Synthesis of the Aphin-related (±)-7,9-Dideoxyquinone A and (±)-7,9-Dideoxyquinone A'

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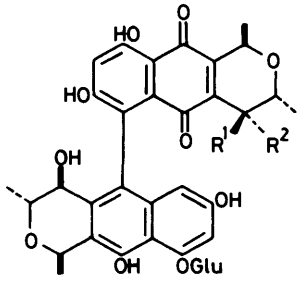
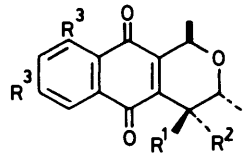
The oxidative cyclisation of 3-(1-hydroxyethyl)-,1,4-dimethoxy-2-prop-1-enylnaphthalene with four equivalents of ceric ammonium nitrate to afford two 4-hydroxy-1,3-dimethylnaphtho[2,3-*c*]pyran-5,10-quinones with the same stereochemistry as quinones A and A', derivatives of the aphid pigments protoaphin-*fb* and protoaphin-*sl*, is described. Certain aspects of the mechanism have been established.

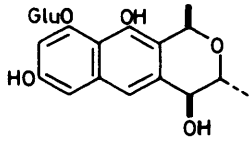
Considerable interest has recently been shown in quinones containing the naphtho[2,3-*c*]pyran ring system.[1] Earlier examples include the aphid pigments protoaphin-*fb* (1) and protoaphin-*sl* (2), each shown [2] to be binaphthyl derivatives containing two such ring systems, the one as a 5,10-quinone and the other as a naphthyl glucoside. Reductive cleavage of protoaphin-*fb* (1) gave quinone A (3) together with glucoside B (9), while protoaphin-*sl* on similar treatment afforded quinone A' (4), epimeric with quinone A at C-4, together with the same glucoside B. Quinone A and glucoside B were subsequently recombined [3] to protoaphin-*fb*; a synthesis of both quinone A and glucoside B would therefore constitute a synthesis of (1), but hitherto neither moiety has been prepared. We now report [4] a synthesis of the 7,9-dideoxy derivatives of both quinone A and quinone A' (5) and (6), respectively, as their racemates, in which the correct stereochemistry about the pyran ring is achieved in a novel cyclisation.



(1) R^1 = OH, R^2 = H
(2) R^1 = H, R^2 = OH



(3) R^1 = R^3 = OH, R^2 = H
(4) R^1 = H, R^2 = R^3 = OH
(5) R^1 = OH, R^2 = R^3 = H
(6) R^1 = R^3 = H, R^2 = OH
(7) R^1 = OAc, R^2 = R^3 = H
(8) R^1 = R^3 = H, R^2 = OAc



(9)

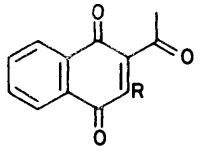
Discussion

2-Acetyl-1,4-naphthoquinone (10) [5] was propylated with butanoic acid in the presence of silver nitrate and potassium peroxodisulphonate to give quinone (11). This was reductively methylated to the dimethoxynaphthalene (12). Compound (12) was brominated with *N*-bromosuccinimide in the presence of either di-t-butyl peroxide or dibenzoyl peroxide to afford the benzylic bromide (13), a process which was confirmed by the ^{1}H n.m.r. spectrum of the product in which the benzylic methylene signal at δ 3.69 in (12) was replaced by a one-proton multiplet at δ 5.42 in (13). Dehydrobromination of the structurally related benzylic bromides (14) [6] and (15) [7] to (16) and (17), respectively, was readily effected in high yield by boiling in lutidine. However, in the case of crude (13), the yield of the required olefin (18) was low (10%), the transformation being accompanied by extensive decomposition. Bromide (13) was best converted into olefin (18) with the base 1,5-diazabicyclo[4.3.0]non-5-ene in dimethylformamide at 45 °C, in a yield of 65%. That solely the *trans*-olefin had been formed was evidenced by the large coupling constant between the olefinic protons (*J* 16 Hz).

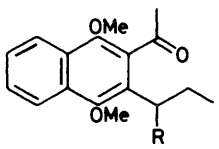
The crowded ketone (18) was slowly reduced to the corresponding alcohol (19) with sodium borohydride in ethanol; in methanol, reduction failed owing to competitive reaction of borohydride with the solvent.[8] Alternatively, lithium aluminium hydride could be used. In a large-scale preparation of alcohol (19), the corresponding acetate (20) was also isolated in a yield of 4% by column chromatography, presumably through transesterification by the eluant ethyl acetate.

Oxidation of the dimethoxynaphthalene (19) with argentic oxide [9] gave the somewhat unstable quinone (21), which showed no tendency to undergo spontaneous cyclisation to the naphtho[2,3-*c*]pyran ring system by intramolecular nucleophilic addition of a hydroxy group to the adjacent alkenyl group.

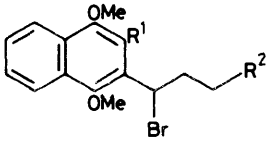
Alternative oxidation of (19) with four moles of ceric ammonium nitrate took a different course, two products with markedly different R_F values being isolated. The ^{1}H n.m.r. spectra of each of these compounds showed, in addition to four aromatic protons and two pairs of doublets due to two methyl groups, three one-proton signals in the δ 4—5 region. For the compound of higher R_F these were a doublet of quartets at δ 4.92 (*J* 7 and 1.5 Hz), a doublet of doublets at 4.47 (*J* 8 and 1.5 Hz), and a doublet of quartets at δ 3.90 (*J* 8 and 6.5 Hz); on this basis structure (5) was assigned, the signals being respectively due to 1-H, 4-H, and 3-H. The large coupling constant of 8 Hz between 3-H and 4-H indicates an arrangement close to *trans*-diaxial between these two protons, the C-3 methyl and C-4 hydroxy groups therefore being equatorial and pseudoequatorial, respectively. The small coupling constant (1.5 Hz) suggests long-range coupling between the pseudoaxial 4-H and 1-H in the pseudoequatorial configuration, the C-1 methyl therefore being pseudoaxial. For the compound of lower R_F, the corresponding signals were a sharp quartet at δ 5.00 (*J* 7 Hz), a sharp doublet at δ 4.52 (*J* 2.5 Hz), and a doublet of quartets at δ 4.00 (*J* 2.5 and 6.5 Hz), allowing the assignment of structure (6). Here, the small coupling constant of 2 Hz between 3-H and 4-H implies that 3-H is axial and 4-H is pseudoequatorial; the C-3 methyl is therefore equatorial and the C-4 hydroxy group pseudoaxial.



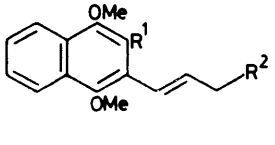
(10) R = H
(11) R = Pr^n



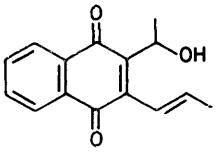
(12) R = H
(13) R = Br



(14) R^1 = H, R^2 = CO_2Me
(15) R^1 = Br, R^2 = Et



(16) R^1 = H, R^2 = CO_2Me
(17) R^1 = Br, R^2 = Et
(18) R^1 = Ac, R^2 = H
(19) R^1 = CH(OH)Me, R^2 = H
(20) R^1 = CH(OAc)Me, R^2 = H



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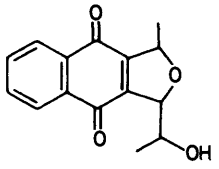

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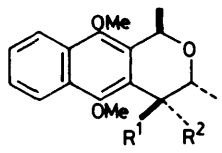
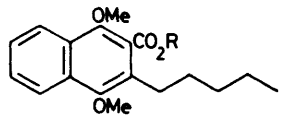
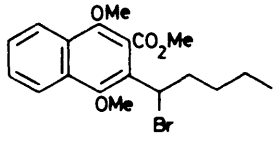


(23) R^1 = OH, R^2 = H
(24) R^1 = H, R^2 = OH



(25) R = H
(26) R = Me



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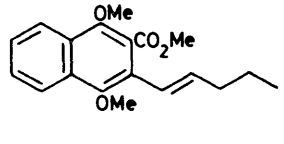

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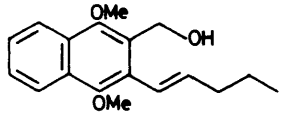

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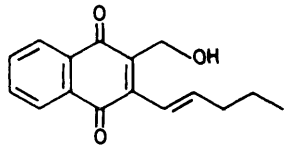

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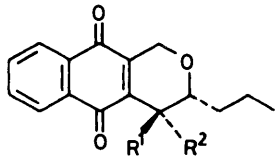
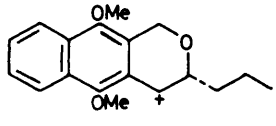


(31) R^1 = OH, R^2 = H
(32) R^1 = H, R^2 = OH
(33) R^1 = ONO_2, R^2 = H
(34) R^1 = H, R^2 = ONO_2



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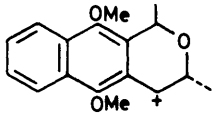

(36)

The lack of long-range coupling between the 1-H and 4-H protons means that 1-H is also pseudoequatorial, the C-1 methyl thus being pseudoaxial. These assignments are entirely consistent with those made for the naturally derived 7,9-dimethoxy analogues.[10] The alternative naphthofuranquinones (22) could be excluded since acetylation of the hydroxy group, affording the acetates (7) and (8), respectively,[10] strongly deshielded the doublet of doublets at δ 4.47 in the case of (5) and the doublet at δ 4.52 in the case of (6).

Mechanistic insight into the oxidative cyclisation was sought. First, the question was raised as to whether the observed, very specific stereochemistry occurred at cyclisation or subsequently by equilibration of a stereoisomeric mixture *via* enolisation of 1-H and 4-H at the quinonoid level; the reaction solutions do in fact become acidic during oxidation. The latter possibility was excluded when the reaction was performed in deuterium oxide and no incorporation of deuterium took place. A second question that arose was whether oxidation preceded cyclisation, requiring quinone (21) as an intermediate. However this quinone, when treated with two moles of ceric ammonium nitrate, did not cyclise to (5) and (6), suggesting cyclisation occurs prior to oxidation. This was confirmed by treating the dimethoxynaphthalene (19) with two moles of oxidant. Chromatography of the reaction mixture, which contained traces of the quinones (5) and (6), gave rise to the two naphthopyrans (23) (9%) and (24) (22%). Oxidation of compound (24) afforded the corresponding quinone (6) in good yield. The ^1H n.m.r. spectra of the intermediates (23) and (24) closely resembled those of the corresponding quinones although, not surprisingly, that of naphthalene (23) showed no long-range coupling between 1-H and 4-H observed in the case of the related quinone (5).

With regard to the stereochemistry of the pyran ring, one would expect that, upon cyclisation, the preferred configuration of the bulkier group at C-3 would be equatorial, while that at C-1 (and C-4) would be pseudoaxial to minimise *peri*-interaction with the neighbouring methoxy groups. Thus the C-1 and C-3 methyls are respectively pseudoaxial and equatorial. On attachment, the C-4 hydroxy group shows preference for the pseudoaxial configuration [see relative yields of (5) and (6)], but two factors presumably mitigate against this being the sole orientation (*cf.* the C-1 methyl); first, the steric requirement of a hydroxy group is much less than that of methyl, and secondly, a pseudoequatorial hydroxy group, being closer to the *peri*-oxygen, can more effectively intramolecularly hydrogen-bond with it. This is supported by compounds (23) and (5) with pseudoequatorial hydroxy groups having higher R_F values than the related (24) and (6).

The generality of the oxidative cyclisation of related naphthalenes was investigated. The naphthoic acid (25) [7] was methylated to afford the ester (26), which was brominated with *N*-bromosuccinimide to give the benzyl bromide (27). This was readily dehydrobrominated in boiling lutidine to the *trans*-olefin (28) [93% from (26)] (*J* 16 Hz), which was in turn reduced to the corresponding alcohol (29) using lithium aluminium hydride.

The dimethoxynaphthalene (29) was oxidised with argentic oxide, giving the relatively unstable quinone (30) as the sole product. On the other hand, when compound (29) was oxidised with four moles of ceric ammonium nitrate, five products were isolated under the conditions used. The un-

saturated quinone (30) was identical with material from the argentic oxide reaction. The remaining four compounds were readily identified as the naphthopyranquinones (31)—(34) from their ^{1}H n.m.r. spectra, the stereochemistry of each compound being derived from the coupling constants of the four protons attached to the pyran ring. For compound (32) [once again of lower R_F than compound (31)], the pseudo-equatorial proton 1-H appeared as a sharp doublet at δ 4.90, geminally coupled (*J* 19 Hz), but without long-range coupling to the pseudoequatorial 4-H. The latter proton appeared as a somewhat broadened singlet at δ 4.60 which collapsed to a triplet (*J* 2 Hz) on shaking with deuterium oxide, being then equally coupled to the axial 3-H and the pseudoaxial 1-H. The axial proton 1-H at δ 4.42 appeared as a doublet of doublets (*J* 19 and 2 Hz). 3-H Gave a doublet of doublet of doublets at δ 3.45 (*J* 2, 6, and 7 Hz) which collapsed to a doublet of doublets (*J* 6 and 7 Hz) on irradiation at 4-H. Compound (31), on the other hand, showed long-range coupling between both 1-H protons and the pseudoaxial 4-H, although the latter was obscured by partial overlap with the pseudoaxial 1-H. Proton 3-H appeared as a doublet of triplets (*J* 2 and 8 Hz) at δ 3.47 which collapsed to a doublet of doublets (*J* 2 and 8 Hz) on irradiation at 4-H, while irradiation of the adjacent propyl methylene group collapsed 3-H to a doublet with large coupling constant (8 Hz), showing 3-H and 4-H to be axial and pseudoaxial, respectively.

The major difference observed for the spectra of the remaining two quinones (33) and (34) was that 4-H was strongly deshielded relative to the two congeners just discussed. Thus, a comparison of the spectrum of (34) with (32) showed in (34) a low-field triplet (*J* 2 Hz) at δ 6.20 for 4-H, being equally coupled to 3-H and the pseudoaxial 1-H at δ 4.45, which appeared as a double doublet (*J* 2 and 19 Hz). The pseudo-equatorial 1-H, being more deshielded by the *peri*-carbonyl, showed only geminal coupling (*J* 19 Hz) at δ 4.96; no long-range coupling to the pseudoequatorial 4-H would be expected.

Compound (33) showed 4-H strongly deshielded at δ 6.00, as a multiplet. Both 1-H signals coincided at δ 4.65.

The formation of these four naphthopyranquinones implied the intermediacy of the carbonium ion (35), benzylic to naphthalene and also stabilised by the *o*-methoxy group. This intermediate presumably arose from naphthalene (29) by a process involving two one-electron oxidative steps by cerium(IV). This carbonium ion could be trapped competitively by the nucleophiles water and nitrate. Presumably a related carbonium ion (36) was involved in the formation of the naphthopyrans (23) and (24) on oxidation of the alcohol (19).

An attempt was made to favour attack by water, by adding more water. However this caused precipitation of the starting material. The problem was solved by maintaining a constant water : acetonitrile ratio, but increasing this solvent volume four-fold while using the same masses of compound (29) and oxidant; thus water was increased relative to nitrate. Under these conditions, only the quinonoid alcohols (31) and (32) were formed in appreciable quantities. Traces of the nitrates (33) (<3%) and (34) (<2%) and none of the quinone (30) were isolated. On the other hand, if water was excluded, the reaction mixture was far more complicated and it was not further investigated. However, if small amounts of water were present, the relative yields of the nitrate esters (33) and (34) were increased.

No compounds other than those described were observed in the product mixtures.

Thus certain aspects of the mechanism of the oxidative cyclisation can be explained. However the factors leading to the initial cyclisation need further study, and these are being investigated.

Experimental

Unless otherwise stated, n.m.r. spectra were measured for solutions in [^{2}H]chloroform, with tetramethylsilane as internal reference, while i.r. spectra were measured for solutions in chloroform. Preparative layer chromatography was performed on glass plates coated with Merck Kieselgel 60 F_{254}, while column chromatography refers to dry packed columns using the same gel (70—230 mesh). Light petroleum refers to the fraction of b.p. 60—80 °C, and ether to diethyl ether. The phrase ' residue upon work-up ' refers to the residue when the organic layer was separated, dried ($MgSO_4$), and the solvent evaporated under reduced pressure.

2-*Acetyl*-3-*propyl*-1,4-*naphthoquinone* (11).—2-Acetyl-1,4-naphthoquinone (2.00 g) and butyric acid (1.32 g) were dissolved in acetonitrile (50 ml). An aqueous solution of silver nitrate (1 g in 1 ml) was added and the mixture stirred at 65—70 °C. Potassium peroxodisulphonate (4.5 g) in water (70 ml) was added slowly during 45 min at constant temperature. The solution was cooled, filtered, thrown into water and extracted with chloroform. The organic phase was separated, washed with sodium hydrogen carbonate and chromatographed (eluant 20% ethyl acetate–light petroleum) to yield an oil (1.33 g, 55%). This solidified and was sublimed, m.p. 54—55 °C (Found: C, 74.65; H, 5.7. $C_{15}H_{14}O_3$ requires C, 74.4; H, 5.8%); δ 0.99 (3 H, t, *J* 6 Hz, 3′-CH_3), 1.58 (2 H, sext., *J* 7 Hz, 2′-CH_2), 2.47 (2 H, t, *J* 7 Hz, 1′-CH_2), 2.51 (3 H, s, $COCH_3$), 7.76 (2 H, m, 6- and 7-H), and 8.11 (2 H, m, 5- and 8-H).

2-*Acetyl*-1,4-*dimethoxy*-3-*propylnaphthalene* (12).—2-Acetyl-3-propyl-1,4-naphthoquinone (400 mg) in ether (50 ml) was shaken with an aqueous solution of sodium dithionite (4 g). The organic phase was separated, dried (Na_2SO_4), filtered and evaporated to dryness. The resulting quinol was immediately dissolved in dry acetone (20 ml) and treated with potassium carbonate (1.14 g) and dimethyl sulphate (1.25 g). The mixture was heated under reflux for 18 h, cooled, the solvent removed and the residue was thrown into water and extracted with chloroform. The chloroform extract was dried and chromatographed (eluant 10% ethyl acetate–light petroleum), to yield a viscous oil (390 mg, 87%) which later solidified, m.p. 37.5—39 °C (methylene dichloride–light petroleum) (Found: C, 74.95; H, 7.15. $C_{17}H_{20}O_3$ requires C, 75.00; H, 7.35); $\nu_{max.}$ 1 705, 1 695, and 1 588 cm^{-1}; δ 0.98 (3 H, t, *J* 7 Hz, 3′-CH_3), 1.63 (2 H, sext., *J* 7 Hz, 2′-CH_2), 2.65 (3 H, s, $COCH_3$), 3.69 (2 H, t, *J* 7 Hz, 1′-CH_2), 3.89 and 3.91 (3 H each, s, OCH_3), 7.52 (2 H, m, 6- and 7-H), and 8.06 (2 H, m, 5- and 8-H).

trans-2-*Acetyl*-1,4-*dimethoxy*-3-*prop*-1-*enylnaphthalene* (18).—Compound (12) (1.00 g), *N*-bromosuccinimide (0.71 g), and benzoyl peroxide (50 mg) were boiled in carbon tetrachloride (10 ml) for 1.5 h. The solution was cooled, the solvent removed and an n.m.r. spectrum run on compound (13); δ 1.02 (3 H, t, *J* 8 Hz, 3′-CH_3), 2.38 (2 H, quint., *J* 8 Hz, 2′-CH_2), 2.76 (3 H, s, $COCH_3$), 3.89 (3 H, s, OCH_3), 4.04 (3 H, s, OCH_3), 5.42 (1 H, t, *J* 8 Hz, 1′-CH), 7.59 (2 H, m, 6- and 7-H), and 8.10 (2 H, m, 5- and 8-H). Compound (13), without purification, was heated with dry dimethylformamide (50 ml) and 1,5-diazabicyclo[4,3,0]non-5-ene (2.5 ml) at 45 °C (external bath temperature) for 90 min. The solution was cooled and poured into water (800 ml). This was repeatedly extracted with ether. Work-up gave a residue which was chromatographed over silica (eluant 5% ethyl acetate–light petroleum) to yield the product (0.65 g, 65%) as an oil (Found: M^+ 270.125 62. $C_{17}H_{18}O_3$ requires *M* 270.125 59); $\nu_{max.}$ 1 710 and 1 585 cm^{-1};

δ 1.93 (3 H, dd, *J* 1.5 and 6 Hz, 3'-CH_3), 2.50 (3 H, s, $COCH_3$), 3.85 (3 H, s, OCH_3), 3.92 (3 H, s, OCH_3), 6.16 (1 H, dq, *J* 6 and 16 Hz, 2'-CH), 6.60 (1 H, dq, *J* 1.5 and 16 Hz, 1'-CH), 7.53 (2 H, m, 6- and 7-H), and 8.10 (2 H, m, 5- and 8-H).

trans-2-(1-*Hydroxyethyl*)-1,4-*dimethoxy*-3-*prop*-1-*enylnaphthalene* (19).—An excess of sodium borohydride was added in portions to a stirred solution of ketone (18) (1.62 g) in dry ethanol (200 ml). The reaction mixture was stirred at room temperature for 12 h, by which time starting material was shown (t.l.c.) to have been consumed. The solvent was evaporated, and the residue taken up in ether, washed with water, dried, and evaporated. Chromatography (eluant 5% ethyl acetate–light petroleum) first afforded 2-(1-*acetoxyethyl*)-1,4-*dimethoxy*-3-*prop*-1-*enylnaphthalene* (20) (78 mg, 4%) as an oil (Found: C, 72.8; H, 7.25. $C_{19}H_{22}O_4$ requires C, 72.6; H, 7.0%); $\nu_{max.}$ (neat) 1 742 and 1 590 cm^{-1}; δ 1.67 (3 H, d, *J* 7 Hz, 2-CH_3), 2.00 (3 H, dd, *J* 1.5 and 6 Hz, 3-CH_3), 2.08 (3 H, s, CH_3CO), 3.79 and 4.00 (3 H each, s, OCH_3), 6.15 (1 H, dq, *J* 6 and 16 Hz, $CH_3CH{=}C$), 6.58 (1 H, q, *J* 7 Hz, CCHO), 6.73 (1 H, dq, *J* 1.5 and 16 Hz, $CH_3C{=}CH$), 7.4—7.6 (2 H, m, 6- and 7-H), and 8.0—8.2 (2 H, m, 5- and 8-H). Later fractions gave the *product* (19) (1.37 g, 85%) as an oil (Found: C, 74.8; H, 7.4. $C_{17}H_{20}O_3$ requires C, 75.0; H, 7.3%); ν_{max} (neat) 3 480 and 1 585 cm^{-1}; δ 1.63 (3 H, d, *J* 7 Hz, 2-CH_3), 1.97 (3 H, dd, *J* 1.5 and 6 Hz, 3-CH_3), 3.74br (1 H, s, OH), 3.79 and 4.03 (3 H each, s, OCH_3), 5.35 (1 H, q, *J* 7 Hz, CHOH), 6.06 (1 H, dq, *J* 6 and 16 Hz, $CH_3CH{=}C$), 6.60 (1 H, dq, *J* 1.5 and 16 Hz, $CH_3C{=}CH$), 7.4—7.6 (2 H, m, 6- and 7-H), and 7.9—8.2 (2 H, m, 5- and 8-H)

trans-2-(1-*Hydroxyethyl*)-3-*prop*-1-*enyl*-1,4-*naphthoquinone* (21).—Compound (19) (98 mg), silver(II) oxide (178 mg) and dioxan (6 ml) were stirred together at room temperature and reaction initiated by addition of nitric acid (6M; 0.4 ml). After 2 min the reaction was stopped by addition of dichloromethane–water (8 : 2; 40 ml), the organic layer washed with aqueous sodium hydrogen carbonate then water. The residue upon work-up was chromatographed (eluant 20% ethyl acetate–light petroleum) to yield the *product* (21) (51 mg, 59%) as an oil (Found: C, 74.05; H, 6.25. $C_{15}H_{14}O_3$ requires C, 74.35; H, 5.85%); δ 1.64 (3 H, d, *J* 6 Hz, 2-CH_3), 2.00 (3 H, d, *J* 5 Hz, 3-CH_3), 3.97 (1 H, d, *J* 12 Hz, OH), 5.07 (1 H, m, CHOH), 6.38 (2 H, m, CH=CH), 7.73 (2 H, m, 6- and 7-H), and 8.06 (2 H, m, 5- and 8-H).

(1R,3R,4S)-4-*Hydroxy*-1,3-*dimethylnaphtho*[2,3-c]*pyran*-5,10-*quinone* (5) *and* (1R,3R,4R)-4-*Hydroxy*-1,3-*dimethylnaphtho*[2,3-c]*pyran*-5,10-*quinone* (6) *and their Enantiomers*.—Compound (19) (100 mg) was dissolved in acetonitrile (10 ml) and ceric ammonium nitrate (858 mg) in water (5 ml) was added during 5 min with stirring, at room temperature. The mixture was stirred for an additional 5 min and then extracted with methylene dichloride. The residue upon work-up was chromatographed (eluant 20% ethyl acetate–light petroleum) to yield the *product* (5) (21 mg, 20%), m.p. 137—138 °C (hexane) (Found: C, 69.65; H, 5.5. $C_{15}H_{14}O_4$ requires C, 69.75; H, 5.45%); δ 1.41 (3 H, d, *J* 6, 5 Hz, 3-CH_3), 1.59 (3 H, d, *J* 7 Hz, 1-CH_3), 3.92br (1 H, s, OH), 3.90 (1 H, dq, *J* 8 and 6.5 Hz, 3-H), 4.47 (1 H, dd, *J* 8 and 1.5 Hz, 4-H), 4.92 (1 H, dq, *J* 7 and 1.5 Hz, 1-H), 7.65—7.85 (2 H, m, 7- and 8-H), and 7.95—8.15 (2 H, m, 6- and 9-H). Later fractions afforded product (6) (62 mg, 59%), m.p. 146—147 °C (hexane) (Found: C, 69.55; H, 5.35. $C_{15}H_{14}O_4$ requires C, 69.75; H, 5.45%); δ 1.41 (3 H, d, *J* 6, 5 Hz, 3-CH_3), 1.52 (3 H, d, *J* 7 Hz, 1-CH_3), 2.26br (1 H, s, OH), 4.00 (1 H, dq *J* 6.5 and 2.5 Hz, 3-H), 4.52 (1 H, d, *J* 2.5 Hz, 4-H), 5.00 (1 H, q, *J* 7 Hz, 1-H), 7.6—7.85 (2 H, m, 7- and 8-H), and 8.9—9.15 (2 H, m, 6- and 9-H).

(1R,3R,4S)-4-*Acetoxy*-1,3-*dimethylnaphtho*[2,3-c]*pyran*-5,10-*quinone* (7) *and its Enantiomer*.—Acetylation of quinone (5) with pyridine and acetic anhydride at room temperature gave material which was chromatographed (eluant 10% ethyl acetate–light petroleum) to give the product (7), m.p. 132—133 °C (methylene dichloride–light petroleum), δ 1.29 (3 H, d, *J* 6 Hz, 3-CH_3), 1.61 (3 H, d, *J* 7 Hz, 1-CH_3), 2.12 (3 H, s, $COCH_3$), 4.13 (1 H, apparent quint., *J* 6 Hz, 3-H), 4.93 (1 H, dq, *J* 7 and 2 Hz, 1-H), 5.78 (1 H, dd, *J* 5 and 2 Hz, 4-H), 7.65—7.85 (2 H, m, 7- and 8-H), and 7.95—8.20 (2 H, m, 6- and 9-H).

(1R,3R,4R)-4-*Acetoxy*-1,3-*dimethylnaphtho*[2,3-c]*pyran*-5,10-*quinone* (8) *and its Enantiomer*.—Acetylation of quinone (6) as for compound (7) above afforded the *acetate* (8), m.p. 186—187.5 °C (hexane) (Found: C, 67.65; H, 5.65. $C_{17}H_{16}O_5$ requires C, 68.0; H, 5.35%); δ 1.28 (3 H, d, *J* 7 Hz, 3-CH_3), 1.56 (3 H, d, *J* 7.5 Hz, 1-CH_3), 2.13 (3 H, s, $COCH_3$), 4.10 (1 H, dq, *J* 7.5 and 2.5 Hz, 3-H), 5.09 (1 H, q, *J* 7 Hz, 1-H), 5.98 (1 H, d, *J* 2.5 Hz, 4-H), 7.72 (2 H, m, 7- and 8-H), and 8.10 (2 H, m, 6- and 9-H).

(1R,3R,4S)-4-*Hydroxy*-1,3-*dimethylnaphtho*[2,3-c]*pyran* (23) *and* (1R,3R,4R)-4-*Hydroxy*-1,3-*dimethylnaphtho*[2,3-c]*pyran* (24) *and their Enantiomers*.—Compound (19) (105 mg, 0.386 mmol) in acetonitrile (15 ml) and water (15 ml) was treated with ceric ammonium nitrate (426 mg, 0.78 mmol) in water (1 ml) during 5 min. After being stirred for a further 5 min the solution was extracted with methylene dichloride, and the residue upon work-up was chromatographed (p.l.c., eluant 10% ethyl acetate–light petroleum) to give *product* (23) (10 mg, 9%) as an oil (Found: M^+ 288.136 000. $C_{17}H_{20}O_4$ requires *M* 288.136 136); δ 1.43 (3 H, d, *J* 6.5 Hz, 3-CH_3), 1.70 (3 H, d, *J* 7 Hz, 1-CH_3), 3.90 and 4.02 (3 H, each s, OCH_3), 3.9—4.3 (2 H, m, 3-H and OH), 4.81 (1 H, dd, *J* 2 and 7 Hz, 4-H, collapsed to d, *J* 7 Hz on D_2O exchange), 5.26 (1 H, q, *J* 7 Hz, 1-H), 7.4—7.65 (2 H, m, 7- and 8-H), and 7.95—8.25 (2 H, m, 6- and 9-H). A band of lower R_F gave *product* (24) (25 mg, 22%) as needles, m.p. 168—168.5 °C (methylene dichloride–light petroleum) (Found: C, 70.7; H, 6.8%; M^+ 288. $C_{17}H_{20}O_4$ requires C, 70.85; H, 6.95%; *M* 288); δ 1.44 (3 H, d, *J* 6.5 Hz, 3-CH_3), 1.61 (3 H, d, *J* 7 Hz, 1-CH_3), 2.15br (1 H, s, OH, D_2O exchangeable), 3.90 and 4.08 (3 H each, s, OCH_3), 4.14 (1 H, dq, *J* 2 and 6.5 Hz, 3-H), 4.78 (1 H, m, 4-H, collapsed to d, *J* 2 Hz, on D_2O exchange), 5.35 (1 H, q, 1-H), 7.4—7.6 (2 H, m, 7- and 8-H), and 7.9—8.2 (2 H, m, 6- and 9-H). Two yellow bands, one of higher R_F than (23) and the other of lower R_F than (24) gave rise to, respectively, quinones (5) (6 mg, 6%) and (6) (6 mg, 6%), each identical with authentic material.

Methyl 1,4-*Dimethoxy*-3-*pentyl*-2-*naphthoate* (26).—Compound (25) [7] (3.58 g), anhydrous potassium carbonate (3 g), and methyl iodide (25 ml) were stirred in dry dimethylformamide (80 ml) at room temperature for 1 h. Dilute hydrochloric acid (350 ml) was added and the mixture extracted with ether. The organic layer was washed with brine, sodium thiosulphate solution, then brine again. The residue upon work-up was chromatographed (2.5% ethyl acetate–light petroleum) to afford the *product* (26) (3.59 g, 96%) as an oil (Found: C, 71.9; H, 7.5. $C_{19}H_{24}O_4$ requires C, 72.2; H, 7.6%); δ 0.91 (3 H, distorted t, *J* 6 Hz, CH_3), 1.1—1.85 (6 H, m, 3 × CH_2), 2.76 (2 H, distorted t, $ArCH_2$), 3.88 (3 H, s, OCH_3), 3.97 (6 H, s, OCH_3), 7.4—7.6 (2 H, m, 6- and 7-H), and 8.0—8.2 (2 H, m, 5- and 8-H).

trans-*Methyl* 1,4-*Dimethoxy*-3-*pent*-1-*enyl*-2-*naphthoate* (28).—The ester (26) (792 mg) in dry carbon tetrachloride

(50 ml) was treated with *N*-bromosuccinimide (500 mg) and di-t-butyl peroxide (10 drops), and the mixture was heated under reflux for 2 h. The solution was chilled in an ice-bath and the solid succinimide was filtered off. The filtrate was stripped of solvent to give the intermediate bromide (27) as an oil; δ 0.88 (3 H, distorted t, *J* 6 Hz, CH_3), 1.1—1.6 (4 H, m, 3- and 4-CH_2), 2.2—2.5 (2 H, m, 2-CH_2), 3.99, 4.01 and 4.15 (3 H each, s, OCH_3), 5.54 (1 H, t, 1-CH), 7.5—7.7 (2 H, m, 6- and 7-H), and 8.0—8.2 (2 H, m, 5- and 8-H). Crude (27) was boiled for 1.5 h in dry lutidine (40 ml) and the reaction mixture was chilled in ice, then filtered to remove precipitated lutidine hydrobromide. The solvent was removed by evaporation and the residue chromatographed (eluant 2% ethyl acetate–light petroleum) to yield the *product* (28) (732 mg, 93%) as an oil (Found: C, 72.1; H, 7.1%; M^+ 314.151 94. $C_{19}H_{22}O_4$ requires C, 72.6; H, 7.0%; *M* 314.151 78); δ 0.98 (3 H, t, *J* 7 Hz, CH_3), 1.50 (2 H, sext., *J* 7 Hz, 4-CH_2), 2.24 (2 H, dq, *J* 1 and 7 Hz, 3-CH_2), 3.84, 3.92, and 3.98 (3 H each, s, OCH_3), 6.19 (1 H, dt, *J* 7 and 16 Hz, 2-H), 6.31 (1 H, dd, *J* 1 and 16 Hz, 1-H), 7.4—7.65 (2 H, m, 6- and 7-H), and 8.0—8.2 (2 H, m, 5- and 8-H).

trans-2-*Hydroxymethyl*-1,4-*dimethoxy*-3-*pent*-1-*enylnaphthalene* (29).—The ester (28) (880 mg) in dry ether (45 ml) was added dropwise during 30 min to a stirred slurry of lithium aluminium hydride (950 mg) in dry ether (40 ml). The mixture was stirred at room temperature for 2 h. Saturated aqueous ammonium chloride was added dropwise until the cessation of effervescence, followed by $MgSO_4$. The mixture was filtered and the residue washed with more ether. The residue upon removal of solvent was chromatographed (eluant 15% ethyl acetate–light petroleum) to give the *product* (29) (737 mg, 92%) as an oil (Found: C, 75.65; H, 7.95. $C_{18}H_{22}O_3$ requires C, 75.5; H, 7.7%); δ 1.00 (3 H, t, *J* 7 Hz, CH_3), 1.57 (2 H, sext., *J* 7 Hz, 4-CH_2), 2.30 (2 H, dq, *J* 1 and 7 Hz, 3-CH_2), 2.50 (1 H, t, *J* 5 Hz, OH, D_2O exchangeable), 3.80 and 3.94 (3 H each, s, OCH_3), 4.90 (2 H, d, *J* 5 Hz, $ArCH_2$), 6.31 (1 H, dt, *J* 7 and 16 Hz, 2-H), 6.68 (1 H, dd, *J* 1 and 6 Hz, 1-H), 7.4—7.6 (2 H, m, 6- and 7-H), and 7.95—8.2 (2 H, m, 5- and 8-H).

trans-2-*Hydroxymethyl*-3-*pent*-1-*enyl*-1,4-*naphthoquinone* (30).—Nitric acid (6M; 0.55 ml) was added to a stirred mixture of compound (29) (139 mg) and silver(II) oxide (242 mg) in dioxan (8 ml) at room temperature. After 10 min the reaction was terminated by the addition of methylene dichloride–water (8 : 2, 50 ml), and the *product* (30) (77 mg, 62%) was isolated as for compound (21) above, m.p. 42—44 °C (methylene dichloride–light petroleum) (Found: M^+ 256.109 898. $C_{16}H_{16}O_3$ requires *M* 256.109 937); δ 0.99 (3 H, t, *J* 7 Hz, CH_3), 1.57 (2 H, sext., *J* 7 Hz, 4-CH_2), 2.2—2.45 (2 H, m, 3-CH_2), 2.84 (1 H, t, *J* 7 Hz, OH, D_2O exchangeable), 4.74 (2 H, d, *J* 7 Hz, $ArCH_2$, collapses to s with D_2O), 6.50 (2 H, m, CH=CH), 7.6—7.8 (2 H, m, 6- and 7-H), and 7.95—8.15 (2 H, m, 5- and 8-H).

(3R,4S)-4-*Hydroxy*-3-*propylnaphtho*[2,3-c]*pyran*-5,10-*quinone* (31), (3R,4R)-4-*Hydroxy*-3-*propylnaphtho*[2,3-c]-*pyran*-5,10-*quinone* (32), *their Respective Nitrate Esters* (33) *and* (34), *and their Enantiomers*.—Compound (29) (184 mg) in acetonitrile (15 ml) was added dropwise with stirring during 5 min to ceric ammonium nitrate (1.415 g) in water (12 ml). The solution was stirred for a further 30 min, and then extracted into methylene dichloride. The residue upon work-up was subjected to p.l.c. (eluant 20% ethyl acetate–light petroleum) to afford, in order of decreasing R_F, *product* (33) (8 mg, 4%) as yellow cubes, m.p. 123.5—124.5 °C (ethanol) (Found: C, 60.55; H, 5.15; N, 3.8. $C_{16}H_{15}NO_6$ requires C, 60.55; H, 4.75; N, 4.4%); δ 0.98 (3 H, distorted t, *J* 7 Hz, CH_3), 1.4—1.8 (4 H, m, CH_2CH_2), 5.9—6.1 (1 H, m, 3-H), 4.65 (2 H, s, 2 × 1-H), 6.00 (1 H, m, 4-H), 7.7—7.9 (2 H, m, 7- and 8-H), and 8.0—8.25 (2 H, m, 6- and 9-H). A second yellow band afforded the *nitrate ester* (34) (15 mg, 7%) as yellow needles, m.p. 174.5—175.5 °C (ethanol) (Found: C, 60.15; H, 4.65; N, 4.15. $C_{16}H_{15}NO_6$ requires C, 60.55; H, 4.75; N, 4.4%); δ 0.97 (3 H, t, *J* 7 Hz, CH_3), 1.4—1.9 (4 H, m, CH_2CH_2), 3.5—3.75 (1 H, m, 3-H), 4.45 (1 H, dd, *J* 2 and 19 Hz, pseudoaxial 1-H), 4.96 (1 H, d, *J* 19 Hz, pseudoequatorial 1-H), 6.20 (1 H, t, *J* 2 Hz, 4-H), 7.7—7.9 (2 H, m, 7- and 8-H), and 8.0—8.25 (2 H, m, 6- and 9-H). A third yellow band provided the *quinone* (31) (26 mg, 15%), m.p. 91—92 °C (ethanol) (Found: C, 70.4; H, 5.8. $C_{16}H_{16}O_4$ requires C, 70.55; H, 5.9%); δ 0.98 (3 H, t, *J* 7 Hz, CH_3), 1.2—2.05 (4 H, m, CH_2CH_2), 3.47 (1 H, dt, *J* 2 and 8 Hz, 3-H), 3.50 (1 H, dd, *J* 2.5 and 19 Hz, pseudoaxial 1-H), 3.76 (1 H, s, OH, D_2O exchangeable), *ca.* 4.6 (1 H, m, 4-H), 4.80 (1 H, dd, *J* 2 and 19 Hz, pseudoequatorial 1-H), 7.6—7.85 (2 H, m, 7- and 8-H), and 7.95—8.2 (2 H, m, 6- and 9-H). A fourth yellow band afforded the quinone (30) (24 mg, 15%), identical with material described earlier. Finally, a fifth yellow band gave the *quinone* (32) (39 mg, 23%) as yellow rhomboids which melt at 122—123 °C and then resolidify to needles, m.p. 135—136 °C (ethanol) (Found: C, 70.3; H, 5.95. $C_{16}H_{16}O_4$ requires C, 70.55; H, 5.9%); δ 0.99 (3 H, t, *J* 7 Hz, CH_3), 1.2—2.0 (4 H, m, CH_2CH_2), 2.1—2.7 (1 H, s, OH, D_2O exchangeable), 3.45 (1 H, ddd, *J* 2, 6, and 7 Hz, 3-H), 4.42 (1 H, dd, *J* 2 and 19 Hz, pseudoaxial 1-H), 4.60br (1 H, m, 4-H), 4.90 (1 H, d, *J* 19 Hz, pseudoequatorial 1-H), 7.6—7.85 (2 H, m, 7- and 8-H), and 7.95—8.2 (2 H, m, 6- and 9-H).

(3R,4S)-4-*Hydroxy*-3-*propylnaphtho*[2,3-c]*pyran*-5,10-*quinone* (31) *and* (3R,4R)-4-*Hydroxy*-3-*propylnaphtho*[2,3-c]-*pyran*-5,10-*quinone* (32) *and their Enantiomers*.—Compound (29) (82 mg) in acetonitrile (20 ml) was treated with ceric ammonium nitrate (636 mg) in water (20 ml) during 5 min. The reaction was stirred for a further 30 min and then extracted with dichloromethane. The residue upon work-up was chromatographed (p.l.c., eluant 20% ethyl acetate–light petroleum) to give product (31) (17 mg, 22%), followed by product (32) (32 mg, 41%). Both these quinones were identical with material described above.

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