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SPECTALININE AND ISO-6-CARNAVALINE, TWO UNPRECEDENTED PIPERIDINE ALKALOIDS FROM THE SEEDS OF *CASSIA SPECTABILIS*

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Abstract—Along with the alkaloïds (+)spectaline (**1**) and (−)iso-6-cassine (**2**), two new piperidinol alkaloïds have been isolated from the seeds of *Cassia spectabilis* DC. They have been shown to possess structures **3** and **4** through chemical and spectral studies.

In a previous paper,[1] we reported the isolation of two new piperidinol alkaloïds: Spectaline (**1**) and iso-6-cassine (**2**) from the leaves of *Cassia spectabilis* DC. We have also examined the basic products obtained from the seeds of the same plant and have isolated spectaline and iso-6-cassine together with two unprecedented piperidine alkaloïds which we have named: (−)spectalinine (**3**) and (−)iso-6-carnavaline (**4**). The four alkaloïds were separated by preparative layer chromatography. Cassine was also identified by TLC but could not be isolated.

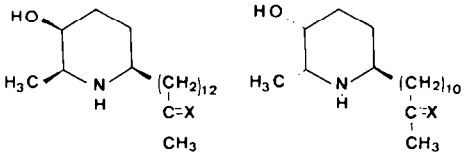
The IR spectra of both new alkaloïds hydrochlorides showed no CO absorption but an intense and extremely broad band at 3360 cm^{-1} and a $-NH_2^+$ absorption at 1570 cm^{-1}. On acetylation, these two bands disappeared with appearance of two intense CO bands at 1740 and 1645 cm^{-1} and an "ester" band at 1245 cm^{-1}.

The mass spectra of spectalinine and iso-6-carnavaline gave a molecular ion less abundant than the M + 1 peak which could be attributed to the fixation of a hydrogen on the N atom to give a stable ammonium ion[2] at *m/e* 328 ($C_{20}H_{42}NO_2$) and *m/e* 300 ($C_{18}H_{38}NO_2$). The peaks at M-15 and M-45 established the presence of a –CHOH–Me group confirmed by the mass spectra of the acetyl derivatives. The fragmentation patterns compared with those of the mass spectra of spectaline, iso-6-cassine[1] and also carnavaline[3] (dihydrocassine) showed that the new alkaloïds are respectively similar to **1** and **2** except for a secondary OH group taking the place of the ketone group.

This was confirmed by PMR spectra which were similar to those of spectaline and iso-6-cassine, except of course for the hydrogen signals of the –CHOH–Me group. The Me group appeared as a doublet at about 1.2 ppm and the –H of the hydroxylic carbon was a broad multiplet centered at $\delta \simeq 3.8$ ppm. The carbinolic –H in the piperidine nucleus was at about 3.6 ppm. On acetylation, the carbinolic hydrogens were shifted to $\delta = 4.30$ and 4.90 ppm respectively, and three peaks appeared at about 2 ppm corresponding to the methyl H of the three acetyl groups.

Information about the stereostructure can be deduced from the signal of the carbinol–H in the piperidine nucleus.[4,5] In spectalinine, this equatorial–H appeared as a broad singlet ($\omega_{1/2} = 6$ Hz) as in spectaline.[1] In iso-6-carnavaline, this carbinol-H was a broad multiplet as in iso-6-cassine[1] (and contrary to carnavaline[3]). The height of the carbinolic hydrogen signal was thus in favour of respectively identical stereochemistry. This was further confirmed by borohydride reduction of spectaline and iso-6-cassine that gave oily compounds and crystalline hydrochlorides which were shown to be identical respectively to spectalinine and iso-6-carnavaline by IR, PMR and TLC in different solvents systems and by a similar identification of their acetates.

The four alkaloïds being in the same plant, we can reasonably think that the absolute configuration of the piperidine nucleus is respectively identical and we can assign structure **3**: 2(*S*)-méthyl 6(*R*)-(13′-hydroxytetradecyl) piperidin 3(*S*)-ol to spectalinine and structure **4**: 2(*R*)-méthyl 6(*R*)-(11′-hydroxydodecyl) piperidin 3(*R*)-ol to iso-6-carnavaline. The absolute configuration of the secondary side chain alcohol has not been determined.



1. x : O
2. x : O
3. x : HOH
4. x : HOH

EXPERIMENTAL

Spectral data. IR spectra were measured in KBr pellets or CCl_4, 100 MHz NMR spectra in $CDCl_3$ (TMS as internal reference). Only significant bands are quoted. MS were determined using direct insertion probe and ionizing voltage of 70 eV.

Chromatography. TLC separations were carried on Merck Silicagel F_{254} plates (0.5 mm) using $CHCl_3$; EtOH; NH_4OH 25%: 9/1/0.5 mixture as developer. Each plate was loaded with 0.05 g of alkaloïdes mixture in 1 ml $CHCl_3$. After developing, the different alkaloïds were desorbed on columns with EtOH; CH_2Cl_2: 1/1 mixture as eluent.

Isolation. Seeds of *C. spectabilis* DC (2.5 kg) were extracted with 24 l. of 1% ethanolic tartaric acid at 50–60°, then treated in the usual way[1] to leave a dark brown oil (4.1 g). This was digested repeatedly with boiling hexane, leaving a insoluble residue of 1.2 g. The hexane soln was concentrated to dryness to leave 2.8 g (0.11%) of a clear yellow oil. This material was dissolved in 20 ml of EtOH and made acid with conc. HCl, diluted with 20 ml of EtOAc, and scratched and chilled until a crystalline ppt formed. The free bases (1.95 g; 0.078%), obtained by dissolving the hydrochlorides in EtOH, diluting with $CHCl_3$, adding NH_4OH and washing the organic phase with water, revealed on TLC the presence of four major alkaloïds and a few minor alkaloïds, one of them identified to cassine by TLC in several solvents systems. Preparative layer chromatography

yielded four pure alkaloïds after repeated crystallisations of their hydrochlorides in EtOAc–EtOH: 0.48 g (0.019%) of 1 (R_f = 0.65); 0.52 g (0.020%) of 2(R_f = 0.40); 0.075 g (0.003%) of 3(R_f = 0.51); 0.060 g (0.0024%) of 4(R_f = 0.23). Cassine (R_f = 0.60), being in too small quantity, could not be separated. The alkaloïds **1** and **2** were shown to be identical with spectaline (**1**) and iso-6-cassine (**2**) isolated from the leaves of *C. spectabilis*,[1] by m.ps, IR, NMR, MS, optical activity and TLC behaviour in several solvents systems and by a similar comparison of their acetates.

Spectalinine (**3**); colorless oil—hydrochloride: m.p. 120°. (Found: C, 65.88; H, 11.80; N, 4.01. $C_{20}H_{41}NO_2$·HCl requires: C, 66.02; H, 11.55; N, 3.85%). IR(KBr): 3360(S, Bd), 2920(S), 2860(M), 1570(M), 1467(M), 1370(M), 720(W) cm^{-1}. Free base: $\alpha_D^{25} = -8.4°$; $\alpha_{250}^{25} = -9.8°$ (c, 0.12 $CHCl_3$) MS: *m/e* = 328 (M^+ + 1, 1.8), 327 (M^+, 0.5), 312 (M^+ − Me, 3.0), 294 (M^+ − Me−H_2O, m^x = 277, 0.6), 282 (M^+ − −CHOH−Me, 1.0), 268(0.6), 254(0.55), 240(0.8), 226(0.6), 212(0.5), 198(0.5), 184(0.6), 170(0.4), 156(1.0), 142(0.7), 128(0.8), 114(100), 96(114 −H_2O, m^x = 80, 84, 18%). PMR ($CDCl_3$): δ = 1.12(d, 3H, J = 6.5 Hz), 1.22(d, 3H, J = 6.5 Hz), 1.28(s, 22H), 2.40(m, 2H), 3.54(s, 1H, bd, $\omega_{1/2}$ = 6 Hz), 3.77(m, 1H) ppm.

Triacétyl spectalinine; IR(CCl_4): 2920(S), 2860(M), 1740(S), 1645(S), 1370(M), 1245(S) cm^{-1}, MS: *m/e* = 453(M^+, 0.5), 438(M^+ − Me, 0.9), 396(1.3), 393(1.5), 292(0.5), 198(100), 156(46), 138(21), 96(20), 43(49%). PMR($CDCl_3$): δ = 2.10(s, 3H), 2.05(s, 3H), 2.01(s, 3H), 4.30(m, 1H), 4.90(m, 2H) ppm.

Iso-6-carnavaline (**4**); colorless oil-hydrochloride: m.p. 123°. Found: C, 64.15; H, 11.50; N, 4.25%. $C_{18}H_{37}NO_2$·HCl requires: C, 64.38; H, 11.33; N, 4.17%. IR(KBr): 3360(S, Bd), 2920(S), 2860(M), 1580(M), 1470(M), 1370(M) cm^{-1}. Free base: α_D^{25} = −5.66° (*c*, 0.03 $CHCl_3$). MS: *m/e* = 300(M^+ + 1, 3.0), 289(M^+, 0.4), 284(M^+-Me, 2.5), 266(M^+-Me-H_2O, m^x = 249.1, 0.8), 254 (M^+-−CHOH−Me, 0.6), 226(0.4), 212(0.5), 138(0.4), 184(0.5), 170(0.6), 156(0.7), 142(0.6), 128(0.5), 114(100), 96(9.0%). PMR ($CDCl_3$): δ = 1.08(d, 3H, J = 6.5 Hz), 1.17(d, 3H, J = 6.5 Hz), 1.28(s, 18H), 2.40(m, 2H), 3.65(m, 1H, bd), 3.80(m, 1H, bd) ppm.

Triacetyl iso-6-carnavaline; IR(CCl_4): 2920(S), 2860(M), 1740(S), 1645(S), 1370(M), 1245(S) cm^{-1}. MS: *m/e* = 425(M^+, 0.5), 410(1.0), 368(1.4), 365(1.7), 264(1.0), 198(100), 156(39), 138(21), 96(20), 43(41%). PMR($CDCl_3$): δ = 2.08 (s, 3H), 2.05(s, 3H), 2.02(s, 3H), 4.30(m, 1H), 4.90(m, 2H) ppm.

Dihydro alkaloïds. A soln of 30 mg alkaloïds in 3 ml of MeOH was treated with 100 mg of $NaBH_4$ then left for 1/2 hr. The soln was made acid with dil. HCl and washed twice with ethyl ether. The acid soln was treated with 10% NaOH and extracted twice with $CHCl_3$ and twice with $CHCl_3$, EtOH 4/1. The organic extracts were concentrated to leave oily reduced alkaloïds.

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