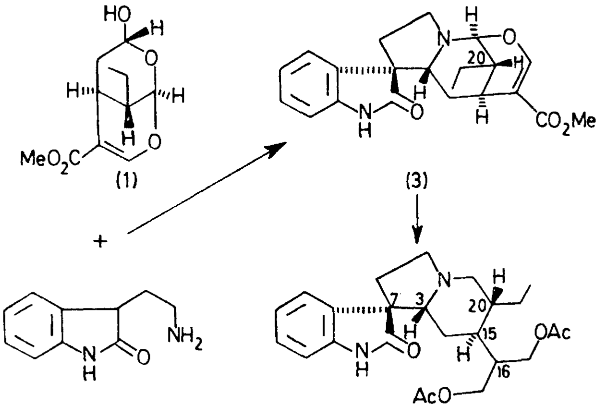
A Unique Series of *Pseudo* Oxindole Alkaloids

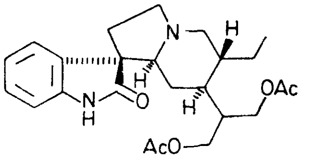
By Richard T. Brown* and Ray Platt
(*Department of Chemistry, The University, Manchester* M13 9PL)

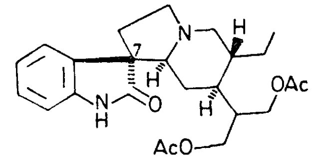
Summary *Corynanthé* oxindole alkaloids of the *pseudo* (3β,15α,20β) configurational series, previously thought to be too unstable to exist, have been synthesised from dihydrosecologanin aglycone.

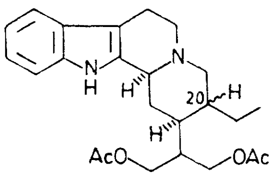
Although *Corynanthé* indole alkaloids of all four configurational types: *normal* (3α,20β), *pseudo* (3β,20β), *allo* (3α,20α), and *epiallo* (3β,20α) are known, among the corresponding oxindole alkaloids the *pseudo* series is unique in being totally unrepresented. Furthermore, attempted oxidative conversion of *pseudo* indole alkaloids invariably results in complete H-3 inversion to the *normal* 3α series, and it has therefore been axiomatic that oxindole alkaloids of *pseudo* stereochemistry were too unstable to exist.[1] We now report the synthesis and characterisation of the first *pseudo* oxindole alkaloid derivatives (**3**), (**4**), and (**8**).

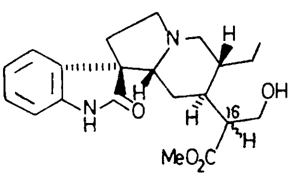


Condensation of dihydrosecologanin aglycone (**1**) and 2-oxytryptamine (**2**) gave 2-oxydihydromancunine, which was assigned structure (**3**) with the important exception of the configuration at C-20.[2] Prolonged reduction with $NaBH_4$ in methanol afforded three isomeric diols, separated and characterised as the diacetates $C_{24}H_{32}N_2O_5$. All exhibited identical mass spectra with major peaks at *m/e* 428 (M^+), 269 ($M - C_7H_{11}O_4$), and 254 ($M - C_{11}H_{12}NO$) in agreement with gross structures (**4**)—(**6**), and the stereochemistry at C-7 and C-3 was readily established from c.d. spectra.[3] The most polar diacetate (25%), $[\alpha]_D^{25}$ + 0·5° ($CHCl_3$), R_f 0·11 (silica, cyclohexane–ethyl acetate, 1 : 1 × 3), had a negative Cotton effect at 260 nm and a positive at 290 nm indicating 3α and 7B configurations respectively; the second (40%), R_f 0·42, $[\alpha]_D^{25}$ + 24° ($CHCl_3$) was found to be 3α, 7A and the third (30%), R_f 0·48, $[\alpha]_D^{25}$ + 9° ($CHCl_3$) 3β, 7B.† For correlation purposes the diacetates of dihydrositsirikine diol (**7b**) and its 20α-epimer (**7a**) were each converted into the corresponding A/B pairs of oxindoles by oxidation with Bu^tOCl and hydrolysis. Direct comparison showed conclusively that the two 3α products from oxydihydromancunine were (**5**) and (**6**), *i.e.* both 20β. Finally, heating in glacial acetic acid for 4 h converted the 3β product into a mixture of (**5**) and (**6**), thus establishing a 20β stereochemistry and the *pseudo* B configuration (**4**).


(5)


(6)


(7)
a; 20α-H
b; 20β-H


(8)

Repetition of the $NaBH_4$ reduction in MeOD resulted in the incorporation of only one deuterium atom at C-16 showing that no inversion of 20-H had occurred, and hence oxydihydromancunine must also belong to the *pseudo* series. Thus it retains the configuration of the ethyl group in the dihydrosecologanin species, unlike 20α-dihydromancunine.[4] A shorter reaction time avoided almost completely both reduction of the methyl ester and C-3–C-7 inversion to give the two C-16 epimers of (**8**) as the major products.

Evidently, *pseudo* oxindole alkaloids can exist and are reasonably stable. There seems no reason why examples from natural sources should not be forthcoming, given care and modern isolation techniques.

We thank the S.R.C. and the I.C.I. Pharmaceuticals Division for a CASE Award.

(*Received*, *8th March* 1976; *Com.* 234.)

---

† Configurations 7A and 7B refer to the configuration at the 7-position in structures (**6**) and (**4**) respectively.

[1] *E.g.*, J. S. Bindra in 'The Alkaloids,' Academic Press, New York, 1973, Vol. 14, p. 103; E. J. Shellard, J. D. Phillipson, and D. G. Gupta, *Planta Med.*, 1969, **17**, 146; E. J. Shellard and P. J. Noughton, *ibid.*, 1971, **20**, 82.

[2] R. T. Brown, C. L. Chapple, and R. Platt, *Tetrahedron Letters*, in the press.

[3] J. L. Pousset and J. Poisson, *Tetrahedron Letters*, 1966, 6283; W. F. Trager, C. M. Lee, J. D. Phillipson, R. E. Haddock, D. Dwama-Badu, and A. H. Beckett, *Tetrahedron*, 1968, **24**, 523.

[4] R. T. Brown, C. L. Chapple, and A. A. Charalambides, *J.C.S. Chem. Comm.*, 1974, 756.