Reflexine, a New Indole Alkaloid of *Rauwolfia reflexa*

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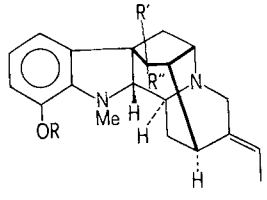
Summary. Reflexine, a new indole alkaloid, has been isolated from the leaves of *Rauwolfia reflexa* Teijsm. and Binn. From spectral studies, chemical reactions and correlation with seredamine, reflexine is shown to be its C-17 epimer (IV).

In the course of our studies on the alkaloids of apocynaceous plants for the search of new biologically active indolic bases, we examined the leaves of *Rauwolfia reflexa* Teijsm. and Binn. Several indolic bases could be isolated. The present communication deals with the characterization of two of them, one of which, designated reflexine, has been proved to be a new indole alkaloid.

The spectral data of one of the basic constituents, $C_{21}H_{24}N_2O_2$ (M^+ 336), m.p. 154–55° (petrol ether-ethyl acetate) suggested its identity with purpeline (I), isolated earlier from *Rauwolfia vomitoria*[2]. But the ^{1}H-NMR-spectrum of this alkaloid recorded in the aromatic region signals at δ 7.08 (1H, d, J_o 8.5 Hz) and 6.30 (2H, dd, J_o 8.5 Hz, J_m 2 Hz) instead of the signal at 6.81 (3H, s) reported for purpeline. Also the signal due to the indoline *N*-methyl at 3.05 in purpeline was observed at 2.79 in our alkaloid. Nevertheless, a direct comparison could not be made because of the non-availability of an authentic sample of purpeline. The identity of our alkaloid with purpeline was subsequently confirmed by its demethylation (with anhydrous $AlCl_3/C_6H_6$, reflux) to mitoridine (II)[2] (superimposable IR-spectra). The isolation of purpeline from *R. reflexa* eventually constitutes its first isolation from this species and also its second occurrence in nature.



(I) R = Me; R′, R″ = 0
(II) R = H; R′, R″ = 0
(III) R = Me; R′ = β-OH; R″ = α-H
(IV) R = Me; R′ = α-OH; R″ = β-H

The second base, designated reflexine, $C_{21}H_{26}N_2O_2$ (M^+ 338) obtained from benzene-chloroform (1:2) eluate crystallized from acetone as stout needles, m.p. 260° (dec.); $[\alpha]_D$ + 126° ($CHCl_3$); Rf 0.2 (silica gel G; MeOH); λ_{max}^{EtOH} 250 and 295 nm (log ε 3.78 and 3.66 respectively), typical of indoline chromophore; ν_{max}^{KBr} 3400 cm^{-1} (–OH). The 100 MHz NMR-spectrum of reflexine (in $CDCl_3$) unfolded the presence of an ethylidene functionality (δ 1.63, 3H, d, J 7 Hz; 5.23, 1H, q, J 7 Hz), an indoline *N*-methyl (2.78, 3H, s), an aromatic methoxyl (3.77, 3H, s) and 3 adjacent aromatic protons (6.30, 2H, dd, J_o 8.5 Hz, J_m 2 Hz; 7.08, 1H, d, J_o 8.5 Hz). The mass spectrum of reflexine recorded the molecular ion-peak at *m/e* 338 (100%) and a somewhat less intense peak at *m/e* 337 (M^+-1; 77%), suggestive[3] of the presence of a tetrahydro-β-carboline moiety. These observations, as well as a group of ion-peaks at *m/e* 293 (43%), 226 (31%), 213 (73%) and 212 (70%), clearly demonstrated that reflexine has the gross structure of dihydropurpeline, bearing a hydroxyl at C-17.

As regards the stereochemistry at the 5 chiral centres in the molecule, mass spectral evidence (presence of peaks at *m/e* 212 and 213, and absence of peak at *m/e* 166) settled[4] the β-orientation of the hydrogen at C-2. A careful examination of the Dreiding model of the molecule in conjunction with biogenetic considerations revealed the same configurations at C-3, C-5, C-7 and C-15 as in purpeline. If the hydroxyl at C-17, whose configuration remains to be determined, is β-, it becomes a known indole alkaloid seredamine (III)[2]. But a marked difference in the physical constants of reflexine and seredamine (Lit[2]. m.p. 297°, $[\alpha]_D$ + 60° ($CHCl_3$)] suggested the non-identity of the two alkaloids. The hydroxyl at C-17 thus stands as α-oriented. To adduce chemical evidence to this logical conclusion, purpeline was reduced with sodium borohydride in methanol in cold when a single product (evidenced by TLC) was obtained. This reduction product, $C_{21}H_{26}N_2O_2$ (M^+ 338), m.p. 263–65° (dec.), $[\alpha]_D$ + 130° ($CHCl_3$) was found to be identical with reflexine in all respects (m.p., m.m.p., co-TLC and superimposable IR-spectra). Since borohydride reduction of purpeline is reported[2] to produce an α-hydroxyl at C-17, this experimentation confirms the assigned stereostructure (IV) of reflexine. The molecular rotation of purpeline, which is considerably higher (M_D + 223°) than that of seredamine, provides further evidence[5] in support of the derived structure.

The present communication constitutes the first report of the occurrence of reflexine, i.e., 17-epi-seredamine from natural sources. It also marks the occurrence of the third epimeric pair of ajmaline-type bases, the previous two pairs being ajmaline-sandwicine (M_D + 122°) and tetraphyllicine-mauiensine (M_D + 501°)[6].

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