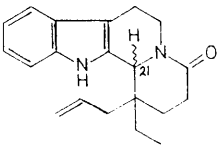
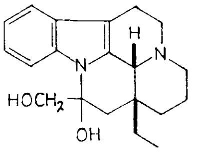
Total Synthesis of *Hunteria* Alkaloids. Stereochemical Considerations and a Total Synthesis of $(\pm)$-Vincaminol

By L. CASTEDO, JOHN HARLEY-MASON,* and T. J. LEENEY
(*University Chemical Laboratory, Lensfield Road, Cambridge*)

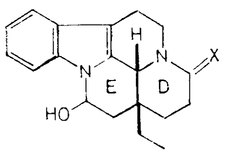
PREVIOUSLY we reported[1] a simple synthesis of $(\pm)$-eburnamine (IV; X = 2H) from the tetracyclic lactam (I) involving hydroxylation of the double bond followed by periodate cleavage of the resulting diol and subsequent reduction with lithium aluminium hydride. We then believed that the lactam (I) was stereochemically homogeneous but have since found that by careful column chromatography all four possible racemates of the diol lactam can be separated from the mixture obtained. These form two pairs (II) and (III), differing within each pair by the configuration at the secondary hydroxy-group. Periodate cleavage of either of the first pair gave eburnamine *N*(6)-lactam (IV; X = O), reduced by lithium aluminium hydride to eburnamine (V; X = 2H) (natural series, *cis* D/E ring junction) while similar treatment of the second pair gave iso-eburnamine[2] (V; X = 2H) (unnatural series, *trans* D/E ring junction). From the proportions of the diols isolated we conclude that the lactam (I) is a mixture of *cis* (ethyl group and C-21 proton *cis*) and *trans* (ethyl group and C-21 proton *trans*) in the ratio of 1 : 6.



(I)



(VI)



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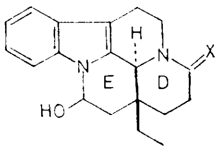

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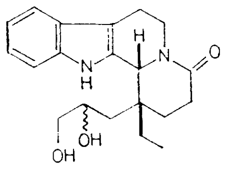
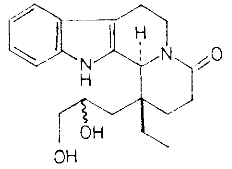
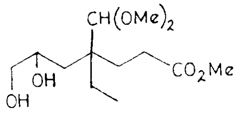


(II)



(III)



(VII)

We have also investigated the effect, on the diols, of another oxidising agent, dimethyl sulphoxide–dicyclohexylcarbodi-imide.[3] In this case oxidation of either of the *cis*-diols (II) followed by lithium aluminium hydride reduction led to the isolation of $(\pm)$-vincaminol (VI), the product obtained[4] by lithium aluminium hydride reduction of the alkaloid vincamine. Identity was proved by direct comparison (t.l.c. and mass spectra) with an authentic sample.† Similar treatment of either of the *trans*-diols gave isovincaminol.

Originally the diols were obtained by osmium tetroxide oxidation of the lactam (I). We have now found that oxidation of the dimethyl acetal[5] of 4-ethyl-4-formylmethylhept-6-enoate with cold permanganate gives the glycol (VII) and that this condenses readily with tryptamine in boiling acetic acid followed by hydrochloric acid to give a similar mixture of stereoisomeric diols, thus obviating the use of an expensive and toxic reagent.

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