

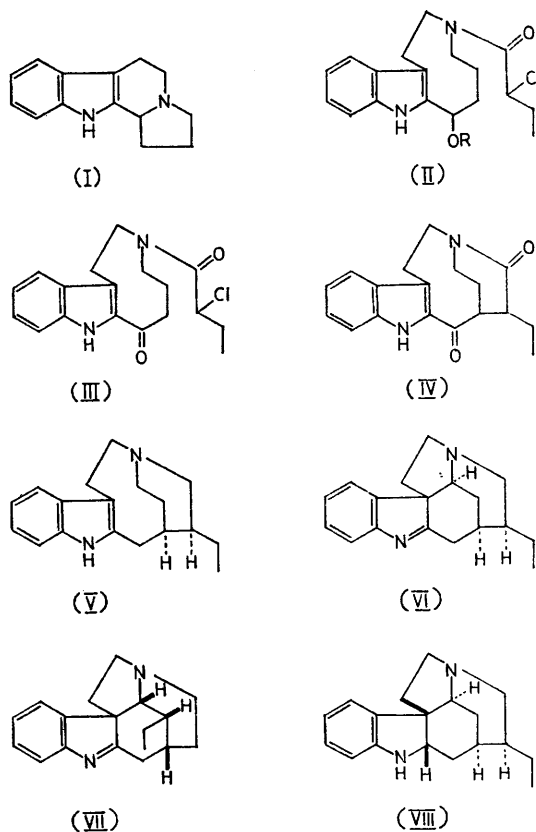
Total Synthesis of (\pm)-Tubifoline, (\pm)-Tubifolidine and (\pm)-Condyfoline

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THE tetracyclic indole derivative (V) is a key degradation product which has been obtained from many alkaloids of the akuammicine¹ and condylocarpine² types. Furthermore, oxidative cyclisation of this degradation product has led to known pentacyclic alkaloids.² We describe a simple synthesis of the indole (V) and its conversion to the racemates of the alkaloids described in the title.

Treatment of the readily available hexahydro-indolo-indolizine (I)³ with $\alpha\alpha'$ -dichlorobutyric anhydride gave the amide-ester (II; R = α -chlorobutyryl).⁴ Cautious alkaline hydrolysis of this gave the hydroxy-amide (II; R = H) which with manganese dioxide gave the ketone (III). Treatment of this ketone with sodium 1,1-dimethylpropoxide then yielded the tetracyclic keto-amide (IV). Wolf-Kishner reduction removed the keto-group and lithium aluminium hydride reduction of the product gave the tetracyclic indole (V). The structure of the product (and hence of the intermediates) was proved by direct comparison (t.l.c. and mass spectra) with a sample prepared by degradation¹ of akuammicine.†

Oxidation of the synthetic indole (V) to (\pm)-tubifoline (VI) and (\pm)-condyfoline (VII) was conducted as described by Schumann and Schmid.² Catalytic hydrogenation of (\pm)-tubifoline gave (\pm)-tubifolidine (VIII). This represents a simple and stereospecific synthetic entry to pentacyclic natural products of this type.



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† Sample kindly supplied by Dr. G. F. Smith.

¹ G. F. Smith and J. T. Wröbel, *J. Chem. Soc.*, 1960, 792.

² D. Schumann and H. Schmid, *Helv. Chim. Acta.*, 1963, **46**, 1966.

³ S. Corsano and S. Algieri, *Ann. Chim. (Italy)*, 1960, **50**, 75.

⁴ Cf. G. H. Foster, J. Harley-Mason, and W. R. Waterfield, *Chem. Comm.*, 1967, 21.