Naphtho[2,3-*c*]pyran-5,10-quinones. Syntheses of the Racemates of Quinone A, Quinone A', and Deoxyquinone A Dimethyl Ethers of 7-Methoxyeleutherin, and of Isoeleutherin

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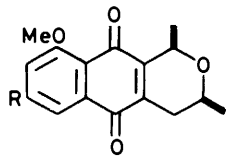
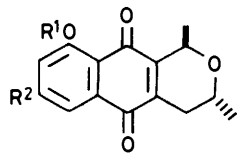
Treatment of 3-(1-hydroxyethyl)-1,4,5,7-tetramethoxy-2-prop-2-enylnaphthalene (**33**) with potassium t-butoxide in dimethylformamide under nitrogen for a short time gave a high yield of *trans*-3,4-dihydro-5,7,9,10-tetramethoxy-1,3-dimethyl-1*H*-naphtho[2,3-*c*]pyran (**41**). This compound, with the same base and solvent, but in air, afforded a mixture comprising its *cis*-epimer (**42**), together with the two possible 4-hydroxy derivatives, namely (**35**) and (**38**). Silver(II) oxide oxidation of compounds (**35**), (**38**), (**41**), and (**42**) gave, respectively, the dimethyl ethers of quinone A, quinone A', and deoxyquinone A, and also 7-methoxyeleutherin.

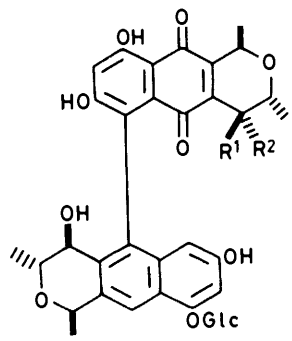
Various naturally occurring compounds are found as 5,10-quinonoid derivatives of the naphtho[2,3-*c*]pyran ring system. Examples include the stereoisomeric eleutherin (**1**) and isoeleutherin (**3**),[1] as well as the aphid pigments deoxyprotoaphin (**6**),[2] protoaphin *fb* (**7**),[3] and protoaphin *sl* (**8**). The latter three compounds undergo facile reductive cleavage to afford three closely related naphthopyranquinones, deoxyquinone A (**4**),[2] quinone A (**10**),[3,4] and quinone A' (**14**), respectively, together with, in each case, the same naphthalenic glycoside, glucoside B (**9**). The quinones (**4**), (**10**), and (**14**) have been subjected to methylation of the phenolic hydroxy groups to afford the respective dimethyl ethers (**5**),[5] (**11**),[3] and (**15**). We describe here[6] the syntheses of these three dimethyl ethers as their racemates,† as well as (±)-7-methoxyeleutherin (**2**),[7] isomeric with (**5**), and (±)-isoeleutherin (**3**).[8] Previous routes to compound (**3**)[8–10] and (±)-deoxyquinone A dimethyl ether (**5**)[5] have been recorded, but they give rise to a mixture of eleutherin and isoeleutherin in the first case, and a mixture of compound (**5**) and its *cis*-dimethyl isomer, (±)-7-methoxyeleutherin (**2**), in the second. The routes described here for isoeleutherin and deoxyquinone A dimethyl ether are highly stereoselective. The formation of the dimethyl ethers of quinones A and A', which is also highly stereoselective, represents the first reported synthesis of degradation products of the aphid pigments protoaphin-*fb* and protoaphin-*sl*.



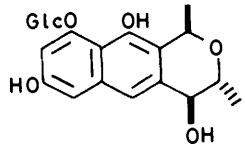
(**1**) R = H
(**2**) R = OMe



(**3**) R^1 = Me, R^2 = H
(**4**) R^1 = H, R^2 = OH
(**5**) R^1 = Me, R^2 = OMe



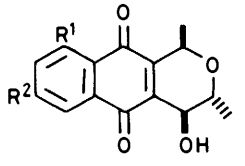
(**6**) R^1 = R^2 = H
(**7**) R^1 = OH, R^2 = H
(**8**) R^1 = H, R^2 = OH



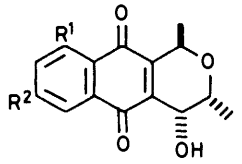
(**9**)

Results and Discussion

The naphthyl ketone (**26**) was available from 3-acetyl-5,7-dimethoxy-1,4-naphthoquinone (**20**)[11] by two routes. The first involved allylation of compound (**20**) with commercially available vinylacetic acid to afford the allylquinone (**21**); however, the yield was mediocre [44% overall in the two steps from 3-acetyl-1,5,7-trimethoxy-4-naphthol (**18**)[11]]. Reductive methylation provided the ketone (**26**) smoothly, in a yield of 32% from compound (**18**). The second route to the product (**26**) was effected by the alternative allylation of the quinone (**20**) using allyltrimethylstannane[10] to afford the adduct (**24**), which was methylated without purification to give the naphthyl ketone (**26**) in an overall yield of 64% from the naphthol (**18**), which made it the method of choice. Conjugation of the allylic double bond of compound (**26**) with base gave only the (*E*)-olefin (**27**), as evidenced by the large coupling constant between the olefinic protons. This ketone was reduced with lithium aluminium hydride to the corresponding alcohol (**30**).



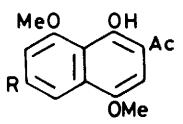
(**10**) R^1 = R^2 = OH
(**11**) R^1 = R^2 = OMe
(**12**) R^1 = OMe, R^2 = H
(**13**) R^1 = R^2 = H



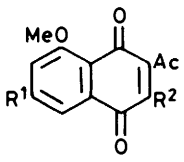
(**14**)
(**15**)
(**16**)
(**17**)

Cerium(IV) ammonium nitrate has recently been shown to oxidise the napthyl alcohol (**32**) to a mixture of (±)-7,9-dideoxyquinones A (**13**) and A' (**17**), the latter predominating.[12] However, when this reagent was applied to the alcohol (**30**), no

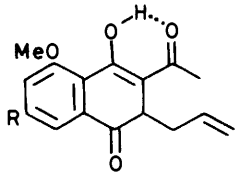
† All synthetic products whose structures are represented as single enantiomers are racemic.



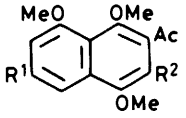
(18) R = OMe
(19) R = H



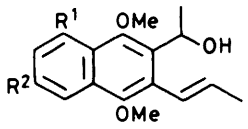
(20) R^1 = OMe, R^2 = H
(21) R^1 = OMe, R^2 = $CH_2CH{=}CH_2$
(22) R^1 = R^2 = H
(23) R^1 = H, R^2 = $CH_2CH{=}CH_2$



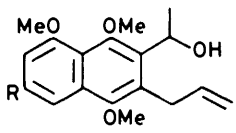
(24) R = OMe
(25) R = H



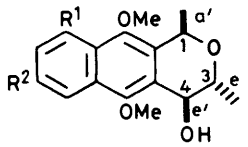
(26) R^1 = OMe, R^2 = $CH_2CH{=}CH_2$
(27) R^1 = OMe, R^2 = (*E*)−CH=CHCH$_3$
(28) R^1 = H, R^2 = $CH_2CH{=}CH_2$
(29) R^1 = H, R^2 = (*E*)−CH=CHCH$_3$

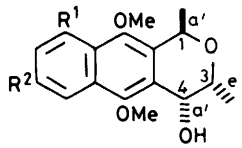


(30) R^1 = R^2 = OMe
(31) R^1 = OMe, R^2 = H
(32) R^1 = R^2 = H



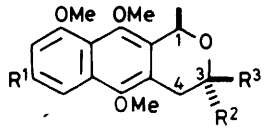
(33) R = OMe
(34) R = H





(35) R^1 = R^2 = OMe
(36) R^1 = OMe, R^2 = H
(37) R^1 = R^2 = H

(38)
(39)
(40)



(41) R^1 = OMe, R^2 = Me, R^3 = H
(42) R^1 = OMe, R^2 = H, R^3 = Me
(43) R^1 = R^3 = H, R^2 = Me
(44) R^1 = R^2 = H, R^3 = Me

product corresponding to either (**11**) or (**15**) could be identified, all the starting material having been consumed. Reaction with two moles of oxidant also provided neither cyclised naphthalene (**35**) nor (**38**), although the corresponding naphthyl alcohol (**32**) gives the naphthopyrans (**37**) and (**40**) under similar conditions.[12]

The non-conjugated naphthyl alcohol (**33**) was available by reduction of the corresponding ketone (**26**). Brief treatment of the alcohol (**33**) with potassium t-butoxide in dimethylformamide under nitrogen afforded a high hield (86%) of the naphthopyran (**41**) together with some of the pseudoequatorial C-4 hydroxylated material (**35**) (5%), the latter assignment being made on the basis of its ^{1}H n.m.r. spectrum (described below). Similar reaction of the conjugated alcohol (**30**) gave the products (**41**) (92%) and (**35**) (2%). Reaction of the allyl alcohol (**33**) with the same base and solvent, but in the presence of air, afforded a much higher proportion (17%) of the hydroxylated product (**35**) relative to (**41**) (58%). Similar results were obtained for the alcohol (**30**) in the presence of air.

When the pyran (**41**) was treated with potassium t-butoxide in dimethylformamide in the presence of air for several hours, three new products were isolated. The first was assigned structure (**42**) (8%), epimeric with (**41**) at C-1.[13] The major product (35%) showed three protons in the ^{1}H n.m.r. spectrum at δ 5.21 (q, *J* 7.5 Hz, 1-H), 4.74 (d, *J* 9 Hz, 4-H), and *ca.* 3.97 (dq, *J* 6.5 and 9 Hz, 3-H) and was identified as the leucotetramethyl ether (**35**) of quinone A, identical with the material described above. The chemical shift of the latter signal is imprecise, owing to partial overlap by the methoxy signals. The third product (7%) showed corresponding signals at δ 5.31 (q, *J* 7 Hz), 4.72 (d, *J* 2 Hz), and *ca.* 4.13 (dq, *J* 2 and 6.5 Hz), and was assigned structure (**38**), being the leucotetramethyl ether of quinone A′.

These results were consistent with our recent findings, which described the related reaction for the 7,9-demethoxy analogue of compound (**41**) and the determination of the stereochemistry of the products (**37**) and (**40**).[13]

Oxidation of the naphthopyran (**41**) with cerium(IV) ammonium nitrate (2 equiv.) did not afford deoxyquinone A dimethyl ether (**5**) or any other identifiable product, a finding consistent with the destruction of the naphthyl alcohol (**30**) by the same oxidant, as described above. However, the alternative oxidation of compound (**41**) with silver(II) oxide gave the desired quinone (**5**) in good yield (82%). Similar treatment of compound (**42**) gave 7-methoxyeleutherin (**2**) (75%).

Oxidation of the tetramethyl ethers (**35**) and (**38**) with silver(II) oxide gave the dimethyl ethers of quinone A, (**11**) (90%), and quinone A′, (**15**) (88%), respectively. The stereochemical assignments for these compounds were confirmed by their ^{1}H n.m.r. spectra, which were identical with those reported for the naturally derived compounds.[14] These results verified the tentative stereochemical assignments made above for the two leucotetramethyl ethers (**35**) and (**38**), where the absence[12] of any long-range coupling between 1-H and 4-H precluded a rigorous determination of the stereochemistry of the 1-Me group in each case.

The allylation of 3-acetyl-5-methoxy-1,4-naphthoquinone (**22**), obtained from the naphthol (**19**),[11] was carried out using vinylacetic acid; the yield of the quinone (**23**) from the naphthol (**19**) was about the same as that for the conversion of compound (**18**) into (**21**). Reductive methylation gave the naphthyl ketone (**28**). After the completion of this work, an alternative synthesis of this compound was reported[10] by the allylation of the quinone (**22**) using allyltrimethylstannane, to give compound (**25**), followed by methylation, as we have subsequently used for the ketone (**26**) above. No doubt the latter method is the one of choice for compound (**28**) as well. Lithium aluminium hydride reduction yielded the alcohol (**34**). When this compound was treated briefly with potassium t-butoxide in dimethylformamide under nitrogen, a high yield (87%) of the *trans*-dimethylnaphthopyran (**43**)[8,9] was obtained, only traces of the *cis*-isomer (**44**) being formed. Oxidation of compound (**43**) gave (±)-isoeleutherin (**3**).

Treatment of the alcohol (**34**) in dimethylformamide with the same base, but for a longer time and in air, afforded a mixture of the pyran (**43**) and its pseudoequatorial hydroxy derivative (**36**). Cerium(IV) ammonium nitrate oxidation of compound (**36**) gave the corresponding quinone (**12**).

Since it had not proved possible to oxidatively cyclise the tetramethoxynaphthyl alcohol (**30**) to the quinones (**11**) and (**15**) with cerium(IV) ammonium nitrate, it was of interest to investigate the reaction of this reagent with the corresponding trimethoxy compound (**31**). This was obtained from the ketone (**28**) by conjugation of the double bond, once again to give the (*E*)-olefin (**29**) only, followed by reduction to the alcohol (**31**). Oxidation with cerium(IV) ammonium nitrate (2 equiv.) gave the hydroxynaphthopyran (**39**) in poor yield. This was oxidised with silver(II) oxide to give the quinone (**16**) in good yield. Presumably, successive addition of methoxy groups to the naphthyl alcohol (**32**) increases the electron density of the system, thereby promoting alternative oxidative pathways to the extent that, with the tetramethoxy compound (**30**), none of the desired oxidative cyclisation to the products (**35**) and (**38**) takes place with the cerium oxidant.

Spectroscopic and thin layer chromatographic comparison of the synthetic with the naturally derived samples of deoxyquinone A, quinone A, and quinone A′ showed each pair to be identical. Unfortunately, natural 7-methoxyeleutherin was no longer available, but the spectra provided agreed entirely with those of our synthetic product.

Experimental

All ^1H n.m.r. spectra were measured for solutions in [^2H]chloroform with tetramethylsilane as internal reference, while 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}, 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 obtained upon work-up' refers to the residue when the organic layer was separated, dried ($MgSO_4$), and the solvent evaporated under reduced pressure.

3-*Acetyl*-5,7-*dimethoxy*-2-*prop*-2-*enyl*-1,4-*naphthoquinone* (**21**).—The quinone (**20**)[11] (302 mg) was dissolved in acetonitrile (35 ml) and water (5 ml) was added, followed by vinylacetic acid (149 mg), and silver nitrate (115 mg) in water (3 ml). The flask was flushed with nitrogen and then potassium peroxodisulphonate (629 mg) in water (4 ml) was added under nitrogen during 45 min to the reaction mixture immersed in an oil-bath maintained at 80 °C, and the reaction mixture was stirred with heating for a further 30 min. The cooled solution was poured into water and extracted with methylene dichloride (3 × 50 ml). The organic layer was then washed with a small amount of saturated aqueous sodium hydrogen carbonate. The residue obtained upon work-up was chromatographed (eluant 30% ethyl acetate–light petroleum) to afford the *product* (**21**) (178 mg, 51%), m.p. 156—157 °C (methylene dichloride–light petroleum) (Found: C, 67.7; H, 5.3. $C_{17}H_{16}O_5$ requires C, 68.0; H, 5.3%); $\nu_{max.}$ 1 709, 1 660, 1 598, and 1 562 cm^{-1}, δ 2.46 (3 H, s, CCH_3), 3.21 (2 H, dd, *J* 1 and 6 Hz, CH_2), 3.95 (6 H, s, OCH_3), 4.9—5.3 (2 H, m, vinyl CH_2), 5.6—6.1 (1 H, m, vinyl CH), 6.73 (1 H, d, *J* 3 Hz, 6-H), and 7.25 (1 H, d, *J* 3 Hz, 8-H).

3-*Acetyl*-1,4,5,7-*tetramethoxy*-2-*prop*-2-*enylnaphthalene* (**26**).—(*a*) The quinone (**21**) (373 mg) in methylene dichloride (50 ml) was reduced with an excess of aqueous sodium dithionite until the organic phase became a very pale yellow. The organic layer was dried and evaporated, and then immediately dissolved in dry acetone (30 ml). Anhydrous potassium carbonate (2.0 g) was added, followed by dimethyl sulphate (2 ml), and the mixture vigorously stirred and boiled for 12 h under nitrogen. The mixture was cooled, filtered, the solvent evaporated, and the residue was taken up in ether, and washed successively with concentrated ammonia, water, dilute hydrochloric acid, and finally water. The residue upon work-up was chromatographed (eluant 30% ethyl acetate–light petroleum) to yield the *product* (**26**) as an oil (369 mg, 90%) (Found: C, 68.9; H, 6.75. $C_{19}H_{22}O_5$ requires C, 69.05; H, 6.65%); $\nu_{max.}$(neat) 1 730, 1 690, 1 620, and 1 583 cm^{-1}; δ 2.58 (3 H, s, CCH_3), 3.55 (2 H, dd, *J* 1 and 6 Hz, CH_2), 3.76, 3.86, 3.93, and 3.98 (3 H each, s, OCH_3), 4.9—5.15 (2 H, m, vinyl CH_2), 5.75—6.2 (1 H, m, vinyl CH), 6.55 (1 H, d, *J* 2 Hz, 6-H), and 7.00 (1 H, d, *J* 2 Hz, 8-H).

(*b*) The naphthol (**18**) (1 g, 3.62 mmol) in acetonitrile (100 ml) and water (25 ml) was treated with cerium(IV) ammonium nitrate (5.1 g, 2.6 equiv.) in water (20 ml) during 8 min, and stirring was continued for a further 15 min. The mixture was thrown into water, extracted with methylene dichloride, and the solution dried. The solution volume was reduced to about 60 ml, and this was then cooled to −78 °C and the flask flushed with nitrogen. Boron trifluoride–ether (0.38 ml, 0.8 equiv. relative to the starting naphthol) was added, whereupon the solution turned dark brown. Allyltrimethylstannane (1.2 g, 1.5 equiv.) was added, and the reaction mixture stirred for 1 h at −78 °C, and warmed to room temperature. Water (200 ml) was then rapidly added and the whole extracted with methylene dichloride (4 × 50 ml). The dried extract was filtered, and the resulting oil, on evaporation of the solvent, was dissolved in dry acetone (100 ml) and treated with potassium carbonate (5 g, 10 equiv.) and dimethyl sulphate (3.5 ml, 10 equiv.). The mixture was boiled with vigorous stirring for 5 h. Work-up as under (*a*) above gave a brown oil which was chromatographed (eluant 15% ethyl acetate–light petroleum) to give the *product* (**26**) (764 mg, 64%), identical with the material from (*a*).

3-*Acetyl*-1,4,5,7-*tetramethoxy*-2-*prop*-1-*enylnaphthalene* (**27**).—Compound (**26**) (504 mg) was treated with potassium t-butoxide (684 mg, 4 equiv.) in dry tetrahydrofuran (60 ml) at 60 °C under nitrogen for 2 h. The reaction mixture was cooled and added to aqueous ammonium chloride, then extracted with dichloromethane. The residue upon work-up was chromatographed (eluant 20% ethyl acetate–light petroleum) to afford the *product* (**27**) (369 mg, 73%), m.p. 98—99 °C (light petroleum) (Found: C, 68.9; H, 6.8. $C_{19}H_{22}O_5$ requires C, 69.05; H, 6.65%); $\nu_{max.}$ 1 704, 1 615, and 1 576 cm^{-1}; δ 1.93 (3 H, d, *J* 6 Hz, $CHCH_3$), 2.50 (3 H, s, $COCH_3$), 3.79, 3.82, 3.95, and 3.99 (3 H each, s, OCH_3), 6.12 (1 H, dq, *J* 6 Hz, $CHCH_3$), 6.56 (1 H, d, *J* 16 Hz, CH=$CHCH_3$), 6.55 (1 H, d, *J* 2 Hz, 6-H), and 7.05 (1 H, d, *J* 2 Hz, 8-H).

3-(1-*Hydroxyethyl*)-1,4,5,7-*tetramethoxy*-2-*prop*-1-*enylnaphthalene* (**30**).—Compound (**27**) (320 mg) in dry ether (20 ml) was added to a stirred suspension of lithium aluminium hydride (250 mg) in ether (20 ml). When t.l.c. showed that all the starting material had been converted into product (*ca.* 20 min), the reaction was worked up by addition of saturated ammonium chloride, followed by anhydrous magnesium sulphate. Work-up of the filtrate gave a residue which was chromatographed (eluant 30% ethyl acetate–light petroleum) to afford the *product* (**30**) (280 mg, 87.5%), m.p. 98—99 °C (light petroleum) (Found: C, 68.55; H, 7.25. $C_{19}H_{24}0_5$ requires C, 68.65; H, 7.25%); $\nu_{max.}$ (liquid film before crystallisation) 3 440, 1 614, 1 580, and 1 490 cm^{-1}; δ 1.63 [3 H, d, *J* 7 Hz, $CH(OH)CH_3$], 1.99 (3 H, dd, *J* 2 and 7 Hz, CH=$CHCH_3$), 3.74, 3.87, 3.93, and 3.97 (3 H each, s, OCH_3), 3.9 (1 H, br s, OH, D_2O exchangeable), 5.35 [1 H, m, $CH(OH)CH_3$], 6.06 (1H, dq, *J* 7 and 16 Hz, CH=$CHCH_3$), 6.55 (1H, d, *J* 2.5 Hz, 6-H), 6.60 (1 H, dq, *J* 2 and 16 Hz, CH=$CHCH_3$), and 7.05 (1 H, d, *J* 2.5 Hz, 8-H).

3-(1-*Hydroxyethyl*)-1,4,5,7-*tetramethoxy*-2-*prop*-2-*enylnaphthalene* (**33**).—Compound (**26**) (2.20 g) in dry ether (20 ml) was added dropwise during 3 min to a stirred suspension of lithium aluminium hydride (1.03 g) in dry ether (80 ml). The mixture was stirred for a further 10 min after which the work-up procedure for compound (**30**) was followed. Chromatography as above gave the *alcohol* (**33**) (2.01 g, 91%). A small portion was subjected to p.l.c. to provide an analytical sample of the oily product (Found: C, 68.85; H, 7.25; $C_{19}H_{24}O_5$ requires C, 68.65; H, 7.25%); $\nu_{max.}$(neat) 3 480, 1 618, 1 580, and 1 492 cm^{-1}; δ 1.63 (3 H, d, *J* 7 Hz, CCH_3), 3.70 (2 H, m, CH_2), 3.82, 3.84, 3.90, and 3.94 (3 H each, s, OCH_3), 4.10 (1 H, br s, OH, D_2O exchangeable), 3.8—4.2 (2 H, m, vinyl CH_2), 5.26 (1 H, m, C*H*CH_3), 5.9—6.3 (1 H, m, vinyl CH), 6.52 (1 H, d, *J* 2.5 Hz, 6-H), and 6.98 (1 H, d, *J* 2.5 Hz, 8-H).

trans-3,4-*Dihydro*-5,7,9,10-*tetramethoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran* (**41**).—(*a*) Compound (**30**) (584 mg) was dissolved in dry dimethylformamide (25 ml) and dry nitrogen was passed through the solution for 5 min. Potassium t-butoxide (1.33 g) was added and the mixture stirred under nitrogen at a bath temperature of 55 °C for 15 min. The mixture was cooled, thrown into water, and extracted exhaustively with ether. The residue obtained upon work-up was chromatographed (eluant 30% ethyl acetate–light petroleum) to afford firstly the *naphthopyran* (**41**) (537 mg, 92%) (Found: C, 68.7; H, 7.4. $C_{19}H_{24}O_5$ requires C, 68.65; H, 7.25%); $\nu_{max.}$ 1 615, 1 595, 1 578, and 1 500 cm^{-1}; δ 1.39 (3 H, d, *J* 6 Hz, 3-CH_3), 1.63 (3 H, d, *J* 7 Hz, 1-CH_3), 2.56 (1 H, dd, *J* 10 and 17 Hz, pseudoaxial 4-H), 3.06 (1 H, dd, *J* 3.5 and 17 Hz, pseudoequatorial 4-H), 3.79, 3.85, 3.94, and 3.98 (3 H each, s, OCH_3), 3.9—4.3 (1 H, m, 3-H), 5.31 (1 H, q, *J* 7 Hz, 1-H), 6.51 (1 H, d, *J* 2.5 Hz, 8-H), and 6.96 (1 H, d, *J* 2.5 Hz, 6-H). Later fractions afforded compound (**35**) (12 mg, 2%), identical with the material described below.

(*b*) Similar treatment of the alcohol (**33**) (2.01 g) gave rise to the *product* (**41**) (1.73 g, 86%), identical with that described above. This was followed by compound (**35**) (100 mg, 5%), indistinguishable from material described below. None of the isomeric compound (**38**) was observed in either reaction (*a*) or (*b*).

(1R,3R,4S)-3,4-*Dihydro*-4-*hydroxy*-5,7,9,10-*tetramethoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran* (**35**) *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* (**38**) *and its Enantiomer and* cis-3,4-*Dihydro*-5,7,9,10-*tetramethoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran* (**42**).—Compound (**41**) (193 mg) was dissolved in dry dimethylformamide (15 ml) and dry air was passed through the solution for 10 min. Potassium t-butoxide (440 mg) was added and the mixture stirred at a bath temperature of 55—60 °C for 2 h under a stream of dry air. The air was turned off, and stirring was continued for 1 h, then the mixture was worked up as for (**41**) above. Chromatography of the residue (eluant 20% ethyl acetate) gave firstly *compound* (**42**) (17 mg, 8%), m.p. 148.5—149.5 °C (methylated spirits) (Found: C, 68.3; H, 7.55. $C_{19}H_{24}O_5$ requires C, 68.65; H, 7.25%); δ 1.40 (3 H, d, *J* 6.5 Hz, 3-CH_3), 1.54 (3 H, d, *J* 6.5 Hz, 1-CH_3), 2.54 (1 H, dd, *J* 11 and 16 Hz, pseudoaxial 4-H), 3.04 (1 H, dd, *J* 2.5 and 16 Hz, pseudoequatorial 4-H), 3.5—3.9 (1 H, m, 3-H, partially obscured), 3.73, 3.87, 3.93, and 3.98 (3 H each, s, OCH_3), 5.21 (1 H, q, *J* 6.5 Hz, 1-H), 6.51 (1 H, d, *J* 2.5 Hz, 8-H), and 6.98 (1 H, d, *J* 2.5 Hz, 6-H). The second fraction afforded starting material (15 mg, 8%), while the third fraction gave *product* (**35**) (70 mg, 35%) as white cubes, m.p. 119.5—120.5 °C (methylene dichloride–light petroleum) (lit.,[3] for the single enantiomer from natural sources, 40 °C. It is possible that the naturally derived sample was impure.) (Found: C, 65.45; H, 7.0. $C_{19}H_{24}O_6$ requires C, 65.5; H, 6.9%), $\nu_{max.}$ 3 520, 1 620, 1 596, 1 584, and 1 497 cm^{-1}; δ 1.42 (3 H, d, *J* 6.5 Hz, 3-CH_3), 1.68 (3 H, d, *J* 7.5 Hz, 1-CH_3), 3.76, 3.92, 3.94, and 3.96 (3 H each, s, OCH_3), 3.85 (1 H, br s, OH), *ca.* 3.97 (1 H, dq, *J* 6.5 and 9 Hz, 3 H, partially obscured by Me), 4.74 (1 H, d, *J* 9 Hz, 4-H), 5.21 (1 H, q, *J* 7.5 Hz, 1-H), 6.55 (1 H, d, *J* 2.5 Hz, 8-H), and 6.92 (1 H, d, *J* 2.5 Hz, 6-H). The last fractions gave rise to *compound* (**38**) (15 mg, 7%), m.p. 133—134 °C (methylene dichloride–light petroleum) (Found: C, 65.2; H, 7.0. $C_{19}H_{24}O_6$ requires C, 65.5; H, 6.9%); $\nu_{max.}$ 3 458, 1 618, 1 595, 1 578, and 1 496 cm^{-1}; δ 1.42 (3 H, d, *J* 6.5 Hz, 3-CH_3), 1.61 (3 H, d, *J* 7 Hz, 1-CH_3), 2.22 (1 H, br s, OH, D_2O exchangeable), 3.79, 3.93, 3.98, and 4.04 (3 H each, s, OCH_3), *ca.* 4.13 (1 H, dq, *J* 2 and 6.5 Hz, 3-H), 4.72 (1 H, d, *J* 2 Hz, 4-H), 5.31 (1 H, q, *J* 7 Hz, 1-H), 6.56 (1 H, d, *J* 2.5 Hz, 8-H), and 7.02 (1 H, d, *J* 2.5 Hz, 6-H).

(±)-cis-3,4-*Dihydro*-7,9-*dimethoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran*-5,10-*quinone* (**2**).—The tetramethyl ether (**42**) (16 mg), silver(II) oxide (40 mg), and dioxane (3 ml) were stirred together at room temperature. Nitric acid (6M; 0.2 ml) was added and the reaction mixture stirred for 4 min. A mixture of chloroform (4 ml) and water (1 ml) was added and the organic layer was separated and washed with more water. The residue obtained upon work-up gave the *product* (**2**) (11 mg, 75%) as a yellow powder, m.p. 185—186 °C (methylene dichloride–light petroleum) (lit.,[5] 179—180 °C). The ^1H n.m.r. spectrum in particular, gave conclusive evidence of the stereochemistry.[5]

(±)-trans-3,4-*Dihydro*-7,9-*dimethoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran*-5,10-*quinone* (**5**).—Compound (**41**) (60 mg) was oxidised as described for compound (**42**) above to give the *product* (**5**) (45 mg, 82%), m.p. 239.5—240.5 °C (ethanol) (lit.,[5] 228—230 °C).

(1R,3R,4S)-3,4-*Dihydro*-4-*hydroxy*-7,9-*dimethoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran*-5,10-*quinone* (**11**) *and its Enantiomer* [(±)-*Quinone A Dimethyl Ether*)].—Compound (**35**) (150 mg) was oxidised as above in dioxane (10 ml) to give the *product* (**11**) (123 mg, 90%) as small yellow rosettes, m.p. 175.5—176.5 °C (propan-2-ol) (lit.,[3] for the single enantiomer from natural sources, 172.5—174 °C) (Found: C, 64.0; H, 5.75. $C_{17}H_{18}O_6$ requires C, 64.1; H, 5.7%); $\nu_{max.}$ 3 555, 1 647, 1 630, 1 597, and 1 562 cm^{-1}; δ 1.38 (3 H, d, *J* 6 Hz, 3-CH_3), 1.57 (3 H, d, *J* Hz, 1-CH_3), 3.80 (1 H, s, OH, D_2O exchangeable), *ca.* 3.81 (1 H, dq, *J* 6 and 8 Hz, 3-H, partly obscured by OMe) 3.96 and 3.97 (3 H each, s, OCH_3), 4.44 (1 H, br d, *J* 8 Hz, 4-H), collapses to dd, *J* 1.5 and 8 Hz, on D_2O exchange), 4.90 (1 H, dq, *J* 1.5 and 7 Hz, 1-H), 6.69 (1 H, d, *J* 2.5 Hz, 8-H), and 7.21 (1 H, d, *J* 2.5 Hz, 6-H).

(1R,3R,4R)-3,4-*Dihydro*-4-*hydroxy*-7,9-*dimethoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran*-5,10-*quinone* (**15**) *and its Enantiomer* [(±)-*Quinone A' Dimethyl Ether*)].—Compound (**38**) (130 mg) was oxidised as above to give the quinone (**15**) (105 mg, 88%) as small yellow rosettes, m.p. 200 °C (decomp.) (propan-2-ol) (lit.,[3] for the single enantiomer from natural sources, 201 °C) (Found: C, 63.7; H, 5.9. $C_{17}H_{18}O_6$ requires C, 64.1; H, 5.7%); $\nu_{max.}$ 3 422, 1 647, 1 599, and 1 560 cm^{-1}; δ 1.38 (3 H, d, *J* 6 Hz, 3-CH_3), 1.51 (3 H, d, *J* 7 Hz, 1-CH_3), 2.3 (1 H, br s, OH, D_2O exchangeable), 3.93 and 3.94 (3 H each, s, OCH_3), *ca.* 3.95 (1 H, dq, *J* 2.5 and 6 Hz, 3-H, obscured by OMe), 4.44 (1 H, br s, 4-H, collapses to d, *J* 2.5 Hz on D_2O exchange), 4.99 (1 H, q, *J* 7 Hz, 1-H), 6.69 (1 H, d, *J* 2.5 Hz, 8-H), and 7.24 (1 H, d, *J* 2.5 Hz, 6-H).

3-*Acetyl*-5-*methoxy*-2-*prop*-2-*enyl*-1,4-*naphthoquinone* (**23**).—Compound (**19**) (600 mg) was oxidised and then allylated as for the preparation of compound (**21**) above, to give the *product* (**23**) (327 mg, 50%) as light orange needles, m.p. 135—136 °C (light petroleum) (Found: C, 71.05; H, 5.2. $C_{16}H_{14}O_4$ requires C,

71.1; H, 5.2%); $\nu_{max.}$ 1 708, 1 656, 1 637, and 1 578 cm^{-1}; δ 2.48 (3 H, s, CCH_3), 3.23 (2 H, dd, *J* 1 and 6 Hz, CH_2), 4.01 (3 H, s, OCH_3), 5.0—5.25 (2 H, m, vinyl CH_2), 5.6—6.1 (1 H, m, vinyl CH), 7.32 (1 H, dd, *J* 2.5 and 8 Hz, 6-H), 7.6—7.85 (2 H, m, 7- and 8-H).

3-*Acetyl*-1,4,5-*trimethoxy*-2-*prop*-2-*enylnaphthalene* (**28**).—Compound (**23**) (320 mg) was reductively methylated as for compound (**21**) above, to afford the *naphthalene* (**28**) (252 mg, 71%) as an oil after chromatography (eluant 15% ethyl acetate–light petroleum) (Found: C, 72.0; H, 6.6. $C_{18}H_{20}O_4$ requires C, 72.0; H, 6.7%); $\nu_{max.}$(neat) 1 684, 1 609, and 1 565 cm^{-1}; δ 2.60 (3 H, s, CCH_3), 3.56 (2 H, dd, *J* 1 and 6 Hz, CH_2), 3.78, 3.87, and 4.00 (3 H each, s, OCH_3), 4.85—5.15 (2 H, m, vinyl CH_2), 5.75—6.2 (1 H, m, vinyl CH), 6.89 (1 H, d, *J* 8 Hz, 6-H), 7.44 (1 H, t, *J* 8 Hz, 7-H), and 7.70 (1 H, d, *J* 8 Hz, 8-H).

3-(1-*Hydroxyethyl*)-1,4,5-*trimethoxy*-2-*prop*-2-*enylnaphthalene* (**34**).—Compound (**28**) (245 mg) was reduced as for compound (**26**) above to give the product (**34**) (221 mg, 90%), whose spectral characteristics corresponded to those reported for this compound prepared by another route.[9]

trans-3,4-*Dihydro*-5,9,10-*trimethoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran* (**43**).—Compound (**34**) (152 mg) was cyclised as described for compound (**33**) above, to afford the product (**43**) (134 mg, 87%) after chromatography (eluant 20% ethyl acetate–light petroleum). This showed spectral characteristics identical with those reported for the same compound obtained by another method.[9]

trans-3,4-*Dihydro*-9-*methoxy*-1,3-*dimethyl*-1H-*naphtho*-[2,3-c]*pyran*-5,10-*quinone* [(±)-*Isoeleutherin*] (**3**).—This was obtained by the method described.[9]

3-*Acetyl*-1,4,5-*trimethoxy*-2-*prop*-1-*enylnaphthalene* (**29**).—Compound (**28**) (252 mg) was conjugated as for the conversion of compound (**26**) into (**27**) described above to give the *product* (**29**) (203 mg, 81%), after chromatography (eluant 15% ethyl acetate–light petroleum), m.p. 78—79 °C (light petroleum) (Found: C, 71.7; H, 6.65. $C_{18}H_{20}O_4$ requires C, 72.0; H, 6.7%); $\nu_{max.}$ 1 699, 1 612, 1 570, and 1 490 cm^{-1}; δ 1.92 (3 H, d, *J* 6 Hz, $CHCH_3$), 2.50 (3 H, s, $COCH_3$), 3.91 (6 H, s, OCH_3), 3.99 (3 H, s, OCH_3), 6.20 (1 H, dq, *J* 6 and 16 Hz, $CHCH_3$), 6.54 (1 H, d, *J* 16 Hz, CH=$CHCH_3$), 6.86 (1 H, d, *J* 8 Hz, 6-H), 7.41 (1 H, t, *J* 8 Hz, 7-H), and 7.74 (1 H, d, *J* 8 Hz, 8-H).

3-(1-*Hydroxyethyl*)-1,4,5-*trimethoxy*-2-*prop*-1-*enylnaphthalene* (**31**).—Compound (**29**) (630 mg) was reduced as described for compound (**27**) above to give the product (**31**) (550 mg, 87%), as an oil after chromatography (Found: C, 71.2; H, 7.4. $C_{18}H_{22}O_4$ requires C, 71.5; H, 7.3%); $\nu_{max.}$(neat) 3 450, 1 608, 1 568, and 1 487 cm^{-1}; δ 1.61 [3 H, d, *J* 7 Hz, $CH(OH)CH_3$], 1.96 (3 H, dd, *J* 2 and 7 Hz, CH=$CHCH_3$), 3.76, 3.90 and 4.00 (3 H, each, s, OCH_3), 4.2 (1 H, br s, OH), 5.22 [1 H, m, $CH(OH)CH_3$], 6.05 (1 H, dq, *J* 7 and 16 Hz, CH=$CHCH_3$), 6.56 (1 H, dq, *J* 2 and 16 Hz, CH=$CHCH_3$), 6.85 (1 H, d, *J* 8 Hz, 6-H), 7.38 (1 H, t, *J* 8 Hz, 7-H), and 7.72 (1 H, d, *J* 8 Hz, 8-H).

(1R,3R,4S)-3,4-*Dihydro*-4-*hydroxy*-5,9,10-*trimethoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran* (**36**) *and its Enantiomer*.—Compound (**31**) (163 mg) was dissolved in dry dimethylformamide (20 ml) and potassium t-butoxide (242 mg) was added. Air was passed over the reaction mixture, which was heated at 60 °C (bath) for 15 min. Work-up as above afforded a residue which was chromatographed (eluant 30% ethyl acetate–light petroleum) to give, firstly, compound (**43**) (26 mg, 15%), followed by the *product* (**36**) (50 mg, 31%) as an oil (Found: C, 67.7; H, 6.8. $C_{18}H_{22}O_5$ requires C, 67.9; H, 6.95%); δ 1.43 (3 H, d, *J* 6.5 Hz, 3-CH_3), 1.70 (3 H, d, *J* 7.5 Hz, 1-CH_3), 3.80, 3.97, and 4.01 (3 H each, s, OCH_3), *ca.* 3.97 (1 H, dq, *J* 6.5 and 8.5 Hz, 3-H, partially obscured by Me), 4.2 (1 H, br s, OH), 4.76 (1 H, d, *J* 8.5 Hz, 4-H), 5.26 (1 H, q, *J* 7.5 Hz, 1-H), 6.88 (1 H, d, *J* 8 Hz, 8-H), 7.40 (1 H, t, *J* 8 Hz, 7-H), and 7.64 (1 H, d, *J* 8 Hz, 6-H).

(1R,3R,4R)-3,4-*Dihydro*-4-*hydroxy*-5,9,10-*trimethoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran* (**39**) *and its Enantiomer*.—Compound (**31**) (205 mg, 0.679 mmol) was dissolved in acetonitrile (70 ml), and water (70 ml) was added. Cerium(IV) ammonium nitrate (743 mg, 2 equiv.) in water (15 ml) was added during 5 min. Stirring was continued for a further 10 min, then the mixture was extracted into methylene dichloride, and the extract was washed with water. The residue obtained upon work-up was subjected to p.l.c. (eluant 15% ethyl acetate–light petroleum) to give the *product* (**39**) (30 mg, 14%), m.p. 170—173 °C (light petroleum) (Found: M^+ 318.1473. $C_{18}H_{22}O_5$ requires *M* 318.1467); δ 1.43 (3 H, d, *J* 6 Hz, 3-CH_3), 1.61 (3 H, d, *J* 7 Hz, 1-CH_3), 2.22 (1 H, d, *J* 8 Hz, OH, D_2O exchangeable), 3.81, 4.02, and 4.05 (3 H each, s, OCH_3), 4.14 (1 H, dq, *J* 2 and 6 Hz, 3-H), 6.76 (1 H, dd, *J* 2 and 8 Hz, 4-H, collapses to d, *J* 2 Hz on D_2O exchange), 5.34 (1 H, q, *J* 7 Hz, 1-H), 6.89 (1 H, d, *J* 8 Hz, 8-H), 7.40 (1 H, t, *J* 8 Hz, 7-H), and 7.72 (1 H, d, *J* 8 Hz, 6-H).

(1R,3R,4S)-3,4-*Dihydro*-4-*hydroxy*-9-*methoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran*-5,10-*quinone* (**12**) *and its Enantiomer*.—The ether (26 mg, 0.818 mmol) in acetonitrile (8 ml) and water (2 ml) was treated with cerium(IV) ammonium nitrate (98 mg, 2.2 equiv.) in water (1 ml) during 3 min with stirring at room temperature. After being stirred for a further 7 min, the mixture was worked up as for (**39**) above and chromatographed (eluant 40% ethyl acetate–light petroleum) to give the *product* (**12**) (16 mg, 67%), m.p. 159—160 °C (methylene dichloride–light petroleum) (Found: C, 66.7; H, 5.65. $C_{16}H_{16}O_5$ requires C, 66.65; H, 5.55%); $\nu_{max.}$ 3 560, 1 662, 1 650, 1 634, and 1 594 cm^{-1}; δ 1.42 (3 H, d, *J* 6 Hz, 3-CH_3), 1.60 (3 H, d, *J* 7.5 Hz, 1-CH_3), 3.80 (1 H, d, *J* 2 Hz, OH, D_2O exchangeable), 3.91 (1 H, dq, *J* 6 and 8 Hz, 3-H), 4.00 (3 H, s, OCH_3), 4.47 (1 H, br d, *J* 8 Hz, 4-H, collapses to dd, *J* 1.5 and 8 Hz on D_2O exchange), 4.93 (1 H, dq, *J* 1.5 and 7.5 Hz, 1-H), 7.31 (1 H, dd, *J* 3 and 8 Hz, 8-H), and 7.55—7.85 (2 H, m, 6- and 7-H).

(1R,3R,4R)-3,4-*Dihydro*-4-*hydroxy*-9-*methoxy*-1,3-*dimethylnaphtho*[2,3-c]*pyran*-5,10-*quinone* (**16**) *and its Enantiomer*.—Compound (**39**) (19 mg) was oxidised with silver(II) oxide as for the conversion of (**42**) into quinone (**2**) above. P.l.c. (eluant 50% ethyl acetate–light petroleum) afforded the quinone (15 mg, 88%) as yellow rosettes, m.p. 173.5—175 °C (methylene dichloride–light petroleum) (Found: M^+ 288.102 00. $C_{16}H_{16}O_5$ requires *M* 288.099 75); $\nu_{max.}$ 3 460, 1 663, 1 653, and 1 587 cm^{-1}; δ 1.41 (d, *J* 6.5 Hz, 3-CH_3), 1.52 (d, *J* 7.5 Hz, 1-CH_3), 2.46 (1 H, br d, *J* 7 Hz, OH, D_2O exchangeable), *ca.* 4.0 (1 H, dq, *J* 2.5 and 6.5 Hz, 3-H), 4.01 (3 H, s, OCH_3), 4.49 (1 H, br d, *J* 7 Hz, 4-H, collapses to d, *J* 2.5 Hz, on D_2O exchange), 5.03 (1 H, q, *J* 7.5 Hz, 1-H), 7.32 (1 H, dd, *J* 2.5 and 8 Hz, 8-H), and 7.55—7.95 (2 H, m, 6-and 7-H).

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