23

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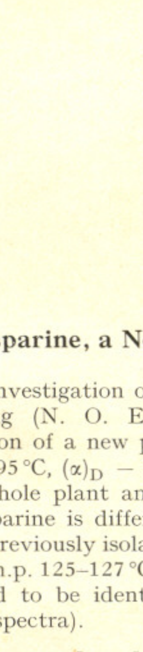
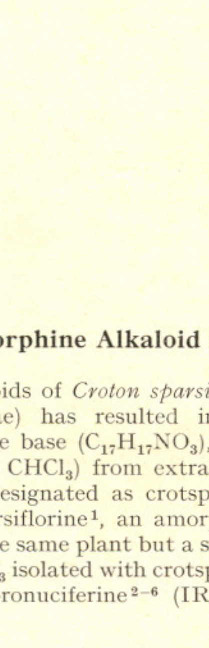
Crotsparine, a New Proaporphine Alkaloid from *Croton sparsiflorus* Morong

Reinvestigation of the alkaloids of *Croton sparsiflorus* Morong (N. O. Euphorbiaceae) has resulted in the isolation of a new proaporphine base ($C_{17}H_{17}NO_3$), m.p. 193–195 °C, $(\alpha)_D$ − 30° (c, 1.22 $CHCl_3$) from extracts of the whole plant and is now designated as crotsparine. Crotsparine is different to sparsiflorine[1], an amorphous base previously isolated from the same plant but a second base m.p. 125–127 °C, $C_{19}H_{21}NO_3$ isolated with crotsparine proved to be identical with pronuciferine[2–6] (IR- and mass-spectra).



(I)



(II)

Crotsparine has been assigned the structure (I, R = R_1 = H). It is susceptible to aerial oxidation and forms a crystalline hydrochloride m.p. 278 °C (decomp.). The presence of a secondary >NH group and a bound -OH group in the crotsparine molecule is suggested by bands at 3490 and 2896 cm^{-1} respectively in its IR-spectrum and is confirmed by the formation of a *N,O*-diacetyl derivative, m.p. 185–186 °C. The IR-spectrum of this derivative also has absorption bands at 1772, 1260 (phenolic OAc), 1642 (amide) and at 1670 cm^{-1} (dienone C=O). Further, IR-bands in the spectrum of crotsparine at 1664 and 1624 cm^{-1} in conjunction with an UV-absorption maxima at 235 nm (log ε, 3.37) are indicative of a cross-conjugated dienone system[7]. The mass-spectrum of crotsparine shows a molecular ion peak (M^+) at m/e 283 and other prominent peaks are m/e 282, 254, 211, 165, 118 and 87. The NMR-spectrum of crotsparine is in agreement with the proposed formula (I, R = R_1 = H). Singlets at 3.40 (1 H), at 6.21 (3 H) τ and multiplets centred around 2.9 (2 H) and 3.6 (2 H) τ are due to an aromatic proton, an OMe group and 4 olefinic protons respectively.

N-methylation of crotsparine with formic acid-formaldehyde affords *N*-methyl crotsparine (I, R_1 = Me, R = H) ($C_{18}H_{19}NO_3$), m.p. 223–225 °C, $(\alpha)_D$ − 113° (c, 1.52 $CHCl_3$). The mass spectrum of this compound shows a molecular ion peak at m/e 297 and other significant peaks at m/e 296, 268, 254, 225, 165, 115 and 97. This fragmentation pattern is the same as has been observed for glaziovine[4]. The IR-spectrum of the *N*-methyl derivative still has a band at 2860 cm^{-1} (bonded OH) but the >NH band at 3490 cm^{-1}, which is present in the spectrum of crotsparine is absent. The dienone system is unaffected during methylation as the compound shows IR-absorption at 1672 cm^{-1}, an UV-maximum at 235 nm and the loss of 28 mass units in the mass spectrum.

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The NMR-spectrum of *N*-methylcrotsparine exhibited sharp singlets at 7.64 (3H), 6.17 (3H), 3.35 (1H) τ on account of a *N*-Me, OMe and one aromatic proton respectively. The 4 vinylic protons are responsible for the signals at 3.40–3.75 τ and 3.30–2.70 τ.

When treated with 3*N* hydrochloric acid, crotsparine is rearranged to apocrotsparine (II, $R_1 = R = H$) ($C_{17}H_{17}NO_3$). Apocrotsparine hydrochloride does not melt below 300 °C and maxima at 266, 276 and 305 nm (log ε, 1.02, 1.3, 0.9) in the UV-spectrum of apocrotsparine are characteristic of an aporphine oxygenated at position 3, 5 and 6[5,8]. Similarly, *N*-methyl crotsparine furnishes apo-*N*-methyl crotsparine (II, R_1 = Me, R = H) ($C_{18}H_{19}NO_3$), $(\alpha)_D$ + 30 °C (c, 0.2 $CHCl_3$) under acidic conditions. This compound is also obtained from apocrotsparine on treatment with formaldehyde-formic acid. The hydrochloride of this aporphine melts at 284–286 °C (decomp.). The UV-spectrum of the product is identical with that of 3, 5-dihydroxy-6-methoxy aporphine[4,8] (II, R_1 = Me, R = H).

Direct comparison of the samples on thin layer chromatography established the identity of *N*-methylcrotsparine with that of glaziovine[4]. *N*-methyl crotsparine is, therefore, an enantiomer of glaziovine.

The proaporphine bases, crotonosine[5], glaziovine[4], pronuciferine[2], and stepharine[6] have positive rotation and D-configuration. The isomerized aporphines of these bases having the same configuration are laevorotatory. *N*-methylcrotsparine is laevorotatory and the isomerized aporphine is dextrorotatory. Crotsparine should, therefore, have the L-configuration.

It is of interest that *C. sparsiflorus* Morong collected around Calcutta (Eastern India), yielded crotsparine with negative rotation whereas the same plant collected in Lucknow (North-Central, India) gave crotsparine with positive rotation[9].

Zusammenfassung. Ein neues Proaporphin Alkaloid, Crotsparine genannt, wurde von *Croton sparsiflorus* Morong isoliert. Es wurde ihm die Formel (I, $R = R_1 = H$) angewiesen.

D. S. Bhakuni and M. M. Dhar

Central Drug Research Institute, Lucknow (India),
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[9] We thank Dr. K. L. Stuart for samples of Crotonosine and Base A, Dr. G. Gilbert for a sample of glaziovine and Dr. R. S. Kapil for mass- and NMR-spectral determinations.