Total Synthesis of (±)-Geissoschizoline

By B. A. DADSON and JOHN HARLEY-MASON*

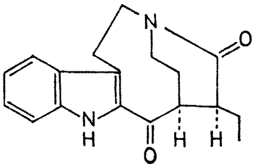
(*University Chemical Laboratory, Lensfield Road, Cambridge* CB2 1EW)

Summary A stereoselective total synthesis of (±)-geissoschizoline in thirteen stages from tryptamine is reported.

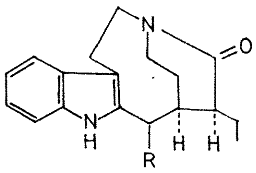
GEISSOSCHIZOLINE (VI) is the pentacyclic strychnine-like moiety of the "dimeric" indole alkaloid geissospermine[1] and is obtained from the latter by acid hydrolysis. We now report a total synthesis of (±)-geissoschizoline as follows. Treatment of the tetracyclic keto-amide[2] (I) with sodium borohydride gave the hydroxy-amide (II; R = OH) which was acetylated to give (II; R = OAc). Reaction of this acetyl derivative with sodium cyanide in dimethyl sulphoxide gave the cyano-compound (II; R = CN) which with methanolic sulphuric acid gave the ester-amide (III). Reduction with lithium aluminium hydride then gave (±)-demethoxycarbonyl-dihydrostemmadenine (IV), which with oxygen in the presence of platinum[3] gave (±)-dehydrogeissoschizoline (V). Reduction of this with diborane gave (±)-geissoschizoline identified by direct comparison with an authentic (optically active) sample kindly supplied by Professor A. R. Battersby.

Apart from one step [conversion of (II; R = OAc) into (II; R = CN) which gave only 40%] yields at all stages were excellent. All intermediates up to and including the ester-amide (III) crystallised well. (IV), (V), and (VI) were gums, but (IV) and (VI) were characterised as crystalline methiodides.

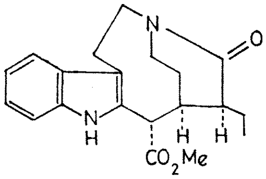
(*Received, April* 28*th*, 1969; *Com.* 583.)



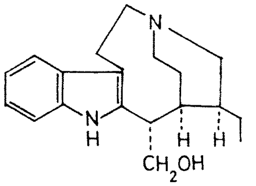
(I)



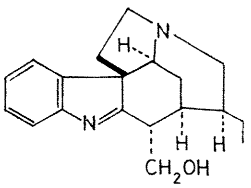
(II)



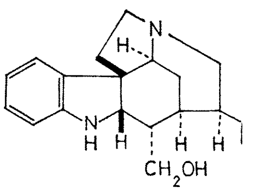
(III)



(IV)



(V)



(VI)

---

[1] M. M. Janot, *Tetrahedron*, 1961, **14**, 113; P. N. Edwards and G. F. Smith, *J. Chem. Soc.*, 1961, **152**; J. R. Hymon and H. Schmid, *Helv. Chim. Acta*, 1966, **49**, 2067.

[2] B. A. Dadson, J. Harley-Mason, and G. H. Foster, *Chem. Comm.*, 1968, 1233.

[3] *Cf.* D. Schumann and H. Schmid, *Helv. Chim. Acta*, 1963, **46**, 1966.