

THE ABSOLUTE CONFIGURATION OF (-)-ARGEMONINE

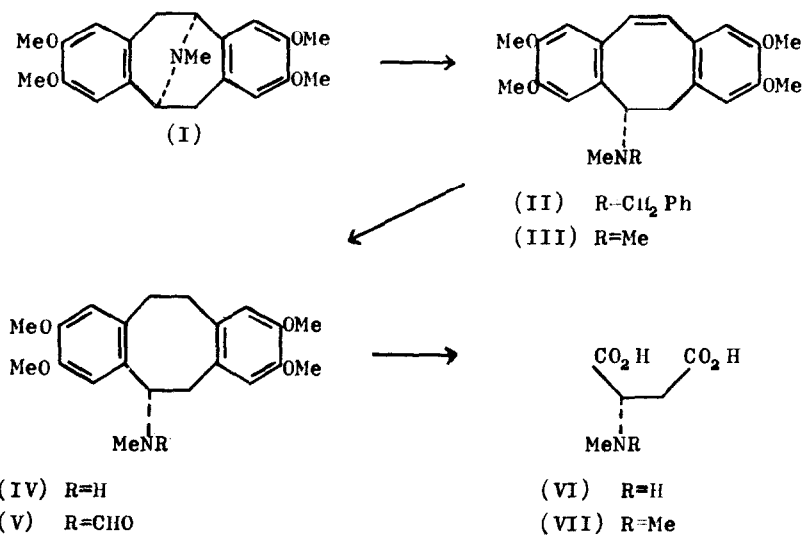
A.C. Barker and A.R. Battersby

Robert Robinson Laboratories, University of Liverpool

(Received 31 October 1966)

A recent communication (1) reporting o.r.d. studies on (-)-argemonine (I) prompts us to outline a rigorous determination of the absolute stereochemistry of this alkaloid.

(±)-N-Methylpavine (2) (racemic I) was resolved through its salt with OO-dibenzoyl-L-tartaric acid and the (-)-form [L(-)-argemonine (3)] was quaternised with benzyl chloride. Hofmann degradation in anhydrous tert. butanol using potassium tert. butoxide afforded the methine (II) which underwent hydrogenation and hydrogenolysis over palladised charcoal. When the product (IV) was heated with formamide, it yielded the amide (V) and this was oxidised first with an excess of ozone and then with performic acid. Fractionation of the resultant complex mixture by ion-exchange chromatography led to an acidic amino-acid fraction, shown by paper chromatography to contain largely N-methyiaspartic acid (VI) and aspartic acid. By methylating this mixture over palladium with formaldehyde and hydrogen, NN-dimethyiaspartic acid (VII) was obtained which, as its di-n-propyl ester, was carefully purified. The product was L(-)-NN-dimethyl di-n-propyl aspartate shown by its rotation ($[\alpha]_D^{20} -20^\circ$ in CHCl_3) to contain ca. 25% of the (+)-form. Partial racemisation has thus occurred at some stage(s) in the degradation; this does not affect the rigorous proof of absolute configuration. From the known stereochemistry of L-aspartic acid, it follows that formula (I) is a complete representation of (-)-argemonine.



The o.r.d. work (1) involved the comparison of a cyclic unsaturated derivative of (-)-argemonine, compound (III), with a saturated acyclic standard of known stereochemistry. The configuration deduced for (-)-argemonine agrees with that established by the foregoing results.

It is probable (4,5) that reticuline is the biological precursor of (-)-argemonine and the present work shows that if this is so, the (+)-form is the appropriate enantiomer. Interestingly, reticuline is present in Argemone hispida plants and the (+)-form predominates (5).

REFERENCES

1. O. Červinka, A. Fábryová and V. Novák, Tetrahedron Letters, 1966, 5375.
2. C. Schöpf, Angew. Chem., 1950, 62, 453; A.R. Battersby and R. Binks, J. Chem. Soc., 1955, 2888.
3. M.J. Martell, T.O. Soine, and L.B. Kier, J. Amer. Chem. Soc., 1963, 85, 1022; F.R. Stermitz, S.-Y. Lwo and G. Kellos, *ibid.*, p. 1551.
4. D.H.R. Barton, R.H. Hesse, and G.W. Kirby, J. Chem. Soc., 1965, 6379.
5. F.R. Stermitz and J.N. Seiber, J. Org. Chem., 1966, 31, 2925.