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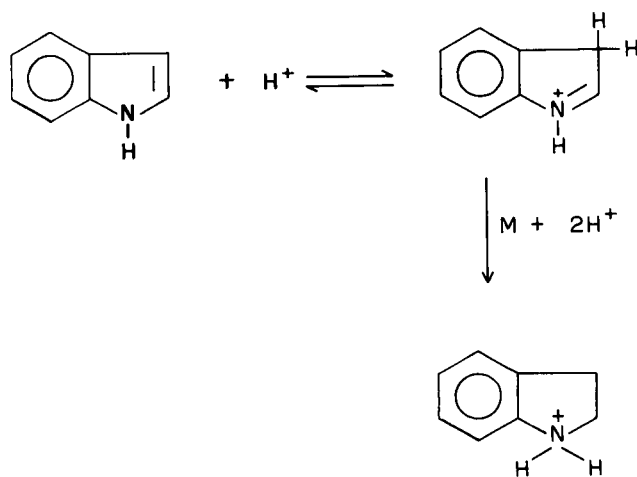
A Convenient Preparation of Indoline (1)

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An efficient method for chemically reducing indole to indoline using zinc dust and 85% phosphoric acid is described. 2,3-Dimethylindole, 1,2,3,4-tetrahydrocarbazole and *N*-methyl-1,2,3,4-tetrahydrocarbazole are also reduced to the corresponding dihydroindoles in somewhat lower yields. Unlike earlier acid-metal reductions of indole little or no polymerization is observed.

Substituted indoles may be reduced in useful yields with tin or zinc dust and hydrochloric acid (4, 5), but indole itself undergoes rapid polymerization (6) under these conditions. The electrolytic reduction of indole gives poor yields and is accompanied by polymer (7).

Recent observations on the behavior of indole in strong acid (8) suggested that metal reductions of indole itself might be accomplished in strongly acidic media. These conditions appeared promising because the conjugate acid of indole is stable only in very acidic media and metal reductions of indole probably take place on the conjugate acid.



When indole was heated with zinc dust and 85% phosphoric acid for 3-4 hours, indoline was obtained in 64-69% yield (9). There was no evidence of the bright orange polymer that forms when hydrochloric acid is used in the reduction. The attempted reduction of indole using Perkin's (5) procedure for the reduction of tetrahydrocarbazole yielded polymeric material and no indoline was obtained. Similarly, when indole was treated with tin and hydrochloric acid at room temperature for 24 hours, no acid-soluble compounds were formed.

Reduction of 2,3-dimethylindole with zinc dust and 85% phosphoric acid afforded a mixture of *cis* and *trans*-2,3-dimethylindoline in 28% yield based on unrecovered 2,3-dimethylindole. The 2,3-dimethylindoline was found to contain approximately 65% of the *cis* isomer and 35% of the *trans* isomer by vapor phase chromatography. The two isomers could be distinguished from comparison of their n.m.r. spectra which have been reported by Anet (10). The tin-hydrochloric acid reduction of 2,3-dimethylindole has been reported to give *cis* and *trans*-2,3-dimethylindoline in the ratio of 3:2 (11).

Similarly, 1,2,3,4-tetrahydrocarbazole, when heated with zinc dust and 85% phosphoric acid, gave pure *cis*-1,2,3,4,4a,9a-hexahydrocarbazole in 49% yield based on unrecovered tetrahydrocarbazole. The reduction appeared to give nearly exclusively *cis* isomer as none of the higher melting *trans* form could be obtained by fractional crystallization of the mother liquors. However, a small amount of the *trans* isomer could go undetected. Perkin (5) reported that the tin-hydrochloric acid reduction of 1,2,3,4-tetrahydrocarbazole gives about 98% of the *cis*-1,2,3,4,4a,9a-hexahydrocarbazole.

Similar reduction of *N*-methyl-1,2,3,4-tetrahydrocarbazole with zinc dust and 85% phosphoric acid gave 67% of crude *N*-methyl-1,2,3,4,4a,9a-hexahydrocarbazole based on unrecovered starting material.

When tin was used in place of zinc dust 1,2,3,4-tetrahydrocarbazole gave no identifiable reduction product but starting material was recovered in 81% yield.

EXPERIMENTAL

General.

All melting points and boiling points are uncorrected. Infrared spectra were determined in chloroform solution with a Beckman IR-5A infrared spectrophotometer and ultraviolet spectra were measured either with a Cary Model 11 spectrophotometer or with a Perkin-Elmer Model 202 spectrophotometer. Anhydrous potassium carbonate was used to dry solutions.

Zinc Dust and Phosphoric Acid Reduction of Indole.

To 23.5 g. (0.36 mole) of untreated zinc dust in a nitrogen atmosphere was added all at once 200 ml. of 85% phosphoric acid. The mixture was rapidly heated to 70-80° on a steam bath and 14.0 g. (0.12 mole) of indole was added in portions during 30 minutes with vigorous mechanical stirring (12). After the addition was complete stirring was continued for 3-4 hours at 80° under nitrogen. Water (100 ml.) was added with cooling and the mixture was basified slowly with 40% aqueous sodium hydroxide. The thick white slurry was steam distilled and extraction of the distillate with chloroform gave, after drying and concentration *in vacuo*, a light yellow oil. Distillation under reduced pressure gave 9.2 g. (64%) of indoline as a colorless oil, b.p. 80-81° (3 mm.) (lit. (13) b.p. 70-75° (2mm.)). The infrared and ultraviolet spectra were superimposable with those of authentic indoline. The picrate, m.p. 174-175° (lit. (14) m.p. 174°), was prepared in the usual manner.

Reduction of 2,3-Dimethylindole.

The same conditions, as described for indole, gave only 4.5% *cis* and *trans* 2,3-dimethylindoline with the recovery of 49% 2,3-dimethylindole.

The use of a cosolvent facilitated addition and increased the yields in all reductions except with indole.

To 13.6 g. (0.21 mole) of zinc dust under nitrogen was added 200 ml. of 85% phosphoric acid and a solution of 7.6 g. (0.052 mole) of 2,3-dimethylindole in 75 ml. of methylene chloride. The temperature was kept at 80-90° with vigorous stirring for 4 days. The mixture was diluted with water and extracted with ether to remove any acid-soluble starting material. This extract yielded 2.5 g. (33%) of crude 2,3-dimethylindole. Basification of the acidic reaction mixture and ether extraction gave a dark oil. Distillation under reduced pressure gave 1.44 g. (19%) of 2,3-dimethylindoline (approximately 65% *cis* - 35% *trans* by vapor phase chromatography on carbowax) b.p. 98-99° (8 mm.) (lit. (15) *cis*, b.p. 74° (2 mm.); *trans*, b.p. 107-109° (12 mm.)). The n.m.r. spectra of samples collected by vapor phase chromatography were in good agreement with those reported by Anet (10).

Reduction of 1,2,3,4-Tetrahydrocarbazole.

To 19.9 g. (0.30 mole) of zinc dust and 200 ml. of 85% phosphoric acid under nitrogen at 80° was added over a 30 minute period 13.0 g. (0.076 mole) of 1,2,3,4-tetrahydrocarbazole as a solution in 75 ml. of methylene chloride. Vigorous stirring at 80-90° was maintained for 24 hours. Dilution with water and extraction of the acid-insoluble material gave 7.9 g. (61%) of crude 1,2,3,4-tetrahydrocarbazole. The mixture was basified and extracted to give 2.5 g. of crude solid. Crystallization from aqueous methanol gave 2.0 g. (19%) of *cis*-1,2,3,4,4a,9a-hexahydrocarbazole as white needles, m.p. 98-99.5° (lit. (5) *cis*, m.p. 99°; *trans*, m.p. 127°). Further concentration of the mother liquors gave none of the *trans* isomer.

Reduction of *N*-methyl-1,2,3,4-Tetrahydrocarbazole (16).

To 5.9 g. (0.09 mole) of zinc dust and 100 ml. of 85% phosphoric acid was added 3.34 g. (0.018 mole) of *N*-methyl-1,2,3,4-tetrahydrocarbazole in 40 ml. of methylene chloride. The mixture was stirred at 90° under nitrogen for 20 hours. The usual workup gave 1.84 g. (58%) of crude starting material and 0.94 g. (28%) of *N*-methyl-1,2,3,4,4a,9a-hexahydrocarbazole as a yellow oil which was not further purified.

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