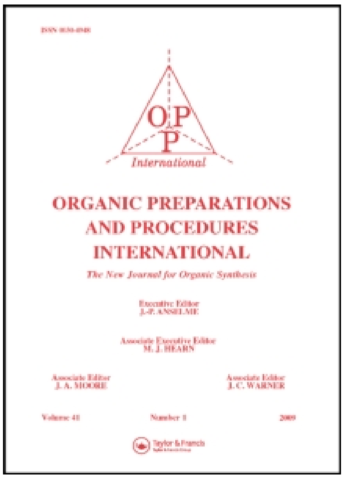

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IMPROVED PROCEDURE FOR THE DISSOLVING METAL REDUCTION OF INDOLE AND CARBAZOLE

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IMPROVED PROCEDURE FOR THE DISSOLVING METAL REDUCTION OF INDOLE AND CARBAZOLE

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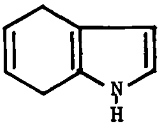
We now report improved procedures for the Birch reduction of indole (I) and carbazole (II) to the corresponding dihydroderivatives III and IV, respectively.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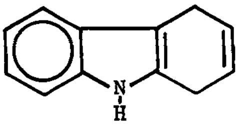
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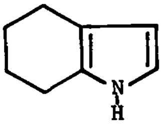
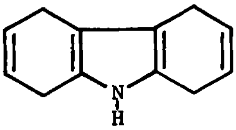

V


VI

Previously III had been prepared as an equimolar mixture[1] with IV and in pure form[2] (63% by gc, purified by preparative gas chromatography) by the dissolving-metal reduction of indole in liquid ammonia. We have been able to increase the yield of III to 80% (by nmr) on a preparative scale by the slow, portionwise addition of lithium wire and methanol to a solution of indole dissolved in methanol (one equiv.) and liquid ammonia at -78°. III was isolated in pure form, bp. 102.5°/5.5 mm, mp. 40-41°, lit.[2] 37-39°, by fractionation of the crude Birch-reduction product through a spinning band column (isolated yeild, 51%).

Attempted preparation of IV by the literature procedure[1] gave a mixture of IV and VI as a difficultly separable pair, with VI predominating. Alteration of the procedure to the use of lithium/isopropanol/liquid ammonia at -78° instead of sodium/ethanol/liquid ammonia, gave IV in 73% yield (recrystallized), mp. 222-224°, lit.[1] mp. 180-210°.

EXPERIMENTAL

All reactions were conducted under a nitrogen atmosphere. Infrared spectra were recorded on a Perkin-Elmer Model 137 spectrophotometer, nmr on a Varian A-60D spectrometer, ultraviolet spectra (in methanol) on a Cary 14 spectrophotometer, and mass spectra on a Hitachi Perkin-Elmer RMU-6D spectrometer. Melting and boiling points are uncorrected. Mallinckrodt AR-grade isopropanol and methanol were used as received.

4,7-Dihydroindole (III).-To a dry, 3-l., three-necked flask equipped with a mechanical stirrer, Dewar condenser and gas inlet and outlet tubes were added 176 g (1.5 moles) of indole and 66 ml (1.5 moles) of methanol. The flask and condenser were cooled to -78° and about 2 l. of liquid ammonia (directly from the commercial cylinder) were condensed into the flask. Lithium wire (41.6 g, 5.95 moles) and methanol (132 ml, 3.0 moles) were slowly added in alternating proportions. The temperature of the reaction was maintained at -78°. After all the lithium had reacted, an nmr spectrum of an aliquot was taken to ensure complete reduction of the indole. The ammonia was removed by evaporation. Distilled water (700 ml) and ether (2 l.) were cautiously added to the residue and the phases were separated. After the aqueous phase was extracted with two 450-ml portions of ether, the organic extracts were combined, dried with $MgSO_4$ and filtered. The crude product remaining after solvent removal was fractionated through a spinning band column (48-inch, stainless steel in this instance, although a shorter column with a Teflon band was equally effective), yielding pure 4,7-dihydroindole as a colorless oil that solidified on standing; yield, 92 g, 51%; mp. 40-41.5°; bp. 102.5°/5.5 mm; mp. 41-42° after crystallization from pentane (recovery very nearly quantitative), lit.[2] 37-39°; nmr (CCl_4/TMS) δ 3.11 (s, 4H), 5.81 (m 3H), 6.40 (t, J = 3Hz, 1H), 7.17 (broad s, 1H); infrared 3400 cm^{-1} (N-H).

1,4-Dihydrocarbazole (IV).-To a dry, 3-l., three-necked flask equipped with a mechanical stirrer, Dewar condenser and gas inlet and outlet tubes were added 50 g (0.30 mole) of carbazole. The flask and condenser were cooled to -78° and about 1.5 liters of liquid ammonia were condensed into the flask from the commercial cylinder. Lithium wire (7.08 g, 1.01 moles) and isopropanol (100 ml) were added in alternating portions. The reaction was maintained at -78°. An nmr spectrum of an aliquot was taken after all of the lithium had reacted to ensure complete reduction of the carbazole. After the ammonia had been allowed to evaporate, distilled water (500 ml) and ether (2 l.) were cautiously added. The aqueous phase was extracted with methylene chloride (2 x 1.0 l.). The ether and methylene chloride phases were combined, dried over $MgSO_4$, filtered and concentrated by solvent evaporation. The crude product was crystallized from absolute ethanol (1800 ml, that had been flushed out with nitrogen) to yield 37 g (73%) of white plates: mp. 222-224°, lit.[1] 180-210°; nmr (d_6-acetone/TMS) δ 3.40 (s, 4H), 5.95 (s, 2H), 6.90-7.50 (m, 4H), N-H not observed; infrared (Nujol) 3400 cm^{-1} (N-H); ultraviolet (methanol) 226 nm (ε 21,000), 278 nm (ε 4,200), 287 nm (sh, ε 3,500); mass spectrum m/e 169 (P^+ 75%, base peak 168).

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