Chemical Communications

(The Journal of The Chemical Society, Section D)

NUMBER 4/1970 18 FEBRUARY

The Isolation of Monomeric Secodine-type† Alkaloids from *Rhazya* Species

By G. A. Cordell, G. F. Smith,* and G. N. Smith

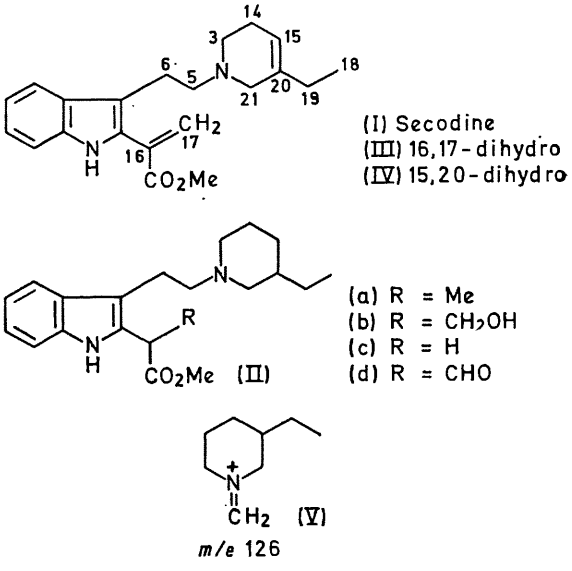
(*Department of Chemistry, The University, Manchester* M13 9PL)

Summary Tetrahydrosecodine (IIa) and a dihydrosecodine [most probably (III)] have been isolated from *Rhazya stricta* and tetrahydrosecodin-17-ol (IIb) from *R. orientalis*; (IIb), (III), and 15,20-dihydrosecodine (IV) have been synthesised.

Extensive fractionation of the petrol-insoluble bases of *Rhazya stricta* leaves by a combination of countercurrent and reversed-phase buffer chromatography yielded two closely related fractions, which on further purification by repeated t.l.c. afforded tetrahydro- and dihydro-secodine as colourless gums (10 mg, *ca.* 0·001% of total bases, and 0·8 mg, respectively). Fractionation of the total methanolic extract of *Rhazya orientalis* roots similarly gave tetrahydrosecodinol (1 mg, *ca.* 0·005% dry weight). The small amounts of these biogenetically significant alkaloids at present available has precluded their detailed study, although their structures, excluding stereochemistry, have been assigned on the following evidence.

16,17,15,20-Tetrahydrosecodine, $C_{21}H_{30}N_2O_2$, $[\alpha]_D^{25}$ −6·5 ±1° ($CHCl_3$), 0 ± 1° (EtOH), forms a crystalline picrolonate m.p. 216—218° dec. The base has a typically indolic u.v. spectrum; the i.r. ($CHCl_3$) and n.m.r. ($CDCl_3$) spectra support the presence of an $\alpha\beta$-disubstituted indole nucleus [ν_{max} 3445 cm^{-1}: τ 1·54s (1H) exchangeable with D_2O, 2·4 — 3·0 m (4H)] directly attached to a CH_3CHCO_2Me group [ν_{max} 1725 cm^{-1}; τ 6·29 s (3H), 5·9 q (1H) J 7·5 Hz., 8·43 d (3H) J 7·5 Hz.] The mass spectrum, *m/e* 342 (8·1), 311 (0·7), 283 (0·4), 230 (1·1), 216 (1·4), 170 (3·5), 157 (4·2), 156 (7·2), 143 (1·6), 127 (12·2), 126 (100), and 124 (5) is notable for the intensity of ion (V) which is characteristic of alkaloids containing the secodine skeleton with a saturated piperidine ring[2] and has played a central role in their discovery and isolation.

The co-occurrence of tetrahydrosecodine with the dimeric alkaloids the secamines[2] and presecamines,[3] which are known to contain the secodine skeleton, together with the above spectroscopic data clearly favoured structure (IIa). Direct chromatographic and spectroscopic comparison of the alkaloid with the synthetic mixture of two racemates (IIa)[4] confirmed this assignment.



Dihydrosecodine, $C_{21}H_{28}N_2O_2$, has a simple indolic u.v. spectrum and is practically indistinguishable from tetrahydrosecodine (IIa) by t.l.c. The two bases are however completely resolved by reversed-phase buffer chromatography. The mass spectrum of dihydrosecodine closely parallels that of (IIa) and allows the double bond to be located in the piperidine unit.

† The name secodine is suggested for structure (I), numbered according to biogenetic principles.[1]

Biogenetic reasoning and the co-occurrence of dihydrosecodine with the secamines and presecamines clearly favours position 15,20 for the additional unsaturation. Reduction of the acrylic ester function of secodine (I)[3] yielded 16,17-dihydrosecodine, also obtained by independent synthesis, which has so far proved indistinguishable from the natural dihydrosecodine by t.l.c. and mass spectrometry.

The u.v. spectrum of tetrahydrosecodinol is again that of a simple indole and its structure was deduced mainly on mass spectroscopic evidence. The molecular ion *m/e* 358 (3·6), $C_{21}H_{30}N_2O_3$, readily loses water (*m** 322·9) to give the radical ion *m/e* 340 (2·0) which corresponds to the molecular ion of 15,20-dihydrosecodine (IV). As is to be expected therefore, all the fragments in the mass spectrum of (IV)[3] are also represented in that of tetrahydrosecodinol. Furthermore an ion *m/e* 328 (0·9) corresponding to loss of CH_2O (*m** 300·4) strongly suggests position 17 for the hydroxy-group. Direct comparison of the alkaloid with synthetic (IIb), (prepared by the general route outlined by Battersby *et al.*[5] for 16,17-dihydrosecodin-17-ol‡) by t.l.c. and mass spectroscopy confirmed their identity.

On attempted acetylation, tetrahydrosecodin-17-ol readily dehydrated to give a high yield of a product shown to be 15,20-dihydrosecodine (IV) by comparison (t.l.c., u.v., mass spectra) with the product of pyrolysis of tetrahydropresecamine[3] and by reduction to tetrahydrosecodine (IIa). In view of the dimerisation of (IV) reported in the accompanying communication,[3] this conversion completes a partial synthesis of tetrahydropresecamine, and hence of one of the racemates of tetrahydrosecamine, from (IIc).

We thank Drs. D. A. Evans and Z. Z. Dąbrowski, who carried out preliminary isolation work, Drs. M. A. Wahid and S. A. Wersi of the Pakistan C.S.I.R. for *Rhazya stricta* leaves, and the S.R.C. for a grant (G.A.C.).

(*Received, November 14th, 1969; Com.* 1733.)

‡ We thank Professor Battersby for sending us his paper before submission.

[1] J. Le Men and W. I. Taylor, *Experientia*, 1965, **21**, 508.
[2] D. A. Evans, G. F. Smith, G. N. Smith, and K. S. J. Stapleford, *Chem. Comm.*, 1968, 859; P. A. Crooks, B. Robinson, and G. F. Smith, *ibid.*, p. 1210.
[3] G. A. Cordell, G. F. Smith, and G. N. Smith, accompanying communication.
[4] R. T. Brown, G. F. Smith, K. S. J. Stapleford, and D. A. Taylor, accompanying communication.
[5] A. R. Battersby and A. K. Bhatnagar, accompanying communication.