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A TOTAL SYNTHESIS OF dl-EBURNAMONINE

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WE have recently described the isolation and determination of the structure of four alkaloids from Hunteria eburnea Pichon.[1] It was shown how they could be interconverted, eburnamonine (I) being the key compound and their relationship to aspidospermine (II)[2] was pointed out. Both (I) and (II) appear to have been formed from a tryptamine moiety plus a residue (III) either by an α-type condensation[3] in the case of (I) or a β-type for (II). The fragment (III) is patently a C_6-C_2-C_1 unit derived from a one carbon source[4] and an aromatic precursor such as dopa which undergoes fission[5] at some stage. Alternatively (III) may have had its genesis in a hydroaromatic compound such as prephenic acid.[6]

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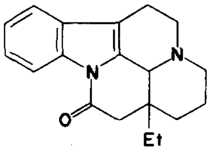
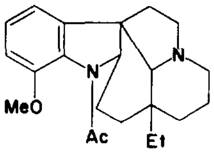
[1] M. F. Bartlett, W. I. Taylor and Raymond-Hamet, C. R. Acad. Sci., Paris 249, 1259 (1959).

[2] J. F. D. Mills and S. C. Nyburg, Tetrahedron Letters No. 11, 1 (1959).

[3] For the use of these terms see R. Robinson, Structural Relations of Natural Products p. 100 et seq. Clarendon Press (1955); the biogenetic ideas elaborated in this note have also been considered by Sir Robert Robinson (private communication of a brief note submitted to Tetrahedron Letters).



I



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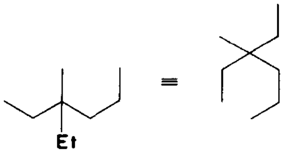

III

We have carried out a total synthesis of eburnamonine which although starting from p-ethylphenol can be regarded as a formal model for either of the routes alluded to above. p-Ethylphenol subjected to a Reimer - Tiemann reaction furnished 4-dichloromethyl-4-ethyl-cyclohexa-2:5-dienone, m.p. 61-62° (Found: C, 53.0; H, 5.0. $C_9H_{10}OCl_2$ requires: C, 52.7; H, 4.9) which with palladium-charcoal in ethanol yielded 4-dichloromethyl-4-ethylcyclohexanone, m.p. 58° (Found: C, 51.5; H, 6.8. $C_9H_{14}OCl_2$ requires: C, 51.6; H, 6.7). Oxidation of the latter compound with concentrated nitric acid gave β-dichloromethyl-β-ethyladipic acid, m.p. 126° (Found: C, 42.0; H, 5.5. $C_9H_{14}O_4Cl_2$ requires: C, 42.0; H, 5.5). Heating an aqueous solution of the dicarboxylic acid in a sealed tube at 200° gave the aldehydo-diacid (V), characterized as the γ-lactone (IV), m.p. 102-3° (Found: C, 53.4; H, 7.0. $C_9H_{14}O_5$ requires: C, 53.5, H, 7.0). Upon heating the lactone with

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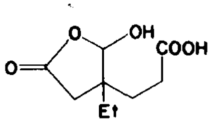
[4] Perhaps the same one that yields the C_{21} carbon of yohimbine.

[5] R. B. Woodward, Nature, Lond. **162**, 155 (1948).

[6] For a comprehensive review on this subject see E. Wenkert, Experientia **15**, 165 (1959).

tryptamine in dilute aqueous hydrochloric acid eburnamonine lactam (VI) was obtained in 5-10% yield, m.p. 217° (Found: C, 73.7; H, 6.7. $C_{19}H_{20}O_2N_2$ requires: C, 74.0; H, 6.5). The lactam was reduced quantitatively by lithium aluminium hydride in ether to a mixture of eburnamine (VII) and iso-eburnamine (VII) which was oxidized directly with chromic oxide in pyridine to dl-eburnamonine (I) in very high yield, m.p. 203-4° (Found: C, 77.3; H, 7.7. $C_{19}H_{22}ON_2$ requires: C, 77.5; H, 7.5). Its infrared spectrum measured in a Nujol mull was indistinguishable from that of a similarly prepared sample of eburnamonine.



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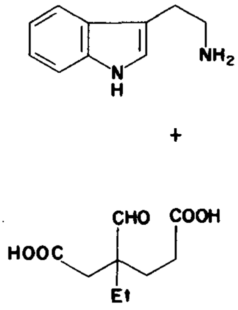

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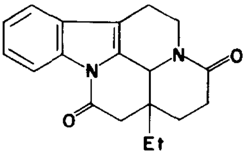
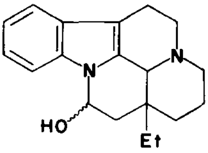


VI



VII