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TROPINE 1,2-DITHIOLANE-3-CARBOXYLATE, A NEW ALKALOID FROM BRUGUIERA SEXANGULA.

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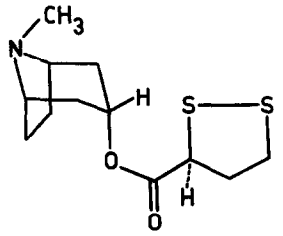
Bruguiera sexangula (Lour.) Poir. (Rhizophoraceae) is a tropical mangrove. Stem bark collected at Lae, New Guinea, was found to contain 0.08% of alkaloids although no alkaloids were detected in the leaves. The bark alkaloids were shown by gas and paper chromatography to be a complex mixture but the major base, which we have called brugine, could be isolated by counter-current distribution between chloroform and a phosphate buffer (pH 6.5). Brugine, $[\alpha]_D^{24}$ -24° (c, 4 in chloroform), was a pale yellow glass which darkened and polymerised on standing and decomposed on attempted vacuum distillation; hydrogen sulphide was evolved on pyrohydrolysis with manganese sulphate. Brugine had an empirical formula $C_{12}H_{19}NO_2S_2$ by elemental analysis and gave a mass spectrum with a molecular ion (43% of the base peak at m/e 124) at 273 with isotopic ion peaks at M + 1 and M + 2 in accord with this formula.

Brugine, with carbonyl absorption at ν_{max} 1720 cm^{-1}, was an ester which was hydrolysed with cold ethanolic sodium hydroxide to the amino-alcohol, tropine, and 1,2-dithiolane-3-carboxylic acid. Tropine, after distillation at 80°/0.5 mm, melted at 63.5° and gave NMR, IR and mass spectra identical with those of an authentic sample while the mixed

m.p. was undepressed. Although accompanied by polymeric material, the acid from the hydrolysis was obtained crystalline, m.p. 80°, after chromatography on silicic acid and it was identical with racemic synthetic 1,2-dithiolane-3-carboxylic acid[1] on comparison of NMR, UV and IR spectra; the mixed m.p. was undepressed. Further support for brugine being tropine 1,2-dithiolane-3-carboxylate (I) came from its ultraviolet absorption, λ_{max}^{EtOH} 277, 320 (Sh) mμ (ε 350, 130), which is similar to that of the synthetic thio-acid, λ_{max}^{EtOH} 277, 325 mμ (ε 300, 162).



(I)

Desulphurisation of brugine with Raney nickel in ethanol gave an oil which was characterised by its NMR, IR and mass spectra and picrate which were the same as those of synthetic tropine n-butyrate.

In the NMR spectrum of brugine the signals from the protons of the tropine moiety were sufficiently distinguishable from those of the esterifying acid for structural inferences to be made. The five protons of the acyl group appeared as three multiplets whose chemical shifts and splitting patterns closely resembled the corresponding signals of 1,2-dithiolane-3-carboxylic acid and differed significantly from the signals of 2,4-dimercaptobutyric acid; none of the protons of the alkaloid were exchanged with deuterium oxide. A one-proton quartet centred at δ 4.15 was assigned to the proton on the carbon atom bearing the ester carbonyl group and the coupling (J 7.5, 4.3 c/s) was consistent with an adjacent

methylene with non-equivalent hydrogen atoms. This methylene appeared as a two-proton multiplet at δ 2.50 and the remaining two-proton multiplet was centred at δ 3.25.

The UV and NMR spectra are conclusive evidence of the intact 1,2-dithiolane ring in brugine (I) and the instability of the alkaloid is in accord with the known properties of the esterifying acid. Other related 1,2-dithiolanes occurring naturally are lipoic acid which is widely distributed, nereistoxin, 4-dimethylamino-1,2-dithiolane, which is a neurotoxin from a marine annelid, Lumbriconereis heteropoda[2], and a compound found in asparagus which is probably 1,2-dithiolane-4-carboxylic acid[3].

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