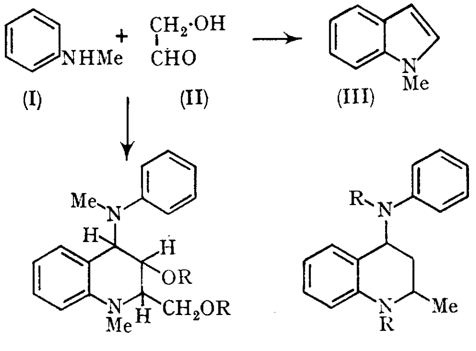
A Novel Transformation of a Doebner–Miller Intermediate

By A. B. TURNER

(*Department of Chemistry, University of Aberdeen, Aberdeen,* AB9 2UE)

CONDENSATION of *N*-methylaniline (I) with hydroxyacetaldehyde (II) in hot aqueous ethanol yields *N*-methylindole (III).[1] We have now found that the indole is not formed when the reaction is run at room temperature. Instead, the dimeric diol (IV), m.p. 163—165°, is obtained in 45% yield.† This forms a diacetate (V), m.p. 71—72°, the n.m.r. spectrum of which indicates that it is a single isomer. It shows the benzylic proton at C-4 as a doublet centred at τ 4·70 (J 11 Hz) and the C-3 proton as a quartet (τ 4·4; J 11, 5 Hz). The C-2 proton appears as a multiplet at τ 6·31, and the non-equivalent side-chain methylene protons resonate as a double quartet (τ 5·38 and 5·90; J 12, 6, 3·5 Hz).

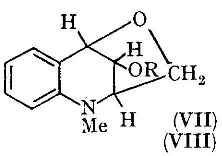
Related Doebner–Miller intermediates (VI) from the condensation of acetaldehyde with aniline and its alkyl derivatives have been extensively studied by Zalukaev and Spitsina.[2] These compounds are converted into quinolines by pyrolysis or acid treatment. The diol (IV) also readily loses methylaniline, on being heated at its melting point, but the tetrahydroquinoline structure is retained in the resulting secondary alcohol, m.p. 87—89°, which we formulate as the bridged compound (VII). Its n.m.r. spectrum shows that the protons on the heterocyclic ring are only weakly coupled (s, C-4 H, τ 5·47; d, C-3 H, τ 5·35, J 1·5 Hz; m, C-2 H, τ 6·48).



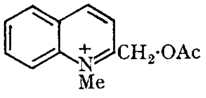
(I) (II) (III)

(IV) R=H
(V) R=Ac

(VI)



(VII) R=H
(VIII) R=Ac

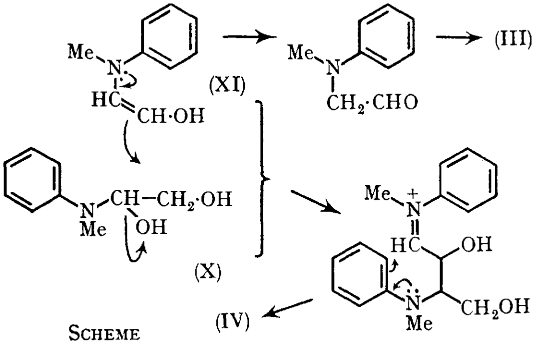


(IX)

---

† Satisfactory elemental analyses have been obtained for all new compounds reported.

The mass spectra of the bridged alcohol (VII), and its monoacetate (VIII), m.p. 70—71°, show strong ($M - 1$) peaks at m/e 190 and 232, respectively. The base peak in each spectrum is at m/e 144. This corresponds to the quaternary methylquinolinium ion, which apparently arises in both cases by the simultaneous cleavage of three bonds. The mass spectrum of the diol (IV) is also dominated by the m/e 144 ion, and peaks at m/e 191, 107, and 106 indicate a combination of electronic effects with the thermal process already described. The base peak in the spectrum of the diacetate (V) occurs at m/e 216, and corresponds to the quaternary quinoline (IX) resulting from loss of acetic acid and PhNMe. This diacetate (V) distils unchanged at 180° *in vacuo*, confirming hydroxy-group participation in the fragmentation of the diol (IV).



Scheme

The formation of indoles and tetrahydroquinolines in this reaction may be rationalised by the Scheme shown, in which the key intermediate is the enaminol (XI). This can either tautomerise to the aldehyde (XII), the likely precursor of the indole (III), or mount a nucleophilic attack upon the primary adduct (X), thereby providing a mechanism for the linkage of the two hydroxyacetoldehyde units. Further evidence for such a pathway, which does not require the intermediate formation of an $\alpha\beta$-unsaturated aldehyde, is currently being sought.

(*Received, October* 11*th*, 1968; *Com.* 1390.)

---

[1] J. Harley-Mason, *Chem. and Ind.*, 1955, 355; *cf.* A. B. Turner and H. C. S. Wood, *J. Chem. Soc.*, 1965, 5270.

[2] L. P. Zalukaev, *Doklady Akad. Nauk S.S.S.R.*, 1956, **110**, 791; L. Zalukaev and L. Y. Spitsina, *Zhur. obshchei Khim.*, 1961, **31**, 3067; 1964, **34**, 3392.