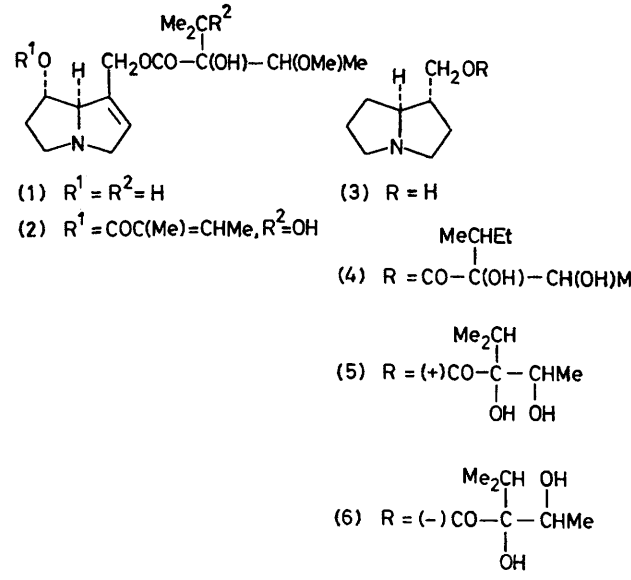
Curassavine, an Alkaloid from *Heliotropium curassavicum* Linn. with a C_8 Necic Acid Skeleton

By SUBRAMANIAM MOHANRAJ and POLUR S. SUBRAMANIAN*
(*Department of Chemistry, Presidency College, Madras* 600005, *India*)
and CLAUDE C. J. CULVENOR, JOHN A. EDGAR, JOHN L. FRAHN, LESLIE W. SMITH, and PETER A. COCKRUM
(*C.S.I.R.O. Division of Animal Health, Private Bag* 1, *Parkville, Victoria* 3052, *Australia*)

Summary Curassavine, the major alkaloid of *Heliotropium curassavicum* Linn. is shown to be an ester of trachelanthamidine with 3-carboxy-4-methylhexane-2,3-diol (homoviridifloric acid), the first example of a monocarboxylic necic acid with a C_8 skeleton; the minor alkaloids, coromandalin and heliovicine are esters of trachelanthamidine with (+)-viridifloric and (−)-trachelanthic acids, respectively, the former providing the first example of natural occurrence of a (+)-viridiflorate.

Heliotropium curassavicum Linn. is a weed of saline areas in the U.S.A., Europe, India, and Australia. It was recently reported by Rajagopalan and Batra[1] to contain heliotrine (**1**), lasiocarpine (**2**), and 7-angelylheliotridine, all known esters of heliotridine. We have found that a sample of the plant collected near Madras does not contain these alkaloids, but contains alkaloids which are new esters of trachelanthamidine. The structural differences between these alkaloids and those reported by Rajagopalan and Batra suggest that this widespread species may have developed two or more markedly different populations.

The major alkaloid (after Zn–H_2SO_4 reduction), curassavine, $[\alpha]_D^{25}$ + 0·9° (EtOH), isolated in 0·3% yield, was non-crystalline but was initially isolated as a crystalline *N*-oxide, $C_{16}H_{29}NO_5$, $[\alpha]_D^{25}$ −6·6° (EtOH), m.p. 186–188 °C. The n.m.r. spectrum of the tertiary base in $CDCl_3$ was similar to that expected for an ester of a monohydroxynecine with viridifloric acid but the mass spectrum (*M*+, *m/e* 299) agreed with the formula $C_{16}H_{29}NO_4$, *i.e.* one CH_2 group more than an ester of viridifloric acid. Alkaline hydrolysis gave trachelanthamidine (**3**) and an acid, m.p. 106–110 °C, $[\alpha]_D^{25}$ + 7·4° (ethanol), the methyl ester and butyl boronate derivatives of which had mass spectra corresponding with the formula $C_8H_{16}O_4$. Although the n.m.r. spectrum of the acid in $CDCl_3$ showed signals for MeCHOH and an apparent isopropyl group, the spectrum measured in [$^2H_5$]pyridine showed clear evidence of an ethyl group (3H triplet at δ 0·96). The latter spectrum included two 3H doublets, δ 1·19 (>CH*Me*) and 1·66 [–CH(OH)*Me*],



signals at δ 2·32 [1H, m, –C*H*(Me) Et] and 4·54 [1H, q, –C*H*(OH)Me], and a broad multiplet centred near δ 1·7 (2H, –CH_2Me) appropriate for an acid of structure $MeCH_2$–CHMe–C(OH)(CO_2H)–CH(OH)Me. Oxidation of the methyl ester of the acid with periodate gave a product whose mass spectrum [*m/e* 144 (M^+), 88, 85, 57, 41, and 29] strongly indicated the presence of the ketone EtCH(Me)$COCO_2$Me. The absence of ions at *m/e* 71 and 43 eliminated alternative structures with an isopropyl group.

Curassavine can thus be written as (**4**). Comparison of its electrophoretic mobilities in carbonate and borate buffers indicates that the esterifying acid contains a glycol group of the *erythro* configuration as in viridifloric acid.[2] Furthermore the methyl esters of viridifloric and the new acid have comparable anionic mobilities in borate buffer, and the name 'homoviridifloric acid' for the new acid is therefore appropriate.

The two minor alkaloids, coromandalin, gum, $[\alpha]_D^{25}$ −6·86° (EtOH), M^+, *m/e* 285, and heliovicine, gum, $[\alpha]_D^{25}$ −2·74° (EtOH), M^+, *m/e* 285, isolated in 0·1 and 0·05% yields were characterised as trachelanthamidine esters of (+)-viridifloric (**5**) and (−)-trachelanthic (**6**) acids, respectively. Alkaline hydrolysis of (**5**) gave trachelanthamidine and an acid, m.p. 122—124 °C, $[\alpha]_D^{25}$ + 3·12° (EtOH), whose methyl boronate derivative had the same g.l.c. retention time as that of viridifloric acid but different from that of the same derivative of trachelanthic acid. Alkaline hydrolysis of (**6**) gave trachelanthamidine and an acid, m.p. 91—92 °C, $[\alpha]_D^{25}$ − 1·9° (EtOH), whose methyl boronate derivative had the same g.l.c. retention time as that of trachelanthic acid. Besides, the n.m.r. spectra of the hydrolysate acids were identical with those of the authentic acids. This is the first recorded natural occurrence of (+)-viridifloric acid and only the second of (−)-trachelanthic acid. The more commonly isolated (−)-viridifloric and (+)-trachelanthic acids have the same (*S*) configuration at the α-carbon,[3] so both minor alkaloids contain acids of abnormal (*R*) configuration at this point.

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