Base-induced Cyclisations of Naphthalenes into Naphtho[2,3-*c*]pyrans. Application to Stereospecific Syntheses of (±)-Isoeleutherin and (±)-Deoxyquinone A Dimethyl Ether

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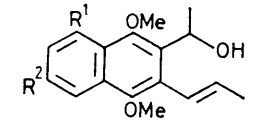
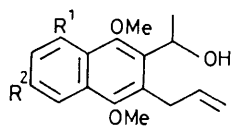
2-(Alk-2-enyl)-3-(1-hydroxyalkyl)-1,4-dimethoxynaphthalenes are cyclised and then oxidised to naphtho[2,3-*c*]pyran-5,10-quinones which are naturally occurring quinones or their derivatives.

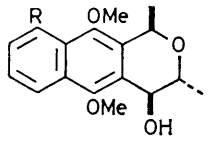
We recently reported[1] the oxidative cyclisation of the naphthalene (**1**) to the aphin-related 7,9-dideoxyquinones A (**9**) and A′ (**11**), using cerium(IV) ammonium nitrate (CAN), a reaction shown to proceed *via* the hydroxynaphthopyrans (**6**)



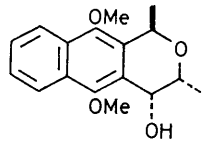
(1) $R^1 = R^2 = H$
(2) $R^1 = OMe$, $R^2 = H$



(3) $R^1 = R^2 = H$
(4) $R^1 = OMe$, $R^2 = H$
(5) $R^1 = R^2 = OMe$



(6) R = H
(7) R = OMe



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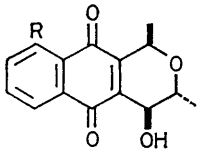
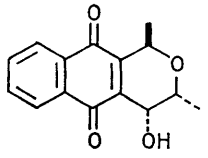


(9) R = H
(10) R = OMe



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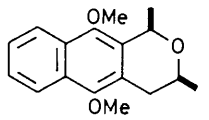
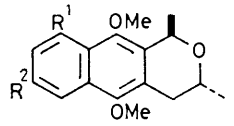
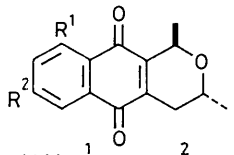


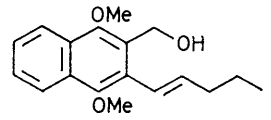
(12)



(13) $R^1 = R^2 = H$
(14) $R^1 = OMe$, $R^2 = H$
(15) $R^1 = R^2 = OMe$



(16) $R^1 = OMe$, $R^2 = H$
(17) $R^1 = R^2 = OMe$



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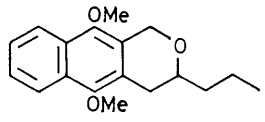
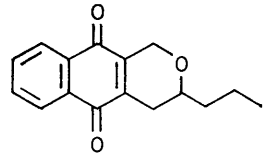


(19)



(20)

and (**8**).[2] Others[3] have converted the isomeric prop-2-enylnaphthalene (**3**) into a *cis–trans*-mixture of the naphthopyrans (**12**) and (**13**), using phenylselenoetherification.

We now describe the anaerobic base-catalysed cyclisation of compound (**3**) into (**13**), in which the methyl groups are stereospecifically *trans*, and the corresponding aerobic cyclisation to give the 4-hydroxy-derivatives (**6**) and (**8**). The anaerobic reaction is also used to convert the related naphthalenes (**4**) and (**5**) into (±)-isoeleutherin (**16**)[4] and (±)-deoxyquinone A[5] dimethyl ether (**17**) respectively.

Compound (**3**), when treated with potassium t-butoxide in dimethylformamide at 60 °C for 15 min under nitrogen, gave (**13**) (50%), free of the *cis*-isomer (**12**). Similar treatment of (**3**) for a longer period in the presence of air afforded the hydroxylated derivative (**6**)[2] (28%) together with minor amounts (7%) of the epimeric (**8**).†

The trimethoxy-compound (**4**)[3,6] was treated under nitrogen, using the above conditions, to yield the *trans*-dimethylnaphthopyran (**14**) (88%), uncontaminated by the *cis*-isomer.‡ Oxidation of (**14**) with CAN gave (±)-isoeleutherin (**16**) (83%) only.

An alternative reaction of compound (**2**)§¶ in air gave the hydroxynaphthopyran (**7**)§ (15%) together with (**14**) (31%). CAN oxidation of (**7**) afforded the methoxyquinone (**10**)§ (66%).

When the tetramethyl ether (**5**)§ was treated in the absence of air, the product (**15**)§ (58%) was isolated, once again without any *cis*-isomer being observed. This was oxidised using silver(II) oxide[7] to (±)-deoxyquinone A dimethyl ether (**17**)§ (72%).[8]

No doubt base-catalysed conjugation of the isolated double bond in compounds (**3**), (**4**), and (**5**) precedes cyclisation, a suggestion supported by the formation of products (**7**) and (**14**) from (**2**). This was confirmed by reaction of (**18**)[1,2] under nitrogen to give (**19**)§ (83%), which was in turn oxidised (CAN) to the quinone (**20**)§ (90%).

We are currently studying how to optimise the yields of the aerobic reactions.

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References

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8 This compound has been independently prepared by an alternative route which provided a mixture of the *cis*- and *trans*-isomers; D. W. Cameron, personal communication.

† It is noteworthy that in this reaction the epimer (**6**) predominates, while in the CAN oxidation of (**1**), the epimer (**8**) predominates (see ref. 2).

‡ Previous syntheses report a mixture of the *cis*- and *trans*-isomers (see refs. 3 and 6).

§ All new compounds gave satisfactory elemental analyses and their spectroscopic data were in accord with the assigned structures.

¶ Prepared from 3-acetyl-5-methoxy-1,4-naphthoquinone (T.A. Chorn, R. G. F. Giles, I. R. Green, V. I. Hugo, and P. R. K. Mitchell, *Tetrahedron Lett.*, 1982, **23**, 3299) by a method similar to that described for compound (**1**) (see refs. 1 and 2).