Oxidative Coupling. Part 11.[1] Approaches to the Synthesis of Bikaverin

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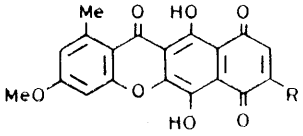
The synthesis of orcinoylhydroquinones has been achieved by photochemical Fries rearrangement of their esters. A study of their oxidation (DDQ) shows that oxidative coupling occurs to produce a spirocyclohexenedione which can be thermally isomerised to the xanthone. The synthesis of a tetracyclic xanthone (related to bikaverin) is described.

BIKAVERIN, an orange-red pigment first obtained from the fungus *Gibberella fujikuroi* [2] was identified by chemical [3] and spectroscopic [4] studies and shown to possess the



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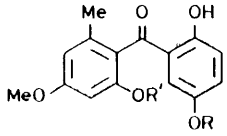

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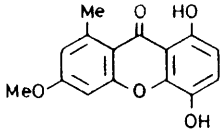

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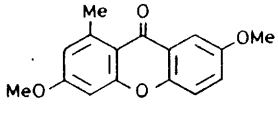

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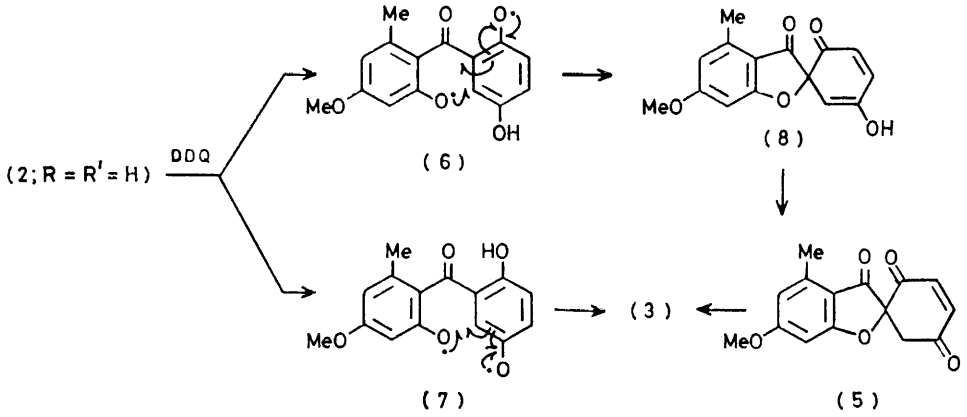
xanthenonobenzoquinone structure (1; R = OMe). Two independent syntheses [5,6] have since confirmed this structural assignment. Our synthetic approach to this ring system stemmed from the already well established synthetic route to xanthones by oxidative coupling of 2,3′-dihydroxybenzophenones.[7,8] For the synthesis of the 'orcinoyl xanthone' section of bikaverin (rings B, C, D) we chose as a model the benzophenone (2; R = R′ = H), since it was expected to give xanthone (3) upon oxidation by analogy with the reported oxidations of 2,2′,5′-trihydroxybenzophenones using potassium hexacyanoferrate(III), which produced 1,4,6-trihydroxyxanthones.[9] Benzophenones (2; R = H or Me, R′ = Me) could not be synthesised by direct Friedel–Crafts condensation of 2,4-dimethoxy-6-methylbenzoyl chloride with the appropriate phenol, but photochemical Fries rearrangement [10] of 4-(2,4-dimethoxy-6-methylbenzoyloxy)methoxybenzene gave benzophenone (2; R = R′ = Me) in 37% yield, while 4-(2,4-dimethoxy-6-methylbenzoyloxy)phenol gave (2; R = H, R′ = Me) in 33% yield under similar conditions. Preparation of these esters was most satisfactorally achieved by direct condensation of 2,4-dimethoxy-6-methylbenzoic acid with the appropriate phenol in the presence of polyphosphoric ester.[11] Confirmation of the structure of benzophenone (2; R = R′ = Me) was obtained by its base-catalysed [12] cyclisation to yield 1-methyl-3,7-dimethoxyxanthen-9-one (4). Demethylation of (2; R = H, R′ = Me) selectively at C-2 was achieved by BCl_3 in CH_2Cl_2 at 0 °C, giving the required benzophenone (2; R = R′ = H).

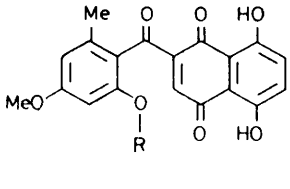
Treatment of (2; R = R′ = H) with potassium hexacyanoferrate(III) gave extensive decomposition in both alkaline and aqueous carbonate solutions but two compounds were produced by oxidation with DDQ.



SCHEME 1

The yellow minor component isolated by t.l.c. (5% yield at 0 °C, 20% at 14 °C) showed a typical xanthone chromophore [$\lambda_{max.}$ (MeOH) 235, 254, 278, and 380 nm] and was identified as 1-methyl-3-methoxy-5,8-dihydroxyxanthen-9-one (3) by mass and n.m.r. spectroscopy. The colourless major component (5) (84% yield at 0 °C, 73% at 14 °C) was isomeric with (3) and upon heating showed a double melting point (145—190 and 220—230 °C)

reminescent of that reported by Whalley and co-workers [9] for 2-(2,4-dihydroxy-3-methylbenzoyl)-*p*-quinone which they found could be thermally converted into 1,4,6-trihydroxy-5-methylxanthen-9-one. However the n.m.r.



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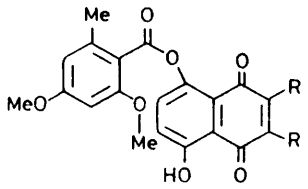

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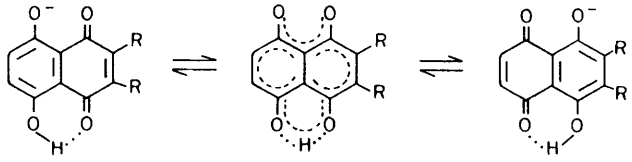
spectrum of our oxidation product showed two AB quartets centred at δ 3.18 and 6.96 with coupling constants of 16 and 10 Hz respectively, the latter quartet corresponded to the methine protons, while the upfield quartet could be assigned to a methylene group associated with a cross-conjugated cyclohexenedione ring. The absence of any acidic protons and the mass spectroscopic loss of keten and diketen supported structure (5) for this compound. The formation of the cross-conjugated cyclohexenedione (5) and xanthone (3) through oxidation of the benzophenone (2; R = R′ = H) could be envisaged (Scheme 1) *via* formation of the diradicals (6) and (7) which could lead directly, through (8) followed by ketonisation to give the stable isomer (5) or through (7), by conventional *ortho*-directed phenol coupling and enolisation, to give (3). Franck and Zeidler [13] have also shown that oxidation of a 2-hydroxybenzoyl-*p*-quinone can lead to a spiro-product. The spiro-compound (5) was stable to hot methanol and acetic acid, but on heating to 200 °C with or without DMSO was converted into xanthone (3). Oxidation of the hydroxybenzophenone (2; R = R′ = H) thus proceeds *via* radical (6) or (7) leading directly to xanthone (3) or through (6) and (8) to the spiro-compound (5) and thence by thermal rearrangement to (3).

Our strategy for the synthesis of bikaverin revolved around the synthesis of the benzophenone (9; R = H) which we considered suitable for oxidative conversion to the benzoxanthone (1; R = H), which in turn could be oxidised to norbikaverin (1; R = OH) in an analogous manner to the conversion of naphthazarin into naphthopurpurin.[13] Condensation of naphthazarin with 2,4-dimethoxy-6-methylbenzoic acid gave the ester (10; R = H) but we were unable to effect its rearrangement to benzophenone (9; R = Me). Fission, but no re-combination, occurred in methanol to give naphthazarin



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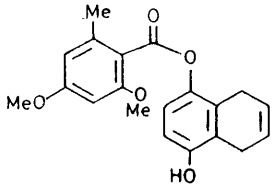
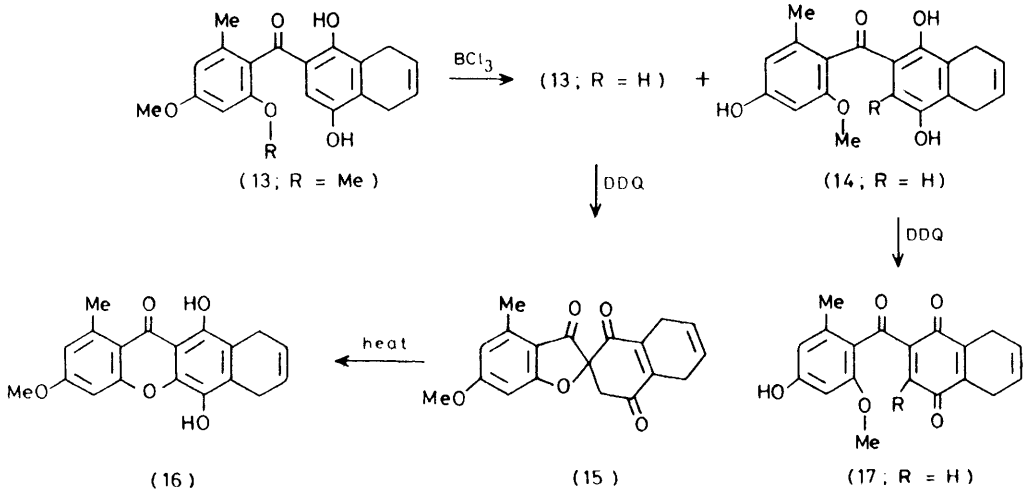


(12)

and dimethylorsellaldehyde, while in benzene no reaction took place, presumably due to the absence of a proton donor. The dichloronaphthazarin ester (10; R = Cl) also failed to give a benzophenone upon photolysis and other Lewis-acid Friedel–Crafts catalysts ($FeCl_3$, $TiCl_4$, $SnCl_4$) were also unsuccessful in achieving rearrangement. We attribute the failure to achieve rearrangement of the naphthazarin esters to be due to the inability of any acylium cation produced to attack the conjugate anion (11; R = H or Cl) due to the latter's stabilisation, re-combination or H-abstraction consequently taking place. In contrast, removal of the *peri*-



(13; R = Me)

(13; R = H)

(14; R = H)

(16)

(15)

(17; R = H)

Scheme 2

carbonyl group enabled Fries rearrangement to recur, thus 1,4-dihydroxy-5,8-dihydronaphthalene gave ester (12), which rearranged smoothly in benzene to give the benzophenone (13; R = Me). Confirmation that the photochemical rearrangement had taken place *ortho* was confirmed by the n.m.r. spectrum of (13; R = Me) which showed a singlet at δ 6.47 corresponding to a single aromatic proton. The u.v. and i.r. spectra also supported a benzophenone structure with a hydrogen-bonded carbonyl group.

Demethylation of benzophenone (13; R = Me) with boron trichloride gave two products, the structures of which were determined by oxidation as indicated in Scheme 2. The slower running component (14; R = H) showed the presence of two non-bonded hydroxy-groups as broad singlets at δ 8.63 and 7.08, respectively. It was decomposed upon treatment with potassium hexacyanoferrate(III) in aqueous sodium carbonate solution, but upon treatment with DDQ a hydroxy-quinone was produced whose spectral data indicated structure (17; R = H) and which upon treatment with methanol gave the methoxyhydroquinone (14; R = OMe). The faster-running component obtained from the demethylation of (13; R = Me) showed the presence of three hydroxy-groups, one hydrogen-bonded (δ 12.27) and the others resonating at δ 8.55 and 7.87. Upon DDQ oxidation (13; R = H) gave a neutral compound which showed properties resembling those of the spiro-compound produced previously (5). It possessed a double m.p. and its n.m.r. indicated the spiro-hydronaphthalenedione structure (15). On heating above its m.p. (>202 °C), it isomerised to xanthone (16), but this product failed to give the required xanthenonobenzoquinone (1; R = H) when it was oxidised with DDQ.

EXPERIMENTAL

All irradiation experiments were carried out with a medium-pressure u.v. lamp in a quartz reaction vessel. U.v. spectra were measured in methanol, i.r. spectra were obtained from KBr discs, and the n.m.r. spectra were recorded in $CDCl_3$ solution unless otherwise stated. Light petroleum was of b.p. 60—80 °C unless stated otherwise.

4-(2′,4′-Dimethoxy-6′-methylbenzoyloxy)methoxybenzene.—2,4-Dimethoxy-6-methylbenzoic acid was converted into its acid chloride,[14] this (2.82 g) was dissolved in dry AnalaR acetone (100 ml) containing 4-methoxyphenol (1.6 g) and K_2CO_3 (anhydrous, 4 g) and the mixture refluxed for 2 h. Filtration and removal of the solvent left an oil which was dissolved in ether and the ethereal solution shaken successively with 2M NaOH (2×), water, and $MgSO_4$ (dry). Removal of the ether left an oil which crystallised from methanol to give *4-(2′,4′-dimethoxy-6′-methylbenzoyloxy)-methoxybenzene* as prisms, m.p. 74—75 °C (852 mg, 22%); $\lambda_{max.}$ 252 (log ε 3.85) and 278 nm (3.71); $\nu_{max.}$ 1 746 cm^{-1} (ester CO); δ 2.41 (3 H, s, Ar-*Me*), 3.80 (6 H, s, 2 × OMe), 3.84 (3 H, s, OMe), 6.36 (2 H, s, 3′,5′-H), and 7.05 (4 H, A_2X_2 q, *J* 9 Hz, Ar-H); *m/e* 302 (1%), 187 (7), 179 (100), 164 (0.6), 85 (16), and 83 (32) (Found: C, 67.5; H, 6.2. $C_{17}H_{18}O_5$ requires C, 67.5; H, 6.0%).

Condensation of the dimethoxy-acid (1 g) and 4-methoxyphenol (633 mg) in $CHCl_3$ (25 ml) with polyphosphoric ester[15] (10 g) gave, after 18 h at room temperature, the above *ester* (647 mg, 42%), m.p. and mixed m.p. 74—75 °C. Replacing chloroform with dimethylformamide gave an improved yield (85%).

2′-Hydroxy-2,4,5′-trimethoxy-6-methylbenzophenone (2; R = R′ = Me).—4-(2′,4′-Dimethoxy-6′-methylbenzoyloxy)methoxybenzene (0.8 g) in AnalaR benzene (500 ml) in an atmosphere of nitrogen was photolysed for 4 h. The benzene was removed under reduced pressure and the residue treated with ether (100 ml); after filtration and removal of the ether-insoluble material the residue was purified by preparative t.l.c. on silica by elution with chloroform–light petroleum (1 : 1) to yield, after crystallisation from ether–light petroleum, *2′-hydroxy-2,4,5′-trimethoxy-6-methylbenzophenone* (2; R = R′ = Me) (300 mg, 37.5%), m.p. 120—123 °C; $\lambda_{max.}$ 227 (log ε 4.43), 260 (4.15), and 368 nm (3.66); $\nu_{max.}$ 3 400 (bonded OH) and 1 635 cm^{-1} (bonded C=O); δ 2.15 (3 H, s, Ar-*Me*), 3 62 (3 H, s, OMe), 3 69 (3 H, s, OMe), 3.84 (3 H, s, OMe), 6.38 (2 H, br s, 3,5-H), 6.74 (1 H, *J* 2.5 Hz, 6′-H), 6.95 (1 H, d, *J* 9 Hz, 3′-H), 7.14 (1 H, dd, d, *J* 2.5 and 9 Hz, 4′-H), and 11.85 (1 H, s, H-bonded OH); *m/e* 302 (5.5%), 287 (1.5), 210 (4.5), 179 (17), 152 (100), and 150 (35) (Found: C, 67.4; H, 6.0. $C_{17}H_{16}O$ requires C, 67.5; H, 6.0%).

4-(2′,4′-Dimethoxy-6′-methylbenzoyloxy)phenol.—2,4-Dimethoxy-6-methylbenzoic acid (1 g), hydroquinone (1.68 g), and polyphosphoric ester (PPE) (25 g) were dissolved in AnalaR DMF (30 ml) and left at room temperature for 24 h. The solution was poured into water and the solid which was produced was filtered to yield *4-(2′,4′-dimethoxy-6′-methylbenzoyloxy)phenol* (1.22 g, 83%), m.p. 123—127 °C. An analytical sample was obtained as prisms by crystallisation from ether–light petroleum, m.p. 127—128 °C; $\lambda_{max.}$ 252 (log ε 3.80) and 280 nm (3.73); $\nu_{max.}$ 3 430 (OH) and 1 715 cm^{-1} (C=O); δ 2.42 (3 H, s, Ar-*Me*), 3.81 (3 H, s, OMe), 3.83 (3 H, s, OMe), 4.90 (br s, OH), 6.37 (2 H, br s, 3′,5′-H), and 6.92 (4 H, A_2X_2 q, *J* 9 Hz, Ar-H); *m/e* 288 (1%), 193 (4.5), 180 (4.5), 179 (100), and 136 (2) (Found: C, 66.8; H, 5.9. $C_{16}H_{16}O_5$ requires C, 66.7; H, 5.6%).

2,4-Dimethoxy-2′,5′-dihydroxy-6-methylbenzophenone (2; R = H, R′ = Me).—The ester (1 g) was dissolved in AnalaR benzene, photolysed, and the reaction worked up as described previously to give the *benzophenone* (2; R = H, R′ = Me) (329 mg, 33%), m.p. 228—229 °C; $\lambda_{max.}$ 225sh (log ε 4.32), 262 (3.99), and 372 nm (3.67); $\nu_{max.}$ 3 250 (OH) and 1 635 cm^{-1} (H-bonded CO); δ(CD_3COCD_3) 2.09 (3 H, s, Ar-*Me*), 3.69 (3 H, s, OMe), 3.85 (3 H, s, OMe), 6.53 (2 H, br s, 3,5-H), 6.70 (1 H, br d, *J* 2.5 Hz, 6′-H), 6.84 (1 H, d, *J* 9 Hz, 3′-H), 7.15 (1 H, dd, *J* 2.5 and 9 Hz, H-4′), 8.10 (1 H, br s, OH), and 11.66 (1 H, s, H-bonded OH); *m/e* 288 (7%), 273 (2), 257 (2), 179 (4.5), and 152 (100) (Found: C, 66.8; H, 5.9. $C_{16}H_{16}O_5$ requires C, 66.7; H, 5.6%).

3,7-Dimethoxy-1-methylxanthen-9-one (4).—The benzophenone (2; R = R′ = Me) (45 mg) was dissolved in methanol (5 ml) containing KOH (5 ml, 30% solution) and the mixture refluxed for 1 h; after cooling the methanol was removed under reduced pressure. The resulting solid was filtered and crystallised from methanol to give *3,7-dimethoxy-1-methylxanthen-9-one* (35 mg, 87%) as needles, m.p. 123—125 °C; $\lambda_{max.}$ 241 (log ε 4.56), 262sh (4.16), 310 (4.19), and 345sh nm (3.79); $\nu_{max.}$ 1 645 cm^{-1} (C=O); δ 2.88 (3 H, s, Ar-*Me*), 3.89 (6 H, s, OMe), 6.69 (2 H, d, *J* 2.5 Hz, 2,4-H), 7.27 (2 H, m, 5- and 6-H), and 7.66 (1 H, d, *J* 2.5 Hz, 8-H); *m/e* 270 (100%), 255 (18), 240 (10), 227 (5.5), 212 (2), 199 (18), and 184 (13). A similar cyclisation occurred when

the benzophenone (2; R = R′ = Me) was dissolved in DMSO (5 ml) and treated with NaH (110 mg, 50%) at room temperature for 2 days. On addition of dilute HCl the dark solid produced was filtered off and purified on t.l.c. to give the *xanthone* (4) (20 mg, 17%), m.p. and mixed m.p. 123—125 °C (Found: C, 70.8; H, 5.4. $C_{16}H_{14}O_4$ requires C, 71.1; H, 5.2%).

2,2′,5′-Trihydroxy-4-methoxy-6-methylbenzophenone (2; R = R′ = H).—The methoxybenzophenone (2; R = H, R′ = Me) (400 mg) was dissolved in dry AnalaR dichloromethane (30 ml), cooled to 0 °C, BCl_3 (5 ml) added, and the mixture sealed and left at room temperature for 5 days. The mixture was diluted with iced water and the organic layer separated, dried, and evaporated to give a solid (408 mg) which crystallised from ether–CH_2Cl_2 as yellow prisms. *2,2′,5′-Trihydroxy-4-methoxy-6-methylbenzophenone* (2; R = R′ = H) (312 mg, 82%) had m.p. 176—179 °C; $\lambda_{max.}$ 229 (log ε 4.27), 263 (3.98), and 371 nm (3.67); $\nu_{max.}$ 3 250 (OH) and 1 635 cm^{-1} (H-bonded CO); δ(CD_3COCD_3) 2.10 (3 H, s, Ar-*Me*), 3.79 (3 H, s, OMe), 6.39 (2 H, overlapping d, *J* 2 Hz, 3,5-H), 6.76 (1 H, d, *J* 2 Hz, 6′-H), 6.83 (1 H, d, *J* 7 Hz, 3′-H), and 7.06 (1 H, dd, *J* 2 and 7 Hz, 4′-H); *m/e* 274 (25%), 259 (7), 257 (8), 165 (11), 138 (100), 137 (100), and 136 (56) (Found: C, 65.7; H, 5.0. $C_{15}H_{14}O_5$ requires C, 65.7; H, 5.1%).

Oxidation of 2-Hydroxybenzophenone (2; R = R′ = H).—(i) $K_3Fe(CN)_6$. The benzophenone (50 mg) was dissolved in methanol (2 ml) and added to a solution of $K_3Fe(CN)_6$ (181 mg) in NaOH solution (35 ml, 2M) at pH 14. After 10 min the solution was acidified with dilute HCl and extracted with ethyl acetate. T.l.c. examination of the product showed only base-line material. A similar oxidation in sodium carbonate solution also showed that extensive decomposition had taken place.

(ii) *DDQ*. The hydroxybenzophenone (2; R = R′ = H) (55 mg) was dissolved in dry benzene (50 ml) at 0 °C, DDQ (45.6 mg) was added, and the mixture was stirred at 0 °C for 16 h. The precipitated $DDQH_2$ was removed by filtration and the filtrate was evaporated under reduced pressure to give a solid which crystallised from ether to give *6-methoxy-4-methylbenzo[6]furan-2-spirocyclohex-3′-ene-2′,3,4′-trione* (5), m.p. 145—190 and 220—230 °C; $\lambda_{max.}$ 215 (log ε 4.4), 226sh (4.3), 238sh (4.0), 278 (4.3), and 318 nm (3.88); $\nu_{max.}$ 1 675, 1 685, and 1 700 cm^{-1} (C=O groups); δ 2.45 (3 H, s, Ar-*Me*), 3.18 (2 H, AB q, *J* 16 Hz, ring-CH_2), 3.87 (3 H, s, OMe), 6.42 (1 H, d, *J* 2 Hz, H-2 or -4), 6.48 (1 H, d, *J* 2 Hz, H-4 or -2), and 6.96 (2 H, AB q, *J* 10 Hz, quinonoid CH=CH); *m/e* 272 (100%), 244 (6), 230 (13), 215 (5), 202 (11), 191 (89), and 190 (63) (Found: C, 66.0; H, 4.4. $C_{15}H_{12}O_5$ requires C, 66.2; H, 4.6%). The mother-liquors were chromatographed on p.l.c. (silica gel) to give a further quantity of the spiro-compound (total weight 46 mg, 84%) and *5,8-dihydroxy-3-methoxy-1-methylxanthen-9-one* (3) (3 mg, 5.5%) which crystallised from ether as yellow needles, m.p. 233—236 °C; $\lambda_{max.}$ 214 (log ε 4.26), 235 (4.35), 254 (4.13), 278 (4.25), 299sh (4.12), and 380 nm (3.57); $\nu_{max.}$ 3 530 (OH) and 1 640 cm^{-1} (H-bonded CO); δ(CD_3COCD_3) 2.80 (3 H, s, Ar-*Me*), 3.94 (3 H, s, OMe), 6,54 (1 H, d, *J* 9 Hz, H-6 or -7), 6.75 (1 H, d, *J* 2 Hz, H-2 or -4), 6.85 (1 H, d, *J* 2 Hz, H-4 or -2), 7.19 (1 H, d, *J* 9 Hz, H-7 or -6), 8.20 (1 H, broad, 5-OH), and 12.44 (1 H, s, 8-OH); *m/e* 272 (100%), 257 (0.3), 229 (5) (Found: C, 66.2; H, 4.1. $C_{15}H_{12}O_5$ requires C, 66.2; H, 4.4%). A repeat oxidation at room temperature gave the spiro-compound (40 mg, 73%) and xanthone (11 mg, 20%).

Conversion of the Spiro-cyclohexenedione (5) *into Xanthone* (3).—The spiro-compound (5) (10 mg) was heated in a vacuum at 200 °C for 15 min and the residue recrystallised from ether to give the *xanthone* (3) (3 mg), m.p. and mixed m.p. 233—235 °C. Heating (5) in methanol or acetic acid gave no rearrangement, but heating to 200 °C in DMSO gave the xanthone.

5,8-Dihydroxy-1,4-naphthoquinone (11; R = H).—Naphthazarin (11; R = H) and its dichloro-derivative (11; R = Cl) were prepared by condensation of 1,4-dimethoxybenzene and maleic anhydride or dichloromaleic anhydride.[16] Naphthazarin had m.p. 230—240 °C (sublimes), δ 7.13 (4 H, s, ring protons) and 12.35 (2 H, s, H-bonded OH) (no splitting of these resonances was observed down to −40 °C); *m/e* 190 (100%), 198 (18), 152 (8), 151 (8), 136 (2), 134 (6), and 108 (11). δ_C 172.9 (26%; C-1, C-4, C-5, C-8), 134.6 (100%; C-2, C-3, C-6, C-7), and 111.9 (7%, C-9, C-10). Dichloronaphthazarin had m.p. 198—199 °C; [16] δ 7.27 (2 H, s, ring protons) and 12.25 (2 H, s, H-bonded OH); *m/e* 260 (50%), 258 (100), 225 (11), 223 (50), 197 (2), 195 (7), and 178 (2); δ_C 177.1 (15%; C-1, C-4), 161.4 (35%; C-5, C-8), 142.7 (9%; C-2, C-3), 131.2 (100%; C-6, C-7), and 110.4 (8%, C-9, C-10). Oxidation of naphthazarin with potassium superoxide and 18-crown-6 in DMSO gave naphthopurpurin, m.p. 200—210 °C,[16] yield >93%.

5-(2′,4′-Dimethoxy-6′-methylbenzoyloxy)-8-hydroxy-1,4-naphthoquinone (10; R = H).—Naphthazarin (600 mg) and 2,4-dimethoxy-6-methylbenzoic acid (930 mg) were dissolved in AnalaR DMF (30 ml) containing PPE (20 g) and the reaction left for 5 days at 80—90 °C before being poured into water. The organic material was extracted into ether and purified on p.l.c. (silica gel, eluting with $CHCl_3$–light petroleum) to give an orange product (632 mg, 54%) which crystallised from ether as orange needles of (10; R = H) m.p. 174—176 °C; [11] $\lambda_{max.}$ 211 (log ε 4.52), 254 (4.04), and 428 nm (3.45); $\nu_{max.}$ 3 420 (bonded OH), 1 738, 1 662, and 1 638 cm^{-1} (C=O groups); δ 2.54 (3 H, s, Ar-*Me*), 3.82 (3 H, s, OMe), 3.87 (3 H, s, OMe), 6.38 (2 H, br d, *J* 2 Hz, H-2 and -4), 6.86 (2 H, d, *J* 2 Hz, H-2 and -3), 7.37 (2 H, q, *J* 9 Hz, H-6 and -7), and 12.35 (1 H, s, H-bonded OH); *m/e* 190 (5%) and 179 (100).

2,3-Dichloro-5-(2′,4′-dimethoxy-6′-methylbenzoyloxy)-8-hydroxy-1,4-naphthoquinone (10; R = Cl).—2,3-Dichloronaphthazarin (500 mg) and 2,4-dimethoxy-6-methylbenzoic acid (570 mg) were condensed in PPE [16] at 80—90 °C as described previously. On work-up and p.l.c. purification in the usual way, orange needles of the *dichloro-ester* (10; R = Cl) were obtained from ether (416 mg, 49%), m.p. 176—179 °C; $\lambda_{max.}$ 219 (log ε 4.58), 263 (4.16), 283 (4.19), and 434 nm (3.56); $\nu_{max.}$ 3 440 (H-bonded OH), 1 745, 1 680, and 1 630 cm^{-1} (C=O); δ 2.52 (3 H, s, Ar-*Me*), 3.82 (3 H, s, OMe), 3.86 (3 H, s, OMe), 6.38 (2 H, br d, *J* 2 Hz, H-2 and -4), 7.42 (2 H, q, *J* 9 Hz, H-6 and -7), and 12.08 (1 H, s, H-bonded OH); *m/e* 258 (2%) and 179 (100) (Found: C, 54.8; H, 3.2. $C_{20}H_{14}Cl_2O_7$ requires C, 70.6; H, 5.9%).

Attempted Rearrangement of Esters (10; R = H) *and* (10; R = Cl).—Ester (10; R = H) (1 g) was dissolved in AnalaR methanol (500 ml) and photolysed for 0.5 h; t.l.c. examination of the solution showed the presence of naphthazarin and 2,4-dimethoxy-6-methylbenzaldehyde only. The dichloro-ester (10; R = Cl) (1 g) produced dichloronaphthazarin and 2,4-dimethoxy-6-methylbenzaldehyde also.

Treatment of the ester with $TiCl_4$ in $CHCl_3$ gave only naphthazarin (or its dichloro-analogue) and 2,4-dimethoxy-6-methylbenzoic acid, as did NaCl–$AlCl_3$ fusion at 200 °C.

5,8-Dihydro-4-(2′,4′-dimethoxy-6′-methylbenzoyloxy)-1-naphthol (12).—2,4-Dimethoxy-6-methylbenzoic acid (1 g) and 5,8-dihydronaphthalene-1,4-diol [17] (1.65 g) were dissolved in AnalaR DMF (30 ml) containing PPE (30 g) and left at room temperature overnight. The solution was poured into water and the resulting oil scratched to produce crystals. The *ester* (12) (1.25 g, 72%) was crystallised from ether–light petroleum as needles, m.p. 181—183 °C; $\lambda_{max.}$ 215 (log ε 4.37), 253 (3.79), and 278 nm (3.65); $\nu_{max.}$ 3 470 (OH) and 1 725 cm^{-1} (ester CO); δ(CD_3COCD_3) 2.37 (3 H, s, Ar-*Me*), 3.28 (4 H, s, 5-H_2 and 8-H_2), 3.81 (3 H, s, OMe), 3.88 (3 H, s, OMe), 5.87 (2 H, s, H-6 and -7), 6.47 (2 H, d, *J* 2 Hz, H-3′ and -5′), and 6.77 (2 H, AB q, *J* 8 Hz, H-2 and 3); *m/e* 340 (0.3%), 193 (4.5), and 179 (100) (Found: C, 70.6; H, 6.2. $C_{20}H_{20}O_5$ requires C, 70.6; H, 5.9%).

2-(2′,4′-Dimethoxy-6′-methylbenzoyl)-5,8-dihydronaphthalene-1,4-diol (13; R = Me).—The ester (12) (1 g) was dissolved in AnalaR benzene (500 ml) and photolysed for 2 h, after which the benzene was removed under reduced pressure and the residue dissolved in ether and purified by p.l.c. (silica gel); elution with ether–light petroleum (1 : 1) gave the *benzophenone* (13; R = Me) as yellow needles from ether, m.p. 196—198 °C; $\lambda_{max.}$ 212 (log ε 4.37), 226 (4.31), 283 (4.04), and 379 nm (3.77); $\nu_{max.}$ 3 480 (OH) and 1 620 cm^{-1} (H-bonded CO); δ 2.12 (3 H, s, Ar-*Me*), 3.32 (4 H, m, 5-H_2 and 8-H_2), 3.67 (3 H, s, OMe), 3.82 (3 H, s, OMe), 4.35 (1 H, broad s, 4-OH), 5.90 (2 H, m, H-6 and -7), 6.35 (2 H, s, H-3′ and -5′), 6.47 (1 H, s, H-3), and 12.23 (1 H, s, 1-OH); *m/e* 340 (56%), 325 (6), 309 (18), 188 (100), 179 (18), 153 (13), and 152 (79) (Found: C, 70.5; H, 5.8. $C_{20}H_{20}O_5$ requires C, 70.6; H, 5.9%).

5,8-Dihydro-2-(2′-hydroxy-4′-methoxy-6′-methylbenzoyl)-naphthalene-1,4-diol (13; R = H).—The 2′-methoxybenzophenone (13; R = Me) (250 mg) was dissolved in dry AnalaR CH_2Cl_2 (30 ml), cooled to 0 °C, and BCl_3 (5 ml) added; after 3·5 days at room temperature the solution was washed with cold water, dried, evaporated under reduced pressure, and the residue separated by p.l.c. (silica gel) using ether–light petroleum (1 : 1) to give three major bands. The slower-running band yielded a solid (52 mg) which was identified as starting material, m.p. and mixed m.p. 196—198 °C; the second band produced a solid (33 mg, 17%) which crystallised from benzene as yellow needles to give the *2′-hydroxybenzophenone* (13; R = H), m.p. 197—202 °C and 256—258 °C; $\lambda_{max.}$ 227 (log ε 4.22), 283 (3.97), and 378 nm (3.71); $\nu_{max.}$ 3 425 (OH), and 1 635 cm^{-1} (H-bonded CO); δ(CD_3COCD_3) 2.08 (3 H, s, Ar-*Me*), 3.29 (4 H, s, 5-H_2 and 8-H_2), 3.78 (3 H, s, OMe), 5.90 (2 H, br s, H-6 and -7), 6.39 (2 H, br s, H-3′ and -5′), 6.63 (1 H, s, H-3), 7.87 (1 H, br d, 4-OH), 8.55 (1 H, br s, 2′-OH), and 12.29 (1 H, s, 1-OH); *m/e* 326 (50%), 309 (3.5), 189 (89), and 188 (100) (Found: C, 69.6; H, 5.8. $C_{19}H_{18}O_5$ requires C, 69.9; H, 5.5%).

The faster-running band yielded a solid (42 mg, 22%) which crystallised from ether as yellow prisms of the *4′-hydroxybenzophenone* (14; R = H), m.p. 256—258 °C; $\lambda_{max.}$ 212 (log ε 4.41), 226 (4.32), 282 (4.08), and 378 nm (3.79); $\nu_{max.}$ 3 340 (OH) and 1 635 cm^{-1} (H-bonded CO); δ(CD_3COCD_3) 2.07 (3 H, s, Ar-*Me*), 3.29 (4 H, s, 5-H_2 and 8-H_2), 3.64 (3 H, s, OMe), 5.90 (2 H, br s, H-6 and -7), 6.41 (2 H, br s, H-3′ and -5′), 6.55 (1 H, s, H-3), 7.88 (1 H, s, 4-OH), 8.64 (1 H, s, 4′-OH), and 12.28 (1 H, s, 1-OH) (Found: C, 69.7; H, 5.6. $C_{19}H_{18}O_5$ requires C, 69.9; H, 5.5%).

Oxidation of 2′-Hydroxybenzophenone (13; R = H).—(i) $K_3Fe(CN)_6$. The 2′-hydroxybenzophenone (13; R = H) (5 mg) was dissolved in Na_2CO_3-buffered NaOH solution (2 ml), $K_3Fe(CN)_6$ (20 mg) in water (2 ml) added, and the mixture left at room temperature for 30 min. After acidification and extraction with ether, t.l.c. indicated that decomposition had taken place, only base-line material being present.

(ii) *DDQ*. The 2′-hydroxybenzophenone (13; R = H) (40 mg) was dissolved in dry AnalaR benzene (20 ml), DDQ (28 mg) added, and the mixture stirred at room temperature overnight. After work-up in the usual way a yellow oil remained, which after p.l.c. on silica gel eluting with benzene gave a solid (22 mg) which crystallised from ether as colourless prisms. *2,3,5,8-Tetrahydro,-6′-methoxy-4′-methylnaphthalene-2-spiro-2′-benzo*[b]*furan-1,3′,4-trione* (15) showed a double m.p. at 160—170 °C, re-solidifying and re-melting at 238—241 °C; $\lambda_{max.}$ 219 (log ε 4.46), 235 (4.51), 282 (4.48), and 317 nm (4.16); $\nu_{max.}$ 1 703, 1 677, and 1 670 cm^{-1} (CO); δ 2.45 (3 H, s, Ar-*Me*), 3.08 (2 H, AB q, *J* 16 Hz, CH_2-2), 3.23 (4 H, d, *J* 8 Hz, 5-H_2 and 8-H_2), 3.90 (3 H, s, OMe), 5.82 (2 H, br s, H-6 and -7), 6.48 (1 H, br s, H-3′ or -5′), and 6.52 (1 H, d, *J* 2 Hz, H-5′ or -3′); *m/e* 324 (100%), 322 (35), 307 (7), 296 (4.5), and 280 (10) (Found: C, 69.7; H, 5.2%; *M*$^+$, 324.099 5. $C_{19}H_{16}O_5$ requires C, 70.3; H, 5.0%; *M*, 324.099 7).

Oxidation of 4′-Hydroxybenzophenone (14; R = H). The 4′-hydroxybenzophenone (14; R = H) (25 mg) was dissolved in dry benzene (5 ml) and dioxan (5 ml), DDQ (18 mg) was added, and the solution stirred overnight. After work-up a dark oil was isolated which crystallised from ether to give the *5,8-dihydro-1,4-naphthoquinone* (17; R = H), m.p. 220—224 °C; $\lambda_{max.}$ 210 (log ε 4.41), 246 (3.90), 281 (3.68), and 310 nm (3.54); $\nu_{max.}$ 3 380 (OH) and 1 660—1 630 cm^{-1} (CO); δ 2.40 (3 H, s, Ar-*Me*), 3.07 (4 H, s, 5-H_2 and 8-H_2), 3.63 (3 H, s, OMe), 5.85 (2 H, s, H-6 and -7), 6.28 (1 H, d, *J* 2.5 Hz, H-3′ or -5′), 6.40 (1 H, d, *J* 2.5 Hz, H-5′ or -3′), 6.63 (1 H, s, H-3), and 8.79 (1 H, s, 4′-OH); *m/e* 326 (8%), 324 (11), 322 (14), 189 (20), 188 (20), and 165 (100) (Found: *M*$^+$, 324.099 5. $C_{19}H_{16}O_5$ requires *M*, 324.099 7).

2-(2′-Methoxy-4′-hydroxy-6′-methylbenzoyl)-3-methoxy-5,8-dihydro-1,4-naphthoquinone (17; R = OMe).—The quinone (17; R = H), (5 mg) was refluxed in methanol (2 ml) for 1 h. Removal of the solvent left an oil which crystallised from ether to give the *methoxybenzophenone* (17; R = OMe) (2 mg) as yellow needles, m.p. 236—239 °C; $\lambda_{max.}$ 222 (log ε 4.01), 281 (3.78), and 376 nm (3.39); *m/e* 356 (0.3%), 326 (32), 189 (89), and 188 (100) (Found: *M*$^+$, 356.125 6. $C_{20}H_{20}O_6$ requires *M*, 356.125 9).

7,10-Dihydro-6,11-dihydroxy-3-methoxy-1-methylbenzoxanthen-12-one (16).—The dihydrospiro-compound (15) (12 mg) was sublimed under vacuum to give a yellow solid (11 mg) which crystallised from methanol, m.p. 238—241 °C; $\lambda_{max.}$ 227 (log ε 4.30), 252 (4.22), 271 (4.41), 293 (4.38), and 380 nm (3.4); $\nu_{max.}$ 3 510 (OH) and 1 635 cm^{-1} (H-bonded CO); δ(CD_3COCD_3) 2.45 (3 H, s, Ar-*Me*), 3.27 (4 H, s, 5-H_2 and 8-H_2), 3.94 (3 H, s, OMe), 5.85 (2 H, s, H-2 or -4), 6.75 (2 H, s, H-4 or -2), and 12.44 (1 H, s, 8-OH), *m/e* 324 (14%), 323 (63), 322 (100), 321 (50), 307 (1.5), 283 (5), 279 (9), and 277 (6), (Found: *M*$^+$, 324.099 5. $C_{19}H_{16}O_5$ requires *M*, 324.099 7).

Oxidation of Xanthone (16).—The xanthone (16) (5 mg) was dissolved in dry AnalaR benzene (5 ml) and dioxan (5 ml), DDQ (10 mg) was added, and the mixture refluxed for

1 h. After work-up in the usual way, t.l.c. indicated only base-line material being present.

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