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THE ABSOLUTE CONFIGURATION OF TAZETTINE

R. J. Highet and P. F. Highet

Laboratory of Metabolism, National Heart Institute

Bethesda, Maryland, 20014

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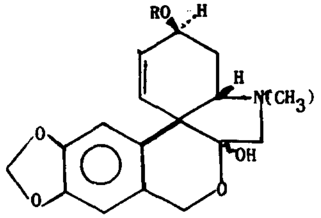
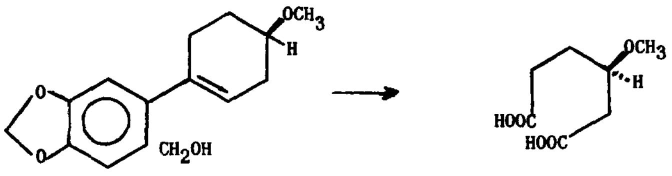
Some thirty alkaloids have been related to tazettine (I) by means which, with a few exceptions, have demonstrated the relative stereochemistry of the ring systems and the substituents.[1] The absolute configuration of the group has been assigned as shown by application of Mills' empirical rules to such epimeric pairs of allylic alcohols as tazettinol (II) and isotazettinol (II, the allylic alcohol and hydrogen atom being interchanged),[2] but the anomalous rotatory dispersions in the group have caused this assignment to be questioned.[3] Recently, determination of the correct structure of dihydrotazettine methine alcohol (III)[4] provided a material which retains only one asymmetric center of the complex stereochemistry of tazettine, and suggested that more secure knowledge of the absolute stereochemistry might be obtained from further degradative study of this derivative.



I, R = CH_3

II, R = H



III IV

Exhaustive ozonization of III, followed by hydrolysis of the ozonide by refluxing performic acid[5] produced β-methoxy adipic acid, (IV) identified by GLC and mass spectrum; the conversion was approximately 50%. Clearly this material can arise from III only from the alicyclic ring in the manner shown. Isolation of the methyl ester by GLC provided dimethyl (+)-R-methoxyadipate,[6] $[\alpha]_D$ + 8.3°, the infrared spectrum identical with that of known material. Thus the absolute configuration previously assigned is confirmed.

REFERENCES

1. Review articles list the following related alkaloids: Crinine (crinidine), vittatine, (+)-epicrinine, powelline, buphanidrine, buphanisine, undulatine, crinamidine, flexinine, nerbowdine, buphanamine, haemanthamine, haemanthidine, 6-hydroxycrinamine, criwelline, isotazettine and haemultine. Cf. W. C. Wildman in "The Alkaloids," Vol. VI, R. H. F. Manske, Ed., Academic Press, Inc., New York, N.Y., 1960, p. 289; H.-G. Boit, "Ergebnisse der Alkaloid-Chemie bis 1960," Academie-Verlag, Berlin, 1961, p. 410. Later work has assigned the following alkaloids to this group: (a) montanine, coccinine and manthine, Y. Inubushi, H. M. Fales, E. W. Warnhoff, and W. C. Wildman, J. Org. Chem., 25, 2153 (1960); (b) crinamine, H. M. Fales and W. C. Wildman, J. Am. Chem. Soc., 82, 197 (1960); (c) epihaemanthidine, J. Goosens, P. W. Jeffs, J. Graham, F. L. Warren and W. G. Wright, J. Chem. Soc., 1088 (1960); (d) epibuphanisine,

H. Hauth and D. Stauffacher, *Helv. chim. Acta*, *45*, 1307 (1962); (e) ambelline, P. Naegeli, E. W. Warnhoff, H. M. Fales, R. E. Lyle and W. C. Wildman, *J. Org. Chem.*, *28*, 206 (1963); (f) acetylnerbowdine, H. Hauth and D. Stauffacher, *Helv. chim. Acta*, *46*, 810 (1963); (g) crispaline, W. Doepke, *Arch. Pharm.*, *295*, 868 (1962); (h) squamigerine, S. H. Hung and K. E. Ma, *Yao Hsueh Hsueh Pao*, *11*, 1 (1964); *Chem. Abstr.*, *61*, 3154 (1964); (i) amaryllisine, A. L. Burlingame, H. M. Fales and R. J. Highet, *J. Am. Chem. Soc.*, *86*, 4976 (1964); (j) macronine, C. F. Murphy and W. C. Wildman, *Tetrahedron Letters*, 3857 (1964); (k) tubispacine, W. Doepke, *Arch. Pharm.*, *298*, 704 (1965).

2. T. Ikeda, W. I. Taylor, Y. Tsuda, S. Uyeo and H. Yajima, *J. Chem. Soc.*, 4749 (1956).
3. W. C. Wildman, private communication; cf. H. M. Fales and W. C. Wildman, *J. Am. Chem. Soc.*, *82*, 3389 (1960).
4. R. J. Highet, P. F. Highet and J. C. N. Ma, *Tetrahedron Letters*, 1049 (1966).
5. H. Corrodi and E. Hardegger, *Helv. chim. Acta*, *39*, 889 (1956).
6. (+)-Methoxyadipic acid is known to have the *R* configuration; cf. M. Viscontini and H. Köhler, *Helv. chim. Acta*, *37*, 41 (1954). To demonstrate that the corresponding ester has the same sign of rotation, (-)-S-β-methoxyadipic acid $[\alpha]_D$ -10° (reported -14.5°) was converted to the dimethyl ester $[\alpha]_D$ -8.3°; C, 0.182, chloroform).