

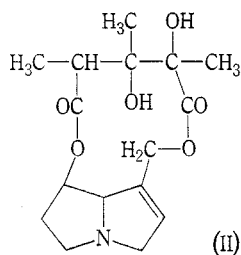
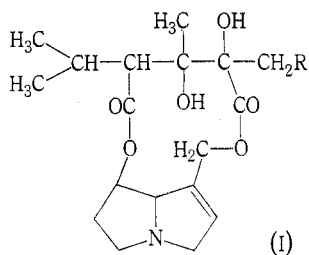
ALKALOIDS OF *CROTALARIA RUBIGINOSA* WILLD.

TRICHODESMINE AND JUNCEINE*

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Crotalaria rubiginosa Willd. is a shrub native to south India and occurring in other countries of the Orient. An examination has been made of the seed alkaloids of the variety *C. rubiginosa* Willd. var. *wightiana* J. G. Baker (syn. *C. wightiana* R. Grah. ex Wight and Walk.-Arn.), which grows in the Nilgiri, Pulney, and Travancore hills of the Western Ghats.

Of five alkaloids present, the two major constituents have been isolated and characterized as $C_{18}H_{27}NO_6$, m.p. 154–155°, and $C_{18}H_{27}NO_7$, m.p. 188–189°. Their nuclear magnetic resonance spectra (cf. Table 1) indicated molecular structures corresponding to trichodesmine (I; $R = H$)^{1,2} and junceine (I; $R = OH$)³ and identity with these alkaloids has been confirmed by direct comparison with authentic samples kindly supplied by Professor R. Adams.



The macrocyclic ring in trichodesmine and junceine is 11-membered as in monocrotaline (II). Although their n.m.r. spectra are rather difficult to interpret in the δ 4 region, it is fairly certain that the differences in shift of the H 9 protons (ΔH 9) are 0.64 p.p.m. for trichodesmine, 0.17 p.p.m. for junceine, when measured in deuteriochloroform. The solubility of junceine in $CDCl_3$ is so low that it was necessary to obtain a computer-averaged spectrum. A spectrum of junceine in D_2SO_4 appeared to have ΔH 9 c. 0.35 p.p.m. These ΔH 9 values are within the range previously encountered for 11-membered ring diesters of retronecine (0.00–0.73 p.p.m.) and show that the H 9 protons are more symmetrically disposed with respect to the plane of the primary ester group than is the case with the

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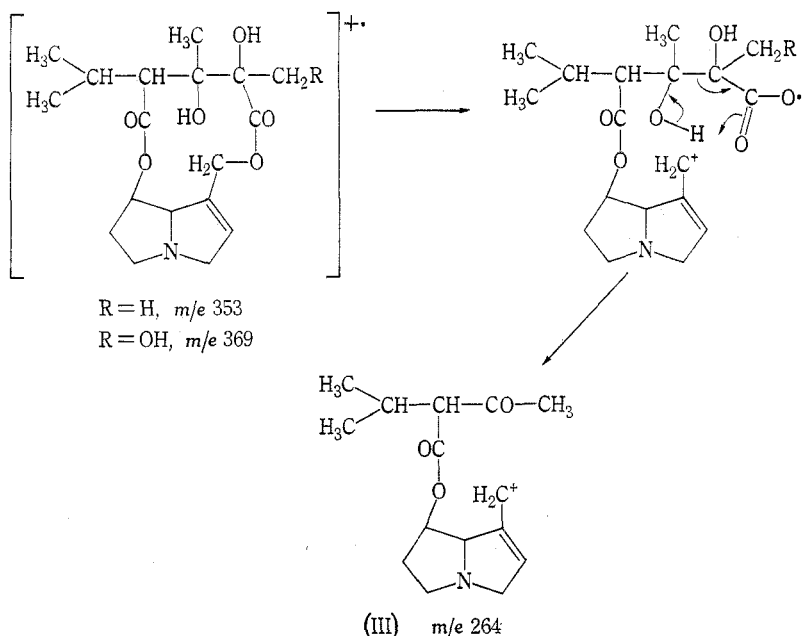
¹ Adams, R., and Gianturco, M., *J. Am. chem. Soc.*, 1956, **78**, 1922.

² Yunusov, S. Yu., and Plekhanova, N. V., *J. gen. Chem. U.S.S.R.*, 1959, **29**, 670.

³ Adams, R., and Gianturco, M., *J. Am. chem. Soc.*, 1956, **78**, 1926.

12-membered ring diesters.^{4,5} In trichodesmine, the width of the H7 multiplet, ΣJ_7 , c. 11 c/s, is also typical of this class of diester, indicating a largely *exo*-buckled retronecine ring.⁴ In junceine, however, the H7 multiplet is broader and poorly defined, apparently indicating that the retronecine ring flips between *exo*- and *endo*-buckled conformations.

The electron-impact fragmentation of trichodesmine and junceine is closely analogous to that of monocrotaline (II) which has been described by Neuner-Jehle *et al.*⁶ Corresponding to the strong M-89 (*m/e* 236) peak of monocrotaline is a strong peak of *m/e* 264, which is M-89 for trichodesmine and M-105 for junceine. This peak is due to the ion (III) whose formation may be depicted as follows:



Junceine is subject to greater thermal degradation than most pyrrolizidine diesters, a molecular ion being obtained only when the sample is inserted directly into the ion chamber. Apart from (III), the strong peaks in the spectra are at *m/e* 138, 136, and lower mass numbers which arise from the pyrrolizidine nucleus. The structures of these fragments have been illustrated by Neuner-Jehle *et al.*⁶ and by Atal *et al.*⁷

Experimental

Microanalyses were made by the Australian Microanalytical Service, Melbourne. The solvent used in paper chromatography was the upper phase resulting from shaking *n*-butanol

⁴ Culvenor, C. C. J., and Woods, W. G., *Aust. J. Chem.*, 1965, **18**, 1625.

⁵ Culvenor, C. C. J., *Tetrahedron Lett.*, 1966, 1091.

⁶ Neuner-Jehle, N., Nesvadba, H., and Spittler, G., *Mh. Chem.*, 1965, **96**, 321.

⁷ Atal, C. K., Kapur, K. K., Culvenor, C. C. J., and Smith, L. W., *Tetrahedron Lett.*, 1966, 537.

with an equal volume of 5% acetic acid. Thin-layer plates were coated with silica gel and developed in chloroform/methanol/ammonia (d 0.880) (85:14:1).⁸

(a) *Extraction of Alkaloids*

Milled, dehusked seeds of *Crotalaria rubiginosa* (600 g) were defatted with light petroleum, b.p. 60–80°, and then extracted with methanol in a Soxhlet extractor. After removal of solvent, the dark brown residue (145 g) was triturated with 5% H_2SO_4 (100 ml). The solution was reduced for 12 hr by the addition of Zn dust (15 g). The mixture was filtered and the filtrate made alkaline with aqueous ammonia and extracted with $CHCl_3$. The extracted base (2.2 g) showed five spots on a thin-layer chromatogram, the two major spots having R_F 0.27, 0.49. Crystallization from $CHCl_3$ gave brown crystals (470 mg). Recrystallization from acetone gave colourless crystals R_F (thin-layer chromatography) 0.27, 0.49.

TABLE I
CHEMICAL SHIFTS (δ , p.p.m.) AND COUPLING CONSTANTS (c/s) OF
PROTONS OF TRICHODESMINE AND JUNCINE

Proton	Trichodesmine (in $CDCl_3$)	Junceine (in D_2SO_4)
$(CH_3)_2CH$	0.96, 1.04 (J 6.0)	0.96, 0.99 (J 6.5)
CH_3-C-OH	1.35 (or 1.38)	1.42
$CH_3-C(OH)-CO$	1.38 (or 1.35)	—
$HO-CH_2-C(OH)-CO$	—	3.77, 4.10
$CH-O-CO$ (H 7)	5.11 (ΣJ_7 , c. 11.0)	5.37
CH_2-O-CO (H 9)	c. 4.47, 5.11	c. 4.36, c. 4.71
$CH=C$	6.0	6.29

(b) *Separation of Alkaloids*

The alkaloid mixture (250 mg) was chromatographed on a column of silica gel. The alkaloid of R_F 0.27 was eluted with $MeOH/CHCl_3$ (7:3). Crystallization from methanol gave colourless prisms, R_F (paper chromatography) 0.31; R_F (thin-layer chromatography) 0.27; m.p. 188–189° undepressed on admixture with junceine (Found: C, 58.2; H, 7.5; N, 3.9. $C_{18}H_{27}NO_7$ requires C, 58.5; H, 7.4; N, 3.8%). The alkaloid had infrared and n.m.r. spectra identical with those of junceine.

Crystallization of the crude alkaloid mixture (200 mg) from methanol and concentration of the mother liquor yielded successive crops of junceine contaminated with the second major alkaloid. After removal of most of the junceine, the final mother liquor was evaporated to dryness and the residue crystallized from acetone to give colourless prisms, R_F (paper chromatography) 0.49; R_F (thin-layer chromatography) 0.49; m.p. 154–155°, undepressed on admixture with trichodesmine. Insufficient of the pure alkaloid was obtained for analysis but the molecular formula was confirmed by the mass spectrum, which was identical with that of authentic trichodesmine. The n.m.r. and i.r. spectra were also identical with those of authentic trichodesmine.

(c) *Alkaline Hydrolysis of Junceine*

Junceine (200 mg) was refluxed for 15 min with alcoholic KOH (15%, 15 ml). The solvent was evaporated and the residue extracted with ether. Crystallization of the ether extracted material from acetone gave colourless needles, R_F 0.19, m.p. 116–117°, undepressed on admixture with retronecine.

Acknowledgments

The authors are indebted to Mr J. L. Occolowitz, Defence Standards Laboratories, Melbourne, for the measurement of mass spectra.

⁸ Sharma, R. K., Khajuria, G. S., and Atal, C. K., *J. Chromat.*, 1965, **19**, 433.