A quinonoid naphthopyranone as a model for the synthesis of the pigment xylindein. Photochemical formation of the lactone ring

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3-Propyl-3,4,5,10-tetrahydronaphtho[2,3-c]pyran-1,5,10(1H)-trione (5) has been synthesized with a view to determining a satisfactory pathway to its 7,9-dihydroxy-analogue (4), which it is hoped will ultimately provide a route to the extended quinonoid pigment, xylindein. A key step in the reaction sequence is the photo-rearrangement of 1,4-dimethoxy-trans-3-pent-1-etyl-naphthalene-2-carboxylic acid (11) into the related δ-lactone (12) having the required ring system. Subsequent silver(II) oxide oxidative demethylation affords the target quinone (5).


3-Propyl-3,4,5,10-tetrahydronaphtho[2,3-c]pyran-1,5,10(1H)-trione (5) was synthesized in order to find a practical route to its 7,9-dihydroxy-analogue (4), which it is hoped will ultimately provide a route to the extended quinonoid pigment, xylindein. A key step in the reaction sequence is the photo-rearrangement of 1,4-dimethoxy-trans-3-pent-1-etyl-naphthalene-2-carboxylic acid (11) into the related δ-lactone (12) having the required ring system. Subsequent silver(II) oxide oxidative demethylation affords the target quinone (5).


The naturally occurring pigment xylindein has been assigned the extended quinonoid structure (I). In considering a possible synthesis of the fused ring system, it was noted that Cameron et al. had effected the anaerobic coupling of the aphid degradation product (2) to afford xylaphin (3), which differs from xylindein only in the construction of the two heterocyclic rings. It therefore appeared that a likely synthetic precursor of xylindein would be the quinonoid naphthopyranone (4). We describe here a synthesis of the dideoxy-analogue (5) which possesses the required ring system.

2-Bromonaphthoquinone (6) was alkylated with hexanoic acid in the presence of silver nitrate and...
ammonium persulphate to afford the quinone (7) (90%), which was in turn converted into the hydroquinone dimethyl ether (8) (95%) by reductive methylation. Bromination of this naphthalene with N-bromosuccinimide in the presence of di-t-butyl peroxide cleanly yielded the product (9) of benzylic bromination; the $^1$H n.m.r. spectrum of this material showed the benzylic proton as a pair of triplets centred at $\delta$ 5.93 ($J$ 7 Hz) owing to restricted rotation about the naphthalene-benzylic carbon bond through steric crowding. Variable temperature measurements in toluene-$d_8$ afforded a coalescence temperature of 70 °C. Without further purification, the benzylic bromide was boiled in lutidine, which gave the trans-olefin (10) as the sole product (88% from 8). Treatment of the trans-olefin (10) with butyl-lithium in ether followed by carbon dioxide gave rise to the unsaturated acid (11) (76%). The stereochemistry about the double bond was clearly indicated by the coupling constant (16 Hz) of the olefinic protons in compound (11).

Formation of the lactone ring system from the unsaturated acid (11) was accomplished using a novel photochemical ring closure. The acid (11) was irradiated in solution in cyclohexane through quartz using a vycor filter to afford the lactone (12) (40%). The n.m.r. spectrum of this fused $\delta$-lactone showed inter alia the methine proton as a multiplet at $\delta$ 4.42 coupled to the two benzylic protons, which each appeared as a pair of doublets at $\delta$ 3.37 ($J$ 2,5 and 11 Hz), whereas irradiation of the methine proton collapsed the benzylic protons into a geminally coupled pair of doublets ($J$ 16 Hz), thus providing confirmation of the assignment of structure (12). For comparison purposes, the alternative $\gamma$-lactone (13) was prepared by the following sequence. The bromo-naphthalene (8) was converted into the naphthalenic acid (14) (92%) by treatment with butyl-lithium, followed by carbon dioxide. The product (14) was brominated with N-bromosuccinimide in the presence of di-t-butyl peroxide to afford the intermediate bromo-acid (15). On boiling the crude product in lutidine, it gave rise to the lactone (13) (70% from 14) by intramolecular displacement of bromide ion by the neighbouring carboxylate group. The $^1$H n.m.r. spectrum of this lactone exhibited the signal for the methine proton as a doublet at $\delta$ 5.68 ($J$ 3 and 8 Hz), coupled to a high-field multiplet centred at $\delta$ 2.28.

While the photochemical formation of a lactone ring in the above manner appears to have no literature precedent, a not unrelated thermal ring closure has been reported for the conversion of the stilbene acid, hydrangea acid (16), into hydrangeol (17). However, on heating the unsaturated acid (11), decarboxylation occurred to afford 2-pent-1-enyl-1,4-dimethoxynaphthalene (18) as the sole product observed, identical with material obtained as a by-product in the conversion of the trans-bromo-olefin (10) into the acid (11). It may be conjectured that in the transformation 16→17 an alternative mechanism may be operating, for example via a quinone methide.

Lactone (12) was converted into the quinone (5) (80%) by oxidative demethylation using silver(ll) oxide. 

![Chemical structures](image)

**Experimental**

N.m.r. spectra were measured on a Varian XL-100 instrument for solutions in $^1$HCl-$d_4$-chloroform with tetramethylsilane as internal reference. Dry column chromatography was performed using Merck Kieselgel 60 (70–230 mesh). Light petroleum refers to the fraction, b.p. 60–80 °C.

2-Bromo-3-pentyl-1,4-naphthoquinone (7)

A mixture of 2-bromo-1,4-naphthoquinone (6) (550 mg), silver nitrate (400 mg), and benzoic acid (400 mg) in water-acetonitrile (12:12 ml) was heated at 60–65 °C with vigorous stirring and treated over 1 h with a freshly prepared aqueous solution of ammonium peroxodisulphonate (800 mg in 10 ml water). The dark solution was stirred for a further 10 min at the same temperature, then cooled and the excess of acid was neutralized with solid sodium carbonate. The mixture was filtered, extracted with ether (2 X 25 ml), and the organic layer was dried and evaporated. The crude orange residue was chromatographed (ethyl acetate-light petroleum, 1:19) to afford the product (640 mg, 90%) as yellow needles, n.p. 90–91 °C (from methylene chloride-light petroleum). $\lambda_{max}$ (CCl$_4$) 1670, 1596, and 1470 cm$^{-1}$, $\beta$ 0.92 (3H, t, $J$ 1 Hz, CH$_3$), 1.16–1.80 (6H, m, 3 X CH$_2$), 2.83 (2H, t, $J$ 7 Hz, 1' CH$_3$).
The quinone (7) (1.50 g) in ether (50 ml) was shaken with sodium dithio-
ate (300 mg) and dimethyl sulphate (4 ml). The mixture was heated
under reflux with vigorous stirring for 3 h. The solid was filtered off and
washed with acetone. The combined filtrate and washings were evap-
orated, and the oily residue was dissolved in ether and washed with a
cold 5% sodium carbonate. A small quantity of 1% aqueous sodium hy-
droxide. Work-up of the organic layer gave the oily 1,4 dimethoxy-
benzyl naphthalene (11). The acid (11) (100 mg) in cyclohexane (60 ml)
was irradiated under nitrogen with di-t-butyl peroxide as for compound (9). Work-up as before gave the
bromide (15), 1,22-1,64 (4H, m, 2XCH; 3,89 (3H, s, OCH3); 2,70-2,92 (2H, m, 1'-CH; 7,34-7,43 (2H, m, 6- and 7-H); and 8,02-8,22 (2H, m, 5- and 8-H).Found: C, 67; H, 5.6. Calc.
for C19H14O2: C, 60; H, 5.7%.

1,4-Dimethoxy-trans-3-1-methoxyphenyl-2-carboxylic acid (11)
A solution of the olef1nic bromide (10) (270 mg) in dry carbon tetrachloride
(15 ml) was treated with N bromosuccinimide (160 mg) and a catalytic
amount of ti-butyli peroxide, and the mixture was heated under gentle
reflux for 2 h. The solution was cooled, filtered, and reduced to afford the
crude dibromide (15), 1.12-1.16 (4H, m, 2XCH; 3,88 (3H, s, OCH3); 2,70-2,92 (2H, m, 1'-CH; 7,34-7,43 (2H, m, 6- and 7-H); and 8,02-8,22 (2H, m, 5- and 8-H).Found: C, 67; H, 5.6. Calc.
for C19H14O2: C, 60; H, 5.7%.

1,4-Dimethoxy-trans-3-4-bromophenyl-2-carboxylic acid (12)
A solution of the bromide (8) (1.35 g) in dry ether (60 ml) was treated
with N-bromosuccinimide and carbon disulfide as described for com-
 pound (11). Work-up as before gave, from the aqueous layer, the product
(1.11 g, 92%), mp, 85-90 °C (from light petroleum), δ 0.92 (3H, d, 3-CH3; 1.35-2,11 (4H, m, 1'- and 2'-CH2); 2,99 (2H, d, 1- and 4'-CH2); 7,46-7,64 (2H, m, 6- and 7-H); and 8,03-8,19 (211, m and 8 II). Without further purification, the
material was heated under reflux in 2.6-lutidine (15 ml) for 2.5 h. The
solution was cooled, filtered, and evaporated under reduced pressure.

The dark residue was chromatographed (ethyl acetate-light petroleum,
1:49) to afford the concentrated ammonia solution (5 ml), water, dilute hydrochloric acid, and saturated brine. Upon work-up, the residue was chromatographed
(ethyl acetate-light petroleum, 1:49) to afford the

1,4-Dimethoxy-trans-3-ethyl-2-carboxylic acid (14)
The acid (14) (150 mg) was brominated with N-bromosuccinimide and di-t-butyl peroxide as for compound (9). Work-up as before gave the bromide (15), δ 0.78-1.04 (3H, m, CH3); 1.22-1,64 (4H, m, 2XCH; 3,89 (3H, s, OCH3); 2,70-2,92 (2H, m, 1'-CH; 7,34-7,43 (2H, m, 6- and 7-H); and 8,02-8,22 (2H, m, 5- and 8-H).Found: C, 67; H, 5.6. Calc.
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References
Soc., 1962, 327; (b) G.M. Blackburn, D.E.V. Ekong, A.H. Nielsen,
(C), 1966, 1836.
4 S.M. McElvain and E.L. Engelhardt, J. Am. Chem. Soc., 1944, 66,
1077.

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129