Crotsparinine, a Dihydroproaporphine Alkaloid from *Croton sparsiflorus*[1]

We recently reported the isolation of 2 proaporphine alkaloids, crotsparine and N, O-dimethyl crotsparine, from *Croton sparsiflorus* Morong[2]. Further search for new bases from this source has now yielded a new dihydroproaporphine alkaloid ($C_{17}H_{19}NO_3$), m.p. 184–185 °C, $(\alpha)_D + 215°$ (*c*, 2.37, $CHCl_3$); provisionally designated as crotsparinine.

Crotsparinine has been assigned the structure (I, R = Me; R′ = R″ = H). The presence of a secondary NH group, an –OH group and an enone system in the molecule was suggested by bands at 3485, 2890, 1665, 1604 and 1600 cm^{-1} in its IR-spectrum and by maxima at 228 nm (log ε, 4.28), and 285 nm (log ε, 3.10) in its UV-spectrum. The NMR-spectrum of crotsparinine revealed the presence of a methoxy group (τ 6.21) and confirmed the presence of the α,β-unsaturated ketone system which gives rise to an AB quartet at τ 3.88 and 3.06 (J_{AB},10 cps). The lone aromatic proton is responsible for a singlet at τ 3.5.

In the mass spectrum of the base, the molecular ion peak (M^+) is seen at m/e 285 and a M^{++} at m/e 142.5. Other significant peaks are at m/e 284, 256 and 223.

N-Methylation of crotsparinine with formaldehyde-formic acid yields N-methyl crotsparinine (I, R = R″ = Me, R′ = H) ($C_{18}H_{21}NO_3$), m.p. 160–161°, $(\alpha)_D + 244$ (*c*, 0.92, $CHCl_3$). This compound is isomeric with linearisine[3] (I, R′ = R″ = Me; R = H) and its mass spectrum (M^+, m/e 299; M^{++}, m/e 149.5 and similar fragmentation as observed with crotsparinine) and NMR-spectrum are in agreement with the structure (I, R = R″ = Me, R′ = H).

Crotsparinine, when treated with excess of methyl iodide in the presence of K_2CO_3 in acetone, gave N, O-dimethyl-crotsparinine methiodide, m.p. 239–241° identical with O-methyl linearine methiodide[4] and hydrogenation of N-methyl crotsparinine in the presence of Pd/C afforded N-methyldihydro crotsparinine ($C_{18}H_{23}NO_3$), m.p. 112–114°, identical with N-methyltetrahydro crotsparine (II). This compound has been obtained by reduction under similar conditions of N-methylcrotsparine[5]. Crotsparinine, therefore, has the structure I (R = Me, R′ = R″ = H)[6].

Zusammenfassung. Crotsparinin, ein neuer Vertreter der Proaporphine, wurde aus *Croton sparsiflorus* isoliert und seine Struktur aufgeklärt.

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Central Drug Research Institute,
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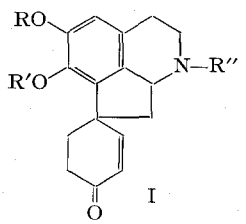

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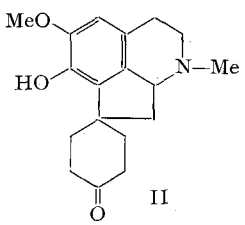

II

[1] Communication No. 1323 from the Central Drug Research Institute.
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[6] We thank Dr. K. L. Stuart for a sample of linearisine and Dr. R. S. Kapil for mass spectra.

The Synthesis of Isohalfordin

In 1956, isohalfordin ($C_{14}H_{12}O_6$) was isolated, together with halfordin, from the bark of *Halfordia scleroxyla* F. Muell by Hegarty and Lahey[1]. The structure of isohalfordin was proposed as 3,5,6-trimethoxyfuro[2′,3′:7,8]coumarin (I) or 3,7,8-trimethoxyfuro[2′,3′:5,6]coumarin (II). Recently, on the basis of the NMR spectral analysis and degradative experiments, however, the revised structure was assigned as 3,4,8-trimethoxyfuro-[3′,2′:6,7]coumarin (III)[2]. In continuation of the syntheses of furocoumarin derivatives[3], the present paper will describe the total synthesis of III from 6,7-dihydroxy-2,3-dihydrobenzo[*b*]furan (IV)[4], confirming the revised structure of the natural compound.

Hoesch condensation of the benzofuran IV with methoxyacetonitril yielded 5-(ω-methoxyacetyl)-6,7-dihydroxy-2,3-dihydrobenzo[*b*]furan (V, m.p. 135–135.5°). The partial methylation of V with diazomethane gave 7-methoxy-derivative (V, m.p. 88–90°, IR 1625 cm^{-1} (Nujol). Found: C, 60.56; H, 5.98. $C_{12}H_{14}O_5$ requires: C, 60.50; H, 5.92%). By the procedure of Robertson's 4-hydroxycoumarin synthesis[5], the condensation of VI with ethyl carbonate in the presence of sodium gave 4′,5′-dihydrofuro[3′,2′:6,7]-3,8-dimethoxy-4-hydroxy-coumarin (VII, m.p. 175–176.5°, UV λ_{max}^{EtOH} nm (log ε): 244_{sh} (3.95), 295_{sh} (3.98), 319 (4.23), IR 3100_{sh}, 1700_{sh}, 1685, 1623, 1583 cm^{-1} (Nujol). Found: C, 58.82; H, 4.62. $C_{13}H_{12}O_6$ requires: C, 59.09; H, 4.58%) (Acetate of VII, m.p. 162.5–164°, IR 1775, 1712 cm^{-1} (Nujol)). Dihydroisohalfordin (VIII, m.p. 161.5–163°, UV λ_{max}^{EtOH} nm (log ε): 320 (4.21), IR 1690, 1623, 1587 cm^{-1} (Nujol). Found: C, 60.48; H, 5.14. $C_{14}H_{14}O_6$ requires: C, 60.43; H, 5.09%) was obtained by the methylation of VII. The dehydrogenation of VIII was carried out with 10% Pd-C in diphenyl ether giving a desired coumarin (III, m.p.

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