Sequential Intermediates in the Doebner–Miller Reaction

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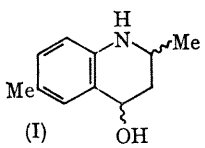
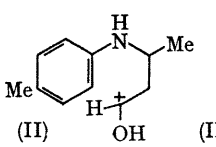
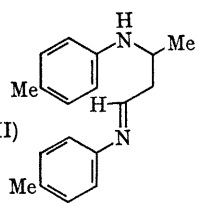
THE mechanism of the Doebner–Miller reaction has been the subject of much speculation.[1] Two isomeric alcohols (I) were isolated from the reaction of *p*-toluidine with acetaldehyde in aqueous hydrochloric acid at room temperature.[2] The formation of (I) was considered by later workers[3] to be evidence for the ring closure *via* the protonated aldehyde (II). A further product of this reaction,[2] isolated after a shorter time, was assigned the double Schiff base structure (III). We have isolated this compound and found that it has the structure (IV); n.m.r.: τ 7·74 and 7·80 (each s, aromatic Me), 8·87 (d, other Me, J 6 Hz), 6·50 (m, 2-H), 8·6 and 7·7 (3-H, AB portion of an ABXY system; J_{AB} 12·5, J_{AX} 11, J_{AY} 11, J_{BX} 2·5, J_{BY} 5·5 Hz), (4-H), and 2·7—3·7 (aromatic protons).



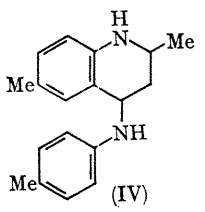
(I)



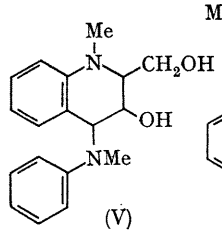
(II)



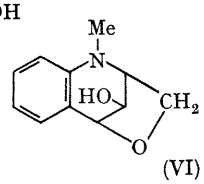
(III)



(IV)



(V)



(VI)

Thin-layer chromatography shows that the diamine (IV) is formed initially and disappears as the alcohols (I) are formed. The fact that (IV) is a precursor of (I) indicates that the ring closure occurs *via* a Schiff base and not the free aldehyde. Turner[4] has recently reported the isolation of a similar intermediate (V) which undergoes a displacement of *N*-methylaniline to give the compound (VI). This novel transformation is analogous to the normal course of the Doebner–Miller reaction except that the aromatic amine is displaced by an internal OH instead of water.

We thank the National Research Council of Canada for financial support.

(*Received, January 27th*, 1969; *Com.* 119.)

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[3] G. M. Badger, H. P. Crocker, B. C. Ennis, J. A. Gayler, W. E. Matthews, W. G. C. Raper, E. L. Samuel, and T. M. Spotswood, *Austral. J. Chem.*, 1963, **16**, 814.
[4] A. B. Turner, *Chem. Comm.*, 1968, 1659.