Rotenoid Synthesis Circumventing 6a,12a-Dehydro Intermediates

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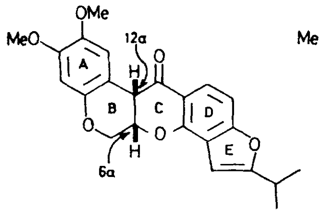
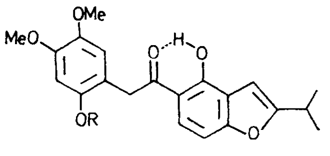
Summary A deoxybenzoin-based rotenoid synthesis, producing the rotenoid directly at the desired oxidation level, is described.

Only two recent synthetic approaches to rotenoid [*e.g.* isorotenone (**1**)] synthesis, a sulphonium ylide,[1] and an acetylene cyclisation method,[2] lead directly to the B/C ring system at the correct oxidation level. Other methods, including those employing 2,2′-dihydroxybenzoins as intermediates [*e.g.* (**2a**)], lead to 6a,12a-dehydrorotenoids (**3**) which must be 1,4-reduced with sodium borohydride, and the 12-carbonyl re-introduced by oxidation (*e.g.* Oppenauer) of the 12-alcohol finally formed.[3] We now report a deoxybenzoin-based route which circumvents these steps.

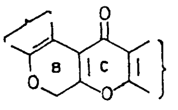
Allylation (or propargylation) of 2,2′-dihydroxydeoxybenzoin in the presence of potassium carbonate leads mainly to the *C*-allylation product (**4**) rather than the desired 2-*O*-allylation product.[4] The deoxybenzoin (**2a**) was therefore treated with sodium and ethyl orthoformate to form the isoflavone (**5a**), m.p. 185 °C, thus protecting the future 12a-centre and the D-ring hydroxyl. Treatment with allyl bromide, sodium hydride, and dimethylformamide led smoothly to (**5b**) m.p. 145—146 °C, which was hydrolysed to (**2b**) m.p. 92 °C with removal of the protective carbons of the isoflavone. The aldehyde (**2c**) [oil, δ 9·65 (CHO), 13·92 (chelated hydroxyl), characterised by oxidation to isoderrisic acid] was formed from (**2b**) by treatment with osmium tetroxide–periodate. On heating (30 min) in pyridine (**2c**) condensed [*cf.* (**6**)] to give (±)-isorotenone (**1**), m.p. and mixed m.p. 166 °C, spectrally identical with authentic material.[5]



(1)



(2a); R = H
(2b); R = $CH_2CH{:}CH_2$
(2c); R = CH_2CHO



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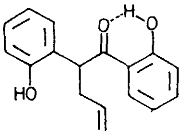
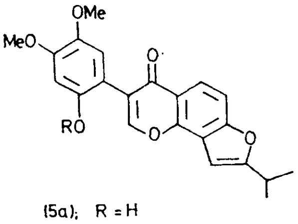
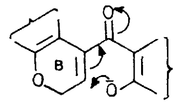


(4)



(5a); R = H
(5b); R = $CH_2CH{:}CH_2$



(6)

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