

A New Berbine Synthesis

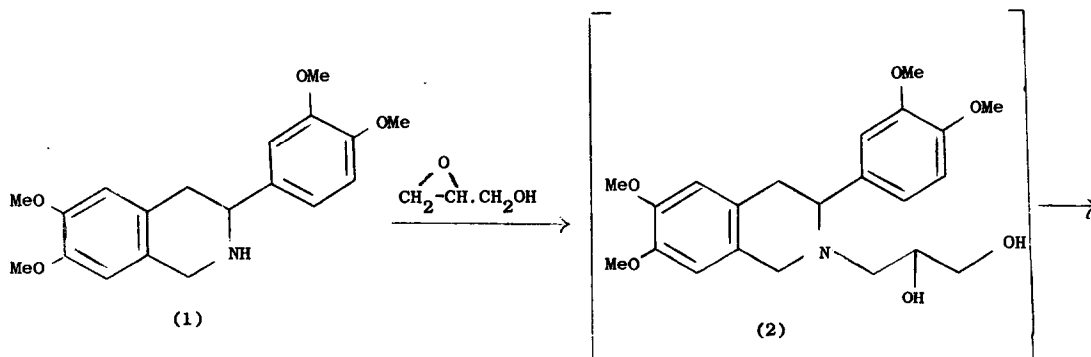
D.W. Brown, S.F. Dyke, G. Hardy and M. Sainsbury

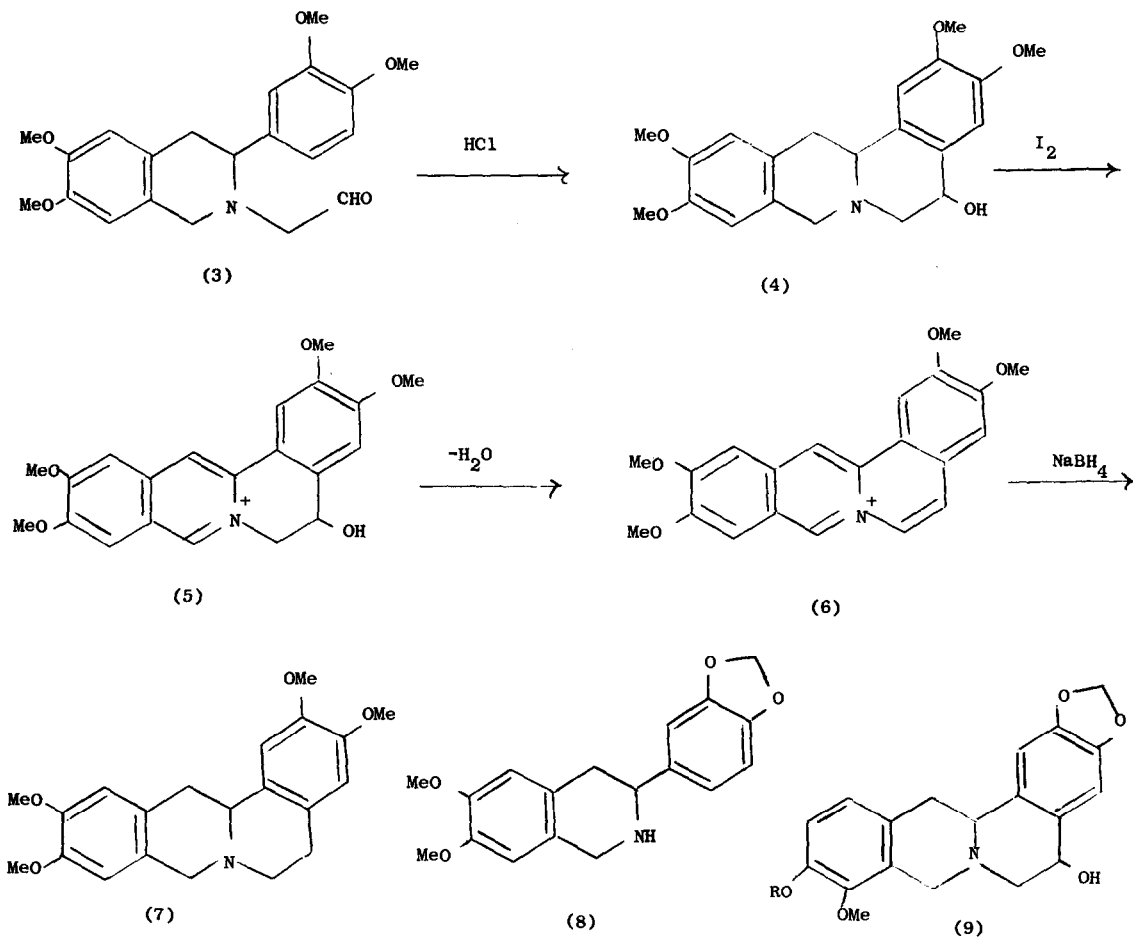
School of Chemistry and Chemical Engineering,
Bath University of Technology, Claverton Down,
Bath BA2 7AY, Somerset, England.

(Received in UK 6 September 1968; accepted for publication 18 September 1968)

In a continuation of our studies on the synthesis of berbine derivatives^{1,2} we now wish to report a new approach which constitutes the first synthesis of 5-hydroxyberbines. The known³ 3-aryl-1,2,3,4-tetrahydroisoquinoline (1) was reacted with glycidol and the intermediate amino-glycol derivative (2) was, without isolation, oxidised with periodic acid to provide the aldehyde⁴ (3). When the latter compound was left in contact with 6N HCl at room temperature for 16 hours, cyclisation occurred and the 5-hydroxyberbine (4) could be isolated in 70% yield as the hydrochloride $C_{21}H_{25}NO_5 \cdot HCl$, m.p. 228-229°. The IR spectrum indicated the presence of a hydroxyl group, but was devoid of carbonyl absorption, and the NMR spectrum exhibited resonances attributable to only FOUR aromatic protons. Dehydrogenation of the cyclisation product with iodine gave the quaternary salt (5) and this was easily dehydrated to the known⁵ dibenzo[a,g]quinolinium salt (6). Finally, reduction of (6) with sodium borohydride yielded norcoralydine (7), identical with an authentic specimen. The entire sequence of reactions has been repeated with the 3-aryl-1,2,3,4-tetrahydroisoquinoline (8) with similar results.

With this route to 5-hydroxyberbines established, we are currently investigating the synthesis of berberastine (9, R=Me) and thalidastine⁷ (9, R=H).





References

1. D.W. Brown and S.F. Dyke, *Tetrahedron*, **22**, 2429 (1966).
2. D.W. Brown, S.F. Dyke, G. Hardy and M. Sainsbury, *Tetrahedron Letters*, 1968, 2609.
3. A.R. Battersby and R. Binks, *J.Chem.Soc.*, 4333 (1958).
4. Satisfactory analyses and spectral data have been obtained for all new compounds reported.
5. C.K. Bradsher and N.L. Dutta, *J.Amer.Chem.Soc.*, **82**, 1145 (1960).
6. M.M. Nijband, *Pharm. Weekblad*, **98**, 301 (1963).
7. M. Shamma and B.S. Dudock, *Tetrahedron Letters*, 3825 (1965).