Synthesis of the Quinoline Alkaloids, Platydesmine and Isobalfourodine

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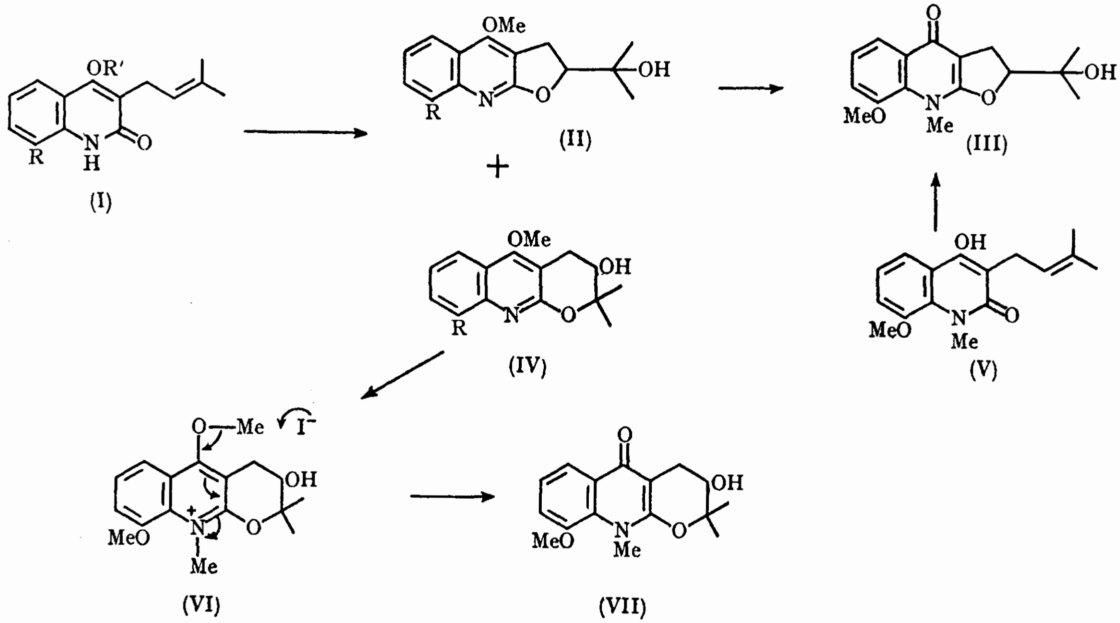
The alkaloid, platydesmine, is a component of *Platydesma campanulata* Mann, and Werny and Scheuer[1] suggested the constitution (II; R=H) on the basis of ultraviolet, infrared, and mass spectra of the base, and analysis of the picrate. By extension of our proposal[2] for the related alkaloid, balfourodine (III), the biosynthesis of platydesmine may proceed by oxidative cyclisation of an isopentenylquinoline (I). Our aim was to establish the structure of platydesmine by synthesis, and we chose a method illustrative of the probable biosynthetic pathway.

Diethyl (3-methylbut-2-enyl)malonate[3] with aniline in refluxing diphenyl ether afforded the 2,4-dihydroxyquinoline (I; R,R′=H) (26%), which was converted into the 4-methoxy-derivative (I; R=R, R′=Me) (79%) by brief treatment with diazomethane. Reaction of the quinolone (I; R=H; R′=Me) with peroxylauric acid furnished the furano-derivative (II; R=H) (40%), and the isomeric pyrano-compound (IV; R=H) (28%). Comparison with a sample of natural (+)-platydesmine showed that the major oxidation product was (±)-platydesmine.

The structures of the oxidation products were established by n.m.r. spectroscopy. In deuterochloroform solution, the hydroxyl resonances of the two isomers appear as broad singlets, because of proton exchange. In dimethyl sulphoxide, however, strong hydrogen-bonding to the solvent reduces the rate of exchange,[4] and the hydroxyl resonances of the tertiary alcohol (II; R=H) and of the secondary alcohol (IV; R=H) become a sharp singlet and a doublet, respectively; splitting of the latter peak is due to spin–spin coupling with the adjacent CH proton.



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[1] F. Werney and P. J. Scheuer, *Tetrahedron*, 1963, **19**, 1293.

[2] E. A. Clarke and M. F. Grundon, *J. Chem. Soc.*, **1964**, 4196.

[3] E. A. Clarke and M. F. Grundon, *J. Chem. Soc.*, **1964**, 438.

[4] *cf.* O. L. Chapman and R. W. King, *J. Amer. Chem. Soc.*, 1964, **86**, 1256.

The alkaloids balfourodine (III) and isobalfourodine (VII) occur together in *Balfourodendron riedelianum* Engl. and their respective enantiomers in *Lunasia amara* Blanco.[5] We showed previously[2] that oxidation of the *N*-methylquinolone (V) with peroxylauric acid gave (±)-balfourodine (III) almost quantitatively. We have now achieved a rational synthesis of the isomeric alkaloid isobalfourodine (VII) by applying to the 8-methoxy-series the platydesmine synthesis described above. Reaction of the 8-methoxyquinolone (I; R=OMe, R′=Me) with peracid provided a mixture of the secondary alcohol (IV; R=OMe) and the isomeric tertiary alcohol (II; R=OMe), which were distinguished by their n.m.r. spectra in dimethyl sulphoxide. Heating the secondary alcohol (IV; R=OMe) with methyl iodide furnished (±)-isobalfourodine, presumably by the mechanism (IV) → (VI) → (VII).[3,6] In a similar way, the tertiary alcohol (II; R=OMe) was converted into (±)-balfourodine (III).

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[5] H. Rapoport and K. G. Holden, *J. Amer. Chem. Soc.*, 1959, **81**, 3738; 1960, **82**, 4395; S. Goodwin, A. F. Smith. A. A. Velasquez, and E. C. Horning, *ibid.*, 1959, **81**, 6209; H. C. Beyerman and R. W. Rooda, *Proc. k. ned. Akad, Wetenskap.*, 1959, **62**, *B*, 187; 1960, **63**, *B*, 427.

[6] *cf.* J. R. Price, *Austral. J. Chem.*, 1959, **12**, 458.