Syntheses of the Aphid Pigment Derivatives Quinone A, Quinone A', and Deoxyquinone A as Racemates

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3-Acetyl-5-methoxy-1,7-bisisopropoxy-4-naphthol (**11**) was converted in a number of high yielding transformations into the title quinones. Key steps were the stereospecific base-induced cyclisation in almost quantitative yield of 2-allyl-4,7-bisbenzyloxy-3-(1-hydroxyethyl)-1,5-dimethoxynaphthalene (**18**) into 7,10-bisbenzyloxy-3,4-dihydro-5,9-dimethoxy-*trans*-dimethyl-1*H*-naphtho[2,3-*c*]pyran (**20**) followed by the oxygenation of (**20**) to afford its two C-4 hydroxy epimers (**23**) and (**26**) in high combined yield, by potassium t-butoxide in dimethyl sulphoxide in the presence of oxygen. The efficient conversion of the major pseudoequatorial hydroxy compound (**23**) into the minor pseudoaxial hydroxy epimer (**26**) *via* the corresponding pseudoaxial chloro derivative was useful in providing increased quantities of precursors to quinone A'.

In the preceding paper,[1] a convenient route to 3-acetyl-1,5,7-trialkoxy-4-naphthols† was investigated with a view to synthesizing Quinone A (**1**), Quinone A' (**2**), and Deoxyquinone A (**3**), derivatives obtained by reductive cleavage of the aphid pigments protoaphin-*fb* (**8**), protoaphin-*sl* (**9**), and deoxyprotoaphin (**10**). 3-Acetyl-1,7-bisisopropoxy-5-methoxy-4-naphthol (**11**) was prepared, and in this paper its conversion into the quinones (**1**)—(**3**) as racemates is described. This is the first synthesis of these derivatives of the aphid pigments to be reported.

Results and Discussion

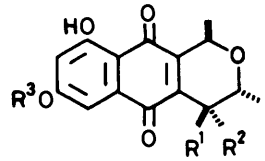
The naphthol (**11**) was oxidised in high yield (90%) to afford the quinone (**12**). This quinone was allylated[2] with allyltrimethylstannane in the presence of boron trifluoride, and the derived crude adduct was methylated directly with dimethyl sulphate and potassium carbonate in acetone to afford the allylnaphthalenone (**13**) in a yield of 61% from the starting naphthol (**11**).

Although it is known[3] that the isopropyl group may be removed from aromatic ethers with boron trichloride, there was little precedent for such use in more complex systems such as the quinones (**28**) and (**29**). It was therefore deemed prudent to retain the bulk of the material as the acetylnaphthalene (**13**) while carrying forward to the quinones (**28**) and (**29**) just sufficient material to attempt the ultimate deprotection. These transformations were effected through the series (**13**) ⟶ (**17**) ⟶ (**19**) ⟶ (**22**) ⟶ (**28**) and (**19**) ⟶ (**29**) by a series of reactions corresponding to those to be described later for the benzyl analogues. However, on treatment of the quinone (**28**) with boron trichloride in methylene dichloride at 0 °C, only the methoxy group was cleaved, while isopropyl remained attached to oxygen, affording the product (**4**). Cleavage of the isopropoxy group to yield Quinone A could not be achieved under any of the conditions attempted for the complete deprotection of Quinone A dimethyl ether already described,[1] without destruction of the moderately sensitive ring system. Similarly, the diprotected derivative (**29**) of Deoxyquinone A afforded only the demethylated product (**5**).

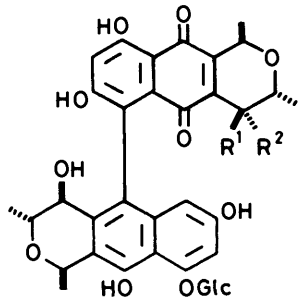
† For clarity, the oxy substituents in all tetraoxygenated naphthalene referred to here are numbered 1,4,5,7, although strictly speaking a principal group (*e.g.* -ol) should be assigned lowest locant (as *e.g.* 4,6,8-trialkoxy-1-naphthol).

Treatment of the naphthalene (**13**) with boron trichloride in methylene dichloride removed the methyl from oxygen *ortho* to the acetyl group at −78 °C, while the isopropoxy group was cleaved smoothly at 0 °C. The derived crude naphthalenediol (**14**) was immediately benzylated with benzyl bromide and anhydrous potassium carbonate in acetone to afford the dibenzyl ether (**15**) as the major product, together with a 9% yield of the *C*-benzyl derivative (**16**). Although it proved necessary at this stage to change the protecting group for O-7 from isopropyl to benzyl, this was the route of choice, since this transformation was effected in an overall yield of 67% for the two steps. The alternative use of 3-acetyl-1,7-bisbenzyloxy-5-methoxy-4-naphthol to afford the quinones (**30**)—(**32**), and hence the target molecules (**1**)—(**3**), would no doubt have been possible, but the yield of that naphthol from benzoquinone was very poor indeed in comparison with the conversion of the benzoquinone into the naphthol (**11**).[1] After chromatographic separation, compound (**15**) was reduced with lithium aluminium hydride in high yield to give the alcohol (**18**). This alcohol was readily and stereospecifically cyclised in 97% yield to the *trans*-1,3-dimethylnaphtho[2,3-*c*]pyran (**20**) with potassium t-butoxide in dry dimethylformamide.[4,5] In contrast to cyclisations of the corresponding dimethoxy[6] and tetramethoxy analogues,[4] which gave some of the *cis*-dimethylnaphthopyrans if the base-induced cyclisations were allowed to proceed for longer than recommended, the conversion of the alcohol (**18**) into the pyran (**20**) did not afford any of the *cis*-stereoisomer. This was ascribed in the present case to a greater degree of crowding with a benzyloxy rather than a methoxy substituent on C-10, which would discourage the C-1 methyl from assuming the more crowded pseudoequatorial configuration. This was supported in the ^{1}H n.m.r. spectrum of the pyran (**20**) by the fact that one of the two benzylic methylene signals appears as a singlet, whereas the other, no doubt due to the more crowded group, appears as a pair of doublets (J 11 Hz) at δ 4.75 and 5.10. Finally, the relative stereochemistry of the methyl groups could be assigned as *trans* on account of both the chemical shift[6,7] of the axial proton on C-3 [δ 4.0—4.25 (m)] and the fact that the naphthalene (**20**) was readily oxidised with silver(II) oxide[8] to the corresponding 5,10-quinone (**30**), the ^{1}H n.m.r. spectrum of which showed unambiguously that its stereochemistry was that of the isoeleutherin rather than the eleutherin series.[9]

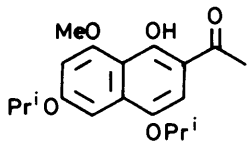
Oxygenation of the naphthopyran (**20**) was achieved in dimethylformamide containing potassium t-butoxide in the presence of air,[4,5] giving the C-4 pseudoequatorial hydroxy



(1) R^1 = OH, R^2 = R^3 = H
(2) R^1 = R^3 = H, R^2 = OH
(3) R^1 = R^2 = R^3 = H
(4) R^1 = OH, R^2 = H, R^3 = Pr^i
(5) R^1 = R^2 = H, R^3 = Pr^i
(6) R^1 = R^2 = H, R^3 = CH_2Ph
(7) R^1 = H, R^2 = OH, R^3 = CH_2Ph



(8) R^1 = OH, R^2 = H
(9) R^1 = H, R^2 = OH
(10) R^1 = R^2 = H



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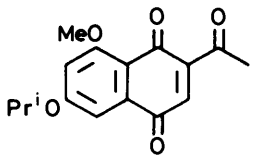

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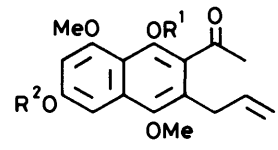
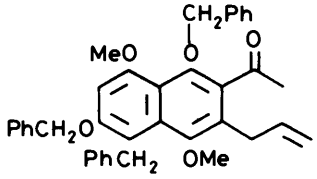


(13) R^1 = Me, R^2 = Pr^i
(14) R^1 = R^2 = H
(15) R^1 = R^2 = CH_2Ph



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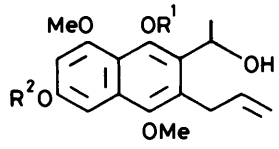
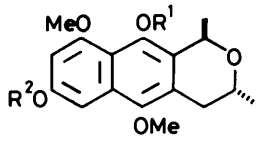
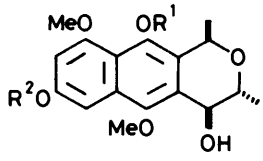


(17) R^1 = Me, R^2 = Pr^i
(18) R^1 = R^2 = CH_2Ph

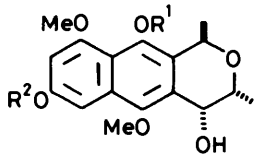
† Structures drawn as single enantiomers represent racemates, other than those of natural products and their derivatives, for which the correct configuration is depicted.



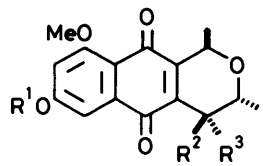
(19) R^1 = Me, R^2 = Pr^i
(20) R^1 = R^2 = CH_2Ph
(21) R^1 = R^2 = Me



(22) R^1 = Me, R^2 = Pr^i
(23) R^1 = R^2 = CH_2Ph
(24) R^1 = R^2 = Me



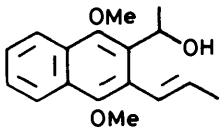
(25) R^1 = Me R^2 = Pr^i
(26) R^1 = R^2 = CH_2Ph
(27) R^1 = R^2 = Me



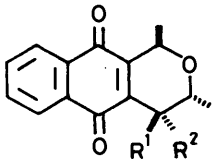
(28) R^1 = Pr^i, R^2 = OH, R^3 = H
(29) R^1 = Pr^i, R^2 = R^3 = H
(30) R^1 = CH_2Ph, R^2 = R^3 = H
(31) R^1 = CH_2Ph, R^2 = OH, R^3 = H
(32) R^1 = CH_2Ph, R^2 = H, R^3 = OH

derivative (**23**) as the major product (41%), together with the pseudoaxial epimer (**26**) (5%). These yields were consistent with those previously described for the oxygenation of the related tetramethoxynaphthopyran (**21**), which afforded the C-4 hydroxy derivatives (**24**) and (**27**) in yields of 35 and 7%, respectively. Various conditions were attempted to increase the yields of these oxygenation reactions. A major improvement was established when the naphthopyrans were dissolved in dry dimethyl sulphoxide through which oxygen was bubbled during the reaction. Thus, the bisbenzyloxynaphthopyran (**20**) afforded the hydroxylated products (**23**) and (**26**) in yields of 60 and 24%, respectively. Similar treatment of the tetramethoxynaphthopyran (**21**) gave rise to the hydroxy derivatives (**24**) and (**27**) in yields of 63 and 23%, respectively. This discovery led to a major increase in the overall yields of the Quinones A and A′ over those which would otherwise have been possible.

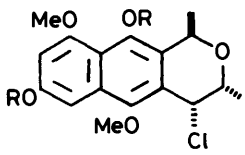
The oxidation of naphthopyran (**20**) to the quinone (**30**) (in 86% yield) has already been mentioned. Similar oxidation of the pyran (**23**) with silver(II) oxide afforded the corresponding 5,10-quinone (**31**), while oxidation of the pyran (**26**), the C-4 epimer of (**23**), provided the quinone (**32**). Deprotection of the quinones (**30**) and (**31**) with an excess of boron trichloride removed both *O*-methyl and *O*-benzyl groups, giving rise smoothly to racemic Deoxyquinone A (**3**) and Quinone A (**1**), respectively. In the conversion of compound (**30**) into the quinone (**3**), the product (**6**), of demethylation only, was obtained as a minor constituent. However, similar deprotection of the corresponding quinone



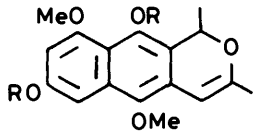
(33)



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



(39) R = Me
(40) R = CH_2Ph



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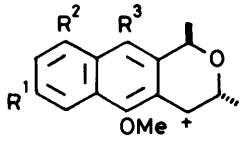

(36) R^1 = R^2 = H, R^3 = OMe
(37) R^1 = R^3 = OCH_2Ph, R^2 = OMe
(38) R^1 = R^2 = R^3 = OMe

(32) did not readily lead to the isolation of pure racemic Quinone A′ (2), although this compound was clearly visible as a major product on t.l.c. investigation of the crude product (identified by comparison with authentic, naturally derived Quinone A′). A possible explanation is that in Quinone A′ the axial and pseudoaxial configurations of the adjacent hydrogen and hydroxy at C-3 and C-4, respectively, may enable more ready elimination of water followed by further decomposition, such elimination conceivably being encouraged by the conditions under which Quinone A′ was being formed. A milder method for the formation of Quinone A′ was therefore indicated, but neither of the precursors (26) nor (32) remained, as the former was the minor product in the hydroxylation of the naphthopyran (20). On the other hand, quantities of the major product (23) of this reaction were available, and a method for the efficient conversion of compound (23) into the epimer (26) was sought.

The first synthesis[10] of derivatives of Quinones A and A′ involved the oxidative cyclisation with cerium(IV) ammonium nitrate of the naphthalene (33) to afford the 7,9-dideoxy derivatives (34) and (35), respectively. The stabilised carbocation (36) was suggested as an intermediate, attacked by the nucleophile water to afford naphthopyrans epimeric with respect to the C-4 hydroxy substituent. However in that reaction the pseudoaxial compound predominated, giving rise after oxidative demethylation to the Quinone A′ analogue (35) as the major product; no doubt the pseudoaxial epimer was favoured since *peri*-interactions with the neighbouring methoxy group were less than in the alternative pseudoequatorial alcohol. This reasoning led to the speculation that if it were possible to generate the carbocation (37) from the pseudoequatorial hydroxy compound (23) in the presence of water, the major product would be the pseudoaxial epimer (26) contaminated by a small quantity of compound (23).

In order to conserve compound (23), the analogue (24)[4] was chosen as a model. Initial experiments designed to protonate either the alcohol (24) or its esters with a variety of acids gave only starting material or products of decomposition. Aprotic removal of the C-4 hydroxy group was then investigated, and the conversion of (23) into (26) was successfully achieved in practice as follows. Treatment of compound (24) with phosphorus pentachloride in dry ether afforded only the pseudoaxial 4-chloro derivative (39), as the major product in high yield (87%), together with a little of the naphthopyran (41) (9%). The stereochemistry of the chloro substituent was established from the coupling constant (1.3 Hz) between 3-H and 4-H, which showed these protons to be in an axial–pseudoequatorial relationship. Similar treatment of the epimeric alcohol (27) afforded the same chloro compound (39), suggesting the intermediacy of the carbocation (38) in these chlorination reactions as well, chloride then attacking to form the sterically least hindered product in both cases. The olefin (41) would be derived from the carbocation (38) by loss of 3-H. The chloro compound (39) was then treated in acetonitrile with an excess of silver nitrate in water, which gave rise to the desired pseudoaxial hydroxy compound (27) (36%), the pseudoequatorial epimer (24) (10%), and starting material (39) (7%). The yields were considerably improved when the intermediate chloro compound was not purified. Thus the alcohol (24) was converted directly into a mixture of the epimer (27) (70%), starting material (24) (18%), and the chloro compound (39) (6%). The related conversion of the bisbenzyloxy analogue (23) gave parallel results, affording compound (26) (55%), starting material (23) (22%), the naphthopyran (42) (7%), and the chloro compound (40) (13%)

Having obtained further quantities of compound (26), we converted it into the quinone (32) as already described. The quinone was demethylated with a limited amount of boron trichloride (2 mol equiv.) to afford Quinone A′ benzyl ether (7). Pure compound (7) was hydrogenolysed and Quinone A′ (2) was obtained upon aerial re-oxidation of the derived hydroquinone.

The synthetic racemates (1)—(3) were identical with naturally derived samples of Quinone A, Quinone A′, and Deoxyquinone A in respect of t.l.c. behaviour, and had i.r. and ^{1}H n.m.r. data closely similar to reported values.[9,11]

With routes to the quinones (1)—(3) established, the total synthesis of the naturally occurring aphid insect pigments protoaphin-*fb*, protoaphin-*sl*, and deoxyprotoaphin then requires the preparation of Glucoside B.[12,13]

Experimental

All ^{1}H n.m.r. spectra were measured for solutions in [^{2}H]chloroform with tetramethylsilane as internal reference; i.r. spectra were measured for Nujol mulls, unless otherwise stated. Preparative layer chromatography (p.l.c.) was performed on glass plates coated with Merck Kieselgel 60 F_{254}; column chromatography refers to dry-packed columns of 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 obtained upon work-up' refers to the material remaining when the organic layer was separated, dried ($MgSO_4$), and evaporated under reduced pressure.

3-Acetyl-7-isopropoxy-5-methoxy-1,4-naphthoquinone (12).—A solution of cerium(IV) ammonium nitrate (12.46 g, 22.7 mmol) in water (15 ml) was added dropwise over 10 min to a stirred solution of the naphthol (11) (3.49 g, 10.3 mmol) in acetonitrile (285 ml) and deionised water (49 ml). The solution was stirred for a further 15 min then quenched with water and partitioned with methylene dichloride. The residue obtained

upon work-up gave the *product* (2.72 g, 90%) as yellow needles, m.p. 133—135 °C (from propan-2-ol) (Found: C, 66.6; H, 5.7. $C_{16}H_{16}O_5$ requires C, 66.7; H, 5.6%); $\nu_{max.}$ 1 700 (C=O), 1 670 (C=O), and 1 605 cm^{-1} (C=C); δ 1.40 [3 H, d, *J* 6 Hz, $CH(CH_3)_2$], 2.60 (3 H, s, $COCH_3$), 3.98 (3 H, s, OCH_3), 4.79 [1 H, sept, *J* 6 Hz, $CH(CH_3)_2$], 6.73 (1 H, d, *J* 2 Hz, 6-H), 6.91 (1 H, s, 2-H), and 7.17 (1 H, d, *J* 2 Hz, 8-H); *m/z* 288 (M^+, 100%), 246 (55), 231 (100), and 203 (65).

3-*Acetyl*-7-*isopropoxy*-1,4,5-*trimethoxy*-2-*prop*-2-*enylnaphthalene* (**13**).—The freshly prepared impure quinone (**12**) (3.02 g, 10.5 mmol; quantitative yield assumed) was dissolved in dry methylene dichloride (302 ml) under nitrogen and cooled to −78 °C. Boron trifluoride–ether complex (1.30 ml, 10.3 mmol) was added with vigorous stirring followed dropwise by allyltrimethylstannane (2.75 g, 13.4 mmol). The dark red solution was stirred for 1 h at −78 °C, then water was added to quench the reaction before the usual work-up. The resulting orange oil was immediately dissolved in dry acetone (260 ml) under nitrogen then dimethyl sulphate (13.03 g, 0.10 mol) and anhydrous potassium carbonate (14.27 g, 0.10 mol) were added and the solution was boiled and vigorously stirred for 4 h. The mixture was cooled, filtered, and evaporated, and the residue taken up in diethyl ether, and washed successively with concentrated ammonia, water, dilute hydrochloric acid, and finally water. The residue obtained upon work-up was chromatographed (15% ethyl acetate–light petroleum) to afford the *product* as an oil (2.28 g, 61%) (Found: C, 70.4; H, 7.6. $C_{21}H_{26}O_5$ requires C, 70.4; H, 7.3%); $\nu_{max.}$(film) 1 710 (C=O) and 1 625 and 1 590 cm^{-1} (C=C); δ 1.43 [6 H, d, *J* 6 Hz, $CH(CH_3)_2$], 2.67 (3 H, s, $COCH_3$), 3.60 (2 H, dd, *J* 6 and 1 Hz, CH_2), 3.80, 3.92, and 4.07 (each 3 H, s, OCH_3), 4.83 [1 H, sept, *J* 6 Hz, $CH(CH_3)_2$], 4.8—5.2 (2 H, m, vinyl CH_2), 5.75—6.4 (1 H, m, vinyl CH), 6.67 (1 H, d, *J* 2 Hz, 6-H), and 7.12 (1 H, d, *J* 2 Hz, 8-H); *m/z* 358 (M^+, 100%), 343 (78), 329 (15), 301 (60), and 286 (50).

3-(1-*Hydroxyethyl*)-7-*isopropoxy*-1,4,5-*trimethoxy*-2-*prop*-2-*enylnaphthalene* (**17**).—Lithium aluminium hydride (216 mg, 5.7 mmol) was added in portions to a stirred solution of the ketone (**13**) (509 mg, 1.4 mmol) in dry diethyl ether (30 ml). The mixture was stirred for a further 10 min then quenched by slow addition of saturated aqueous ammonium chloride followed by anhydrous magnesium sulphate. The solution was filtered and evaporated under low pressure to afford the *product* (456 mg, 89%) as a glassy gum (Found: C, 69.4; H, 7.9. $C_{21}H_{28}O_5$ requires C, 69.9; H, 7.8%); $\nu_{max.}$(film) 3 550 (OH) and 1 625 and 1 595 cm^{-1} (C=C); δ 1.42 [6 H, d, *J* 6 Hz, $CH(CH_3)_2$], 1.67 [3 H, d, *J* 6 Hz, $CH(OH)CH_3$], 3.75 (2 H, m, CH_2), 3.87, 3.93, and 4.03 (each 3 H, s, OCH_3), 4.04br (1 H, s, OH, D_2O-exchangeable), 4.77 [1 H, sept, *J* 6 Hz, $CH(CH_3)_2$], 4.8—5.3 (2 H, m, vinyl CH_2), 6.0—6.4 (1 H, m, vinyl CH), 6.62 (1 H, d, *J* 2 Hz, 6-H), and 7.07 (1 H, d, *J* 2 Hz, 8-H); *m/z* 360 (M^+, 100%), 345 (30), 303 (18), and 285 (15).

(±)-3,4-*Dihydro*-7-*isopropoxy*-5,9,10-*trimethoxy*-r-1,c-3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran* (**19**).—The alcohol (**17**) (422 mg, 1.2 mmol) was dissolved in dry dimethylformamide (20 ml) and dry nitrogen was passed through the stirred solution for 10 min. The solution was heated at 60 °C before the addition of potassium t-butoxide (1.58 g, 14 mmol) and stirring was continued for 7 min before the darkened solution was quenched with water, cooled, and extracted with ether. The usual work-up and chromatography (15% ethyl acetate–light petroleum) afforded the *product* (367 mg, 87%) as white needles, m.p. 144 °C from (propan-2-ol) (Found: C, 69.6; H, 8.0. $C_{21}H_{28}O_5$ requires C, 69.98; H, 7.8%); $\nu_{max.}$ 1 630, 1 610, and 1 590 cm^{-1} (C=C); δ 1.40 (3 H, d, *J* 6 Hz, 3-CH_3), 1.43 [6 H, d, *J* 6 Hz, $CH(CH_3)_2$], 1.65 (3 H, d, *J* 7 Hz, 1-CH_3), 2.53 (1 H, dd, *J* 17 and 10 Hz, pseudoaxial 4-H), 3.07 (1 H, dd, *J* 17 and 3.5 Hz, pseudoequatorial 4-H), 3.77, 3.82, and 3.95 (each 3 H, s, OCH_3), 3.9—4.3 (1 H, m, 3-H), 4.73 [1 H, sept, *J* 6 Hz, $CH(CH_3)_2$], 5.30 (1 H, q, *J* 7 Hz, 1-H), 6.48 (1 H, d, *J* 2 Hz, 8-H), and 6.97 (1 H, d, *J* 2 Hz, 6-H); *m/z* 360 (M^+, 77%), 345 (100), 303 (35), and 259 (20).

(1R,3R,4S)-3,4-*Dihydro*-4-*hydroxy*-7-*isopropoxy*-5,9,10-*trimethoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran* (**22**) *and its Enantiomer and* (1R,3R,4R)-3,4-*Dihydro*-4-*hydroxy*-7-*isopropoxy*-5,9,10-*trimethoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran* (**25**) *and its Enantiomer*.—A solution of the pyran (**19**) (345 mg, 1.0 mmol) in dimethylformamide (25 ml) was aerated for 10 min before being heated to 60 °C (bath). Potassium t-butoxide (645 mg, 5.6 mmol) was added, causing the solution to darken rapidly, and after 15 min the reaction was quenched with water (50 ml), cooled, and extracted with ether. The ethereal extract was washed with water. After the usual work-up, the residue was chromatographed (10—30% ethyl acetate–light petroleum) to afford first starting material (25 mg, 7%), followed by the pseudoequatorial *alcohol* (**22**) (93 mg, 28% based on starting material consumed) as cream-coloured plates, m.p. 173 °C (from methylene dichloride–light petroleum) (Found: C, 66.9; H, 7.5. $C_{21}H_{28}O_6$ requires C, 67.0; H, 7.5%); $\nu_{max.}$ 3 500 (OH) and 1 630 and 1 600 cm^{-1} (C=C); δ 1.43 [9 H, d, *J* 6 Hz, $C(CH_3)_2$ and 3-CH_3], 1.68 (3 H, d, *J* 7 Hz, 1-CH_3), 3.73, 3.88, and 3.93 (each 3 H, s, OCH_3), *ca.* 4.02 (1 H, dq, *J* 6 and 9 Hz, 3-H, partially obscured), 4.22br (1 H, s, OH, D_2O-exchangeable), 4.70 (1 H, d, *J* 9 Hz, 4-H), 4.72 [1 H, sept, *J* 6 Hz, $CH(CH_3)_2$], 5.18 (1 H, q, *J* 7 Hz, 1-H), 6.50 (1 H, d, *J* 2 Hz, 8-H), and 6.90 (1 H, d, *J* 2 Hz, 6-H); *m/z* 376 (M^+, 99%), 361 (100), 319 (20), and 275 (18). The last fraction gave rise to the pseudoaxial *alcohol* (**25**) (13 mg, 4%) as a viscous oil (Found: M^+, 376.191. $C_{21}H_{28}O_6$ requires *M*, 376.189); $\nu_{max.}$(film) 3 500 (OH) and 1 630 and 1 610 cm^{-1} (C=C); δ 1.42 [9 H, d, *J* 6 Hz, $CH(CH_3)_2$ and 3-CH_3], 1.61 (3 H, d, *J* 7 Hz, 1-CH_3), 2.10 (1 H, d, *J* 10 Hz, OH, D_2O-exchangeable), 3.78, 3.95, and 3.99 (each 3 H, s, OCH_3), 4.14 (1 H, dq, *J* 6 and 2 Hz, 3-H), 4.71 (1 H, d, *J* 2 and 10 Hz, 4-H), 4.73 [1 H, sept, $CH(CH_3)_2$], 5.28 (1 H, q, *J* 7 Hz, 1-H), 6.48 (1 H, d, *J* 2 Hz, 8-H), and 6.96 (1 H, d, *J* 2 Hz, 6-H); *m/z* 376 (M^+, 100%), 361 (75), and 343 (10).

(1R,3R,4S)-3,4-*Dihydro*-4-*hydroxy*-7-*isopropoxy*-9-*methoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran*-5,10-*quinone* (**28**) *and its Enantiomer*.—The naphthopyran (**22**) (93 mg, 0.25 mmol), silver(II) oxide (123 mg, 1.0 mmol), and dioxane (8 ml) were stirred together at room temperature. Nitric acid (6M; 0.3 ml) was added and the mixture stirred for 4 min, then quenched with water and methylene dichloride. The residue obtained upon work-up was flash chromatographed (10—50% ethyl acetate–light petroleum) to afford the *quinone* (75 mg, 91%) as orange needles, m.p. 67—68.5 °C (from ethanol) (Found: M^+, 346.143. $C_{19}H_{22}O_6$ requires *M*, 346.142); $\nu_{max.}$ 3 500 (OH), 1 650 (C=O), and 1 590 and 1 555 cm^{-1} (C=C); δ 1.39 [9 H, d, *J* 6 Hz, $CH(CH_3)_2$ and 3-CH_3], 1.57 (3 H, d, *J* 7 Hz, 1-CH_3), 3.81 (1 H, d, *J* 2 Hz, OH), 3.87 (1 H, dq, *J* 6 and 8 Hz, 3-H), 3.95 (3 H, s, OCH_3), 4.44 (1 H, ddd, *J* 8, 2, and 1.5 Hz, 4-H, collapses to dd, *J* 1.5 and 8 Hz on D_2O exchange), 4.77 [1 H, sept, *J* 6 Hz, $CH(CH_3)_2$], 4.92 (1 H, dq, *J* 7 and 1.5 Hz, 1-H), 6.70 (1 H, d, *J* 2.5 Hz, 8-H), and 7.21 (1 H, d, *J* 2.5 Hz, 6-H); *m/z* 346 (M^+, 7%), 328 (44), 313 (30), 302 (100), 286 (36), 271 (61), 260 (95), and 243 (49).

(1R,3R,4S)-3,4-*Dihydro*-4,9-*dihydroxy*-7-*isopropoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran*-5,10-*quinone* (**4**) *and its Enantiomer*.—The quinone (**28**) (16 mg, 0.048 mmol) was dissolved in dry methylene dichloride (5 ml) and cooled to 0 °C. Boron trichloride (33 mg, 0.28 mmol) in dry methylene dichloride (1.2

ml) was added at once and the mixture was stirred for 20 min at that temperature. Water and more methylene dichloride were added. The residue obtained upon work-up was chromatographed (50% ethyl acetate–light petroleum) to afford the *product* (**4**) (14 mg, 92%) as pale orange-yellow needles, m.p. 125—127 °C (decomp.) (from propan-2-ol) (Found: C, 64.4; H, 6.3. $C_{18}H_{22}O_6$ requires C, 64.65; H, 6.6%); $\nu_{max.}$ 3 530 (OH), 1 653 and 1 639 (C=O), and 1 615 and 1 562 cm^{-1} (C=C); δ 1.37 [6 H, d, *J* 6 Hz, $CH(CH_3)_2$], 1.40 (3 H, d, *J* 6 Hz, 3-CH_3), 1.60 (3 H, d, *J* 6.5 Hz, 1-CH_3), 3.87 (1 H, dq, *J* 6 and 8 Hz, 3-H), 3.9br (1 H, s, OH, D_2O-exchangeable), 4.43 (1 H, dd, *J* 2 and 8 Hz, 4-H), 4.66 [1 H, sept, *J* 6Hz, $CH(CH_3)_2$], 4.91 (1 H, dq, *J* 2 and 6.5 Hz, 1-H), 6.60 (1 H, d, *J* 2.5 Hz, 8-H), 7.12 (1 H, d, *J* 2.5 Hz, 6-H), and 12.13 (1 H, s, OH, D_2O-exchangeable); *m/z* 332 (M^+, 1%), 288 (100), 246 (54), 218 (95), and 43 (83).

(±)-3,4-*Dihydro*-7-*isopropoxy*-9-*methoxy*-r-1,t-3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran*-5,10-*quinone* (**29**).—The naphthopyran (**19**) (134 mg, 0.4 mmol) was oxidised and purified as for the preceding naphthopyran to afford the recrystallised *product* (90 mg, 75%) as yellow needles, m.p. 158—159 °C (from ether–propan-2-ol) (Found: C, 69.1; H, 6.8. $C_{19}H_{22}O_5$ requires C, 69.1; H, 6.7%); $\nu_{max.}$ 1 660 (C=O) and 1 610 cm^{-1} (C=C); δ 1.33 (3 H, d, *J* 6 Hz, 3-CH_3), 1.40 [6 H, d, *J* 6 Hz, $CH(CH_3)_2$], 1.57 (3 H, d, *J* 7 Hz, 1-CH_3), 2.20 (1 H, ddd, *J* 19, 10, and 2 Hz, pseudoaxial 4-H), 2.69 (1 H, dd, *J* 19 and 4 Hz, pseudoequatorial 4-H), 3.96 (3 H, s, OCH_3), *ca.* 3.97 (1 H, m, 3-H), 4.78 [1 H, sept, *J* 6 Hz, $CH(CH_3)_2$], 5.02 (1 H, dq, *J* 2 and 7 Hz, 1-H), 6.70 (1 H, d, *J* 2 Hz, 8-H), and 7.28 (1 H, d, *J* 2 Hz, 6-H); *m/z* 330 (M^+, 100%), 315 (19), 288 (20), 273 (60), and 257 (50).

(±)-3,4-*Dihydro*-9-*hydroxy*-7-*isopropoxy*-r-1,t-3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran*-5,10-*quinone* (**5**).—A solution of the quinone (**29**) (47 mg, 0.14 mmol) in dry methylene dichloride (6 ml) was cooled with stirring to 0 °C, then boron trichloride (153 mg, 1.4 mmol) dissolved in dry methylene dichloride (1.2 ml) was added at a fast drip. The colour of the solution immediately turned dark red and faded to a deep yellow before the mixture was quenched with water after 25 min. After partitioning and the usual work-up, the residue was purified by flash chromatography (10—40% ethyl acetate–light petroleum) to afford the *product* (29 mg, 64%) as orange-yellow needles, m.p. 128 °C (from ether–propan-2-ol) (Found: C, 68.1; H, 6.4. $C_{18}H_{20}O_5$ requires C, 68.3; H, 6.4%); $\nu_{max.}$ 3 550br (OH), 1 680 and 1 650 (C=O), and 1 615 cm^{-1} (C=C); δ 1.35 (3 H, d, *J* 6 Hz, 3-CH_3), 1.37 [6 H, d, *J* 6 Hz, $CH(CH_3)_2$], 1.54 (3 H, d, *J* 7 Hz, 3-CH_3), 2.20 (1 H, ddd, *J* 18, 10, and 2 Hz, pseudoaxial 4-H), 2.74 (1 H, dd, *J* 18 and 3 Hz, pseudoequatorial 4-H), 3.99 (1 H, m, 3-H), 4.68 [1 H, sept, *J* 6 Hz, $CH(CH_3)_2$], 5.00 (1 H, dq, *J* 7 and 2 Hz, 1-H), 6.59 (1 H, d, *J* 2 Hz, 8-H), 7.13 (1 H, d, *J* 2 Hz, 6-H), and 12.45 (1 H, s, OH); *m/z* 316 (M^+, 100%), 301 (20), 274 (35), 258 (60), 242 (27), and 226 (37).

3-*Acetyl*-4,7-*bisbenzyloxy*-1,5-*dimethoxy*-2-*prop*-2-*enylnaphthalene* (**15**) *and* 3-*Acetyl*-8-*benzyl*-4,7-*bisbenzyloxy*-1,5-*dimethoxy*-2-*prop*-2-*enylnaphthalene* (**16**).—The ether (**13**) (6.29 g, 17.6 mmol) was dissolved with stirring in dry methylene dichloride (500 ml) and cooled to 0 °C before the addition of boron trichloride (10 equiv.) dissolved in dry methylene dichloride (50 ml). When the addition was complete (9 min) the mixture was stirred for 1 h, then quenched with water, partitioned, and worked up. The crude product (**14**) [δ 1.80br (1 H, s, 7-OH), 2.60 (3 H, s, $COCH_3$), 3.59 (2 H, dt, *J* 1.5 and 7 Hz, CH_2), 3.78 and 4.03 (each 3 H, s, OCH_3), 4.94 (1 H, dq, *J* 1.5 and 20 Hz, 3′-H), 4.99 (1 H, dq, *J* 1.5 and 8.5 Hz, 3′-H), 5.7—6.2 (1 H, m, 2′-H), 6.47 (1 H, d, *J* 3 Hz, 6-H), 6.95 (1 H, d, *J* 3 Hz, 8-H), and 9.31 (1 H, s, 4-OH)] was immediately dissolved in dry acetone (400 ml), and benzyl bromide (9.01 g, 53 mmol) and anhydrous potassium carbonate (7.27 g, 53 mmol) were added. The mixture was stirred and boiled under nitrogen overnight, cooled, filtered, and evaporated to afford an oil which was chromatographed (5—10% ethyl acetate–light petroleum) to yield two compounds. The first *product* (**15**) (5.68 g, 67%) was isolated as long white needles, m.p. 133—134 °C (from chloroform–propan-2-ol) (Found: C, 77.1; H, 6.3. $C_{31}H_{30}O_5$ requires C, 77.2; H, 6.3%); $\nu_{max.}$ 1 710 (C=O) and 1 630 and 1 595 cm^{-1} (C=C); δ 2.55 (3 H, s, CCH_3), 3.55 (2 H, dt, *J* 6 and 2 Hz, allyl CH_2), 3.79 and 3.89 (each 3 H, s, OCH_3), 4.85 (2 H, s, CH_2Ph), 4.9—5.1 (2 H, m, vinyl CH_2), 5.22 (2 H, s, CH_2Ph), 5.8—6.1 (1 H, m, vinyl CH), 6.65 (1 H, d, *J* 2.5 Hz, 6-H), 7.10 (1 H, d, *J* 2.5 Hz, 8-H), and 7.3—7.6 (10 H, m, C_6H_5); *m/z* 482 (M^+, 25%), 420 (10), 391 (55), and 91 (100). The second *product* (**16**) (1.52 g, 9%) was isolated as an oil (Found: C, 79.8; H, 6.6. $C_{38}H_{36}O_5$ requires C, 79.7; H, 6.3%); $\nu_{max.}$(film) 1 690 (C=O) and 1 600 and 1 590 cm^{-1} (C=C); δ 2.52 (3 H, s, CCH_3), 3.34 (3 H, s, OCH_3), 3.46 (2 H, dq, *J* 1.5 and 7 Hz, allyl CH_2), 3.78 (3 H, s, OCH_3), 4.72, 4.80, and 5.14 (each 2 H, s, CH_2Ph), 4.86—5.24 (2 H, m, vinyl CH_2), 5.63—6.07 (1 H, m, vinyl CH), 6.71 (1 H, s, 6-H), and 7.05, 7.24, and 7.32 (each 5 H, s, C_6H_5); *m/z* 572 (M^+, 17%), 530 (70), 481 (25), and 91 (100).

When the ether (**13**) was treated with boron trichloride as before, but at −78 °C and then thrown into water without warming to room temperature, an oily product was obtained which was identified as 3-acetyl-2-allyl-7-isopropoxy-1,5-dimethoxy-4-naphthol on the basis of its ^1H n.m.r. spectrum: δ 1.44 [6 H, d, *J* 6 Hz, $C(CH_3)_2$], 2.59 (3 H, s, $COCH_3$), 3.60 (2 H, td, *J* 1.5 and 7 Hz, CH_2), 4.00 and 4.24 (each 3 H, s, OCH_3), 4.76 [1 H, sept, *J* 6 Hz, $CH(CH_3)_2$], 4.98 (1 H, dq, *J* 1.5 and 20 Hz, 3′-H), 5.01 (1 H, dq, *J* 1.5 and 8.5 Hz, 3′-H), 5.7—6.2 (1 H, m, 2′-H), 6.47 (1 H, d, *J* 3 Hz, 6-H), 6.93 (1 H, d, *J* 3 Hz, 8-H), and 9.33 (1 H, s, 4-OH).

4,7-*Bisbenzyloxy*-3-(1-*hydroxyethyl*)-1,5-*dimethoxy*-2-*prop*-2-*enylnaphthalene* (**18**).—The ketone (**15**) (4.75 g) was reduced as for the ketone (**13**). After chromatography (12% ethyl acetate–light petroleum) the *product* (4.74 g, 98%) was isolated as a colourless gum (Found: C, 76.9; H, 6.7. $C_{31}H_{32}O_5$ requires C, 76.8; H, 6.7%); $\nu_{max.}$ 3 500 (OH) and 1 625 and 1 590 cm^{-1} (C=C); δ 1.60 (3 H, d, *J* 6 Hz, CCH_3), 3.46br (1 H, s, OH, D_2O-exchangeable), 3.74 (2 H, m, allyl CH_2), 3.76 and 3.81 (each 3 H, s, OCH_3), 4.8—5.4 (7 H, superimposed m, 4- and 7-CH_2Ph, $CHCH_3$, vinyl CH_2), 5.9—6.3 (1 H, m, vinyl CH), 6.62 (1 H, d, *J* 2.5 Hz, 6-H), 7.08 (1 H, d, *J* 2.5 Hz, 8-H), and 7.35—7.65 (10 H, m, C_6H_5); *m/z* 484 (M^+, 8%), 466 (15), 393 (11), 375 (58), and 91 (100).

(±)-7,10-*Bisbenzyloxy*-3,4-*dihydro*-5,9-*dimethoxy*-trans-*dimethyl*-1H-*naphtho*[2,3-c]*pyran* (**20**).—Compound (**18**) (4.74 g, 9.8 mmol) was cyclised with potassium t-butoxide (4.39 g, 39 mmol) as described for the formation of compound (**19**). The residue obtained upon work-up with ethyl acetate as the extraction solvent was chromatographed (8% ethyl acetate–light petroleum) to afford the *product* (4.64 g, 97%) as white cubes, m.p. 121.5 °C (from ether–light petroleum followed by propan-2-ol) (Found: C, 76.8; H, 6.7. $C_{31}H_{32}O_5$ requires C, 76.8; H, 6.7%); $\nu_{max.}$ 1 630, 1 610, and 1 590 cm^{-1} (C=C); δ 1.38 (3 H, d, *J* 6 Hz, 3-CH_3), 1.67 (3 H, d, *J* 7 Hz, 1-CH_3), 2.61 (1 H, dd, *J* 17 and 11 Hz, pseudoaxial 4-H), 3.09 (1 H, dd, *J* 3.5 and 17 Hz, pseudoequatorial 4-H), 3.80 and 3.85 (each 3 H, s, OCH_3), 4.0—4.25 (1 H, m, 3-H), 4.75 and 5.10 (each 1 H, d, *J* 11 Hz, 10-OCH_2), 5.22 (2 H, s, 7-OCH_2), 5.37 (1 H, q, *J* 7 Hz, 1-H), 6.59 (1 H, d, *J* 2 Hz, 8-H), 7.06 (1 H, d, *J* 2 Hz, 6-H), and 7.3—7.6 (10 H, m, C_6H_5); *m/z* 484 (M^+, 18%), 393 (55), 361 (10), and 91 (100).

(1R,3R,4S)-7,10-*Bisbenzyloxy*-3,4-*dihydro*-4-*hydroxy*-5,9-*dimethoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran* (**23**) *and its Enantiomer, and* (1R,3R,4R)-7,10-*Bisbenzyloxy*-3,4-*dihydro*-4-

hydroxy-5,9-*dimethoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran* (**26**) *and its Enantiomer*.—(*a*) Compound (**20**) (4.61 g, 9.5 mmol) was oxygenated in dimethylformamide as described for compound (**19**), for 1 h, before cooling, dilution with water (1.6 l), and extraction with 30% diethyl ether–ethyl acetate (to enhance phase separation). Work-up and chromatography (10—30% ethyl acetate–light petroleum) first afforded starting material (184 mg, 4%), then *compound* (**23**) (1.86 g, 41% based on starting material consumed) as cream-coloured rhombic crystals, m.p. 119.5—120 °C (from methanol) (Found: C, 74.3; H, 6.5. $C_{31}H_{32}O_6$ requires C, 74.4; H, 6.5%); $\nu_{max.}$ 3 550 (OH) and 1 640, 1 610, and 1 590 cm^{-1} (C=C); δ 1.40 (3 H, d, *J* 6 Hz, 3-CH_3), 1.68 (3 H, d, *J* 7 Hz, 1-CH_3), 3.86 and 3.89 (each 3 H, s, OCH_3), 4.03 (1 H, dq, *J* 6 and 8 Hz, 3-H), 4.30 (1 H, d, *J* 3 Hz, OH, D_2O-exchangeable), 4.69 (1 H, d, *J* 10 Hz, 10-OCH), 4.74 (1 H, dd, *J* 3 and 8 Hz, 4-H), 5.06 (1 H, d, *J* 10 Hz, 10-OCH), 5.20 (1 H, q, *J* 7 Hz, 1-H), 5.20 (2 H, s, CH_2Ph), 6.64 (1 H, d, *J* 2 Hz, 8-H), 7.02 (1 H, d, *J* 2 Hz, 6-H), and 7.35—7.65 (10 H, m, C_6H_5); *m/z* 500 (M^+, 5%), 482 (10), 409 (5), 391 (20), 377 (15), and 91 (100); and thirdly *compound* (**26**) (238 mg, 5%) as off-white needles, m.p. 141—142 °C (from propan-2-ol) (Found: C, 74.4; H, 6.5. $C_{31}H_{32}O_6$ requires C, 74.4; H, 6.5%); $\nu_{max.}$ 3 550 (OH) and 1 630, 1 610, and 1 590 cm^{-1} (C=C); δ 1.41 (3 H, d, *J* 6 Hz, 3-CH_3), 1.60 (3 H, d, *J* 7 Hz, 1-CH_3), 2.20 (1 H, d, *J* 9 Hz, OH, D_2O-exchangeable), 3.85 and 3.96 (each 3 H, s, OCH_3), 4.16 (1 H, *J* 2 and 6 Hz, 3-H), 4.72 (1 H, dd, *J* 2 and 9 Hz, 4-H), 4.74 and 5.08 (each 1 H, d, *J* 10 Hz, 10-OCH_2), 5.21 (2 H, s, CH_2Ph), 5.29 (1 H, q, *J* 7 Hz, 1-H), 6.68 (1 H, d, *J* 2 Hz, 8-H), 7.08 (1 H, d, *J* 2 Hz, 6-H), and 7.3—7.6 (10 H, m, C_6H_5); *m/z* 500 (M^+, 8%), 482 (17), 408 (8), 391 (30), 377 (18), and 91 (100).

(*b*) Compound (**20**) (114 mg, 0.24 mmol) was dissolved in dry dimethyl sulphoxide (8 ml) and dry oxygen was bubbled into the solution. Potassium t-butoxide (106 mg, 0.94 mmol) was added and the solution was stirred vigorously at 55 °C. More base (4 mol equiv. in total) was added after 0.5 and 1 h. Stirring was continued for a further 7 h. The mixture was quenched with ice-water and extracted exhaustively with ethyl acetate. The residue obtained upon work-up was chromatographed as in (*a*) to afford starting material (32 mg, 28%), the product (**23**) (51 mg, 43%; 60% based on starting material consumed), and the product (**26**) (20 mg, 17%; 24% based on starting material consumed).

(*c*) Compound (**23**) (46 mg, 0.092 mmol) was dissolved in dry ether (5 ml) and phosphorus pentachloride (40 mg, 0.184 mmol) was added in one batch. The mixture was stirred for 6 min at room temperature, then quenched with water (20 ml). More ether was added and the organic phase was washed exhaustively with deionised water (5 × 15 ml). The residue obtained upon work-up was immediately redissolved in acetonitrile (5 ml) and then deionised water (1 ml) containing silver nitrate (83 mg, 0.491 mmol) was added. The mixture was stirred for 3.5 h at room temperature during which time a white precipitate formed. The mixture was then partitioned between water and ether. The residue obtained upon work-up afforded an oil which was chromatographed (10% ethyl acetate–light petroleum), giving the oily olefin (**42**) (3 mg, 7%), followed by the chloro compound (**40**) (6 mg, 13%); both were identical with material described later. The third compound obtained was the pseudoequatorial alcohol (**23**) (10 mg, 22%), which was followed by the pseudoaxial alcohol (**26**) (25 mg, 55%).

(1R,3R,4S)-3,4-*Dihydro*-4-*hydroxy*-5,7,9,10-*tetramethoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran* (**24**) *and its Enantiomer, and* (1R,3R,4R)-3,4-*Dihydro*-4-*hydroxy*-5,7,9,10-*tetramethoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran* (**27**) *and its Enantiomer*.—(*a*) The pyran (**21**) (97 mg, 0.292 mmol) was dissolved in dry dimethyl sulphoxide (10 ml) and dry oxygen was bubbled through the solution for 10 min at room temperature. Potassium t-butoxide (220 mg, 1.96 mmol) was added and the solution was stirred for 30 min while bubbling of oxygen was continued. The mixture was quenched with water and exhaustively extracted with ether. The residue obtained upon work-up was chromatographed (20% ethyl acetate–light petroleum) to afford the product (**24**) (61.3 mg, 63%) followed by the product (**27**) (22 mg, 23%). These compounds were identical with those reported previously.[4]

(*b*) The chloro compound (**39**) (44 mg, 0.12 mmol) described later was dissolved in acetonitrile (5 ml). Water (1 ml) and silver nitrate (102 mg, 0.6 mmol) were added, and the mixture was stirred for 4.5 h at room temperature. Water and ether were added, and the residue obtained upon work-up was subjected to p.l.c. (30% ethyl acetate–light petroleum) to afford starting material (3 mg, 7%) followed by the *product* (**24**) (4 mg, 10%) and then *compound* (**27**) (15 mg, 36%).

(*c*) Compound (**24**) (50 mg, 0.144 mmol) was dissolved in dry ether (10 ml). Phosphorus pentachloride (60 mg, 0.288 mmol) was added and mixture stirred for 10 min at room temperature. The reaction was then quenched with water (20 ml). More ether (80 ml) was added and the organic phase was washed with deionised water (5 × 10 ml). The residue obtained upon work-up was immediately redissolved in acetonitrile (10 ml). Water (1.1 ml) and silver nitrate (122 mg, 0.72 mmol) were added and the mixture was stirred for 5 h at room temperature. More water and ether were added. The residue obtained upon work-up afforded the chloro compound (**39**) (3 mg, 6%), the product (**24**) (9 mg, 18%), and finally the product (**27**) (35 mg, 70%) by the method described in (*b*).

(1R,3R,4R)-4-*Chloro*-3,4-*dihydro*-5,7,9,10-*tetramethoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran* (**39**) *and its Enantiomer, and* 5,7,9,10-*Tetramethoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran* (**41**).—(*a*) Compound (**24**) (48 mg, 0.138 mmol) was dissolved in dry ether (5 ml) and chlorinated with phosphorus pentachloride (57 mg, 0.276 mmol). When t.l.c. showed that all starting material had been consumed, the reaction was stopped with water (30 ml) and the mixture partitioned with ether. The organic layer was twice extracted with deionised water. The yellow oily residue obtained upon work-up was subjected to p.l.c. (20% ethyl acetate–light petroleum) to give first the *pyran* (**41**) (4 mg, 9%) as an oil (Found: C, 69.15; H, 6.7. $C_{19}H_{22}O_5$ requires C, 69.1; H, 6.7%); $\nu_{max.}$(film) 1 647, 1 616, 1 600, and 1 581 cm^{-1} (C=C); δ 1.44 (3 H, d, *J* 7 Hz, 1-CH_3), 1.98 (3 H, s, 3-CH_3), 3.83, 3.86, 3.93, and 3.98 (each 3 H, s, OCH_3), 5.72 (1 H, q, *J* 7 Hz, 1-H), 5.91 (1 H, s, 4-H), 6.44 (1 H, d, *J* 2.3 Hz, 8-H), and 6.95 (1 H, d, *J* 2.3 Hz, 6-H); *m/z* 330 (M^+, 100%) and 315 (74). This was followed by the *chloro compound* (**39**) (44 mg, 87%) as an oil (Found: C, 62.35; H, 6.1. $C_{19}H_{23}ClO_5$ requires C, 62.2; H, 6.3%); $\nu_{max.}$(film) 1 620, 1 595, and 1 581 (C=C), and 679 and 650 cm^{-1} (C–Cl); δ 1.46 (3 H, d, *J* 6 Hz, 3-CH_3), 1.58 (3 H, d, *J* 6 Hz, 1-CH_3), 3.83, 3.94, 3.98, and 4.07 (each 3 H, s, OCH_3), 4.27 (1 H, dq, *J* 1.3 and 6 Hz, 3-H), 5.29 (1 H, d, *J* 1.3 Hz, pseudoequatorial 4-H), 5.37 (1 H, q, *J* 6 Hz, 1-H), 6.54 (1 H, d, *J* 2.3 Hz, 8-H), and 6.94 (1 H, d, *J* 2.3 Hz, 6-H); *m/z* 368 (M^+, 8%), 366 (M^+, 24), 330 (100), and 315 (89).

(*b*) Compound (**27**) (48 mg, 0.138 mmol) was treated similarly with phosphorus pentachloride (57 mg, 0.276 mmol). The chloro compound (**39**) (32 mg, 64%) and the olefin (**41**) (4 mg, 9%) were obtained as before.

(1R,3R,4R)-7,10-*Bisbenzyloxy*-4-*chloro*-3,4-*dihydro*-5,9-*dimethoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran* (**40**) *and its Enantiomer, and* 7,10-*Bisbenzyloxy*-5,9-*dimethoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran* (**42**).—The alcohol (**23**) (52 mg, 0.104 mmol) was chlorinated as already described. P.l.c. (20% ethyl acetate–light petroleum) afforded first the oily *olefin* (**42**) (4 mg, 8%) (Found: M^+, 482.207. $C_{31}H_{30}O_5$ requires *M*, 482.209); δ

1.44 (3 H, d, *J* 6.6 Hz, 1-CH_3), 1.98 (3 H, d, *J* 0.8 Hz, 3-CH_3), 3.79 and 3.84 (each 3 H, s, OCH_3), 4.79 and 5.09 (each 1 H, d, *J* 10.7 Hz, 10-OCH_2), 5.19 (2 H, s, 7-OCH_2), 5.73 (1 H, q, *J* 6.6 Hz, 1-H), 5.92 (1 H, d, *J* 0.8 Hz, 4-H), 6.53 (1 H, d, *J* 2.3 Hz, 8-H), 7.03 (1 H, d, *J* 2.3 Hz, 6-H), and 7.3—7.55 (10 H, m, C_6H_5). This was followed by the *chloro compound* (**40**) (48 mg, 89%) as colourless crystals, m.p. 62 °C (from methylene dichloride–light petroleum) (Found: C, 71.65; H, 6.05. $C_{31}H_{31}ClO_5$ requires C, 71.75; H, 6.0%); $\nu_{max.}$(film) 1 618, 1 595, and 1 581 (C=C), and 734 and 696 cm^{-1} (C–Cl); δ 1.47 (3 H, d, *J* 6 Hz, 3-CH_3), 1.59 (3 H, d, *J* 6.5 Hz, 1-CH_3), 3.85 and 3.97 (each 3 H, s, OCH_3), 4.26 (1 H, dq, *J* 1.3 and 6 Hz, 3-H), 4.78 and 5.09 (each 1 H, d, *J* 9 Hz, 10-OCH_2), 5.21 (2 H, s, 7-OCH_2), 5.29 (1 H, d, *J* 1.3 Hz, 4-H), 5.41 (1 H, q, *J* 6.5 Hz, 1-H), 6.63 (1 H, d, *J* 2.3 Hz, 8-H), 7.01 (1 H, d, *J* 2.3 Hz, 6-H), and 7.3—7.55 (10 H, m, C_6H_5).

(±)-7-*Benzyloxy*-3,4-*dihydro*-9-*methoxy*-r-1,t-3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran*-5,10-*quinone* (**30**).—The naphthalene (**20**) (142 mg) was oxidised as for compound (**19**). Flash chromatography (30% ethyl acetate–light petroleum) and crystallisation afforded the *product* (95 mg, 86%) as yellow needles, m.p. 160 °C (methylene dichloride–light petroleum) (Found: C, 73.0; H, 5.9. $C_{23}H_{22}O_5$ requires C, 73.0; H, 5.9%); $\nu_{max.}$ 1 660 (C=O) and 1 610 cm^{-1} (C=C); δ 1.31 (3 H, d, *J* 6 Hz, 3-CH_3), 1.52 (3 H, d, *J* 7 Hz, 1-CH_3), 2.16 (1 H, ddd, *J* 20, 10, and 2 Hz, pseudoaxial 4-H), 2.66 (1 H, dd, *J* 20 and 4 Hz, pseudoequatorial 4-H) 3.90 (3 H, s, OCH_3), *ca.* 3.96 (1 H, m, 3-H), 4.96 (1 H, dq, *J* 2 and 7 Hz, 1-H), 5.16 (2 H, s, CH_2Ph), 6.75 (1 H, d, *J* 2 Hz, 8-H), 7.29 (1 H, d, *J* 2 Hz, 6-H), and 7.37br (5 H, s, C_6H_5); *m/z* 378 (M^+, 30%), 363 (5), 267 (8), 259 (10), and 91 (100).

(1R,3R,4S)-7-*Benzyloxy*-3,4-*dihydro*-4-*hydroxy*-9-*methoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran*-5,10-*quinone* (**31**) *and its Enantiomer*.—The naphthalene (**23**) (101 mg) was oxidised as before and the *product* (41 mg, 51%) was isolated as yellow rosettes, m.p. 177.5—178.5 °C (from methylene dichloride–propan-2-ol) (Found: C, 69.8; H, 5.7. $C_{23}H_{22}O_6$ requires C, 70.05; H, 5.6%); $\nu_{max.}$ 3 550 (OH), 1 660 (C=O), and 1 600 cm^{-1} (C=C); δ 1.39 (3 H, d, *J* 6 Hz, 3-CH_3), 1.59 (3 H, d, *J* 7 Hz, 1-CH_3), 3.76 (1 H, d, *J* 2 Hz, OH, D_2O-exchangeable), 3.86 (1 H, dq, *J* 9 and 6 Hz, 3-H, partly obscured by the OMe), 3.92 (3 H, s, OCH_3), 4.42 (1 H, ddd, *J* 9, 2, and 1.5 Hz, 4-H, collapses to dd, *J* 9 and 1.5 Hz on D_2O exchange), 4.92 (1 H, dq, *J* 7 and 1.5 Hz, 1-H), 5.18 (2 H, s, CH_2Ph), 6.79 (1 H, d, *J* 2 Hz, 8-H), 7.30 (1 H, d, *J* 2 Hz, 6-H), and 7.39br (5 H, s, C_6H_5); *m/z* 394 (M^+, 8%), 376 (20), 350 (100), 285 (30), 259 (50), 231 (29), and 91 (100).

(1R,3R,4R)-7-*Benzyloxy*-3,4-*dihydro*-4-*hydroxy*-9-*methoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran*-5,10-*quinone* (**32**) *and its Enantiomer*.—The naphthopyran (**26**) (245 mg) was oxidised as before; flash chromatography (30% ethyl acetate–light petroleum) afforded the *quinone* (125 mg, 65%) as yellow rosettes, m.p. 174 °C (from methylene dichloride–propan-2-ol) (Found: C, 70.05; H, 5.65. $C_{23}H_{22}O_6$ requires C, 70.05; H, 5.6%); $\nu_{max.}$ 3 490 (OH), 1 660 and 1 640 (C=O), and 1 620 cm^{-1} (C=C); δ 1.40 (3 H, d, *J* 6 Hz, 3-CH_3), 1.46 (3 H, d, *J* 7 Hz, 1-CH_3), 2.57 (1 H, d, *J* 7 Hz, OH, D_2O-exchangeable), 3.94 (3 H, s, OCH_3), 3.98 (1 H, dq, *J* 6 and 2.5 Hz, 3-H), 4.24 (1 H, dd, *J* 7 and 2.5 Hz, 4-H, collapses to d, *J* 2.5 Hz on D_2O exchange), 5.02 (1 H, q, *J* 7 Hz, 1-H), 5.21 (2 H, s, CH_2), 6.82 (1 H, d, *J* 2.5 Hz, 8-H), 7.38 (1 H, d, *J* 2.5 Hz, 6-H), and 7.35—7.5 (5 H, m, C_6H_5); *m/z* 394 (M^+, 2%), 376 (20), 361 (10), 350 (95), 285 (20), 259 (40), 231 (32), and 91 (100).

(±)-7-*Benzyloxy*-3,4-*dihydro*-9-*hydroxy*-r-1,t-3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran*-5,10-*quinone* (**6**) *and* (±)-3,4-*Dihydro*-7,9-*dihydroxy*-r-1,t-3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran*-5,10-*quinone* (**3**) [(±)-*Deoxyquinone A*].—The naphthopyran (**30**) (500 mg, 1.32 mmol) was treated with boron trichloride (10.6 mmol) in dry methylene dichloride at 0 °C for 5 min in the usual manner. The residue obtained upon work-up was flash chromatographed (20—30% ethyl acetate–light petroleum) to afford first the *product* (**6**) (53 mg, 11%) as orange needles, m.p. 143—144 °C (from methylene dichloride–cyclohexane) (Found: C, 72.5; H, 5.6. $C_{22}H_{20}O_5$ requires C, 72.5; H, 5.5%); $\nu_{max.}$ 1 659 and 1 640 (C=O) and 1 606 cm^{-1} (C=C); δ 1.28 (3 H, d, *J* 6 Hz, 3-CH_3), 1.48 (3 H, d, *J* 6.5 Hz, 1-CH_3), 2.21 (1 H, ddd, *J* 1.5, 10, and 19 Hz, pseudoaxial 4-H), 2.68 (1 H, dd, *J* 4 and 19 Hz, pseudoequatorial 4-H), 3.98 (1 H, dd, *J* 6 and 10 Hz, 3-H), 5.01 (1 H, dq, *J* 1.5 and 6.5 Hz, 1-H), 5.18 (2 H, s, CH_2), 6.69 (1 H, d, *J* 2.5 Hz, 8-H), 7.25 (1 H, d, *J* 2.5 Hz, 6-H), 7.41 (5 H, m, C_6H_5), and 12.06 (1 H, s, OH); *m/z* 364 (M^+, 27%), 349 (7), and 91 (100). This was followed by (±)-*Deoxyquinone A* (232 mg, 64%) as orange needles, m.p. 229—230.5 °C (decomp.) from methylene dichloride–cyclohexane) [lit.,[11] for the natural product, m.p. 207.5—209 °C (decomp.)] (Found: C, 65.3; H, 5.2%; M^+ 274.085. $C_{15}H_{14}O_5$ requires C, 65.7; H, 5.3%; *M*, 274.084); $\nu_{max.}$ 3 450 (OH), 1 650 (C=O), and 1 630, 1 610, and 1 590 cm^{-1} (C=C); δ [$(CD_3)_2CO$] 1.30 (3 H, d, *J* 6.5 Hz, 3-CH_3), 1.50 (3 H, d, *J* 7 Hz, 1-CH_3), 2.08 (1 H, ddd, *J* 22, 11, and 2.5 Hz, pseudoaxial 4-H), 2.69 (1 H, dd, *J* 22 and 4 Hz, pseudoequatorial 4-H), 4.0 (1 H, m, 3-H), 4.88 (1 H, dq, *J* 7 and 2.5 Hz, 1-H), 6.56 (1 H, d, *J* 2 Hz, 8-H), 7.05 (1 H, d, *J* 2 Hz, 6-H), and 12.20 (1 H, s, OH, D_2O-exchangeable); *m/z* 274 (M^+, 100%), 259 (70), 245 (25), 231 (30), 230 (36), and 216 (18).

(1R,3R,4S)-3,4-*Dihydro*-4,7,9-*trihydroxy*-1,3-*dimethylnaphtho*[2,3-c]*pyran*-5,10-*quinone* (**1**) *and its Enantiomer* [(±)-*Quinone A*].—The naphthopyran (**31**) (23 mg) was treated with boron trichloride at −5 °C for 20 min as just described. The residue obtained upon work-up was flash chromatographed (30% ethyl acetate–light petroleum) to afford racemic *Quinone A* (10 mg, 59%) as red-orange cubes, which charred at 185—200 °C (from benzene–cyclohexane) (lit.,[11] for the natural product 200 °C) (Found: C, 61.8; H, 5.0. $C_{15}H_{14}O_6$ requires C, 62.05, H, 4.9%); $\nu_{max.}$ 3 300 (OH), 1 640 (C=O), and 1 615 cm^{-1} (C=C); δ [$(CD_3)_2CO$] 1.30 (3 H, d, *J* 6.5 Hz, 3-CH_3), 1.56 (3 H, d, *J* 7 Hz, 1-CH_3), 2.89br (2 H, s, 4- and 7-OH, D_2O-exchangeable), 3.85 (1 H, dq, *J* 7 and 6.5 Hz, 3-H), 4.34 (1 H, dd, *J* 7 and 2 Hz, 4-H), 4.81 (1 H, dq, *J* 7 and 2 Hz, 1-H), 6.53 (1 H, d, *J* 2.5 Hz, 8-H), 7.04 (1 H, d, *J* 2.5 Hz, 6-H), and 12.05 (1 H, s, OH, D_2O-exchangeable); *m/z* (10 eV) 290 (M^+, 2%), 272 (2), 257 (3), 246 (13), and 218 (78).

(1R,3R,4R)-7-*Benzyloxy*-3,4-*dihydro*-4,9-*dihydroxy*-1,3-*dimethylnaphtho*[2,3-c]*pyran*-5,10-*quinone* (**7**) *and its Enantiomer* [(±)-7-O-*Benzyl Quinone A'*].—The quinone (**32**) (82 mg, 0.21 mmol) in dry methylene dichloride (10 ml) was cooled to 0 °C and boron trichloride (0.42 mmol) was added in the same solvent (2 ml). The mixture was stirred for 6 min then quenched with water (40 ml) and shaken with methylene dichloride (4 × 30 ml). The residue obtained upon work-up was chromatographed (p.l.c.; 50% ethyl acetate–light petroleum under nitrogen) to afford the *quinone* (27 mg, 34%) as orange crystals, m.p. 152—153 °C (from methylene dichloride–cyclohexane) (Found: C, 69.2; H, 5.3. $C_{22}H_{20}O_6$ requires C, 69.45; H, 5.3%); $\nu_{max.}$ 3 481 (OH), 1 661 and 1 638 (C=O), and 1 609 cm^{-1} (C=C); δ 1.36 (3 H, d, *J* 6.5 Hz, 3-CH_3), 1.50 (3 H, d, *J* 7 Hz, 1-CH_3), 3.97 (1 H, dq, *J* 2 and 6.5 Hz, 3-H), 4.47 (1 H, d, *J* 2 Hz, 4-H), 4.67 (1 H, s, 4-OH, D_2O-exchangeable), 4.97 (1 H, q, *J* 7 Hz, 1-H), 5.12 (2 H, s, CH_2), 6.68 (1 H, d, *J* 2.5 Hz, 8-H), 7.24 (1 H, d, *J* 2.5 Hz, 6-H), 7.38 (5 H, s, C_6H_5), and 12.14 (1 H, s, 9-OH, D_2O-exchangeable).

(1R,3R,4R)-3,4-*Dihydro*-4,7,9-*trihydroxy*-1,3-*dimethylnaphtho*[2,3-c]*pyran*-5,10-*quinone* (**2**) *and its Enantiomer* [(±)-

Quinone A'].—Adams' catalyst (5 mg) was suspended in dry methanol (5 ml) and stirred under a stream of hydrogen until the brown suspension turned black. To this was added a solution of the quinone (**7**) (11 mg, 0.029 mmol) in dry methanol (10 ml), whereupon the yellow colour disappeared immediately. The mixture was stirred under hydrogen for 30 min and then air was admitted to oxidise the derived hydroquinone. The catalyst was removed by filtration and the solvent by evaporation, to leave racemic *Quinone A'* (8 mg, 95%) as red-orange crystals, m.p. 227—230 °C (decomp.) (from methanol followed by benzene) (lit.,[12] for the natural product 236 °C) (Found: C, 61.75; H, 4.95%; M^+ 290.079. $C_{15}H_{14}O_6$ requires C, 62.05; H, 4.9%; *M*, 290.079); $\nu_{max.}$ 3 445 (OH), 1 659 and 1 641 (C=O), and 1 613 cm^{-1} (C=C); δ [$(CD_3)_2CO$] 1.29 (3 H, d, *J* 6.5 Hz, 3-CH_3), 1.48 (3 H, d, *J* 7 Hz, 1-CH_3), 3.98 (1 H, dq, *J* 2 and 6.5 Hz, 3-H), 4.38br (1 H, s, 4-H, sharpens to d, *J* 2 Hz on D_2O exchange), 4.84 (1 H, q, *J* 7 Hz, 1-H), 6.62 (1 H, d, *J* 2.5 Hz, 8-H), 7.09 (1 H, d, *J* 2.5 Hz, 6-H), 7.34 (1 H, s, 7-OH, D_2O-exchangeable), and 12.18 (1 H, s, 9-OH, D_2O-exchangeable); *m/z* 290 (M^+, 2%), 288 (2), 272 (12), 246 (100), and 216 (80).

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