406. (—)-3α : 6β-*Ditigloyloxytropane, a New Alkaloid, from the Roots of* Datura.

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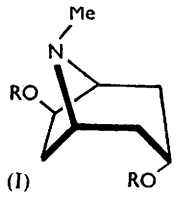
A new alkaloid isolated from the roots of *Datura innoxia* and *D. stramonium* was shown by hydrolysis to be the ditigloyl ester of (+)-tropane-3α : 6β-diol. This constitution was confirmed by comparison of the natural alkaloid with (—)-3α : 6β-ditigloyloxytropane prepared by partial synthesis.

The roots of *Datura stramonium* L. have long been known to contain hyoscyamine [1] and more recently paper chromatography has indicated its co-occurrence with hyoscine, *apo*atropine, meteloidine, two unknown alkaloids,[2] and cuscohygrine.[3] 3 : 6-Ditigloyloxytropan-7-ol has been isolated from the weakly basic fractions of a root extract.[4] *Datura innoxia* Miller roots are reported to contain cuscohygrine,[3] hyoscyamine, hyoscine, and two uncharacterised bases.[5]

[1] Feldhaus, *Arch. Pharm.*, 1905, **243**, 328.
[2] Romeike, *Pharmazie*, 1953, **8**, 668; *Flora*, 1956, **143**, 67.
[3] Reinouts van Haga, *Nature*, 1954, **174**, 833.
[4] Evans and Partridge, *J.*, 1957, 1102.
[5] Steinegger and Gessler, *Pharm. Acta Helv.*, 1955, **30**, 279.

An acid solution of the total bases extracted from *D. innoxia* roots yielded to chloroform an alkaloid which was isolated as the picrate, $C_{18}H_{27}O_4N,C_6H_3O_7N_3$. From it a lævorotatory base was regenerated and this furnished a chloroplatinate, $(C_{18}H_{27}O_4N)_2,H_2PtCl_6$. An identical alkaloid was recovered from the mother-liquors of the crystallisation of 3 : 6-ditigloyloxytropan-7-ol hydrobromide [4] from a root extract of *D. stramonium*. The yield of base from the two plants was 0·001 and 0·0002% respectively.



(I)

Hydrolysis of the base with aqueous-ethanolic barium hydroxide furnished (+)-tropane-3α : 6β-diol (I; R = H) and tiglic acid. The yield of the latter indicated a ditigloyl ester (I; R = Me·CH:CMe·CO).

Hyoscine and valeroidine are both β-orientated at $C_{(6)}$ and α-orientated at $C_{(3)}$.[6,7] (±)-Tropane-3 : 6-diol obtained by hydrogenation and subsequent hydrolysis of hyoscine [6] and the (—)-isomer from the hydrolysis of valeroidine [8,9] have similar configurations. The identity of the new alkaloid with (—)-3α : 6β-ditigloyloxytropane prepared by the esterification of (+)-tropane-3α : 6β-diol with tigloyl chloride confirmed its structure. The (+)-isomer was prepared from the alkamine of valeroidine. Recrystallisation of a mixture of equal weights of the (+)- and the (—)-alkaloid picrate afforded a racemic compound of different crystalline structure from, and m. p. 24° above, the natural derivative. There were no significant differences between the infrared spectra of the natural alkaloid picrate and that of the synthesised (—)-picrate crystallised under similar conditions, when determined by the potassium chloride pressed disc technique. The differences between the infrared spectra of the similarly recrystallised (—)-, (+)-, and (±)-isomers are consistent with the general observations on the effect of spatial configuration on infrared absorption in the solid state. In this instance the differences were sufficient for the detection of partly racemised salts.

Experimental

Isolation of the Alkaloid Picrate.—(i) The powdered roots of *D. innoxia* (32 kg.) were moistened with water, mixed with calcium hydroxide (1·6 kg.), and after 2 hr. exhaustively extracted by continuous percolation with industrial methylated spirit. Removal of most of the solvent from the percolate (90 l.) left a brown viscous liquid. This was rendered alkaline and the liberated bases were collected in chloroform. Neutralisation of the crude alkaloid mixture with N-sulphuric acid indicated a basic equivalent of 128 g. of hyoscyamine. The faintly acid solution of the alkaloid sulphates was filtered and repeatedly shaken with chloroform. Evaporation of the solvent afforded a brown gum, which by paper chromatography was shown to consist of alkaloids of high R_F values. A neutral solution of the gum in dilute hydrochloric acid, when treated with sodium picrate solution, gave a flocculent mass which crystallised on addition of ethanol followed by warming. The solid was filtered off; then, overnight, the filtrate deposited a *picrate* which crystallised from aqueous ethanol as filamentous needles (0·02 g./kg. of root), m. p. 150—151° (Found: C, 52·5; H, 5·6; N, 10·2. $C_{18}H_{27}O_4N,C_6H_3O_7N_3$ requires C, 52·4; H, 5·5; N, 10·2%).

(ii) The mother-liquors from the crystallisation of 3 : 6-ditigloyloxytropan-7-ol hydrobromide [4] derived from the roots of *D. stramonium*, on treatment with sodium picrate, afforded a picrate (0·004 g./kg.) identical with that obtained from *D. innoxia* roots (Found: C, 52·4; H, 5·4%).

Base and Chloroplatinate.—A solution of the picrate in chloroform was washed with aqueous ammonia and the base recovered as a colourless gum, $[\alpha]_D^{20}$ −21·5° (*c* 3·1 in EtOH, *l* 5 cm.). The base, in dilute hydrochloric acid, furnished with chloroplatinic acid a *chloroplatinate* as

[6] Fodor and Kovács, *J.*, 1953, 2341.
[7] Fodor, Vincze, and Tóth, *Experientia*, 1957, **13**, 183; Fodor, *ibid.*, 1955, **11**, 129.
[8] Barger, Martin, and Mitchell, *J.*, 1937, 1820.
[9] Stoll, Lindenmann, and Jucker, *Helv. Chim. Acta*, 1953, **38**, 1506.

orange rosettes which crystallised from very dilute hydrochloric acid as plates, m. p. 230° (decomp.) [Found: C, 40·8; H, 5·4; Pt, 18·8. $(C_{18}H_{27}O_4N)_2,H_2PtCl_6$ requires C, 41·1; H, 5·3; N, 2·7; Pt, 18·5%].

Hydrolysis.—The base (0·03 g.) in ethanol (1 ml.) was refluxed with a solution of barium hydroxide (0·3 g.) in water (5 ml.) for 2 hr. The turbid suspension was washed with chloroform, and the barium removed as sulphate. From the filtrate, acidified with dilute sulphuric acid, ether removed tiglic acid (0·015 g., 79%), m. p. and mixed m. p. 62·5° (Found: C, 59·8; H, 7·8. Calc. for $C_5H_8O_2$: C, 60·0; H, 8·0%). The aqueous solution, neutralised by the addition of barium carbonate, was filtered and evaporated to dryness under reduced pressure. The residual sulphate, $[\alpha]_D^{20}$ +10·9° (*c* 1·1 in EtOH, *l* 5 cm.), was dissolved in water and with sodium picrate afforded (+)-tropane-3α : 6β-diol picrate, m. p. and mixed m. p. 249° (decomp.) [Found: C, 43·4; H, 4·7. Calc. for $C_8H_{15}O_2N,C_6H_3O_7N_3$: C, 43·5; H, 4·7%]. Fodor and Kovács [6] give m. p. 251—252° and Wolfes and Hromatka [10] m. p. 253° (decomp.) for (+)-tropane-3α : 6β-diol and Stoll, Becker, and Jucker [11] record m. p. 248° (decomp.) for the (±)-salt. The low m. p. of our (+)-salt was probably due to admixture with a small quantity of the (±)-picrate produced by the easy racemisation of the parent alkaloid.

(−)-3α : 6β-*Ditigloyloxytropane and its Derivatives.*—(+)-Tropane-3α : 6β-diol (+)-tartrate was prepared from the (±)-base by Fodor and Kovács's method.[6] Tigloyl chloride (0·14 g.) was added to the (+)-salt (0·08 g.), and the mixture kept at 105° for 3 hr., then at room temperature overnight. The unchanged tigloyl chloride was decomposed with water (5 ml.), the liberated acid removed with ether, and the alkaloid salt collected in chloroform. The residue remaining after the removal of the solvent was dissolved in water (4 ml.) and with sodium picrate furnished (−)-3α : 6β-*ditigloyloxytropane picrate* (0·08 g., 43%) as needles (from aqueous ethanol), m. p. and mixed m. p. with natural alkaloid picrate, 149° (Found: C, 52·1; H, 5·5%). The base, $[\alpha]_D^{20}$ −12·0 (*c* 2·5 in EtOH, *l* 5 cm.), liberated from the picrate solution with ammonia and collected in chloroform, was neutralised with dilute hydrochloric acid. With chloroplatinic acid it furnished a *chloroplatinate* which crystallised from very dilute hydrochloric acid as plates, m. p. 232° (decomp.) (Found: C, 41·4; H, 5·3; Pt, 18·3%).

(+)-3α : 6β-*Ditigloyloxytropane and its Derivatives.*—These were prepared in a similar way to the (−)-compounds but from the (−)-base (0·1 g.), obtained by the hydrolysis of valeroidine.[8] The *picrate* (0·07 g., 71·4%) crystallised from aqueous ethanol as needles, m. p. 151—152°, mixed m. p. with natural alkaloid picrate and synthesised (−)-alkaloid picrate, 170° (Found: C, 52·2; H, 5·4%). The base was obtained as a gum, $[\alpha]_D^{20}$ +18·6° (*c* 3·7 in EtOH, *l* 5 cm.), and the *chloroplatinate* formed plates, m. p. 230° (decomp.) (Found: C, 41·4; H, 5·6; N, 2·4; Pt, 18·8%). Equal weights of the picrate and the natural alkaloid picrate, mixed and recrystallised from aqueous ethanol, afforded prisms, m. p. 173—175°.

The infrared spectrum of the (+)-alkaloid picrate differed from that of the (−)-isomer in the following respects: a doublet at 730 and 740 $cm.^{-1}$, a shoulder at 715 $cm.^{-1}$, a sharpening of the band at 782 $cm.^{-1}$, a splitting of the band at 1133 $cm.^{-1}$, enhancement of the bands at 1228, 1342, and 3030 $cm.^{-1}$, and numerous minor differences. Differences in the spectrum of the (±)-alkaloid picrate included an enhanced band at 1026 $cm.^{-1}$, a splitting of the band at 1072 $cm.^{-1}$, and a 1133 $cm.^{-1}$ doublet.

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[10] Wolfes and Hromatka, *Ber.*, 1934, **47**, 45.
[11] Stoll, Becker, and Jucker, *Helv. Chim. Acta*, 1952, **35**, 1263.