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'ONE-POT' BIOMIMETIC SYNTHESIS OF DIHYDROMANCUNINE.

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Some time ago we proposed a hypothetical intermediate mancunine (5a) to explain why the 3β isomer vincoside (3a) rather than its 3α-epimer acts as exclusive precursor in the biosynthesis of Corynanthé indole alkaloids[1]. To support this idea we synthesised from dihydrosecologanin (2), a dihydromancunine (5c) which was easily converted into the tetracyclic Corynanthé skeleton[2]. Since dihydrovincoside (3c) lactamised very readily and also enzymatic removal of the sugar under standard conditions resulted in cyclisation of N-4 to C-17 rather than C-21, an N(b)-benzyl blocking group on the tryptamine moiety was used to give 3b. Debenzylation of the aglycone by hydrogenolysis in acetic acid then afforded essentially only 5c, where the configuration of the ethyl group had been inverted from that of the starting material.

Although achieving the initial objective such a reaction sequence bore little resemblance to likely in vivo processes. However, as a consequence of our investigations on secologanin aglycone[3] we have now found that treatment of a mixture of dihydrosecologanin (2) and tryptamine (1a) with β-glucosidase in pH5 buffer at 37° for 4 - 12 hours produced dihydromancunine directly in up to 30% yield. Moreover the product contained an appreciable quantity of the 20β epimer (5b) which was separated by chromatography, m.p.177-180°. Its structure was assigned from spectral data and confirmed by prolonged $NaBH_4$ reduction and acetylation to a diacetate $[\alpha]_D^{25}$ + 50° ($CHCl_3$) (6b), followed by inversion of H-3 by consecutive $Pb(OAc)_4$ oxidation and $NaBH_4$ reduction to give the known dihydrositsirikine diol diacetate (6a) $[\alpha]_D^{25}$ 0° ($CHCl_3$). Formation of 5b may occur via the aglycone 4, or that of dihydrovincoside (3c).

20β-Dihydromancunine was considerably less stable than the 20α-epimer into which it was largely converted on standing in solution for a few hours - the equilibrium mixture containing only a few per cent of the former. When pure 20β-epimer was dissolved in MeOD and $NaBH_4$ added after 30 minutes, two major products were obtained after acetylation. From the mass spectra, one contained one deuterium at C-16 and was shown to be a 20β compound (6d) by inversion to dihydrositsirikine acetate (6c); the other contained two deuteriums at C-16 and C-20 and corresponded to the 20α analogue 6e. As anticipated, the inversion must therefore occur by

reversible ring-opening to 7 and thence to the enamine 8.

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