NOVEL NAPHTHOQUINONES AND THEIR DERIVATIVES

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DOCTOR OF PHILOSOPHY

by

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CONTENTS

ABBREVIATIONS

The following abbreviations are used in the course of this thesis.

IR	Infrared
UV	Ultraviolet
n.m.r.	nuclear magnetic resonance
m.p.	melting point
b.p.	boiling point
mm	millimeters of mercury
hr	hour(s)
ml	millilitres
g	gram
mg	milligram
nm	nanometer (10^{-9}m)
$LiAlH_4$	lithium aluminium hydride
THF	tetrahydrofuran
NBS	N-bromosuccinimide
DME	dimethoxyethane
DMS	dimethylsulphate
DMSO	dimethylsulphoxide
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DMF	dimethylformamide
t.l.c.	thin layer chromatography

SUMMARY

This dissertation deals with some novel routes investigated towards the synthesis of 1H-benz[f]indene-4,9-dione.

The first chapter deals with a classical approach in which a benzindane nucleus was synthesised, followed by various attempts to insert a double bond into the five-membered ring. This was achieved with 1-bromo-4,9-diacetoxy-6,7-dimethylbenz[f]indane by dehydrobromination with lutidine. However hydrolysis of the dehydrobrominated product yielded 6,7-dimethylbenz[f]indane. Experimental evidence indicated that the desired benzindenequinone was unstable and decomposed readily in the presence of air and heat.

In the second chapter some novel routes utilising pyrolysis of certain Diels-Alder adducts, in which thermally allowed $\left[\pi^4_s + \pi^2_s\right]$ cycloreversion reactions are feasable, are discussed. Once again experimental evidence indicated that the desired quinone had been transiently produced during the various pyrolyses but that it was unstable towards heat, oxygen and acidic media. Attempts to trap the benzindenequinone upon its formation were also unsuccessful.

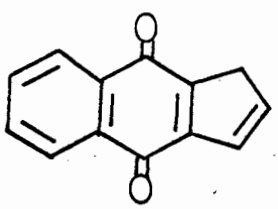
The third chapter deals with a novel rearrangement of a bicyclo [2.2.1] quinone-epoxide system which was discovered during the course of this project. A mechanism has been proposed based on the known steriochemistry of the particular epoxide that underwent the rearrangement. The merits and scope of the rearrangement to include [2.2.2] systems have not yet

been fully investigated.

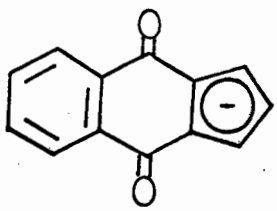
In the appendix variable temperature n.m.r. studies on some 2-amino-1,4-naphthoquinones have been discussed in the context of the relative ability of the cyclic secondary amino substituents in becoming involved in delocalisation with the quinone system.

INTRODUCTION

Stabalised carbanions have for many years interested the organic chemist both in deriving routes to their formation and in studying their chemical nature and reactivity. The present study was initiated to investigate possible ways of preparing 1H-benz[f]indene-4,9-dione (1) and to study the chemistry of the anion (2) which might be anticipated to be formed by treatment of quinone (1) with a base. Extensive delocalisation of the negative charge, not only about the five-membered ring of carbanion (2), but also into the quinone functional group to form the canonical form (3) could be expected to stabalise the molecule in much the same way as the 1,2-diacyl-cyclopentadienes (4) are stabalised by tautomerism to the corresponding 2-acyl-6-hydroxyfulvenes (5), so much so, that, whereas (4) undergoes normal electrophilic substitution reactions at position 4, the anion (6) undergoes diazotisation at position 3.[1] This is explained in terms of initial attack of the diazonium cation on the oxygen atom of the acyl group followed by subsequent migration on to the 3 position of the cyclopentadiene ring.[1]



(1)



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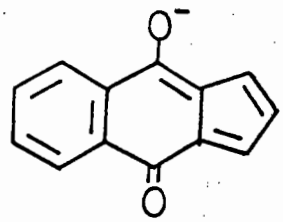

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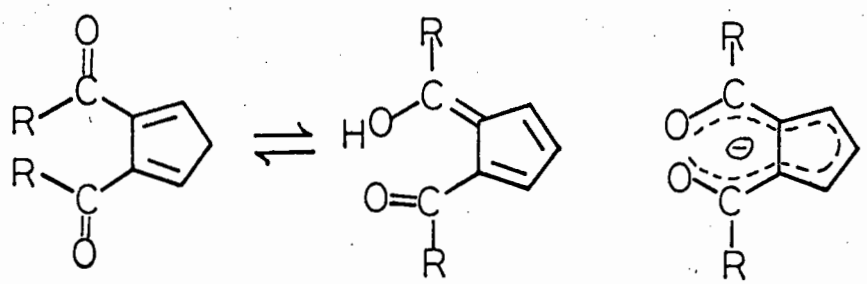
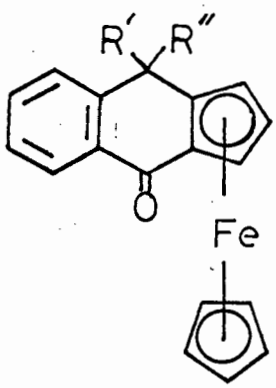


(4) (5) (6)

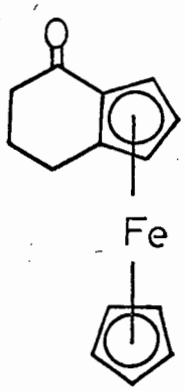
A violet ferrocene derivative (7) of quinone (1) has been synthesised by the oxidation of ferroceneanthrone (8) with manganese dioxide suspended in benzene. [2] Under these same conditions an analogous oxidation was effected on the 1,2-(α-oxotetramethylene) ferrocene (9) which was converted in low yield to the violet ferrocenebenzoquinone (10). [3] The chemistry of these ferrocenequinones has not been studied in much detail although reduction of (10) with sodium hydrosulphite or polarographically yielded the corresponding unstable hydroquinone which rapidly reoxidised aerobically back to the starting material. [3] Other workers [4] have shown that catalytic hydrogenation of the ferrocenequinone (10) produced ketols such as (11) where the quinone ring underwent reduction in preference to the ferrocene ring. Even under drastic hydrogenation conditions that reduced the aromatic ring in the conversion (12)→(13), the one carbonyl group remained uneffected. Furthermore catalytic hydrogenation of the ferrocenequinone

(10) has been shown to produce the endo-6-hydroxyferroceno(1,2)cyclohex-1-en-3-one (11) [4] while hydroxylation of ferrocene (9) with the mould Sporotrichum sulfurescens gave the exo isomer of (11) by an asymmetrical enzymatic hydroxylation reaction. [5] However no mention has been made in the literature of any attempt to disrupt the ferrocenes (7) and (10) in order to isolate the free quinones (1) and (14), neither of which are known, although ferrocene has been reduced with lithium in ethylamine to give cyclopentadiene and iron. [6]



(7) $R' R'' = O$

(8) $R' = R'' = H$



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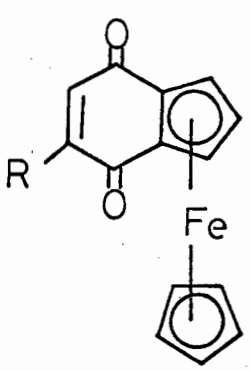
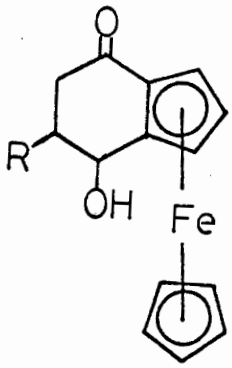


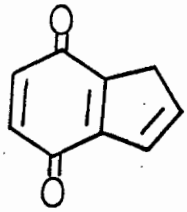
(10) R = H

(12) R = Ph



(11) R=H

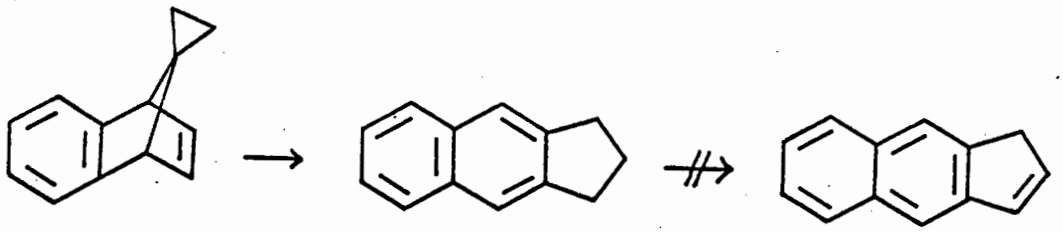
(13) R = C_6H_{11}



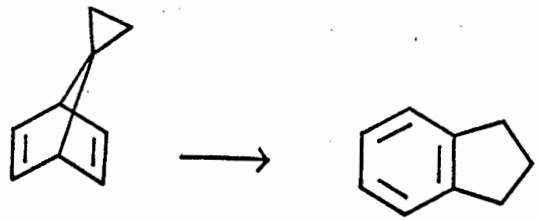
(14)

CHAPTER 1

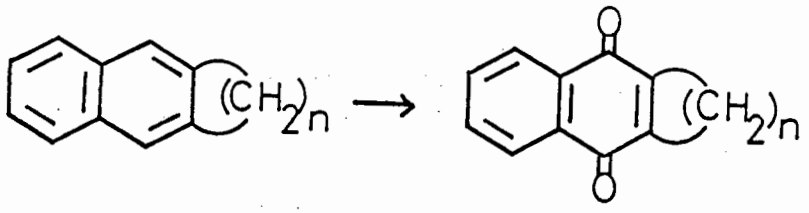
Classical methods employed in the synthesis of polynuclear hydrocarbons containing a fused five-membered ring such as benzindane (15) have been well documented. [7,8,9] Recently, [10] a novel route for the synthesis of benzindane was reported which involved the high temperature pyrolysis of the spirocyclopropane adduct (16). The generality of this rearrangement been demonstrated albeit in lower yield (25% as opposed to 60%), by the pyrolysis of an analogous adduct (17) to indane (18). [11] The main drawbacks of this technique were that only small quantities (1g) of material could be handled and that a fairly intricate experimental set up was required to obtain the high (440°) temperatures needed for rearrangement to be effected. It has also been reported [8] that the attempted dehydrogenation of benzindane (15) to benzindene (19) with selenium powder left the five-membered ring unchanged. In spite of this it was not anticipated that the introduction of a double bond into the five-membered ring of benzindane would present an insurmountable problem. Furthermore since facile oxidation of the hydrocarbons (20 → 22) into their corresponding quinones (23 → 25) has been achieved, [12] it seemed likely that no undue difficulty would be encountered in the oxidation of 5,6-benzindene (19) to the corresponding 5,6-benzindenequinone (1).



(16) (15) (19)



(17) (18)



(20) n = 2
(21) n = 3
(22) n = 4

(23) n = 2
(24) n = 3
(25) n = 4

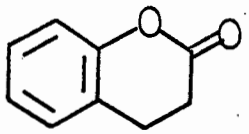
The experimental technique employed for the pyrolysis of (16) to (15) did not present an attractive method for large scale preparations although yields of up to 60% were obtained on 1g quantities. [11] The present investigation was undertaken with the explicit purpose of attempting to devise novel routes towards the synthesis of the benzindenequinone (1) by starting with initial fragments of the polynuclear system containing oxygen atoms in the appropriate positions.

Substituted indanones have been synthesised by classical ring closure techniques [13, 14, 15] and have become incorporated by the chemist as

fairly routine. Intramolecular cyclisations of aryl substituted aliphatic acids, as well as Fries rearrangements have been shown to be readily effected in 2 minutes at 180 - 200° in a molten mixture of aluminium chloride and sodium chloride although the method is restricted to small scale preparations, and by alkyl group migrations. [16] However several stages were still normally involved for the synthesis of the precursors for the cyclisation step. In the present investigation cyclisation from a readily available precursor was initially attempted. Dihydrocoumarin (27) could be fairly easily obtained by catalytic hydrogenation of coumarin [17] and appeared to satisfy the requirements since subjection of the former to a Fries rearrangement was reported to give rise to crude yields of up to 67% of 4-hydroxyindanone (28). [18, 19] Use could then be made of the carbonyl functional group of the indanone (28) in order to introduce a double bond into the five-membered ring.

Of the many methods available for effecting the desired introduction of the olefinic bond, there was one which appeared to show particular promise. This method, which involved conversion of the carbonyl group into its tosylhydrazone followed by elimination of tosylhydrazine by an alkyllithium to form the olefin, has found wide application in a number of different fields of synthetic organic chemistry. [20, 21, 22, 23] In certain instances where the tosylhydrazone appeared to be fairly reactive, passage through a column of activated alumina followed by brief irradiation, heat or acid treatment also yielded olefins. [24] Of particular interest was the report by Shapiro and Heath [25] that reaction of 1-indanonetosyl-

hydrazone (29) with one equivalent of methyllithium yielded a mixture of indene (30) which represented the elimination product and 1-methylindane (31) representing a nucleophilic substitution product. The predominating product was nevertheless indene (30).



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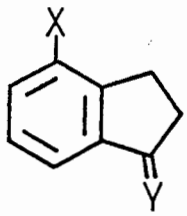


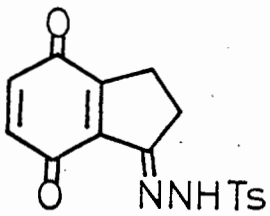
(28) X=OH, Y=O

(29) X=H, Y=NNHTs

(31) X=H, Y=CH_3 and H

(32) X=OH, Y=NNHTs

(30)



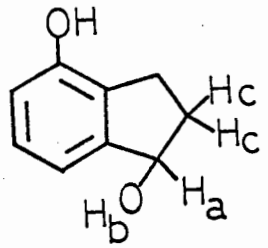
(33)

Conversion of 4-hydroxyindanone (28) to its tosylhydrazone (32) was effected in good yield by utilising a method similar to that employed by Dürr.[26] At this stage it was realised that, before reaction between methyllithium and the tosylhydrazone (32) could be carried out, the hydroxyl group of the latter compound would have to be protected in such a manner as to be stable under the strong basic conditions that it would be subjected to. A possible protecting group was envisaged to be the

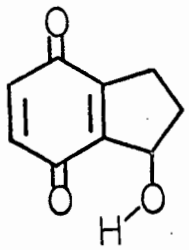
methoxymethylether ($-CH_2OCH_3$) which has been shown to be stable under these conditions. Furthermore regeneration of the phenolic group could easily be effected by treatment with acid. [27, 28] As an alternative to protection of the phenolic group in (32), oxidation to the quinone (33) also presented an attractive route as it involved the least number of steps in the synthesis and also it was anticipated that reaction between the quinone (33) and methyllithium would form the indenequinone (14) in spite of the fact that some nuclear alkylation at the quinone functional group might be expected to occur. Frémy salt oxidation [29, 30] of phenol (32) gave only a very low yield of the quinone (33) which proved to be difficult to handle and thus other routes were considered whereby the same objectives could be achieved, namely the synthesis of quinone (14).

Reduction of 4-hydroxyindanone (28) with lithium aluminium hydride ($LiAlH_4$) in tetrahydrofuran (THF) gave a fairly low yield of the 1,4-dihydroxyindane (34). The n.m.r. spectrum indicated coupling between the aliphatic proton H_a and the alcoholic proton H_b. The appearance of H_a as a quartet at 4.85τ (J = 6Hz) was ascribed to coupling with the two methylene protons H_c as well as the alcoholic proton H_b which appeared as a doublet at 5.75τ (J = 6Hz). On washing with D_2O, the signal due to H_a collapsed to a triplet (J = 6Hz) and the doublet due to H_b was removed. These results seem to indicate that although the dihedral angles between protons H_c and H_a are different as one would expect, J_{ac} cis and J_{ac} trans are at their larger and smaller limits respectively

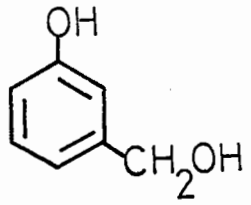
and in the present case J cis = J trans.



(34)



(35)

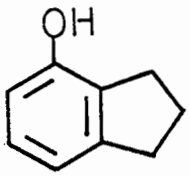


(36)

The purpose behind synthesising diol (34) was to oxidise it to the quinone (35) as it was hoped that dehydration of the latter or conversion of the alcoholic functional group into a good leaving group such as its N-carboalkoxysulphonate salt, [31] followed by elimination would lead to the formation of the indenequinone (14). Again a very poor yield (10%) of what appeared to be the quinone (35) was obtained on Frémy salt oxidation of phenol (34). In this case a red oil was obtained which proved very difficult to handle. Unambiguous assignment of structure (35) to the product was not possible due to lack of reliable elemental analysis, although ultraviolet (UV), infrared (IR) and n.m.r. spectral data were compatible with structure (35). The IR spectrum showed bands at 3450, 1650, 1588 and 1046 cm^{-1} while $\lambda_{max.}$ values of 433, 405, 320 and 250 nm were present in the UV spectrum. The n.m.r. spectrum showed a singlet at 3.27τ (2H) assigned to the quinone protons; a multiplet at 4.64τ (1H) assigned to the methine proton on the carbon atom carrying

the OH group and a broad multiplet at between 7 and 8τ (5H) which integrated for four protons after washing with D_2O. Similar difficulties in oxidising a related phenol (36) have been encountered [32] where oxidation with Frémy salt also proved to be very unsatisfactory. Due to the difficulties encountered with the indane quinones it was decided to delay insertion of the double bond in the five-membered ring to a later stage.

By analogy with the indanes, the benzindanes could be expected to be easier to handle, firstly since Frémy salt oxidation of 4-hydroxy-indane (37) should proceed smoothly as there are no substituents in the five-membered ring to cause complications and secondly, additional benzannelation would be expected to give rise to compounds which could lend themselves more readily toward chemical manipulation. It seemed more likely that the introduction of a double bond into the five-membered ring of a system such as (39) would be more successful than with a quinone system such as (38) and thus efforts were concentrated on the preparation of the benzindane quinone system (39).



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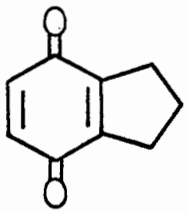

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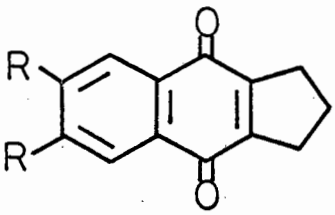
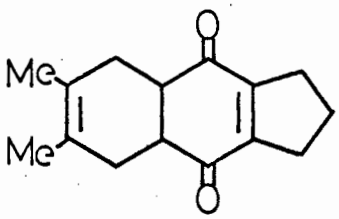


(39) R=H

(40) R=Me

Clemmensen reduction of the indanone (28) [18, 19] gave 4-hydroxyindane (37) which was oxidised [30] to 4,7-indandione (38) in fairly good yield. This quinone also proved slightly difficult to handle since it was not easily obtained in a solid form and was consequently used immediately upon isolation for the next step in the synthetic pathway. This involved Diels-Alder addition to 2,3-dimethylbutadiene which formed the dienone (41) in quantitative yield. Had quinone (61) (vide infra) been prepared successfully, butadiene or cyclohexa-1,3-diene would have been used in this step in order to prepare quinone (1). Base catalysed enolisation of adduct (41) gave a high yield of the quinol (42) and a small (5%) amount of the quinone (40). The structure of quinol (42) was confirmed by its conversion to the diacetate (43) which was synthesised under different conditions involving the reductive acetylation of quinone (44), which in turn was prepared by the silver oxide oxidation of quinol (42). Aromatisation of the six-membered ring of quinone (44) would give rise to the desired benzindanequinone (40). This proved to be very successful since conversion of the quinol (42) into quinone (40) was achieved in quantitative yield by employing a similar procedure used by Fieser [33] in a similarly related type of synthesis using firstly nitrous acid in glacial acetic acid followed by aqueous sodium dichromate at a temperature between 70 - 100°. That quinone (44) was a probable intermediate in the conversion of quinol (42) to quinone (40) was demonstrated by the fact that treatment of (44) in glacial acetic acid

with an aqueous solution of sodium dichromate at 70° yielded quinone (40) quantitatively whereas treatment of (44) with nitrous acid did not yield quinone (40).



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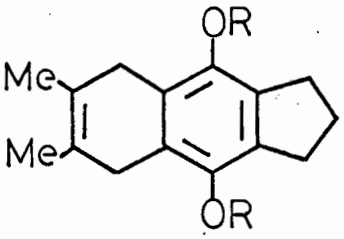
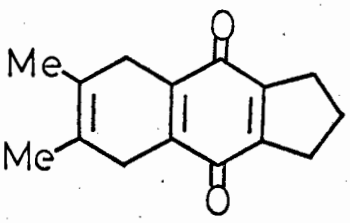


(42) R=H

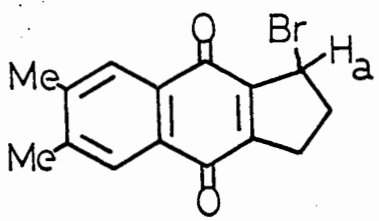
(43) R=Ac



(44)

The most simple and obvious method of introducing a double bond into the five-membered ring of quinone (40) seemed to involve bromination at C_1 followed by dehydrobromination. It has been shown that benzindane (15) underwent bromination at C_1 with N-bromosuccinimide [34] (NBS) and consequently quinone (40) might be anticipated to behave similarly towards this reagent as was indeed found to be the case. Although the bromo-quinone (45) proved to be very unstable, it was possible to run its n.m.r. spectrum immediately upon its isolation which showed the following feature: the methine proton H_a appeared as a poorly resolved triplet at 4.50τ (J = 6Hz) indicating that it was being deshielded by the bromine atom [*c.f.* τ value of 7.12 for the α-methylene protons in the unsubstituted five-membered ring of quinone (40)]. All attempts to dehydrobrominate

the bromoquinone (45) including silver oxide in benzene, [35] potassium hydroxide in ethanol, [36] silver nitrate in ethanol, [36] potassium t-butoxide in t-butanol, [37] potassium hydroxide in dimethylformamide (DMF) and lithium bromide in DMF [38] failed to give the desired product. This failure to effect dehydrobromination may be attributed to the profound tendency of the bromoquinone (45) to decompose upon exposure to the atmosphere and in the various solvents that were used such as ethanol, chloroform and DMF. This instability finds precedent in the literature [40] where analogously related brominated quinones such as (46) have been shown to decompose upon storage although not as rapidly. Alternatively the methine hydrogen atom may be removed from the bromoquinone (45) upon attempted dehydrobromination to yield the carbanion (47) from which loss of a bromide ion is unlikely to occur.



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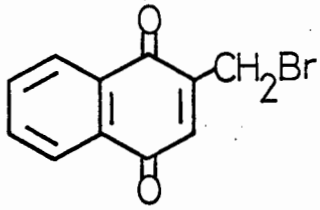

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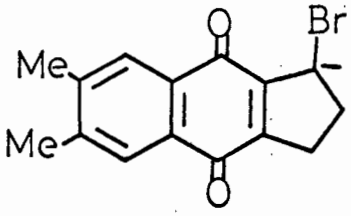
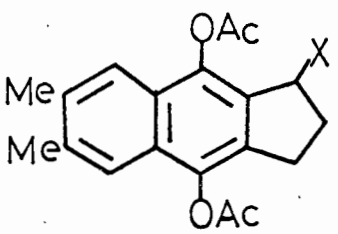


(47)

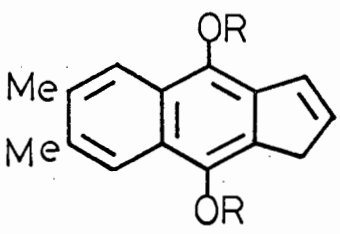
The product of bromination (48) of the diacetate (49), which was prepared by the reductive acetylation of quinone (40), was anticipated to be representative of a more stable system than that of (45) and

consequently it was hoped that dehydrobromination of the bromodiacetate (48) would be more easily effected relative to that attempted on the bromoquinone (45). This proved to be the case since the benzindene-diacetate (50) was obtained in 40% yield by dehydrobromination of (48) in neat anhydrous lutidine with a trace of p-t-butylcatechol to inhibit polymerisation. Hydrolysis of the benzindenediacetate (50) proved to be a less simple process than was originally expected in that isolation of the benzindenequinol (51) proved to be impossible. This failure to isolate quinol (51) from the hydrolysis finds some analogy in a recent paper by Storck and Manecke [41] who hydrolised the vinyldiacetate (52) with alkali and obtained no corresponding quinol but did manage to isolate dimeric products [42] from the reaction mixture.



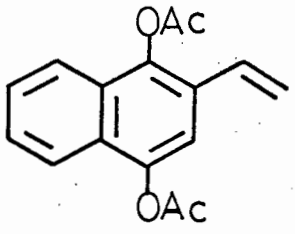
(48) X = Br

(49) X = H



(50) R=Ac

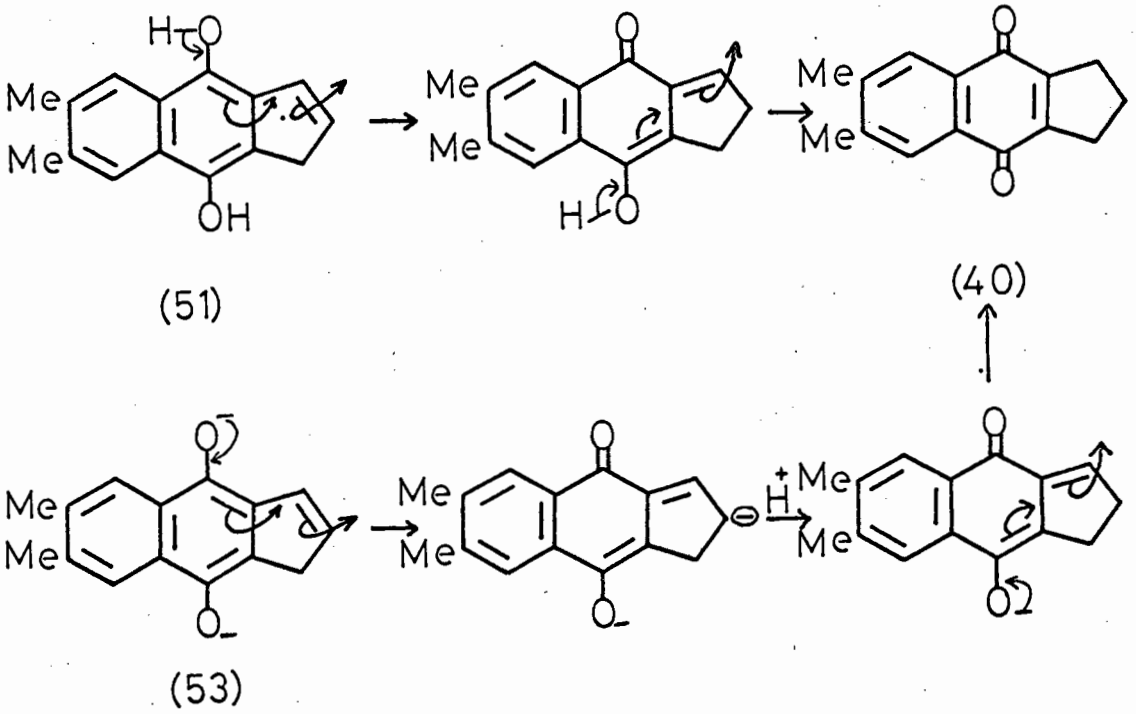
(51) R=H



(52)

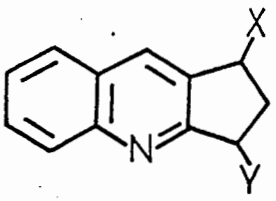
Of the various methods employed to hydrolyse the diacetate (50) e.g. $LiAlH_4$ in solvents such as THF, dimethoxyethane (DME) and ether

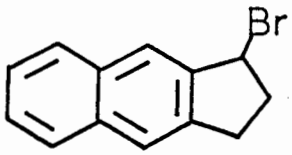
all of which led only to black decomposed material, alcoholic potassium hydroxide was the only one from which it was possible to isolate a product, albeit in 15% yield, which was subsequently shown to be the benzindanequinone (40). Formation of this quinone from the tautomeric quinol (51) could be rationalised either in terms of the series of 1,5 prototropic shifts given in Scheme I or by alternatively considering the corresponding mesomeric shifts of the aromatic dianion (53) before the reaction mixture was neutralised with either dilute acetic acid or aqueous ammonium chloride. Neutralisation is naturally essential for the formation of the final product (40).

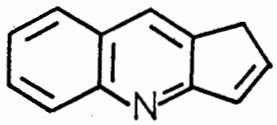


SCHEME 1

In this connection it should perhaps be mentioned that a somewhat related system such as the cyclopenteno [b] quinoline (54) also evaded the usual methods of introducing a double bond into the five-membered ring to yield (58). [44] The bromo-derivative (55) has also been reported to be too unstable for analysis. [43] The double bond was eventually inserted by dehydration of the alcohol (56) [43] or by treatment of the methyliodide salt of (54) with chloranil. [44] Furthermore 1-bromobenzindane (57) has also been reported to decompose upon isolation and has consequently been used immediately upon preparation. [34] The fully aromatic cyclopentadieno [b] quinoline (58) is not all that stable either and has to be stored under nitrogen at 0° since it decomposes in the presence of oxygen and at temperatures of 50 - 60°. [44]







(54) X=Y=H

(55) X=Br, Y=H

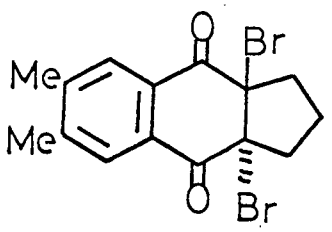
(56) X=H , Y=OH

(57)

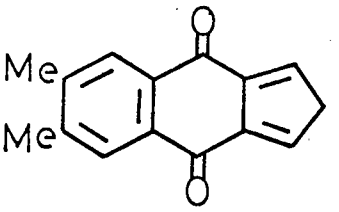
(58)

Addition of bromine to the quinone (40) in glacial acetic acid under a stream of N_2 gas gave the dibromo-adduct (59), presumably the

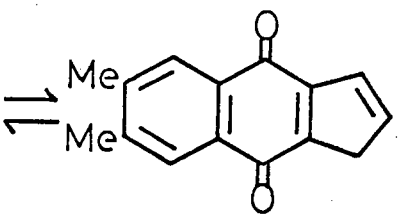
trans isomer as indicated, in quantitative yield. It was hoped that the elements of HBr could be removed from this dibromo-adduct to give the diene (60) which would probably tautomerise to the expected thermodynamically more stable isomer (61). It has also been shown that although quinone (23) reacted normally as a dienophile in the Diels-Alder reaction, it could also react as a diene at elevated temperatures by thermal rupture of the cyclobutene ring to generate a transient true diene intermediate (62) which has been trapped by reaction with N-phenylmaleimide.[45] It has also been shown that the somewhat similarly related systems, i.e. (63),[46] (64 and 65),[47] (66)[48] and more recently (67),[49] are quite stable although they differ in that they contain heteroatoms or metals in the five-membered ring as well as potentially electron-donating substituents which are most likely to be the major factors contributing towards the stability of these compounds.



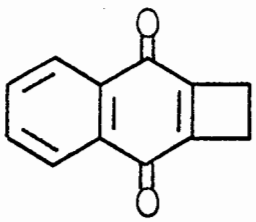
(59)



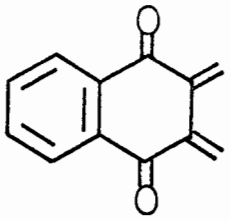
(60)



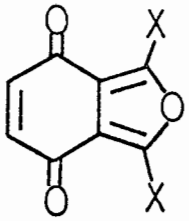
(61)



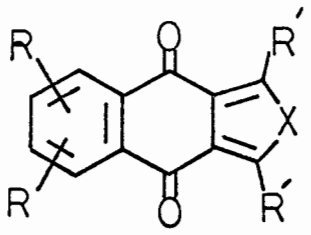
(23)



(62)



(63) X=H or Me



(64) R=H, Me R´= Me, Ph X=O

(65) R=Me R´=Me X=N-C_4H_9

(66) R=OH R´=Me X=O

(67) R=H R=Me X=RhL_2Cl

L=ligand

Treatment of the dibromo-adduct (59) with triethylamine in anhydrous benzene failed to induce dehydrobromination. Instead the elements of bromine were removed from the molecule giving back the starting material (40) in 92% yield. Although there does not seem to be any immediate reason forthcoming for the preference of debromination over dehydrobromination there is precedent in the literature where for instance the Lewis base triphenylphosphine has been employed to debrominate both methyl- and ethylmethacrylate dibromides to the corresponding unsaturated esters in yields of 60%.[50] Even thiourea has been reported to debrominate

vic-dibromides in good yields.[51]

Use of the high potential quinone 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in the dehydrogenation of hydroaromatic rings to aromatic compounds, is well known.[52, 53] Thus dehydrogenation of the benzindanequinone (40) was also attempted but proved to be unsuccessful even for reflux periods of up to 80 hr in benzene.

EXPERIMENTAL

Unless otherwise stated, the following conditions apply to all experimental sections in this thesis.

Infrared (IR) spectra were measured as nujol mulls on a Perkin Elmer 237 spectrometer while ultraviolet (UV) spectra were measured in 95% ethanol on a Beckman D.B. spectrophotometer. Nuclear magnetic resonance (n.m.r.) spectra were measured in deuterochloroform with tetramethylsilane as internal reference on a Varian A60 spectrometer. During the latter part of this project the n.m.r. spectra were measured on a Varian XL-100 spectrometer using deuterium as the lock signal. Petrol ether refers to the fraction having b.p. between 60 and 80°. All melting points which are uncorrected were determined on a Fisher-Johns m.p. apparatus. Thin layer chromatography (t.l.c.) was carried out on aluminium foil plates of Kieselgel F254, while the silica gel used for column chromatography had a mesh rating of 30 - 60. All photolyses were conducted under an atmosphere of nitrogen using a Hanovia high pressure quartz 450 W mercury-vapour lamp and pyrex filter.

Ia Reduction of coumarin

2,3-Dihydrocoumarin (27) was prepared in 84% yield as a colourless oil by the catalytic hydrogenation of coumarin.[17] The product had b.p. 270 - 272° (Lit.[54] 271 - 273°).

Ib(i) 4-Hydroxyindanone (28)

Fries rearrangement of dihydrocoumarin according to the method of London gave 4-hydroxyindanone in 50% yield as yellow plates (from ethanol) m.p. 240° (Lit.[18] m.p. 239 - 240°), $\lambda_{max.}$ 312 and 257 nm (log ε 3.43 and 4.94); $\nu_{max.}$ 3165, 1675 cm^{-1}; n.m.r. τ 2.80 (m, 3H), 3.30 (broad singlet, 1H, D_2O exchangeable), 6.90 (t, 2H, J 6.5 Hz), 7.2 (t, 2H, J 6.5 Hz).

Ib(ii) 4-Hydroxyindanonetosylhydrazone (32)

A mixture of the indanone (1 g) and tosylhydrazine (1.38 g) in ethanol (40 ml) were heated together under reflux for 1 hr in the presence of one drop of concentrated sulphuric acid. The ethanol was taken off under vacuum and the residue dissolved in the minimum volume of chloroform. Trituration with petrol ether yielded 4-hydroxyindan-1-tosylhydrazone (32) in 67% yield as white crystals (from chloroform/petrol ether) m.p. 185° (dec.). [Found: C, 60.5; H, 5.1; N, 8.9; S, 10.2. $C_{16}H_{16}N_2O_3S$ requires C, 60.75; H, 5.1; N, 8.9; S, 10.1%]; $\lambda_{max.}$ 277 and 221 nm (log ε 4.17 and 4.43).

Ib(iii) Frémy salt oxidation of the tosylhydrazone (32)

A solution of the hydrazone (300 mg) in methanol (25 ml) was added to an aqueous solution of Frémy salt (5 g) in water (200 ml) containing a 0.2 M buffer solution of potassium hydrogen phosphate (80 ml) and the resulting solution stirred for 1.5 hr after which it was extracted with ether (6 x 50 ml). The dried (Na_2SO_4) extract was concentrated to 15 ml and chilled to precipitate an orange solid which was recrystallised from methanol to give 4,7-indandione-1-tosylhydrazone (33) as orange needles (20 mg) with m.p. 165 - 170° (dec.). [Found: N, 8.3. $C_{16}H_{14}N_2O_4S$ requires N, 8.5%]; $\lambda_{max.}$ 410, 274 and 220 nm (log ε 3.16, 4.28 and 4.46); $\nu_{max.}$ 3510, 3150, 1653, 1593, 1169 cm^{-1}; n.m.r. (Acetone-d_6) τ 2.13 (dxd, 2H, J 6 and 6 Hz), 2.66 (d, 2H, J 8 Hz), 2.92 (d, 1H, J 2 Hz), 3.28 (d, 1H, J 2 Hz), 7.23 (sharp multiplet, 5H, after D_2O wash this multiplet integrated for 4H), 7.62 (s, 3H).

Ib(iv) Reduction of 4-hydroxyindanone (28) with $LiAlH_4$

A solution of 4-hydroxyindanone (2.9 g) in THF (100 ml) was added to a refluxing mixture of THF (500 ml) and $LiAlH_4$ (1.0 g) and the resulting mixture heated under reflux for a further 3 hr and then cooled. An aqueous (10%) solution of NH_4Cl was added to destroy any remaining $LiAlH_4$. The separated aqueous layer was extracted once with ether which was combined

with the THF layer and dried ($MgSO_4$). Evaporation of the solvents yielded a brown gum which crystallised after 24 hr to yield the 1,4-dihydroxyindane (34) as white needles (1.5 g) (from ether/petrol ether) m.p. 118°. [Found: C, 71.7; H, 6.9. $C_9H_{10}O_2$ requires C, 72.0; H, 6.7%]; $\lambda_{max.}$ 279 and 272 nm (log ε 3.10 and 3.11); $\nu_{max.}$ 3380, 1039 cm^{-1}; n.m.r. (Acetone-d_6) τ 1.90 (s, 1H, D_2O exchangeable), 3.20 (m, 3H), 4.85 (q, 1H, J 6 Hz. This signal collapsed to a triplet with J 6 Hz after the sample was shaken with D_2O), 5.75 (d, 1H, J 6 Hz. This signal disappears on D_2O exchange), 7.50 (m, 4H).

1c(i) Clemmenson reduction of 4-hydroxyindanone (28)

4-Hydroxyindane (37) was obtained by the Clemmenson reduction of 4-hydroxyindanone as white waxy plates m.p. 37 - 38°, b.p. 88°/1.3 mm in a 40% yield (Lit.[18] m.p. 48 - 49°, 42°[19]).

Ic(ii) Frémy salt oxidation of 4-hydroxyindane (37)

4,7-Indandione (38) was obtained as a red oil in 57% yield according to the method of Teube.[30] On standing the oil solidified to a yellow solid m.p. 35° (Lit.[30] 42°, 41 - 42°[13]). $\nu_{max.}$ 1662 cm^{-1}; n.m.r. τ 3.33 (s, 2H), 7.17 (t, 4H, J 7.5 Hz), 7.90 (m, 2H).

Id(i) Addition of 2,3-dimethylbutadiene to the indanquinone (38)

A solution of 2,3-dimethylbutadiene (3 ml) and the quinone

(550 mg) in dry benzene (60 ml) were heated under reflux for 20 hr after which time the solvent was removed to yield 6,7-dimethyl-4a,5,8,8a-tetrahydrobenz[f]indan-4,9-dione (41) as white needles (830 mg) (from petrol ether) m.p. 139 - 140°. [Found: C, 78.4; H, 7.8. $C_{15}H_{18}O_2$ requires C, 78.3; H, 7.8%]; $\lambda_{max.}$ 261 nm (log ε 3.99); $\nu_{max.}$ 1670 and 1619 cm^{-1}; n.m.r. τ 6.84 (m, 2H), 7.25 (t, 4H, J 7.2 Hz), 7.83 (m, 6H), 8.38 (s, 6H).

Id(ii) Enolisation of adduct (41)

Sodium hydroxide (0.5 ml x 2 M) was added to a solution of the adduct (750 mg) in methanol (45 ml) and the resulting solution stirred for 10 minutes. The pH was then adjusted to 6 by the addition of dilute HCl and the solid material filtered off * and dried to yield the quinol (42) in 94% yield (704 mg). The pure quinol was obtained as light pink needles (from methanol) m.p. 300°. [Found: C, 78.2; H, 7.8. $C_{15}H_{18}O$ requires C, 78.3; H, 7.8%]; $\lambda_{max.}$ 284 nm (log ε 3.40); $\nu_{max.}$ 3290, 1123 cm^{-1}.

* The mother liquors yielded 35 mg of 6,7-dimethylbenz[f]indan-4,9-dione (40) when worked up.

Id(iii) Acetylation of 6,7-dimethyl-5,8-dihydrobenz[f]indan-4,9-diol (42)

Pyridine (2 ml) was added to a solution of the diol (100 mg)

in acetic anhydride (2 ml) and the resulting solution kept in the dark for 12 hr and then poured into water. The white solid was filtered off and dried to yield 6,7-dimethyl-5,8-dihydrobenz[f]indan-4,9-diacetate (43) quantitatively (148 mg). The diacetate formed long white needles (from methanol) m.p. 170.5°. [Found: C, 72.4; H, 7.0. $C_{19}H_{22}O_4$ requires C, 72.6; H, 7.0%]; $\nu_{max.}$ 1750, 1208, 1024 cm^{-1}; n.m.r. τ 6.93 (s, 4H), 7.22 (t, 4H, J 7 Hz), 7.69 (s, 6H), 7.93 (m, 2H), 8.27 (s, 6H).

Id(iv) Oxidation of 6,7-dimethyl-5,8-dihydrobenz[f]indan-4,9-diol (42)

Silver oxide (1 g) was added to a solution of the quinol (175 mg) in dry benzene (20 ml) and the resulting mixture shaken for 2 hr and then filtered. Evaporation of the solvent gave 6,7-dimethyl-5,8-dihydrobenz[f]indan-4,9-dione (44) (170 mg) as yellow needles (from methanol) m.p. 110° (dec.). [Found: C, 78.8; H, 7.1. $C_{15}H_{16}O_2$ requires C, 79.0; H, 7.0%]; $\lambda_{max.}$ 343, 271 and 261 nm (log ε 2.89, 4.20 and 4.19); $\nu_{max.}$ 1655, 1644, 1620 cm^{-1}; n.m.r. τ 7.03 (s, 4H), 7.21 (t, 4H, J 7.2 Hz), 7.94 (m, 2H), 8.28 (s, 6H).

This quinone is light sensitive and decomposes to a black material when exposed to the air and/or sunlight.

Id(v) Reductive acetylation of the quinone (44)

A solution of the quinone (100 mg) in acetic anhydride (3 ml)

was treated with zinc dust (200 mg) and heated on a waterbath for 0.5 hr after which the solution was rapidly filtered. Hot water (50 ml) was added to the filtrate and on cooling a white solid formed which was filtered off to yield the diacetate (43) (135 mg) as long white needles (from methanol) m.p. 170.6°. This diacetate was identical in all respects to (43) as prepared in Id(iii).

Ie(i) Preparation of 6,7-dimethylbenz[f]indan-4,9-dione (40)

A solution of sodium nitrite (1.1 g in 1.7 ml water) was added dropwise to a stirred solution of the quinol (42) (677 mg) in glacial acetic acid (30 ml) at 100°. After the evolution of gas had ceased, the temperature was adjusted to 70° and a solution of sodium dichromate (1 g in 0.7 ml water) was added together with one drop of concentrated H_2SO_4. The resulting solution was kept at 70° for an additional hour and then poured into iced water (150 ml). The yellow solid was filtered off to yield 6,7-dimethylbenz[f]indan-4,9-dione (40) as long yellow plates (from methanol) (620 mg) m.p. 150 - 151°. [Found: C, 79.5; H, 6.1. $C_{15}H_{14}O_2$ requires C, 79.7; H, 6.1%]; $\lambda_{max.}$ 347, 281, 258 and 254 nm (log ε 3.45, 4.19, 4.37 and 4.33) $\nu_{max.}$ 1660, 1624 cm^{-1}; n.m.r. τ 2.31 (s, 2H), 7.12 (t, 4H, J 7 Hz), 7.65 (s, 6H), 7.90 (m, 2H).

Ie(ii) Bromination of the quinone (40)

A solution of the quinone (32 mg) and NBS (26 mg) in carbon tetrachloride (10 ml) was heated in the presence of benzoyl-peroxide (2 mg) for 0.25 hr. The succinimide that was produced was filtered off and the solvent was removed from the filtrate under high vacuum at room temperature to leave a yellow crystalline mass which decomposed on exposure to the atmosphere. Rapid crystallisation from methanol yielded olive-green plates of 2-bromo-6,7-dimethylbenz[f]indan-4,9-dione (45) (10 mg) m.p. 140 - 150° (dec.). $\nu_{max.}$ 1660, 1597, 1339, 740 cm^{-1}; n.m.r. τ 2.12 (s, 2H), 4.50 (t, 1H, J 6 Hz), 7.0 (m, 2H), 7.42 (m, 2H), 7.58 (s, 6H).

No reliable analysis could be obtained from this compound due to its very rapid mode of decomposition.

Ie(iii) Reductive acetylation of quinone (40)

Zinc dust (100 mg) was added to a solution of the quinone (100 mg) in acetic anhydride (3 ml) and the mixture rapidly stirred at 90° for 0.5 hr after it was filtered hot. The filtrate was treated with hot water (40 ml) and allowed to cool to yield (130 mg) of 6,7-dimethylbenz[f]indan-4,9-diacetate (49) as long white needles (from methanol) m.p. 159°. [Found: C, 72.9; H, 6.3. $C_{19}H_{20}O_4$ requires C, 73.0; H, 6.5%];

$\lambda_{max.}$ 296, 286, 277, 268, 258 and 232 nm (log ε 3.67, 3.82, 3.78, 3.64, 3.52 and 4.08); $\nu_{max.}$ 1752, 1150 cm^{-1}; n.m.r. τ 2.52 (s, 2H), 7.08 (t, 4H, J 7 Hz), 7.57 (s, 6H), 7.60 (s, 6H), 7.90 (m, 2H).

Ie(iv) Bromination of diacetate (49)

NBS (590 mg) and the diacetate (1 g) in carbon tetrachloride (50 ml) were heated under reflux in the presence of benzoyl-peroxide (12 mg) for 0.5 hr. After removal of the succinimide by filtration the solvent was removed from the filtrate to yield a white gum which could not be induced to crystallise. This product was assumed to be the 2-bromo-6,7-dimethylbenz[f]indan-4,9-diacetate (48) as indicated by its n.m.r. τ 2.48 (s, 2H), 3.42 (t, 1H, J 4 Hz), 6.98 (m, 2H), 7.32 (m, 2H), and three singlets at 7.49, 7.54 and 7.60 (12H).

Ie(v) Dehydrobromination of the bromodiacetate (48)

Anhydrous lutidine (30 ml) was added to the bromodiacetate (650 mg) together with p-t-butylcatechol (300 mg) and the resulting solution was heated on a waterbath for 0.75 hr after which time it was poured into water (500 ml). The purplish solid that formed was filtered off and dried. Sublimation of this solid yielded 310 mg of 1H-4,9-diacetoxy-6,7-dimethyl-benz[f]indene (50) as white needles (from methanol) m.p. 174.6°. [Found: C, 73.2; H, 5.8. $C_{19}H_{18}O_4$ requires C, 73.5;

H, 5.8%]; $\lambda_{max.}$ 309, 296, 286, 251, 243 and 234 nm (log ε 3.90, 4.00, 3.90, 4.53, 4.54 and 4.59); $\nu_{max.}$ 1754, 1655, 1626 cm^{-1}; n.m.r. τ 2.48 (s, 2H), 3.23 (dxt, 1H, J 5.8 and 2 Hz), 3.51 (dxt, 1H, J 5.8 and 2 Hz), 6.62 (t, 2H, J 2 Hz), 7.60 (m, 12H).

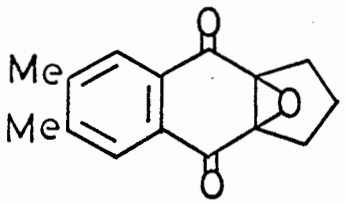
Ie(vi) Hydrolysis of the indenediacetate (50)

A mixture of the diacetate (60 mg), 10% aqueous KOH (3 ml) and ethanol (1 ml) were heated under reflux for 0.75 hr and then cooled. The red solution was neutralised with dilute acetic acid. A black precipitate formed which was filtered off and chromatographed over silica gel using chloroform as the eluent. A yellow crystalline compound (6 mg) was the only product isolated from the column and was shown to be 6,7-dimethylbenz[f]indan-4,9-dione (40) by comparison of its mass spectrum with the previously prepared material.

Ie(vii) Epoxidation of the benzindanequinone (40)

30% Hydrogen peroxide (0.5 ml) in aqueous sodium carbonate (50 mg in 1 ml water) was added to a solution of the quinone (95 mg) in ethanol (3.5 ml) and the resulting mixture allowed to stand for 12 hr. The white solid that formed was filtered off to yield (110 mg) 3a,9a-epoxy-6,7-dimethylbenz[f]indan-4,9-dione as white needles (from methanol) m.p. 150°. [Found: C, 74.3; H, 5.8. $C_{15}H_{14}O_3$ requires C, 74.5; H, 5.8%];

$\nu_{max.}$ 1690, 1600, 949 cm^{-1}; n.m.r. τ 2.33 (s, 2H), 7.65 (s, 6H), 7.80 (m, 6H). This data is consistant with the structure given below.



Ie(viii) Bromination of 6,7-dimethylbenz [f] indan-4,9-dione (40) with bromine

Bromine (6 drops) was added to a solution of the quinone (200 mg) in acetic acid (10 ml) and the resulting solution was stirred in the dark under N_2 for 12 hr during which time a white crystalline material formed. The reaction mixture was poured into water (50 ml) and the white solid (330 mg) was filtered off to yield 3a,9a-dibromo-6,7-dimethylbenz [f] indan-4,9-dione (59) as white needles (from methanol) m.p. 124°. [Found: Br, 42. $C_{15}H_{14}O_2Br_2$ requires Br, 41.5%]; $\lambda_{max.}$ 316 and 269 nm (log ε 3.79 and 4.22); $\nu_{max.}$ 1699, 1598, 942 cm^{-1}; n.m.r. τ 2.09 (s, 2H), 7.20 (m, 6H), 7.59 (s, 6H).

The compound decomposes slowly on exposure to the air.

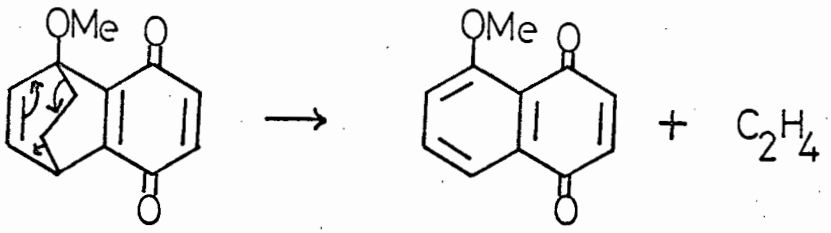
Ie(ix) Treatment of the dibromide (59) with triethylamine

Anhydrous triethylamine (0.25 ml) was added to a solution of the dibromide (50 mg) in dry benzene (10 ml) and the resulting solution heated under reflux for 5 hr and then evaporated down to a yellowish solid which was chromatographed through a column of silica gel using chloroform as eluent. The only product isolated was 6,7-dimethylbenz[f]indan-4,9-dione (40) (27 mg).

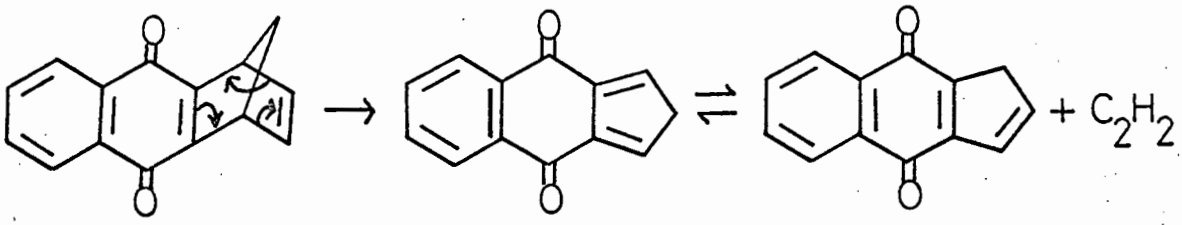
CHAPTER II

Pyrolysis has been utilised for many years as an effective technique in the preparation of organic compounds that would otherwise prove difficult and tedious to obtain.[55, 56] In pericyclic reactions one is not limited by the thermal instability of a compound as a prerequisite for the desired pyrolysis since these compounds could be photochemically labile and could be induced to undergo the required changes upon irradiation.[57, 58, 59] The rules governing the cleavage or formation of bonds *via* either thermal or photochemical excitation and the manner in which the bonds undergo these pericyclic reactions have been proposed by Woodward and Hoffmann.[60] It is thus essential to prepare the precursor having the correct geometry to effect the desired type of reaction under the appropriate conditions.

Birch *et al.*[61] have shown that thermal elimination of an ethylene bridge from adducts such as (68) has been highly successful in forming the quinone (69) and ethylene. This represents a typical example of a thermally allowed reverse $\left[\pi^4_s + \pi^2_s\right]$ cycloaddition reaction. With this in mind the 1,4-methanoanthroquinone (70) was synthesised by a modification of the method of Diels and Alder[62] and also subjected to pyrolysis. It seemed conceivable that under pyrolytic conditions the retro $\left[\pi^4_s + \pi^2_s\right]$ Dields-Alder reaction could be induced to yield the diene (71) which would immediately tautomerise to the quinone (1), and acetylene as shown in Scheme 2.



(68) (69)



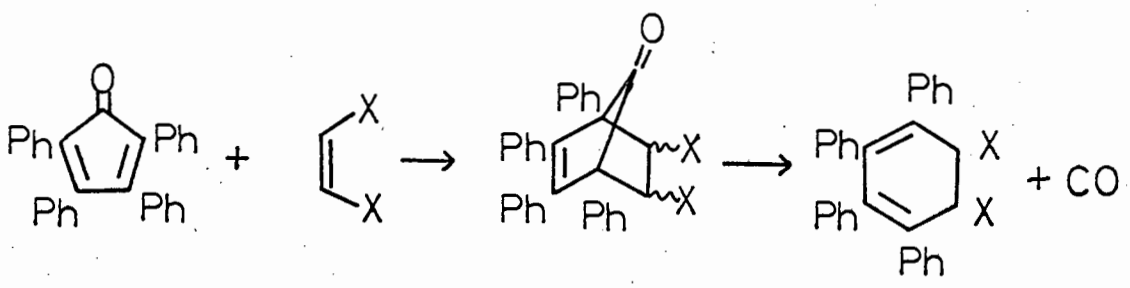
(70) (71) (1)

SCHEME 2

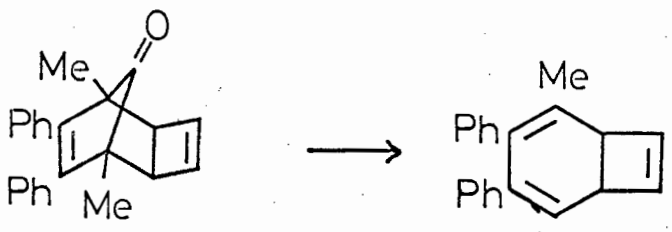
Pyrolysis of the quinone (70) at temperatures of up to 200° and in a nitrogen atmosphere yielded no new products. Extensive decomposition occurred to yield a black tar from which only starting material was isolated. A possible explanation for failure of the pyrolysis reaction to take place might in part be due to the fact that bicyclo [2.2.1] heptadiene (78) has been shown to rearrange to several products on pyrolysis although amongst these cyclopentadiene and acetylene have been identified.[63] Thus in essence the approach envisaged in Scheme 2

did have precedent to work although a more successful route for removing the ethylene bridge from quinone (70) would have to be investigated.

It is well known that tetracyclone (72) and its analogues undergo Diels-Alder additions with ethylenic dienophiles to give carbonyl bridged adducts such as (73) in some cases, while in others, the derived dihydroaromatic analogues such as (74), resulting from elimination of carbon monoxide which depended on the reaction temperature involved. [64] In addition the cheletropic elimination of a carbon monoxide bridge from cyclic β,γ-unsaturated ketones has been observed to occur both under thermal and photochemical conditions. [60] Recently use of the well documented photodecarbonylation of β,γ-unsaturated ketones [65] was made by McKay and Warrener [67] who employed this technique as an effective means of entry into the bicyclooctatriene system which had previously been shown to be thermally labile and to isomerise to the cyclooctatetraene form. [66] Thus low temperature (-50° to +40°) irradiation of the tricyclononadienone (75) caused rapid decarbonylation to yield the bicyclooctatriene (76) which was shown to be appreciably stable at temperatures of up to 65°. [67]

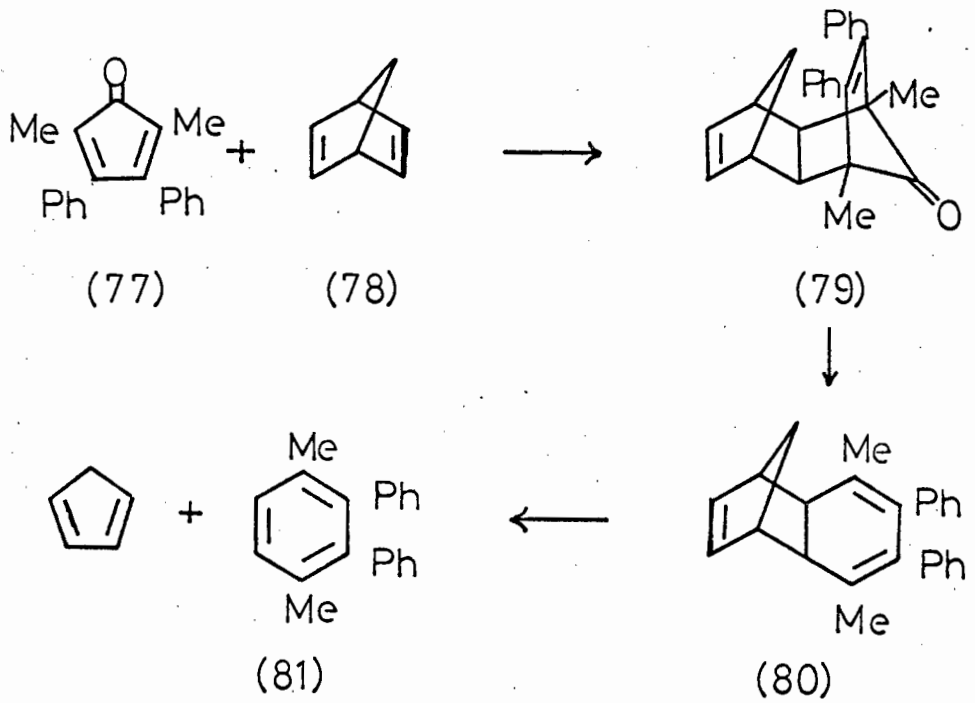


(72) (73) (74)



(75) (76)

Of particular interest to the present study was a recent publication by Wilson and Warrener [68] who successfully synthesised the thermally labile tricycloundecatriene (80) by low temperature (-40°) irradiation of the ketone (79) as shown in Scheme 3. They furthermore established that reaction was initiated by initial loss of carbon monoxide to produce the triene (80) followed by a symmetry allowed $\left[\pi^4_s + \pi^2_s\right]$ cycloreversion reaction to produce the aromatic moiety (81) and cyclopentadiene.



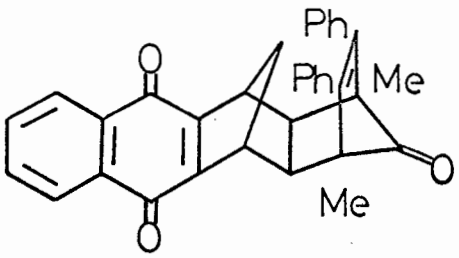
(77) (78) (79) (80) (81)

SCHEME 3

The pertinent feature of the above reaction sequence was that it provided an excellent method of effectively removing an ethylene bridge from norbornadiene (78). Furthermore the undecatriene systems are particularly labile towards retro $\left[\pi^4_s + \pi^2_s\right]$ cleavage, when the $\left[\pi^2_s\right]$ component becomes part of an aromatic system providing an additional driving force for the reaction.[69, 70] It appeared that a direct analogy between norbornadiene (78) and the methanoanthroquinone (70) could possibly exist with respect to the reaction sequence outlined in Scheme 3 in which case elimination of the ethylene bridge from the quinone <u>via</u> a $\left[\pi^4_s + \pi^2_s\right]$ cycloreversion reaction would lead to the desired quinone (1), again through the postulated diene intermediate (71) which finds precedent by analogy with isoindene systems.[71]

It has been shown that the cyclopentadienone (77) exists as a dimer in the solid state and that it is dissociated to the extent of 20% in benzene under reflux.[72] Consequently it was anticipated that quinone (70) would undergo normal Diels-Alder addition with the dienone (77) to produce the adduct (82). Its steriochemistry has not been proven but is implied by analogy with the steriochemistry of similar adducts <u>i.e.</u> (79)[68] and precedent in the literature.[73, 74] It was hoped that the adduct (82) would undergo an analogous set of reactions as did the ketone (79). However, no addition products were obtained when the two reagents were heated together in benzene under reflux for periods of up to 80 hr. The addition was also attempted in higher

b.p. solvents such as dioxan and toluene since it was hoped that the concentration of monomeric dienone (77) would be increased and thus favour addition. This also proved to be unsuccessful resulting only in extensive decomposition of the quinone (70). Changing the polarity of the solvent by using chlorobenzene and DMF also proved to be ineffective, leading only to decomposition of the quinone (70).

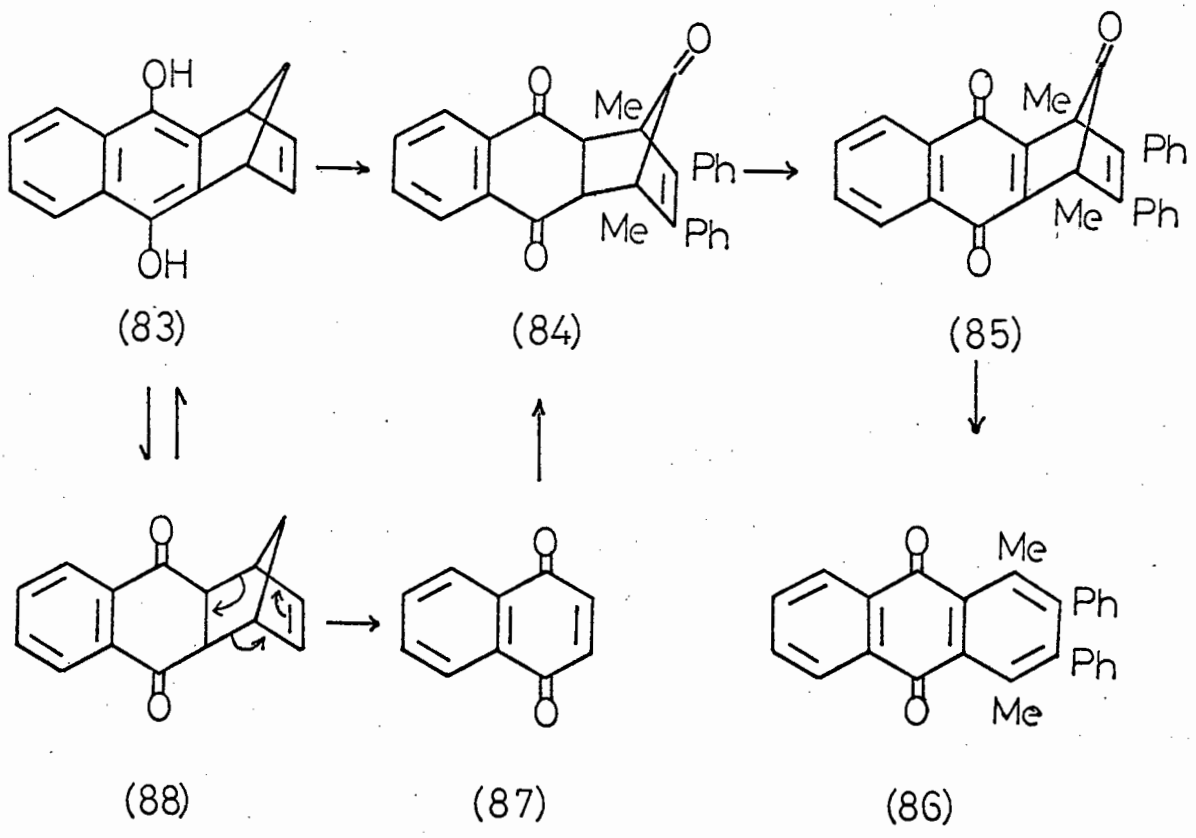


(82)

A suitable explanation for this failure to induce addition to proceed does not seem to be forthcoming. It may be that the olefinic bond of quinone (70) could in some way be influenced by the quinone double bond in its proximity so much so that it becomes electron deficient enough not to react with the dienone (77) which is itself an electron deficient enophile. However there is an argument which takes note of the fact that both benzoquinone [75] and naphthoquinone react with the dienone (77) to give good yields of adducts. This would be inclined to refute the first suggestion since in the latter case addition is being effected between two electron deficient species both of which would be expected to be more electron deficient than the olefinic bond in quinone (70).

Reversal of the electron availability of the olefinic bond in the quinone (70) could be achieved by conversion to the quinol (83) reaction of which with the dienone (77) was expected to be more favourable. However reaction between the quinol (83) and the dienone (77) by heating them in benzene under reflux for 90 hr did not give the expected addition product. Instead the anthroquinone derivative (84) was isolated in 30% yield. The IR spectrum showed carbonyl stretching frequencies at 1792, 1770 and 1680 cm^{-1} while in the n.m.r. spectrum methyl groups appeared at 8.40τ showing that they were attached to an sp^3 hybridised carbon atom (c.f. the τ value of 7.52 for the methyl groups in (86) and carbonyl stretching frequency at 1669 cm^{-1}). Treatment of the keto-adduct (84) with methanolic sodium hydroxide produced the known anthroquinone (86) in quantitative yield. This process presumably involved enolisation followed by aerial oxidation to the keto-anthroquinone (85) with subsequent loss of carbon monoxide from the derived bicyclohepta[2.2.1]diene-7-one system. The latter class of compounds are known to rapidly undergo loss of carbon monoxide to give aromatic derivatives.[76] The keto-adduct (84) was synthesised in 87% yield via an independant route which involved addition between naphthoquinone (87) and the dienone (77). It would thus seem that under the conditions of prolonged heating, the quinol (83) is converted in a very low yield into the keto tautomer (88) which could undergo a reverse Diels-Alder reaction to produce cyclopentadiene

and naphthoquinone (87) which in turn would then react with the diene (77) vide infra to produce the adduct (84).

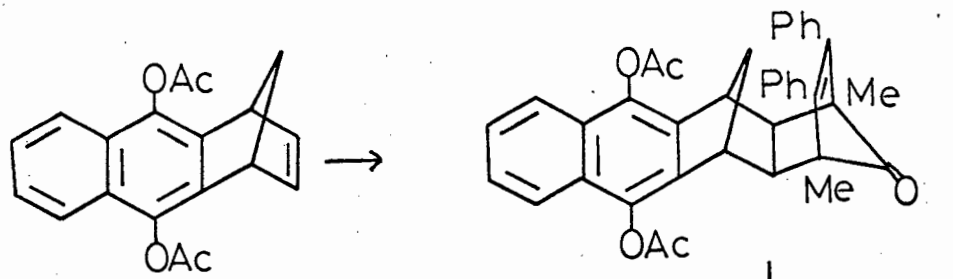


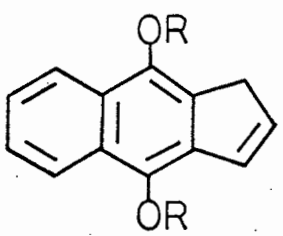
(83) (84) (85)

(88) (87) (86)

In order to inhibit any possibility of the quinol (83) undergoing reversion to the keto tautomer (88), quinol (83) was converted into the diacetate (89) which very readily underwent the anticipated reaction with the dienone (77) to produce the exo-decarbonylated adduct (91) in a yield of 95%. Furthermore this proved that by reversing the electron demand in the aromatic nucleus in the close proximity of the olefinic

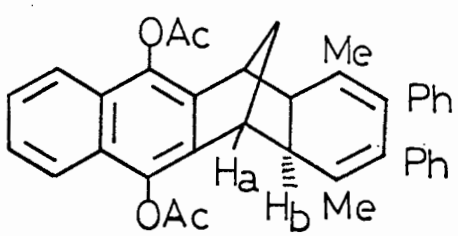
bridge, the latter would function as a normal dienophile. The exo steriochemistry of the adduct (91) is based on a similar type of reaction [68] and also on the lack of coupling between the bridgehead protons H_a at 6.86τ and the adjacent endo protons H_b at 6.12τ [77] since the dihedral angle between the two protons is ca. 90°. Thermal decarbonylation most probably occurred since the presumed intermediate (90) might be expected to be thermally labile [78] due to the steric compression of the syn hydrogen atom of the methano bridge against the π-electron cloud of the etheno bridge in its very close proximity. The relatively high temperature used during the reaction viz. 132° may also be a contributing factor. [64]





(93) R=Ac

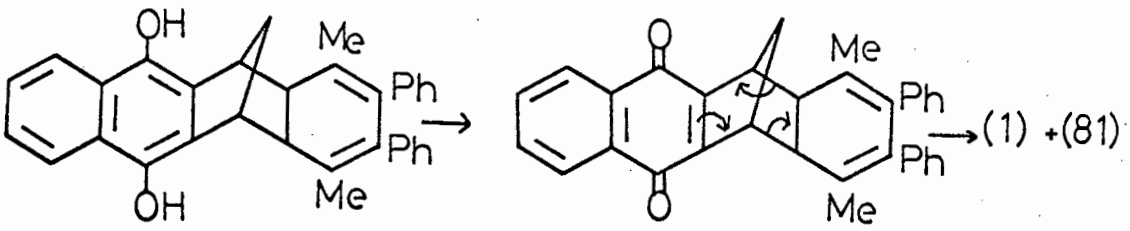
(94) R=H



(91)

All attempts to pyrolyse diacetate (91) even at temperatures of up to 310° failed to yield the expected products derived from a $\left[\pi^8_s + \pi^2_s\right]$ thermally allowed cycloreversion reaction *viz.* the benzindenediacetate (93) and the terphenylene (81). The diacetate (91) actually appeared to be quite stable under these drastic conditions and simply sublimed unchanged. In addition very little decomposition occurred. Further attempts to disrupt the diacetate system (91) at this stage were postponed since on closer examination of the anticipated products of pyrolysis, the expected diacetate (93), is analogous to the benzindenediacetate (50) and similar difficulties were anticipated in attempting the hydrolysis of (93) to quinol (94) as had previously been found (*c.f.* Chapter I Scheme I).

Thus an alternative method was considered whereby the diacetate (91) could be converted in such a way as to render it thermally labile. $LiAlH_4$ reductive hydrolysis of the diacetate (91) was expected to yield the quinol (92) which upon oxidation could be expected to yield the quinone (95). The compound, in the latter form, was in a favourable position to undergo a reverse $\left[\pi^4_s + \pi^2_s\right]$ cycloaddition reaction as outlined in Scheme 4 to yield the desired quinone (1) and the aromatic moiety 3',6'-dimethyl-o-terphenylene (81). [79]



(92) (95)

SCHEME 4

The diacetate (91) was virtually insoluble in most of the solvents e.g. THF and ether, that are normally employed in effecting reduction with $LiAlH_4$. Reduction was carried out in DME to produce a black tar from which it was possible to isolate only one compound viz. the dimethyl-o-terphenylene (81) in 63% yield. Hydrolysis in ethanol with sodium ethoxide under an atmosphere of nitrogen also yielded a black tar from which the aromatic moiety (81) was isolated in 90% yield. These findings seem to substantiate the postulation that the proposed Scheme 4 was essentially feasible and that the quinol (92) which formed on hydrolysis must have a sufficiently low oxidation potential to enable rapid aerobic oxidation to the quinone (95) under the experimental conditions employed. This latter quinone however seemed to be very unstable since as soon as the reaction mixture from the alkaline hydrolysis was neutralised with a weak acid like aqueous ammonium chloride, immediate blackening of the reaction mixture occurred. It thus implied that the $\left[\pi^4_s + \pi^2_s\right]$ cycloreversion reaction had indeed occurred as

predicted and that the benzindenequinone (1) had been transiently produced according to Scheme 4. It was also concluded that the latter quinone (1) was extremely sensitive to the reaction conditions and rapidly decomposed.

Failure to induce pyrolysis of the diacetate (91) to produce the benzindenediacetate (93) posed the problem as to whether there was justification in anticipating the $\left[\pi 8_s + \pi 2_s\right]$ cycloreversion reaction to indeed proceed. In order to clarify the merits of the proposed cycloreversion reaction, it was decided to conduct a similar set of experiments on the dimethylether (96) prepared in good yield by methylation of the quinol (83) as shown in Scheme 5. Diels-Alder addition between the dimethylether (96) and the dienone (77) gave an almost quantitative yield of the exo-decarbonylated adduct (98), presumably derived from the intermediate exo-adduct (97) [68] which would experience steric acceleration in the thermal decarbonylation due to compression between the syn hydrogen of the bridging methylene group and the adjacent π-cloud of the etheno bridge. [78] The steriochemistry of adduct (98) was again demonstrated to be exo by virtue of the absence of coupling between the bridgehead protons H_b at 7.19τ and the adjacent endo proton H_a at 5.95τ.

Pyrolysis of the adduct (98) was conducted at 310° under an atmosphere of nitrogen and gave rise to two products which were separated on a silica gel column. The first component was eluted with petroleum ether and was

shown to be the dimethylterphenylene (81). The second component, light yellow in appearance, was eluted with chloroform. This material was slightly impure and further purification was achieved by passing it through a column of activated alumina, to yield the purified second component 1H-4,7-dimethoxybenz[f]indene (100). Formation of this benzindene must proceed through the isobenzindene (99). It is worthy of note that the aromaticity of both rings in the intermediate (99) is disrupted although it is rapidly restored by tautomerisation. Furthermore formation of (81) and (100) represented a concerted $\left[\pi^8_s + \pi^2_s\right]$ cycloreversion reaction which justified previous predictions i.e. (91)→(93).

The structure of (100) followed from the usual analytical and spectral data. The n.m.r. spectrum (fig. I) showed the allylic methylene protons H_a as a triplet at 6.40τ (J = 2Hz). The vinylic proton H_b appeared as a doublet further split into a pair of triplets centred at 3.49τ (J_{bc} = 5.8Hz and J_{ba} = 2Hz) while the signals due to H_c also appeared as a doublet further split into a pair of triplets centred at 2.86τ (J_{cb} = 5.8Hz and J_{ca} = 2Hz).[80] This finds analogy with the diacetate (50) which showed a similar set of signals for the protons concerned viz. H_a appeared as a triplet at 6.20τ (J = 2Hz); H_b appeared as a doublet further split into a pair of triplets centred at 3.51τ (J_{bc} = 5.8Hz and J_{ba} = 2Hz) while H_c appeared as a pair of triplets centred at 3.23τ (J_{cb} = 5.8Hz and J_{ca} = 2Hz). That pyrolysis of adduct (98) produced the two components (100) and (81), and that these were isolated in

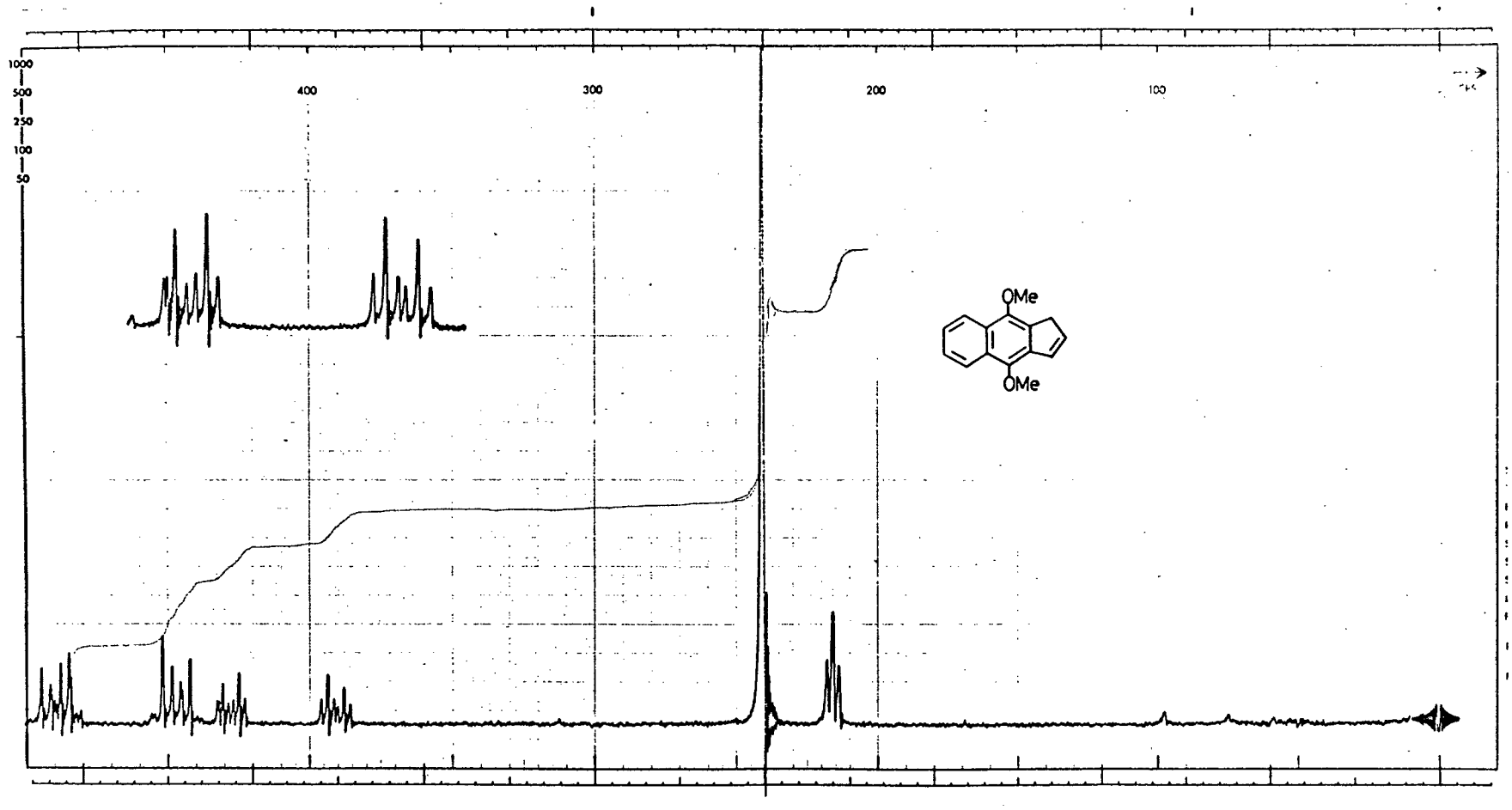
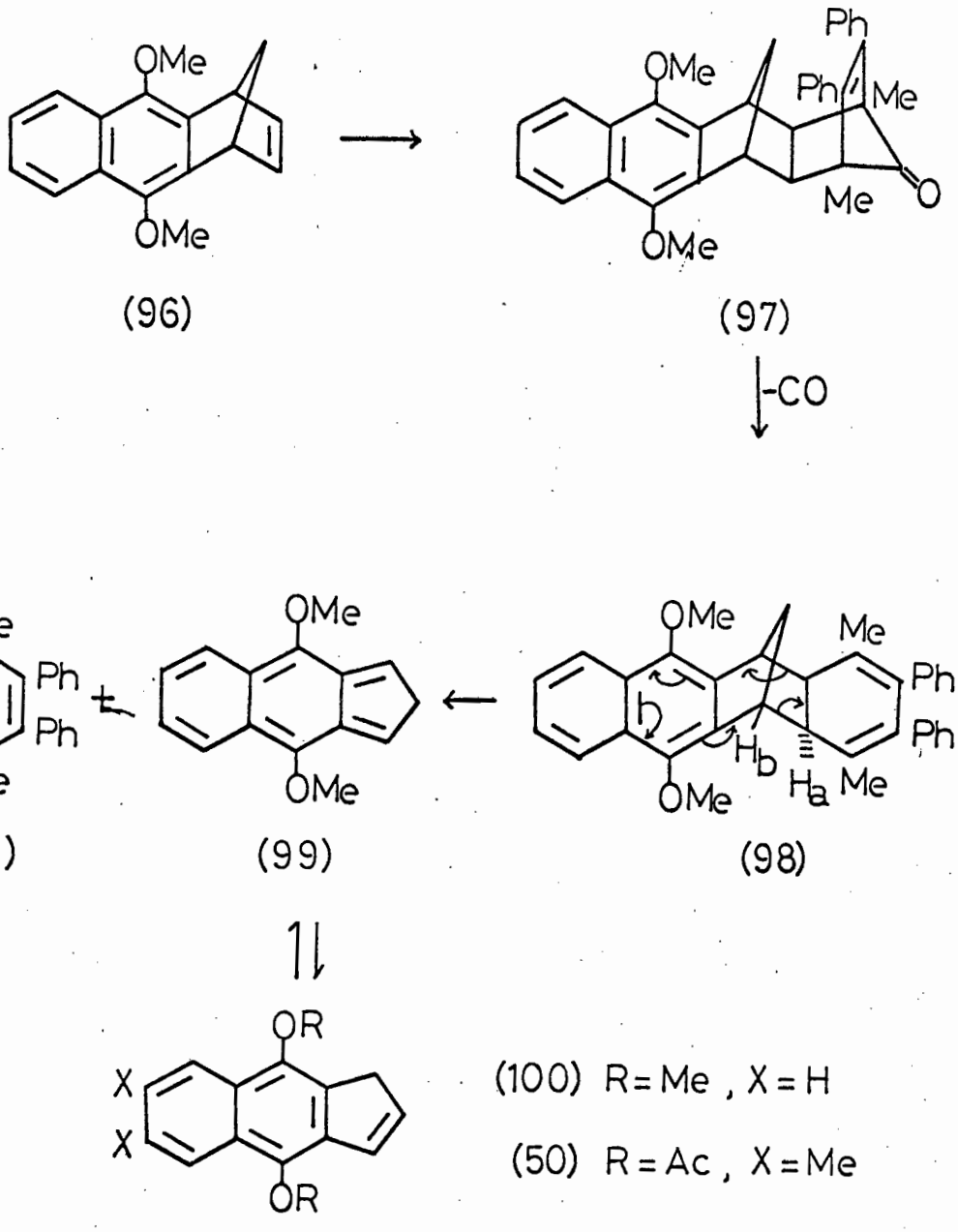


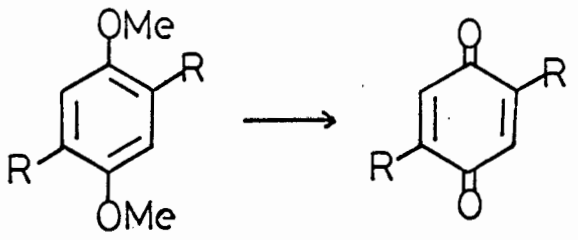
fig. 1


OMe
OMe
(96)
Ph
OMe
Ph
Me
Me
O
OMe
(97)
-CO
Me
Ph
Ph
Me
(81)
OMe
OMe
(99)
OMe
Me
Ph
Ph
b
Hb
Ha
OMe
Me
(98)
OR
X
X
OR
(100) R = Me , X = H
(50) R = Ac , X = Me

SCHEME 5

equimolar quantities, fully justified the postulations incorporated in Scheme 5 and in the conversion of (91) to (93). It would also certainly lend credence to the fact that quinone (1) had been produced according to Scheme 4 but that it had very rapidly undergone decomposition. The adduct (98) was also investigated photochemically in case it should be possible to fragment it into the dimethylterphenylene (81) and the benzindene (100) by a non-concerted process. However its irradiation in benzene led to extensive decomposition although the aromatic moiety (81) was isolated in very low yield.

Methods for demethylation of the dimethylether (100) were then considered bearing in mind the lack of success attending previous attempts to hydrolyse the diacetate (50). Use of nitric [81] and nitrous acids [82] to oxidatively dealkylate aromatic ethers has been effectively employed in the conversion of ethers such as (101) and (102) into the corresponding quinones (103) and (104) respectively. When these methods were applied to the dimethylether (100) in the hope that the desired quinone (1) could be obtained no product was isolated. This seemed to indicate that the quinone (1), if formed during the latter reactions, decomposed under these conditions. It would hence appear that thus far there existed evidence that quinone (1) is unstable towards heat, basic and acidic conditions and thus a neutral reagent for the demethylation of the benzindene (100) would have to be sought.

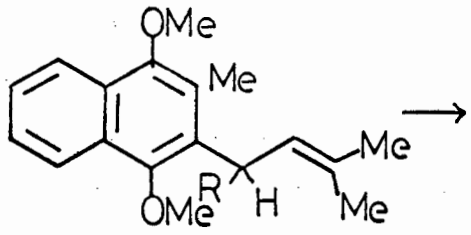


(101) R = CH_2Cl (103) R = CH_2Cl

(102) R = t-butyl (104) R = t-butyl

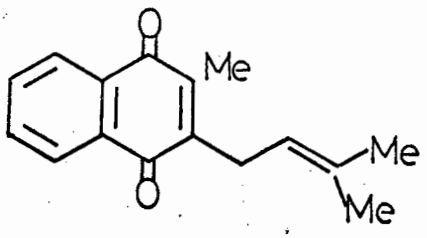
Numerous methods for effecting oxidative demethylation have been recently reviewed by Musgrave.[83] Concentrated nitric acid appeared to be the most generally employed reagent in the oxidative demethylation of p-dimethoxybenzenes whereas when applied to the 1,4-dimethoxyethers of naphthalene nitration on the aromatic nucleus may occur instead of or in addition to oxidative demethylation. The use of inorganic oxidants such as Ce^{4+} and Cr^{3+} has also found widespread application although side reactions are known to prevail in certain instances.[83]

Argentic oxide has been shown to be particularly effective in oxidising various substituted toluenes to the corresponding aldehydes under mildly acidic conditions.[84] It has also been established that activating groups in the ortho- or para- position improve yields especially if these groups are methoxyl although the latter are not effected by the reaction conditions.[84] Recently a novel use for this reagent was reported by Rapoport et al.[85] who, when attempting to oxidise the dimethylether of menaquinol (105) to the anticipated product (106), obtained menaquinone-1 (107) as the only product which must have arisen from oxidative demethylation.



(105) R=H

(106) R=OH



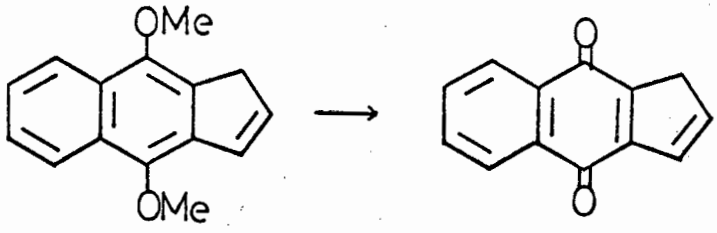
(107)

The scope of the use of argentic oxide as a general method for the oxidative cleavage of hydroquinone ethers has been investigated [86] whereby the superiority of this reagent over the conventional methods was demonstrated by conversion of a number of substituted 1,4-dimethoxynaphthalenes into the corresponding 1,4-naphthoquinones in high yield. In addition, oxidative side chain reactions were shown to be minimal. This seemed to present an attractive route to the desired quinone (1) since treatment of the dimethylether (100) with argentic oxide would be anticipated to yield quinone (1) according to Scheme 6. However all attempts at oxidative demethylation failed to allow isolation of the desired product most likely due to the strong acids that are catalytically employed which possibly cause quinone (1) to decompose. In one instance 3 mg of a yellow product was isolated from 100 mg of the dimethylether (100) when nitric acid was used to initiate the reaction. This product had strong bands at 1675, 1603 and 1353 cm^{-1} in the IR spectrum (measured in chloroform) while the UV spectrum showed $\lambda_{max.}$ at 427, 282(sh), 265 and 236 nm

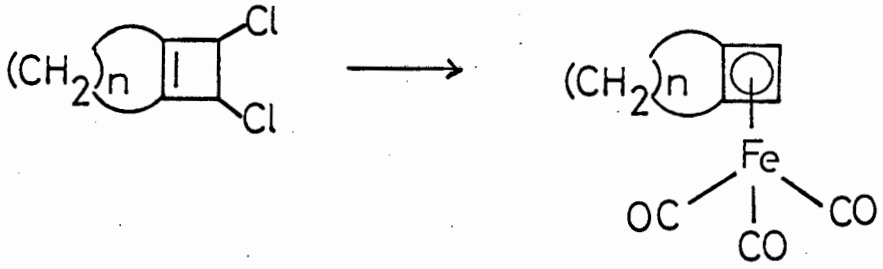
indicating the possible isolation of a quinonoid component. This reaction is however still under investigation.

Iron ennacarbonyl has been shown to readily react with dihalides such as (108) and (109) to form the corresponding complexes (110) and (111) respectively.[87] This method has been effectively employed for the isolation of unstable types of aromatic compounds and would thus be expected to be well suited for the preparation of the complex (113) via the dibromide (112) according to Scheme 6. It was hoped that the iron-tricarbonyl complex (113) would be stable towards the acidic conditions employed to effect oxidative demethylation and that the expected quinone (114) would form in high yield and be stabalised by virtue of the complexing properties of the iron.

The dibromoadduct (112) was synthesised by the pyridine bromide perbromide method[89] and was not purified since it appeared relatively unstable. It was used as such in the next step of the reaction. However no reaction could be induced to proceed between the dibromide and iron-ennacarbonyl.

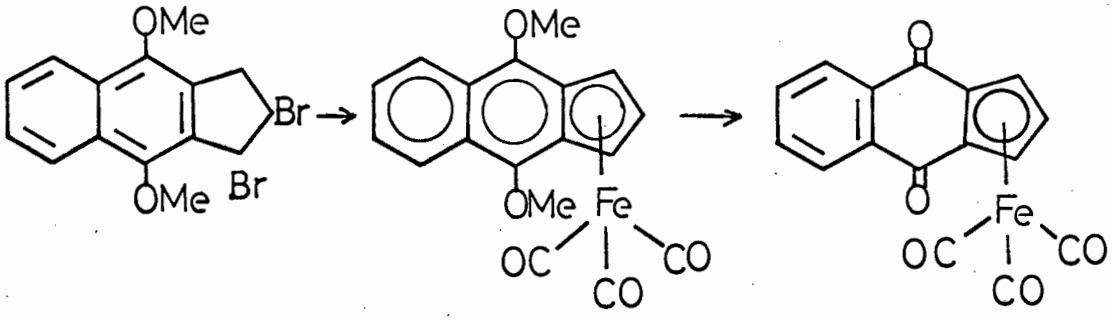


(100) (1)



(108) n = 0 (110) n = 0

(109) n = 4 (111) n = 4

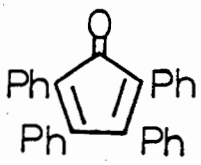


(112) (113) (114)

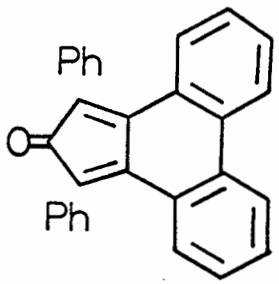
SCHEME 6

That the quinone (70) reacted neither with 2,5-dimethyl-3,4-diphenyl-cyclopentadienone (77) nor with tetraphenylcyclopentadiene (115) has been partially attributed to the fact that both diene and dienophile are electron-deficient species. Of the tetra-substituted cyclopentadienones, the most reactive analogue appears to be phencyclone (116) [90] and thus it was considered that reaction between the latter and quinone (70) might be possible. This in fact proved to be the case for a highly insoluble yellow product was isolated from the reaction mixture after heating the two components together in toluene under reflux for 50 hr. The reaction could be followed visually since the initially intense green colour due to the phencyclone slowly faded to a yellow at the completion of the reaction. Although the reaction proceeded with some decomposition of the quinone (70) the yield of adduct (117) was high, being 71%. The structure of adduct (117) followed from its analysis and spectral characteristics. The IR spectrum showed a strong band at 1793 cm^{-1} indicating the presence of a bridging carbonyl functional group while the quinone carbonyl group appeared at 1656 cm^{-1} as expected. The adduct also proved to be very insoluble in the usual n.m.r. solvents. A fair spectrum was obtained in hot $CDCl_3$. Protons H_a gave rise to a single peak at 6.85τ while the bridgehead protons H_b gave rise to a single peak at 6.23τ. Once again, absence of coupling between H_a and H_b implied an <u>exo</u> adduct. [77] The methylene bridge protons H_c also gave rise to a single peak at 8.37τ. At this stage it is not possible

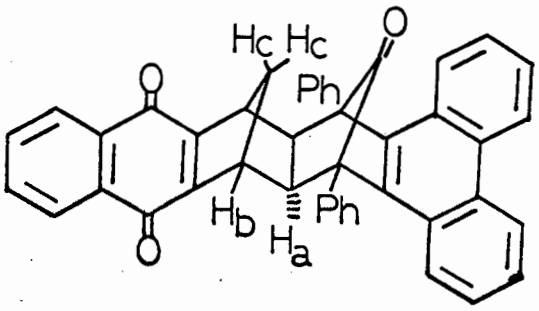
to assign the correct steriochemistry to the rest of the molecule so that the structure of adduct (117) may also be represented by structure (118). Extrapolation of previous results obtained by similar reactions employing the dienone (77) tend to favour structure (117) but this assignment is still ambiguous. It is also interesting to note that whereas the adducts derived from use of the tetraphenylcyclopentadienone (115) lead to adducts which have lost the elements of carbon monoxide, adducts derived from use of phencyclone do not.[79] This may be explained by the fact that loss of the carbonyl from (117) would disrupt the aromaticity of the phenanthrene ring, whereas in the analogous adduct (97) no similar reason for retaining the carbonyl exists.



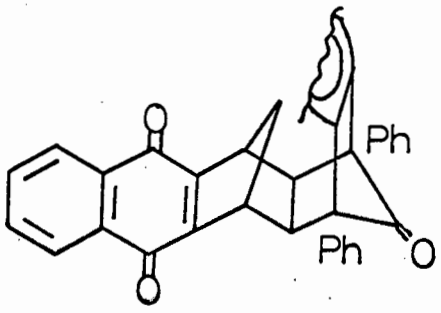
(115)



(116)

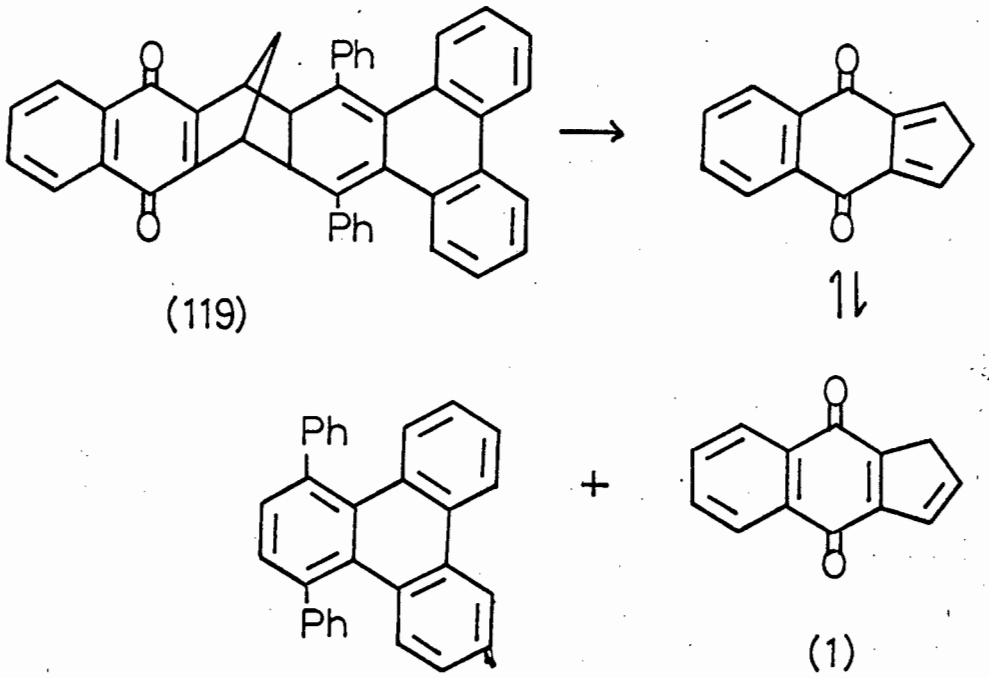


(117)



(118)

Strong heating of adduct (117) was expected to induce thermal decarbonylation [76] at its melting point to produce the diene derivative (119) which could then undergo a thermally allowed $\left[\pi^4_s + \pi^2_s\right]$ cycloreversion reaction to yield the quinone (1) and the aromatic moiety 1,4-diphenyltriphenylene (120) as shown in Scheme 7.



SCHEME 7

Pyrolysis of adduct (117) could be conveniently carried out at 220°C and at low pressures (0.5 mm). Two fractions were observed to collect on the cold finger, the one being yellow and the other being white. However as soon as the cold finger was removed from the nitrogen

atmosphere of the pyrolysis apparatus, the yellow component started to decompose into a black tar. This decomposition seemed to be almost immediate when the fractions were washed from the cold finger with ether, ethanol or chloroform. Chromatographic purification of the sublimate led to the isolation of the predicted aromatic component (120) as the only product. Furthermore irradiation of adduct (119) in acetone led to the isolation of the triphenylene (120) as the only product in very low yield.

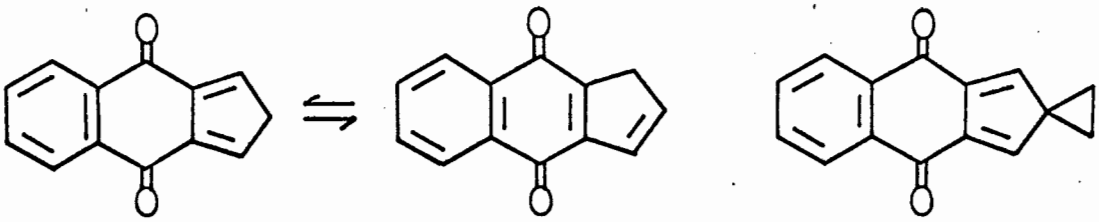
From these results it did seem that pyrolysis of the adduct (117) must have produced the quinone (1) albeit only transiently, which appeared to be particularly unstable towards heat (vide infra) and oxygen. In order to obtain more definite evidence as to the existance of quinone (1) an IR spectrum was run on the sublimate immediately upon removal from the apparatus. The spectrum showed a strong band at 1670 cm^{-1} indicating the presence of a quinone carbonyl stretch. Thus far experimental evidence suggested that the quinone (1) when formed, immediately decomposed and thus it was considered expedient to attempt to trap the quinone by immersing the cold finger into solutions containing various trapping reagents such as cyclopentadiene, N-phenylmaleimide and tetracyanoethylene. In all cases no addition products were isolated.

The thermal instability of the yellow component obtained on pyrolysis of the adduct (117) was demonstrated during a more sophisticated attempt to isolate it. A long thin tube with a bulb at one end containing

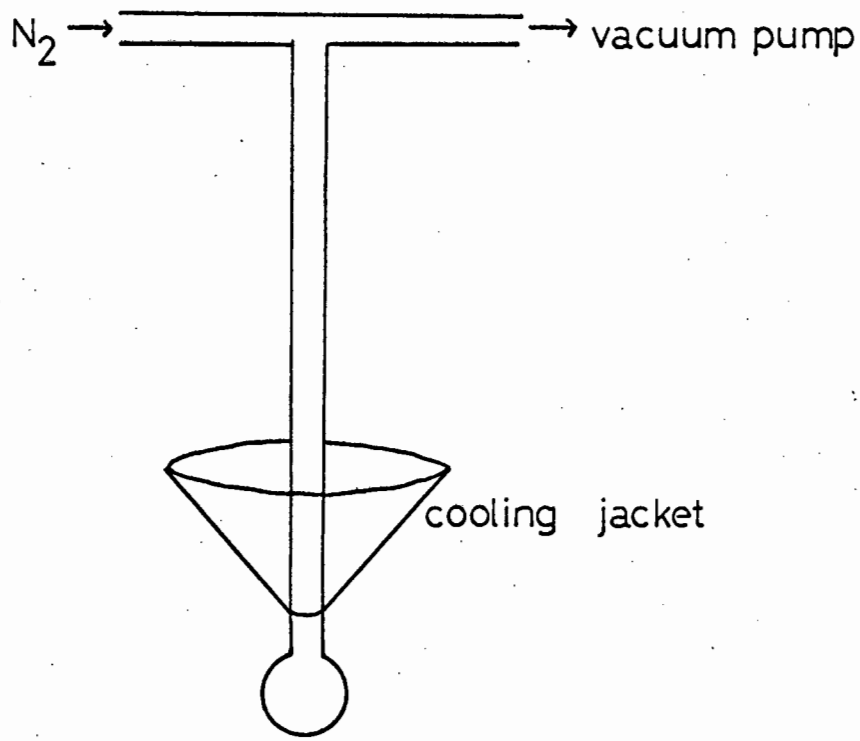
adduct (117) and a sliding dry ice jacket (fig. 2) was flushed with nitrogen and evacuated down to 0.5 mm. Thereafter the bulb was immersed in an oil bath which had been preheated to 220° and pyrolysed for 10 minutes. The cooling jacket, which was filled with dry ice, was about 1 cm above the oil level. A yellow ring of condensate formed inside the tube at the level of the cooling jacket. The oil bath was then cooled to 20°C and the pyrolysis tube immersed to the depth of the yellow ring with the cooling jacket 1 cm above the oil level. The temperature of the oil bath was then slowly raised in the hope that the yellow component would sublime off under the high vacuum, thus giving a separation. However at an oil bath temperature of 30° the yellow component suddenly turned black and all that could be recovered from the black product was the triphenylene (120). Thus even in the absence of oxygen the yellow component, which is thought to be quinone (1), is extremely sensitive towards heat.

Of the possible structures for the observed yellow pyrolysis product either (1a) or (1b) seem to be the most likely. In the thermal reactions proposed in Scheme 7 the intermediate (1a) is postulated as the precursor to (1b). A possible reason for the facile decomposition of (1a) if indeed this were the tautomer which was unstable, could be associated with the methylene protons of the five-membered ring which could undergo 1,5-prototropic shifts to the oxygen atoms. In order to prevent the possibility of these proton migrations an attempt was made to prepare the

diene (121). While it was aniticipated that it might also be too unstable to be isolated as such, it was reasoned that it might be possible to trap it with a dienophile (e.g. N-phenylmaleimide).

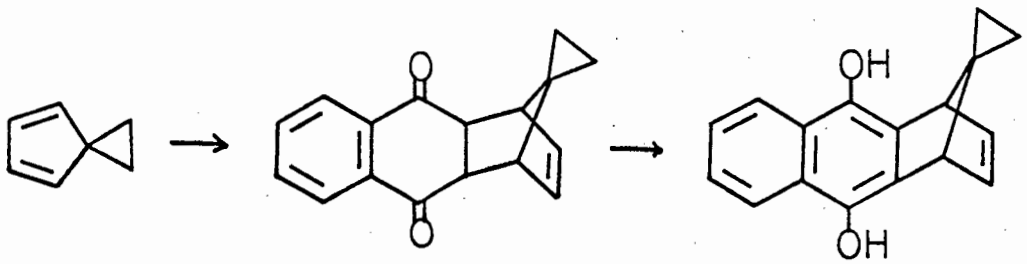


(1a) (1b) (121)

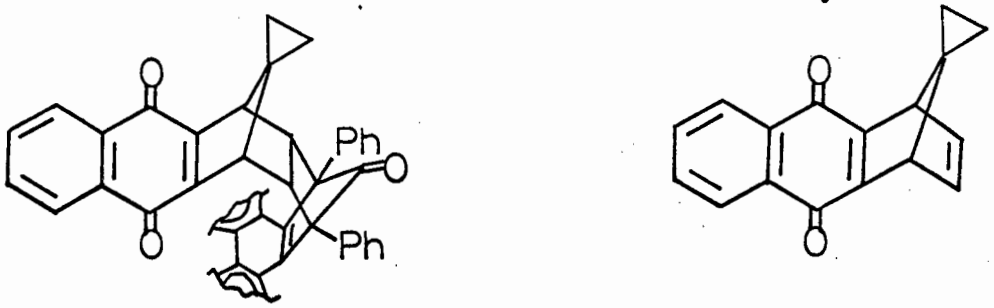


(fig. 2)

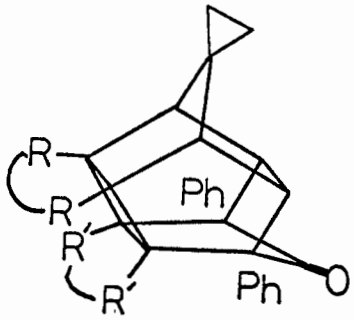
Reaction between 1,4-naphthoquinone (87) and spiro[2.4]hepta-1,3-diene (122) gave a quantitative yield of the endo-adduct (123) which was readily enolised to the quinol (124) in THF with potassium t-butoxide as the basic catalyst. Silver oxide oxidation of quinol (124) produced the quinone (125) which when heated under reflux with phencyclone (116) in toluene for 24 hr gave a 59% yield of the endo-adduct (126) as an orange solid. The IR spectrum showed the bridging carbonyl as a strong band at 1787 cm^{-1} while the quinone carbonyl appeared at 1663 cm^{-1}. No n.m.r. spectrum could be run since the adduct was too insoluble in the solvents available.



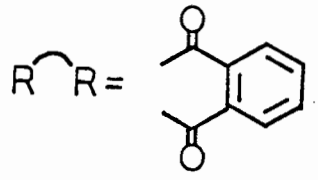
(122) (123) (124)

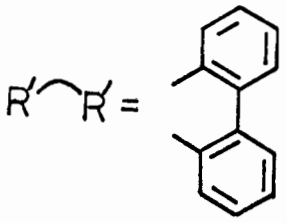


(126) (125)



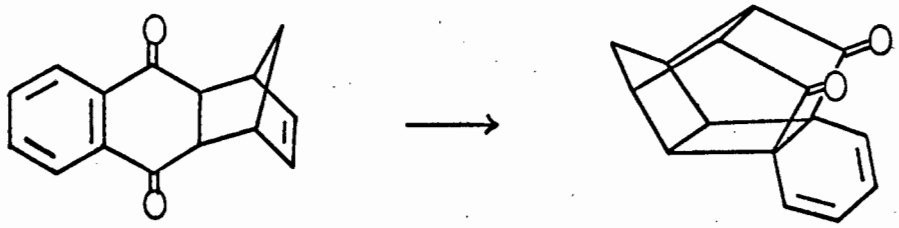
(127)



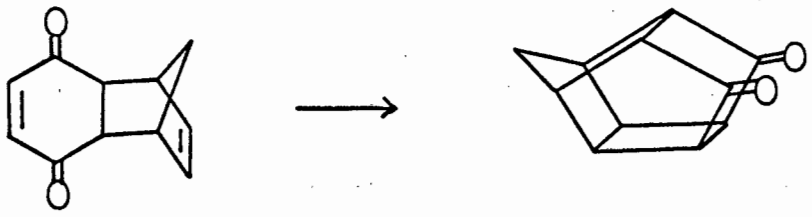


Support for the suggested steriochemistry of adduct (126) was demonstrated by its facile intramolecular photoisomerisation in the solid state. Upon exposure to sunlight the originally orange coloured material slowly photolysed either in the solid state or in solution and within a few days turned white to produce photoisomer (127). The IR spectrum of (127) showed the presence of the bridging carbonyl function by means of a strong band at 1770 cm^{-1} while the original quinone carbonyl stretch had been shifted up to 1680 cm^{-1}. This indicated that the quinonoid double bond had been lost in the isomerisation and it is felt that the only possible way in which the intramolecular isomerisation could occur would be to assign the indicated <u>endo</u> steriochemistry to adduct (126). Recently a similar type of photolysis had been reported by Kushner [91] who found that irradiation of the adduct (128) produced the photoisomer (129) <u>via</u> an intramolecular $\left[\pi^2_s + \pi^6_s\right]$ cycloaddition reaction, which while being analogous to the well documented $\left[\pi^2_s + \pi^2_s\right]$ photochemical cyclisation of

adduct (130) to (131),[92] differs remarkably in that it proceeds with destruction of an aromatic ring. Previously only intermolecular $\left[\pi^2_s + \pi^6_s\right]$ photoadditions involving a benzene ring in which the 6π electron system of the benzene ring is not regenerated have been reported.[93] The photoconversion of adduct (126) to (127) also represented an example of photolytic destruction of an aromatic ring albeit leaving two other aromatic rings intact.



(128) (129)



(130) (131)

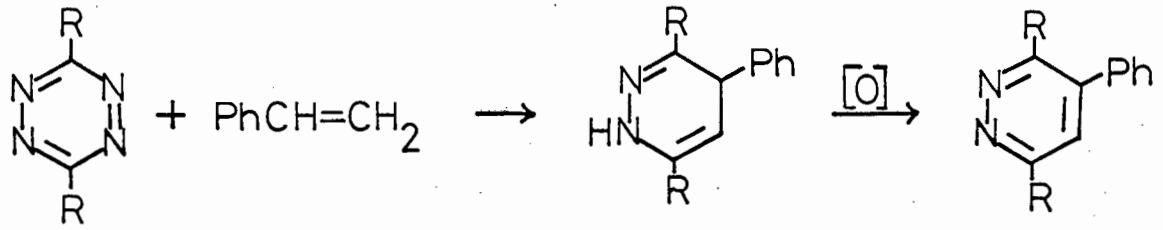
Pyrolysis of adduct (126) led to the isolation of the predicted triphenylene moiety (120) in 62% of the expected yield as the only product in a reaction presumed to be similar to that depicted in Scheme 7.

Again much decomposition accompanied the pyrolysis leaving a black tar in the pyrolysis vessel. Attempts to trap the intermediate (121) also failed. This failure may also be attributed to the fact that other rearrangements may be taking place as happens in related systems such as spiro[2.4]hepta-1,3-diene (122) and its spiro[4.4]- and spiro[5.4]-diene derivatives, which are known to undergo thermal rearrangements.[94, 95]

It would appear from evidence adduced thus far that the desired quinone (1) had been formed, albeit only transiently, by the various techniques employed, but that, once having been formed, rapidly underwent decomposition in the presence of oxygen and heat and also in certain solvents such as ethanol and chloroform. Consequently a method had to be sought which would obviate the rather high temperatures used (220°) in order to effect pyrolysis of the adducts (117) and (126). It was thus not surprising that the quinone (1) largely decomposed at these high temperatures.

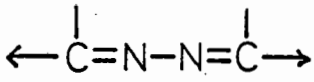
The use of extreme temperatures in order to effect fragmentation places a strict limitation as to the nature of the products sought if they are themselves temperature sensitive.[97] This limitation has been partly offset by flash vacuum pyrolysis as was demonstrated by de Mayo and his co-workers on the synthesis of pentalene.[98] In seeking ways to effect a mild $\left[\pi^4_s + \pi^2_s\right]$ cycloreversion reaction for the preparation of the desired quinone (1) from the quinone (70), certain tetra- and triazines were considered. It has been shown that

s-tetrazines with electron withdrawing groups in positions 3 and 6 e.g. (132) react very readily with a variety of unsaturated compounds e.g. styrene to yield the corresponding dihydropyridazines (133), the reaction being exothermic in certain cases such as the one cited. [99] The dihydropyridazines can be easily oxidised to the corresponding pyridazines (134). However when the substituents in the 3 and 6 position are electron donating e.g. (135) reaction is inhibited and higher temperatures are necessary to effect addition. This enhanced reactivity associated with electron-withdrawing groups on the s-tetrazine nucleus has been interpreted to render the 3 and 6 positions of the diene system (136) more susceptible to attack by dienophiles. [99]



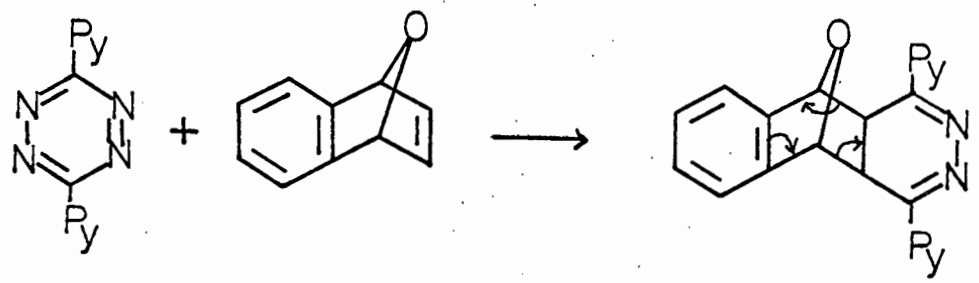
(132) R=CHFCF$_3$ (133) R=CHFCF$_3$ (134) R=CHFCF$_3$

(135) R = Me, Ph

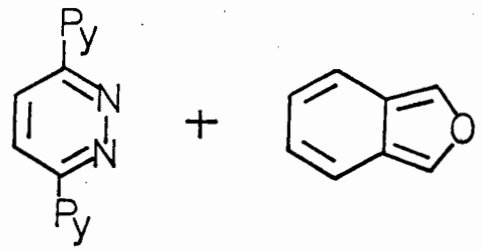


(136)

Warrener [100] has recently employed the high reactivity of an s-tetrazine (137) in the synthesis of isobenzofuran (140) as indicated in Scheme 8. Reaction between the dipyridyl-s-tetrazine (137) and 1,4-dihydro-1,4-endoxynaphthalene (138) occurred rapidly at room temperature in an exothermic manner liberating nitrogen. The exo-dihydropyridazine (139) that was isolated appeared to be fairly stable in solution below -20°. N.m.r. spectroscopy showed that quantitative conversion into the pyridazine (141) and isobenzofuran (140) occurred at room temperature.



(137) (138) (139)

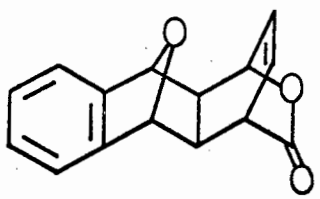


Py = 2′-pyridyl

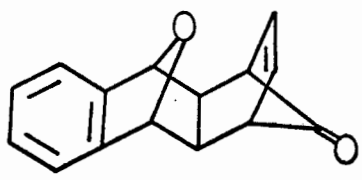
(141) (140)

SCHEME 8

The above procedure presented an easy and convenient method for obtaining isobenzofuran (140) which had previously only been trapped with dienophiles when generated by either the thermolysis of lactone (142) [101] or ketone (143) [78] in solution. Recently Wege [102] was able to isolate isobenzofuran from the pyrolysis of (142) which had previously been adsorbed on to celite. Warrener [100] had effectively removed the ethylene bridge of the endoxynaphthalene (138), the former becoming incorporated into an aromatic system (see Scheme 8) representing a $\left[\pi^4_s + \pi^2_s\right]$ cycloreversion reaction. This observation finds analogies in similarly related types of reactions. [103 - 106] As had been shown, the reverse electronic requirements of the s-tetrazines necessitated the use of electron rich olefins in order to facilitate reaction. [99] However efficient cycloadditions could also be induced with dienophiles activated by ring strain such as norbornadiene (78) although a reaction period of 3 days in benzene under reflux was necessary. [103] Once again the norbornadiene (78) was converted into cyclopentadiene with the loss of an ethylenic bridge.



(142)



(143)

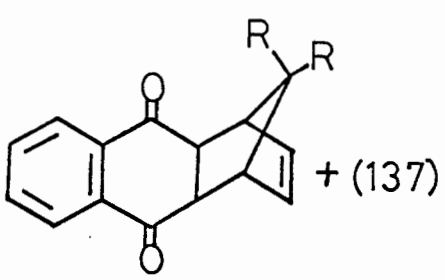
With this in mind reaction of the quinones (70) and (125) with the s-tetrazine (137) were attempted in benzene at room temperature for periods of up to 68 hr. Under these conditions no addition occured as well as when heated under reflux for long periods in the presence of trapping reagents. The reason for adding the trapping reagent was due to the fact that a substantial amount of decomposition was observed to occur which could have been due to the formation of the diene (1a) which subsequently decomposed. It was hoped that the trapping reagent would immediately react with this species if formed. In all cases the starting materials were isolated in 80 - 95% yields by column chromatography. Again no immediate reason for this failure to effect reaction is apparent excepting that the quinone system in the near proximity of the ethylene double bond may cause it to become sufficiently electron deficient so as not to react with the electron deficient s-tetrazine. In order to substantiate this suggestion reactions between the adducts (144) and (123) with the s-tetrazine (137) were carried out since the influence of the quinone double bond was absent in both of these cases. Addition was found to proceed quite readily when the reactants were heated in benzene under reflux and the 1,4-dihydropyridazines (145) and (146) were isolated in yields of 90%. Although no n.m.r. spectra for the 1,4-dihydropyridazine adducts could be obtained due to their high insolubility in the usual solvents, the structures proposed are based on precedent in the literature [99] and also on the strong

absorption bands at 3362 cm^{-1} for the N—H stretching frequency in (145) and at 3280 cm^{-1} for the N—H stretch in (146). In this regard Avram *et al.* [107] have shown that proton shifts of 4,5-dihydro- to 1,4-dihydropyridazines occur quite readily especially when the addends are cyclic. This implied that if the initial adducts obtained had the 4,5-dihydro-structure *i.e.* (147) they would undergo proton migration to produce the 1,4-dihydropyridazines (145) and (146) as shown in Scheme 9.

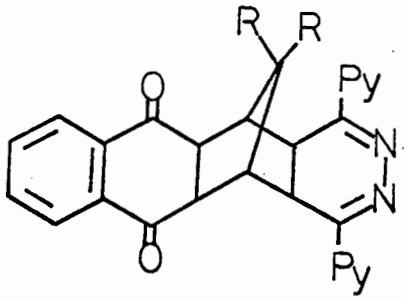
Attempts were made at this stage to oxidise the adducts (145) and (146) to the quinonoid forms (150), since, provided that the 1,4-dihydropyridazine rings were in equilibrium with the isomeric 4,5-dihydro tautomers *i.e.* (150), it might be possible for the molecule to undergo the $\left[\pi^4_s + \pi^2_s\right]$ cycloreversion reaction to yield quinone (1) and pyridazine (141). Attempts to enolise adducts (145) and (146) with base to the corresponding quinols in order to prepare quinones of type (150) did not prove fruitful.

In spite of the fact that the 4,5-dihydropyridazine system is prone to aerial oxidation and that chemical reagents such as DDQ may greatly facilitate this, [104] oxidation with DDQ was attempted on the adducts (145) and (146) since oxidation of the diketo section of the adducts to the quinone level, with concomitant tautomerisation from the 1,4- to the 4,5-dihydropyridazines (150), might prove sufficiently rapid to allow the indicated $\left[\pi^4_s + \pi^2_s\right]$ cycloreversion reaction to occur.

Oxidation of adduct (145) with a molar equivalent of DDQ in hot



+ (137) ⟶

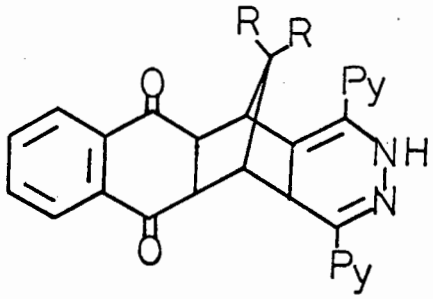


(144) R=R=H

(123) R⌒R = CH_2CH_2

(147)

↓



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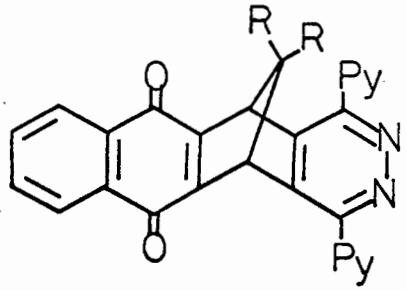
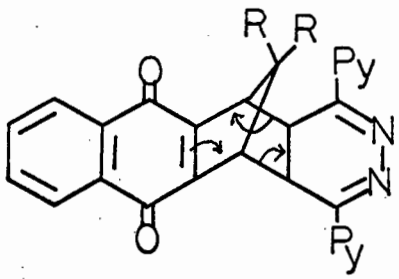


(145) R=R=H

(146) R⌒R = CH_2CH_2

(148) R=R=H

(149) R⌒R = CH_2CH_2

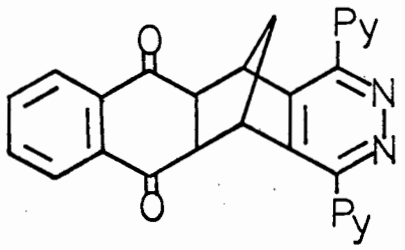


(150)

Py = 2′-pyridyl

SCHEME 9

dioxan produced a mixture of two oxidation products which were separated into a minor fraction (2%) and major fraction (94%) the rest being decomposed material. The minor component is believed to be the diketo-pyridazine (151), the structure of which is based on the chemical analysis and the lack of the N—H stretching frequency in the IR spectrum and the presence of a carbonyl frequency at 1690 cm^{-1}. Furthermore this material is converted to the quinone (148) on further treatment with DDQ in hot dioxan.



Py = 2-pyridyl

(151)

The major component was shown to have structure (148) which showed that complete oxidation had occurred. The IR spectrum showed a strong band at 1665 cm^{-1} due to the carbonyl stretching frequency of the quinone functional group whereas the UV spectrum had peaks at $\lambda_{max.}$ values of 341, 278, 254 and 248 nm. The n.m.r. spectrum featured two of each of the pyridyl ring protons very prominently at τ values of 1.06 and 1.42τ the others overlapped with the signals due to the other aromatic protons.

The bridgehead methine protons appeared as a triplet at 3.96τ (J = 1Hz), being strongly deshielded by the anisotropic effects of the two adjacent pyridyl rings, while the methylene protons of the methano bridge appeared as a triplet at 7.21τ (J = 1Hz). Oxidation of the 1,4-dihydropyridazine (146) with DDQ produced the quinone-pyridazine (149) in 84% yield.

It appears likely, therefore, that oxidation of the dihydropyridazine ring in (147) precedes oxidation of the diketo moiety to the corresponding quinone. If, in fact, the order of the oxidations is reversed, giving riseto the quinone (150), or its 1,4-tautomer as an intermediate, then subsequent oxidation of the heterocyclic ring must be more facile than the retro Diels-Alder reaction.

EXPERIMENTAL

IIa(i) 1,4-Methano-1,4,4a,9a-tetrahydroanthroquinone (88)

The tetrahydroanthroquinone was prepared according to the method of Diels and Alder [62] in 96% yield as white cubes (from petrol ether) m.p. 113° (Lit. [62] 115 - 116°).

IIa(ii) Enolisation of adduct (88)

The adduct (6.1 g) was dissolved in dry THF (250 ml) and flushed with N_2. Potassium t-butoxide (600 mg) was added and the resulting red solution stirred for 0.5 hr after which time the solution was neutralised with dilute HCl, poured into water (300 ml) and extracted with chloroform (6 x 50 ml). The dried ($MgSO_4$) extract was stripped of solvent to yield 6.07 g of 1,4-methano-1,4-dihydroanthroquinol (83) as white crystals (from chloroform/petrol ether) m.p. 168° (dec.). [Found: C, 80.4; H, 5.4. $C_{15}H_{12}O_2$ requires C, 80.1; H, 5.1%]; $\lambda_{max.}$ 340, 327, 310, 280 and 252 nm (log ε 3.58, 3.63, 3.62, 3.57 and 4.40); $\nu_{max.}$ 3280, 1645, 1605, 1080 cm^{-1}; n.m.r. (Acetone-d_6) τ 2.00 (m, 2H), 2.35 (s, 2H, D_2O exchangeable), 2.70 (m, 2H), 3.37 (t, 2H, J 1.6 Hz), 5.68 (t, 2H, J 1.6 Hz), 7.93 (m, 2H).

IIa(iii) Acetylation of the quinol (83)

Redistilled pyridine (2 ml) was added to a solution of the quinol (100 mg) in acetic anhydride (3.2 ml). The mixture was kept at room temperature for three days and then poured into water (50 ml). The white solid that precipi-

tated was filtered off to yield 132 mg (100%) of 1,4-methano-1,4-dihydroanthroquinol diacetate (89) as white needles (from ethanol) m.p. 164°. [Found: C, 74.0; H, 5.4. $C_{19}H_{16}O_4$ requires C, 74.0; H, 5.2%]; $\nu_{max.}$ 1757, 1082 cm^{-1}; n.m.r. τ 2.43 (m, 4H), 3.29 (t, 2H, J 1.6 Hz), 6.07 (t, 2H, J 1.6 Hz), 7.59 (s, 6H), 7.78 (t, 2H, J 1.6 Hz).

IIa(iv) Oxidation of 1,4-methano-1,4-dihydroanthroquinol (83)

A solution of the quinol (6.0 g) in benzene (350 ml) was treated with powdered silver oxide and the mixture shaken for 5 hr and filtered. The yellow filtrate was stripped of solvent to yield 6.0 g (100%) of 1,4-methano-1,4-dihydroanthroquinone (70) as yellow needles (from ethanol) m.p. 157° (Lit.[62] m.p. 158°). $\lambda_{max.}$ 339, 277, 254 and 248 nm (log ε 3.46, 4.20, 4.29 and 4.24); $\nu_{max.}$ 1660, 1640, 1600 cm^{-1}; n.m.r. τ 2.11 (m, 2H), 2.49 (m, 2H), 3.22 (t, 2H, J 2 Hz), 5.83 (sharp multiplet, 2H), 7.69 (t, 2H, J 1 Hz).

IIa(v) 1,4-Methano-1,4-dihydroanthroquinol dimethylether (96)

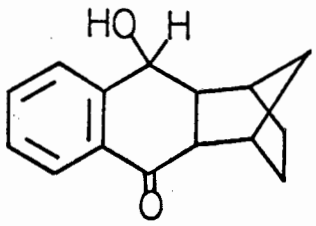
A solution of the quinol (83) (4.5 g) in ethanol (60 ml) was heated to 50° and rapidly stirred while 10 M NaOH (5 ml) and dimethyl sulphate (6 ml) were added alternatively during 5 minutes. Thereafter a further 2 ml of the 10 M NaOH was added and the resulting brown solution was heated on a water bath for 2.5 hr. The solvent was removed under vacuum and

then water (250 ml) was added to the solid material which remained in the flask. The solution was extracted with chloroform (5 x 50 ml), the extracts dried ($MgSO_4$) and concentrated to a brown oil which was chromatographed over silica gel and eluted with benzene. The dimethylether (96) was obtained as pure white crystals (4.68 g; 93%) (from methanol) m.p. 77°. [Found: C, 80.8; H, 6.3. $C_{17}H_{16}O_2$ requires C, 81.0; H, 6.35%]; $\lambda_{max.}$ 281 and 242 nm (log ε 3.77 and 4.57); $\nu_{max.}$ 1645, 1605, 1080 cm^{-1}; n.m.r. τ 2.03 (m, 2H), 2.62 (m, 2H), 3.30 (t, 2H, J 2 Hz), 5.73 (t, 2H, J 1.6 Hz), 6.07 (s, 6H), 7.79 (d, 2H, J 1.6 Hz).

IIa(vi) Catalytic hydrogenation of 1,4-methano-1,4,4a,9a-tetrahydroanthroquinone (88)

A solution of the adduct (4.76 g) in ethanol (160 ml) containing the catalyst 10% Pd/C (100 mg) was shaken in a atmosphere of H_2 for 3 hr after which time two molar equivalents of hydrogen had been absorbed. No plateau was observed in the absorption curve which indicated a steady uptake of H_2 all the time. The solution was filtered and the filtrate stripped of solvent to yield a mass of white crystals (4.60 g). Recrystallisation from petrol ether gave pure 1,4-methano-1,2,3,4,4a,9,9a-heptahydroanthracene-10-one-9-ol m.p. 141°. [Found: C, 78.6; H, 7.1. $C_{15}H_{16}O_2$ requires C, 78.9;

H, 7.0%]; $\lambda_{max.}$ 295 and 258 nm (log ε 3.12 and 3.91); $\nu_{max.}$ 3480, 1663, 1042 cm^{-1}; n.m.r. τ 2.50 (m, 4H), 4.88 (d, 1H, J 5 Hz), 7.22 (m, 5H, the signal integrated for 4H after D_2O exchange), 8.82 (m, 6H). This data is consistant with the structure shown below.



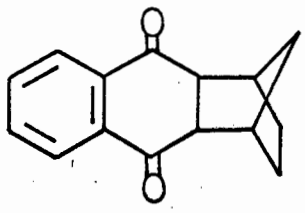
IIa(vii) Oxidation of the adduct from IIa(vi)

The adduct (1.14 g) was dissolved in acetic acid (35 ml) and heated to 100°. A solution of sodium nitrite (2.0 g) in water (1.4 ml) was added to the hot solution with evolution of N_2. The temperature was then adjusted to 70° while a solution of sodium dichromate (2.0 g) in water (1.5 ml) was added with stirring. The temperature was kept at 70° for 1 hr and the solution was poured into ice/water (60 ml). The yellow solid was filtered off and dried to yield 1.0 g of an olive-green product. Purification through a column of silica gel using benzene as eluent gave 1,4-methano-

1,2,3,4-tetrahydroanthroquinone (184) as yellow needles (from ethanol) m.p. 135 - 136° (Lit.[62] 138°). $\lambda_{max.}$ 338, 278, 251, 245 and 241 nm (log ε 3.39, 4.17, 4.18, 4.19 and 4.16); $\nu_{max.}$ 1665, 1658, 1600 cm^{-1}; n.m.r. τ 1.92 (m, 2H), 2.29 (m, 2H), 6.33 (m, 2H), 7.90 - 8.90 (broad multiplet, 6H).

IIa(viii) Repeat hydrogenation on adduct (88) [c.f. IIa(vi)]

The dione (2.30 g) was dissolved in ethanol (60 ml) and the catalyst 10% Pd/C (30 mg) added. The resulting mixture was hydrogenated very carefully and the uptake of H_2 monitored. When exactly one molar equivalent of H_2 had been absorbed, the mixture was filtered and the filtrate stripped of solvent to yield 2.3 g of 1,4-methano-1,2,3,4,4a,9a-hexahydroanthroquinone (vide infra) as glistening white needles (from dilute ethanol) m.p. 114 - 115° (Lit.[62] 117°). [$C_{15}H_{14}O_2$ requires C, 79.6; H, 6.2. Found: C, 79.8; H, 6.0%]; $\lambda_{max.}$ 307, 298, 255 and 226 nm (log ε 3.26, 3.27, 4.37 and 4.59); $\nu_{max.}$ 1690, 1670 cm^{-1}; n.m.r. τ 2.05 (m, 2H), 2.38 (m, 2H), 6.88 (m, 2H), 7.01 (m, 2H), 8.49 (m, 2H), 8.74 (m, 4H). This data is consistant with the structure shown below.



IIa(ix) Oxidative enolisation of the adduct from IIa(viii)

The dione (1.4 g) was dissolved in methanol (45 ml) and stirred rapidly while 2 M NaOH (7 ml) was added. Stirring was continued for 0.5 hr after which time a dense yellow crystalline product had separated. Fractional recrystallisation gave pure quinone (184) in 70% yield.

IIb(i) 2,5-Dimethyl-3,4-diphenylcyclopentadienone (77)

The dimer of the cyclopentadienone (61) was prepared according to the method of Allen and von Allen [72] in 90% yield as white crystals (from ethanol) m.p. 180 - 181° (Lit. [72] 180 - 181°).

IIb(ii) Reaction between the cyclopentadienone (77) and 1,4-methano-1,4-dihydroanthroquinol (83)

The quinol (300 mg) and the cyclopentadienone (348 mg) were heated in benzene (20 ml) under reflux for 90 hr. Removal of solvent yielded a brown oil which was triturated with boiling methanol to yield a white solid 164 mg. Recrystallisation from ethanol yielded pure 1,4-keto-1,4-dimethyl-2,3-diphenyl-4a,9a-dihydroanthroquinone (84) as white cubes m.p. 202°. [Found: C, 83.1; H, 5.1. $C_{29}H_{22}O_3$ requires C, 83.2; H, 5.3%]; $\nu_{max.}$ 1792, 1770, 1680, 1668, 1590 cm^{-1}; n.m.r. τ 2.22 (m, 4H), 3.07 and

3.57 (m, 10H), 4.51 (s, 2H), 8.40 (s, 6H).

IIb(iii) Reaction between 1,4-naphthoquinone and the cyclopentadienone (77)

Naphthoquinone (610 mg) and the cyclopentadienone (1.0 g) were heated under reflux in benzene (30 ml) for 48 hr. Removal of solvent gave a brown crystalline mass which when triturated with methanol gave the adduct (84) in 87% yield shown to be identical in all respects with that prepared in IIb(ii).

IIb(iv) Reaction of base on the adduct (84)

The adduct (320 mg) in methanol (150 ml) was stirred vigorously while 2 M NaOH (1.5 ml) was added dropwise. Stirring was continued until all of the adduct had gone into solution 0.5 hr. The solution was then neutralised with dilute HCl and poured into water (350 ml). The yellow solid was filtered off to yield the 1,4-dimethyl-2,3-diphenyl-anthroquinone (86) in 96% yield as yellow plates (from methanol) m.p. 195° (Lit.[49] 295°). [$C_{28}H_{20}O_2$ requires C, 86.6; H, 5.2. Found: C, 86.8; H, 5.4%]; $\lambda_{max.}$ 357 and 262 nm (log ε 3.75 and 4.57); $\nu_{max.}$ 1669, 1593 and 1542 cm^{-1}; n.m.r. τ 1.85 (m, 2H), 2.28 (m, 2H), 2.96 (m, 10H), 7.52 (s, 6H).

IIb(v) Reaction between diacetate (89) and the dienone (77)

A solution of the diacetate (390 mg) and the dienone

(322 mg) in chlorobenzene (30 ml) were heated under reflux for 50 hr during which time the solution changed colour from bright orange to pale yellow. Removal of the solvent yielded an oil which when triturated with boiling methanol yielded a white crystalline material which was shown to be the exo-adduct (91). The yield was 95%. The purified material appeared as white needles (from DME) and had m.p. 259 - 260° (dec.). [Found: C, 82.0; H, 5.8. $C_{37}H_{32}O_4$ requires C, 82.2; H, 5.9%]; $\nu_{max.}$ 1759, 1171, 1152 cm^{-1}; n.m.r. (Pyridine-d_5 at ca. 50°) τ 2.07 (m, 2H), 2.58 (m, 2H, 3.08 (m, 10H), 6.12 (s, 2H), 6.86 (s, 2H), 7.54 (s, 8H), 8.25 (s, 6H).

This compound did not undergo pyrolysis at temperatures of up to 310°.

IIb(vi) Hydrolysis of the diacetate adduct (91)

(1) $LiAlH_4$: The diacetate (100 mg) was dissolved in hot DME (20 ml). This solution was then run into a suspension of $LiAlH_4$ (50 mg) in DME under reflux and the resulting mixture heated under reflux for a further 1 hr under an atmosphere of N_2. The solution was then cooled and excess $LiAlH_4$ destroyed with moist DME. Celite and $MgSO_4$ were added and the whole brought to the boil and filtered hot. The filtrate was stripped of solvent to yield a black tar, sublimation of which

yielded 3',6'-dimethyl-o-terphenylene (81) in 63% yield as white needles (from methanol) m.p. 110° (Lit.[72] 113°).

(2) NaOEt/EtOH/N_2: The diacetate (100 mg) was heated under reflux in sodium ethoxide (from 30 mg sodium and 60 ml ethanol) under a stream of N_2 gas. After 2 hr the solution was reduced to half its volume and poured into an aqueous solution of ammonium chloride which was then extracted with benzene. The dried ($MgSO_4$) extract was stripped of solvent to yield after sublimation 3',6'-dimethyl-o-terphenylene (81) in 90% yield. No other products were isolated.

IIb(vii) Reaction between the dimethylether (96) and the cyclopentadienone (77)

The dimethylether (4.6 g) and the dienone (4.75 g) were heated under reflux in chlorobenzene (200 ml) for 50 hr. Solvent was removed yielding an oil which crystallised on trituration with hot methanol (200 ml) forming the exo-adduct (98) in 89% yield* as glistening plates (from chloroform/petrol ether) m.p. 195 - 196°. [Found: C, 86.5; H, 6.4. $C_{35}H_{32}O_2$ requires C, 86.8; H, 6.6%]; $\lambda_{max.}$ 299 and 238 nm (log ε 3.94 and 4.88); $\nu_{max.}$ 1640, 1610, 1088, 1039 cm^{-1}; n.m.r. τ 1.87 (m, 2H), 2.55 (m, 2H), 3.09 (m, 10H), 5.95 (s, 8H), 7.19 (s, 2H), 8.28 (s, 8H).

*The mother liquors were evaporated to dryness and an IR spectrum was run on the white solid material. The spectrum was identical to that of adduct (98) except for a band at 1763 cm^{-1} indicating the presence of the bridgehead carbonyl function. Due to the very small yield of this compound it was not purified since sublimation led directly to decarbonylation forming adduct (98).

IIb(viii) Pyrolysis of the adduct (98)

The adduct (900 mg) in the pyrolysis vessel was immersed into an oil bath preheated to 310° and allowed to melt for 5 minutes under an atmosphere of N_2. Sublimation of the brown liquid yielded a light yellow solid (800 mg) which was chromatographed through a column of silica gel. Elution with petrol ether yielded the first component (427 mg; 1.658 mmoles) which was shown to be 3',6'-dimethyl-o-terphenylene (81) by its m.p. and mixed m.p. with authentic material. The second component was eluted with chloroform to yield slightly impure material. Chromatographic separation through a second column using benzene/petrol ether (4:1) as eluent gave pure 1H-4,9-dimethoxybenz[f]indene (100). The yield was 373 mg; 1.650 mmoles. It formed light yellow lusterous plates (from methanol) m.p. 105°. [Found: C, 79.6; H, 6.3.

$C_{15}H_{14}O_2$ requires C, 79.7; H, 6.2%]; $\lambda_{max.}$ 347, 311, 301 and 251 nm (log ε 3.28, 3.91, 3.93 and 4.57); $\nu_{max.}$ 1630, 1607, 1170, 1090 cm^{-1}; n.m.r. τ 1.83 (m, 2H), 2.54 (m, 2H), 2.86 (dxt, 1H, J 5.8 and 2 Hz), 3.49 (dxt, 1H, J 5.8 and 2 Hz), 5.99 (s, 6H), 6.40 (t, 2H, J 2 Hz).

IIc(i) Preparation of phencyclone (116)

Phencyclone was synthesised as black needles in 60% yield according to the method of Dilthey.[108] A solution of phencyclone in benzene appeared green.

IIc(ii) Reaction between phencyclone (116) and quinone (70)

A solution of the quinone (250 mg) and phencyclone (510 mg) were heated under reflux in toluene (40 ml) for 50 hr after which time the solution was allowed to cool. Unreacted phencyclone was removed by filtration and the pale green filtrate was reduced in volume to 5 ml and triturated with hot ethanol. The yellow solid that precipitated from the solution was filtered off to yield (485 mg) of the exo-adduct (117) m.p. 223 - 225° (dec.). [Found: C, 87.3; H, 4.5. $C_{44}H_{28}O_3$ requires C, 87.6; H, 4.6%]; $\nu_{max.}$ 1793, 1656, 1598 cm^{-1}; n.m.r. (hot $CDCl_3$) τ 2.0—3.0 (m, 22H), 6.23 (s, 2H), 6.85 (s, 2H), 8.37 (s, 2H).

IIc(iii) Pyrolysis of the adduct (117)

Pyrolysis of the adduct was carried out by immersing it

under a N_2 atmosphere in a preheated oil bath at 230° and then reducing the pressure inside the apparatus to 0.5 mm. In this way two components, one white and the other yellow could clearly be seen on the cold finger. An IR spectrum done immediately on removal of the cold finger from the apparatus showed a quinone carbonyl at 1670 cm^{-1}. However the yellow component rapidly darkened on exposure to light, heat or oxygen.

The black sublimed material was chromatographed and a single component was eluted with chloroform which was shown to be the 1,4-diphenyltriphenylene (120) which formed white plates (from methanol/benzene) m.p. 221 - 222° (Lit.[79] 223°). When the adduct was pyrolysed in a system previously flushed with N_2 and kept at -30° after pyrolyses, the yellow component seemed to persist for a much longer period. However on warming to room temperature or introducing air into the system decomposition set in.

Trapping experiments

During a number of pyrolyses the cold fingers containing the two components were dipped into ethereal solutions containing potential dienophiles and dienes such as N-phenylmaleimide, cyclopentadiene, tetracyanoethylene and the s-tetrazine (137). In all cases no addition products were isolated.

IId(i) Spiro[2,4]-hepta-4,6-diene (122)

The diene was prepared in 65% yield as a colourless liquid b.p. 30 - 32°/20 mm by the method of Alder [109] who reported the b.p. as 57°/100 mm.

IId(ii) Reaction between 1,4-naphthoquinone and the spiroheptadiene (122)

A solution of naphthoquinone (10 g) and the spiroheptadiene (8.2 g) were heated under reflux in benzene (60 ml) for 12 hr. Removal of the solvent left a grey crystalline mass of 1,4-spirocyclopropyl-1,4,4a,9a-tetrahydroanthroquinone (123) in quantitative yield. It formed white needles (from alcohol) m.p. 159 - 160° (dec.). [Found: C, 81.8; H, 5.6. $C_{17}H_{14}O_2$ requires C, 81.6; H, 5.6%]; $\lambda_{max.}$ 309, 301, 250 and 225 nm (log ε 3.12, 3.13, 3.93 and 4.42); $\nu_{max.}$ 1678, 1589 cm^{-1}; n.m.r. τ 1.99 (m, 2H), 2.30 (m, 2H), 3.96 (t, 2H, J 2 Hz), 6.38 (dxd, 2H, J 1.6 and 1.6 Hz), 6.98 (m, 2H), 9.42 (s, 4H).

IId(iii) Enolisation of adduct (123)

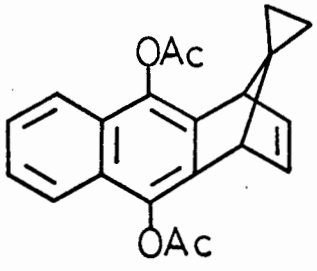
The adduct (7.2 g) was dissolved in anhydrous THF (150 ml). Potassium t-butoxide (1 g) was added and the resulting solution was stirred for 1 hr and then poured into water (300 ml), neutralised with dilute HCl and extracted with chloroform. The dried ($MgSO_4$) extract was evaporated to an orange solid which was fractionally recrystallised from methanol to yield

the quinone (125) as yellow needles m.p. 186° (900 mg).

Evaporation of the mother liquors yielded 7.0 g of the quinol (124) as grey cubes (from benzene) m.p. 168 - 170°. [Found: C, 81.4; H, 5.7. $C_{17}H_{14}O_2$ requires C, 81.6; H, 5.6%]; $\nu_{max.}$ 3260, 1656, 1608, 1080 cm^{-1}.

IId(iv) Acetylation of quinol (124)

Acetic anhydride (2.5 ml) was added to a solution of the quinol (500 mg) in pyridine (2 ml) and the resulting solution kept in the dark for 18 hr and then poured into water (200 ml). The white precipitate was filtered off to give the diacetate (vide infra) in 93% yield. Recrystallisation from ethanol gave pure material m.p. 168°. [Found: C, 75.0; H, 5.4. $C_{21}H_{18}O_4$ requires C, 75.5; H, 5.4%]; $\nu_{max.}$ 1752, 1200, 1172 cm^{-1}; n.m.r. τ 2.25 (m, 2H), 2.51 (m, 2H), 3.20 (t, 2H, J 2 Hz), 6.63 (t, 2H, J 2 Hz), 7.60 (s, 6H), 9.40 (s, 4H).



Reductive acetylation of quinone (125) gave the above diacetate in 97% yield.

IId(v) Oxidation of quinol (124)

The quinol (1.0 g) in benzene (30 ml) containing silver oxide (2.5 g) was shaken for 1 hr and then filtered. The yellow filtrate was evaporated to dryness to give 1,4-spiro-cyclopropyl-1,4-dihydroanthroquinone (125) in 100% yield as yellow needles (from ethanol) m.p. 186.4°. [Found: C, 82.2; H, 4.7. $C_{17}H_{12}O_2$ requires C, 82.3; H, 4.8%]; $\lambda_{max.}$ 340, 278, 254 and 248 nm (log ε 3.38, 3.97, 4.27 and 4.23); $\nu_{max.}$ 1659, 1598 cm^{-1}; n.m.r. τ 1.92 (m, 2H), 2.32 (m, 2H), 3.05 (t, 2H, J 2 Hz), 6.27 (t, 2H, J 2 Hz), 9.37 (s, 4H).

IIe(i) Reaction of quinone (125) with phencyclone (116)

The quinone (1.0 g) and phencyclone (1.1 g) were heated together under reflux in toluene (100 ml) for 24 hr. Then toluene (80 ml) was distilled off and hot ethanol (50 ml) was added to the residue to precipitate on cooling the orange adduct (126) in 59% yield. It formed orange cubes (from benzene/methanol) m.p. 210°. [Found: C, 87.2; H, 4.8. $C_{46}H_{30}O_3$ requires C, 87.5; H, 4.8%]; $\nu_{max.}$ 1787, 1663, 1598 cm^{-1}. The compound was too insoluble in the normal solvents employed for a n.m.r. spectrum to be run.

IIe(ii) Photolysis of adduct (126)

The adduct (500 mg) was spread out thinly on a watch glass and exposed to sunlight for 6 days with occasional

remixing in order to expose new surface areas. The adduct changed from an orange to a white colour. The photo-isomer (127) was thus obtained in quantitative yield as small white cubes (from chloroform/methanol) m.p. $>300^{\circ}$. [Found: C, 87.3; H, 4.5. $C_{46}H_{30}O_3$ requires C, 87.6; H, 4.8%]; $\nu_{max.}$ 1770, 1680, 1594 cm^{-1}. No n.m.r. could be run due to the insoluble nature of the photo-isomer.

IIe(iii) Pyrolysis of adduct (126)

The adduct was pyrolysed under the same conditions as described in IIc(iii). In this case the 1,4-diphenyltriphenylene (120) was isolated in 70% yield after chromatographic separation of the sublimate. No other products arising from pyrolysis were isolated.

IIf(i) 3,6-Di(2'-pyridyl)-s-tetrazine (137)

The s-tetrazine was prepared in 60% yield as red-violet plates (from benzene) m.p. 229° according to the method of Geldard [110] who reported m.p. 229 - 230°.

IIf(ii) Addition attempts between the tetrazine (137) and quinones (70) and (125)

Equimolar amounts of the quinones and s-tetrazine were stirred in benzene (in separate experiments) at room temperature for periods of up to 68 hr. No addition products were detected and starting materials were isolated in 95% yield.

Similarly when the two reaction mixtures were heated in benzene containing trapping reagents like tetracyanoethylene for periods of up to 24 hr at 50°, no reaction could be induced. In these cases the quinones (70) and (125) were isolated in 80 - 85% yield. Changing the solvent to DMS or DMF had no effect either.

IIf(iii) Reaction between the s-tetrazine (137) and adduct (144)

The adduct (1.0 g) and s-tetrazine (1.1 g) were stirred together in benzene (50 ml) at 80° for 4 hr. During this period a yellow precipitate formed which was filtered off to give the 1,4-dihydropyridazine adduct (145) in 90% yield as yellow cubes (from chloroform/methanol) m.p. 218° (dec.). [Found: C, 75.0; H, 4.6; N, 12.9. $C_{27}H_{20}N_4O_2$ requires C, 75.2; H, 4.6; N, 13.0%]; $\nu_{max.}$ 3362, 1678, 1594, 1560 cm^{-1}. The adduct was not soluble enough to have an n.m.r. spectrum run.

IIf(iv) Oxidation of the 1,4-dihydropyridazine adduct (145)

The adduct (500 mg) and DDQ (300 mg) in freshly distilled dioxan (100 ml) were stirred at room temperature for 6 hr and then at 50° for 3 hr. Dichloro-dicyanoquinol (200 mg) was removed by filtration and solvent stripped off from the filtrate to yield a yellow oil which was passed through a

column of silica gel and eluted with chloroform. In this way a brick-red crystalline material was obtained (490 mg). Thin layer chromatography (t.l.c.) showed that this solid had a very small amount of a colourless material present. A recrystallised sample (200 mg) of the brick-red adduct was rechromatographed over silica gel using benzene/chloroform (4:1) as eluent. The front colourless band (10 mg) was recrystallised from chloroform/ethanol into white needles of the diketo-pyridazine adduct (151) m.p. 255 - 256° (dec.). [Found: C, 75.4; H, 3.2; N, 13.1. $C_{27}H_{14}N_4O_2$ requires C, 75.2; H, 3.3; N, 13.15%]; $\nu_{max.}$ 1690, 1598 cm^{-1}. Oxidation of this material with DDQ gave the quinone (148).

The second band eluted from the column gave the pyridazine-quinone (148) as fine yellow cubes (180 mg) from chloroform/ethanol. The sample started to darken at 260° and melted with decomposition at 280°. [Found: C, 75.3; H, 3.7; N, 13.0. $C_{27}H_{16}N_4O_2$ requires C, 75.6; H, 3.7; N, 13.0%]; $\lambda_{max.}$ (4% chloroform in ethanol) 341, 278, 254 and 248 nm (log ε 3.51, 4.46, 4.50 and 4.50); $\nu_{max.}$ 1665, 1598 cm^{-1}; n.m.r. τ 1.06 (dxm, 2H, J 4.6 Hz), 1.42 (dxm, 2H, J 8 Hz), 1.92 - 2.78 (m, 8H), 3.96 (t, 2H, J 1 Hz), 7.21 (t, 2H, J 1 Hz).

IIf(v) Reaction between the s-tetrazine (137) and adduct (123)

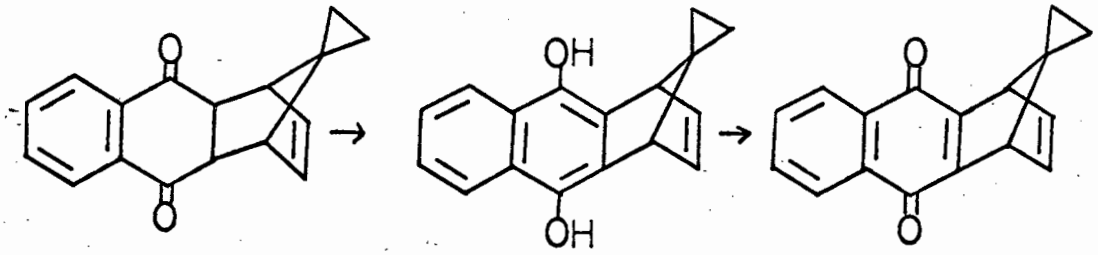
The adduct (1.0 g) and the s-tetrazine (1.0 g) were heated together under reflux in benzene (50 ml) for 4 hr during which time a yellow precipitate had formed which was isolated by filtration to yield the 1,4-dihydropyridazine adduct (146) as yellow cubes (1.60 g) (from chloroform/ethanol) m.p. 215° (dec.). [Found: C, 76.0; H, 4.6; N, 12.0. $C_{29}H_{22}N_4O_2$ requires C, 76.0; H, 4.8; N, 12.2%]; $\nu_{max.}$ 3280, 1677, 1587, 1565 cm^{-1}.

IIf(vi) Oxidation of the 1,4-dihydropyridazine adduct (146)

The adduct (800 mg) and DDQ (480 mg) were stirred together in freshly distilled dioxan (120 ml) at room temperature for 6 hr and then at 50° for 3 hr. The dichloro-dicyanoquinol was filtered off and dried (400 mg) and the filtrate was evaporated to a brown oil which was chromatographed over silica gel and eluted with chloroform to yield 670 mg of the quinone (149) as yellow needles (from chloroform/ethanol) m.p. 275° (dec.). [Found: C, 76.3; H, 4.1; N, 12.3. $C_{29}H_{18}N_4O_2$ requires C, 76.6; H, 4.0; N, 12.3%]; $\lambda_{max.}$ (10% chloroform in ethanol) 341, 283, 254 and 249 nm (log ε 3.48, 4.47, 4.50 and 4.51); $\nu_{max.}$ 1664, 1602, 1597 cm^{-1}; n.m.r. τ 1.42 (m, 2H), 1.71 (m, 2H), 1.98 - 2.23 (m, 8H), 4.42 (s, 2H), 9.18 (m, 4H).

CHAPTER III

During the course of the investigations described in the previous chapter it became necessary to prepare the 1,4-spirocyclopropylanthroquinone derivative (125). By analogy with the procedure adopted for the synthesis of the analogous quinone (70) it was anticipated that treatment of adduct (123) with methanolic sodium hydroxide should cause enolisation to produce the corresponding quinol (124) which was expected to readily undergo oxidation with silver oxide [118] or ferric chloride to yield quinone (125) according to Scheme 10.

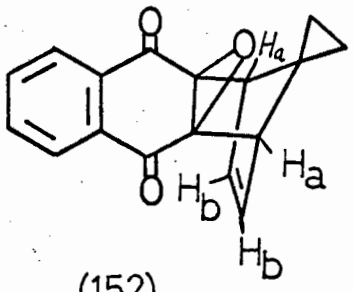


(123) (124) (125)

SCHEME 10

In practice, treatment of adduct (123) with methanolic sodium hydroxide for 2 hr at approximately 40° did not yield the expected quinol (124) but instead gave rise to three isomeric compounds, two of which were separated from the third by fractional crystallisation and column chromatography. The major component (80%) was white in colour while the minor component (3%) was golden yellow. It was immediately obvious that the

major component was not the expected quinol (124) since it would not dissolve in sodium hydroxide. This material which contained a mixture of the exo- and endo-epoxides (152) and (169) was fractionally recrystallised to give the pure exo-isomer m.p. 169°. The IR spectrum showed no O—H stretching frequency but instead a carbonyl stretch at 1691 cm^{-1}. Elemental analysis indicated that an additional oxygen atom had been incorporated into the starting material (123) with the loss of two hydrogen atoms. This, together with the n.m.r. data confirmed that the major product of the reaction was the exo-epoxide (152).*



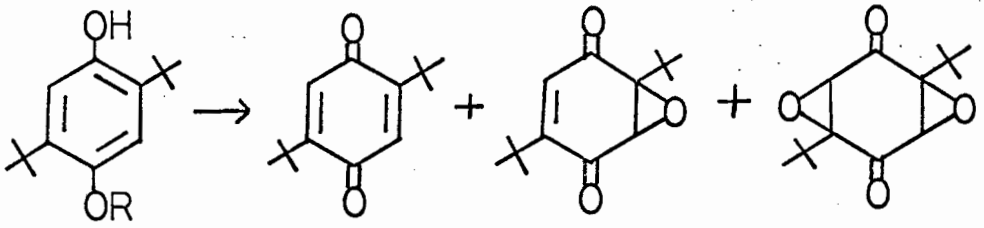
(152)

The allylic bridgehead protons H_a appeared as a triplet at 6.70τ (J = 2Hz) while the vinylic protons H_b appeared as a triplet at 3.78τ (J = 2Hz). A n.m.r. spectrum of the original reaction mixture obtained on attempted enolisation of (123) showed that both the exo- and endo-epoxides (152) and (169) were present in a ratio of 3:2 respectively. A discussion of the assignment of the exo steriochemistry to the major epoxide (152) is dealt with at a later stage in this chapter (see page 104).

*exo with respect to the bicyclo [2.2.1] system

Isolation of the epoxides (152) and (169) rather than quinol (124) under the reaction conditions employed may be rationalised in terms of work by Hewgill and Lee [111] on the autoxidation of 4-methoxy-2,5-di-t-butylphenol (153) and the corresponding demethylated quinol (154). It was shown that both these compounds yielded the same four products under the same conditions of autoxidation (*viz.* ethanolic sodium hydroxide and oxygen) as shown in Scheme 11. In addition it was also shown that if either quinone (155) or epoxide (156) was subjected to the same autoxidation conditions no reaction took place. This led to the postulation that a phenolic group was essential to initiate the autoxidation since oxygen could oxidise the phenoxide anion under these reaction conditions to the phenoxide radical according to equations (A) and (B), while itself becoming reduced to the peroxide anion. The phenoxide radical would be expected to exist largely as the quinonoid tautomer (157) which could then undergo epoxidation by the peroxide anion in the normal way. [112, 113]

Recently Baxter and Phillips [114] reported a similarly unusual formation of the epoxide (158) as one of the products formed from reaction between quinone (155) and neat n-propylamine in the presence of oxygen. However, not all autoxidation reactions of phenols proceed in this fashion as has been demonstrated by Corbett [115] in his studies of the autoxidations of 2-hydroxyhydroquinones. It was shown that the initial product *e.g.* the quinone (159) decomposed to dimeric products as well

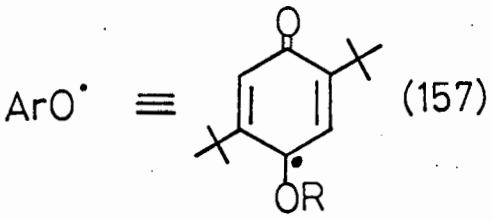


(153) R=Me (155) (156) cis and trans

(154) R=H

$$ArO^- + O_2 \longrightarrow ArO^{\cdot} + O_2^{\cdot -} \quad (A)$$

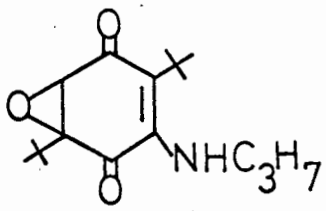
$$ArO^- + O_2 + H^+ \rightarrow ArO^{\cdot} + {}^{-}O_2H \quad (B)$$



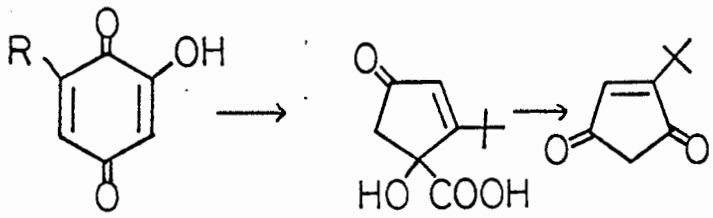
(157)

SCHEME 11

as open chain acids. In certain cases benzilic acid rearrangements have been observed to occur as in the autoxidation of hydroquinones (160) producing the cyclopent-4-ene-1,3-dione (162) via the intermediate (161).[116] In all cases of aromatic triols or hydroxyquinones being autoxidised, no epoxide formation has been observed to have occurred.



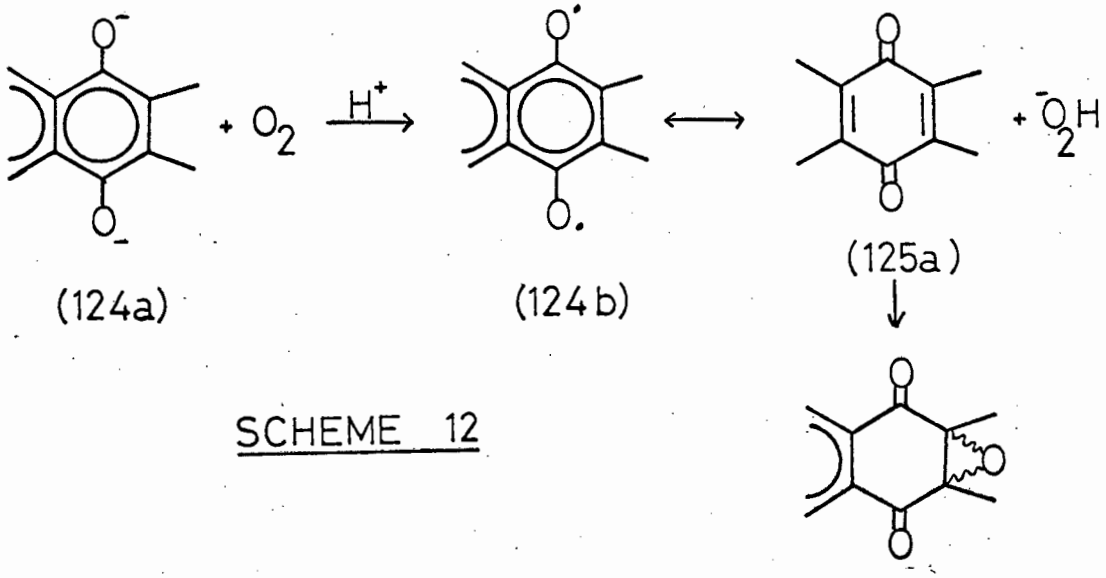
(158)



(159) R=H (161) (162)

(160) R= t-butyl

In the light of these findings the formation of the epoxides (152) and (169) can be rationalised in terms of an analogous autoxidation mechanism as depicted in Scheme 11. The first step envisaged must involve enolisation of the diketo-adduct (123) in the presence of base to produce the enolate dianion represented by partial structure (124a). Oxidation of the dianion by oxygen <u>via</u> the free radical mechanism proposed in Scheme 12 could then proceed to produce the peroxide anion and the diradical (124b) which would most likely exist in the more stable mesomeric form (125a). Epoxidation of the quinonoid tautomer (125a) could then produce a mixture of <u>endo</u>- and <u>exo</u>-epoxides, the <u>exo</u>-isomer (152) being purified by preferential crystallisation.



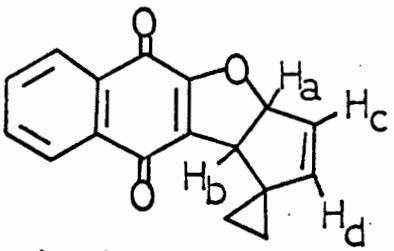
(124a) (124b) (125a)

SCHEME 12

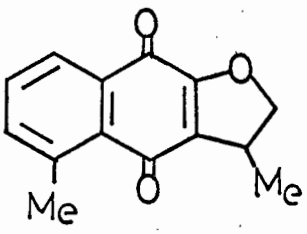
Isolation of a mixture of endo- and exo-epoxides in 90% yield as the only products of treatment of quinol (124) under the same autoxidation conditions as employed with adduct (123) supported the assumption that the initial step in the autoxidation of the latter adduct was indeed enolisation. Further support for the postulated quinone intermediate (125a) was derived by treating this quinone i.e. (125) with alkaline hydrogen peroxide, whereupon a mixture of the epoxides (152) and (169) was obtained in quantitative yield. The forgoing experimental evidence led to the conclusion that epoxidation of adduct (123) could be precluded by performing the enolisation under conditions which would exclude the presence of molecular oxygen. This was indeed shown to be the case since enolisation of adduct (123) in THF using potassium t-butoxide as catalyst and under an atmosphere of nitrogen produced an almost quantitative yield of the quinol (124).

The minor yellow component obtained from the autoxidation of adduct (123) is believed to have structure (163). This represents a very interesting type of rearrangement of an epoxide, albeit in only very low yield. The proposed structure for the rearranged product (163) is based on the elemental analysis and its spectral characteristics. The IR spectrum showed the quinone carbonyl stretching frequencies at 1683 and 1642 cm^{-1}. The UV spectrum showed bands at 393, 327, 282 and 252 nm which exibited certain similarities with somewhat related systems

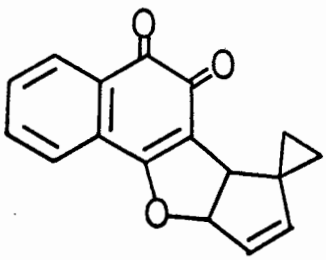
such as (164) [117] and α-lapachone (165) [118] which also showed four major bands but at slightly different wavelengths i.e. $\lambda_{max.}$ 358, 290, 253 and 247 nm for (164) and $\lambda_{max.}$ 375, 332, 282 and 251 nm for (165) respectively. An alternative 1,2-quinone structure such as (166) was ruled out due to the absence of a band at 430 nm in the UV spectrum. [118]



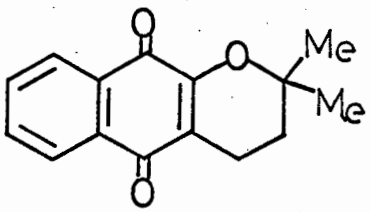
(163)



(164)



(166)



(165)

The n.m.r. spectrum (see fig. 3) showed the aromatic protons to appear as two sets of multiplets at 1.94 and 2.33τ. The prominent doublet at 6.02τ (J_{ba} = 9.1Hz) has been attributed to H_b showing it to be coupled to H_a in a cis manner, while the doublet at 4.38τ (J_{dc} = 5.5Hz) is due to proton H_d which is coupled to H_c across the

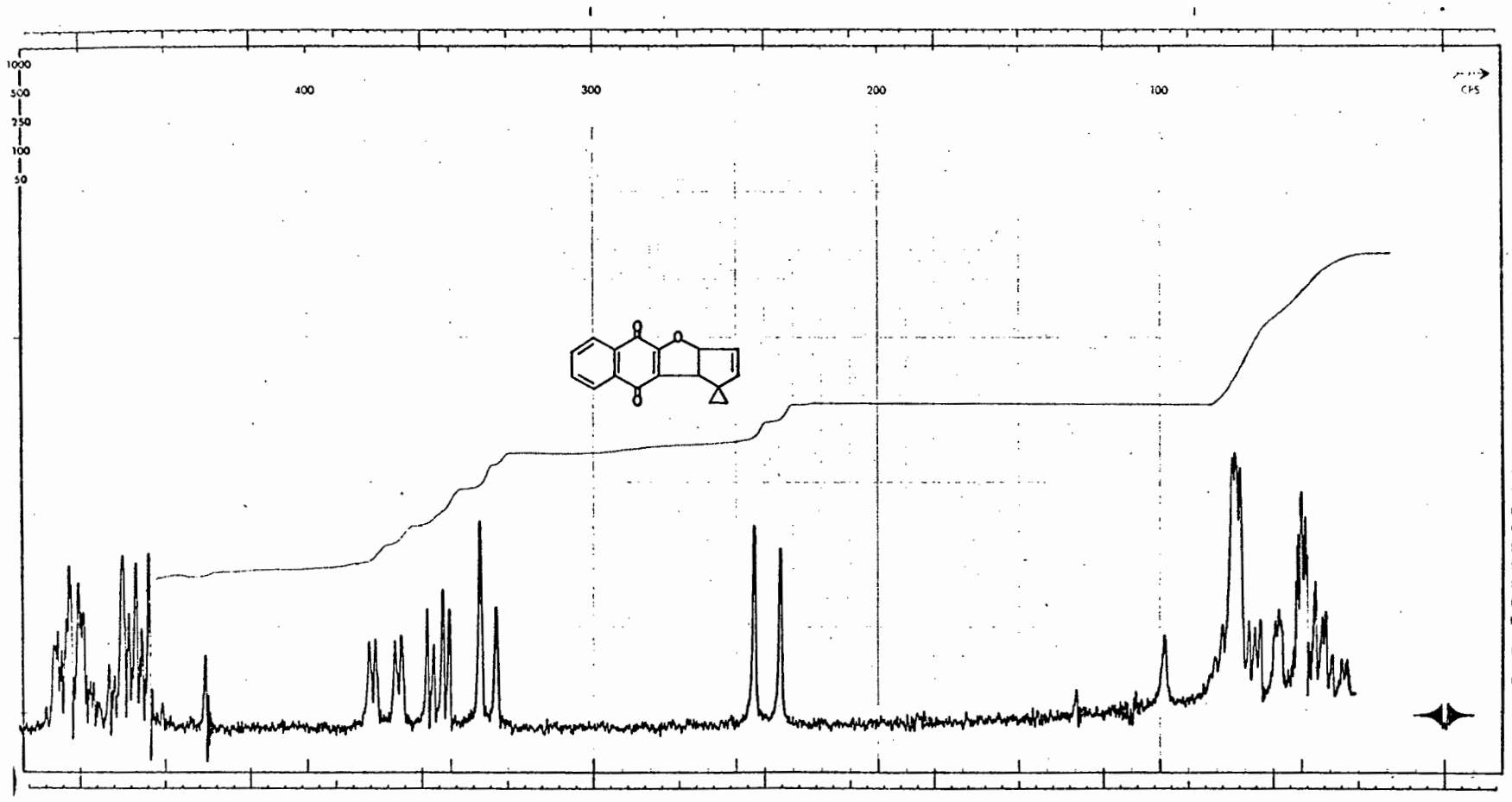
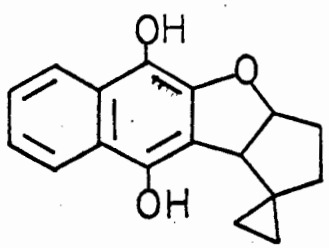


fig. 3

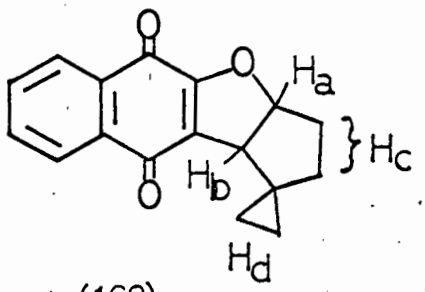
olefinic bond. The doublet of doublets appearing at 4.10τ was attributed to H_c with the major coupling occuring with H_d (J_{cd} = 5.5Hz) while the minor coupling (J_{ca} = 2.2Hz) is consistant with the steriochemical requirements for coupling with H_a as the dihedral angle is approximately 70°. The signal arising from proton H_a also appeared as a doublet of doublets at the rather low field value of 3.78τ most likely due to the fact that it is not only an allylic methine proton but is also adjacent to an oxygen atom which could cause further deshielding. The major coupling (J_{ab} = 9.1Hz) arises from cis coupling with H_b while the minor coupling (J_{ac} = 2.2Hz) is consistant with coupling to H_c. The cyclopropyl group appears as a multiplet centred at 9.18τ.

The presence of the olefinic bond was confirmed by catalytic hydrogeneration of quinone (163) in ethanol with 10% Pd/C as catalyst. A two molar equivalent uptake of hydrogen was measured which was expected since one mole would be required to reduce the olefinic bond while the other mole would be employed in the reduction of the quinone system to the quinol (167). Work up of the reduction mixture indicated that it was comprised of two products, presumably the quinone (168) and quinol (167). Oxidation of the mixture with silver oxide gave a single product viz. quinone (168). The IR spectrum showed strong bands at 1683 and 1644 cm^{-1} due to the quinone carbonyl groups while the UV spectrum was almost identical to quinone (163) and had $\lambda_{max.}$ at 395,

337, 287 and 252 nm. The n.m.r. spectrum showed the aromatic protons to appear as two sets of multiplets at 1.96 and 2.33τ. A prominent doublet at 6.53τ (J_{ba} = 8.2Hz) has been attributed to H_b which is coupled in a cis manner to H_a since irradiation of the multiplet due to H_a at 4.46τ caused this doublet to collapse into a singlet. Irradiation of the multiplet due to the methylene protons H_c at 7.84τ caused the signal due to H_a to change from a multiplet to a doublet (J_{ab} = 8.4Hz) while irradiation of the signal due to H_b caused H_a to appear as a doublet of doublets (J = 11 and 7Hz). These results are consistant with the proposed structure (168).



(167)

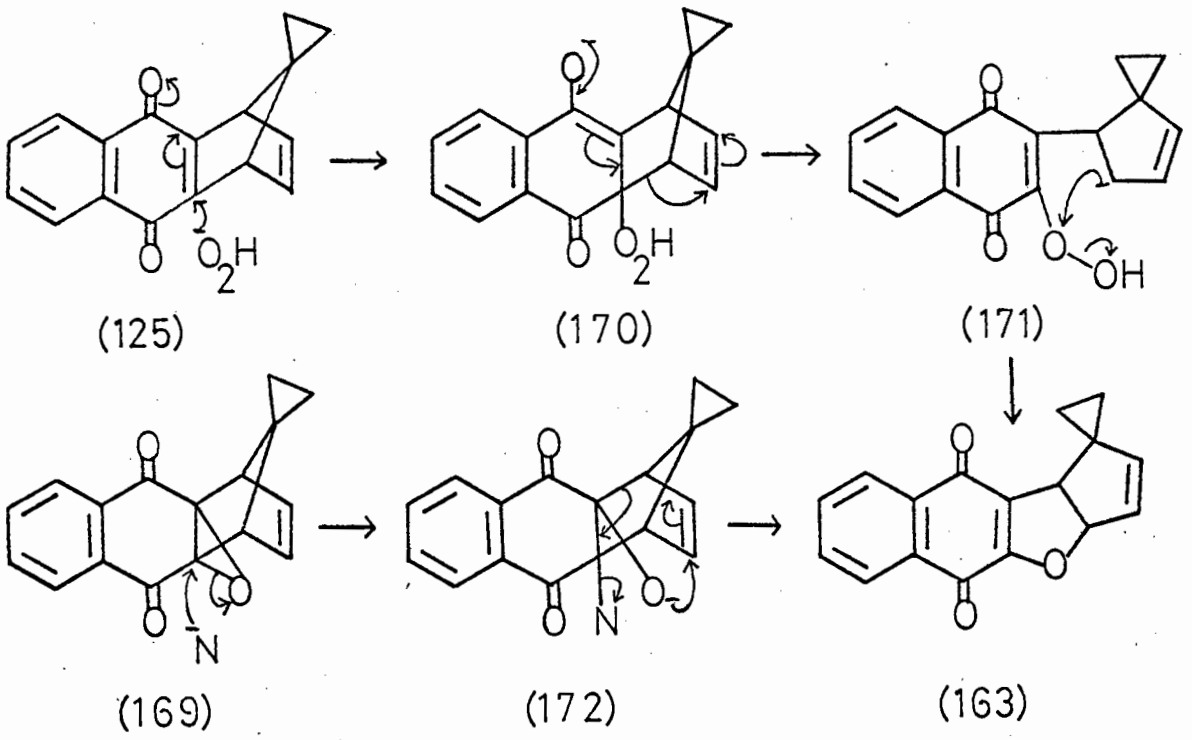


(168)

In postulating a mechanism for the formation of the quinone (163) from attempted enolisation of adduct (123) with methanolic sodium hydroxide, two likely precursors to be considered appeared to be either the quinone (125) or the endo-epoxide (169). Firstly one might envisage a type of Baeyer-Villiger rearrangement taking place whereby the quinone (125) could be attacked by the peroxide anion yielding the

enolate anion (170) which could in turn rearrange as depicted in Scheme 13 giving rise to the carbanion (171). Subsequent nucleophilic displacement of the hydroxyl group could then result in the formation of quinone (163). However it was experimentally shown that treatment of quinone (125) with alkaline hydrogen peroxide did not yield any of the quinone (163). Alternatively after the exo- and endo-epoxides (152) and (169) had been formed during the attempted enolisation of adduct (123), the only species present in the reaction medium to possibly initiate isomerisation were nucleophiles. Attack by a nucleophile may be expected to occur at the carbon atom of the epoxide ring to induce C—O bond cleavage and produce the anion (172) which is not necessarily considered to be a discrete intermediate. Subsequent attack by the oxygen atom at the olefinic bond could then produce the quinone (163) by the expulsion of the nucleophile as shown in Scheme 13. From the proposed mechanism it is implied that only the endo-epoxide (169) is likely to undergo the observed isomerisation as was indeed found to be the case (see later). Heating a mixture of the endo- and exo-epoxides (152) and (169) in methanolic sodium hydroxide gave rise to the formation of quinone (163) lending credence to the proposed mechanism in Scheme 13.

As already mentioned, the primary objective in treating adduct (123) with methanolic base had been to effect its conversion into the quinone (125) via the quinol (124). Since these conditions had led instead to the formation of the epoxides (152) and (169) attempts were then undertaken to convert the epoxides into the desired quinone (125) by removal



SCHEME 13

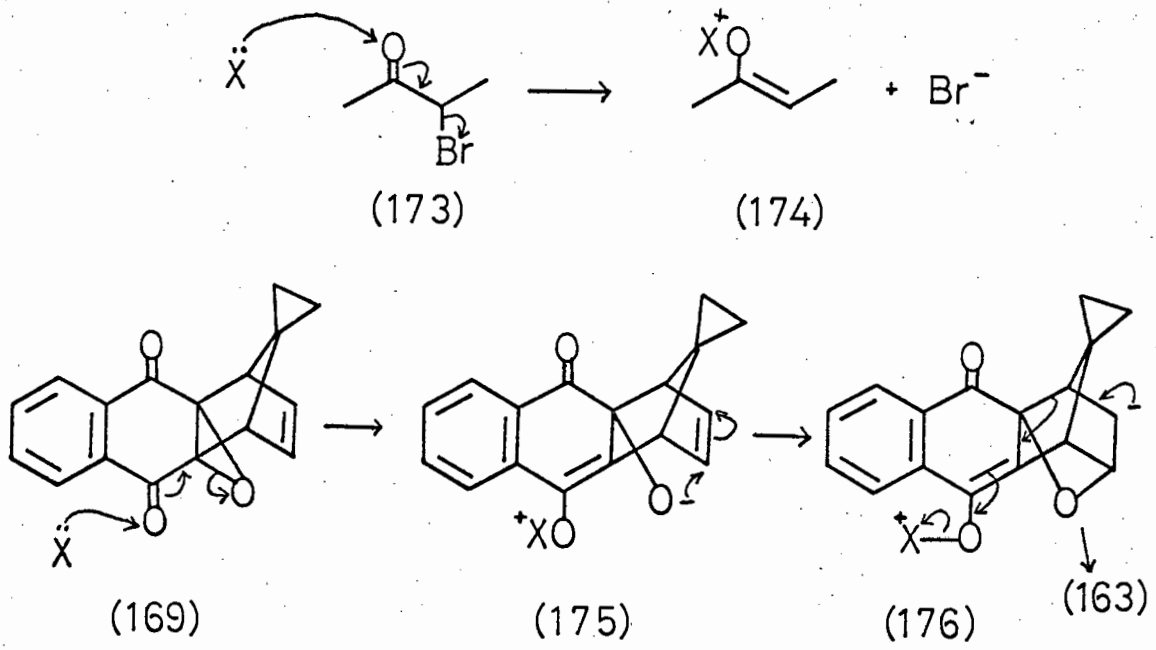
of the epoxide oxygen atom. Triphenylphosphine is known to attack a wide variety of oxygen containing compounds forming triphenylphosphine oxide. Horner and Hoffmann [119] have used this reagent for removing oxygen from compounds like peroxides, nitrones and amine oxides while Wittig and Haag [120] have found that styrene oxide may be effectively deoxygenated to styrene at 165° while the epoxide of ethyl cinnamate is converted in 80% to ethyl cinnamate.

It was found that when equimolar amounts of triphenylphosphine and a mixture of the exo- and endo-epoxides (152) and (169) were heated together under reflux in ethanol for 20 hr a dark brown solution resulted. The crude reaction products were separated from each other by column chromatography to yield triphenylphosphine (100%), the exo-epoxide (152) recovered in 96% yield based on the amount present in the original mixture and the quinone (163) in 58% yield as the only identifiable products from the

reaction mixture. There was a great deal of decomposed material present on the column. Furthermore, treatment of the isolated exo-epoxide (152) with triphenylphosphine under the same conditions for 20 hr failed to produce any isomerisation, the starting materials being recovered quantitatively. It was also shown that the quinone (163) when treated with triphenylphosphine under reflux with ethanol decomposed extensively. This would account for the fact that although all of the endo-epoxide (169) present in the original mixture of epoxides had been consumed during the reaction (as shown by n.m.r.), only 58% of the theoretical quantity of quinone (163) was actually isolated, the rest being decomposed by reaction with triphenylphosphine. This was substantiated in a further experiment in which a mixture of the exo- and endo-epoxides (152) and (169) in the ratio of 3:2 respectively was treated with triphenylphosphine in ethanol under reflux for 2 hr. On work up, the mixture, as shown by n.m.r. spectroscopy, consisted of the epoxides (152) and (169) in the respective ratio of 2:3 showing again that only the endo-epoxide underwent isomerisation. In this case the conversion of epoxide (169) to the quinone (163) was 90% based on unrecovered endo-epoxide (169). Thus the endo-epoxide (169) had undergone a molecular isomerisation reaction instead of deoxygenation while the exo-epoxide was quite unaffected under these conditions.

At this stage of the project it was thought that the triphenylphosphine was catalysing the isomerisation of the endo-epoxide (169) to the quinone (163). At the time this seemed reasonable since it is known that when

triphenylphosphine is reacted with α-bromoketones i.e. (173), reaction may occur at the oxygen atom to expel the bromide ion and form the corresponding olefin (174).[121] If, in the present case, the triphenylphosphine was indeed catalysing the rearrangement, then attack by this reagent might be expected to take place at a carbonyl oxygen atom to generate the anion (175) as depicted in Scheme 14. A molecular rearrangement similar to that postulated in Scheme 13 could generate carbanion (176) (not necessarily considered a discrete intermediate) which could rearrange to quinone (163) by expulsion of the triphenylphosphine. After completion of this work a more detailed study was undertaken to establish the function, if any, of triphenylphosphine in the isomerisation of epoxide (169) to quinone (163) and is discussed at a later stage of this chapter.



X = Ph_3P

SCHEME 14

Thus far it had been mentioned that the endo-epoxide (169) and not the exo-isomer (152) rearranged to the quinone (163) upon treatment with triphenylphosphine in ethanol under reflux. In order to assign chemical shifts unambiguously to the various protons of the endo- and exo-epoxides, quinone (125) was epoxidised with alkaline hydrogen peroxide to give a mixture of the exo- and endo-epoxides (152) and (169) in the ratio of 57:43 respectively. The chelating agent $Eu(FOD)_3$ [122] was then added to this mixture of epoxides in deuterochloroform in increasing amounts and the relative shifts of the various peaks were measured by n.m.r. spectroscopy. The results are summarised in Table 1.

TABLE 1

Protons	Quinone (125)	Epoxides τ		Relative shifts after $Eu(FOD)_3$ was added	
	τ	Endo (169)	Exo (152)	Endo	Exo
Olefinic	2.95	3.23	3.70	1.9	1
Bridgehead	6.20	6.81	6.64	3.2	2.8
Cyclopropyl	9.34	9.20/9.65	9.48	0.7/0.3	1.1

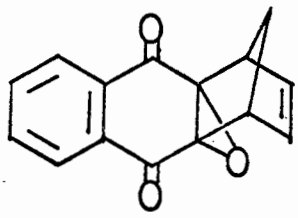
The relative shifts induced by $Eu(FOD)_3$ showed that the olefinic protons resonating at 3.23τ were due to the endo-isomer (169) since the downfield shift of these protons is roughly twice as much as in the exo case implying that the oxygen atom of the former epoxide is in closer proximity to the olefinic protons than in the latter case. Furthermore

the cyclopropyl protons in the exo-epoxide had a downfield shift of 1.6 times as much compared to the endo case where the protons appeared as two sets of triplets at 9.20 and 9.65τ (J = 8Hz). It should also be noted that the signal due to the cyclopropyl group of the endo-epoxide appeared as two sets of triplets in the original reaction mixture prior to addition of $Eu(FOD)_3$ and did not undergo any change other than becoming shifted. In the case of the exo-epoxide the cyclopropyl protons appeared as a single peak which could imply that the $Eu(FOD)_3$ reagent was significantly complexing with the carbonyl oxygen atoms as well as with the epoxide oxygen atom. Hence it was simple to observe which isomer rearranged during the isomerisation by noting which of the signals disappeared from the mixture of epoxides by n.m.r. spectroscopy.

At this stage it seemed to be a reasonable supposition to anticipate that extension of the rearrangement reaction to include the endo-epoxide (177), which also had a built in bicyclo [2.2.1] system, would be possible. Again it was imperative to be able to unambiguously assign chemical shifts to the protons of both the exo- and endo-isomers (178) and (177) * since both these isomers are produced when quinone (70) is epoxidised with alkaline hydrogen peroxide. Hence once the exo- and endo-isomers (178) and (177) were able to be identified by n.m.r. spectroscopy, it would clarify the position regarding which of the two isomers underwent isomerisation when treated with triphenylphosphine. This would add credence to the mechanism as postulated in Scheme 14 if it was found

*exo with respect to the bicyclo [2.2.1] system.

that only the endo-isomer (177) underwent the isomerisation. With this in mind the exo-epoxides (179) and (180) were prepared by treatment of the corresponding quinone (70) and the known dimethyl ester of bicyclo [2.2.1] heptadiene with m-chloroperbenzoic acid in methylene dichloride. These epoxides were synthesised in order to study their respective n.m.r. spectra with special reference to the chemical shifts and multiplicity of the syn and anti protons of the methano bridges.



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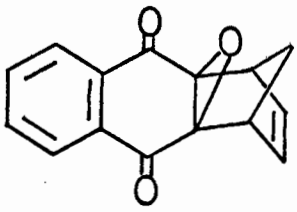

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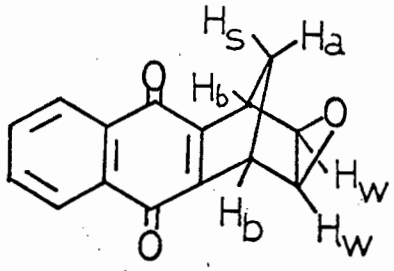

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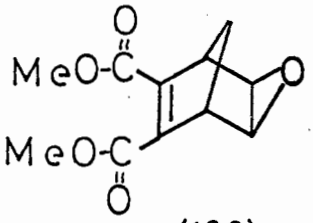
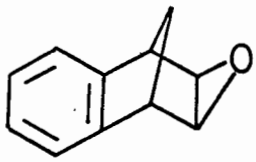


(180)



(181)

The n.m.r. spectrum of the exo-epoxide (179) (see fig. 4) showed the syn proton H_s to be strongly shielded (8.38τ) relative to the anti proton H_a which resonated at 7.99τ. The multiplicity of the signal due to the anti proton H_a appeared as triplets of a doublet arising from geminal coupling with H_s (J_{as} = 9Hz) and vicinal coupling

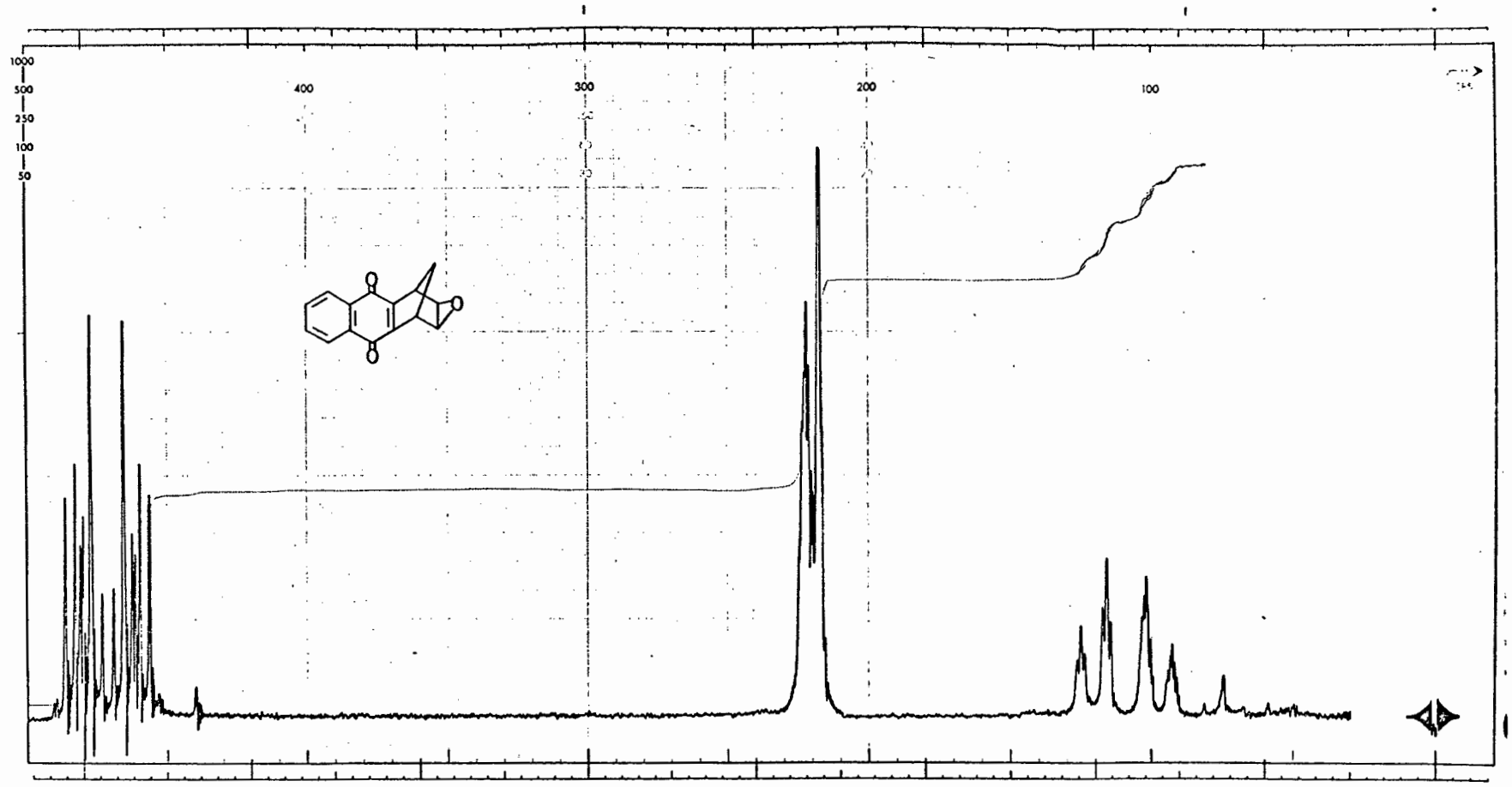


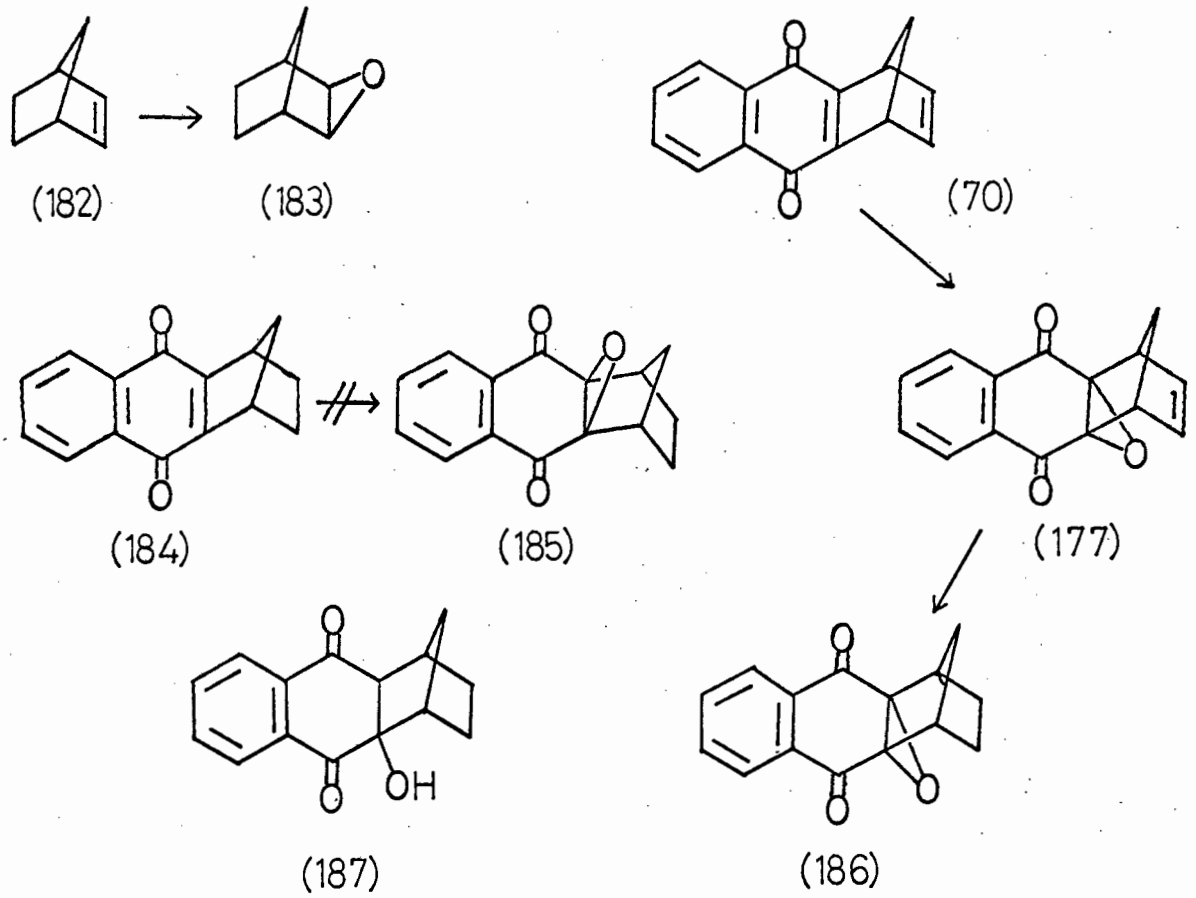
fig. 4

with H_b (J_{ab} = 1.5Hz). The multiplicity of the signal due to the syn proton H_s was analogous to H_a as might be anticipated, but in addition showed "W" coupling [70, 123] with H_w (J_{sw} = 0.5Hz). A very similar pattern for the methano protons of epoxide (180) was also noted. These spectra bore a very close resemblance to the similarly related exo-epoxide (181). [124] The ease with which the exo- and endo-epoxides of the systems (179), (180) and (181) may be distinguished from one another is by virtue of the large difference in the chemical shifts of the syn and anti protons. A reason for this difference may be due to the fact that the syn proton lies above the plane formed by the epoxide ring and will thus be shielded by the anisotropic effect of the ring current generated in the epoxide ring. [125, 126] The anti protons are located in positions where the ring current can not exert any marked effect and are consequently not shielded to any large extent.

Brown et al. [127, 128] have shown that the rate for exo epoxidation, k_{exo}, of norbornene (182) with m-chloroperbenzoic acid is 100 - 200 times as much as k_{endo} and consequently the exo-isomer (183) is produced in an almost quantitative yield. This preference for exo over endo attack may be accounted for by: (a) employing simple steric considerations for the U-shaped molecule which has a relatively open exo face and a hindered endo face [129] and (b) the fact that torsional strain favours exo over endo attack. [130] By analogy with the norbornene

epoxidation, quinone (184) should be expected to give the exo-epoxide (185) upon epoxidation via a concerted process. It was then reasoned that epoxidation of quinone (70) would yield a mixture of exo and endo epoxides from which the endo-epoxide (177) or exo-epoxide (178) could be purified by fractional crystallisation or chromatographic separation. In the present case the endo-epoxide (177) was isolated by crystallisation in 90% purity contaminated by 10% of the exo-epoxide (178) although this was not known at the time. Reduction of the olefinic bond of epoxide (177) under carefully controlled conditions should yield the endo-epoxide (186) as shown in Scheme 15. Comparison of both the n.m.r. and IR spectra of the two epoxides (185) and (186) would establish their relative steriochemistries and thus allow unambiguous assignment of the chemical shifts to the protons in the mixture of epoxides (177) and (178).

Epoxidation of the two quinones (70) and (184) proceeded smoothly. However catalytic hydrogenation of the epoxide (177) proved to be less straightforward since in protic solvents like ethanol quinone (184) was isolated. This most likely arose from reductive cleavage of the epoxide ring producing the diketo-alcohol (187) which rapidly lost water to produce the quinone (184). Reduction in an aprotic solvent such as anhydrous benzene proved much more successful and the fairly strained olefinic bond of epoxide (177) was reduced in preference to the alternative reductive cleavage of the epoxide ring. After



SCHEME 15

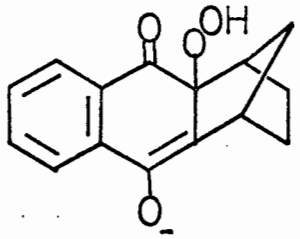
hydrogenation the reaction mixture was chromatographed to yield the quinone (184) and the endo-epoxide (186). Comparison of the IR spectra appeared to indicate no difference between epoxides (185) and (186). The n.m.r. spectra were also practically identical. Unfortunately the spectra were not well enough defined in the 8τ region to allow interpretation since the methylene protons appeared as a complex multiplet. Double irradiation of the bridgehead methine protons at 6.72τ for epoxide

(185) did not alter the multiplet due to the methylene protons much and no major peaks due to the *syn* and *anti* protons were observed. These results indicated that under the reaction conditions employed epoxidation of quinone (184) had in effect produced the *endo*-epoxide (186) and not the *exo*-isomer (185) that was initially expected. Unfortunately no mixed m.p. could be performed since the *endo*-epoxide (186) contained traces of the *exo*-isomer (185) and could not be obtained in a pure isomeric state.

Failure to effect *exo* epoxidation on the quinone (184) may be rationalised in terms of the major difference in the mechanism operating under the conditions of epoxidation *viz*. alkaline hydrogen peroxide. These conditions are necessary since the quinone double bond, being electron deficient, is quite uneffected by electrophilic epoxidising reagents *e.g.* m-chloroperbenzoic acid and peracetic acid. It has been established that when epoxidation proceeds *via* a concerted process, as with m-chloroperbenzoic acid, the steriochemistry of addition is determined by steric effects whereas when epoxidation proceeds *via* a non-concerted process involving intermediate stages, the mode of addition is not sterically controlled. [127, 128]

As previously mentioned, epoxidation of the quinone (184) was effected with alkaline hydrogen peroxide where the HO_2^- was the reactive species. Epoxidation occurred in this instance *via* a non-concerted process which

most likely involved the intermediate enolate anion (187) and consequently one would not anticipate formation of the exo-epoxide (185) but the endo-isomer (186).

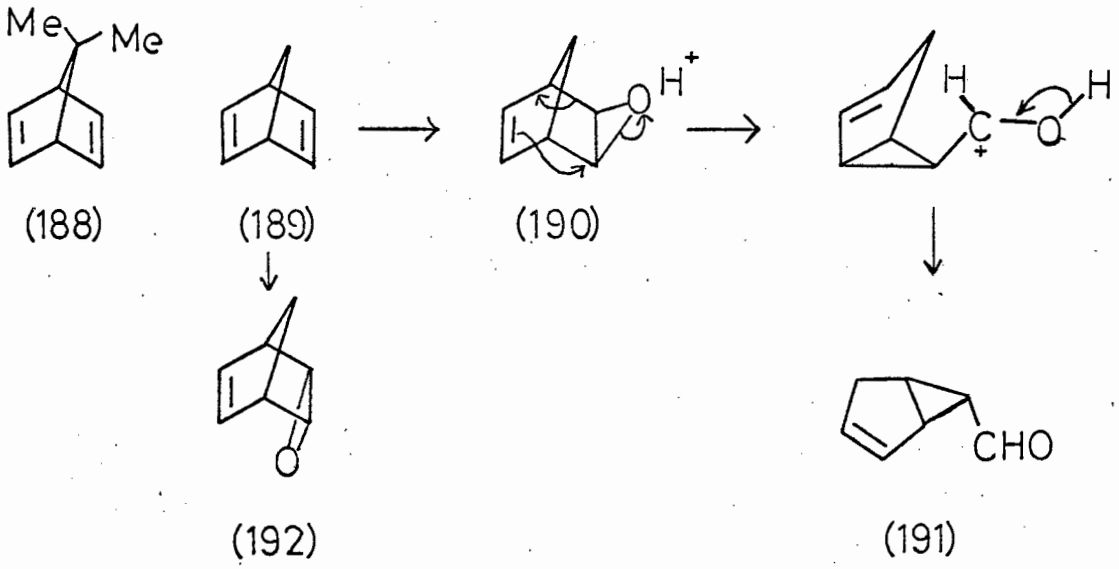


(187)

In this regard it has been shown that oxymercuration and free radical reactions with apobornene (188) proceeded with formation of the exo adducts in yields of 100% and 95% respectively.[127] Thus it may be concluded that epoxidation of quinone (184) in alkaline hydrogen peroxide proceeded in a non-concerted manner giving the endo adduct (186) as by far the major isomeric product which has been varified by comparison of its spectral properties with (186) prepared via a different route. It was not possible to determine by n.m.r. whether there was any of the exo-isomer (185) present.

Extension of this concept, i.e. concerted and non-concerted processess of epoxidation, to include systems such as norbornadiene (189) was inadvertantly undertaken by Meinwald et al.[131] who treated the diene (189) with peracetic acid in order to obtain the exo-epoxide (190). Under these reaction conditions the bicyclo-endo-carboxaldehyde (191) was

obtained as the only product. It was postulated however that the exo-epoxide (190) did form but that it underwent an acid catalysed rearrangement to produce the aldehyde (191). The exo-epoxide (190) was later actually isolated and its structure was proved unambiguously. [132] Other workers [133] have managed to isolate the endo-epoxide (192) of norbornadiene in low yield in addition to the carboxaldehyde (191) by employing different reaction conditions i.e. alkaline hydrogen peroxide in acetonitrile. This may not be entirely unexpected since examples of endo addition by dibromocarbenes to norbornadiene are known. [134] Furthermore it has been suggested that the exo-epoxide (190) underwent preferential rearrangement to the aldehyde (191) leaving the isomeric epoxide (192) unchanged. [132]



Final proof as to the correct assignments of the various protons to the mixture of endo- and exo-epoxides (177) and (178) was derived from n.m.r. studies by noting the relative shifts of the methylene protons in the methano bridges of the epoxides upon addition of the reagent $Eu(FOD)_3$ to deuterochloroform solutions of the mixtures. The results are summarised in Table 2.

TABLE 2

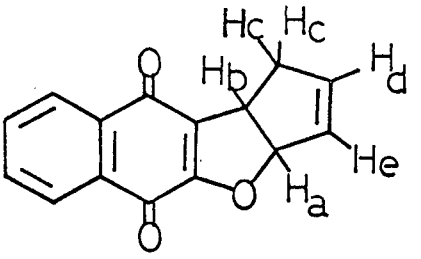
Protons	Quinone (70)	Epoxides τ		Relative shifts induced by $Eu(FOD)_3$	
	τ	Exo (178)	Endo (177)	Exo	Endo
Olefinic	3.00	3.75	3.30	1.0	1.5
Bridgehead	5.70	6.18	6.34	2.9	2.0
Methano	7.62	7.80	8.18/8.34	2.9/0.6	1.3/0.9

From a comparison of the n.m.r. spectra it seemed likely that the olefinic protons resonating at 3.75 τ were due to the exo-isomer since in the endo case these protons were deshielded about 1.5 times as much, as might be anticipated from the proximity of these protons to the oxygen atom of the epoxide ring which complexed with the reagent $Eu(FOD)_3$. An even more striking feature for this assignment is found when considering the shifts undergone by the methano protons. The signal due to the methano protons of the exo-epoxide (178) appeared as a triplet at 7.80τ ($J = 2Hz$). Upon addition of the reagent $Eu(FOD)_3$, this signal was split

into a pair of doublets (J = 9Hz) the relative shifts being 2.9 and 0.6 from the original position of the triplet. This clearly implied that the signal must be due to the exo epoxide methano protons. The methano protons of the endo epoxide appeared as multiplets of doublets at 8.18 and 8.34τ. Upon addition of the reagent $Eu(FOD)_3$ no change in the multiplicity of the signal nor the shape occurred, only a relative shift of the centres of the two sets of signals. These assignments are consistant with the relative integration of the peaks assigned to the mixture of endo and exo epoxides that were produced in yields of 77% and 23% respectively upon epoxidation of quinone (70) with alkaline hydrogen peroxide.

Investigations were then directed towards extending the scope of the isomerisation of epoxide (169) to include the epoxide (177). Heating a mixture of the exo- and endo-epoxides (178) and (177) in ethanol in the presence of triphenylphosphine caused a rapid change in colour of the reaction mixture from colourless to purple. The starting materials were isolated by a column chromatographic separation from a yellow component and were again heated under reflux and again chromatographed. The yellow fractions from the numerous separations were combined to give after re-crystallisation a 30% yield of purified material which was shown to be the cyclopentafuranonaphthoquinone (193).

The structure of quinone (193) followed from its elemental analysis and its spectral characteristics. The IR spectrum showed the quinone carbonyl stretches at 1680 and 1649 cm^{-1}. The UV spectrum, which bore



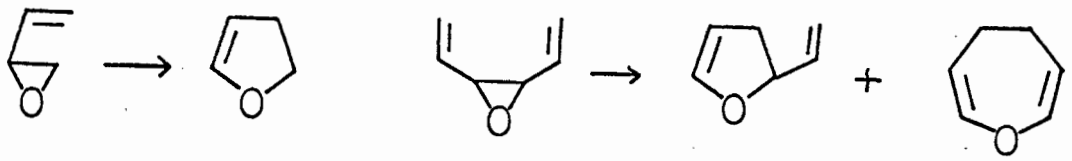
(193)

a close similarity to the analogous quinone (163), had $\lambda_{max.}$ at 391, 338, 286 and 252 nm. The n.m.r. spectrum showed the aromatic protons as multiplets at 1.98 and 2.33τ. The methine proton H_a and vinyl protons H_d and H_e appeared as a multiplet at 3.96τ while H_b appeared as a multiplet at 5.88τ. The methylene protons H_c appeared as a multiplet at 7.17τ.

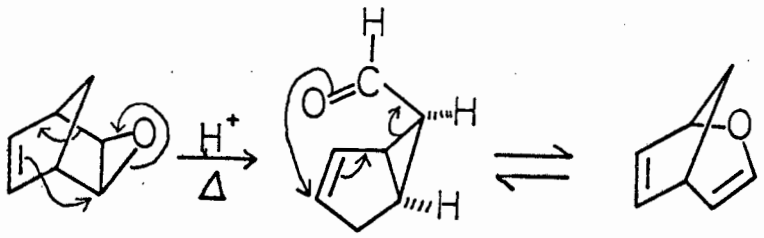
In separate experiments known relative amounts (by n.m.r. spectroscopy) of mixtures of the exo- and endo-epoxides (178) and (177) were subjected to the conditions of rearrangement for various lengths of time of up to 1 hr. The mixtures of epoxides isolated from the yellow component by column chromatography after reaction, were studied by n.m.r. spectroscopy to establish which isomer underwent the rearrangement. The evidence overwhelming indicated that the endo-isomer (177) underwent rearrangement and that the exo-isomer (178) was uneffected. Unfortunately no isomerically pure exo isomer could be isolated but together with the previous findings it was felt that there was little doubt that it was indeed only the endo isomer which underwent the rearrangement under the particular

set of conditions mentioned. It was also shown experimentally that the quinone (193) rapidly underwent decomposition when treated with triphenylphosphine in ethanol under reflux which would account for the low yield of quinone (193) isolated.

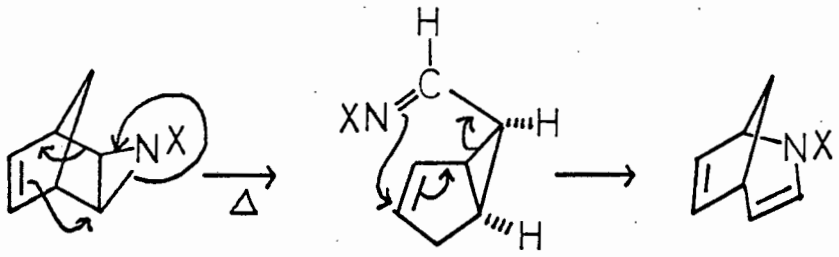
At this stage it is emphasised that all discussions pertaining to the mode by which the epoxide (169) undergoes isomerisation to yield quinone (163) were presented in a strictly chronological order. During the writing of this thesis it was decided to establish the precise function which the triphenylphosphine played in the rearrangement and to determine whether or not it was necessary for the rearrangement. Vinyl epoxides have been shown to thermally undergo 1,3-sigmatropic shifts to produce in the case of (194) the dihydrofuran (195) [135] in much the same way as the divinyl epoxide (196) produced derivatives such as (197) and (198). [136] Ray and Drieding [137] have shown that an equilibrium was formed between the aldehyde (191) and the cyclic ether (199) when the exo-epoxide (190) was treated with a catalytic amount of acid while Grigg and Shelton [138] have shown that this may be achieved thermally in a base washed apparatus. An analogous thermal rearrangement of the nitrogen analogue (200) to (201) has also been reported. [139] These rearrangements may be related to the Cope or Claisen type since similar equilibria are known to be set up by systems such as (202) [140] and (203). [141]



(194) (195) (196) (197) (198)



(190) (191) (199)



(200) (201) X=CN, SO_2Ph

(202) (203)

In order to establish whether the triphenylphosphine was essential in the rearrangement, two parallel sets of experiments were conducted. In one flask a mixture of the endo- and exo-epoxides (169) and (152) was heated in the dark under reflux in ethanol for 2.5 hr after which the reaction mixture was chromatographed. In this way it was shown that a 97% conversion of endo-epoxide (169) to quinone (163) had been effected, based on unrecovered starting material. In an analogous experiment carried out under the same conditions, and in this case in the presence of triphenylphosphine, the endo-epoxide (169) was converted in 80% yield to the quinone (163) again based on unrecovered starting material. The lower yield in the latter case was due to the reaction between quinone (163) and triphenylphosphine which causes it to decompose. It thus appears that triphenylphosphine does not catalyse the isomerisation of epoxide (169) to quinone (163) and in fact gives a poorer conversion than by heating under reflux with ethanol.

Next the role of the solvent was investigated and it was found that when the mixture of exo- and endo-epoxides (152) and (169) was heated in benzene in the dark for 10 hr only a slight degree of isomerisation occurred. In an analogous experiment conducted under the same conditions, but in the presence of triphenylphosphine, it was shown that no improvement in the conversion of epoxide (169) to quinone (163) had occurred again substantiating the fact that this reagent was not necessary for the isomerisation observed.

At this stage it appears to be questionable as to whether the isomerisation is entirely thermally induced or not. Experimental evidence adduced thus far has indicated that heating a mixture of the exo- and endo-epoxides (152) and (169) in ethanol under reflux for 3 hr caused a quantitative conversion of the endo-epoxide (169) into the quinone (163) whereas when a similar mixture was heated in benzene under reflux for 10 hr only a small degree of conversion occurred. Since both solvents have similar boiling points and since the one is polar relative to the other it is tentatively felt that the isomerisation is initiated by a nucleophilic species such as ethanol which could cause ring opening of the epoxide ring to produce the quinone (163) as depicted in Scheme 13.

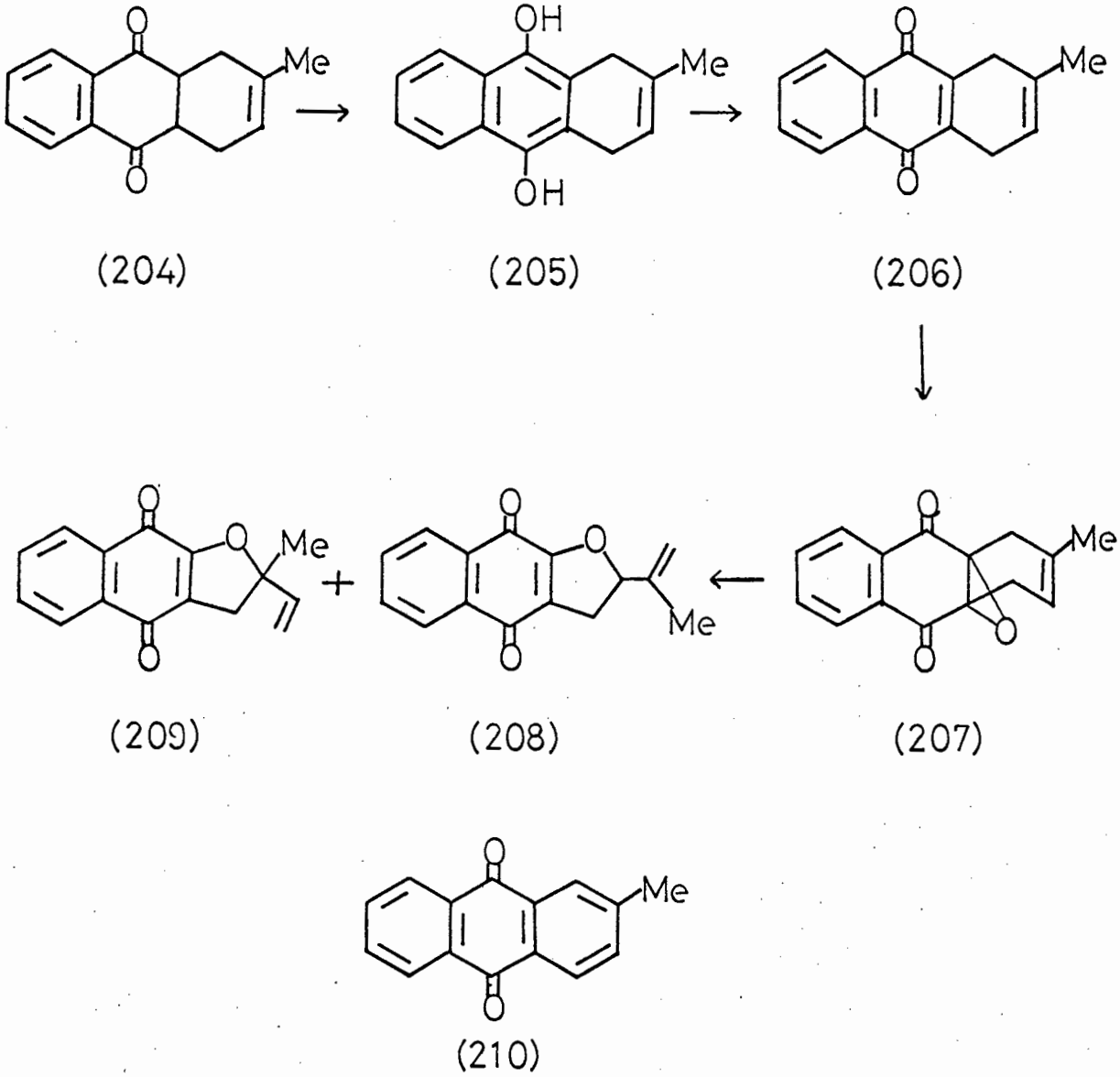
The reason for conducting these experiments in the dark arises from the fact that it was shown in these laboratories that sunlight was able to convert the endo-epoxide (169) into quinone (163) quite rapidly in benzene. When a mixture of the exo- and endo-epoxides (152) and (169) in benzene were allowed to stand in sunlight for 8 hr and then chromatographed, it was shown that the endo-epoxide (169) was converted in 70% yield into the quinone (163) based on unrecovered epoxide (169). This facile photoisomerisation is presently being investigated.

The success that had been achieved in extending the rearrangement of the epoxide (169) to a second bicyclo[2.2.1] epoxide (177), prompted investigation into the less closely related epoxide (207) since the re-

arrangement seemed to provide an attractive route to the as yet unsynthesised α-isopropenyl-dihydronaphthofuranoquinone (208) which has to the time of writing only been isolated from natural sources.[142] It seemed reasonable to expect that heating the epoxide (207), which it was hoped, could be prepared by epoxidation of quinone (206), in ethanol would lead to a similar type of rearrangement, as was previously encountered with the bicyclo[2.2.1] epoxides (169) and (177), producing the desired quinone (208) as shown in Scheme 16. It was fully appreciated that, should the rearrangement occur, a second isomer (209) might also be obtained.

Initial attempts designed to effect enolisation of the diketo-adduct (204) with methanolic base to the quinol (205) gave quantitative yields of 2-methylanthroquinone (210). This has been attributed to the lability of the methylene protons of either (205) or (206), which could both be present in the reaction mixture, towards base. Removal of two of these methylene protons from positions 1 and 4 would cause aromatisation of the six-membered ring yielding the thermodynamically more stable quinone (210). When the adduct (204) was treated with base for shorter periods of time (30 seconds) and the reaction then stopped by neutralisation, the quinone (206) was obtained in 34% yield, the rest of the product being the anthroquinone (210). Various methods of effecting epoxidation of quinone (206), including sodium hypochlorite in aqueous dioxan,[143] t-butylhydroperoxide with Triton-B as catalyst,[144] t-butylhydroperoxide

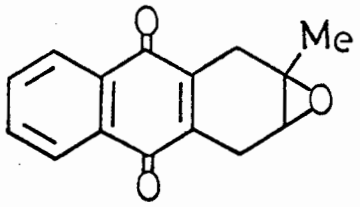
with molybdenum trioxide as catalyst, [145] and various methods employed by Payne [146, 147] and Newman [148] either gave only the anthroquinone (210) or led to decomposition or in some cases to the recovery of starting



SCHEME 16

material. When the solvent was changed to acetonitrile,[149] the situation remained the same, quinone (210) being isolated in quantitative yield. It was obvious from these results that the use of base as a catalyst in effecting the epoxidation of the quinone (206) caused aromatisation of the six-membered ring and hence in order to achieve epoxidation some other method would have to be sought. The major problem of the situation was the electron deficiency of the quinone double bond which naturally influenced the choice of epoxidising agent and the nature of the reaction conditions. Treatment of quinone (206) with peracetic acid according to the method of Koratch et al.[150] or with peracetamic acid according to the method of Lumb[133] failed to cause epoxidation. This was anticipated since these methods involved electrophilic epoxidations and attack would consequently be unlikely to occur at the electron deficient quinone double bond but instead at the olefinic bond. Contrary to expectations this did not occur. However treatment of quinone (206) with m-chloroperbenzoic acid gave a quantitative yield of the epoxide (211). It was considered to be of interest to ascertain whether the quinone double bond of this epoxide (211) could be epoxidised. However, treatment of this quinone-epoxide (211) with alkaline hydrogen peroxide produced a quantitative yield of quinone (210). Even treatment of (211) with peracetic acid under reflux for 72 hr produced a quantitative yield of the anthroquinone (210). Furthermore treatment of the epoxide (212) with methanolic alkali for short periods produced only a 35% yield of

the quinone-epoxide (211) with the remainder of the starting material being converted into the anthroquinone (210).



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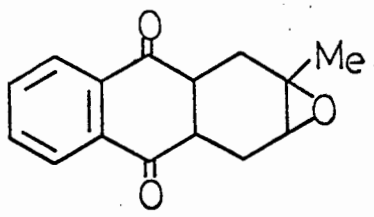
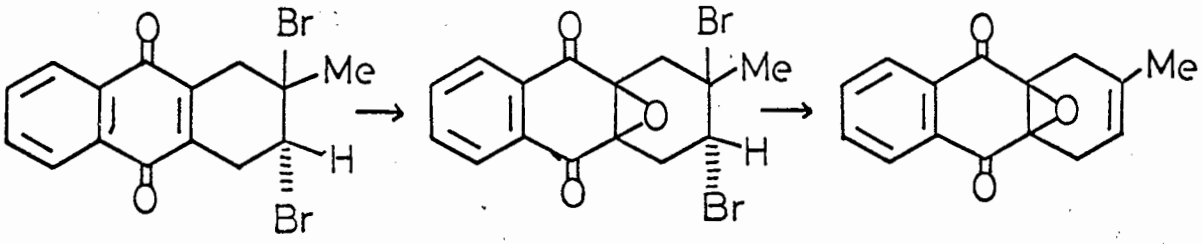


(212)

Thus there appeared to be a very strong driving force towards aromatisation of the six-membered ring of (211) even though an epoxide ring had been introduced with the specific purpose of inhibiting aromatisation. In a further experiment it was envisaged that bromination of the olefinic bond of quinone (206) would yield the trans-dibromoquinone (213) which on epoxidation could yield epoxide (214). Removal of the bromide atoms with zinc dust in ether [79] could then generate the desired epoxide (207) as shown in Scheme 17.



(213) (214) (207)

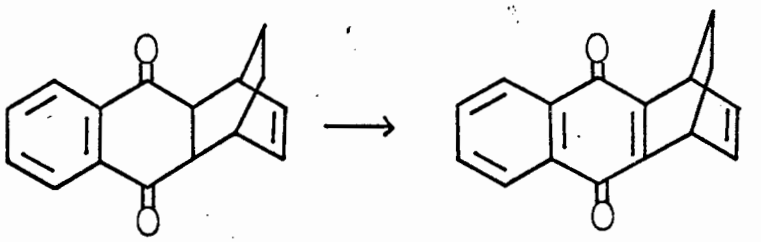
SCHEME 17

Bromination of the olefinic bond of quinone (206) proceeded smoothly and gave a quantitative yield of the trans-dibromoquinone (213). However attempted epoxidation of this quinone under alkaline conditions led to quantitative conversion into the anthroquinone (210) whereas when neutral or acidic conditions were employed no reaction occurred, the starting materials being isolated unchanged. The experimental evidence adduced so far suggested that aromatisation of the six-membered ring of the compounds studied could not be inhibited under basic conditions.

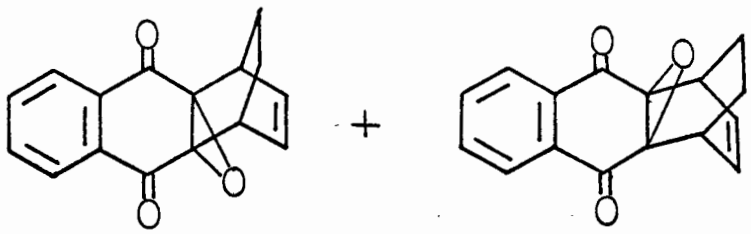
Thus far it had been shown that the epoxide rearrangement took place readily in bicyclo[2.2.1] epoxide systems. Generalisation of this rearrangement to include the bicyclo[2.2.2] epoxide systems was next attempted in order to establish whether or not it would occur with these systems. Treatment of adduct (215) with methanolic alkali for a short period yielded the quinone (216) together with some of the exo-epoxide (217)* which most likely arose from autoxidation of the intermediate dianion (see Scheme 12). Epoxidation of the quinone (216) with alkaline hydrogen peroxide gave a mixture of the endo- and exo-epoxides (218) and (217) in relative yields of 5% and 95% respectively as determined by n.m.r. That the exo-epoxide was the major product was demonstrated by adding the reagent $Eu(FOD)_3$ and comparing the change in the multiplicity of the ethano bridge protons by n.m.r. spectroscopy. Unfortunately the relative shifts induced by the reagent $Eu(FOD)_3$ on both exo and endo

*exo with respect to the bicyclo[2.2.2]system

epoxides could not be ascertained due to the very small quantity of the endo isomer and due to the fact that the ethano and bridgehead protons of the two epoxides had the same chemical shifts. The results are presented in Table 3. The olefinic protons of the endo-epoxide (218) resonate at 3.46τ as a triplet (J = 4Hz).



(215) (216)



(218) (217)

TABLE 3

Protons	Quinone 216 τ	Epoxide (217) τ	Relative shifts induced after addition of $Eu(FOD)_3$
Olefinic	3.55	3.96	1
Bridgehead	5.43	6.15	3.3
Ethano	8.52	8.54	2.7/0.7

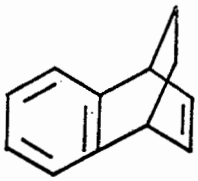
As can be seen from the table the protons of the ethano bridge underwent the expected shift. In the epoxide these methylene protons appeared as a single peak at 8.54τ. Upon addition of the euroshift reagent this single peak separated into a fairly well defined pair of doublets (J = 9Hz) the relative shifts of the doublets being 2.7 and 0.7. Coupling was also apparent between these methylene protons and the bridgehead methine protons. From the relative shifts of this pair of doublets compared to the olefinic proton shift it seemed clear enough that this could only have arisen in the case of the exo-epoxide (217). It is also worthy noting that the olefinic protons undergo an upfield shift on conversion of quinone (216) to the exo-epoxide (217), in line with similar shifts observed in the bicyclo[2.2.1] series.

The preference of exo over endo epoxidation of quinone (216) may again be explained in terms of the mechanism which apparently operated during addition. Whereas electrophilic epoxidation of bicyclo[2.2.2] systems

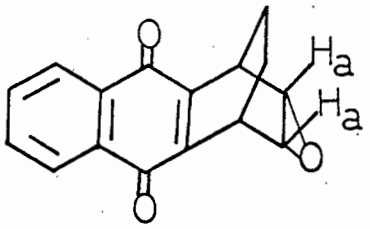
with perbenzoic acid gave only the endo epoxide in the case of (219), [151] a 1:1 mixture of endo and exo isomers was obtained with the benzobicyclo system (220). [152] In both these epoxidations a concerted mechanism is involved with addition being sterically controlled. [127, 128] These findings were substantiated by treatment of quinone (216) with m-chloroperbenzoic acid which, after recrystallisation, gave rise to a single isomer (as shown by n.m.r.) to which the endo structure (221) is tentatively assigned. The structure followed from its analysis and spectral characteristics. The IR spectrum showed the quinone carbonyl stretching frequency at 1665 cm^{-1}. The UV spectrum had $\lambda_{max.}$ 337, 271, 266, 250 and 245 nm which was not very different from the parent quinone (216) which had $\lambda_{max.}$ at 337, 269, 250, 245 and 241 nm. The n.m.r. spectrum showed the bridgehead methine protons as a multiplet at 6.02τ while the epoxide methine protons H_a appeared as a doublet of doublets at 6.58τ (J = 2Hz and 2Hz). The methylene protons of the ethano bridge appeared as two sets of multiplets of doublets at 8.20τ (2H) and 8.60τ (2H) and bore a close similarity to the methylene protons of adduct (215) which appeared as two sets of multiplets of doublets at 8.18τ and 8.58τ. The multiplets of the methylene protons in the ethano bridge of (221) have similar chemical shifts to those of the endo epoxide of (220), but differ substantially from those observed for the corresponding exo isomer. [124] Epoxidation of the quinone double bond in (216) only occurred in alkaline

media and thus via a non-concerted mechanism which is not controlled by steric requirements.[127, 128]

(219)

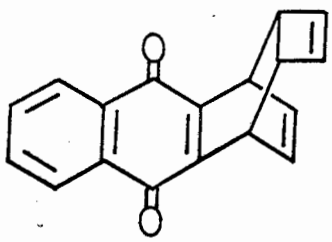


(220)

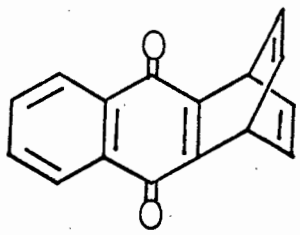


(221)

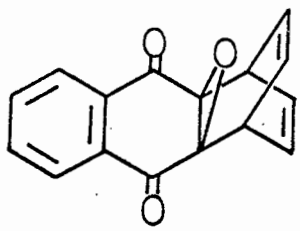
Failure for the exo-epoxide (217) to undergo rearrangement under reflux in ethanol may naturally be attributed to the absence of an olefinic bond in the immediate proximity of the epoxide oxygen atom (c.f. Scheme 13). A means to overcome this apparent hurdle would be to insert a double bond in the ethano bridge of compound (216) to give the symmetrical quinone (223). The steriochemistry of the epoxide (224) of this quinone would be favourable for rearrangement, since epoxidation from either side of the enedione system would give rise to the same epoxide. With this in mind various methods towards the synthesis of the naphthobarrelene-quinone molecule (223) were investigated.



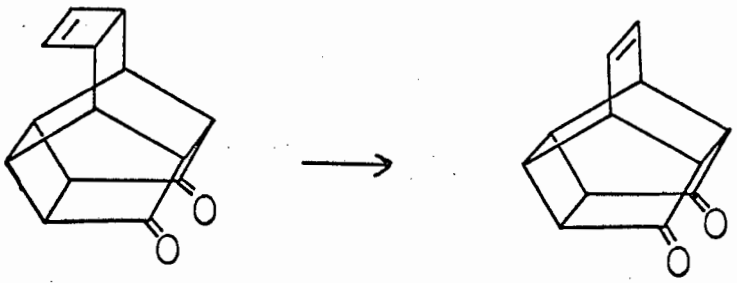
(222)



(223)



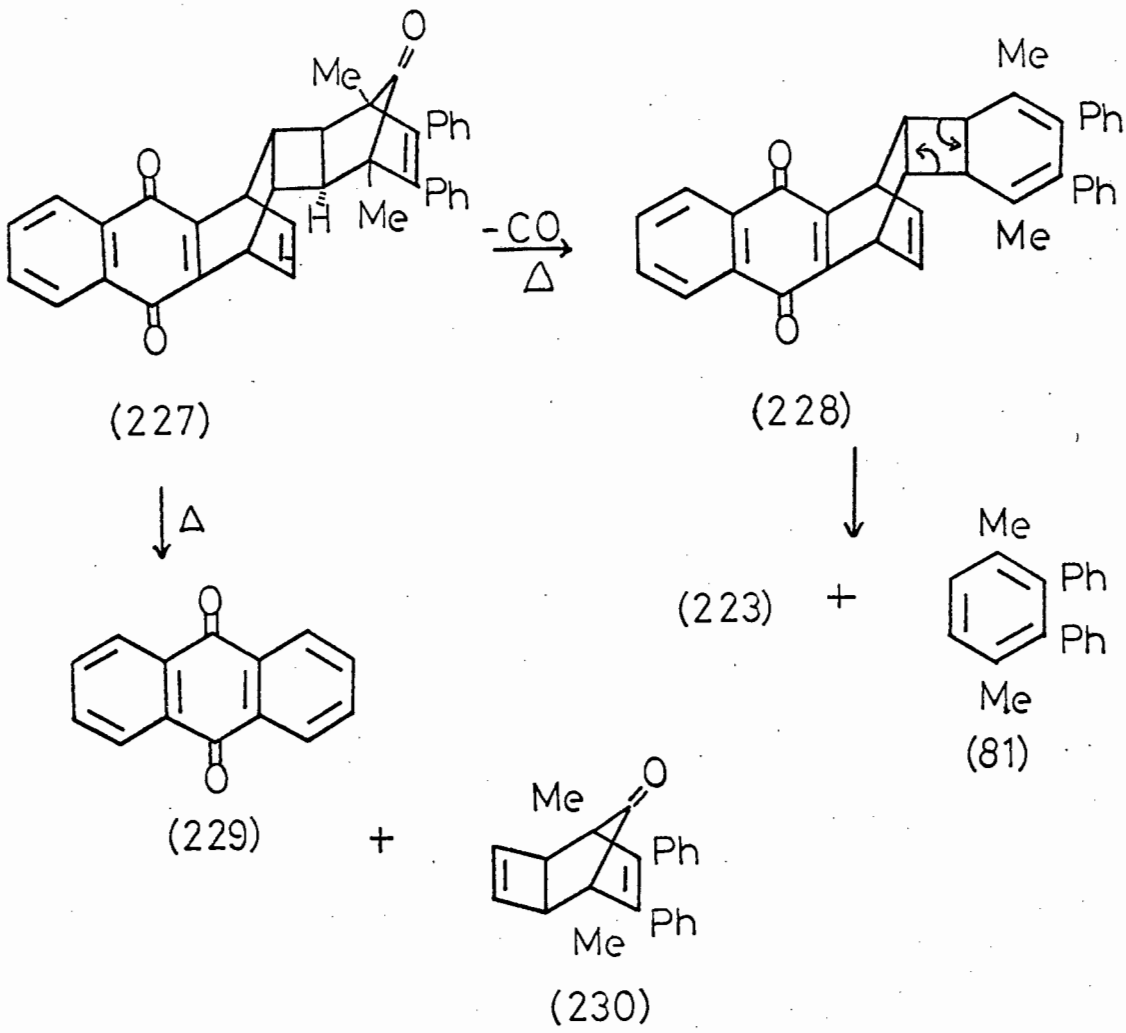
(224)



(225) (226)

It was considered appropriate in this instance to utilise quinone (222) as the starting material in order to prepare the barrelene quinone (223) since it seemed to involve removal of the ethylene bridge in the strained cyclobutene ring formally *via* a $\left[\pi^2_s + \pi^2_s\right]$ cycloreversion reaction. Initially the most convenient method for converting the cyclobutene ring into an olefin appeared to be the one used by Warrener *et al.*[75] who converted the cyclobutene (225) to the olefin (226) in high yield.

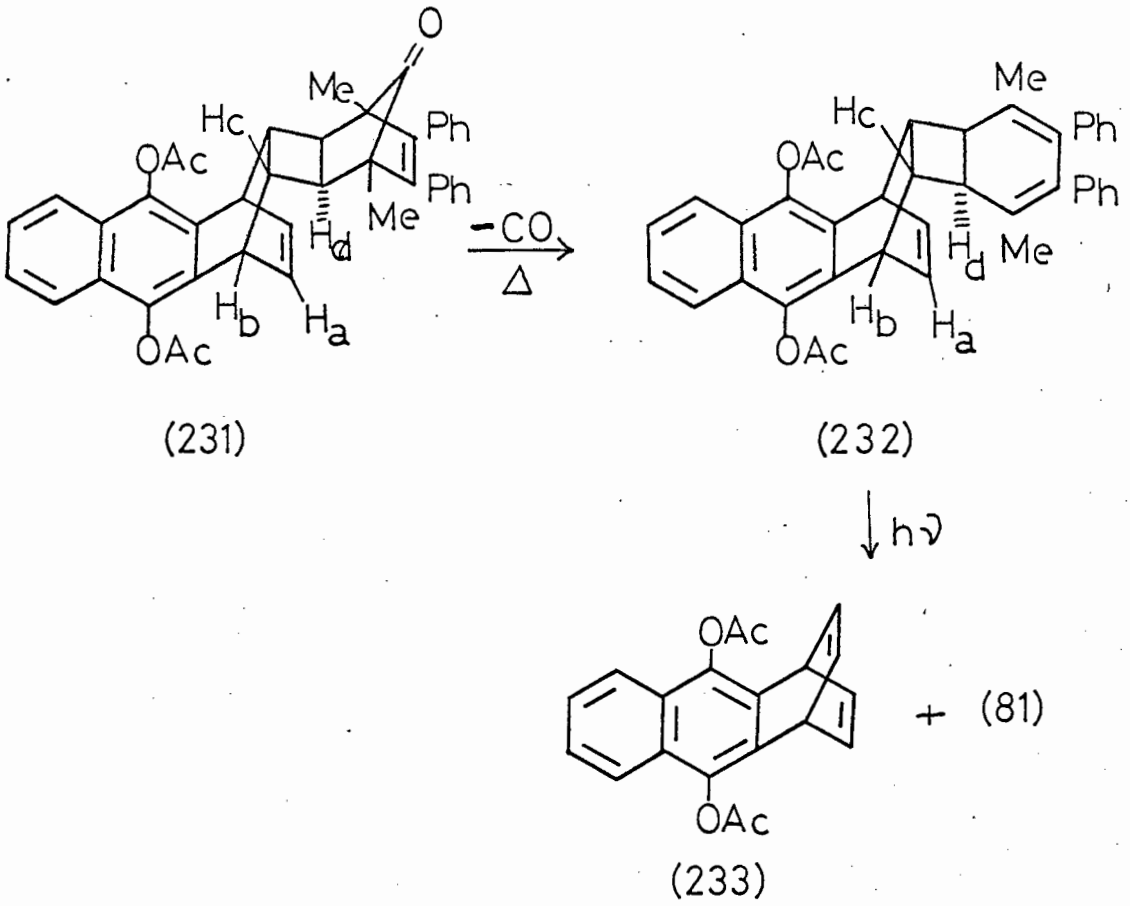
Reaction between quinone (222) and the cyclopentadienone (77) gave a quantitative yield of the adduct (227) which had the steriochemistry shown *i.e.* *trans* substitution about the cyclobutane ring and *exo* annelation of this cyclobutane to the [2.2.1] ring system which was also in line with the findings of Warrener *et al.*[153] It was then hoped that pyrolysis of the adduct would lead to cheletropic elimination of carbon monoxide to yield the triene (228) which under photolytic conditions might be able to undergo a photochemical $\left[\pi^2_s + \pi^2_s\right]$ cycloreversion reaction yielding the desired quinone (223) and the aromatic moiety (81) as shown in Scheme 18.



SCHEME 18

Pyrolysis of adduct (227) under an atmosphere of N_2 at 180 - 200° yielded two products in a 1:1 molar ratio. These products were shown to be anthroquinone (229) and the exo-tricyclononadiene (230) [67, 153] which also confirmed the steriochemistry of adduct (227). It would appear

that the tendency for the quinone nucleus to aromatise *via* the thermally allowed $\left[\pi^4_s + \pi^2_s\right]$ cycloreversion reaction is far greater than the formation of the triene (228) since presumably either the products formed by the former reaction are thermodynamically more stable or that the temperature at which the pyrolysis was conducted favoured the former reaction. However lower temperatures still gave the quinone (229) and ketone (230) as the only products isolated. Photolysis of adduct (227) in acetone led only to decomposition. It was thought that the quinone chromophore of the adduct might be interfering with the desired photolysis and consequently it was decided to irradiate the corresponding diacetate (231). However photolysis in acetone again led to decomposition whereas photolysis in benzene led to the isolation of the aromatic moiety (81) in 23% yield. On the other hand pyrolysis of the diacetate (231) yielded the triene (232) in low yield after a fairly difficult separation on a column. The structure of the triene (232) followed from its analysis and spectral characteristics. The n.m.r. spectra of the two diacetates (231) and (232) are summarised in Table 4. It was not possible to observe the disappearance of the ketonic stretching frequency in the IR spectra in going from (231) to (232) since the ester carbonyl stretching frequencies masked it in the IR spectrum of adduct (231).



SCHEME 19

TABLE 4

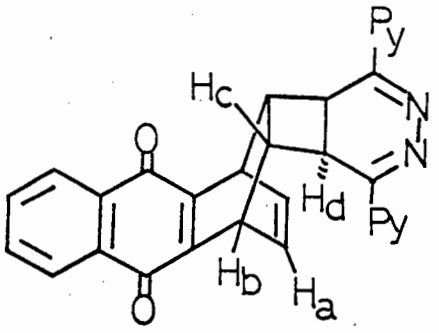
Protons	Adduct (231) τ	Adduct (232) τ
H_a	3.30	3.24
H_b	5.90	5.82
H_c	7.89	7.42
H_d	7.89	7.42
Methyl group	8.78	8.51

From the n.m.r. data it may be adduced that the bicyclo[2.2.1] ring system underwent cheletropic elimination of carbon monoxide to produce a diene system. This can be seen by the downfield shift of the methyl groups implying an alteration of the hybrisation of the ring carbon atom to which they were attached from sp^3 to sp^2. The cyclobutane ring protons H_c and H_d appeared as a single peak at 7.89τ in adduct (231) whereas as a single peak at 7.42τ in the triene (232).

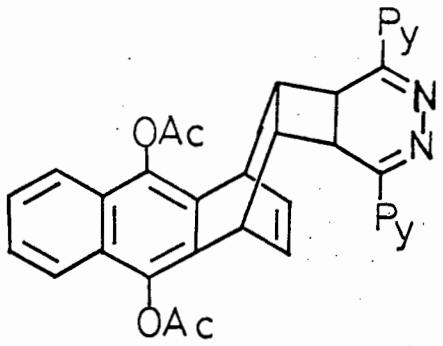
Photolysis of the triene (232) in benzene led to the isolation of the expected aromatic moiety (81) in 37% yield which was derived by a photochemically allowed $[\pi^2_s + \pi^2_s]$ cycloreversion reaction. However no barrelene type of product was isolated from the rest of the reaction mixture which appeared as an intractable tar. It seemed that there had been some conversion of the triene (232) into the barrelene analogue (233) but that under the photolytic conditions further decomposition and/or rearrangements had occurred which finds precedent in the literature.[154, 155, 156] Attention was then directed towards employing the s-tetrazine (137) as a possible means of converting the cyclobutene (222) into the olefin (223).

Reaction between the s-tetrazine (137) and the quinone (222) occurred readily to yield the expected adduct (234) with a trans steriochemistry about the cyclobutane ring. The structure of adduct (234) followed from its analysis and spectral characteristics. The UV spectrum had

$\lambda_{max.}$ at 334, 298, 265, 250 and 245 nm representative of the quinone chromophore while the IR spectrum showed the quinone carbonyl stretching frequency at 1663 cm^{-1}. The n.m.r. spectrum showed the olefinic protons H_a as a triplet at 3.15τ (J = 4Hz) while the bridgehead methine protons H_b appeared as a multiplet at 5.04τ. The allylic protons H_d of the cyclobutane ring appeared as a doublet at 6.60τ (J = 4Hz) while the protons H_c appeared as a multiplet at 7.70τ. Irradiation of the signal at 7.70τ caused the doublet at 6.60τ to collapse into a singlet and the multiplet 5.04τ simplified to a triplet (J = 4Hz).



(234)



(235)

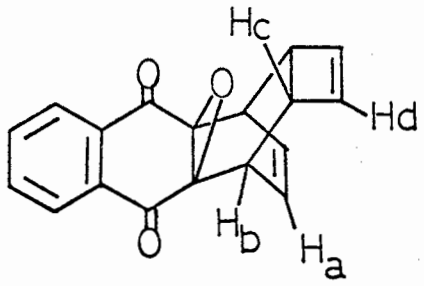
Py = 2′-pyridyl

Pyrolysis of the adduct (234) yielded anthroquinone (229) as expected via a thermally allowed $\left[\pi^4_s + \pi^2_s\right]$ cycloreversion reaction but no nitrogenous material could be isolated from the reaction products (c.f.

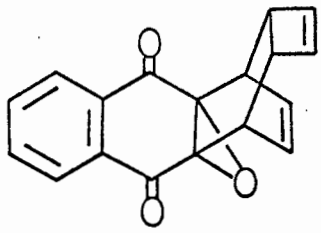
Scheme 18) presumably due to their rapid decomposition at the relatively high (200°) temperatures used for effecting pyrolysis. Photolysis of the diacetate (235) prepared by reductive acetylation of the quinone (234) led to the isolation of a white crystalline compound of unknown structure having the composition $C_{32}H_{24}N_4O_6$ with m.p. 266°. The acetate carbonyl stretching frequency was present at 1752 cm^{-1} in the IR spectrum together with two other rather strong bands at 1698 and 1690 cm^{-1}. When this photo adduct was hydrolysed with aqueous potassium hydroxide anthroquinone (229) was isolated in fair yield together with a yellow gum which could not be induced to crystallise and appeared to be polymeric.

Epoxidation of quinone (222) produced a mixture of the exo- and endo-epoxides (236) and (237)* in 93% and 7% yields respectively. Again it was hoped that the endo isomer could be purified in sufficient quantity to be tested for the thermally induced rearrangement reaction. However this was not possible since the two epoxides had the same solubility and thin layer properties that were investigated. The exo-epoxide (236) was shown to be the major product in the epoxidation of quinone (222) by the use of the reagent $Eu(FOD)_3$, with the induced relative shifts of various peaks being noted. The results are summarised in Table 5.

*Exo by analogy with the nomenclature used in the bicyclo[2.2.1] systems.



(236)



(237)

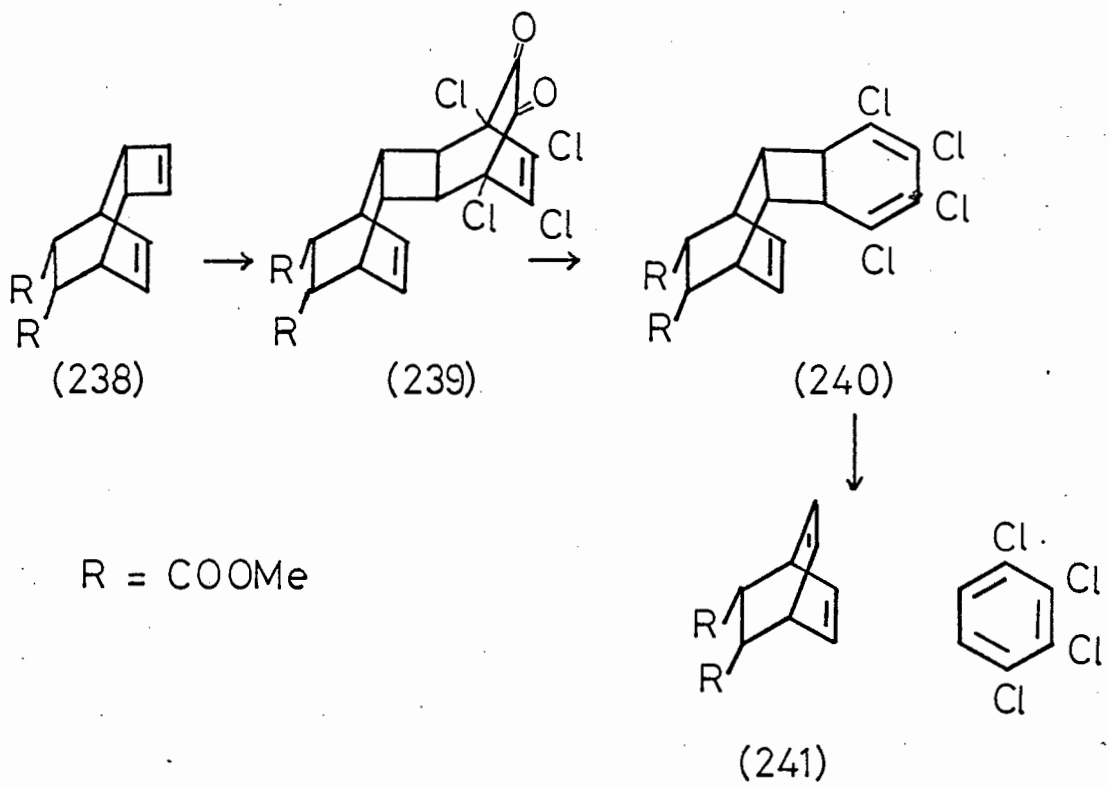
TABLE 5

Protons	Quinone (222) τ	Exo-epoxide (236) τ	Relative shifts induced by $Eu(FOD)_3$
H_a	3.82	4.21	8.0
H_b	5.62	6.12	26.0
H_c	7.32	7.15	22.0
H_d	3.89	4.08	1.0

From the table it can be seen that the H_c protons were shifted far more than either of the olefinic protons implying that the epoxide oxygen atom and the H_c protons are in closer proximity than the epoxide oxygen and the H_d or H_a protons. Furthermore the large shifts undergone by the bridgehead protons H_b seemed to indicate that the chelating euroshift reagent complexed significantly at the carbonyl oxygen atoms as well as to the epoxide oxygen atom.

Recently Warrener *et al.* [157] have reported the successful conversion

of the cyclobutene (238) to the dihydrobarrelene (241) by the photolysis of the intermediate α-diketone (239) formed by a Diels-Alder addition between (238) and o-chloroanil which displays a reverse electron demand in the $\left[\pi^4_s + \pi^2_s\right]$ cycloaddition reaction.[158] The triene (240) has been shown to be the intermediate however, and would correspond to the similarly related adducts (232), (234) and (235) all of which have been studied photochemically in these laboratories. Although there had been no success in the isolation of barrelene type compounds, evidence for their existance had been shown by the fact that isolation of the predicted aromatic moieties in certain cases had been possible (see Scheme 19).



Thus far the epoxide rearrangement has been shown to take place in the bicyclo [2.2.1] epoxide systems (169) and (177) where the steriochemistry of the epoxide rings had been shown to be endo with respect to the bicyclo [2.2.1] ring system. The present inaccessibility of the endo-epoxide (224) has precluded a possible extension of the rearrangement to this particular epoxide. At the time of writing, the epoxides (218) and (237) had been produced in very minor amounts as shown by n.m.r. spectroscopy of the mixtures of epoxides obtained in the epoxidation of quinones (216) and (222) respectively. It is felt that if the epoxides (218) and (237) could be obtained in workable amounts analogous rearrangements could well take place. Studies are presently being undertaken in this direction as well as investigations into the use of heteroatoms other than oxygen in the isomerisation.

EXPERIMENTAL

IIIa(i) Base catalysed enolisation of the adduct (123)

Sodium hydroxide (3 ml x 2 M) was added to a stirred solution of the adduct (2.0 g) in methanol (180 ml) at 35°. Stirring was continued at 35 - 40° for a further 2 hr and then the reaction mixture was neutralised. The solution was poured into water and extracted with chloroform. The dried ($MgSO_4$) extracts were evaporated to a yellow solid 1.95 g. Fractional recrystallisation from ethanol* yielded the r-4a,9a-epoxy-1,4,4a,9a-tetrahydro-cis-1,4-spirocyclopropylanthroquinone (152) as long white needles (1.30 g; 62%) m.p. 169 - 170°. [Found: C, 77.1; H, 4.5. $C_{17}H_{12}O_3$ requires C, 77.3; H, 4.6%]; $\lambda_{max.}$ 298, 258 and 228 nm (log ε 3.33, 3.60 and 4.56); $\nu_{max.}$ 1691, 1598 cm^{-1}; n.m.r. τ 2.04 (m, 2H), 2.28 (m, 2H), 3.78 (t, 2H, J 2 Hz), 6.70 (t, 2H, J 2 Hz), 9.49 (s, 4H).

*The yellow mother liquors were chromatographed over silica gel and eluted with benzene. The first fractions contained a mixture of the endo and exo epoxides (500 mg) while the yellow component eluted (58 mg) was shown to be the cyclopentafuranonaphthoquinone (163). Recrystallisation from ethanol afforded golden yellow plates m.p. 204° (dec.). [Found: C, 77.2; H, 4.6. $C_{17}H_{12}O_3$ requires C, 77.3; H,

4.6%]; $\lambda_{max.}$ 393, 327, 282 and 252 nm (log ε 3.07, 3.45, 4.20 and 4.39); $\nu_{max.}$ 1683, 1642, 1613, 1592 cm^{-1}; n.m.r. τ 1.94 (m, 2H), 2.33 (m, 2H), 3.78 (dxd, 1H, J 9.1 and 2.2 Hz), 4.10 (dxd, 1H, J 5.5 and 2.2 Hz), 4.38 (d, 1H, J 5.5 Hz), 6.02 (d, 1H, J 9.1 Hz), 8.78 (m, 2H), 9.18 (m, 2 Hz).

IIIa(ii) Hydrogenation of quinone (163)

The quinone (260 mg) was dissolved in ethanol (200 ml) containing the catalyst 10% Pd/C (15 mg) which had been prereduced, and the mixture shaken in an atmosphere of H_2. After 35 minutes 2 molar equivalents of H_2 had been absorbed. The solution was filtered and the initially colourless filtrate started to turn yellow. The solution was evaporated to dryness yielding a mass of yellow crystals interspersed with white ones. Benzene (80 ml) was added to this mixture and then freshly precipitated silver oxide (2.5 g) was added and the whole shaken for 1 hr, filtered and the filtrate evaporated to dryness yielding the quinone (168) quantitatively as tiny yellow needles (from ethanol) m.p. 130°. [Found: C, 76.5; H, 5.6. $C_{17}H_{14}O_3$ requires C, 76.7; H, 5.3%]; $\lambda_{max.}$ 395, 337, 287 and 252 nm (log ε 3.10, 3.47, 4.10 and 4.38); $\nu_{max.}$ 1683, 1644, 1613, 1592, 1572 cm^{-1}; n.m.r. τ 1.96 (m, 2H), 2.33 (m, 2H), 4.46 (m, 1H), 6.53 (d, 1H,

J 9.1 Hz), 7.84 (m, 4H), 8.80 - 9.50 (m, 4H).

Irradiation of the multiplet at 4.46τ caused the doublet at 6.53τ to collapse to a singlet while irradiation of the signals at 7.84τ simplified the multiplet at 4.46τ to a doublet (J=9.1Hz) leaving the doublet at 6.53τ unaffected. Irradiation of the doublet at 6.53τ caused the multiplet at 4.46τ to collapse to a doublet of doublets (J=11 and 7Hz).

IIIb(i) Reaction of quinone (125) with alkaline hydrogen peroxide

The quinone (240 mg) was dissolved in hot ethanol (6 ml) and the resulting solution heated with aqueous hydrogen peroxide [0.5 ml x 30% H_2O_2, water (2 ml) and Na_2CO_3 (60 mg)]. The reaction mixture was allowed to stand at room temperature for 0.5 hr and then poured into water (100 ml). A mixture of the endo- and exo-epoxide (169) and (152) was obtained in quantitative yield and shown by n.m.r. spectroscopy to consist of 43% of the endo and 57% of the exo isomer.

IIIb(ii) Conversion of the endo-epoxide (169) into the quinone (163)

A solution of the above mixture (400 mg) of endo and exo epoxides Section IIIb(i) and triphenylphosphine (400 mg) in ethanol (40 ml) were heated together under reflux for 20 hr and evaporated to dryness. The yellow brown solid was chromatographed over aluminium oxide and eluted with benzene/

petrol ether (9:1). Unreacted exo-epoxide (152) was eluted after the triphenylphosphine and amounted to 218 mg. The yellow band which followed contained the isomeric quinone (163) and was obtained in 100 mg yield which is equivalent to a 58% conversion based on the amount of endo epoxide present in the original mixture.

Similar conversions were attempted in benzene, toluene, o-xylene and butanol, the yields ranging from 60% conversion down to less than 1% for n-butanol. Attempted conversion in DMF led to extensive decomposition at 80° within 1 hr.

IIIb(iii) Quantitative evaluation of the conversion of the endo-epoxide (169) into the cyclopentafuranonaphthoquinone (163)

A mixture of the epoxides in the ratio of 60% endo and 40% exo (100 mg) was treated with triphenylphosphine for 2 hr in ethanol under reflux and the products separated by passing the crude reaction product through a column of silica gel and eluting with benzene. The mixture of epoxides eluted (65 mg) was shown by n.m.r. to comprise 60% exo and 40% endo. The amount of the isomeric quinone (163) isolated was 30 mg representing a 90% conversion factor.

IIIb(iv) Autoxidation of the quinol (124)

A solution of the quinol (200 mg) in ethanol (20 ml)

was treated with a 0.1 M solution of NaOH (10 ml) and the resulting black solution aerated until a permanent orange colour was obtained (0.75 hr). The solution was neutralised and diluted with water (100 ml) and extracted with chloroform. The dried ($MgSO_4$) extract was evaporated to a yellow solid and chromatographed over silica gel. Elution with benzene produced a mixture of the endo and exo epoxides in 90% yield in the ratio of 70% exo to 30% endo as shown by n.m.r. The rest of the reaction mixture appeared to be a red tar.

IIIc(i) Expoxidation of quinone (70) with alkaline hydrogen peroxide

30% Hydrogen peroxide (0.7 ml) in aqueous sodium carbonate (100 mg in 2.0 ml water) was added to a warm solution of the quinone (280 mg) in ethanol (15 ml) and allowed to stand at room temperature for 3 hr after which the reaction mixture was poured into water (200 ml) and extracted with chloroform. The dried ($MgSO_4$) extracts were evaporated to yield a white crystalline mass (300 mg) shown by n.m.r. to comprise 23% of the exo and 77% of the endo epoxide. Recrystallisation from methanol gave the fairly pure (91%) endo-isomer (177) m.p. 118°. [Found: C, 75.6; H, 4.5. $C_{15}H_{10}O_3$ requires C, 75.6; H, 4.2%]; $\nu_{max.}$ 1690, 1593, 900 cm^{-1}; n.m.r. τ 1.75 (m, 2H), 2.05 (m, 2H), 3.30 (t, 2H, J 2 Hz), 6.34 (sharp m, 2H), 8.18 and 8.34 (mxd, 2H).

IIIc(ii) Isomerisation of the endo-epoxide (177)

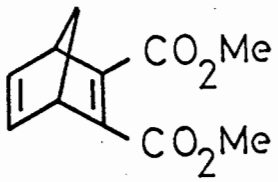
A mixture of triphenylphosphine (600 mg) and a mixture (600 mg) of the epoxides (177) and (178) as obtained from Section IIIc(i) were heated under reflux in ethanol (80 ml) for 0.5 hr by which time the solution had assumed a purple colour. The purple gum obtained on evaporation of the reaction mixture was chromatographed over alumina and eluted with benzene/petrol ether (9:1). The initial colourless components were shown to be starting materials while the yellow band isolated was kept. The mixture of starting materials was then refluxed for a further 0.5 hr and again chromatographed. This process was continued until most of the endo epoxide had been used up. The total yield of the quinone (176) was 139 mg; 30% yield. Recrystallisation from ethanol gave the pure quinone as brown needles m.p. 189 - 190°. [Found: C, 75.6; H, 4.4. $C_{15}H_{10}O_3$ requires C, 75.6; H, 4.2%]; $\lambda_{max.}$ 391, 338, 286 and 252 nm (log ε 3.05, 3.41, 4.08 and 4.36); $\nu_{max.}$ 1680, 1649, 1620, 1594, 1570 cm^{-1}; n.m.r. τ 1.98 (m, 2H), 2.33 (m, 2H), 3.87 and 4.05 (sharp multiplets, 3H), 5.88 (m, 1H), 7.17 (m, 2H).

IIId(i) Epoxidation of quinone (70) with m-chloroperbenzoic acid

A solution of the quinone (500 mg) and m-Cl-perbenzoic acid (500 mg) in dichloromethane were refluxed together for

6 hr. The resulting solution was cooled and extracted with aqueous sodium bicarbonate (3 x 20 ml), washed with water (2 x 20 ml) and dried ($MgSO_4$). Evaporation of the solvent gave r-2,3-epoxy-1,2,3,4-tetrahydro-cis-1,4-methanoanthroquinone (179) in 100% yield as yellow cubes (from ethanol) m.p. 156 - 157°. [Found: C, 75.6; H, 4.2. $C_{15}H_{10}O_3$ requires C, 75.6; H, 4.2%]; $\lambda_{max.}$ 344, 281, 252, 246 and 243 nm (log ε 3.33, 3.92, 4.17, 4.18 and 4.14); $\nu_{max.}$ 1658, 1598 cm^{-1}; n.m.r. τ 1.98 (m, 2H), 2.29 (m, 2H), 6.29 (sharp multiplet, 2H), 6.37 (s, 2H), 7.99 (dxt, 1H, J 9 and 1.5 Hz), 8.38 (dxm, 1H J 9, 1.5 and 0.5 Hz).

IIId(ii) 2,3-Dimethylbicyclo[2.2.1]hepta-2,5-diene dicarboxylate



The dicarboxylate was prepared in 70% yield as a colourless oil b.p. 105 - 106°/2 mm according to the method of Nienburg [159] who quoted the b.p. as 134 - 135°/10 - 11 mm.

IIId(iii) Epoxidation of the bicyclo-dicarboxylate from IIId(ii)

The ester (3 g) and m-chloroperbenzoic acid (2.6 g) were

heated together under reflux in carbontetrachloride (30 ml) for 6 hr. After the usual work up the exo-epoxide (180) was obtained as a colourless oil (2.6 g) b.p. 126 - 128°/ 1.44 mm. [Found: C, 59.1; H, 5.5. $C_{11}H_{12}O_5$ requires C, 59.0; H, 5.4%]; $\nu_{max.}$ 1718, 1617, 860 cm^{-1}; n.m.r. τ 6.12 (s, 6H), 6.27 (sharp multiplet, 2H), 6.56 (sharp multiplet, 2H), 8.14 (dxt, 1H J 9 and 2 Hz), 8.40 (dxm, 1H, J 9, 2 and 0.5 Hz).

Irradiation of the signal at 6.56τ simplified the multiplicity of the signals at 8.14 and 8.40τ to a pair of doublets at 8.20 and 8.42τ (J10Hz).

IIId(iv) Epoxidation of quinone (184)

The quinone (280 mg) was epoxidised with alkaline hydrogen peroxide in the usual manner to produce the endo-epoxide (186) in quantitative yield as white needle-like plates (from ethanol) m.p. 152°. [Found: C, 75.0; H, 5.2. $C_{15}H_{12}O_3$ requires C, 75.0; H, 5.0%]; $\nu_{max.}$ 1690, 1598, 910 cm^{-1}; n.m.r. τ 1.76 (m, 2H), 2.03 (m, 2H), 6.72 (sharp multiplet, 2H), 8.10 - 9.00 (m, 6H).

Irradiation of the signals at 6.72τ did not simplify the multiplet pattern between 8.10 - 9.00τ.

IIId(v) Reduction of the endo-epoxide (177)

The endo epoxide (350 mg) was dissolved in a mixture of

dry benzene (150 ml) containing prereduced PtO_2 and the resulting mixture hydrogenated until exactly two molar equivalents of hydrogen had been absorbed. Chromatographic separation of the products from the reduction mixture over silica gel using benzene as the eluent gave two fractions namely a yellow one which was shown to be the quinone (184) by comparison of its IR and n.m.r. spectra with that of the material prepared previously in Section IIa(vii).

The second component (which was eluted firstly) recrystallised from ethanol to give white crystals m.p. 140 - 145°. This was shown to be a mixture of the exo- and endo-epoxides (185) and (186) by n.m.r. Again irradiation of the sharp multiplet at 6.76τ did not simplify the shape of the multiplet at 8.10 - 9.00 τ. The IR spectrum appeared to be almost identical to that of the endo epoxide prepared in Section IIId(iv).

IIIe(i) 1,4,4a,9a-tetrahydro-2-methylanthroquinone (204)

The above adduct was prepared in 88% yield as white needles (from petrol ether) m.p. 81° according to the method of Diels and Alder [62] who report m.p. 81°. $\nu_{max.}$ 1690, 1598 cm^{-1}; n.m.r. τ 1.97 (m, 2H), 2.31 (m, 2H), 4.58 (m, 1H), 6.64 (dxd, 2H, J 11 and 6 Hz), 7.72 (m, 4H), 8.32 (s, 3H).

IIIe(ii) Enolisation of adduct (204) for 30 seconds

A solution of the adduct (1.0 g) in methanol (80 ml) was rapidly stirred while 3 M NaOH (3 drops) were added. The resulting solution was stirred for 30 seconds, neutralised with dilute HCl, poured into water (250 ml) and extracted with chloroform. The dried ($MgSO_4$) extract was evaporated to a yellow solid 1.0 g. Fractional recrystallisation from ethanol gave 1,4-dihydro-2-methylanthroquinone (206) as long yellow needles m.p. 162° in 34% yield. (The other product being 2-methylanthroquinone (210) in 66% yield). [Found: C, 80.2; H, 5.5. $C_{15}H_{12}O_2$ requires C, 80.4; H, 5.4%]; $\lambda_{max.}$ 332 and 247 nm (log ε 3.47 and 4.38); $\nu_{max.}$ 1660, 1641, 1591 cm^{-1}; n.m.r. τ 1.96 (m, 2H), 2.35 (m, 2H), 4.47 (m, 1H), 6.85 (broad singlet, 4H), 8.19 (s, 3H).

An alternative procedure for enolisation was attempted whereby dilute HCl was added to the initial reaction mixture and then the NaOH added slowly afterwards. The pH was adjusted to just >7 by the alternate addition of alkali and acid. However no improvement in the yield was obtained.

IIIe(iii) Epoxidation of quinone (206) with m-chloroperbenzoic acid

A mixture of the quinone (110 mg) and the perbenzoic acid (185 mg) in dichloromethane (20 ml) was stirred together for

12 hr and after the usual work up gave a quantitative yield of the 2,3-epoxy-1,2,3,4-tetrahydro-2-methylanthroquinone (211) as yellow cubes (from ethanol) m.p. 139°. [Found: C, 75.0; H, 5.0. $C_{15}H_{12}O_3$ requires C, 75.0; H, 5.0%]; $\lambda_{max.}$ 333, 260, 249 and 244 nm (log ε 3.41, 4.17, 4.26 and 4.27); $\nu_{max.}$ 1665, 1639, 1595, 952, 850 cm^{-1}; n.m.r. τ 2.00 (m, 2H), 2.35 (m, 2H), 6.35 - 7.60 (m, 5H), 8.51 (s, 3H).

IIIe(iv) Epoxidation of adduct (204) with m-chloroperbenzoic acid

A solution of the adduct (2.26 g) and m-chloroperbenzoic acid (2.0 g) in methylenedichloride (60 ml) were heated together under reflux for 12 hr to give after the usual work up a quantitative yield of the 2,3-epoxy-1,2,3,4,4a,9a-hexahydro-2-methylanthroquinone (212) as long white needles from (petrol ether) m.p. 118°. [Found: C, 74.4; H, 5.6. $C_{15}H_{14}O_3$ requires C, 74.4; H, 5.8%]; $\nu_{max.}$ 1690, 1592, 840, 745 cm^{-1}; n.m.r. τ 2.00 (m, 2H), 2.24 (m, 2H), 6.72 (m, 2H), 6.93 (d, 1H, J 2 Hz), 7.90 (m, 4H), 8.64 (s, 3H).

IIIe(v) Bromination of the 1,4-dihydro-2-methylanthroquinone (206)

A solution of the quinone (770 mg) in chloroform (10 ml) was treated with a molar equivalent of bromine in chloroform. Evaporation of the solvent gave a quantitative yield of the trans-2,3-dibromo-1,4-dihydro-2-methylanthroquinone (213)

as canary yellow cubes (from ethanol) m.p. 168 - 169°. [Found: C, 46.8; H, 3.3; Br, 42.0. $C_{15}H_{12}Br_2O_2$ requires C, 47.0; H, 3.1; Br, 41.7%]; $\lambda_{max.}$ 334, 256, 250 and 246 nm (log ε 3.63, 4.32, 4.38 and 4.43); $\nu_{max.}$ 1664, 1631, 1592, 698 cm^{-1}; n.m.r. τ 1.92 (m, 2H), 2.28 (m, 2H), 5.30 (m, 1 H), 6.34 (m, 2H), 6.60 (m, 2H), 7.90 (s, 3H).

IIIf(i) Reaction between 1,4-naphthoquinone and 1,3-cyclohexadiene

The reaction was carried out in ethanol according to the method of Diels and Alder [62] to give the 1,4-ethano-1,4,4a,9a-tetrahydroanthroquinone (215) in 97% yield as white needles (from ethanol) m.p. 134° (Lit. [62] m.p. 135°). $\nu_{max.}$ 1678, 1594 cm^{-1}; n.m.r. τ 1.96 (m, 2H), 2.31 (m, 2H), 3.82 (t, 2H, J 4 Hz), 6.62 (m, 2H), 6.75 (sharp multiplet, 2H), 8.18 (dxd, 2H, J 10 and 2 Hz), 8.58 (dxd, 2H, J 10 and 2 Hz).

IIIf(ii) Base catalysed enolisation of adduct (215)

A solution of the adduct (2.82 g) in methanol (120 ml) was treated with 2 M NaOH (1.5 ml) for 15 minutes at room temperature. The colour changed from red to yellow. The solution was then neutralised and the yellow solid filtered* off to give the 1,4-ethano-1,4-dihydroanthroquinone (216) in 54% yield as yellow plates (from ethanol) m.p. 155° (with

explosive violence due to the ethylene liberated at the m.p.). $\lambda_{max.}$ 337, 269, 250, 245 and 241 nm (log ε 3.37, 4.24, 4.22, 4.12 and 4.20); $\nu_{max.}$ 1660, 1630, 1595 cm^{-1}; n.m.r. τ 1.92 (m, 2H), 2.34 (m, 2H), 3.55 (t, 2H, J 4 Hz), 5.43 (m, 2H), 8.52 (m, 4H). Diels and Alder [62] reported no m.p. for this quinone except to state that it lost ethylene when heated to 150 - 190°.

*The filtrate was extracted with chloroform to give a light yellow product (1.26 g) shown by IR to be comprised of the quinone (216) and the exo-epoxide (217). This product was treated with alkaline hydrogen peroxide to give the r-4a,9a-epoxy-cis-1,4-ethano-1,4,4a,9a-tetrahydroanthroquinone (217) in quantitative yield as white needles (from ethanol) m.p. 146 - 147°. [Found: C, 76.5; H, 4.8. $C_{16}H_{12}O_3$ requires C, 76.2; H, 4.8%]; $\nu_{max.}$ 1690, 1596, 908, 892 cm^{-1}; n.m.r. τ 2.05 (m, 2H), 2.31 (m, 2H), 3.96 (t, 2H, 4 Hz), 6.15 (sharp multiplet, 2H), 8.54 (s, 4H).

Irradiation of the signals at 6.15τ caused the triplet at 3.96τ to collapse to a singlet while irradiation of the signals at 8.54τ simplified the multiplet at 6.15τ into a triplet (J4Hz).

Epoxidation of the quinone (216) with alkaline hydrogen peroxide gave a mixture of endo and exo epoxides in the ratio

of 5:95 as shown by n.m.r.

IIIf(iii) Epoxidation of the quinone (216) with m-chloroperbenzoic acid

The quinone (500 mg) and m-Cl-perbenzoic acid (650 mg) were heated together under reflux for 5 hr in dichloromethane (40 ml). After the usual work up a quantitative yield of r-2,3-epoxy-trans-1,4-ethano-1,2,3,4-tetrahydroanthroquinone (221) was obtained as yellow plates (from ethanol) m.p. 166 - 167°. [Found: C, 76.5; H, 4.5. $C_{16}H_{12}O_3$ requires C, 76.2; H, 4.7%]; $\lambda_{max.}$ 337, 271, 266, 250 and 245 nm (log ε 3.37, 4.13, 4.12, 4.19 and 4.21); $\nu_{max.}$ 1665, 1622, 1595, 831 cm^{-1}; n.m.r. τ 1.93 (m, 2H), 2.34 (m, 2H), 6.02 (sextet, 2H, J 2 Hz), 6.58 (dxd, 2H, J 2 and 2 Hz), 8.20 (m, 2H), 8.60 (m, 2H).

IIIg(i) Reaction between 1,4-naphthoquinone and cyclooctatetraene

This reaction was carried out according to the method of Reppe [160] to give the quinone (222) in an overall yield of 30% as yellow plates (from methanol) m.p. 205 - 206° (Lit. [160] m.p. 192°). [$C_{18}H_{12}O_2$ requires C, 83.1; H, 4.6. Found: C, 82.9; H, 4.7%]; $\lambda_{max.}$ 338, 262, 251 and 245 (log ε 3.39, 3.97, 4.30, 4,31); $\nu_{max.}$ 1658, 1622, 1598 cm^{-1}; n.m.r. τ 1.95 (m, 2H), 2.15 (m, 2H), 3.82 (t, 2H, J 4 Hz), 3.89 (s, 2H), 5.62 (m, 2H), 7.32 (sharp multiplet, 2H).

IIIg(ii) Addition between the cyclooctatetraenenaphthoquinone (222) and 2,5-dimethyl-3,4-diphenylcyclopentadienone (77)

A solution of the quinone (670 mg) and the dienone (670 mg) in benzene (40 ml) were heated together under reflux for 30 hr. Evaporation of the solvent yielded the exo-adduct (227) as canary yellow crystals (1.34 g). Recrystallisation from ethanol gave the pure material as canary yellow needles m.p. 195° (dec.). [Found: C, 85.3; H, 5.5. $C_{37}H_{28}O_3$ requires C, 85.5; H, 5.4%]; $\lambda_{max.}$ 336, 264, 251, 245 and 240 nm (log ε 3.45, 4.30, 4.48, 4.49 and 4.48); $\nu_{max.}$ 1773, 1659, 1599 cm^{-1}; n.m.r. τ 1.91 (m, 2H), 2.31 (m, 2H), 2.90 (m, 10H), 3.35 (t, 2H, J 4 Hz), 5.35 (m, 2H), 7.94 (s, 2H), 8.01 (s, 2H), 8.75 (s, 6H).

Irradiation of the signal at 5.35τ caused the triplet at 3.35τ to collapse to a singlet.

IIIg(iii) Pyrolysis of the exo-adduct (227)

The adduct (100 mg) was pyrolysed at 180 - 230° under N_2. The total yield of sublimed material wat 95 mg which was chromatographed through a column 1.5 metres long and 0.03 metre in diameter of silica gel and elution was effected with benzene. Since both components of the sublimate were virtually colourless, the progress of the separation had to be monitored by t.l.c.

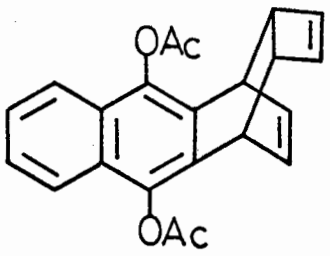
Component 1: Evaporation of the solvent gave 57 mg of a colourless crystalline mass which formed white needles (from petrol ether) m.p. 135°. $\nu_{max.}$ 1768 cm^{-1}; n.m.r. τ 2.78 (m, 10H), 3.38 (s, 2H), 6.80 (s, 2H), 8.76 (s, 6H). This component was shown to be the tricyclo[4.2.1.$0^{2,5}$]nona-3,7-dien-9-one (230) (Lit.[153] m.p. 137°).

Component 2: Pale yellow crystals (38 mg). This was shown to be anthroquinone by comparison of melting points and mixed melting points and IR spectra with authentic material.

IIIg(iv) Reductive acetylation of the cyclooctatetraenenaphthoquinone (222)

A solution of the quinone (1.0 g) in acetic anhydride (30 ml) was stirred at the boiling point in the presence of zinc dust (800 mg) for a period of 3 hr, rapidly filtered and the filtrate poured into water (250 ml). The white solid obtained was recrystallised from ethanol to give 640 mg of diacetate (vide infra). Purification of the solid obtained from the mother liquors by chromatography gave starting material (280 mg) and diacetate (120 mg). This showed an overall conversion of 80% into the diacetate based on recovered starting material. The diacetate formed white needles (from ethanol) m.p. 182 - 183°. [Found: C, 76.2; H, 5.3.

$C_{22}H_{18}O_4$ requires C, 76.4; H, 5.2%]; $\nu_{max.}$ 1700, 1608, 1168 cm^{-1}; n.m.r. τ 2.21 (m, 2H), 2.52 (m, 2H), 3.69 (t, 2H, J 4 Hz), 3.92 (s, 2H), 6.02 (broad singlet, 2H), 7.12 (broad s, 2H), 7.46 (s, 6H).



IIIg(v) Reductive acetylation of the cyclooctatetraenenaphthoquinone-cyclopentadienone adduct (227)

The quinone (500 mg) in acetic anhydride (15 ml) containing zinc dust (500 mg) was heated under reflux for 20 minutes, filtered hot and the filtrate poured into water. The diacetate (231) was obtained in quantitative yield as white needles (from ethanol) m.p. 226 - 227° with gas evolution. [Found: C, 81.0; H, 5.4. $C_{41}H_{34}O_5$ requires C, 81.2; H, 5.6%]; $\nu_{max.}$ 1761, 1170 cm^{-1}; n.m.r. τ 2.19 (m, 2H), 2.50 (m, 2H), 2.87 (m, 10H), 3.30 (t, 2H, J 4 Hz), 5.90 (broad singlet, 2H), 7.50 (s, 6H), 7.89 (s, 4H), 8.78 (s, 6H).

IIIg(vi) Pyrolysis of the diacetate (231)

The diacetate (390 mg) was pyrolysed at 230° for 20 minutes to yield a brown oil which was chromatographed through a

silica gel column and eluted with a mixture of benzene and chloroform (2:1). Again separation was monitored by t.l.c. and the band desired was eluted after many other minor components had been eluted. Starting material (100 mg) was eluted last. From this pyrolysis the triene (232) was obtained in 28% yield as white needles (from ethanol) m.p. 210°. [Found: C, 83.1; H, 5.9. $C_{40}H_{34}O_4$ requires C, 83.1; H, 5.9%]; $\nu_{max.}$ 1770, 1758, 1610, 1168 cm^{-1}; n.m.r. τ 2.21 (m, 2H), 2.52 (m, 2H), 3.12 (m, 12H), 5.82 (m, 2H), 7.42 (sharp multiplet, 4H), 7.49 (s, 6H), 8.51 (s, 6H).

IIIg(vii) Photolysis of the above triene (232)

Photolysis of the triene (60 mg) in benzene (200 ml) under a constant stream of N_2 gas for 2 hr yielded a polymeric gum which was chromatographed over silica gel and eluted with benzene to yield 3',6'-dimethyl-o-terphenylene (81) as colourless plates (10 mg).

IIIh(i) Reaction between the cyclooctatetraenenaphthoquinone (222) and the s-tetrazine (137)

The quinone (260 mg) and the s-tetrazine (238 mg) were gently heated together in chloroform (20 ml) for 1 hr during which time the solution changed colour from purple to light yellow. The solvent was removed and the residue recrystallised

from benzene or chloroform/petrol ether to give the 4,5-dihydropyridazine derivative (234) in 64% yield as yellow-brown needles m.p. 198 - 200° (dec.). [Found: C, 76.7; H, 4.4; N, 11.8. $C_{30}H_{20}N_4O_2$ requires C, 76.9; H, 4.3; N, 12.0%]; $\lambda_{max.}$ 334, 298, 265, 250 and 245 nm (log ε 3.78, 4.11, 4.29, 4.41 and 4.41); $\nu_{max.}$ 1663, 1600 cm^{-1}; n.m.r. τ 1.27 (dxd, 2H, J 1 and 4 Hz), 1.58 (dxd, 2H, J 1 and 8 Hz), 1.92 - 2.73 (m, 8H), 3.15 (t, 2H, J 4 Hz), 5.04 (m, 2H), 6.60 (d, 2H, J 4 Hz), 7.70 (d, 2H, J 4 Hz).

Irradiation of the signals at 5.04τ caused the triplet at 3.15τ to collapse to a singlet while irradiation of the doublet at 7.70τ caused the doublet at 6.60τ to collapse to a singlet while simplifying the multiplet at 5.04τ to a triplet (J 4Hz).

IIIh(ii) Reaction between diacetate from section IIIg(iv) and the s-tetrazine (137)

A solution of the diacetate (420 mg) and the s-tetrazine (282 mg) in benzene (30 ml) were heated under reflux for 3 hr during which time the colour of the solution changed from purple to yellow. Removal of the benzene gave the 4,5-dihydropyridazine adduct (235) in quantitative yield as yellow plates (from chloroform/petrol ether) m.p. 238° (dec.). [Found: C, 74.8; H, 4.7; N, 10.1. $C_{34}H_{26}N_4O_4$ requires

C, 74.7; H, 4.5; N, 9.8%]; $\nu_{max.}$ 1754, 1593, 1170 cm^{-1}; n.m.r. τ 1.28 (txd, 2H, J 1 and 5 Hz), 1.50 (dxd, 2H, J 8 and 1 Hz), 2.06 - 2.80 (m, 8H), 2.98 (t, 2H, J 4 Hz), 5.47 (m, 2H), 6.49 (d, 2H, J 4 Hz), 7.40 (sharp multiplet, 2H), 7.52 (s, 6H).

IIIh(iii) Photolysis of the 4,5-dihydropyridazine adduct (235)

The adduct (300 mg) in benzene (500 ml) was irradiated for 1.5 hr after which time no starting material was present as shown by t.l.c. The photo products were separated on a silica gel column and eluted with chloroform. The major component was obtained as a gum (170 mg) which crystallised on trituration with ethanol. It was recrystallised from DMSO as white rods m.p. 265 - 266°. Alternatively it may also be recrystallised from chloroform/petrol ether. [Found: C, 72.0; H, 4.5; N, 5.1. $C_{32}H_{24}N_2O_6$ requires C, 72.3; H, 4.5; N, 5.3%]; $\nu_{max.}$ 1752, 1698, 1690, 1580, 1168 cm^{-1}.

When this photo product was hydrolysed with aqueous KOH, anthroquinone (229) was isolated together with a yellow gum which was polymeric and could not be induced to crystallise.

IIIi(i) Epoxidation of quinone (222)

The quinone was converted into the exo-epoxide (236) in quantitative yield by methods previously described see Section IIc(i) as white needles (from ethanol) m.p. 178 -

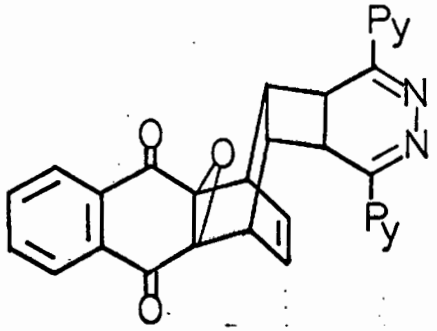
179°. [Found: C, 78.2; H, 4.5. $C_{18}H_{12}O_3$ requires C, 78.4; H, 4.35%]; $\nu_{max.}$ 1690, 1600, 890 cm^{-1}; n.m.r. τ 2.05 (m, 2H), 2.31 (m, 2H), 4.08 (s, 2H), 4.21 (t, 2H, J 4 Hz), 6.12 (m, 2H), 7.15 (d, 2H, J 2 Hz).

Irradiation of the multiplet at 6.12τ caused the triplet at 4.21τ to collapse to a singlet as well as the doublet at 7.15τ to collapse to a singlet.

The n.m.r. also showed the presence of 7% of the endo isomer where the olefinic protons of the bicyclo[2.2.2]system resonated as a triplet at 3.61τ (J = 4Hz).

IIIi(ii) Reaction between the epoxide (236) and s-tetrazine (137)

The epoxide (300 mg) and s-tetrazine (259 mg) were heated together in benzene under reflux for 12 hr and then evaporated down to an orange solid which was boiled up with ethanol and filtered to give the 4,5-dihydropyridazine adduct (vide infra) in 75% yield as yellow plates (from chloroform/petrol ether) m.p. 242 - 243° (dec.). [Found: C, 74.5; H, 4.2; N, 11.9. $C_{30}H_{20}N_4O_3$ requires C, 74.4; H, 4.1; N, 11.6%]; $\nu_{max.}$ 1692, 1598, 1560, 890 cm^{-1}; n.m.r. τ 1.11 (dxm, 2H, J 8 Hz), 1.44 (dxm, 2H, J 10 Hz), 2.00 - 2.68 (m, 8H), 3.40 (t, 2H, J 4 Hz), 5.51 (m, 2H), 6.36 (d, 2H, J 4 Hz), 7.40 (m, 2H).

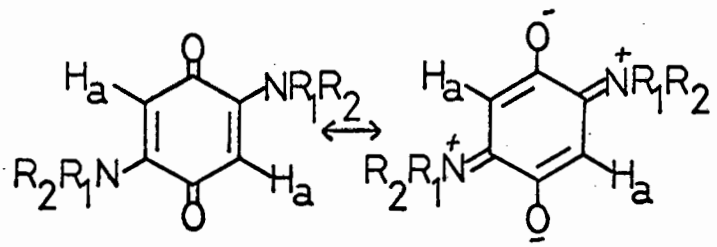


Py = 2′-pyridyl

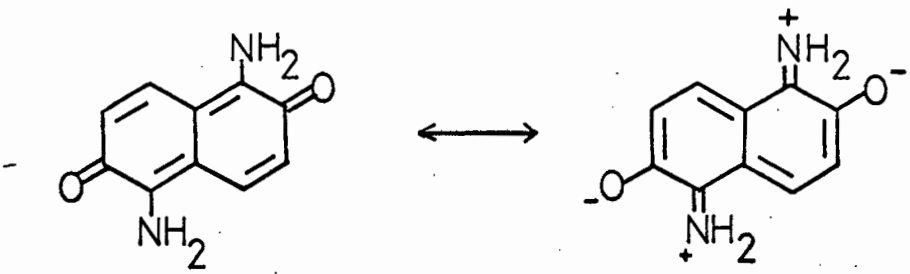
APPENDIX

Earlier workers [161 - 164] had shown by various methods that 2,5-bisaminated-1,4-benzoquinones exist as resonance hybrids of the two extreme canonical forms (242) and (243) there being a significant contribution by the quadrupolar form (243), although some workers [165] maintained that these quinones are true quinones in their ground state. Their quadrupolar nature found precedent since the 1,5-diamino-2,6-naphthoquinone (244) had also been shown to have a contribution by the quadrupolar merocyanine form (245) to the true structure. [166] Dähne et al. [162] have demonstrated the use of n.m.r. spectroscopy in establishing the existance of the quadrupolar form (243) by measuring the chemical shifts of the quinonoid protons H_a for a series of 2,5-bisaminated-1,4-benzoquinones. It was shown that the quinonoid protons H_a were strongly shielded [162, 166, 167] (ca. 4.60τ) relative to 1,4-benzoquinone (3.24τ). The upfield shift has been ascribed to a high degree of quinone-nitrogen double bond character in the immediate vicinity of the quinone protons H_a which would be anticipated to cause strong shielding. [162] Variable temperature n.m.r. studies have recently [167] been carried out on a series of cyclic 2,5-bisaminated-1,4-benzoquinones (246)→(250) to determine the coalescence temperature, Tc, for the signals due to R_1 and R_2, which, because of the C = N double bond character, are in different environments at low temperatures, and hence have different chemical shifts. From the coalescence temperatures Tc [169] the following order was obtained for the

series: azetidino (246)>pyrrolidino (247)>hexamethyleneamino (248) [170] >piperidino (249)>aziridino (250). Measurement of the half-wave potentials [168] for these bisaminated quinones (246)→(250) relative to 1,4-benzoquinone gave an order which was in qualitative agreement with that obtained from variable temperature measurements with the exception that the relative order of the first two amines was reversed.



(242) (243)



(244) (245)

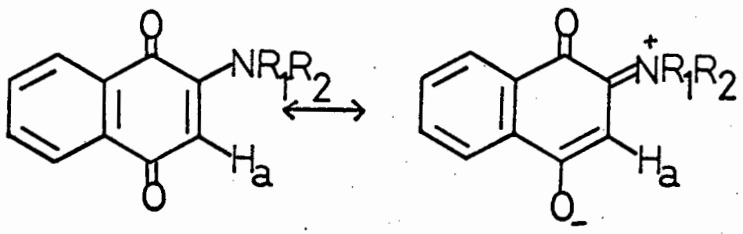
TABLE 6

NR_1R_2		Tc °C	Quinone H (τ)	$\Delta E^{o}_{\frac{1}{2}}$ Half-wave potential
(246)	Azetidino	65	5.08	-0.463
(247)	Pyrrolidino	25	4.75	-0.481
(248)	Hexamethyleneamino	-10	4.62	-0.442
(249)	Piperidino	< -60	4.50	-0.299
(250)	Aziridino	< -60	4.05	-0.199
(251)	Monomethylamino	No coalescence temp. observed	4.72	-0.510
(252)	Dimethylamino	-45	4.67	-0.346

The monomethylamino- and dimethylamino analogues were included for comparison purposes. The bis- and monomethylamino quinones (251) and (260) are the only compounds within each series bearing hydrogen atoms attached to the nitrogen and consequently might be expected to behave anomolously. It has been suggested that hydrogen bonding may occur in these systems [173] which would, if this were the case, tend to inhibit rotation and the methyl resonances would therefore always appear at a single chemical shift (split into a doublet by the neighbouring hydrogen).

It was anticipated that if the series was extended to include the 2-aminated-1,4-naphthoquinones, the same order of effective electron donation within the series of secondary cyclic amino substituents would be observed as with the bisaminated-1,4-benzoquinones. Thus a fully

representative range of cyclic secondary aminated-1,4-naphthoquinones was prepared in order that variable temperature n.m.r. studies could be performed. The effects of these amino substituents on the 1,4-naphthoquinone nucleus (253), i.e. the relative importance of the dipolar contributor (254) to the true structure in the ground state, were examined in terms of three main criteria that had previously been employed.[167] These are (i) polarographic half-wave potentials $E^{o}_{\frac{1}{2}}$ (ii) the approximate coalescence temperatures Tc of the proton signals on the carbon atoms α- to the nitrogen atoms of the amino substituents and (iii) shielding of the quinone proton H_a by the adjacent amino moiety. The results are summarised in Table 7.



(253) (254)

TABLE 7

NR_1R_2	Tc °C	Quinone H (τ)	$\Delta E^{\circ}_{\frac{1}{2}}$ *
(255) Azetidino	30	4.58	-0.221
(256) Pyrrolidino	20	4.30	-0.264
(257) Hexamethyleneamino	-30	4.14	-0.214
(258) Piperidino	< -60	3.94	-0.149
(259) Aziridino	< -60	3.67	-0.089
(260) Monomethylamino	No coalescence temp. observed	4.32	-0.274
(261) Dimethylamino	-60	4.19	-0.194

*$\Delta E^{\circ}_{\frac{1}{2}}$ with respect to 1,4-naphthoquinone i.e. $\Delta E^{\circ}_{\frac{1}{2}} = E^{\circ}_{\frac{1}{2}}(NR_1R_2) - E^{\circ}_{\frac{1}{2}}(H)$. The half-wave potentials were measured at various pH's and the values at pH 7 were used.

Comparison of the n.m.r. results indicated that two effects were particularly noteworthy in proceeding along the series (255)→(259). At relatively higher temperatures the n.m.r. spectra of these compounds showed absorption due to the hydrogens attached to the carbon atoms α- to the nitrogen as a single peak. On lowering the sample temperature, this single peak broadened and in some cases separated into two new signals. This change with temperature could be attributed to restricted rotation about the quinone-nitrogen bond and was dependant on the nature of the cyclic amine. Consequently a high degree of quinone-nitrogen double bond character, i.e. the more that the dipolar form (254) contributes

to the true structure, is reflected by a relatively higher coalescence temperature. Secondly, the chemical shifts of the quinone protons H_a paralleled the findings obtained from Tc measurements very well as shown in Table 7 and may perhaps be used as a more definite guide in deducing the relative order of effective electron donation by the various secondary amino substituents. Thus by the n.m.r. criteria the order of effective electron donation was azetidino (255)>pyrrolidino (256) > hexamethyleneamino (257)>piperidino (258)>aziridino (259). This implied that interaction between the nitrogen non-bonding electrons and the quinone chromophore followed the same order and consequently led to the prediction that the 2-azetidino-1,4-naphthoquinone (255) would have the lowest oxidation potential within the series while the 2-aziridino-1,4-naphthoquinone (259) should have the highest. From polarographic measurements the relative order was the same as determined by the n.m.r. methods with the exception that the order of the first two was reversed as was found in the benzoquinone series.

When the n.m.r. data for the corresponding members of the naphthoquinone and benzoquinone series (Table 7 and Table 6 respectively) were compared it became apparent that the former series exibited both a lower degree of shielding of the quinone proton H_a as well as lower coalescence temperatures than the latter series. This led to the conclusion that for a particular secondary amino substituent, the dipolar contributor (254) was of less significance to an animated naphthoquinone than was the

corresponding quadrupolar contributor (243) to the bisaminated benzoquinone. It was particularly interesting to note that from the polarographic measurements the effect of a particular amino substituent was rather similar in the two series. A further striking feature emerging from comparison of the $\Delta E^{o}_{\frac{1}{2}}$ values for the two series was that the values found for the aminated-naphthoquinones were approximately half the corresponding values as determined in the bisaminated-benzoquinone series.

In order to attempt to rationalise the differing influences of the cyclic amino substituents, the effect of ring strain was initially regarded as a predominant criterion. However the similar effects demonstrated by the azetidino and pyrrolidino groups on the quinone nucleus were apparent even though they would not have been predictable on the basis of the conciderable differences existing between cyclobutyl and cyclopentyl ring systems. Furthermore appreciable differences were observed between the pyrrolidino and hexamethyleneamino groups which would also not be anticipated by analogy to the comparable data quoted for cyclopentyl and cycloheptyl ring systems.[172] It appeared that in both series, relative to pyrrolidino, there was a greater contribution to dipolar forms (243) and (254) by the azetidino substituent than by the hexamethyleneamino substituent than would possibly have been predicted on the grounds of ring strain alone. It is suggested that the protons α- to the nitrogen atom may sterically interact with the neighbouring

oxygen atom and quinonoid proton H_a which could destabalise the polar contributors (243) and (254) as the ring size of the amine increased.

On the other hand if one were to compare the pyrrolidino- and piperidino-quinones (256) and (258) respectively, the greater contribution of (254) in the pyrrolidino case relative to the piperidino analogue may be explained by the fact that the quinone-nitrogen double bond in the dipolar form (254) is exo to a five-membered ring in the former case, while exo to a six-membered ring in the latter.[171] The marked anomolous nature of the aziridino analogue (259) where Tc is far lower and the quinonoid proton H_a much less shielded, could at least be partially due to the nitrogen lone pair orbital having high s character in the aziridine ring resulting in a reluctance for these electrons to be delocalised over the quinone chromophore.

IVa 2,5-Bishexamethyleneamino-1,4-benzoquinone (248)

A solution of hexamethyleneamine (23 ml) in ethanol (25 ml) was added to a mixture of hydroquinone (5 g) in water (30 ml) and the mixture aerated for 8 hr. The red solution was filtered and the filter cake washed with chloroform to leave unreacted hydroquinone (1.0 g). The red filtrate was evaporated to dryness and treated with dilute H_2SO_4 (6 ml concentrated acid in 180 ml water). Extraction with chloroform yielded the bisaminated-quinone (248) as bright red needles (from methanol) m.p. 159°. The total yield which includes material isolated from mother liquors was 40%. [Found: C, 71.8; H, 8.7; N, 9.2. $C_{18}H_{26}N_2O_2$ requires C, 71.5; H, 8.6; N, 9.3%]; $\lambda_{max.}$ 523, 379, and 228 nm (log ε 2.66, 4.35 and 4.38); $\nu_{max.}$ 1614, 1551 cm^{-1}; n.m.r. τ 4.59 (s, 2H), 6.29 (t, 8H, J 5.2 Hz), 8.33 (broad singlet, 16H).

IVb 2-Aziridino-1,4-naphthoquinone (259)

Aziridine (1.3 ml) was added to a solution of 1,4-naphthoquinone (1.5 g) in ethanol (50 ml) and the resulting brown solution stirred in the dark for 20 hr and then filtered. The yellow brown paste was recrystallised from ethanol into yellow brown needles m.p. 170 - 178° (dec.) (Lit. [174] 175 - 182°, 173.5 - 178.5° [175]). $\lambda_{max.}$ 385, 334, 287 and 252 nm (log ε 3.45, 3.56, 4.18 and 4.39); $\nu_{max.}$ 1678, 1655, 1591, 1571 cm^{-1}; n.m.r. τ 1.96 (m, 2H), 2.32 (m, 2H), 3.74 (s, 1H), 7.73 (s, 4H).

IVc 2-Azetidino-1,4-naphthoquinone (255)

Azetidine [176] (4.0 ml) was added to a mixture of cupric acetate (2.4 g) and methanol (60 ml) and the resulting solution aerated for 5 minutes after which a solution of 1,4-naphthoquinone (2.0 g) in methanol (80 ml) was added to the reaction mixture and then aerated for a further 3 hr. The solution was evaporated to dryness and treated with dilute H_2SO_4 (150 ml x 3 M) and extracted rapidly with ether (4 x 60 ml). Very little of the product was extracted. The aqueous solution was filtered to yield the azetidino-quinone (255) in 41% yield as red needles (from methanol) m.p. 174°. [Found: C, 73.1; H, 5.3; N, 6.5. $C_{13}H_{11}NO_2$ requires C, 73.2; H, 5.2; N, 6.6%]; $\lambda_{max.}$ 473, 277 and 239 nm (log ε 3.68, 4.40 and 4.18); $\nu_{max.}$ 1680, 1613, 1591, 1565 cm^{-1}; n.m.r. τ 2.00 (m, 2H), 2.40 (m, 2H), 4.58 (s, 1H), 5.70 (very broad doublet, 4H), 7.54 (m, 2H).

IVd 2-Pyrrolidino-1,4-naphthoquinone (256)

Freshly distilled pyrrolidine (1.7 ml) in ethanol (5 ml) was added to a solution of 1,4-naphthoquinone (1.0 g) in ethanol (30 ml) and the red solution stirred for 20 hr in the dark. The reaction mixture was then chilled and the red solid filtered to yield 1.3 g of the pyrrolidino-quinone (256) as long red plates (from aqueous methanol) m.p. 159°. [Found: C, 73.7; H, 5.6; N, 6.0. $C_{14}H_{13}NO_2$ requires C, 74.0; H, 5.7; N, 6.2%]; $\lambda_{max.}$ 474, 277 and

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238 nm (log ε 3.74, 4.40 and 4.22); $\nu_{max.}$ 1672, 1616, 1589, 1556 cm^{-1}; n.m.r. τ 2.00 (m, 2H), 2.40 (m, 2H), 4.30 (s, 1H), 6.36 (broad singlet, 4H), 8.02 (sharp multiplet, 4H).

IVe 2-Piperidino-1,4-naphthoquinone (258)

The piperidino-quinone was prepared in 82% yield as deep purple needles m.p. 95° according to the method of Crosby and Lutz [177] who reported m.p. 94 - 96°. $\lambda_{max.}$ 466, 276, 243 and 238 nm (log ε 3.69, 4.34, 4.18 and 4.19); $\nu_{max.}$ 1673, 1628, 1588, 1559 cm^{-1}; n.m.r. τ 2.00 (m, 2H), 2.37 (m, 2H), 4.00 (s, 1H), 6.52 (s, 4H), 8.31 (sharp multiplet, 6H).

IVf 2-Hexamethyleneamino-1,4-naphthoquinone (257)

Hexamethyleneamine (8 ml) was added to a solution of 1,4-naphthoquinone (900 mg) in ethanol (30 ml) and the resulting red solution stirred for 15 hr and then evaporated to a deep red oil. Ether (50 ml) was added to the oil followed by 3 M H_2SO_4 (60 ml). The aqueous layer was rapidly extracted with ether (3 x 50 ml). The dried extracts were evaporated to a red oil which was extracted with boiling cyclohexane (4 x 50 ml). These extracts were evapotated to a red solid which was recrystallised from aqueous methanol to give red needles of the hexamethyleneamino-quinone (257) in 73% yield, m.p. 98°. [Found: C, 75.2; H, 6.9; N, 5.4. $C_{16}H_{17}NO_2$ requires C, 75.4; H, 6.7; N, 5.5%]; $\lambda_{max.}$ 469, 278 and 241 nm (log ε

3.72, 4.35 and 4.19); $\nu_{max.}$ 1669, 1615, 1587, 1576, 1549 cm^{-1}; n.m.r. τ 2.02 (m, 2H), 2.42 (m, 2H), 4.14 (s, 1H), 6.36 (t, 4H, J 4 Hz), 8.14 and 8.38 (broad singlets, 8H).

IVg 2-Monomethylamino-1,4-naphthoquinone (260)

The aminated-naphthoquinone was prepared in 60% yield as long red needles m.p. 240° by the method of Inoue [178] who report the m.p. to be 232°. $\lambda_{max.}$ 446, 327 and 278 nm (log ε 3.54, 3.35 and 5.35); $\nu_{max.}$ 3370, 1670, 1601, 1566 cm^{-1}; n.m.r. τ 1.98 (m, 2H), 2.40 (m, 2H), 4.32 (s, 1H), 4.10 (broad s, 1H, D_2O exchangeable), 7.11 (d, 3H, J 6 Hz).

IVh 2-Dimethylamino-1,4-naphthoquinone (261)

The aminated-naphthoquinone was prepared in 85% yield as orange needles m.p. 121.6° by the method of Grinev [179] who reported m.p. of 121.5°. $\lambda_{max.}$ 459, 310, 274 and 236 nm (log ε 3.67, 3.36, 4.34 and 4.20); $\nu_{max.}$ 1670, 1611, 1588, 1560 cm^{-1}; n.m.r. τ 2.02 (m, 2H), 2.40 (m, 2H), 4.19 (s, 1H), 6.83 (s, 6H).

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