Naphthopyrans by Ring-closure of Substituted Naphthalenes using Potassium t-Butoxide in Dimethylformamide

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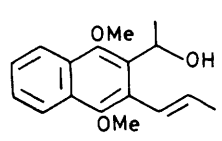
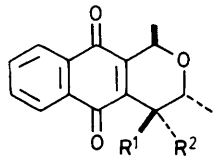
Two 2-alkenyl-3-hydroxyalkyl-1,4-dimethoxynaphthalenes are cyclised with potassium t-butoxide in dimethylformamide to give 3-alkyl-3,4-dihydro-5,10-dimethoxynaphtho[2,3-*c*]pyrans under anaerobic conditions. One of these products is treated with the same solvent and base, but in air, to give the two possible 4-hydroxy derivatives.

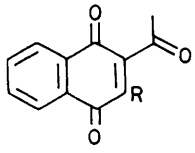
We recently reported[1] the oxidative cyclisation of the naphthalene dimethyl ether (1) with cerium(IV) ammonium nitrate to give a mixture of the isomeric quinones (2) and (3), the latter predominating. These quinones are related to the aphid pigments, *e.g.* protoaphin *fb* and protoaphin *sl*. The *trans*-prop-1-enyl substituent of (1) was derived from propyl by bromination–dehydrobromination but, for this particular system, certain difficulties were encountered which prompted us to seek alternative routes to (1) by conjugation of an allyl group. This has been achieved and, in the course of this investigation, novel cyclisations of compounds related to (1) were discovered which are useful in the synthesis of naturally occurring quinones. The work leading to these cyclisations is described in this paper.



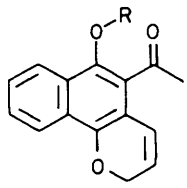
(1)



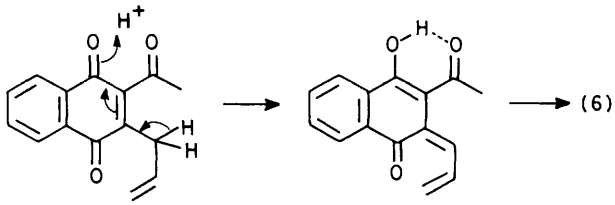
(2) R^1 = OH, R^2 = H
(3) R^1 = H, R^2 = OH



(4) R = H
(5) R = $CH_2CH{=}CH_2$



(6) R = H
(7) R = Me



(5)

Results and Discussion

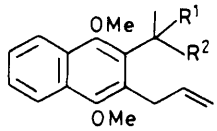
2-Acetyl-1,4-naphthoquinone (4) was allylated with commercially available vinylacetic acid in the presence of silver nitrate and potassium peroxodisulphate to give the quinone (5) in 43% yield. Small quantities of a second yellow product, isomeric with (5) and difficult to separate from it, were observed, but this compound proved not to be quinonoid. The ^{1}H n.m.r. spectrum showed, *inter alia*, a two-proton doublet of doublets at δ 4.80 (*J* 1 and 4 Hz), a one-proton doublet of triplets at δ 5.91 (*J* 4 and 10 Hz), a one-proton doublet of doublets at δ 6.78 (*J* 1 and 10 Hz), and a very-low-field one-proton singlet at δ 13.86. This enabled the assignment of structure (6) to the compound, which presumably arises through acid-catalysed enolisation of quinone (5), followed by cyclisation, as shown. Because of the difficulty of separating this compound from the quinone (5), it was characterised as its methyl ether (7), after being carried through the next step of the reaction sequence, where the naphthalenes (7) and (8) were more readily separated.

The quinone (5), contaminated with a little (6), was reductively methylated to the naphthalene dimethyl ether (8) with sodium dithionite followed by dimethyl sulphate and potassium carbonate in acetone. After purification of ketone (8) its allylic double bond was readily conjugated with potassium t-butoxide in tetrahydrofuran (THF) to give the ketone (10) in which the stereochemistry of the resulting double bond was solely *trans*, as shown by the coupling constant (16 Hz) of the olefinic protons. This compound was identical with material described earlier.[1] Reduction of this ketone with lithium aluminium hydride gave the alcohol (1).

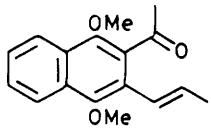
In an effort to improve the yield of the allylation, the reaction was performed on the hydroxyethyl quinone (12) and gave compound (13), but the yield (42%) was similar. The quinone (12) was obtained from 2-acetyl-1,4-dimethoxynaphthalene[2] by sodium borohydride reduction to the alcohol (11), which was in turn oxidised to the quinone (12) with cerium(IV) ammonium nitrate in excellent yield. The allyl quinone was reductively methylated to the alcohol (9). This compound was also available from the ketone (8) by lithium aluminium hydride reduction.

During the course of our work, the allylation of quinone (4) using allyltrimethylstannane and boron trifluoride–diethyl ether was reported,[3] and the crude product, after methylation, gives considerably improved yields of the ketonic naphthalene (8).

The possibility of conjugation of the allylic double bond of the alcohol (9) to give the isomer (1) was also investigated. When treated at 60 °C in dimethylformamide (DMF) under nitrogen with four equivalents of potassium t-butoxide, starting material was rapidly consumed with the initial formation of one product almost exclusively. The reaction was conveniently monitored by t.l.c. After two minutes the reaction mixture showed only one product, although a small proportion of starting material remained. After five minutes all starting material had been consumed, although traces of a product of slightly higher R_F value than the first product



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



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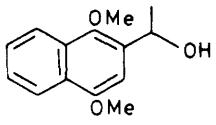

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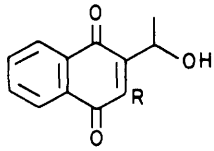
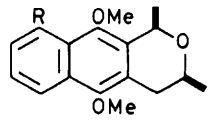
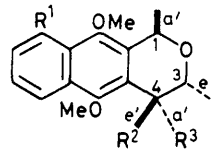


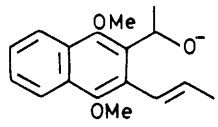
(12) R = H
(13) R = $CH_2CH{=}CH_2$



(14) R = H
(15) R = OMe



(16) R^1 = R^2 = R^3 = H
(17) R^1 = OMe, R^2 = R^3 = H
(18) R^1 = R^3 = H, R^2 = OH
(19) R^1 = R^2 = H, R^3 = OH



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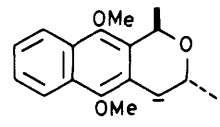

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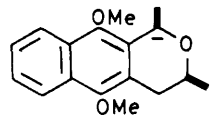


(22)

started to appear. Upon work-up, a ^{1}H n.m.r. spectrum of the first product, which was formed almost quantitatively, showed it to be the *trans*-dimethylnaphthopyran (16).[3] A repeat of this reaction, but for ten minutes, showed compound (16) contaminated with rather more (15%) of the less polar product (ratios estimated by n.m.r. integration). After fifteen minutes the contaminant had increased to about 30% of the still-almost-quantitative overall yield of recovered material. After 1.25 h the overall recovered yield had fallen to 93%, with the individual yields of (16) and new product being 53 and 40%, respectively. A ^{1}H n.m.r. spectrum of the latter showed it to be the *cis*-dimethylnaphthopyran (14).[3] Although the n.m.r spectra of neither of these compounds appear to be published as yet, a comparison with those reported [4] for the trimethoxy analogues (17) and (15) enables a distinction to be made. In particular, the 3-H multiplets differ substantially in chemical shift; those for the *trans* isomers (16) and (17) fall in the range δ 3.9—4.3, while those for the *cis* isomers (14) and (15) appear at δ 3.5—3.8. The chemical shifts of the 1-H quartets also differ, those for the *trans* compounds appearing at δ *ca.* 5.3 while those of the *cis* compounds occur at δ *ca.* 5.2.

Treatment of the alcohol (9) for times much longer than the 1.25 quoted above did not convert all of the *trans* isomer (16) into the *cis* isomer (14). However, in apparent contradiction, when the *cis* isomer (14) was treated under identical conditions, none of the *trans* isomer was detected by either t.l.c. or n.m.r. spectroscopy. An explanation of this anomaly was provided when compound (9) was treated with a large excess (twenty-fold) of butoxide for several hours, whereupon the *cis* compound (14) became the major of the two isomers. However, side-reactions were also taking place under these conditions, which detracted from its being used as a route to (14). These facts suggested that the efficacy of the base was reduced with time.

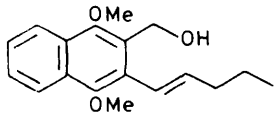
Existing methods [3,4] for preparing naphthopyrans always give a mixture and, in general, favour the *cis* isomer; the method we report here, however, can be used selectively to provide, virtually exclusively and in high yield, either the *trans* isomer, or a *cis*/*trans* mixture, depending on the reaction conditions.

The conjugated alcohol (1) was also found to cyclise to compound (16) under the above conditions, the formation of the *cis* isomer (14) again being observed for longer reaction times.

Similar conjugation of the alcohol (9) without the exclusion of air, and for longer reaction times, afforded a moderate combined yield (35%) of the two isomeric products (18) and (19) in the ratio 4 : 1 and which were readily identified by their characteristic ^{1}H n.m.r. spectra. These compounds had been isolated earlier [1] as intermediates in the cerium(IV) ammonium nitrate oxidative cyclisation of the naphthalene (1) to the isomeric quinones (2) and (3), but it is noteworthy that, in the cerium reaction, the product with the pseudo-axial (a′) hydroxy group predominated, the reverse being true in the base-induced reaction, where the compound with the hydroxy group pseudo-equatorial (e′) was more abundant.[5,6]

The hydroxynaphthopyrans (18) and (19) were most conveniently prepared from the *trans*-dimethylpyran (16) by treating this compound with potassium t-butoxide in DMF at 60 °C in the presence of air for 2 h. Under these conditions three products were formed. These were the *cis*-naphthopyran (14), formed in 12% yield, and the isomeric 4-hydroxypyrans (18) (28%) and (19) (7%). Starting material was isolated in 23% recovery. The yields of products, based on consumed starting material, were 16, 36, and 9%, respectively.

It was imperative to establish the relative stereochemistry of the three chiral centres in compounds (18) and (19) beyond doubt, as the possibility arose that the C-1 methyl was pseudo-equatorial (and not pseudo-axial as drawn), which would be due to hydroxylation of the *cis* pyran (14) having taken place. This proved not to be the case. The stereochemistry was easy to confirm at C-3 and C-4 for compounds (18) and (19) on the reasonable assumption that the C-3 methyl adopted the equatorial configuration in each case. The coupling constant of 8 Hz between 3-H and 4-H for (18) confirmed the former as axial and the latter as pseudo-axial. For (19), the smaller coupling constant of 2 Hz, indicated a smaller dihedral angle which, with 3-H again axial, required 4-H pseudo-equatorial. However, for the naphthopyrans (18) and (19), the long-range coupling between 1-H and 4-H is too small to enable the definitive assignment of stereochemistry at C-1. For crystalline (19), the stereochemistry was established by m.p. and mixed m.p. comparison with authentic (19).[1] The assignments of structures (18) and (19) were confirmed by oxidation to the quinones (2) and (3). In the former, long-range coupling between 1-H and 4-H was apparent in the ^{1}H n.m.r. spectrum, which was identical with that reported.[1] In the spectrum of the



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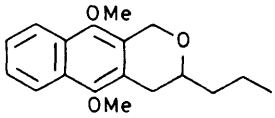

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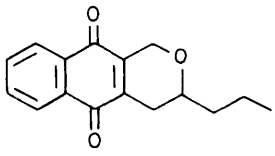

(25)

latter, no long-range coupling was observed. M.p.s and mixed m.p.s were also identical in each case.

Further support for the stereochemical assignments was adduced from the fact that when the *cis*-dimethylnaphthopyran (14) was treated with base in DMF under aerobic conditions as for (16) above, no reaction took place, even when the mixture was left for 18 h.

The mechanisms of the cyclisation of alcohols (9) and (1) under anaerobic conditions, and the oxygenation of the pyran (16) under aerobic conditions, warrant discussion, although the following explanations can only be tentative and speculative at this stage.

Under the strongly basic conditions generated by butoxide in the dipolar aprotic solvent, the alkoxide anion (20) is produced, which undergoes cyclisation to the *trans*-dimethylpyran anion (21), favoured kinetically because the methyl group at C-3 prefers the less crowded equatorial position, while that at C-1 goes pseudo-axial to reduce *peri* interactions.[1] Anion (21) then undergoes protonation to form the product. Longer treatment with base converts (16) into (14), and this may occur by one of several routes. Compound (16) may be deprotonated at C-4 to afford the anion (21) again, which reverts to (20) before reclosing to form the *cis* compound (14), or, alternatively, initial protonation of anion (21) to form (16) may not occur, since (21), as soon as it is formed, may ring-open again to (20), which then recyclises to form the thermodynamic product (14). A second possibility is that deprotonation of (16) takes place at C-1 rather than at C-4, to give the anion (22), thermodynamically preferred under the reaction conditions. The former suggestion, giving rise to the anion (21), seems more likely in view of the oxygenation of (16) at C-4 described above.

In the case of the oxygenation reactions the anion (21), regenerated from the pyran (16) can undergo oxidation either to the corresponding carbonium ion followed by reaction with traces of adventitious moisture to form the products, or to the corresponding radical which reacts with molecular oxygen to form the products, or conceivably, the anion may react with molecular oxygen directly.

Further work needs to be undertaken to distinguish between the various mechanistic possibilities.

A further example of the anaerobic cyclisation was sought. Compound (23) [1] gave a high yield (83%) of the naphthopyran (24). The five heterocyclic ring protons gave the following ^{1}H n.m.r. spectral absorptions: two doublets (*J* 16 Hz) at δ 5.26 and 4.84 were assigned to the pseudo-equatorial and pseudo-axial C-1 protons, respectively. A slight broadening of the latter signals relative to the former indicates a slightly greater degree of long-range coupling for the pseudo-axial proton, but no splitting of the signal due to this effect was observed whatsoever (at normal sweep width). The axial 3-H proton appeared as a multiplet at δ 3.5—3.9 which collapsed to a doublet of doublets (*J* 3.5 and 11 Hz) on irradiation of the adjacent propyl methylene. The pseudo-equatorial 4-H gave rise to a doublet of doublets at δ 3.10 (*J* 3.5 and 17 Hz), and the pseudo-axial 4-H appeared as another doublet of doublets at δ 2.66 (*J* 11 and 17 Hz). The latter signal also indicated broadening relative to that at δ 3.10, but the effect was less obvious than that observed for the 1-H protons because of the increased coupling associated with the 4-H protons.

Cerium(IV) ammonium nitrate oxidative demethylation of (24) afforded the corresponding quinone (25) in high yield. The ^{1}H n.m.r. spectrum of this compound was of particular note in view of the previous reports on the spectra of naphtho-[2,3-*c*]pyran-5,10-quinones.[1,5,6] The 5 heterocyclic ring protons gave the following signals: a doublet of doublets at δ 4.88 with coupling constants of 3 and 19 Hz was due to the pseudo-equatorial 1-H, this being somewhat deshielded from the pseudo-axial 1-H [see also for compound (24)], the smaller coupling constant being due to splitting by the pseudo-axial (but not pseudo-equatorial) 4-H. The pseudo-axial 1-H appeared as a doublet of triplets at δ 4.46, this proton being almost equally coupled (*J* 3.5 Hz) to both 4-H protons. The 3-H signal appeared as a multiplet at δ 3.3—3.7. The pseudo-equatorial 4-H appeared as a doublet of triplets at δ 2.76 with coupling constants 3.5 and 19 Hz, the latter being due to geminal coupling, and the former due to approximately equal coupling to the pseudo-axial 1-H and to 3-H. The pseudo-axial 4-H appeared at δ 2.28 as a sixteen-line signal; this arose from geminal coupling (*J* 19 Hz), vicinal coupling to 3-H (*J* 10 Hz), coupling to pseudo-equatorial 1-H (*J* 3 Hz), and coupling to pseudo-axial 1-H (*J* 3.5 Hz).

It is our intention to use the reactions described in this paper for the syntheses of naturally derived naphtho[2,3-*c*]-pyran-5,10-quinones. Whether or not the hydroxylation of naphthopyrans without oxygen at C-5 takes place remains to be seen. If it does, this might provide a route to aphin-derived glucoside B.[7]

Experimental

All ^{1}H n.m.r. spectra were measured for solutions in [^{2}H]-chloroform with tetramethylsilane as internal reference, while *i.r. spectra were measured for Nujol mulls. 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. 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.

2-Acetyl-3-prop-2-enyl-1,4-naphthoquinone (5).—A solution of freshly recrystallised 2-acetyl-1,4-naphthoquinone (4) (1.00 g, 5 mmol) in acetonitrile (35 ml) containing vinylacetic acid (0.65 g, 7.5 mmol) was treated with a solution of silver nitrate (0.6 g) in water (1 ml). The mixture was stirred at 70 °C while a solution of potassium peroxodisulphate (2.70 g, 10 mmol) in water (30 ml) was added dropwise during 45 min. The mixture was stirred for a further 2 h. The usual work-up [1] afforded a residue which was chromatographed (eluant 10% ethyl acetate–light petroleum). Early fractions afforded the naphthol (6) (28 mg, 2%) which was further purified by p.l.c., m.p. 125 °C (light petroleum) (Found: M^+, 240. $C_{15}H_{12}O_3$ requires *M*, 240); δ 2.64 (3 H, s, CCH_3), 4.80 (2 H, dd, *J* 1 and 4 Hz, CH_2), 5.91 (1 H, dt, *J* 4 and 10 Hz, 3-H), 6.78 (1 H, dd, *J* 1 and 10 Hz, 4-H), 7.5—7.8 (2 H, m, 8- and 9-H), 8.1—8.2 and 8.4—8.5 (each 1-H, m, together 7- and 10-H), and 13.86

(1 H, s, OH, D_2O-exchangeable). Later fractions afforded the *title compound* (5) (0.52 g, 43%) as an oil. A portion was re-chromatographed for analysis (p.l.c.) Found: C, 74.7; H, 5.4. $C_{15}H_{12}O_3$ requires C, 75.0; H, 5.0%); $\nu_{max.}$ (neat) 2 930, 1 707, 1 660, and 1 595 cm^{-1}; δ 2.48 (3 H, s, CCH_3), 3.26 (2 H, dd, *J* 7 and 1 Hz, CH_2), 5.0—5.3 (2 H, m, vinyl CH_2), 5.6—6.1 (1 H, m, vinyl CH), 7.6—7.85 (2 H, m, 6- and 7-H), and 7.9—8.15 (2 H, m, 5- and 8-H).

2-*Acetyl*-1,4-*dimethoxy*-3-*prop*-2-*enylnaphthalene* (8) *and* 5-*Acetyl*-6-*methoxy*-2H-*naphtho*[1,2-b]*pyran* (7).—A solution of the quinone (5) above (200 mg, 0.83 mmol) in diethyl ether (50 ml) was shaken with an aqueous solution of an excess of sodium dithionite (2 × 50 ml). The organic layer was dried and evaporated to give a red oil which was immediately dissolved in dry acetone (30 ml) and anhydrous potassium carbonate (575 mg, 4.2 mmol) and dimethyl sulphate [525 mg (0.4 ml), 4.2 mmol] were added. The mixture was stirred under nitrogen under reflux for 18 h. The usual work-up gave an oil which was chromatographed (eluant 10% ethyl acetate–light petroleum) to give, firstly, the *dimethyl ether* (8) (145 mg, 64%) as an oil (Found: C, 75.6; H, 6.9. $C_{17}H_{18}O_3$ requires C, 75.55; H, 6.65%); $\nu_{max.}$ (neat) 3 100, 1 709, 1 692, 1 640, and 1 590 cm^{-1}; δ 2.60 (3 H, s, CCH_3), 3.61 (2 H, dd, *J* 1 and 6 Hz, CH_2), 3.86 and 3.88 (each 3 H, s, OCH_3), 4.8—5.15 (2 H, m, vinyl CH_2), 5.7—6.2 (1 H, m, vinyl CH), 7.4—7.65 (2 H, m, 6- and 7-H), and 7.95—8.2 (2 H, m, 5- and 8-H). Later fractions afforded the *naphthopyran* (7) as an oil (8 mg, 4%) (Found: C, 75.2; H, 5.6. $C_{16}H_{14}O_3$ requires C, 75.6; H, 5.5%); $\nu_{max.}$ (neat) 1 673br, 1 628, 1 601, and 1 585 cm^{-1}; δ 2.64 (3 H, s, CCH_3), 3.84 (3 H, s, OCH_3), 4.87 (2 H, dd, *J* 1 and 4 Hz, CH_2), 5.78 (1 H, dt, *J* 4 and 10 Hz, 3-H), 6.45 (1 H, dd, *J* 1 and 10 Hz, 4-H), 7.3—7.7 (2 H, m, 8- and 9-H), and 7.9—8.2 (2 H, m, 7- and 10-H).

2-(1-*Hydroxyethyl*)-1,4-*dimethoxy*-3-*prop*-2-*enylnaphthalene* (9).—(*a*) To a stirred suspension of lithium aluminium hydride (0.62 g, 16.2 mmol) in dry diethyl ether (100 ml) was added the ketone (8) (1.10 g, 4.07 mmol) at a rapid drip rate. The mixture was stirred for 10 min after the addition was complete, by which time t.l.c. indicated the consumption of all starting material. The reaction was quenched by the addition of saturated ammonium chloride, followed by anhydrous magnesium sulphate. The solid material was filtered off and the filtrate was evaporated to give a residue which was chromatographed (eluant 15% ethyl acetate–light petroleum) to give the *product* (9) as an oil (1.05 g, 95%), identical with that described below.

(*b*) A solution of the quinone (13) (216 mg, 0.89 mmol) in diethyl ether (75 ml) was shaken with a solution of an excess of sodium dithionite in water (2 × 50 ml). The organic layer was dried and stripped of solvent to give a yellow solid. This was immediately dissolved in dry acetone and the solution was stirred under reflux in the presence of anhydrous potassium carbonate (1 g, 7 equiv.) and dimethyl sulphate (0.7 ml, 7 equiv.). The mixture was boiled under nitrogen for 24 h. The usual work-up afforded an oil which was chromatographed (eluant 15% ethyl acetate–light petroleum) to yield the *product* (9) (194 mg, 80%) as an oil (Found: C, 75.2; H, 7.35. $C_{17}H_{20}O_3$ requires C, 75.0; H, 7.35%); $\nu_{max.}$ 3 420, 1 638, and 1 594 cm^{-1}; δ 1.63 (3 H, d, *J* 6.5 Hz, CCH_3), 3.68 (2 H, m, CH_2), 3.86 and 3.98 (each 3 H, s, OCH_3), 3.9 (1 H, br s, OH, D_2O-exchangeable), 4.8—5.15 (2 H, m, vinyl CH_2), 5.25 (1 H, m, $CHCH_3$), 5.85—6.3 (1 H, m, vinyl CH), 7.35—7.45 (2 H, m 5- and 8-H), and 7.9—8.15 (2 H, m, 6- and 7-H).

2-*Acetyl*-1,4-*dimethoxy*-3-*prop*-1-*enylnaphthalene* (10).—Compound (8) (2.25 g, 8.33 mmol) was dissolved in dry THF under nitrogen. Solid potassium t-butoxide (3.73 g, 33.3 mmol) was added and the solution was heated at 60 °C for 1.5 h during which time the nearly colourless solution turned dark red. The solution was treated with aqueous ammonium chloride (30%) and was extracted with methylene dichloride. The residue obtained upon work-up was chromatographed (eluant 10% ethyl acetate–light petroleum) to give the oily product (1.98 g, 88%), identical with authentic material.[1]

2-(1-*Hydroxyethyl*)-1,4-*dimethoxynaphthalene* (11).—A solution of 2-acetyl-1,4-dimethoxynaphthalene (2.30 g, 10 mmol) in ethanol (60 ml) was added to a suspension of an excess of sodium borohydride in the same solvent. The usual work-up gave an oil (2.35 g) which was chromatographed (eluant 15% ethyl acetate–light petroleum) to give the *product* (11) (220 mg, 95%), m.p. 101—102 °C (light petroleum) (Found: C, 72.4; H, 7.0. $C_{14}H_{16}O_3$ requires C, 72.4; H, 6.9%); $\nu_{max.}$ 3 330 and 1 598 cm^{-1}; δ 1.53 (3 H, d, *J* 6 Hz, CCH_3), 2.90 (1 H, s, OH, D_2O-exchangeable), 3.82 and 3.90 (each 3 H, s, OCH_3), 5.40 (1 H, q, *J* 6 Hz, $CHCH_3$), 6.84 (1 H, s, 3-H), 7.3—7.6 (2 H, m, 6-H and 7-H), and 7.9—8.05 and 8.1—8.3 (each 1 H, m, together 5- and 8-H).

2-(1-*Hydroxyethyl*)-1,4-*naphthoquinone* (12).—A solution of compound (11) (835 mg, 3.6 mmol) in acetonitrile (80 ml) and water (40 ml) was treated with a solution of cerium(IV) ammonium nitrate (3.945 g, 7.2 mmol) in water (5 ml) during 5 min. The solution turned purple then yellow. After being stirred for a further 5 min the mixture was extracted with methylene dichloride. The residue obtained upon work-up was chromatographed (eluant (30% ethyl acetate–light petroleum) to give a yellow oil (710 mg, 98%) which crystallised with time, m.p. 88—89 °C (as rosettes from light petroleum) (Found: C, 71.4; H, 4.9. $C_{12}H_{10}O_3$ requires C, 71.3; H, 4.95%); $\nu_{max.}$ 3 500, 1 662, and 1 592 cm^{-1}; δ 1.52 (3 H, d, *J* 7 Hz, CH_3), 2.72 (1 H, d, *J* 4 Hz, OH, D_2O-exchangeable), 5.02 (1 H, dq, *J* 4 and 7 Hz, CH_3CH), 7.03 (1 H, s, 3-H), 7.65—7.85 (2 H, m, 6- and 7-H), and 7.95—8.2 (2 H, m, 5- and 8-H).

cis-3,4-*Dihydro*-5,10-*dimethoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran* (14) *and* trans-3,4-*Dihydro*-5,10-*dimethoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran* (16).—(*a*) Nitrogen was bubbled through a solution of the alcohol (9) (106 mg, 0.39 mmol) in dry DMF (10 ml) for 0.5 h before the addition of potassium t-butoxide (175 mg, 1.56 mmol). After the addition the flask was immersed in an oil-bath preheated to 60 °C, the contents were stirred, and nitrogen was blown onto the surface of the solution. The reaction was quenched after 5 min by the addition of water (30 ml), and the mixture was cooled and extracted with diethyl ether (4 × 10 ml). The extract was backwashed with water (50 ml) and evaporated to give the *product* (16) virtually quantitatively, and which was shown to be pure by ^1H n.m.r. spectroscopy.

(*b*) Using the above procedure, the alcohol (9) (1.022 g, 3.76 mmol), dry DMF (50 ml), and base (1.686 g, 15 mmol) were warmed at 60 °C under nitrogen for 1.25 h. Work-up gave an oil (0.955 g, 93%). A portion (135 mg) was chromatographed by p.l.c. (developer 4% ethyl acetate–light petroleum) to give *compound* (14) as the product with the higher R_F value (55 mg, 40%) as cubes, m.p. 82—82.5 °C (ethanol) (Found: C, 74.65; H, 7.4. $C_{17}H_{20}O_3$ requires C, 74.95; H, 7.4%); $\nu_{max.}$ 1 590 cm^{-1}; δ 1.43 (3 H, d, *J* 6 Hz, 3-CH_3), 1.73 (3 H, d, *J* 6 Hz, 1-CH_3), 2.60 (1 H, dd, *J* 11 and 16 Hz, pseudo-axial 4-H), 3.10 (1 H, dd, *J* 3 and 16 Hz, pseudo-equatorial 4-H), 3.4—3.9 (1 H, m, 3-H), 3.87 and 3.92 (each 3 H, s, OCH_3), 5.22 (1 H, q, *J* 6 Hz, 1-H), 7.4—7.6 (2 H, m, 7- and 8-H), and 8.0—8.15

(2 H, m, 6- and 9-H). *Compound* (16) (72 mg, 53%), of lower R_F value, was obtained as needles, m.p. 99.5—100.5 °C (light petroleum) (Found: C, 74.6; H, 7.4%); $\nu_{max.}$ 1 590 cm^{-1}; δ 1.39 (3 H, d, *J* 6 Hz, 3-CH_3), 1.63 (3 H, d, *J* 6 Hz, 1-CH_3), 2.59 (1 H, dd, *J* 11 and 16 Hz, pseudo-axial 4-H), 3.11 (1 H, dd, *J* 3.5 and 16 Hz, pseudo-equatorial 4-H), 3.88 and 3.90 (each 3 H, s, OCH_3), 3.9—4.3 (1 H, m, 3-H), 5.35 (1 H, q, *J* 6 Hz, 1-H), 7.35—7.6 (2 H, m, 7- and 8-H), and 7.9—8.15 (1 H, m, 6- and 9-H).

(1*R*,3*R*,4*S*)-3,4-*Dihydro*-4-*hydroxy*-5,10-*dimethoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran* (18) *and its Enantiomer, and* (1R,3R,4R)-3,4-*Dihydro*-4-*hydroxy*-5,10-*dimethoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran* (19) *and its Enantiomer*.—(*a*) *From compound* (9). Compound (9) (89 mg) and potassium t-butoxide (146 mg, 4 equiv.) were heated together at 70—80 °C (bath) in DMF (15 ml) in the presence of air for 19 h. The reaction mixture was then cooled, thrown into water, and extracted with diethyl ether. The residue obtained upon work-up was chromatographed (eluant 15% ethyl acetate–light petroleum) to give, firstly, racemic (18) (26 mg, 28%), followed by racemic (19) (7 mg, 7%). Both (18) and (19) were identical with authentic material.

(b) *From compound* (16). Air was bubbled through a solution of compound (16) (1.08 g, 3.97 mmol) in dry DMF for 20 min. Potassium t-butoxide (1.78 g, 16.0 mmol) was added and the flask was immersed in an oil-bath maintained at 60 °C and the contents were stirred for 2 h. Water was added and the mixture was worked up as for (16) above. Column chromatography gave, firstly, compound (14) (134 mg 12%), followed by starting material (243 mg, 23%), then compound (18) (323 mg, 28%) as an oil. The last compound to be identified was compound (19) (76 mg, 7%), m.p. 166 °C (lit.,[1] 168 °C), mixed m.p. with authentic material 166 °C.

(1R,3R,4S)-3,4-*Dihydro*-4-*hydroxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran*-5,10-*quinone* (2) *and its Enantiomer*.—A solution of cerium(IV) ammonium nitrate (960 mg, 1.74 mmol) in water (1.5 ml) was added dropwise, during 5 min, to a vigorously stirred solution of compound (18) (174 mg, 0.58 mmol) in acetonitrile (20 ml) and water (20 ml). After the mixture had been stirred for a further 5 min water was added and the solution was extracted with methylene dichloride. Work-up of the organic layer afforded the *quinone* virtually quantitatively as yellow plates, m.p. 138—138.5 °C (methylene dichloride–light petroleum), undepressed by authentic material (lit.,[1] 137—138 °C).

(1R,3R,4R)-3,4-*Dihydro*-4-*hydroxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran*-5,10-*quinone* (3) *and its Enantiomer*.—Compound (19) (68 mg) was oxidised as for (18) above to give the quinone (3) virtually quantitatively as yellow needles, m.p. 148—150 °C (decomp.) (methylene dichloride–light petroleum), mixed m.p. with authentic material 147.5—149 °C (decomp.) (lit.,[1] 146—147 °C).

3,4-*Dihydro*-5,10-*dimethoxy*-3-*propyl*-1H-*naphtho*[2,3-c]*pyran* (24).—Compound (23) (106 mg) was dissolved in dry DMF (20 ml) which had been flushed with nitrogen. Potassium t-butoxide (200 mg) was added and the reaction mixture, under nitrogen, was immersed in an oil-bath, maintained at 65 °C, for 20 min. Work-up as for (16) above gave the *product* (24) (87 mg, 83%), m.p. 104—105 °C (methanol) (Found: C, 75.4; H, 7.75. $C_{18}H_{22}O_3$ requires C, 75.5; H, 7.75%); δ 1.00 (3 H, distorted t, *J* 7 Hz, CH_3), 1.64 (4 H, m, CH_2CH_2), 2.66 (1 H, dd, *J* 11 and 17 Hz, pseudo-axial 4-H), 3.10 (1 H, dd, *J* 3.5 and 17 Hz, pseudo-equatorial 4-H), 3.5—3.9 (1 H, m, 3-H), 4.84 (1 H, d, *J* 16 Hz, pseudo-axial 1-H), 5.26 (1 H, d, *J* 16 Hz, pseudo-equatorial 1-H), 7.35—7.6 (2 H, m, 7- and 8-H), and 7.9—8.15 (2 H, m, 6- and 9-H).

3,4-*Dihydro*-3-*propyl*-1H-*naphtho*[2,3-c]*pyran*-5,10-*quinone* (25).—To a stirred solution of compound (24) (104 mg) in acetonitrile (15 ml) and water (5 ml) was added a solution of cerium(IV) ammonium nitrate (442 mg) in water (1 ml) during 10 min. Water was then added and the mixture was extracted with methylene dichloride to give the *product* (25) (83 mg, 90%), m.p. 123—124 °C (methanol–chloroform) (Found: C, 74.6; H, 6.1. $C_{16}H_{16}O_3$ requires C, 74.95; H, 6.2%); δ 0.98 (3 H, distorted t, *J* 7 Hz, CH_3), 1.2—1.95 (4 H, m, CH_2CH_2), 2.28 (1 H, dddd, *J* 3, 3.5, 10, and 19 Hz, pseudo-axial 4-H), 2.76 (1 H, dt, *J* 3.5 and 19 Hz, pseudo-equatorial 4-H), 3.3—3.7 (1 H, m, 3-H), 4.46 (1 H, dt, *J* 3.5 and 19 Hz, pseudo-axial 1-H), 4.88 (1 H, dd, *J* 3 and 19 Hz, pseudo-equatorial 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).

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