217. *7-Hydroxy-3 : 6-ditiglyloxytropane, a New Alkaloid isolated from the Roots of* Datura.

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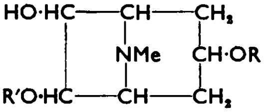
A hitherto unknown alkaloid, shown by hydrolysis to be a ditiglyl ester of 3 : 6 : 7-trihydroxytropane, has been isolated from the roots of three species of *Datura*. The formation of 6 : 7-dihydroxy-3-tiglyloxytropane (meteloidine) by partial hydrolysis establishes the constitution of the new base as 7-hydroxy-3 : 6-ditiglyloxytropane.

MEMBERS of the genus *Datura* have long been known to contain in their aerial parts alkaloids of the tropane group, notably hyoscyamine, hyoscine, and meteloidine. Little is known of the alkaloids occurring in the roots of these plants, except for mention of hyoscyamine in *D. stramonium* L.[1] and *D. tatula* L.[2]

The crude mixture of bases resulting from extraction of the basified, powdered root with ether furnished an apparently homogeneous base as a colourless gum on fractional elution from a phosphate buffer–kieselguhr column. The base afforded an optically inactive, crystalline hydrobromide of molecular formula, $C_{18}H_{27}O_5N,HBr$, a picrate $C_{18}H_{27}O_5N,C_6H_3O_7N_3$, and a chloroplatinate $(C_{18}H_{27}O_5N)_2,H_2PtCl_6$. In the roots of *D. stramonium* L. and *D. tatula* L. var. *inermis*, this alkaloid formed about 10% of the total alkaloids present, whereas in *D. ferox* L. it accounted for 30% of the total basic constituents.

Evidence for its structure was obtained by hydrolysis. On being heated with aqueous-ethanolic barium hydroxide, it underwent complete hydrolysis and furnished 3 : 6 : 7-trihydroxytropane (teloidine) (I; R = R′ = H) and tiglic acid. The yield of the acid indicated that the parent compound was a ditiglyl ester of teloidine. The formation of 6 : 7-dihydroxy-3-tiglyloxytropane (meteloidine) (I; R = $CH_3\cdot CH{:}CMe\cdot CO$, R′ = H) on partial hydrolysis by aqueous barium hydroxide served to orientate the position of both ester groups. The new alkaloid is clearly (±)-7-hydroxy-3 : 6-ditiglyloxytropane (I; R = R′ = $CH_3\cdot CH{:}CMe\cdot CO$). Confirmation of this structure is provided by its ultraviolet absorption: meteloidine and the new alkaloid both exhibit maxima at 217 mμ (ε 12,200 and 23,900, respectively). Methyl tiglate is reported by Dreiding and Pratt[3] to have $\lambda_{max.}$ 214 mμ (ε 11,300).



(I)

EXPERIMENTAL

Extraction of the Alkaloid.—(i) The powdered root (1 kg.) was moistened with water (500 ml.), kept overnight, mixed with calcium hydroxide (100 g.), and exhaustively extracted by percolation with ether. After removal of the solvent, the dark green residue was stirred with aqueous-ethanolic hydrochloric acid; non-basic material was removed with chloroform, and the bases were liberated by ammonia and collected in chloroform. The crude mixture was transferred to a column prepared from kieselguhr (50 g.) and 0·5M-phosphate buffer (pH 6·6; 50 ml.); the first fraction eluted with light petroleum (b. p. 60—80°) was shown by paper chromatography[4] to be homogeneous and was recovered as a colourless gum. The yields obtained were: *D. ferox* L., 0·05; *D. tatula* L. var. *inermis*, 0·01; *D. stramonium* L., 0·01%.

(ii) For large-scale extractions, the root was percolated with ether as described in the foregoing experiment, the whole process being followed by paper chromatography. The initial fractions of the percolate, which were richest in materials of highest R_F value, were combined

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[1] Feldhaus, *Arch. Pharm.*, 1905, **243**, 328.

[2] Klein, "Handbuch der Pflanzenanalyse," Springer, Vienna, 1933, Vol. IV, p. 768.

[3] Dreiding and Pratt, *J. Amer. Chem. Soc.*, 1954, **76**, 1902.

[4] Evans and Partridge, *J. Pharm. Pharmacol.*, 1954, **6**, 702.

and concentrated. Basic material was collected in 3N-sulphuric acid supported on a column of kieselguhr and, after removal of non-basic material from the column by irrigation with ether, the bases were liberated by irrigation with ammoniacal chloroform. The recovered basic material was neutralised to pH 4 with 0·1N-sulphuric acid, fractionally liberated with 0·1N-sodium hydroxide, and collected in chloroform. The first few fractions, which were shown to be homogeneous by paper chromatography, afforded a colourless gum (0·05 g./kg. of root) on evaporation of the solvent.

Salts.—An ethanolic solution of the base on the addition of aqueous hydrobromic acid gave a *hydrobromide* which crystallised from ethanol as aggregated prisms, $\alpha = 0°$, m. p. 215—216° (Found: C, 51·4; H, 6·6; N, 3·3. $C_{18}H_{27}O_5N,HBr$ requires C, 51·7; H, 6·7; N, 3·35%), $\lambda_{max.}$ in H_2O, 217 mμ (ε 23,900). The *picrate*, prepared by interaction of the hydrobromide and sodium picrate, crystallised from aqueous ethanol as plates, m. p. 184—185° (Found: C, 50·7, 51·0; H, 5·3, 5·1; N, 9·7, 10·0. $C_{18}H_{27}O_5N,C_6H_3O_7N_3$ requires C, 50·9; H, 5·3; N, 9·9%). A neutral solution, prepared by dissolving the gum in dilute hydrochloric acid, furnished with chloroplatinic acid a *chloroplatinate* as orange rosettes which crystallised from very dilute hydrochloric acid as prisms, m. p. 252—253° (decomp.) [Found: C, 40·1; H, 5·6; N, 2·7, 2·4; Pt, 18·0, 18·0. $(C_{18}H_{27}O_5N)_2,H_2PtCl_6$ requires C, 39·9; H, 5·2; N, 2·6; Pt, 18·0%]. An attempt to prepare an oxalate gave partially hydrated prisms, m. p. 128—130° (decomp.).

Hydrolysis.—(i) The alkaloid hydrobromide (0·1 g.), dissolved in ethanol (2 ml.) and mixed with a solution of barium hydroxide (0·5 g.) in water (15 ml.), was heated at 100° in a sealed tube for 2½ hr. Barium was removed from the solution as its carbonate. The filtrate, after being thoroughly washed with ether, gave a crystalline solid on removal of the solvent under reduced pressure. Acetone-soluble material was extracted from this and crystallised from aqueous ethanol as aggregated prisms, m. p. 297—298° (decomp.), undepressed on admixture with teloidine hydrobromide prepared by hydrolysis of meteloidine [Pyman and Reynolds[5] give m. p. 295° (decomp.)]. A second portion of the filtrate when treated with aqueous sodium picrate yielded teloidine picrate which crystallised from aqueous ethanol as needles, m. p. 221—222° (decomp.), undepressed by teloidine picrate derived from meteloidine. Schöpf and Arnold[6] describe teloidine picrate as needles, m. p. 218—219° (decomp.). A third portion of the filtrate gave, with aqueous ammonium reineckate, *teloidine reineckate* which separated from aqueous acetone as leaflets m. p. 195—196° (decomp.); mixed m. p. with a sample of the reineckate obtained from the hydrolysis products of meteloidine, 196—197° (decomp.) {Found: C, 29·4; H, 4·2. $C_8H_{15}O_3N,H[Cr(SCN)_4(NH_3)_2]$ requires C, 29·3; H, 4·5%}.

(ii) The hydrobromide (0·064 g.) was hydrolysed as described in the foregoing experiment. After acidification with hydrobromic acid, ether removed from the solution tiglic acid (0·026 g., 85%), m. p. and mixed m. p. 63·5° (Found: C, 59·8; H, 7·8. Calc. for $C_5H_8O_2$: C, 60·0; H, 8·0%).

(iii) The suspension obtained when the hydrobromide (0·1 g.) was added to barium hydroxide (0·5 g.) in water (10 ml.) was heated with stirring at 100° for 90 min. and kept overnight. The clear, supernatant liquid was extracted with chloroform and, after being concentrated, this solution furnished meteloidine which crystallised as rosettes of needles, m. p. and mixed m. p. 138—139°. When mixed with meteloidine, it behaved as a homogeneous substance on paper chromatography. Its picrate crystallised from aqueous ethanol as nodules, m. p. 177—178°; mixed m. p. with meteloidine picrate 177° (Pyman and Reynolds[5] give m. p. 177—180°). The *reineckate* crystallised from aqueous acetone as plates which collapsed to a viscous mass at 140° and then decomposed slowly both alone and after mixing with meteloidine reineckate {Found: C, 35·3; H, 4·9. $C_{13}H_{21}O_4N,H[Cr(SCN)_4(NH_3)_2]$ requires C, 35·5; H, 4·9%}.

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[5] Pyman and Reynolds, *J.*, 1908, **93**, 2077.

[6] Schöpf and Arnold, *Annalen*, 1947, **558**, 109.