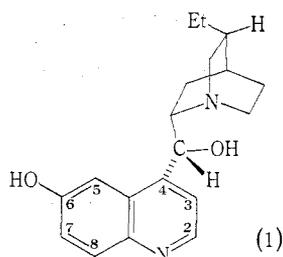


# THE IDENTIFICATION OF A NEW ALKALOID FROM *TIMONIUS KANIENSIS* (RUBIACEAE) AS DIHYDROCUPREINE

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The major alkaloid isolated from the bark of *Timonius kaniensis* Val. (family Rubiaceae) has been shown to be dihydrocupreine (1).<sup>1</sup> Dihydrocupreine has not previously been isolated as an alkaloid, but its preparation from quinine by successive hydrogenation to give dihydroquinine and demethylation by heating with hydrobromic acid has been described.<sup>1</sup> Dihydrocupreine prepared from quinine by this procedure has been shown to be identical with the *Timonius* alkaloid, and the sign and magnitude of the optical rotation of the alkaloid confirm that it

has the same absolute configuration as dihydrocupreine.

Dihydrocupreine is obtained as a glassy non-crystalline solid but it is readily converted into a crystalline hydrochloride or picrate. Dihydrocupreine from *T. kaniensis* shows  $[\alpha]_D -143^\circ$  in ethanol, and the mass spectrum ( $M^+ 312$ ) has the fragmentation expected on the basis of its similarity to cinchonine and quinine.<sup>2</sup> Details of the n.m.r. spectrum of the *O,O*-diacetyl derivative of dihydrocupreine are recorded in the Experimental section.

*T. kaniensis* occurs as a large rain-forest tree in New Guinea. The bark gives a positive field test for alkaloids, and laboratory extraction has afforded a 0.05% yield of crude bark alkaloids which consist mainly of dihydrocupreine. The identification of this alkaloid from a *Timonius* species represents an extension of the genera known to contain *Cinchona*-type alkaloids.

## Experimental

Bark of *T. kaniensis* was collected from a tree (60 ft high and 10 in. in diameter) growing in rain forest in the Oomsis Creek area along the Lae-Bulolo Road (long.  $146^\circ 47' E.$ , lat.  $6^\circ 43' S.$ ). Herbarium voucher specimens are preserved at Lae, New Guinea, and at the Arnold Arboretum, Harvard (voucher number TGH 10008).

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<sup>1</sup> Heidelberger, M., and Jacobs, W. A., *J. Am. chem. Soc.*, 1919, **41**, 817.

<sup>2</sup> Budzikiewicz, H., Djerassi, C., and Williams, D. H., "Structure Elucidation of Natural Products by Mass Spectrometry." p. 220. (Holden-Day: San Francisco 1964.)

Extraction of the milled, dried bark (12 kg) by the procedure recorded previously<sup>3</sup> afforded the crude alkaloids (6.1 g). The alkaloids were chromatographed on neutral alumina but as no crystalline fractions were obtained, all the fractions eluted by chloroform and mixtures of chloroform and methanol were combined and dissolved in ethanol. On addition of a solution of picric acid in ethanol, a crystalline picrate separated immediately. This picrate was sparingly soluble in ethanol, from which it was purified by recrystallization. Ammonia was added to a suspension of the picrate in water and, after warming gently on a steam-bath, the free base was extracted with chloroform. Evaporation of the dried chloroform extracts left a colourless glassy residue which was readily obtained as a colourless foam when the solvent was removed under vacuum. This substance had  $[\alpha]_D -143^\circ$  (*c*, 0.7 in ethanol) (lit.<sup>1</sup>  $[\alpha]_D -148^\circ$  for dihydrocupreine in ethanol), and the i.r. spectrum ( $\text{CHCl}_3$  solution) was identical with that of dihydrocupreine. The mass spectrum showed a molecular ion peak at *m/e* 312 (9%) with major fragmentation peaks at *m/e* 138 (100%) and 174 (40%). The hydrochloride, indefinite m.p., *c.* 220° with decomposition at higher temperature, which was sparingly soluble in aqueous hydrochloric acid, and the picrate, m.p. 250–252°, were identical with those prepared from dihydrocupreine (mixed m.p. determinations, i.r. spectra as KBr disks). The 100-MHz n.m.r. spectrum and i.r. spectrum of the *O,O*-diacetyl derivatives (non-crystalline) from the *Timonius* alkaloid and dihydrocupreine were identical. The n.m.r. spectrum ( $\text{CDCl}_3$  solution) of *O,O*-diacetyldihydrocupreine had signals at  $\delta$  2.09 (3H, s, OAc), 2.35 (3H, s, OAc), 0.84 (3H, t, *J* 6.5 Hz,  $\text{CH}_2\text{CH}_3$ ), 6.38 (1H, d, *J* 7.8 Hz, CHOAc), 8.84 (1H, d, *J* 4.5 Hz, C2-H), 7.39 (1H, d, *J* 4.5 Hz, C3-H), 7.93 (1H, d, *J* 2.5 Hz, C5-H), 7.44 (1H, q, *J* 2.5, 9.2 Hz, C7-H), 8.11 (1H, d, *J* 9.2 Hz, C8-H).

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<sup>3</sup> Johns, S. R., Lamberton, J. A., and Sioumis, A. A., *Aust. J. Chem.*, 1966, **19**, 2331.