The role of the oxygen atom in benzylic hydroxylations of naphthopyrans

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Benzylic hydroxylation of 5,10-dimethoxy-2,2-dimethylnaphtho[2,3-*b*] pyran followed by oxidative demethylation afforded the naturally occurring 4-hydroxy-α-lapachone as its racemate, in 72% yield. Treatment of *trans*-1,2,3,4-tetrahydro-5,10-dimethoxy-1,3-dimethylanthracene under similar conditions failed to hydroxylate the 4-position. It would thus appear that the naphthopyran ring-oxygen facilitates benzylic hydroxylations at C(4) in both naphtho[2,3-*b*] - and naphtho[2,3-*c*]pyrans.

Bensiliese hidroksilering van 5,10-dimetoksi-2,2-dimetielnafto[2,3-*b*]piraan gevolg deur oksidatiewe demetilering, lewer die natuurproduk 4-hidroksi-α-lapasjoon as 'n rasemaat, in 72% opbrengs. Behandeling van *trans*-1,2,3,4-tetrahidro-5,10-dimetoksi-1,3-dimetielantraseen onder dieselfde kondisies het die 4-posisie nie gehidroksileer nie. Dit wil voorkom asof die naftopiraanringsuurstof bensiliese hidroksilering by C(4) in beide nafto[2,3-*b*] - en nafto[2,3-*c*]pirane vergemaklik.

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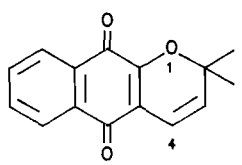
It has been shown earlier that naphtho[2,3-*c*]pyrans can be hydroxylated at the benzylic C(4) position by the use of potassium t-butoxide in dimethylformamide at moderate temperatures.[1—3] In all the compounds investigated, the heterocyclic ring oxygen atom formed an integral part of the molecular environment for the reaction. Consequently, it was considered possible that the oxygen atom of the naphtho-[2,3-*c*]pyran system might play a role in the mechanism of hydroxylation. To this end, a study of autoxidations on both α- and β-tetralones was undertaken, where the oxygen atom was not part of the ring system, but exocyclic to it. The results showed that the carbonyl oxygen atom did not favour similar benzylic hydroxylations to the same extent, using identical conditions.[4]

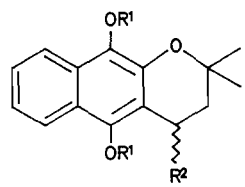
In order to test the generality of earlier findings, it was decided to investigate the hydroxylation reaction on a naphtho[2,3-*b*]pyran system where the influence of the ring oxygen atom relative to the benzylic position was 1,4-, instead of 1,3- as in the earlier systems.[1—3]

Thus, dehydro-α-lapachone (1) was synthesized in good yield (80%) from the precursor isolapachol.[5,6] Reduction of the Δ^3-bond was easily achieved with concomitant reduction of the quinonoid ring system under catalytic conditions. The intermediate quinol (2) was not isolated but was converted into the dimethyl ether (3) (82%) by base-catalysed methylation. A further compound isolated from the reaction mixture was α-lapachone (5) (13%) derived by the aerial oxidation of the quinol (2). In large scale reductive methylations of dehydro-α-lapachone (1), an additional compound was isolated in 5% yield and was assigned the further reduced naphthopyran structure (6). Reductions of a similar nature in the xyloidone systems have been reported by Ferreira *et al.*[7]

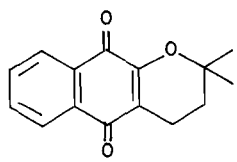
Treatment of the naphthopyran (3) with potassium t-butoxide in dimethylformamide produced the desired 4-hydroxy derivative (4) in a best yield of 37% direct (72%, based upon recovered starting material). This yield is in keeping with



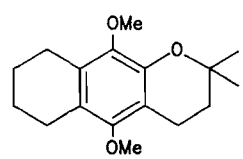
(1)



(2) R¹ = H; R² = H
(3) R¹ = Me; R² = H
(4) R¹ = Me; R² = OH



(5)



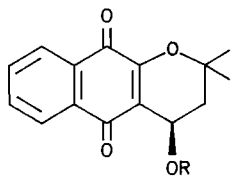
(6)

those found for the naphtho[2,3-*c*]pyran series.[1—3] Assignment of the structure (4) to the product was based on the following spectral evidence. A strong absorption in the i.r. spectrum at 3450 cm^{-1} indicated the presence of a hydroxy group. In the ^1H n.m.r. spectrum, the signals for the 2-methyl groups appeared as singlets at δ 1,45 and 1,52. The three heterocyclic ring protons gave a typical ABX multiplet. Thus, signals at δ 2,08 (dd, *J* 14 and 7 Hz) and 2,16 (dd, *J* 14 and 6 Hz) were assigned to the 3-protons. The hydroxy group gave a broad signal superimposed on those of the 3-protons. A doublet of doublets at δ 5,29 (*J* 7 and 6 Hz) was assigned to the 4-proton. Irradiation of the signals centred at δ 2,08 and 2,16 caused the doublet of doublets at δ 5,29 to collapse to a singlet, while irradiation of the signal at δ 5,29 caused the upfield signals to simplify into two doublets (*J* 14 Hz).

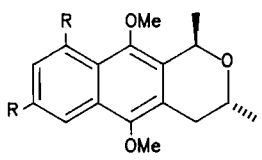
Silver oxide-mediated oxidative demethylation[8] of the dimethyl ether (4) in the presence of nitric acid afforded

racemic 4-hydroxy-α-lapachone (7)[9] in quantitative yield. This quinone, a yellow syrup, proved to be rather difficult to handle and was converted into the crystalline racemic 4-acetoxy-α-lapachone (8) whose spectral data were identical with those of the acetate derived from the natural material.[9]

Thus, the generality of the benzylic hydroxylation reaction already found for the naphtho[2,3-*c*]pyrans has been extended to include the isomeric naphtho[2,3-*b*]pyrans. It was now considered prudent to ascertain whether or not the oxygen atom of the pyran ring does play a role in the mechanism of hydroxylation. With this in mind, a target molecule was chosen, resembling the naphthopyrans (9) and (10) on which the initial hydroxylation procedures were effected.[1–3]



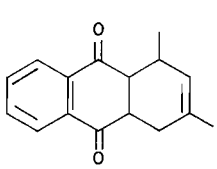
(7) R = H
(8) R = $COCH_3$



(9) R = H
(10) R = OMe

The most suitable carbocyclic analogue to be tested for hydroxylation appeared to be *trans*-tetrahydrodimethoxydimethylanthracene (21), in which the heterocyclic oxygen atom has been replaced by a methylene group. Additionally, it was felt that the inclusion and position of the methyl groups was necessary to allow regio- and stereochemical events, if any, to have the same impact as in the cases related to the ethers (9) and (10).

Reaction between naphthoquinone and *trans*-2-methylpenta-1,3-diene produced, after chromatography, the quinone (12) (67%) representing the oxidized level of the anticipated Diels–Alder adduct (11). A second component eluted from the column appeared to be yellow whilst in solution. However, upon evaporation of the solvent a blueish-black crystalline mass of the charge transfer quinhydrone complex (13)[10] was deposited (26%). It was found that this quinhydrone complex could be converted into the quinone (12) in 47% yield by the simple process of heating under reflux in acetone.



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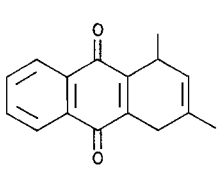

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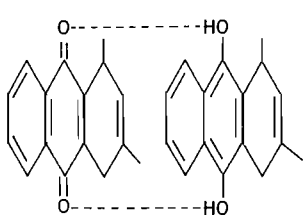


(13)

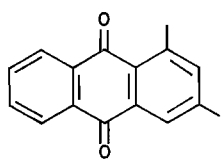
The sensitivity of the benzylic hydrogens of the quinone (12) to attack by mild base was demonstrated by quantitative conversion into the known anthraquinone (14),[12] by treatment with a mild base such as potassium carbonate in refluxing acetone.

In exploratory reactions, it was decided to attempt to convert the quinone (12) into the diacetate (16) by reductive acetylation, in the expectation that this would lead to the formation of the diacetates (20) and (22) upon catalytic hydrogenation. Hydrolysis of these diacetates followed by methylation would yield the desired ethers (21) and (23).

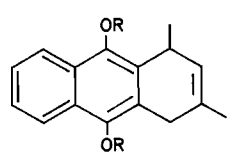
Reductive acetylation of quinone (12) in the presence of zinc powder and acetic anhydride led to the formation of three compounds, successfully separated by column chromatography, and structurally assigned as the 9-anthrone (17) (16%), the 9-anthrol acetate (18) (17%), and the diacetate (19) (51%). Thus, the propensity for the terminal ring to aromatize was clearly demonstrated in all three products isolated, and an alternative synthesis of the desired diacetate (16) was sought.

Catalytic hydrogenation of the quinone (12), followed by base-induced methylation of the crude quinol, yielded the dimethyl ether (15) (78%) with the double bond still intact. This indicated that the quinonoid group in compound (12) could be selectively reduced in the presence of the double bond. Two minor components present in the reaction mixture were separated with difficulty, and shown to be unchanged quinone (12) (4%) and the fully aromatized anthraquinone (14) (6%).

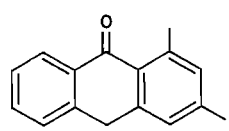
Alternatively, catalytic hydrogenation of quinhydrone (13) followed by methylation under basic conditions afforded the desired ether (15) in quantitative yield. Further hydrogenation of the isolated double bond of this material under the



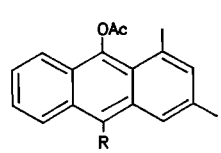
(14)



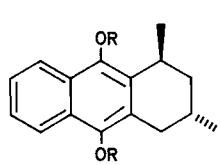
(15) R = Me
(16) R = $COCH_3$



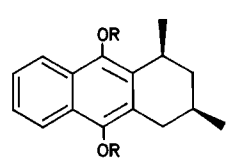
(17)



(18) R = H
(19) R = OAc



(20) R = $COCH_3$
(21) R = Me

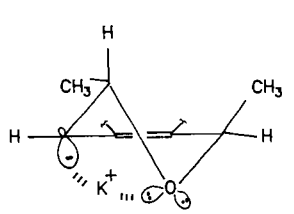


(22) R = $COCH_3$
(23) R = Me

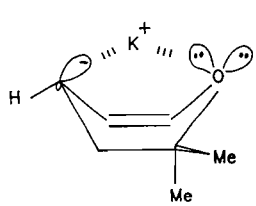
normal conditions produced a quantitative yield of a mixture comprising the two isomers (**21**) and (**23**). The two stereoisomers had very similar t.l.c. behaviour in a range of solvent systems. However, it was possible to purify the major component, which was tentatively assumed to be the *trans* (**21**) rather than the *cis* isomer (**23**), for the same reason that the *trans*-dimethylnaphthopyran (**9**) is favoured over the corresponding *cis* compound. In the latter pair, it has been shown that the 3-methyl group adopts the equatorial configuration as anticipated on steric grounds and confirmed by coupling constants for the 3- and 4-protons in the ^{1}H n.m.r. spectrum, while the 1-methyl group is *pseudoaxial* to minimize *peri* interactions with the neighbouring methoxy substituent.[2] This *trans* stereochemistry for compound (**9**) was confirmed beyond doubt by oxidative demethylation to afford 9-demethoxy-*iso*-eleutherin[2] whose stereochemistry is well documented.[13]

When this material or a mixture of the ethers (**21**) and (**23**) were subjected to the hydroxylation conditions employed before,[1—4] only unchanged starting material was isolated with some decomposition of the starting materials being evident upon extended treatment.

It appears from this and our earlier work[1—3] that the oxygen atom of the pyran ring plays a role in facilitating benzylic hydroxylation of both naphtho[2,3-*c*]- and naphtho-[2,3-*b*]pyrans and, to a minor extent, in the α-tetralones.[4] Bearing in mind the paucity of available evidence at this stage, the following is offered as a tentative explanation. The lone pairs of electrons on the pyran oxygen atoms of the naphtho[2,3-*c*]- and naphtho[2,3-*b*]pyrans assist in the stabilization of the initially formed benzylic carbanion by allowing the potassium cation to bridge the benzylic position and the lone pairs, as depicted in **24** and **25** respectively, prior to the oxidation and hydroxylation stages.



(24)



(25)

Possible oxygenation routes for the two carbanions (**24**) and (**25**) are through oxidation, either to the corresponding carbocations followed by reaction with water to form the products, or to the corresponding radicals which could then react with molecular oxygen to form the products, or conceivably, the carbanions may even react with oxygen directly. Further work using labelled oxygen would need to be undertaken to distinguish between the various mechanistic possibilities.

Experimental

^{1}H N.m.r. spectra were recorded in deuteriochloroform on either a Varian EM 360 at 60 MHz or a Varian XL-100 spectrometer at 100 MHz. I.r. spectra were measured as Nujol mulls on a Pye–Unicam SP 300 spectrophotometer. Melting points are uncorrected. Column chromatography was carried out on dry columns using silica gel (70—230 mesh). Light petroleum refers to that fraction of boiling range 60—80°C. 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.

3,4-*Dihydro*-5,10-*dimethoxy*-2,2-*dimethylnaphtho*[2,3-b]-*pyran* (**3**) *and* 3,4,6,7,8,9-*hexahydro*-5,10-*dimethoxy*-2,2-*dimethylnaphtho*[2,3-b]*pyran* (**6**)

Dehydro-α-lapachone (840 mg; 3,5 mmol)[5,6] in dry ethyl alcohol (200 ml) containing platinum(IV) oxide (80 mg) was hydrogenated under atmospheric pressure and room temperature until the uptake of hydrogen ceased. The reaction mixture was rapidly filtered under nitrogen and the filtrate was evaporated to yield a light-yellow oil, which was immediately taken up in dry acetone (250 ml) and treated with anhydrous potassium carbonate (3 g; 21,8 mmol) and dimethyl sulphate (2,74 g; 21,7 mmol), and heated under reflux with stirring under nitrogen for 48 h. The cooled mixture was filtered and the filtrate was evaporated to leave an oily residue. This was taken up in ether (300 ml) and washed with concentrated ammonia (80 ml) and water (100 ml), and then dried ($MgSO_4$). The residue obtained upon work-up was chromatographed using ethyl acetate–light petroleum (1 : 5) as eluent, to give the *dimethyl ether* (**3**) (780 mg; 82%) as white rods, m.p. 86—87°C (from light petroleum); ν_{max} 1250 cm^{-1}, δ 1,44 [6H, s, 2-$(CH_3)_2$], 1,9 (2H, t, *J* 7 Hz, 3-H_2), 3,0 (2H, t, *J* 7 Hz, 4-H_2), 3,92 and 3,95 (each 3H, s, OCH_3), 7,38 (2H, m, 7- and 8-H), and 8,04 (2H, m, 6- and 9-H) (Found: C, 75,0; H, 7,35. Calc. for $C_{17}H_{20}O_3$: C, 75,0; H, 7,35%); α-lapachone (**5**) (110 mg; 13%), which formed yellow cubes from petroleum ether, m.p. 115—116 °C (lit.,[11] m.p. 119°C); and the *hydroquinone dimethyl ether* (**6**) (42 mg; 5%) as a viscous, colourless oil; ν_{max} (film) 1245 cm^{-1}; δ_H 1,37 [6H, s, 2-$(CH_3)_2$], 1,75 (6H, m, 3-, 7-, and 8-H_2), 2,75 (6H, m, 4-, 6-, and 9-H_2), and 3,72 and 3,78 (each 3H, s, OCH_3) (Found: C, 73,65; H, 8,6. Calc. for $C_{17}H_{24}O_3$: C, 73,9; H, 8,7%).

3,4-*Dihydro*-4-*hydroxy*-5,10-*dimethoxy*-2,2-*dimethylnaphtho*[2,3-b]*pyran* (**4**)

Naphthopyran (**3**) (96 mg; 0,35 mmol) in dry dimethylformamide (20 ml) at 60°C was stirred under dry ($CaCl_2$) aerobic conditions and treated with potassium t-butoxide (176 mg; 157 mmol). Stirring was continued for 24 h, then the orange-coloured liquid was cooled and poured into saturated ammonium chloride (100 ml) and extracted with ether (5 × 30 ml). The residue obtained upon work-up was chromatographed using ethyl acetate–light petroleum (1 : 5) as eluent then ethyl acetate–light petroleum (1 : 1). The first fraction eluted was unchanged naphthopyran (**3**) (46 mg; 48%), followed by the *hydroxynaphthopyran* (**4**) (38 mg; 37%) as a thick, colourless oil; ν_{max} (film) 3450 cm^{-1}; δ 1,45 (3H, s, CH_3), 1,52 (3H, s, CH_3), 2,08 (1H, dd, *J* 14 and 7 Hz, 3-H), 2,16 (1H, dd, *J* 14 and 6 Hz, 3-H), 3,96 and 4,04 (each 3H, s, OCH_3), 5,29 (1H, t, *J* 6 Hz, 4-H), 7,4 (2H, m, 7- and 8-H), and 8,0 (2H, m, 6- and 9-H) (the *OH* signal lies underneath those of 3-H_2) (Found: C, 70,6; H, 6,6. Calc. for $C_{17}H_{20}O_4$: C, 70,8; H, 6,9%).

4-Hydroxy-α-lapachone (7)

Dimethyl ether (4) (64 mg; 0,22 mmol) in dioxan (6,5 ml) containing silver(II) oxide (110 mg; 0,89 mmol) was rapidly stirred and treated with 6M-nitric acid (0,74 ml) for 3,5 min. The silver(II) oxide was consumed and the yellow solution was stirred for an extra 0,5 min, then treated with dichloromethane (16 ml) and water (8 ml), rapidly stirred, and allowed to partition. The residue after work-up of the orgnic phase was rapidly chromatographed over a short column using ethyl acetate–light petroleum (3 : 10) as eluent, to yield *quinone* (7) (57 mg; 100%) as a yellow syrup, ν_{max} (film) 3450 and 1665 cm^{-1}; δ 1,55 (3H, s, CH_3), 1,66 (3H, s, CH_3), 2,2 (2H, poorly defined d, *J* 6 Hz, 3-H_2), 4,5 (1H, s, D_2O exchangeable, 4-OH), 5,17 (1H, t, *J* 6 Hz, 4-H), 7,93 (2H, m, 7- and 8-H), and 8,35 (2H, m, 6- and 9-H) (Found: C, 69,45; H, 5,1. Calc. for $C_{15}H_{14}O_4$: C, 69,8; H, 5,4%). (This information is recorded here since none is available in the literature.)

4-Acetoxy-α-lapachone (8)

4-Hydroxy-α-lapachone (7) was acetylated by the usual method to afford the 4-acetoxy-α-lapachone (8) (94%) as yellow rods from ethanol, m.p. 141—142°C (lit.,[9] m.p. 139,5—140,5°C). The compound had spectral data identical with those published.[9]

1,4-*Dihydro*-1,3-*dimethylanthracene*-5,10-*dione* (12) *and the quinhydrone* (13)

Trans-2-methylpenta-1,3-diene (5 g; 61 mmol) in dry benzene (80 ml) was stirred at reflux temperature and treated with freshly recrystallized naphthoquinone (7,2 g; 45,5 mmol) in three batches over a period of 3 h. The mixture was heated for a further 18 h under reflux. Removal of the solvent under reduced pressure yielded a yellow crystalline mass which was chromatographed using ethyl acetate–light petroleum (1 : 5) as eluent. The first product eluted was the *naphthoquinone* (12) (7,30 g; 67%), m.p. 107—108°C (yellow rods from cyclohexane); ν_{max} 1663 cm^{-1}; δ 1,25 (3H, d, *J* 7 Hz, 1-CH_3), 1,85 (3H, br. s, 3-CH_3), 3,13 (2H, m, 4-H_2), 5,56 (1H, m, 2-H), 7,73 (2H, m, 6- and 9-H), and 8,1 (2H, m, 5- and 8-H) (Found: C, 80,5; H, 5,9. Calc. for $C_{16}H_{14}O_2$: C, 80,7; H, 5,9%). Further elution afforded the *quinhydrone* (13) (2,78 g; 26%) as black plates, m.p. 167—168°C (from acetone); ν_{max} 3420, 1644, 1592, and 1300 cm^{-1}; δ (acetone - d_6) 1,24 (6H, overlapping d, *J* 7 Hz, 1- and 1′-CH_3), 1,82 and 1,88 (each 3H, s, 3- and 3′-CH_3), 2,8—4,0 (6H, m, 1- and 1′-H, 4- and 4′-H_2), 5,58 and 5,64 (2H, m, 2- and 2′-H), 7,43 and 7,75 (4H, m, 6-, 6′-, 7-, and 7′-H), and 8,06 and 8,2 (4H, m, 5-, 5′-, 8-, and 8′-H) (Found: C, 80,3; H, 6,5. Calc. for $C_{32}H_{30}O_4$: C, 80,3; H, 6,3%).

Quinhydrone (2,76 g) in acetone (75 ml) was heated under reflux for 1 h and then reduced in volume to 50 ml and allowed to cool. The black crystals of the quinhydrone were filtered off (1,44 g) and evaporation of the mother liquors afforded an additional crop of the naphthoquinone (12) (1,26 g; 47% conversion).

1,3-*Dimethylanthraquinone* (14)

A mixture of the quinone (12) (238 mg; 1 mmol) and anhydrous potassium carbonate (276 mg; 2 mmol) in anhydrous acetone (50 ml) was stirred and heated under reflux for 2 h. The cooled solution was filtered and the filtrate was evaporated, to yield a residue that was chromatographed using ethyl acetate–petroleum ether (1 : 20) as eluent to afford the anthraquinone (14) (236 mg; 100%), m.p. 163—164°C (yellow needles from ethanol) (lit.,[12] m.p. 162°C); ν_{max} 1667 cm^{-1}; δ 2,43 (3H, s, 3-CH_3), 2,77 (3H, s, 1-CH_3), 7,31 (1H, d, *J* 2 Hz, 2-H), 7,9 (3H, m, 4-, 6-, and 7-H), and 8,27 (2H, m, 5- and 8-H).

1,4-*Dihydro*-1,3-*dimethyl*-5,10-*dimethoxyanthracene* (15)

(a) The quinone (12) (960 mg; 4 mmol) in ethyl alcohol (120 ml) containing platinum(IV) oxide (40 mg) was hydrogenated under ambient temperature and pressure until uptake of hydrogen ceased (*ca* 1 h). The colourless residue was filtered under nitrogen and the filtrate was evaporated to an oil, which was taken up in dry acetone (120 ml) and treated with anhydrous potassium carbonate (2,56 g; 20 mmol) and dimethyl sulphate (2,52; 20 mmol) with vigorous stirring under reflux in a nitrogen atmosphere for 3,5 h. The cooled reaction mixture was filtered, and evaporation of the filtrate afforded an oil which was taken up in ether (150 ml) and washed with concentrated ammonia (1 × 40 ml), water (100 ml), and brine (100 ml). The residue obtained upon work-up was chromatographed using ethyl acetate–light petroleum (1 : 10) as eluent. The first component to be eluted was the *naphthalene* (15) (840 mg; 78%) as a thick syrup, ν_{max} (film) 1596 and 1070 cm^{-1}; δ 1,3 (3H, d, *J* 7 Hz, 1-CH_3), 1,83 (3H, br. s, 3-CH_3), 3,5 (2H, m, 4-H), 4,0 (7H, s, 2 × OCH_3 and 1-H), 5,83 (1H, m, 2-H), 7,53 (2H, m, 6- and 7-H), and 8,17 (2H, m, 5- and 8-H) (Found: C, 80,4; H, 7,3. Calc. for $C_{18}H_{20}O_2$: C, 80,6; H, 7,5%). Further elution yielded starting material (12) (40 mg; 4%) followed by the *dimethylanthraquinone* (14) (60 mg; 6%). The separation was rather difficult to achieve, and quoted yields were obtained after rechromatography.

(b) The quinhydrone mixture (13) (1,4 g; 5,88 mmol) in warm (30°C) ethanol (130 ml) containing platinum-(IV) oxide (30 mg) was hydrogenated at atmospheric pressure until uptake ceased. The solution was filtered under nitrogen, and careful removal of the ethanol under nitrogen on a rotary evaporator afforded a residue, which was taken up in dry acetone (120 ml) and treated with anhydrous potassium carbonate (3,25 g; 23,5 mmol) and dimethyl sulphate (2,96 g; 23,5 mmol), and rapidly stirred and heated under reflux under nitrogen for 28 h. Work-up as before gave the *dimethyl ether* (15) (1,58 g; 100%) as a lemon-yellow syrup, identical with the material prepared in (a).

1,3-*Dimethyl*-9-*anthrone* (17), 9-*acetoxy*-1,3-*dimethylanthracene* (18), *and* 5,10-*diacetoxy*-1,3-*dimethylanthracene* (19)

Quinone (12) (300 mg; 1,26 mmol) in acetic anhydride (20 ml) containing zinc dust (1,5 g; 23,7 mmol) was stirred and heated under reflux for 15 h. Acetic acid (50 ml) was added and the mixture was brought to the boil and then rapidly

filtered. The filtrate was poured into water (200 ml) and extracted with dichloromethane. The residue obtained upon work-up, after washing the extract with saturated sodium hydrogen carbonate (3 × 60 ml) was chromatographed using ethyl acetate–light petroleum (1:10) as eluent. The first compound eluted was the *anthrone* (**17**) (46 mg; 16%), m.p. 115—116°C (white needles from petroleum ether); ν_{max} 1647 cm^{-1}; δ 2,34 (3H, s, 3-CH_3), 2,79 (3H, s, 1-CH_3), 4,04 (2H, s, 10-H), 7,0 (1H, d, *J* 2 Hz, 2-H), 7,06 (1H, d, *J* 2 Hz, 4-H), 7,44 (2H, m, 6- and 7-H), and 8,22 (2H, m, 5- and 8-H) (Found: C, 86,6; H, 6,5. Calc. for $C_{16}H_{14}O$: C, 86,5; H, 6,3%).

Further elution afforded the *acetoxyanthracene* (**18**) (56 mg; 17%), m.p 151—152°C (light yellow needles from light petroleum); ν_{max} 1748 cm^{-1}; δ 2,42 (3H, br. s, $W_{1/2}$ 2 Hz, 3-CH_3), 2,52 (3H, s, CH_3CO), 2,82 (3H, br. s, $W_{1/2}$ 2 Hz, 1-CH_3), 7,04 (1H, d, *J* 2 Hz, 2-H), 7,4 (2H, m, 6- and 7-H), 7,55 (1H, d, *J* 2 Hz, 4-H), 7,84 (2H, m, 5- and 8-H), and 8,17 (1H, s, $W_{1/2}$ 2 Hz, 10-H) (Found: C, 81,5; H, 6,3. Calc. for $C_{18}H_{16}O_2$: C, 81,8; H, 6,1%). The third compound eluted was the *diacetate* (**19**) (210 mg; 51%), m.p. 167—168°C (yellow needles from ethanol); ν_{max} 1753 and 1220 cm^{-1}; δ 2,40 (3H, br. s, $W_{1/2}$ 2 Hz, 3-CH_3), 2,48 and 2,53 (each 3H, s, OAc), 2,78 (3H, br. s, $W_{1/2}$ 2 Hz, 1-CH_3), 7,03 (1H, d, *J* 2 Hz, 2-H), 7,42 (3H, m, 4-, 6-, and 7-H), and 7,76 (2H, m, 5- and 8-H) (Found: C, 74,65; H, 5,8. Calc. for $C_{20}H_{18}O_4$: C, 74,5; H, 5,6%).

trans-1,2,3,4-*Tetrahydro*-5,10-*dimethoxy*-1,3-*dimethylanthracene* (**21**)

Dimethyl ether (**15**) (268 mg; 1 mmol) in ethanol (10 ml) containing platinum(IV) oxide (5 mg) was hydrogenated at ambient temperature and atmospheric pressure until 1 mol equivalent of hydrogen had been taken up. Removal of the solvent yielded a residue which was chromatographed using ethyl acetate–light petroleum (1:20) as eluent, to give a mixture of the isomeric *dimethyl ethers* (**21**) and (**23**) (270 mg; 100%). A sample (40 mg) of this material was purified by p.l.c. with ethyl acetate–light petroleum (3:100) to yield a pure dimethyl ether, tentatively assigned structure (**21**) (25 mg), together with a mixture of isomers. Pure ether (**21**), the second fraction, is a colourless syrup, ν_{max} 1600 and 1295 cm^{-1}; δ 1,12 (3H, d, *J* 7 Hz, 3-CH_3), 1,4 (3H, d, *J* 7 Hz, 1-CH_3), 2,0—2,4 (3H, m, 2- and 3-H), 3,04—3,5 (3H, m, 4- and 1-H), 3,84 and 3,86 (each 3H, s, OCH_3), 7,4 (2H, m, 6- and 7-H), and 8,0 (2H, m, 5- and 8-H) (Found: C, 80,0; H, 8,1. Calc. for $C_{18}H_{22}O_2$: C, 80,0; H, 8,15%).

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