Electrolytic Oxidation of Armepavine and its Derivatives

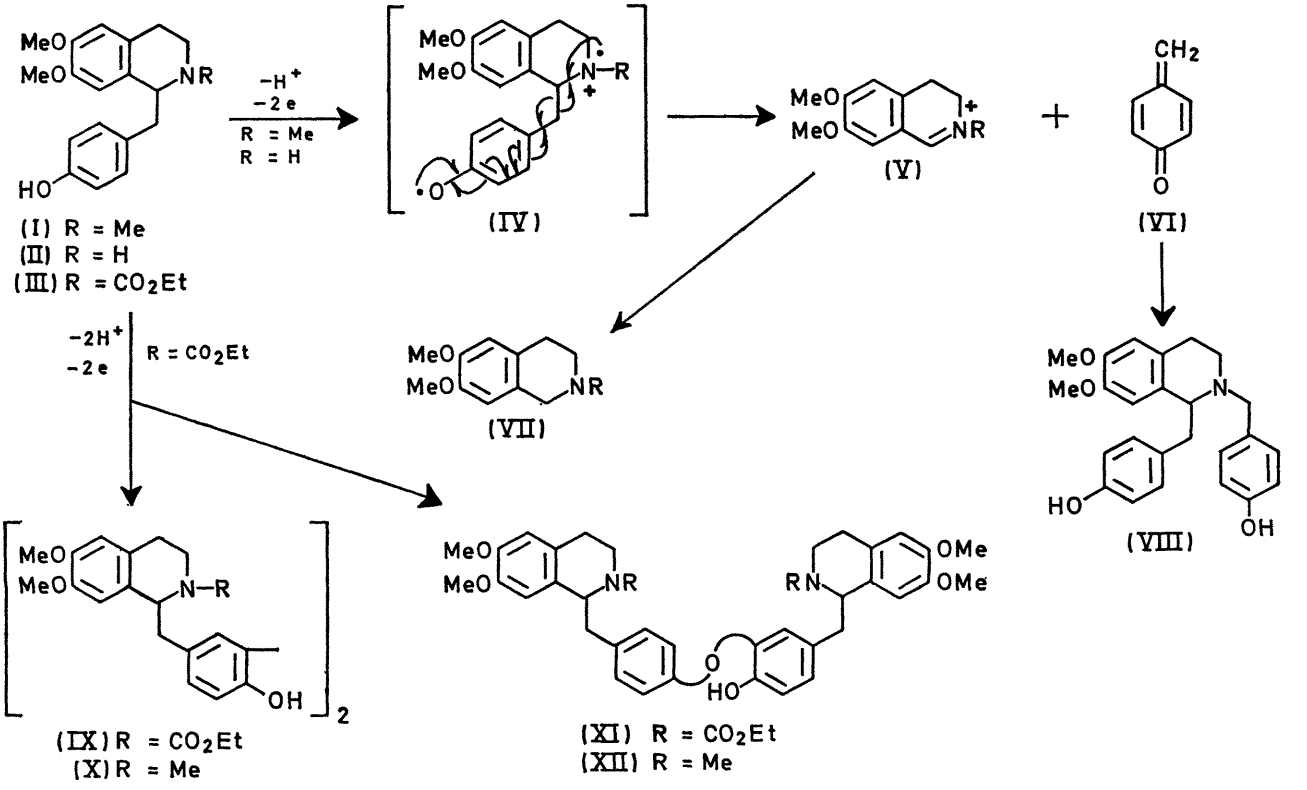
By J. M. BOBBITT* and R. C. HALLCHER

(*Department of Chemistry, University of Connecticut, Storrs, Connecticut* 06268)

Summary Electrolytic oxidation of armepavine and *N*-norarmepavine leads to fragmentation, but the oxidation of *N*-carbethoxy-*N*-norarmepavine yields carbon–carbon dimers and, for the first time, the carbon–oxygen dimer skeleton of the alkaloid, dauricine.

THE synthesis of the dauricine skeleton (XII) by oxidative coupling of armepavine (I) or its derivatives has been studied by several groups.[1–3] In one case,[3] a dimer was obtained, but the carbon–carbon skeleton (X) has not yet been found in nature.

The electrolytic oxidation of the sodium salts of racemic armepavine (I) and *N*-norarmepavine (II) led to the same fragmentation observed by Inubushi and his co-workers[4] when (I) was oxidized enzymatically. It was suggested that the cation diradical (IV) which fragments as shown to (V) and (VI) was involved. On electrolysis,† armepavine (I) gave the 3,4-dihydroisoquinoline (V; R = Me) (86%) which was characterized spectroscopically and reduced to the known compound (VII; R = Me)[6] for identification. *N*-Norarmepavine (II) gave the corresponding dihydroisoquinoline (V; R = H) (32%) which was also characterized spectroscopically and reduced to the known compound (VII; R = H)[7] for identification. Compound (VI) reacted with (II) to produce (VIII) (5%) which was characterized by its spectra (i.r., n.m.r., and mass) as well as those of its diacetate and its crystalline methiodide, m.p. 234—237°. The yields were much higher than in the enzymatic reactions, and no coupled products were observed. These two reactions which take place on an enzyme and on an electrode may well represent a synchronous double oxidation which is characteristic of a surface reaction. The fragmentation is effectively stopped when the nitrogen is acylated [as in (III)].



Oxidation of the sodium salt of racemic (III) led to a mixture which gave (IX) (45%) on preparative t.l.c. Benzylation ($PhCH_2Cl$–Na_2CO_3), reduction ($LiAlH_4$[2]), and debenzylation (H_2–Pd–C) led to (X).‡ Treatment of (X) with methyl iodide gave the same methiodide, m.p. 228—230°, as that previously isolated and proved by synthesis,[3] (lit. m.p. 228—230°). The materials had identical i.r. and n.m.r. spectra. In addition, (IX) was characterized by its spectra and those of its diacetate.

When the reaction mixture from (III) was benzylated,

† The electrolyses were carried out in wet acetonitrile (10% water) using a graphite felt anode and a platinum cathode and $(Et)_4NClO_4$ as electrolyte. An excess of NaOMe (3·3 mols per mol of compound) was present, and the potentials were controlled with a potentiostat against a standard calomel electrode. Oxidations of (I) and (II) were carried out at potentials of +0·1 V in a two-compartment cell. Compound (III) was oxidized at +0·3 V in a one-compartment cell, for general procedures see ref. 5.

‡ Direct reduction of the phenols (IX and XI) without blocking them by benzylation led to difficulties and decomposition.

reduced, and debenzylated as described above, a product was obtained which gave (XII), m.p. 110—111°, (lit.[8] 109—110°) (8%) yield on preparative t.l.c.; its i.r. spectrum was identical with and its n.m.r. spectrum was essentially similar to those of natural dauricine. It yielded a crystalline distyphnate, m.p. 147—150°, (lit.,[8] 146—149°). The ethoxycarbonyl (XI) was not isolated.

Compounds (IX), (X), and (XII) may represent mixtures of diastereoisomers or (±) enantiomers. This ambiguity existed in the previous work which yielded the known materials for comparison.[3,8] We hope to extend our studies to optically pure samples of (III) in order to resolve this.

We thank the National Science Foundation and the National Institutes of Health for financial support.

(*Received, March 29th*, 1971; *Com.* 412.)

[1] B. Franck, G. Blaschke, and G. Schlingloff, *Angew. Chem. Internat. Edn.*, 1964, **3**, 192.
[2] M. P. Cava and K. T. Buck, *Tetrahedron*, 1969, **25**, 2795.
[3] A. M. Choudhury, I. G. C. Coutts, A. K. Durbin, K. Schofield, and D. J. Humphreys, *J. Chem. Soc.* (*C*), 1969, 2070.
[4] Y. Inubushi, Y. Aoyagi, and M. Matsuo, *Tetrahedron Letters*, 1969, 2363.
[5] J. M. Bobbitt, H. Yagi, S. Shibuya, and J. T. Stock, *J. Org. Chem.*, in the press.
[6] T. Kametani, "The Chemistry of the Isoquinoline Alkaloids," Hirokawa Publishing Co., Inc., Tokyo, 1968, p. 25.
[7] J. M. Bobbitt, J. M. Kiely, K. L. Khanna, and R. Ebermann, *J. Org. Chem.*, 1965 **30**, 2247.
[8] T. Kametani and K. Fukumoto, *J. Chem. Soc.* (*C*), 1964, 6141.