ERYTHRINA ALKALOIDS

III.* OCCURRENCE OF (+)-*N*-NORPROTOSINOMENINE AND OTHER ALKALOIDS IN *ERYTHRINA LITHOSPERMA* (LEGUMINOSAE)

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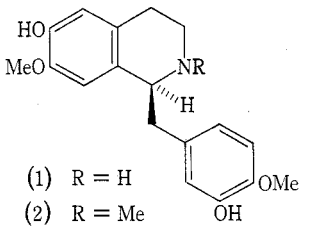
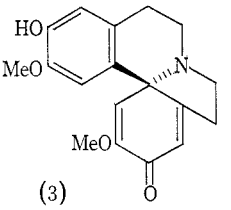
[Manuscript received June 2, 1971]

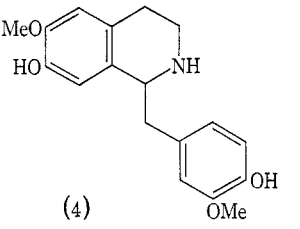
Erythrina lithosperma Blume (Leguminosae) is a tall tree, native to the Philippines and Java; it has been naturalized in India in the plains of Bengal.[1] No previous phytochemical work of this species was reported. The alkaloids identified are *N*-norprotosinomenine (1), protosinomenine (2), erysodienone (3), β-erythroidine, erysopine, erythraline, erythramine, erysodine, erysotrine, erythratine, *N*,*N*-dimethyltryptophan, and hypaphorine. Of these, alkaloids (1)–(3) were not previously reported in nature.



(1) R = H
(2) R = Me



(3)



(4)

It was shown[2,3] by tracer studies that aromatic *Erythrina* alkaloids are biosynthesized from (+)-*N*-norprotosinomenine (1) by phenol oxidation to give erysodienone (3). Subsequent transformation (*O*-methylation, reduction, dehydration, etc.) of the dienone (3) gives rise to aromatic *Erythrina* alkaloids. The isolation of the two primary building units from *E. lithosperma* is thus significant from a biogenetic point of view and also complementary to the reported co-occurrence of spiroamine and isoquinoline bases in menispermaceous plants.[4,5] Recently, Kazuo *et al.*[6] reported the occurrence of another isoquinoline alkaloid, *N*-nororientaline (4), in the leaves of *Erythrina indica* Lam. The existing data in the literature would seem to indicate that

* Part II, *J. pharm. Sci.*, 1971, **60**, in press.

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[1] Hooker, J. D., "Flora of British India." Vol. II, p. 190. (Govt. Printer: London 1879.)
[2] Barton, D. H. R., James, R., Kirby, G. W., Turner, D. W., and Widdowson, D. A., *J. chem. Soc.* (*C*), 1968, 1529.
[3] Barton, D. H. R., Boar, R. B., and Widdowson, D. A., *J. chem. Soc.* (*C*), 1970, 1208, 1213.
[4] Tomita, M., and Yamaguchi, H., *Pharm. Bull., Tokyo*, 1956, **4**, 225.
[5] Wada, K., Marumo, S., and Munakata, K., *Tetrahedron Lett.*, 1966, 5179.
[6] Kazuo, I., Hiroshi, F., and Hitoshi, T., *Chem. Commun.*, 1970, 1076.

N-nororientaline does not lie on the natural biogenetic pathway to the *Erythrina* alkaloids and is only a by-product which accumulates in the plant.

Experimental

The dried and ground pods (10 kg) of *E. lithosperma* were continuously extracted with light petroleum (60–80°) for 36 hr. The petroleum extract was kept aside for further processing for very weak bases. The defatted material was continuously extracted with EtOH for 36 hr. Evaporation of the solvent gave a thick brown slurry (356 g) which was extracted with 2N HCl (1 l.) to leave an amorphous residue (192 g) which was rejected. The clarified acidic solution was partly basified with NH_4OH to pH 5 and extracted with $CHCl_3$ (three 250-ml portions) to yield, after evaporation, the weak base fraction (22 g). The remaining aqueous solution was decanted from the residue, basified to pH 9 with NH_4OH, and extracted with $CHCl_3$ (three 250-ml portions) to give the strong base fraction (5·6 g). The aqueous mother liquor was treated with an excess of saturated solution of ammonium reineckate whereupon water-soluble strong bases separated as the complex salt. The mother liquor was cooled, acidified (4N H_2SO_4), and ammonium reineckate was again added; the reineckate salt of water-soluble weak bases separated.

Alkaloids from the Weak Base Fraction

Erysopine[7] (48 mg) separated from a concentrated solution of the weak-base fraction in $CHCl_3$ (20 ml). The $CHCl_3$ mother liquor was chromatographed on Brockman neutral alumina. Elution with petroleum (40–60°)–benzene (1:1) gave β-erythroidine[7] (27 mg). Benzene eluted erysotrine[8] (52 mg), erythraline[7] (58 mg), and erythramine[7] (14 mg), which were separated by repeated column chromatography. The first fractions of the $CHCl_3$ eluates afforded erysodienone (18 mg) while the later fractions yielded erysodine[7] (76 mg) and another unidentified *Erythrina* alkaloid, R_F 0·32 (BuOH–AcOH–H_2O 4:1:5), λ_{max} 235–238, 282–285, 305–310sh nm. $CHCl_3$–MeOH (99:1) eluted erythratine[2] (16 mg) plus two Dragendorff-positive (orange) and Ehrlich-positive (purple, changing to blue on standing) compounds in traces. The latter two compounds showed similar u.v. absorption spectra: λ_{max} 220–224, 230–235 (infl.), 284–288, 300–305sh nm. $CHCl_3$–MeOH (95:5) eluted a complex mixture of bases (three major Dragendorff- and Ehrlich-positive spots on t.l.c.).

Erysodienone (3).—This crystallized from EtOH as straw coloured needles, m.p. 222–224° (lit.[9] 223°); ν_{max} 3525, 3305, 1672, 1648, 1620 cm^{-1}; λ_{max} 238–242 (log ε 4·18) and 282–285 nm (log ε 3·50); *m/e* 313 (M^+) (62%), 298 (17%), 282 (base peak).

Reduction of erysodienone (8 mg) with $NaBH_4$ (32 mg) in MeOH (5 ml) gave the dienol, m.p. 128–130° (lit.[9] 131°); ν_{max} 3512 (OH), 1642 (C=C) cm^{-1}; *m/e* 315 (M^+), significant peaks at *m/e* 300, 284, 241.

Alkaloids from the Strong Base Fraction

N-*Norprotosinomenine* (1).—A portion (*c.* 2 g) of the strong base fraction was triturated with absolute EtOH (12 ml); a brown solid (67 mg), m.p. 245–252°, separated. T.l.c. and mass spectral determinations of this solid indicated the presence of two major phenolic bases (M^+, 315 and 329) together with a polymeric indolic compound. An EtOH solution of the solid was treated with a drop of 2N HCl; the hydrochloride of the major base, *N*-norprotosinomenine, separated as colourless needles (24 mg), $C_{18}H_{21}NO_4$,HCl, m.p. 242–244° (lit.[3] 245°). It showed $[\alpha]_D^{25}$ +18° (*c*, 0·88 in H_2O); λ_{max} 222–225 (hump) (log ε 4·13) and 284–285 nm (log ε 3·84); ν_{max} (base) 3342, 3304, 1611 cm^{-1}; δ 8·98 (broad s, 1H, NH), 8·87 (s, 1H, OH), 6·76 (broad s, 3H), 6·62 (s, 1H), 6·36 (s, 1H), 4·50 (broad m, 1H), 3·72 (s, 3H, OMe), 3·69 (s, 3H, OMe), 2·50–4·1 (complex 8H); *m/e* 315 (M^+, <1%), significant peaks at *m/e* 178 (base

[7] Boit, H.-G., "Ergebnisse der Alkaloid-Chemie bis 1960." (Akademie-Verlag: Berlin 1961.)

[8] Ghosal, S., Ghosh, D. K., and Dutta, S. K., *Phytochemistry*, 1970, **9**, 2397.

[9] Mondon, A., and Ehrhardt, M., *Tetrahedron Lett.*, 1966, 2557.

peak), 163 (32%), 137 (16%), 122 (9%), 94 (6%). The above properties of the alkaloid are indistinguishable from those reported for *N*-norprotosinomenine.[3]

Protosinomenine (2).—The EtOH mother liquor, after separation of *N*-norprotosinomenine hydrochloride, gave a brown residue upon evaporation of the solvent. The residue was dissolved in water (10 ml), the solution was basified, and the liberated bases extracted with $CHCl_3$. Column chromatography of the $CHCl_3$ concentrate gave a pale brown gum (17 mg) from the first C_6H_6–$CHCl_3$ (1:1) eluates; R_F 0·52; λ_{max} 220–222 (infl.) (log ϵ 4·22) and 282–286 nm (log ϵ 3·78); *m/e* 329 (M^+, <2%), significant peaks at *m/e* 192 (base peak), 177 (22%), 137 (25%).

The picrolonate crystallized from EtOH as yellow needles, m.p. 172–174° (lit.[10] 177–178° with sintering from 170°) (Found: C, 58·2; H, 5·2; N, 11·3. Calc. for $C_{29}H_{30}N_5O_9$: C, 58·7; H, 5·0; N, 11·8%).

Conversion of protosinomenine into laudanosine.—A portion (5 mg) of the above basic gum was dissolved in MeOH (1 ml) and excess of ethereal diazomethane was added. After 24 hr (t.l.c. control) the solution was evaporated to give laudanosine, crystallized from light petroleum as needles, m.p. and mixed m.p. 83–85°.

Water-Soluble Bases

From the reineckate salt, separated under basic condition, choline was obtained in the usual way[11] and was identified as the picrate. The reineckate salt separated under acidic conpitions was also processed in the same way. Hypaphorine (19 mg) and *N*,*N*-dimethyltryptophan (37 mg) were obtained as the only two identifiable alkaloids.

[10] Robinson, R., and Sugasawa, S., *J. chem. Soc.*, 1933, 280.

[11] Ghosal, S., Banerjee, P. K., and Banerjee, S. K., *Phytochemistry*, 1970, **9**, 429.