Course of the Condensation between 5,7-Dihydroxycoumarin and Citral: A Reinvestigation of the Constitution of Bruceol and Deoxybruceol from *Eriostemon brucei*

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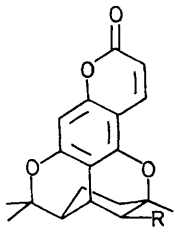
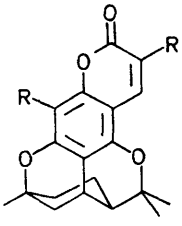
Summary Although deoxybruceol is derived by heating the chromen (**7**) in pyridine, *X*-ray work shows that rearrangement has occurred and its structure must be revised from (**2**) to (**3**), whilst that of bruceol is sustained as (**1**); both (**2**) and (**3**) are synthesised by an alternative route.

THE Australian species *Eriostemon brucei* contains the meroterpenoid bruceol (**1**),† a structure for which *X*-ray evidence is available.[1] Deoxybruceol, which co-occurs, has hence been tacitly assumed to have the structure (**2**). A synthesis of (±)-deoxybruceol, identical in all respects with natural deoxybruceol, except for chirality, has been reported.[2] This involves condensation of 5,7-dihydroxycoumarin with citral in the presence of pyridine and in view of what we have learned from other systems[3] we have re-examined this reaction. Treatment of the coumarin (**5**), with citral and pyridine (1 : 1 : 2) at 90 °C for 18 h afforded two monochromens and a trace of bischromen. The monochromens (**6**), m.p. 113—115 °C, and (**8**), m.p. 136—138 °C were assigned their structures on n.m.r. grounds using NOE measurements on the methyl ethers (**7**) and (**9**) for orientation purposes. Irradiation of the OMe signal in (**7**) led to signal enhancement only of the aromatic proton (21%), and in (**9**) to enhancement of both aromatic and β-coumarin hydrogens (36% and 15% respectively); neither product gave a positive Gibbs reaction.

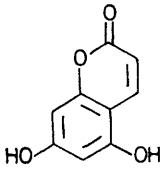
The chromen (**6**) was heated in pyridine‡ at 110 °C for 96 h. Two citrans (**2**) and (**3**) could be observed in the product by n.m.r. one being present in a minor amount. The major product was isolated pure by crystallisation and was identical with the synthetic specimen obtained earlier,[2] and, in chromatographic and spectroscopic properties, with natural deoxybruceol. Treatment with bromine in dioxan gave the (±)-dibromoderivative (**4**), $C_{19}H_{18}O_4Br_2$, m.p. 164—166 °C crystallising in space group $P2_1/c$, $a = 10{\cdot}34$, $b = 9{\cdot}62$, $c = 18{\cdot}30$ Å, $\beta = 105{\cdot}49°$, $Z = 4$. 1592 Significant observed reflexions were recorded with an automatic four-circle diffractometer using Mo-K_α radiation. The



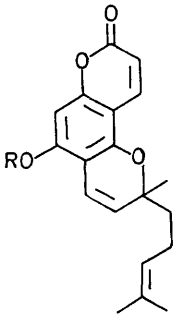
(1); R = OH
(2); R = H



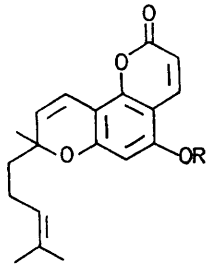
(3); R = H
(4); R = Br



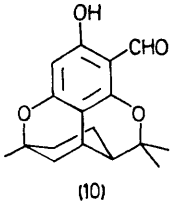
(5)



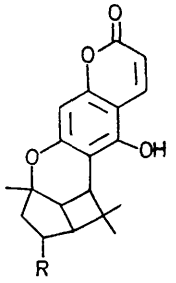
(6); R = H
(7); R = Me



(8); R = H
(9); R = Me



(10)



(11); R = H
(12); R = OH

† Absolute stereochemistry is not implied by the formulae.
‡ Heating the chromen (**8**) in pyridine affords a 'cyclol' (isomeric with eriobrucinol[6]), since citran formation is not permitted in this case.

structure was solved by the heavy-atom routine and with refinement still proceeding R stands currently at 13·6% Deoxybruceol is thus revealed as the citran (**3**), not (**2**) as hitherto believed.

In further confirmation, (±)-deoxybruceol was unambiguously prepared by reaction of the formyl citran (**10**), whose structure rests on X-ray analysis by direct methods,[3a] with 1,1-dimethoxy-1-dimethylaminoethane.[4] Isodeoxybruceol (**2**) can be similarly prepared from the isomer of (**10**). Deoxybruceol and isodeoxybruceol have very similar, yet distinguishable, ^{1}H and ^{13}C n.m.r. spectra. The reaction pathway from chromen (**6**) to deoxybruceol (**3**) must involve isomerisation of the chromen before bicyclisation, in the manner discussed in the preceding communication;[3b] in this case stabilisation by delocalisation is supplied by the chromen ring.

Since difficulties were encountered in the original X-ray investigation of bromobruceol[1] (performed with limited photographic data), the structure of bruceol itself was checked by direct methods. Natural bruceol, $C_{19}H_{20}O_5$, crystallised in space group $P2_12_12_1$, $a = 10{\cdot}34$, $b = 12{\cdot}01$, $c = 13{\cdot}09$, $Z = 4$. Observed data (2685 reflections) were collected as above and the structure was solved by use of the Multan procedure.[5] Refinement has progressed to $R = 7{\cdot}4\%$, and structure (**1**) is confirmed.

Bruceol and deoxybruceol, although occuring side by side in the same plant,[1] do not, therefore, have the same citran orientation and the assumed close biosynthetic linkage, *i.e. via* biological hydroxylation, is severed. Their biosyntheses must diverge before the putative chromen intermediates are formed unless the coumarin ring is inserted at a late stage. On the other hand, the orientation of deoxybruceol (**3**), is related, in terms of chromen intermediate, to that of eriobrucinol (**11**) and its hydroxy-derivative (**12**) which have also been discovered in *E. brucei*.[6]

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