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Functionalisation at C-20 in Diterpenoids

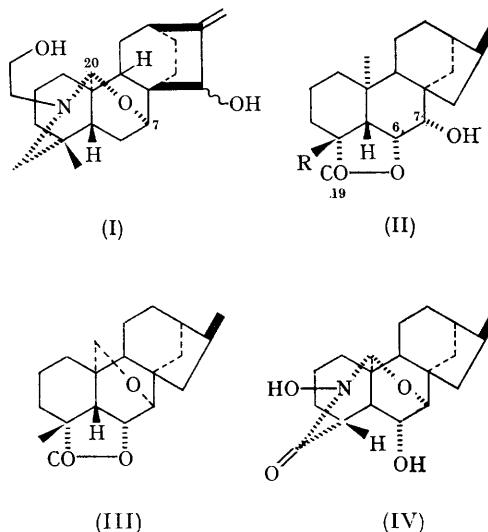
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THE functionality of the C-20 angular group is an important feature of the chemistry of the tetracyclic diterpenoids. Thus amongst the interesting facets of the chemistry of the diterpene alkaloids such as ajaconine (I) are the transannular hydrogen transfer and ether formation reactions between C-7 and C-20.¹ Now the magnitude of the coupling constant between the 6β - and 7α - and 7β -protons of the kaurenolides suggested that ring B existed in a twisted boat conformation with C-6 at one of the points.² In this the 7α -hydroxyl lies close to the angular methyl group. Therefore, although it implied a seven-membered transition state, we investigated photolytic activation of C-20 from C-7.

Irradiation of the 7α -alcohol (II; R=Me), derived from 7β -hydroxykaurenolide,³ in benzene solution in the presence of iodine and lead tetraacetate⁴ gave an ether (III) in high yield. Comparison of the nuclear magnetic resonance spectrum of the ether with that of the starting material revealed the loss of the C-20 methyl resonance and the appearance of a methyleneoxy-group (τ 6.42). The C-7 proton remained coupled to the C-6 proton. Further evidence that no C-C bond fission had taken place was obtained by reduction of the

γ -lactone to a diol and subsequent oxidation to a 19 \rightarrow 6 lactonol. The C-7 resonance then collapsed to a singlet. Reduction of the lactonol regenerated the parent γ -lactone ether. Photolysis of the nitrite⁵ of the 7α -alcohol (II; R=H) derived from



¹ D. Dvornik and O. E. Edwards, *Tetrahedron*, 1961, **14**, 54. S. W. Pelletier, *Experientia*, 1964, **20**, 1.

² C. Djerassi and W. Klyne, *Proc. New York Acad. Sci.*, 1962, **48**, 1093.

³ B. E. Cross, R. H. B. Galt, and J. R. Hanson, *J. Chem. Soc.*, 1963, 2944.

⁴ C. Meystre, K. Heusler, J. Kalvoda, P. Wieland, G. Anner, and A. Wettstein, *Experientia*, 1961, **17**, 475; *Helv. Chim. Acta*, 1962, **45**, 1317.

⁵ D. H. R. Barton, J. M. Beaton, L. E. Geller, and M. M. Pechet, *J. Amer. Chem. Soc.*, 1960, **82**, 2640; 1961, **83**, 476. A. L. Nussbaum and C. H. Robinson, *Tetrahedron*, 1962, **17**, 35.

7,18-dihydroxykaurenolide⁶ gave a lactam, $C_{19}H_{27}O_4N$, ν_{\max} 3470, 3150, and 1640 cm^{-1} . Again the nuclear magnetic resonance spectrum revealed the loss of the angular methyl group and the appearance of a 1-proton singlet at τ 4.9. We formulate this product as (IV) by analogy with the chemistry of ajaconine (I).¹ The structure is based on the initial formation of the expected⁵ oxime followed by C-7→C-20 ether formation. The resultant hydroxylamine in turn attacks the

lactone ring with the formation of a hydroxy-lactam. The reaction clearly has potential for the partial synthesis of ajaconine.

Both cyclisation reactions on to C-20 require a seven-membered transition state, which is unusual for nitrite and hypiodite reactions.⁷

We have also shown, not unexpectedly, that the angular methyl group at C-20 can be attacked from the 6α -ol.

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⁶ B. E. Cross, R. H. B. Galt, and J. R. Hanson, *J. Chem. Soc.*, 1963, 3783.

⁷ Cf. J. W. ApSimon and O. E. Edwards, *Canad. J. Chem.*, 1962, **40**, 896; W. L. Meyer and A. S. Levinson, *Proc. Chem. Soc.*, 1963, 15; R. F. C. Brown, *Austral. J. Chem.*, 1964, **17**, 47; and references there cited.