566. *Reactions of Cyclohexadienes. Part III.*[1] *Conversion of Some 1-Methoxycyclohexa-1,3-dienes into Polycyclic Quinones.*

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1-Methoxy- and 1,3-dimethoxy-cyclohexa-1,3-diene react with benzoquinone, naphthaquinone, or quinoline-5,8-dione to form adducts which, after conversion of the enedione ring into a quinone ring, lose the bridge on heating, to give polycyclic aromatic quinones in good yields. Two bridges can be eliminated simultaneously; *e.g.*, pyrolysis of the diethano-anthracene (VII) gives anthrarufin dimethyl ether.

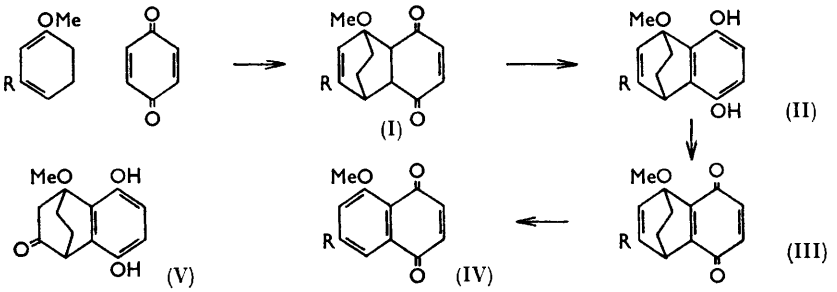
Work on the structure of phomazarin, to be reported later, required a new method for the synthesis of some model aza-anthraquinones with *peri*-methoxy- or -hydroxy-groups. We report some general aspects of the method devised, which constitutes a new polycyclic aromatic quinone synthesis.

Ready thermal elimination of a bridge containing two carbon atoms across the 1,4-positions of a cyclohexa-2,5-diene derivative is known to occur, to generate an aromatic compound. Bridged compounds of this type are usually obtainable, directly or indirectly, by Diels–Alder reactions, and the prototype of the thermal elimination is the reaction of dimethyl acetylenedicarboxylate with cyclohexa-1,3-dienes to yield, finally, an olefin corresponding to the bridge together with a dimethyl phthalate.[2] A number of 1-methoxycyclohexa-1,3-dienes are now readily available, and yield adducts with benzoquinone;[1] conversion of the enedione ring of these, *e.g.*, (I), into a quinone ring (III) generates a bridged ring which would be expected to undergo thermal elimination of the bridge to produce the aromatic quinone (IV). This expectation was confirmed using the adduct (I; R = H). Aromatisation was accomplished by the action of N-aqueous ammonia, the quinol (II; R = H) being directly extractable from the solution by chloroform; with stronger bases rapid aerial oxidation occurred. It could also be satifactorily carried out by refluxing with sodium hydrogen carbonate in methanol. Oxidation of the quinol with silver oxide gave the quinone (III; R = H) which, when heated above its melting point, gave juglone methyl ether (IV; R = H) in good yield.

In an attempt to perform the same reactions on the adduct (I; R = OMe), from 1,3-dimethoxycyclohexa-1,3-diene, difficulties were encountered because the intermediate quinol is an enol ether and is apparently sufficiently acidic to catalyse its own hydrolysis to a ketone in the presence of water. The ketone (V) was the main product from attempts to isolate the quinone (II; R = OMe), although the infrared spectrum of the crude product indicated that a small proportion of the quinone was present. The pure ketone (V) was readily obtained after acid treatment, and showed the expected stability to heat, as did the

[1] Part II, preceding Paper.
[2] Alder and Rickert, *Ber.*, 1937, **70**, 1354.

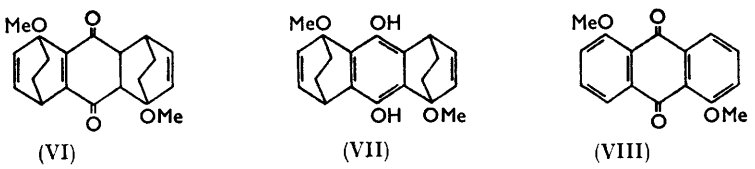
corresponding quinone. The carbonyl group could not be converted into an enol acetate. The aromatisation of the enedione ring of (I; R = OMe) was best accomplished by means of N-aqueous ammonia, since chloroform directly extracted a product from the aqueous solution, which was mainly, though not exclusively, the diol (II; R = OMe). Owing to



its instability, the crude product was oxidised immediately by silver oxide to the desired quinone (III; R = OMe). This was converted by heating to 200° into 5,7-dimethoxy-1,4-naphthaquinone (IV; R = OMe).

A similar series of reactions using 1,4-naphthaquinone instead of benzoquinone resulted in formation of 1-methoxyanthraquinone and 1,3-dimethoxyanthraquinone from (I; R = H) and (I; R = OMe), respectively. With quinoline-5,8-dione and cyclohexa-1,3-diene or 1-methoxycyclohexa-1,3-diene, without isolation of intermediates, were obtained, respectively, about 50% of 1-aza-anthraquinone, and a mixture of 5- and 8-methoxy-1-aza-anthraquinone in the ratio 2 : 3, readily separated by chromatography. The assignment of structure was based on spectral evidence. In 1-aza-anthraquinone itself the carbonyl bands occur at 1671 and 1686 cm.$^{-1}$, the higher corresponding to the carbonyl α to the nitrogen. The electronic effect of the 5-methoxyl group should augment the difference (1665 and 1685 cm.$^{-1}$) between the two carbonyl bands, whilst that of the 8-methoxyl group should diminish it (1670 and 1680 cm.$^{-1}$). Assignment on this basis is supported by other evidence to be presented with the phomazarin work.

A further illustration of the possibilities of the reaction is the synthesis of anthrarufin dimethyl ether (VIII). The quinone (III; R = H) reacted with 1-methoxycyclohexa-1,3-diene to give what appeared to be a mixture of the two possible adducts, one of which,



(VI), was obtained crystalline. It was readily aromatised to the diol (VII), which could be oxidised to the corresponding quinone. However, direct pyrolysis of the diol gave the pure dimethyl ether in practically quantitative yield; presumably the necessary oxidation is effected by atmospheric oxygen.

The methods are clearly very useful within the limitations of the methoxycyclohexadienes available. These have been prepared so far only from the products of metal–ammonia reduction of methoxybenzene derivatives. Owing to the structural limitations of dienes prepared in this way, it is not possible in particular to provide compounds with vicinal oxygen atoms in the diene portion. Some of the methoxycyclohexadienes, such as the 1,4-dimethoxy-derivative, are also rather too readily oxidised by the quinone to give good yields in the Diels–Alder reaction. A further limitation is the production of structurally isomeric adducts from unsymmetrical compounds.

Experimental

Juglone Methyl Ether.—The adduct (2 g.) from 1-methoxycyclohexa-1,3-diene and benzoquinone [1] was boiled under reflux in aqueous methanolic potassium hydrogen carbonate (15 c.c.; 5%) for 10 min., poured into water, and extracted with ether, to give 1,4-*dihydro*-5,8-*dihydroxy*-1-*methoxy*-1,4-*ethanonaphthalene* (1·96 g.), m. p. 119—121·5° from ethyl acetate (Found: C, 71·95; H, 6·35. $C_{13}H_{14}O_3$ requires C, 71·5; H, 6·5%). The quinol (208 mg.) was left overnight with acetic anhydride (1 c.c.) in pyridine (2 c.c.). The resulting *diacetyl derivative* had m. p. 148—150° (from benzene–light petroleum) (Found: C, 67·4; H, 6·1. $C_{17}H_{18}O_5$ requires C, 67·5; H, 6·0%). Hydrogenation of the quinol in pure benzene with palladium on charcoal (10%) gave 1,2,3,4-*tetrahydro*-5,8-*dihydroxy*-1-*methoxy*-1,4-*ethanonaphthalene*, m. p. 144—145° (from ethyl acetate–light petroleum) (Found: C, 70·7; H, 7·6. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%).

The above dihydro-quinol (1·79 g.) was shaken in benzene (80 c.c.) with silver oxide (10 g.) for 2 hr. After filtration and evaporation, the yellow 1,4-*dihydro*-1-*methoxy*-1,4-*ethanonaphthalene*-5,8-*dione* (1·67 g.) had m. p. 76—77° (from benzene–light petroleum) (Found: C, 72·4; H, 5·7. $C_{13}H_{12}O_3$ requires C, 72·2; H, 5·6%), $\lambda_{max.}$ 251 mμ (log ε 4·28). It was sublimed at 0·5 mm., to give juglone methyl ether (5-methoxy-1,4-naphthaquinone, m. p. 189° undepressed by an authentic specimen.

5,7-*Dimethoxy*-1,4-*naphthaquinone.*—The adduct [2] from benzoquinone and 1,3-dimethoxycyclohexa-1,3-diene (1 g.), after warming with N-aqueous methanolic ammonia solution or with potassium hydrogen carbonate in methanol, gave, after very careful acidification and crystallisation from methanol, 1,2,3,4-*tetrahydro*-5,8-*dihydroxy*-1-*methoxy*-3-*oxo*-1,4-*ethanonaphthalene* (0·63 g.), m. p. 207—208° (Found: C, 66·5; H, 6·0. $C_{13}H_{14}O_4$ requires C, 66·6; H, 6·0%), $\nu_{max.}$ 1708 cm.$^{-1}$. Warming of the adduct with acid gave a higher yield of somewhat purer material. Acetylation with sodium acetate–acetic anhydride or with isopropenyl acetate gave a *diacetyl derivative*, m. p. 151—153° (Found: C, 64·1; H, 5·6. $C_{17}H_{18}O_6$ requires C, 64·1; H, 5·7%). Oxidation by boiling with silver oxide in chloroform gave the *quinone*, m. p. 148—150° (Found: C, 67·1; H, 5·3. $C_{13}H_{12}O_4$ requires C, 67·2; H, 5·2%). The naphthaquinone containing the enol ether was prepared as follows. The adduct (18·5 g.) in methanol (370 c.c.) and aqueous ammonia (460 c.c.; 10%) was left for 1 hr. The brown solution was extracted with chloroform (5 × 150 c.c.), and the extract rapidly dried and evaporated under reduced pressure. The residue was taken up in benzene (300 c.c.) and refluxed with silver oxide (25 g.) for 20 min. Filtration and evaporation gave a crystalline solid (9·3 g.), a portion of which was crystallised from benzene, to give 1,4-*dihydro*-1,3-*dimethoxy*-1,4-*ethanonaphthalene*-5,8-*dione*, m. p. 122—123° (Found: C, 68·35; H, 5·8. $C_{14}H_{14}O_4$ requires C, 62·3; H, 5·7%).

The above crude quinone was sublimed slowly at 0·5 mm. (bath temp. 120—160°), to give 5,7-dimethoxy-1,4-naphthaquinone (5·3 g.), m. p. 152—154° (from methanol) (Found: C, 66·1; H, 4·6; OMe, 28·8. Calc. for $C_{12}H_{10}O_4$: C, 66·1; H, 4·6; OMe, 28·8%), $\lambda_{max.}$ 258 and 410 mμ (log ε 4·19 and 3·59). It was converted by hydrogenation (Pd–C) into 1,4-*dihydroxy*-5,7-*dimethoxynaphthalene*, m. p. 140—142° (Found: 66·7; H, 5·4. $C_{12}H_{12}O_4$ requires C, 66·4; H, 5·5%), which, on methylation in acetone with potassium carbonate and methyl iodide, gave 1,3,5,8-*tetramethoxynaphthalene*, m. p. 131—132° (Found: C, 67·9; H, 6·4. $C_{14}H_{16}O_4$ requires C, 67·7; H, 6·5%).

1-*Methoxyanthraquinone.*—Crude 1-methoxycyclohexadiene (5·5 g.) and 1,4-naphthaquinone (8·7 g.) were refluxed in dry benzene (100 c.c.) for 3 hr., and the mixture worked up as usual to give 1,4,4a,9a-*tetrahydro*-1-*methoxy*-1,4-*ethanoanthracene*-9,10-*dione* prisms (9·3 g.), m. p. 100—101° (from ether–light petroleum) (Found: C, 75·9; H, 6·0. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%), $\lambda_{max.}$ 225, 254, 295, 304, and 345 mμ (log ε 4·62, 3·16, 3·11, 3·10, and 2·48).

The crude adduct (900 mg.) was added in methanol (7 c.c.) to a solution from sodium (0·3 g.) in methanol (8 c.c.), and after 1 min. 5N-hydrochloric acid (10 c.c.) was added. Chloroform extraction, chromatography on Florisil, and crystallisation from benzene gave 1,4-*dihydro*-9,10-*dihydroxy*-1-*methoxy*-1,4-*ethanoanthracene*, m. p. 192—194° (Found: C, 76·1; H, 6·3. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%), $\lambda_{max.}$ 242·5, 272 (infl.), and 337 mμ (log ε 4·40, 3·69, and 3·73). The total crude product was boiled in benzene with silver oxide (0·7 g.) for 30 min. and the product chromatographed on Florisil, to give 1-*methoxy*-1,4-*ethanoanthraquinone* (170 mg.), m. p. 126—128° (from ether) (Found: C, 76·5; H, 5·2. $C_{17}H_{14}O_3$ requires C, 76·7; H, 5·3%), $\lambda_{max.}$ 243, 268, and 334 mμ (log ε 4·30, 4·15, and 3·47). This quinone (287 mg.) was

heated to 150° for 10 min. and then slowly sublimed at 0·5 mm., to give 1-methoxyanthraquinone (214 mg.), m. p. 172—173°, identical (spectra and mixed m. p.) with an authentic specimen.

1,3-*Dimethoxyanthraquinone.*—The adduct from 1,4-naphthaquinone (3·6 g.) and crude 1,3-dimethoxycyclohexadiene (6 g.) was taken up in methanol (30 c.c.), and 2N-potassium hydroxide (30 c.c.) added. Air was bubbled through the mixture for 15 min., and the precipitated yellow solid (7·06 g.) was filtered off, to give 1,3-*dimethoxy*-1,4-*ethanoanthraquinone* m. p. 135—137° (from benzene) (Found: C, 73·1; H, 5·6. $C_{18}H_{16}O_4$ requires C, 73·0; H, 5·4%). The crude product (433 mg.), after heating and sublimation as above, gave 1,3-dimethoxyanthraquinone (340 mg.), m. p. 151—153°, identical (spectra and mixed m. p.) with an authentic specimen.

1-*Aza-anthraquinone.*—5,8-Dihydroquinoline-5,8-dione (1 g.) and cyclohexa-1,3-diene (3 g.) were heated under reflux in dry benzene (70 c.c.) for 12 hr. The crude adduct, m. p. 106—112°, was dissolved in methanol (12 c.c.) and 2N-potassium hydroxide (4 c.c.). After 10 min. the mixture was acidified to pH 6 and extracted with chloroform (4 × 15 c.c.). The extract was evaporated and the residue refluxed with silver oxide (2·3 g.) in ether (70 c.c.) for 1 hr. The resulting crude quinone, m. p. 130° (decomp.), was sublimed at 220°, to give 1-aza-anthraquinone (0·63 g.), m. p. 273—275°. The tetrahydro-derivative, required for other purposes, was prepared in quantitative yield by hydrogenation in methanol with Adams catalyst, followed by chromatography on alumina (Spence H). The 1,2,3,4-*tetrahydro*-1-*aza-anthraquinone* formed red needles m. p. 182—183° (from methanol (Found: C, 72·3; H, 5·1; N, 6·55. $C_{13}H_{11}NO_2$ requires C, 73·2; H, 5·2; N, 6·6%), $\lambda_{max.}$ 236, 241, 268sh, 276, 290sh, 330sh, and 470 mμ (log ε 4·27, 4·27, 4·32, 4·43, 4·19, and 3·70).

Anthrarufin Dimethyl Ether.—1,4-Dihydro-1-methoxy-1,4-ethanonapthalene-5,8-dione (1·52 g.) in benzene (10 c.c.) was refluxed with crude 1-methoxycyclohexa-1,3-diene (9·5 g.) for 12 min. The initial dark red colour rapidly faded to a pale yellow. The solvent and dihydroanisole were removed under reduced pressure and the residue crystallised from a small amount of ether, to yield a solid (1·2 g.) which gave 1,4,4a,5,8,9a-*hexahydro*-1,5-*dimethoxy*-1,4:5,8-*diethano-anthracene*-9,10-*dione* (VI), m. p. 119—122° (decomp.) (from ether), $\nu_{max.}$ 1660 cm.$^{-1}$ (Found: C, 73·4; H, 6·95. $C_{20}H_{12}O_4$ requires C, 73·6; H, 6·8%). This substance (48 mg.) was dissolved in methanol and heated on a steam-bath with aqueous sodium carbonate (5 c.c.; 10%) for 10 min. After addition of water and adjustment to pH 8·8, the quinol (44 mg.) was extracted with ether, m. p. 213—215° (decomp.) (from benzene) $\nu_{max.}$ (Nujol) 1610 and 3340 cm.$^{-1}$. After heating above the m. p. and cooling to 190° this solidified, m. p. 236—236·5°, undepressed by authentic anthrarufin dimethyl ether (1,5-dimethoxyanthraquinone), m. p. 235—236°. The enedione (232 mg.) was dissolved in ethanol, an equal volume of N-aqueous potassium hydroxide added, and air sucked through for 30 min. After addition of water the precipitated 1,5-dimethoxy-1,4:5,8-diethanoanthraquinone (194 mg.) was filtered off, m. p. 221° (decomp.) (from ethanol), $\nu_{max.}$ 1660 with no band in the 3000 cm.$^{-1}$ region. Heating above the m. p. again produced anthrarufin dimethyl ether, m. p. 235—236°.

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