Bis-methylene Transfer to 2′-Hydroxyisoflavones by Dimethylsulphoxonium Methylide

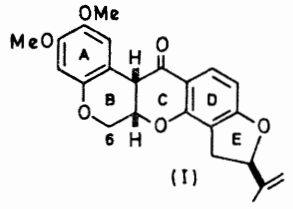
By L. CROMBIE,*† J. S. DAVIES, and D. A. WHITING†
(*Department of Chemistry, University College, Cathays Park, Cardiff*)

Summary Isoderritol isoflavone and an excess of dimethylsulphoxonium methylide undergo a novel reaction in which two methylenes are transferred to give (Va).

NATURAL rotenoids [*e.g.* rotenone (I)] are differentiated from isoflavanoids by a cyclic methylene group (C-6) supplied *in vivo* by methionine[1] or its equivalent. Speculation concerning the function of *S*-adenosylmethionine as an *S*-ylide in this process has stimulated us, and others, to investigate the reaction between isoflavones and sulphoxonium methylides as possible models. Thus, Ollis and his co-workers[2] have shown that 2′-hydroxyisoflavones react with 1 mol. of dimethylsulphoxonium methylide (IIa) to give not rotenoids, but the isomeric vinylcoumaranones (*cf.* IV).

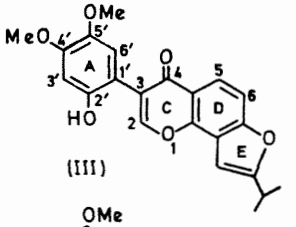
We have been investigating the action of methylide (IIa) with isoderritol isoflavone[3] (III). With 1 mol. of methylide, the vinylcoumaranone (IV), $C_{23}H_{22}O_6$, was indeed isolated, ν_{max} 3280 and 1685 cm^{-1} with a vinyl ABX system apparent in the n.m.r. (τ_A 4·48, τ_B 4·68, and τ_X 3·67; J_{AX} 17, J_{BX} 10, and J_{AB} 1·5 Hz). However, when 5 mol. of methylide was employed the reaction took a novel course. The major product, m.p. 144—145°, $C_{24}H_{24}O_6$, was found to arise from double methylene transfer to the isoflavone, and on the basis of the following evidence is assigned structure (Va). No carbonyl absorption was observed, but ν_{max} (mull) 3460 and 3170 cm^{-1} were apparent. ^{1}H n.m.r. indicated that rings A, D, and E were intact, although 5-H was no longer deshielded by carbonyl [3·18: *cf.* τ 1·84 in (III)]. The olefinic double bond was suggested by the 2-H signal (τ 4·2) and confirmed by the formation of a dihydro-derivative (VIa). One tertiary hydroxy-group was indicated by conversion into the ether (Vc) in acidic methanol; a bathochromic shift in base in the u.v. spectrum characterised the phenolic group. Structure elucidation was aided by the use of fully deuteriated methylide (IIb),[4] which reacted with isoderritol isoflavone to yield the trideuterio-derivative (Vb), demonstrating a methylene→methine transformation. The coumaranone (IV) also yields the alcohol (Va) on treatment with dimethylsulphoxonium methylide (IIa), and is thus likely to be the intermediate in the (III) → (Va) conversion.

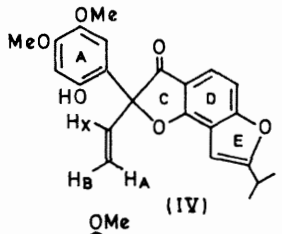
The dihydro-derivative (VIa) has the relative stereochemistry expected from less hindered addition of hydrogen to the *cis*-B/C-fused system (Va). This is confirmed by the ^{1}H n.m.r. spectrum which shows 5-H (VIa) positively shielded (τ 3·95; *cf.* 6-H at τ 3·38) by aryl ring A, only possible in this arrangement. The dihydro-derivative forms a monoacetate (VIc) which has a hydroxylic proton at τ 7·4. This hydroxy-function is readily replaced in acidic methanol to give (VIb): the new methyl is strongly shielded by rings A and/or D, and appears in the ^{1}H n.m.r. spectrum at τ 6·91. Under different acid conditions, alcohol (VIa) is converted into the hexacyclic product (VIIIa). Since the *cis*-fusions of the 5-membered rings appear obligatory, either 1a-H or 4-H must epimerise. Repetition of the reaction using deuterium chloride gave the monodeuterio-product (VIIIb). The benzodifuran (VII) is thus a likely intermediate in the cyclisation. It has been isolated, and as expected, yields the ether (VIIIa) on acid treatment.

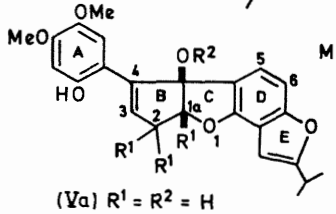


$(CH_3)_2\overset{+}{S}O\cdot\bar{C}H_2$ (IIa)

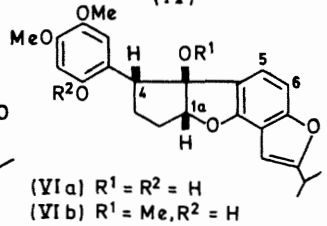
$(CD_3)_2\overset{+}{S}O\cdot\bar{C}D_2$ (IIb)



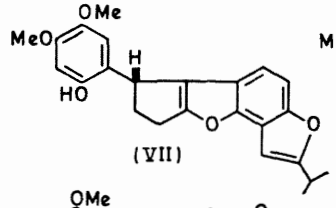


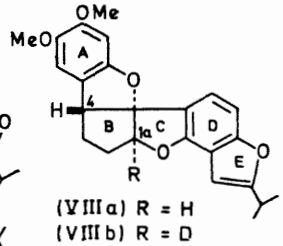


(Va) $R^1 = R^2 = H$
(Vb) $R^1 = D, R^2 = H$
(Vc) $R^1 = H, R^2 = Me$

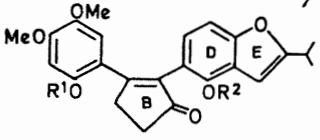


(VIa) $R^1 = R^2 = H$
(VIb) $R^1 = Me, R^2 = H$
(VIc) $R^1 = H, R^2 = Ac$

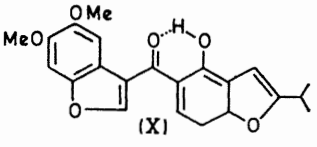




(VIIIa) R = H
(VIIIb) R = D



(IXa) $R^1 = R^2 = H$
(IXb) $R^1 = R^2 = Ac$
(IXc) $R^1 = Ac, R^2 = H$



The allylic alcohol (Va) itself rearranged very readily in acid to a yellow crystalline cyclopentenone (IXa), $C_{24}H_{24}O_6$, ν_{max} 3460, 3180, and 1668 cm.$^{-1}$, displaying a stilbene-like chromophore [λ_{max} 247·5 (ϵ 23,700), 256 i (22,200), 286 (7900), and 352 (11,900) nm]. A diacetate (IXb) was formed, λ_{max} 1705 cm^{-1}. A monoacetate (IXc), ν_{max} 3190 and 1670 cm^{-1}, was obtained from acetylation of the

† Present address: Department of Chemistry, University of Nottingham, Nottingham, NG7 2RD.

unsaturated alcohol (Va) which concurrently rearranged. The ^{1}H n.m.r. spectrum of the cyclopentenone (IXa) fully characterised rings A, D, and E, and showed in addition a symmetrical multiplet at τ 6·7—7·4 (4H), which was assigned to the ring-B methylene protons.

A second and minor product obtained from the reaction of the methylide (IIa) with the isoflavone (III), proved to be decarboxyisorotenononic acid (X),[5] formed by rearrangement of the isoflavone induced by an excess of sodium hydride.

Satisfactory mechanistic rationalisation may be written for all reactions outlined above, and will be discussed in full elsewhere.

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