243. *The Minor Alkaloids of* Duboisia myoporoides. *Part IV. Valeroidine.*

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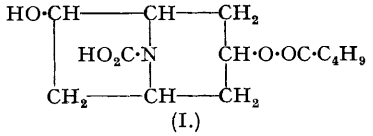
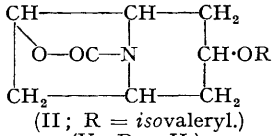
A final structure for valeroidine (*J.*, 1937, 1821; 1940, 1155) is proposed. The product of oxidation with permanganate in acetone is suggested to be an inner urethane, explaining the formation of norvaleroidine on acid hydrolysis. An explanation of the demethylating action of thionyl chloride on valeroidine hydrobromide is also proposed.

VALEROIDINE has been shown (Part I, *J.*, 1937, 1821) to be a mono*iso*valeryldihydroxytropane. The parent tropanediol differed from the known 2 : 3- and 6 : 7-diols but was shown to be identical with the " dioxytropane " isolated from Peruvian coca leaves by Wolfes and Hromatka (*Merck's Jahresber.*, 1933, **47**, 45) and which they suggested to be tropane-3 : 6-diol. In further work (Part III, *J.*, 1940, 1155) the diacetyl and di*iso*valeryl derivatives of the tropanediol were prepared and attempts were made to determine the positions of the free and esterified hydroxyl groups in valeroidine. Oxidation with various reagents in acid aqueous solution gave no positive results, but with potassium permanganate in acetone, besides a small yield of norvaleroidine [compare preparation of nortropine from tropine (Willstätter, *Ber.*, 1896, **29**, 1580), norscopoline from scopoline (Lubold, *Arch. Pharm.*, 1898, **236**, 22), etc.], a new neutral compound was obtained. At that time analysis indicated the formula $C_{13}H_{21}O_4N$ for this compound. On boiling with alcoholic hydrochloric acid the compound was converted into norvaleroidine. This was an unexpected result which could not then be explained.

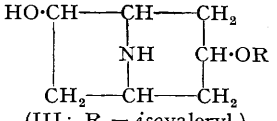
It is now suggested that the oxidation product is an inner urethane (II) formed by elimination of water from a labile carbamic acid (I) initially produced by oxidation of the *N*-methyl group. Formula (II) requires $C_{13}H_{19}O_4N$, with which later analyses were in closer agreement; it would explain the formation of norvaleroidine (III) by elimination of carbon dioxide on acid hydrolysis. It is probable that the rather ill-defined base obtained, along with *iso*valeric acid, on alkaline hydrolysis of the oxidation product was a mixture of nortropane-3 : 6-diol (IV) and the corresponding inner urethane (V).



(I.)

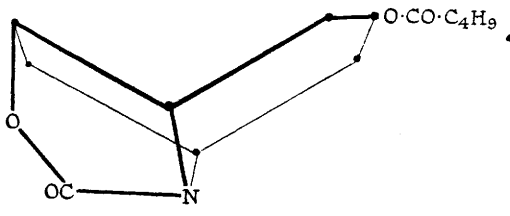


(II; R = *iso*valeryl.)
(V; R = H.)

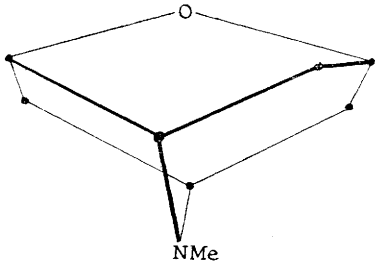


(III; R = *iso*valeryl.)
(IV; R = H.)

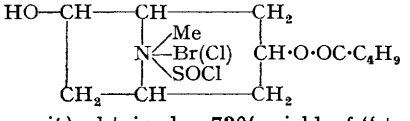
By analogy with hyoscyamine, hyoscine, etc., it is reasonable to assume that the esterified hydroxyl group is in position 3. On this assumption the comparative stability of the oxidation compound would appear to exclude the possibility that the free hydroxyl group in valeroidine could be attached to carbon 1 (or 5) since this would require the presence of a four-membered urethane ring in the oxidation product. The fairly ready formation of the latter would rather suggest that the free hydroxyl group was attached to carbon 6 (or 7), so that the oxidation product would be spatially represented by (VI).



(VI.)



(VII.)



(VIII.)

Wolfes and Hromatka (*loc. cit.*) obtained a 73% yield of " tropene oxide ", in which they postulated the presence of an ether linkage, by treating their tropanediol with a mixture of

phosphorus oxychloride and pentachloride. This compound, more correctly termed desoxyscopoline, can be spatially represented by (VII).

In Part III (*loc. cit.*) attempts to replace the free hydroxyl group in valeroidine by chlorine were also described. These were unsuccessful, but on treating valeroidine hydrobromide (the free base did not give the reaction) with thionyl chloride the curious fact was noted that norvaleroidine was obtained in good yield. It is now suggested that this reaction proceeds through the formation of a labile compound (VIII) which, by loss of methyl chloride (or bromide) and subsequent hydrolysis, yields norvaleroidine (III).

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