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APPLICATION OF THE FISCHER INDOLE SYNTHESIS TO THE PREPARATION OF BENZOFURANS

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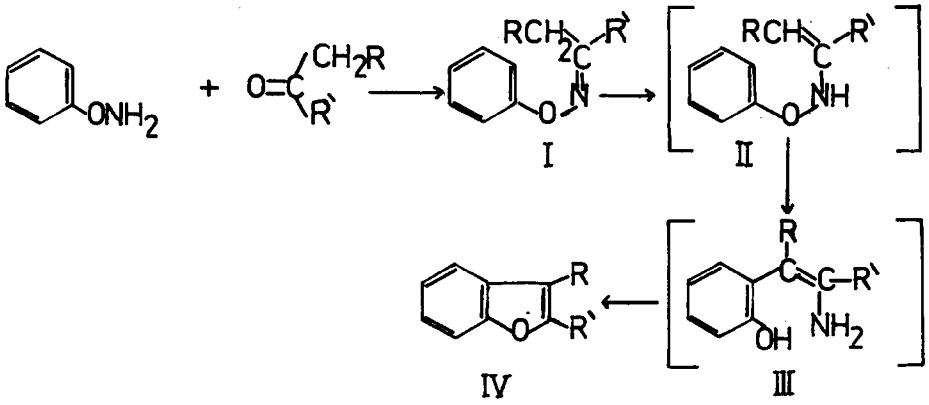
The Fischer cyclization of phenylhydrazones to indoles is considered to be the most versatile synthesis of indole derivatives (1). We studied its application to the synthesis of other heterocyclic systems isoelectronic with indoles and wish to report here the extension of this procedure to the cyclization of O-phenyloximes to benzofurans.



The starting O-phenyloximes (I) were prepared by refluxing equimolar amounts of the appropriate carbonyl compound and O-phenylhydroxylamine (2) in ethanol containing a trace of hydrochloric acid. Evaporation yielded crude compounds of type I which were used for the next step without furthur purification. Pure samples of I were obtained by vacuum distillation as colourless liquids which decomposed rapidly and turned dark red within a few hours. The compounds prepared are: acetone O-phenyloxime (Ia), b.p. 84-85°/10 mm, n_D^{24} 1.5989, (Found: N, 9.4. $C_9H_{11}NO$ requires: N, 9.4); acetophenone O-phenyloxime (ib), b.p. 94-96°/3 mm, n_D^{24} 1.5871, (Found: N, 6.9. $C_{14}H_{13}NO$ requires: N, 6.7); cyclohexanone O-phenyloxime (Ic), b.p. 84-85°/6 mm, n_D^{24} 1.5460, (Found: N, 7.5. $C_{12}H_{15}NO$ requires: N, 7.4).

Boron trifluoride etherate in acetic acid (3) at 100° was used as cyclization catalyst. Reaction times were 30 minutes for Ia and Ib and 2 hours for Ic. The benzofurans were isolated after pouring the reaction mixture into water. The compounds prepared are (4): (yields are based on the starting ketones) 2-methylbenzofuran (IVa) (71%) b.p. 190-191°, n_D^{24} 1.5551, picrate m.p. 73-76°; 2-phenylbenzofuran (92%) m.p. 121°, λ_{max}^{EtOH} 302 mμ (log ε 4.36), 314 mμ (log ε 4.22); 1,2,3,4-tetrahydrobiphenyleneoxide (IVc) (74%), b.p. 152-155/20 mm, n_D^{24} 1.5674 λ_{max}^{EtOH} 251 mμ (log ε 4.03) 277 mμ (log ε 3.51) 284 mμ (log ε 3.41), picrate m.p. 97-98°.

The mechanism of the reaction is probably similar to the one suggested for the indole synthesis (1) and proceeds through intermediates II and III.

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