Chemistry of Quinones. Part 7.[1] Synthesis of Anthracyclinone Analogues *via* Diels–Alder Reactions of 1,4-Anthraquinones

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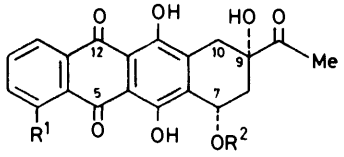
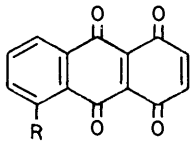
Diels–Alder adducts were formed by reaction of 1,4-anthraquinone with buta-1,3-diene, with 1-acetoxy-, 1-methyl-, 2-methyl-, and 2,3-dimethyl-buta-1,3-diene, and with cyclohexa-1,3-diene. Adducts were also prepared by reaction of 9-chloro-10-hydroxy-1,4-anthraquinone with buta-1,3-diene and with 2-methylbuta-1,3-diene. Some of the linear tetracyclic adducts were transformed to 1,2,3,4-tetrahydro-1,5,12-trihydroxynaphthacene-6,11-quinone (21) and 2-acetyl-1,2,3,4-tetrahydro-2,5,12-trihydroxynaphthacene-6,11-quinone (7). The latter has been converted by other workers into 4-demethoxydaunomycinone (48) and 4-demethoxydaunomycin (8).

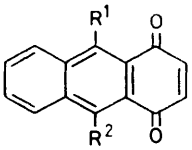
THE useful anti-tumour activity of daunomycin (1) and other anthracyclins has led to great interest in the synthesis of compounds of this general type.[2,3] One of the first and most efficient syntheses of the aglycone daunomycinone (2) used as a key step the Diels–Alder reaction between the 'external' double bond of 5-methoxyquinizarinquinone (3) and 2-acetoxybuta-1,3-diene.[4] This synthetic approach to anthracyclinones is, however, not general, since many dienes, including 2-methylbuta-1,3-diene, add mainly or exclusively to the 'internal' double bond of quinizarinquinone (4).[5,6] Addition to the 'external' double bond can be ensured by blocking the 'internal' double bond by, for example, epoxide formation.[7] Another solution to the problem is to use 1,4-anthraquinones as the dienophiles. We report here Diels–Alder reactions of 1,4-anthraquinone (5) and 9-chloro-10-hydroxy-1,4-anthraquinone (6) with various dienes and the transformation of some of the tetracyclic adducts into anthracyclinone derivatives.



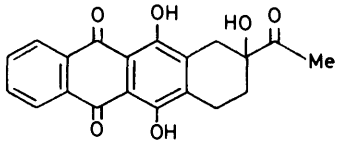
(1) R^1 = OMe, R^2 = daunosamine
(2) R^1 = OMe, R^2 = H
(8) R^1 = H, R^2 = daunosamine
(48) R^1 = R^2 = H



(3) R = OMe
(4) R = H



(5) R^1 = R^2 = H
(6) R^1 = Cl, R^2 = OH
(19) R^1 = OH, R^2 = H



(7)

These include 2-acetyl-1,2,3,4-tetrahydro-2,5,12-trihydroxynaphthacene-6,11-quinone (7) which other workers have converted into 4-demethoxydaunomycin (8),[8,9] an analogue with 8—10 times the biological activity of daunomycin (1).[9]

RESULTS AND DISCUSSION

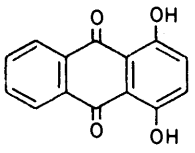
Diels–Alder Reactions.—The use of 1,4-anthraquinone (5) as a dienophile does not appear to have been investigated even though it is readily available in quantity by the reduction (sodium borohydride; acidic work-up) of quinizarin (9).[10] We find it reacts smoothly with buta-1,3-diene, with 1-acetoxy-, 1-methyl-, 2-methyl-, and 2,3-dimethyl-buta-1,3-diene, and with cyclohexa-1,3-diene to give Diels–Alder adducts (10), (11), (12), (13), (14), and (15) respectively. By analogy with other Diels–Alder reactions,[11] these adducts are assumed to have the stereochemistry shown.

9-Chloro-10-hydroxy-1,4-anthraquinone (6) is readily prepared by treating quinizarin (9) with thionyl chloride,[12] and Winkler has investigated its reactions with several dienes.[13] We have repeated the reaction with buta-1,3-diene to see if the adduct (16) could be transformed into anthracyclinone derivatives more readily than the corresponding adduct (10) from 1,4-anthraquinone (5).

In anthracyclinone syntheses based on Diels–Alder reactions, achieving regioselectivity is a major problem. A possible solution is to use reactions between derivatives of 9-substituted-1,4-anthraquinones and unsymmetrical dienes. We therefore repeated the reaction between quinone (6) and 2-methylbuta-1,3-diene to see whether it proceeds with any significant regioselectivity. The product we obtained had properties similar to those reported by Winkler.[13] It was shown by ^{1}H n.m.r. spectroscopy to be a *ca.* 50 : 50 mixture of the two possible adducts (17) and (18). Since our work was completed it has been reported[14] that 9-hydroxy-1,4-anthraquinone (19) also reacts with 2-methylbuta-1,3-diene to give both possible adducts in comparable yields. However, if an excess of boron triacetate is added to the reaction mixture, the Diels–Alder reaction proceeds regiospecifically and gives adduct (20) in good

yield. It is probable that Diels–Alder adducts prepared from dienophiles similar to quinone (19) could be transformed into anthracyclinones using methods similar to those discussed below.

Transformations of the Diels–Alder Adducts.—Having established that 1,4-anthraquinones react readily with various dienes, we sought to transform some of the linear tetracyclic adducts into anthracyclinone analogues, the strategy being to aromatise the adducts to anthracene



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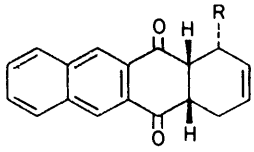
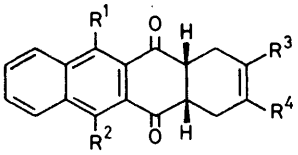
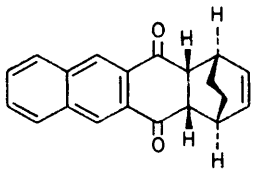


(11) R = OAc
(12) R = Me



(10) $R^1 = R^2 = R^3 = R^4 = H$
(13) $R^1 = R^2 = R^4 = H$; $R^3 = Me$
(14) $R^1 = R^2 = H$; $R^3 = R^4 = Me$
(16) $R^1 = OH$, $R^2 = Cl$, $R^3 = R^4 = H$.
(17) $R^1 = OH$, $R^2 = Cl$, $R^3 = Me$, $R^4 = H$



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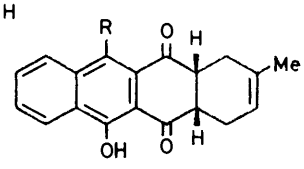
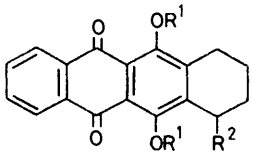


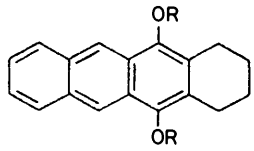
(18) R = Cl
(20) R = H

derivatives which could then be oxidized to 9,10-anthraquinone derivatives. Since this work was completed other synthetic routes which involve the oxidation of anthracene derivatives, prepared by different methods, have been reported.[8,15]

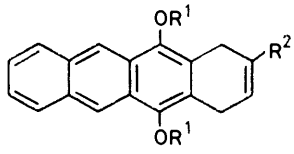
(a) *Synthesis of tetrahydrotrihydroxynaphthacenequinone* (21). Our first objective was the synthesis of the simple known analogue (21).[16,17] The butadiene–1,4-anthraquinone adduct (10) in benzene was selectively hydrogenated using Wilkinson's catalyst [18] and the product reacted with acetic anhydride–sodium acetate to give the anthracene (22). The alternative sequence of conversion into the anthracene (23), followed by hydrogeneration, was experimentally less convenient due to the low solubility of the anthracene (23) in benzene. Chromic acid oxidation of the anthracene (22) gave a mixture of quinones (24)—(26), the proportions being very sensitive to the reaction conditions. Thus, under optimum conditions the yield of the desired diacetoxytetrahydronaphthacenequinone (24) was 80% but under other conditions the yield of the monoacetoxyquinone (25) was 59%. The conversion of derivatives of 1,4-diacetoxyanthracene into 9-acetoxy-1,4-anthraquinones



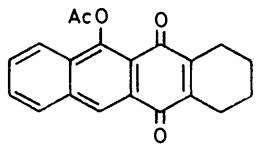
(21) $R^1 = H$, $R^2 = OH$
(24) $R^1 = Ac$, $R^2 = H$
(27) $R^1 = Me$, $R^2 = H$
(31) $R^1 = R^2 = H$
(32) $R^1 = Ac$, $R^2 = Br$
(33) $R^1 = H$, $R^2 = OCOCF_3$
(34) $R^1 = H$, R^2 = -O-daunosamine



(22) R = Ac
(29) R = Me



(23) $R^1 = Ac$, $R^2 = H$
(28) $R^1 = Me$, $R^2 = H$
(39) $R^1 = Ac$, $R^2 = Me$



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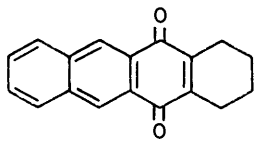

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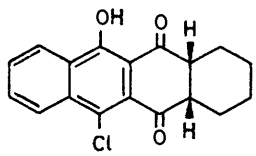

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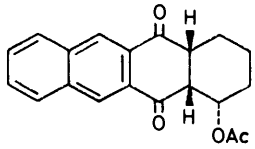

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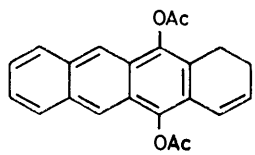


(36)

on treatment with chromic acid has been observed before,[15,19] and such reactions may provide a useful route to compounds of this type.

An attempt to prepare the dimethoxytetrahydronaphthacenequinone (27) by an analogous series of reactions, *i.e.* (10) → (28) → (29) → (27), was unsuccessful because chromic acid oxidation of the dimethoxyanthracene (29) under various conditions gave a

complex mixture of products, the main one being quinone (26).

A shorter, but less efficient, synthesis of the diacetoxytetrahydronaphthacenequinone (24) used the butadiene–9-chloro-10-hydroxy-1,4-anthraquinone adduct (16). The latter was hydrogenated and the product (30) treated with various reagents in an attempt to obtain a quinizarin derivative. The most successful was silver(II) oxide which gave dihydroxytetrahydronaphthacenequinone (31) in 12% yield. Acetylation of this gave the desired quinone (24).

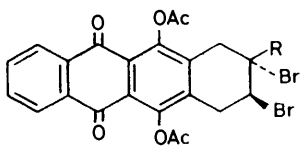
The diacetoxytetrahydronaphthacenequinone (24) was converted into the tetrahydrotrihydroxynaphthacenequinone (21) using the usual approach, *i.e.* benzylic bromination then replacement of the bromide by hydroxy.[16,17] It is, however, interesting to note that treatment of the bromide (32) with silver acetate in trifluoroacetic acid not only displaced the bromide but also hydrolysed the acetoxy-groups to give the dihydroxytrifluoroacetate (33). We have since shown that many α-acetoxyquinones are rapidly hydrolysed by trifluoroacetic acid containing small amounts of water.[1] Hydrolysis of the dihydroxytrifluoroacetate (33) with ammonium hydroxide gave the tetrahydrotrihydroxynaphthacenequinone (21). This has been coupled with daunosamine to give the simple daunomycin analogue (34).[20]

An attempt to synthesise the trihydroxyquinone (21) more directly using the 1-acetoxybutadiene–1,4-anthraquinone adduct (11) was unsuccessful because the hydrogenated adduct (35) reacted with acetic anhydride–sodium acetate to give the olefin (36). Hydrogenation of the latter over Wilkinson's catalyst [18] gave the anthracene (22) discussed above.

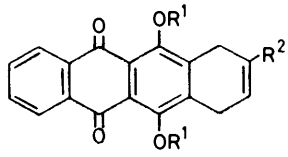
(b) *Synthesis of* 2-*acetyl*-1,2,3,4-*tetrahydro*-2,5,12-*trihydroxynaphthacene*-6,11-*quinone* (7). To prepare this quinone it was necessary to oxidize the anthracene (23) with retention of the olefinic bond. It was successfully protected by formation of the dibromide, but since bromine adds across the central ring of the anthracene moiety at a similar rate, the anthracene (23) was reacted with *two* moles of bromine prior to chromic acid oxidation. This procedure gave the dibromide (37) in excellent yield. Debromination (zinc dust–acetic acid in ether or chromous chloride) gave the known [16] olefin (38).

Using an analogous reaction sequence the 2-methylbutadiene–1,4-anthraquinone adduct (13) was converted [(13) ⟶ (39) ⟶ (40) ⟶ (41)] into olefin (41). Krohn and Rösner have shown that the corresponding ethyl compound (42) can be converted into 4-deoxy-γ-rhodomycinone.[21]

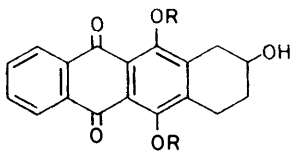
Treatment of olefin (38) with borane followed by alkaline hydrogen peroxide gave a complex mixture, probably because the acetoxy-groups as well as the olefinic group reacted. In agreement with this the corresponding dimethyl ether (43), prepared from olefin (38) by hydrolysis to compound (44) followed by methylation, reacted with the same reagents to give the alcohol (45) in high yield. Demethylation gave the triol (46), which was oxidized to the ketone (47) as described by Lee *et al.*[16] Reaction of this with an excess of ethynylmagnesium bromide and treatment of the crude product with sulphuric acid and mercuric ion gave 2-acetyl-1,2,3,4-tetrahydro-2,5,12-trihydroxynaphthacene-6,11-quinone (7). Since this quinone has been converted into 4-demethoxydaunomycinone (48) [8] and 4-demethoxydaunomycin (8) [9] by other workers, the combination of these and the above reactions constitute a synthetic route to these compounds. An attractive feature of the route is that it uses relatively cheap starting materials and that the early stages can be carried out readily on a large scale without the need for chromatography.



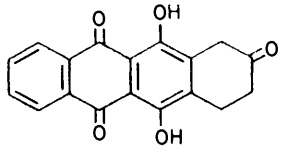
(37) R = H
(40) R = Me



(38) R^1 = Ac, R^2 = H
(41) R^1 = Ac, R^2 = Me
(42) R^1 = Ac, R^2 = Et
(43) R^1 = Me, R^2 = H
(44) R^1 = R^2 = H



(45) R = Me
(46) R = H



(47)

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. Organic solutions were dried with magnesium sulphate. Tetrahydrofuran (THF) was distilled from calcium hydride and stored over molecular sieves. Unless indicated otherwise i.r. spectra were recorded on Nujol mulls, u.v. spectra on ethanol solutions, and ^{1}H n.m.r. spectra on solutions in deuteriochloroform containing tetramethylsilane as an internal reference. In describing ^{1}H n.m.r. spectra the following abbreviations are used: s = singlet, d = doublet, m = multiplet, br = broad.

1,4-*Anthraquinone* (5).[10]—Sodium borohydride (10 g) was added in portions to a vigorously stirred solution of quinizarin (9) (20.0 g) in methanol (400 ml) and the mixture was refluxed for 24 h. The mixture was then cooled and poured into water (1 l). The resultant red solution was acidified with hydrochloric acid and the precipitate filtered off, washed with water, and dried to give 1,4-anthraquinone (5) (17.0 g, 98% yield). Recrystallisation from ethanol gave red needles,* m.p. 216—218 °C (lit.,[22] 225 °C); $\nu_{max.}$ 1 675 cm^{-1}; $\lambda_{max.}$ 234, 288, 299, and 410 nm (log ε 4.67, 3.93, 3.97,

* The pure quinone is yellow but if traces of quinizarin are present it is red.[22] For similar reasons the adduct (13) may have been obtained as pale pink rather than white needles.

and 3.38); δ 6.86 (s, 2-H and 3-H), 7.45 (m, 6-H and 7-H), 7.84 (m, 5-H and 8-H), and 8.34 (s, 9-H and 10-H).

Reaction of 1,4-*Anthraquinone with Buta*-1,3-*diene*.—A mixture of 1,4-anthraquinone (17.0 g), chloroform (500 ml), and buta-1,3-diene (20 ml) was heated at 100 °C under 30 atm of nitrogen in an autoclave for 60 h. The cold reaction mixture was filtered and the solvent evaporated to give the crude adduct (19.8 g) as a pale brown solid. Recrystallisation from acetone gave 1,4,4a,12a-*tetrahydronaphthacene*-5,12-*dione* (10) (16.2 g, 75%) as needles, m.p. 189—191 °C; $\nu_{max.}$ 1 690 and 1 620 cm^{-1}; $\lambda_{max.}$ 266, 348, and 362 nm (log ε 4.81, 3.40, and 3.52); δ 2.40 (br m, 1-H and 4-H), 3.42 (m, 4a-H and 12a-H), 5.72 (s, 2-H and 3-H), 7.64 (m, 8-H and 9-H), 8.04 (m, 7-H and 10-H), and 8.60 (s, 6-H and 11-H) (Found: C, 82.6; H, 5.5. $C_{18}H_{14}O_2$ requires C, 82.5; H, 5.4%).

Reaction of 1,4-*Anthraquinone with* 1-*Acetoxybuta*-1,3-*diene*.—A mixture of 1,4-anthraquinone (5.0 g), 1-acetoxybuta-1,3-diene (12 ml),[23] and chloroform (200 ml) was refluxed for 22 h. The cold mixture was filtered and evaporated to dryness. Recrystallisation of the crude product (5.8 g) from ethanol gave 1-*acetoxy*-1,4,4a,12a-*tetrahydronaphthacene*-5,12-*dione* (11) (4.5 g, 58%) as white needles, m.p. 175—177 °C; $\nu_{max.}$ 1 750 and 1 690 cm^{-1}; $\lambda_{max.}$ 266, 346, and 362 nm (log ε 4.83, 3.60, and 3.62); δ 1.15 (s, OAc), 3.18—3.52 (br m, 4-, 4a-, and 12a-H), 5.53 (br s, 1-H), 6.06 (m, 2-H and 3-H), 7.70 (m, 8-H and 9-H), 8.09 (m, 7-H and 10-H), and 8.71 (s, 6-H and 11-H) (Found: C, 75.5; H, 4.9. $C_{20}H_{16}O_4$ requires C, 75.1; H, 5.0%).

Reaction of 1,4-*Anthraquinone with* 1-*Methylbuta*-1,3-*diene*.—A mixture of 1,4-anthraquinone (2.00 g), 1-methylbuta-1,3-diene (5 ml, commercial mixture of geometrical isomers), and chloroform (50 ml) was refluxed for 72 h. The cold mixture was filtered and evaporated to dryness. Recrystallisation of the crude product from ethanol gave 1-*methyl*-1,4,4a,12a-*tetrahydronaphthacene*-5,12-*dione* (12) (1.28 g, 48%) as a buff powder, m.p. 189—191 °C; $\nu_{max.}$ 1 690, 1 660, and 1 620 cm^{-1}; $\lambda_{max.}$ 267, 348, and 363 nm (log ε 4.70, 3.71, and 3.55); δ 0.85 (d, *J* 7 Hz, Me), 2.0—3.0 (br m, 1-H and 4-H), 3.25—3.70 (br m, 4a-H and 12a-H), 5.70 (br s, 2-H and 3-H), 7.85 (m, 8-H and 9-H), 8.04 (m, 7-H and 10-H), and 8.54 and 8.61 (2 × s, 6-H and 11-H) (Found: C, 82.2; H, 5.6. $C_{19}H_{16}O_2$ requires C, 82.6; H, 5.8%).

Reaction of 1,4-*Anthraquinone with* 2-*Methylbuta*-1,3-*diene*.—A mixture of 1,4-anthraquinone (16.0 g), chloroform (500 ml), and 2-methylbuta-1,3-diene (10 ml) was refluxed for 72 h. The cold mixture was filtered and evaporated to dryness. The crude product (18.8 g) was recrystallised from ethanol to give 2-*methyl*-1,4,4a,12a-*tetrahydronaphthacene*-5,12-*dione* (13) (15.2 g, 72%) as pale pink needles,* m.p. 172—174 °C; $\nu_{max.}$ 1 700 cm^{-1}; $\lambda_{max.}$ 265, 345, and 367 nm (log ε 4.79, 3.57, and 3.56); δ 1.65 (s, Me), 2.32 (br m, 1-H and 4-H), 3.40 (m, 4a-H and 12a-H), 5.42 (br s, 3-H), 7.64 (m, 8-H and 9-H), 8.01 (m, 7-H and 10-H), and 8.56 (s, 6-H and 11-H) (Found: C, 82.8; H, 5.8. $C_{19}H_{16}O_2$ requires C, 82.6; H, 5.8%).

Reaction of 1,4-*Anthraquinone with* 2,3-*Dimethylbuta*-1,3-*diene*.—A mixture of 1,4-anthraquinone (2.00 g), 2,3-dimethylbuta-1,3-diene (5 ml), and chloroform (30 ml) was refluxed for 24 h. The cold mixture was filtered and evaporated to dryness. Recrystallisation of the residue from acetone gave 2,3-*dimethyl*-1,4,4a,12a-*tetrahydronaphthacene*-5,12-*dione* (14) (1.90 g, 68%) as needles, m.p. 229—232 °C; $\nu_{max.}$ 1 687 and 1 623 cm^{-1}; $\lambda_{max.}$ 264, 347, and 362 nm (log ε 4.78, 3.51, and 3.60); δ 1.63 (br s, 2 × Me), 2.33 (br m, 1-H and 4-H), 3.33 (br m, 4a-H and 12a-H), 7.58 (m, 8-H and 9-H), 7.92 (m, 7-H and 10-H), and 8.45 (s, 6-Hand 11-H) (Found: C, 82.9; H, 6.1. $C_{20}H_{18}O_2$ requires C, 82.8; H, 6.2%).

Reaction of 1,4-*Anthraquinone with Cyclohexa*-1,3-*diene*.—A mixture of 1,4-anthraquinone (8.0 g), cyclohexa-1,3-diene (12 ml, 75% pure), and chloroform (150 ml) was refluxed for 72 h. The cold reaction mixture was filtered and then evaporated to dryness. The crude product (12.0 g) was recrystallised from ethanol to give 1,4-*ethano*-1,4,4a,12a-*tetrahydronaphthacene*-5,12-*dione* (15) (6.1 g, 55%) as needles m.p. 202—204 °; $\nu_{max.}$ 1 690 cm^{-1}; $\lambda_{max.}$ 263, 267, 348, and 362 nm (log ε 4.78, 4.80, 3.52, and 3.57); δ 1.2—2.0 (m, $-CH_2CH_2-$), 3.3—3.5 (br m, 1-H, 4-H, 4a-H, and 12a-H), 6.15 (m, vinyl-H), 7.70 (m, 8-H and 9-H), 8.00 (m, 7-H and 10-H), and 8.50 (s, 6-H and 11-H) (Found: C, 83.6; H, 5.7. $C_{20}H_{16}O_2$ requires C, 83.4; H, 5.6%).

9-*Chloro*-10-*hydroxy*-1,4-*anthraquinone* (6).[12]—A mixture of quinizarin (9) (30.0 g) and thionyl chloride (120 g) was refluxed for 30 h, then set aside to cool. 9-Chloro-10-hydroxy-1,4-anthraquinone (6) crystallised out and was collected (25.0 g, 75%). The red needles had m.p. 232—233 °C (lit.,[12] 225—226 °C); $\nu_{max.}$ 1 670 and 1 640 cm^{-1}.

Reaction of 9-*Chloro*-10-*hydroxy*-1,4-*Anthraquinone with Buta*-1,3-*diene*.—A mixture of the quinone (6) (12.0 g), chloroform (500 ml), and an excess of buta-1,3-diene was heated at 100 °C under 30 atm of nitrogen in an autoclave for 60 h. The product was isolated in the usual manner. Recrystallisation of the crude 6-chloro-11-hydroxy-1,4,4a,-12a-tetrahydronaphthacene-5,12-dione (16) (10.0 g) from ethanol gave needles (8.2 g, 57%), m.p. 160—161 °C (lit.,[13] 176 °C from benzene); $\nu_{max.}$ ($CHCl_3$) 1 706 cm^{-1}. The ^1H n.m.r. spectrum was in good agreement with that in the literature.[13]

Reaction of 9-*Chloro*-10-*hydroxy*-1,4-*anthraquinone with* 2-*Methylbuta*-1,3-*diene*.—A mixture of the quinone (6) (11.0 g), and an excess of 2-methylbuta-1,3-diene in chloroform (400 ml) was heated under reflux for 72 h. The product was isolated in the usual manner. Recrystallisation of the crude adduct from chloroform–ethanol gave pale buff needles (11.1 g), m.p. 175—186 °C (lit.,[13] 175 °C), identified as a mixture of 6-chloro-11-hydroxy-2-methyl-1,4,4a-12a-tetrahydronaphthacene-5,12-dione (17) and 11-chloro-6-hydroxy-2-methyl-1,4,4a,12a-tetrahydronaphthacene-5,12-dione (18) (80% yield). It had $\nu_{max.}$ 1 690 and 1 620 cm^{-1}; $\lambda_{max.}$ 258, 278, 379, and 392 nm (log ε 4.73, 4.70, 4.21, and 4.18); δ 1.70 and 1.74 (2 s, ratio 52 : 48, Me), 2.3—2.6 (br m, 1-H and 4-H), 3.2—3.6 (br m, 4a-H and 12a-H), 5.43 (br s, 3-H), 7.6—7.9 (br m, 8-H and 9-H), 8.4—8.6 (br m, 7-H and 10-H), and 14.42 and 14.43 (2 s, ratio 47 : 53, OH). The signals at δ 1.70 and 1.74 became sharper when the sample was irradiated at δ 2.45 or at 5.4.

Conversion of 1,4,4a,12a-*Tetrahydronaphthacene*-5,12-*dione* (10) *into* 5,12-*Diacetoxy*-1,2,3,4-*tetrahydronaphthacene* (22).—(*a*) A solution of the adduct (10) (10.6 g) and tris(triphenylphosphine)rhodium chloride (1.0 g) in benzene (400 ml) at 20 °C was vigorously stirred under hydrogen for 20 h. Evaporation of the solvent gave the crude product contaminated with the catalyst. ^1H N.m.r. analysis showed that the vinyl signal present at δ 5.72 in the starting material had disappeared.

A mixture of the crude hydrogenation product (10.0 g),

* See footnote on page 691.

acetic anhydride (250 ml), and sodium acetate (3 g) was refluxed for 30 min. The mixture was then cooled and added to water (1.5 l). The precipitate was collected, washed with water, and dried. A solution in chloroform was filtered through a column of alumina. The eluate was evaporated and the residue (10.75 g) recrystallised from ethanol to give 5,12-*diacetoxy*-1,2,3,4-*tetrahydronaphthacene* (22) as yellow needles, m.p. 239—241 °C; $\nu_{max.}$ 1 760 cm^{-1}; $\lambda_{max.}$ 252, 260, 334, 350, 370, and 390 nm (log ε 4.43, 5.03, 3.62, 3.90, 3.90, and 3.80); δ 1.82 (br m, 2-H and 3-H), 2.50 (s, OAc), 2.76 (br n, 1-H and 4-H), 7.40 (m, 8-H and 9-H), 7.92 (m, 7-H and 10-H), and 8.22 (s, 6-H and 11-H) (Found: C, 76.2; H, 5.75. $C_{22}H_{20}O_4$ requires C, 75.9; H, 5.8%).

(*b*) A mixture of the adduct (10) (3.5 g), acetic anhydride (50 ml), and sodium acetate (1 g) was refluxed for 30 min. The reaction mixture was cooled and poured into water (500 ml). The resulting precipitate was collected, washed with water, and dried. The crude product (4.2 g, 91%) was recrystallised from glacial acetic acid to give 5,12-*diacetoxy*-1,4-*dihydronaphthacene* (23) as yellow needles, m.p. 274—276 °C; $\nu_{max.}$ 1 760 cm^{-1}; $\lambda_{max.}$ 254, 262, 334, 352, 371, and 392 nm (log ε 4.44, 5.03, 3.63, 3.89, 3.91, and 3.81); δ 2.02 (s, OAc), 3.40 (br s, 1-H and 4-H), 5.93 (br s, 2-H and 3-H), 7.40 (m, 8-H and 9-H), 7.95 (m, 7-H and 10-H), and 8.30 (s, 6-H and 11-H) (Found: C, 76.2; H, 5.2. $C_{22}H_{18}O_4$ requires C, 76.4; H, 5.2%).

A solution of the diacetate (23) (400 mg) and tris(triphenylphosphine)rhodium chloride (40 mg) in benzene (600 ml) was stirred under hydrogen at 20.°C for 20 h. The product, isolated as in the previous hydrogenation, was recrystallised from acetone. This gave 5,12-diacetoxy-1,2,3,4-tetrahydronaphthacene (22) (173 mg, 43%) as needles, m.p. 239—241 °C. It was spectroscopically identical with the sample prepared in (*a*).

Chromic Acid Oxidation of 5,12-*Diacetoxy*-1,2,3,4-*tetrahydronaphthacene* (22).—(*a*) A mixture of chromic anhydride (788 mg), water (1 ml) and glacial acetic acid (10 ml) was added dropwise over 10 min to a solution of 5,12-diacetoxy-1,2,3,4-tetrahydronaphthacene (22) (1.0 g) in glacial acetic acid (50 ml) at reflux temperature. After refluxing for a further 15 min the solution was cooled and added to water (500 ml). The precipitate was collected, washed with water, and dried. T.l.c. analysis indicated the presence of four components, (i)—(iv). The three main ones were isolated by preparative t.l.c. Component (i) (R_F 0.18) was identified as 5,12-diacetoxy-1,2,3,4-tetrahydronaphthacene-6,11-dione (24) (114 mg, 19%), m.p. 234—236 °C (lit.,[24] 235—236 °C); $\nu_{max.}$ 1 770 and 1 675 cm^{-1}; $\lambda_{max.}$ 262 and 347 nm. Component (ii) (R_F 0.32) was identified as 6-*acetoxy*-1,2,3,4-*tetrahydronaphthacene*-5,12-*dione* (25) (354 mg, 59%), m.p. 209—211 °C; $\nu_{max.}$ 1 765 and 1 665 cm^{-1}; $\lambda_{max.}$ 232, 274, 282, 294, and 400 nm (log ε 4.61, 4.40, 4.35, 4.31, and 3.52); δ 1.70 (br m, 2-H and 3-H), 2.32 (br m, 1-H and 4-H), 2.55 (s, OAc), 7.61 (m, 8-H and 9-H), 8.01 (m, 7-H and 10-H), and 8.90 (s, 11-H) (Found: C, 75.0 H, 4.5. $C_{20}H_{16}O_4$ requires C, 75.0; H, 5.0%). Component (iii) (R_F 0.56) was identified as 1,2,3,4-*tetrahydronaphthacene*-5,12-*dione* (26) (78 mg, 13%), yellow needles, m.p. 203—206 °C, $\nu_{max.}$ 1 660 and 1 620 cm^{-1}; $\lambda_{max.}$ 230, 272, 282, 295, and 400 nm (log ε 4.63, 4.46, 4.38, 4.31, and 3.58); δ 1.72 (m, 2-H and 3-H), 2.60 (m, 1-H and 4-H), 7.61 (m, 8-H and 9-H), 7.98 (m, 7-H and 10-H), and 8.40 (s, 6-H and 11-H) (Found: C, 82.5; H, 5.1. $C_{18}H_{14}O_2$ requires C, 82.5; H, 5.4%).

(*b*) A mixture of chromic anhydride (4.3 g), water (12 ml), and glacial acetic acid (48 ml) was added rapidly to a vigorously stirred solution of 5,12-diacetoxy-1,2,3,4-tetrahydronaphthacene (22) (3.0 g) in glacial acetic acid (300 ml) at 70 °C. The mixture was kept at 70 °C for 24 h, then added to water (2 l). The precipitate was collected, washed, and dried to give the crude product (2.6 g, 80%). Recrystallisation from ethanol gave 5,12-diacetoxy-1,2,3,4-tetrahydronaphthacene-6,11-dione (24) as orange needles, m.p. 234—236 °C; spectroscopic data as above.

Preparation of 1,4-*Dihydro*-5,12-*dimethoxynaphthacene* (28).—A vigorously stirred mixture of 1,4,4a,12a-tetrahydronaphthacene-5,12-dione (10) (4.5 g), methyl iodide (6.0 g), anhydrous potassium carbonate (15.5 g), and dry acetone (150 ml) was refluxed for 6 h. The solution was filtered and evaporated to dryness. The residue was dissolved in ether, and the solution washed with water. The ethereal solution was dried, then evaporated to dryness to give the crude product (4.6 g, 92%). Recrystallisation from ethanol gave 1,4-*dihydro*-5,12-*dimethoxynaphthacene* (28) as yellow plate-like crystals, m.p. 135—138 °C; $\nu_{max.}$ 1 662 and 1 625 cm^{-1}; $\lambda_{max.}$ 264, 290, 343, 359, 376, and 396 nm (log ε 5.03, 4.02, 3.63, 3.89, 3.90, and 3.82); δ 3.56 (d, 1-H and 4-H), 3.95 (s, OMe), 6.04 (m, 2-H and 3-H), 7.35 (m, 8-H and 9-H), 8.04 (m, 7-H and 10-H), and 8.57 (s, 6-H and 11-H) (Found: C, 83.1; H, 6.3. $C_{20}H_{18}O_2$ requires C, 82.8; H, 6.3%).

Preparation of the 5,12-*Dimethoxy*-1,2,3,4-*tetrahydronaphthacene* (29).—A mixture of 1,4-dihydro-5,12-dimethoxynaphthacene (28) (2.00 g), benzene (100 ml), and tris(triphenylphosphine)rhodium chloride (100 mg) was stirred under hydrogen at 20 °C and atmospheric pressure for 48 h. The solution was evaporated to dryness, and the residue dissolved in ether and filtered through alumina to remove the catalyst. The ethereal solution was evaporated to dryness to give the crude product (1.98 g, 98%). Recrystallisation from ethanol gave 5,12-*dimethoxy*-1,2,3,4-*tetrahydronaphthacene* (29) as long orange needles, m.p. 132—133 °C; $\lambda_{max.}$ 256, 263, 342, 358, 376, and 396 nm (log ε 4.30, 5.06, 3.64, 3.89, 3.91, and 3.84); δ 1.83 (m, 2-H and 3-H), 3.02 (br m, 1-H and 4-H), 3.92 (s, OMe), 7.42 (m, 8-H and 9-H), 8.02 (m, 7-H and 10-H), and 8.57 (s, 6-H and 11-H) (Found: C, 82.6; H, 6.75. $C_{20}H_{20}O_2$ requires C, 82.3; H, 6.9%).

Chromic Acid Oxidation of 5,12-*Dimethoxy*-1,2,3,4-*tetrahydronaphthacene* (29).—To a stirred solution of compound (29) (100 mg) in glacial acetic acid (20 ml) was added during 10 min chromic acid, made by dissolving chromic anhydride (170 mg) in a mixture of water (1 ml) and glacial acetic acid (3.8 ml). After standing for 24 h at 75 °C, the reaction mixture was poured into water (200 ml). The yellow precipitate was filtered off, washed with water, and dried to give 1,2,3,4-tetrahydronaphthacene-5,12-dione (26) (32 mg, 29% yield), m.p. 200—202 °C, spectroscopically identical with the sample described above.

Conversion of 6-*Chloro*-11-*hydroxy*-1,4,4a,12a-*tetrahydronaphthacene*-5,12-*dione* (16) *into* 5,12-*Dihydroxy*-1,2,3,4-*tetrahydronaphthacene*-6,11-*dione* (31).—The adduct (16) (4.0 g) in benzene (120 ml) was hydrogenated over palladium–charcoal (80 mg) at 20 °C and atmospheric pressure. The catalyst was filtered off, the solvent evaporated, and the crude product recrystallised from ethanol. This gave 6-chloro-11-hydroxy-1,2,3,4,4a,12a-hexahydronaphthacene-5,12-dione (30) (3.7 g) as red platelets, m.p. 165 °C; $\nu_{max.}$ 1 690 and 1 610 cm^{-1}; δ 1.68 (br m, 1—4-H), 3.25 (br m,

4a-H and 12a-H), 7.75 (m, 8-H and 9-H), 8.5 (m, 7-H and 10-H), and 14.7 (s, OH).

Silver(II) oxide [25] was added to the above product (1.0 g) in dioxan (50 ml) and nitric acid (6N, 3 ml) and the mixture was stirred for 1 h at 20 °C. Water (250 ml) was added and the mixture extracted with ether. The dried extracts were evaporated to dryness and the residue recrystallised from ethanol–chloroform. This gave 5,12-dihydroxy-1,2,3,4-tetrahydronaphthacene-6,11-dione (31) (120 mg, 12%), m.p. >300 °C (decomp.) (lit.,[16] >300 °C); $\nu_{max.}$ 1 638 and 1 590 cm^{-1}, identical by i.r. and u.v. spectroscopy with a sample obtained by treating diacetoxyquinone (24) with commercial trifluoroacetic acid.[1]

Conversion of 5,12-*Diacetoxy*-1,2,3,4-*tetrahydronaphthacene*-6,11-*dione* (24) *into* 1,2,3,4-*Tetrahydro*-1,5,12-*trihydroxynaphthacene*-6,11-*dione* (21).—(*a*) A mixture of the quinone (24) (2.00 g), *N*-bromosuccinimide (945 mg), benzoyl peroxide (100 mg), and dry carbon tetrachloride (150 ml) was refluxed for 45 min under dry nitrogen. The solution was then concentrated to *ca.* 20 ml under reduced pressure and cooled. The precipitated succinimide was filtered off and the filtrate evaporated to dryness to give 1-bromo-5,12-diacetoxy-1,2,3,4-tetrahydronaphthacene-6,11-dione (32) (2.39 g, 98%), m.p. 67—69 °C; $\nu_{max.}$ 1 770 and 1 670 cm^{-1}; δ 2.2—2.8 (br m, 2-H, 3-H, and 4-H), 2.50 (s, OAc), 2.51 (s, OAc), 5.6 (br m, 1-H), 7.7 (m, 8-H and 9-H), and 8.15 (m, 7-H and 10-H).

(*b*) A mixture of bromide (32) (1.00 g), silver acetate (458 mg), and trifluoroacetic acid (25 ml) was refluxed for 15 min. The solution was cooled and added to water (200 ml). The red precipitate was filtered off, washed with water, and dried to give the 5,12-dihydroxy-1,2,3,4-tetrahydro-1-trifluoroacetoxynaphthacene-6,11-dione (33) (689 mg, 78%), m.p. >300 °C; $\nu_{max.}$ 1 780 and 1 620 cm^{-1}.

(*c*) A mixture of the dihydroxytrifluoroacetate (33) (150 mg), acetone (150 ml), and dilute ammonium hydroxide (2 ml, 3M) was stirred at 20 °C for 24 h. The solution was concentrated to *ca.* 20 ml, then poured into dilute hydrochloric acid. The red precipitate was collected, washed and dried. Recrystallisation from chloroform gave 1,2,3,4-tetrahydro-1,5,12-trihydroxynaphthacene-6,11-dione (21) as red needles, m.p. 300 °C (decomp.) [lit.,[17] 292—294 °C (decomp.)]; $\nu_{max.}$ 1 620 cm^{-1} (Found: C, 69.45, H, 4.3. Calc. for $C_{18}H_{14}O_5$: C, 69.7; H, 4.55%).

Conversion of 1-*Acetoxy*-1,4,4a,12a-*tetrahydronaphthacene*-5,12-*dione* (11) *into* 5,12-*Diacetoxy*-1,2-*dihydronaphthacene* (36).—(*a*) A vigorously stirred solution of 1-acetoxy-1,4,4a,12a-tetrahydronaphthacene-5,12-dione (11) (2.00 g), benzene (200 ml) and tris(triphenylphosphine)rhodium chloride (200 mg) was hydrogenated at 20 °C and atmospheric pressure for 14 h. The solution was evaporated to give crude 1-acetoxy-1,2,3,4,4a,12a-hexahydronaphthacene-5,12-dione (35) (2.2 g), contaminated with the spent catalyst; δ 1.25 (s, OAc), 1.7 (br s, 2-H and 3-H), 2.5—3.3 (br m, 4-H, 4a-H, and 12a-H), 5.37 (br s, 1-H), 7.65 (m, 8-H and 9-H), 8.06 (m, 7-H and 10-H), and 8.61 (s, 6-H and 11-H).

(*b*) A mixture of the above product (35) (1 g), acetic anhydride (30 ml), and sodium acetate (0.5 g), was heated at 100 °C for 30 min. The solution was then cooled and poured into water (300 ml). The resulting precipitate was filtered off, washed with water, and dried to give the product (1.06 g, 96% yield). Recrystallisation from ethanol gave 5,12-*diacetoxy*-1,2-*dihydronaphthacene* (36) as needles, m.p. 264—266 °C; $\nu_{max.}$ 1 768 cm^{-1}; $\lambda_{max.}$ 264, 275, 285.5, 319, 334, 350, 370, and 391 nm (log ε 4.49, 5.07, 4.13, 4.09, 3.65, 3.91, 3.94, and 3.83); δ 2.50 (s, OAc and 1-H), 2.82 (d, 2-H), 6.14—6.76 (m, 3-H and 4-H), 7.42 (m, 8-H and 9-H), 7.94 (m, 7-H and 10-H), and 8.2 (s, 6-H and 11-H) (Found: C, 76.0; H, 5.4. $C_{22}H_{18}O_4$ requires C, 76.4; H, 5.2%).

Hydrogenation of 5,12-*Diacetoxy*-1,2-*dihydronaphthacene* (36).—A vigorously stirred solution of the above diacetoxy-compound (36) (150 mg), benzene (50 ml), and tris(triphenylphosphine)rhodium chloride (15 mg) was hydrogenated at 20 °C and atmospheric pressure for 40 h. The product, isolated in the usual way, was 5,12-diacetoxy-1,2,3,4-tetrahydronaphthacene (22) (147 mg, 97% yield), m.p. 238—240 °C. Spectral data the same as for the sample prepared above.

Bromination and Chromic Acid Oxidation of 5,12-*Diacetoxy*-1,4-*dihydronaphthacene* (23).—To a stirred solution of compound (23) (5.0 g) in methylene chloride (500 ml) cooled below 0 °C was added dropwise during 15 min a solution of bromine (2 mol. equiv., 4.63 g) in methylene (25 ml). The solvent was evaporated to give an oil. The oil was dissolved in glacial acetic acid (400 ml) and chromic acid [made by dissolving chromic anhydride (7.24 g) in a mixture of water (7 ml) and glacial acetic acid (28 ml)] was added. The mixture was left at 20 °C for 1 h and thereafter at 60 °C for 5 h. The solution was cooled and poured into water (1.2 l). The yellow precipitate was filtered off, washed with water, and dried to give 5,12-*diacetoxy*-2,3-*dibromo*-1,2,3,4-*tetrahydronaphthacene*-6,11-*dione* (37) (7.26 g, 94% yield), m.p. 240—242 °C; $\nu_{max.}$ 1 750 and 1 660 cm^{-1}; $\lambda_{max.}$ 259, 278, and 348 nm (log ε 4.79, 4.64 and 4.52); δ 2.52 (s, OAc), 3.58 (br m, 1-H and 4-H), 4.74 (br s, 2-H and 3-H), 7.70 (m, 8-H and 9-H), and 8.12 (m, 7-H and 10-H) (Found: C, 49.25; H, 2.9. $C_{22}H_{16}O_6Br_2$ requires C, 49.2; H, 2.8%).

Debromination of 5,12-*Diacetoxy*-2,3-*dibromo*-1,2,3,4-*tetrahydronaphthacene*-6,11-*dione* (37).—(*a*) A mixture of the dibromide (37) (1.0 g), zinc dust (5.0 g), glacial acetic acid (10 ml), and sodium-dried ether (400 ml) was stirred at 20 °C for 1 h. The mixture was then filtered and the filtrate washed with water. The ethereal solution was dried and evaporated to give 5,12-*diacetoxy*-1,4-*dihydronaphthacene*-6,11-*dione* (38) (444 mg, 63% yield). Recrystallisation from ethanol gave needles, m.p. 260—262 °C; $\nu_{max.}$ 1 760 and 1 670 cm^{-1}; $\lambda_{max.}$ 260 and 337 nm (log ε 4.64 and 4.37); δ 2.50 (s, OAc), 3.33 (s, 1-H and 4-H), 5.85 (br s, 2-H and 3-H), 7.71 (m, 8-H and 9-H), and 8.17 (m, 7-H and 10-H) (Found: C, 69.6; H, 4.2. $C_{22}H_{16}O_6$ requires C, 70.2; H, 4.3%).

(*b*) To a stirred solution of the dibromide (37) (200 mg) in acetone (100 ml) was added chromous chloride solution [26] (30 ml). After stirring for 1 h at 20 °C the reaction mixture was poured into water (250 ml). The precipitate was filtered off, washed with water, and dried to give the quinone (38) (145 mg, 60% yield). Recrystallisation from ethanol gave needles, m.p. 260—262 °C. The spectral data were identical to those obtained for the product prepared in (*a*).

Preparation of 5,12-*Diacetoxy*-1,4-*dihydro*-2-*methylnaphthacene* (39).—A mixture of 2-methyl-1,4,4a,12a-tetrahydronaphthacene-5,12-dione (13) (10.0 g), acetic anhydride (50 ml), and sodium acetate (2 g) was refluxed for 1 h. The mixture was then cooled and poured into water (1.5 l). The precipitate was filtered off, washed with water, and dried to give 5,12-*diacetoxy*-1,4-*dihydro*-2-*methylnaphthacene* (39) (12.6 g, 97%). Recrystallisation from ethanol gave yellow needles, m.p. 235—238 °C; $\nu_{max.}$ 1 750 cm^{-1}; $\lambda_{max.}$ 251, 258, 279, 350, 367, and 390 nm (log ε 4.26, 4.14, 3.63, 3.15, 3.15, and 3.12); δ 1.87 (s, Me), 2.54 (s, OAc), 3.28 (br m, 1-H and

4-H), 5.60 (br s, 3-H), 7.50 (m, 8-H and 9-H), 7.90 (m, 7-H and 10-H), and 8.20 (s, 6-H and 11-H) (Found: C, 76.4; H, 5.8. $C_{23}H_{20}O_4$ requires C, 76.7; H, 5.6%).

Bromination and Chromic Acid Oxidation of 5,12-*Diacetoxy*-1,4-*dihydro*-2-*methylnaphthacene* (39).—The diacetoxy-compound (39) (3.0 g) was converted into the dibromide (40) using a similar procedure to that given above for the preparation of the dibromide (37). 5,12-*Diacetoxy*-2,3-*dibromo*-2-*methyl*-1,2,3,4-*tetrahydronaphthacene*-6,11-*dione* (40) (3.76 g, 82%) on recrystallisation from ethanol was obtained as yellow needles, m.p. 224—226 °C; $\nu_{max.}$ 1 750 and 1 660 cm^{-1}; $\lambda_{max.}$ 259, 278, and 347 nm (log ε 4.81, 4.67, and 4.53); δ 2.10 (s, Me), 2.52 (s, OAc), 3.61 (m, 1-H and 4-H), 4.70 (br m, 3-H), 7.68 (m, 8-H and 9-H), and 8.13 (m, 7-H and 10-H).

Debromination of 5,12-*Diacetoxy*-2,3-*dibromo*-2-*methyl*-1,2,3,4-*tetrahydronaphthacene*-6,11-*dione* (40).—The dibromide (40) (200 mg) was debrominated with chromous chloride [26] using a procedure similar to that described above. 5,12-*Diacetoxy*-1,4-*dihydro*-2-*methylnaphthacene*-6,11-*dione* (41) (90 mg, 63% yield) recrystallised from ethanol as yellow needles, m.p. 203—205 °C; $\nu_{max.}$ 1 760 and 1 665 cm^{-1}; $\lambda_{max.}$ 259, 275(s), and 340 nm (log ε 4.67, 4.53, and 4.40); δ 1.77 (br s, Me), 2.41 (s, OAc), 2.45 (s, OAc), 3.12 (br m, 1-H and 4-H), 5.51 (br m, 3-H), 7.65 (m, 8-H and 9-H), and 8.10 (m, 7-H and 10-H) (Found: C, 70.6; H, 4.3. $C_{23}H_{18}O_6$ requires C, 70.8; H, 4.6%).

Preparation of 1,4-*Dihydro*-5,12-*dihydroxynaphthacene*-6,11-*dione* (44).—The diacetate (38) (1.0 g) was dissolved in trifluoroacetic acid (10 ml). On heating a red precipitate formed. Water (200 ml) was added and the precipitate filtered off, washed with water, and dried to give 1,4-dihydro-5,12-dihydroxynaphthacene-6,11-dione (44) as deep red needles (766 mg, 99% yield), m.p. >300 °C (lit.,[16] >310 °C); $\nu_{max.}$ 1 628 cm^{-1}; $\lambda_{max.}$ ($CHCl_3$) 259, 458, 484, 507, and 519 nm.

Preparation of 1,4-*Dihydro*-5,12-*dimethoxynaphthacene*-6,11-*dione* (43).—A vigorously stirred mixture of dihydroxyquinone (44) (10.0 g), dimethyl sulphate (15 ml), anhydrous potassium carbonate (50 g), and methyl ethyl ketone (400 ml) was refluxed for 6 h. The solution was then filtered and evaporated to dryness. The residue was taken up in chloroform, washed with water, dried, and the solvent evaporated to give 1,4-dihydro-5,12-dimethoxynaphthacene-6,11-dione (43). Recrystallisation from ethanol gave bright yellow needles (6.47 g, 59% yield), m.p. 190—192 °C (lit.,[16] 190—191 °C); $\nu_{max.}$ 1 670 and 1 595 cm^{-1}.

Conversion of 1,4-*Dihydro*-5,12-*dimethoxynaphthacene*-6,11-*dione* (43) *into* 5,12-*Dimethoxy*-2-*hydroxy*-1,2,3,4-*tetrahydronaphthacene*-6,11-*dione* (45).—A solution of borane in THF (23 ml, 0.75M) was added to a stirred solution of compound (43) (5.0 g) in THF (150 ml) under nitrogen. After 15 min at 20 °C the solution was treated carefully with sodium hydroxide solution (60 ml, 6M) and hydrogen peroxide (16 ml, 30%) then left to stir for a further 15 min at 20 °C. The organic layer was separated and evaporated to dryness. The residue was taken up in chloroform and the solution washed with water, dried, and evaporated to give 5,12-dimethoxy-2-hydroxy-1,2,3,4-tetrahydronaphthacene-6,11-dione (45) as a yellow solid (4.57 g, 87% yield), m.p. 181—182 °C (lit.,[16] 182—183 °C); $\nu_{max.}$ 3 400 and 1 670 cm^{-1}; $\lambda_{max.}$ 210, 226, 262, and 372 nm.

Demethylation of 5,12-*Dimethoxy*-2-*hydroxy*-1,2,3,4-*tetrahydronaphthacene*-6,11-*dione* (45).—A mixture of compound (45) (430 mg), nitrobenzene (20 ml), and aluminium chloride (2 g) was stirred at room temperature for 12 h and then poured into a mixture of ice (100 g), water (50 ml), and concentrated hydrochloric acid (30 ml). The solution was left standing at 20 °C for 7 days. The precipitated red 1,2,3,4-tetrahydro-2,5,12-trihydroxynaphthacene-6,11-dione (46) was collected (220 mg, 55%), m.p. >300 °C (lit.,[16] 313—315 °C); $\nu_{max.}$ 3 420 and 1 615 cm^{-1}; $\lambda_{max.}$ 252, 256(s), 287, 326, 457, 481, and 514 nm.

Oxidation of 1,2,3,4-*Tetrahydro*-2,5,12-*trihydroxynaphthacene*-6,11-*dione* (46).—Compound (46) (200 mg) was oxidised using dicyclohexylcarbodi-imide and dimethyl sulphoxide essentially as described by Lee *et al.*[16] 5,12-Dihydroxy-1,2,3,4-tetrahydronaphthacene-2,6,11-trione (47) (132 mg, 66%) had m.p. >300 °C (lit.,[16] >310 °C); $\nu_{max.}$ 1 720 and 1 630 cm^{-1}.

Conversion of 5,12-*Dihydroxy*-1,2,3,4-*tetrahydronaphthacene*-2,6,11-*trione* (47) *into* 2-*Acetyl*-1,2,3,4-*tetrahydro*-2,5,12-*trihydroxynaphthacene*-6,11-*dione* (7).—Ethylmagnesium bromide (5 mmol) in THF (10 ml) was added dropwise over 3 h to dry THF (20 ml) at 20 °C through which a stream of acetylene as passed. The ketone (47) (103 mg) in THF (20 ml) was added and the mixture stirred vigorously for 80 h at 25 °C. Addition of the mixture to saturated ammonium chloride solution (300 ml) gave a red precipitate. This was collected, washed with water, then added to a vigorously stirred mixture of water (6 ml), concentrated sulphuric acid (1 ml), and yellow mercury(II) oxide (0.1 g). After stirring for 6 h at 60 °C, water (20 ml) was added to the mixture and the insoluble material filtered off, then washed with water, a small amount of ethanol, and ether. This left 2-acetyl-1,2,3,4-tetrahydro-2,5,12-trihydroxynaphthacene-6,11-dione (7) (31 mg, 26%) as a red powder, m.p. 204—206 °C (lit.,[6] 193—195°); $\nu_{max.}$ 3 440 (br), 1 705, and 1 623 cm^{-1}; one spot, R_F 0.24, on t.l.c. [stationary phase, silica gel; chloroform–ethanol (98 : 2) as eluant].

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