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Reduction of 2-Methyl β-Carboline Anhydronium Base by Sodium Borohydride

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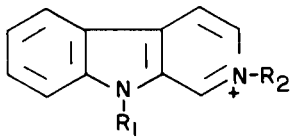
In connection with another synthetic problem we undertook the reduction of a complex β-carbolinium salt (I, R_1 = H) with sodium borohydride. In the course of the reaction the β-carbolinium salt underwent an immediate color change from yellow to deep orange when treated with sodium borohydride, and this color slowly faded to afford the final reduction product (*cf.* II). The color change suggested intermediate formation of a β-carboline anhydronium base (III) that occurs when certain β-carbolinium salts (I, R_1 = H) are allowed to react with alkali (I).

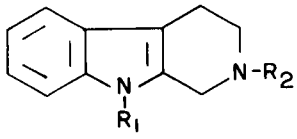
To determine whether this course of the reaction was feasible, and in particular whether the β-carboline anhydronium bases (III) can be reduced under these mild conditions since contrary claims have been made (2), we examined separately the behavior of 2-methyl-β-carboline anhydronium base (III, R_2 = CH_3) toward sodium borohydride. In both cases the same product, identified as 2-methyl-1,2,3,4-tetrahydro-β-carboline (II, R_1 = H, R_2 = CH_3) was obtained as the sole isolable product in good yield.

Earlier Witkop had shown that semperverine methochloride (partial structure I, R_1 = CH_3) could be reduced by sodium borohydride to a perhydro-derivative analogous to II, but he reported that neither semperverine, corresponding to the β-carboline anhydronium base (*cf.* III) nor the anhydronium base from α-carboline (IV) was affected by sodium borohydride (2). Still in the α-carboline series, compound V which is incapable of anhydronium base formation was reduced, presumably to VI. By contrast with Witkop's findings, Gray, Spinner and Cavallito were able to reduce harman methobromide, which is 1,2-dimethyl-β-carbolinium bromide, but they did not explore the behavior of the anhydronium base toward this reagent (3).

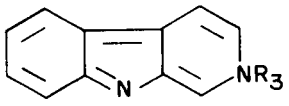
Our reductions were carried out in aqueous methanol (4), and under these conditions the β-carboline anhydronium base is reduced efficiently to the 1,2,3,4-tetrahydro-β-carboline derivative.



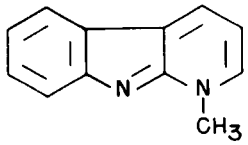
I



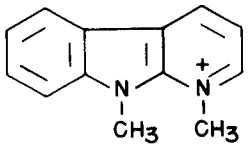
II



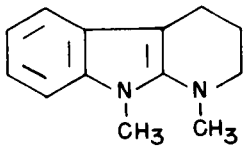
III



IV



V



VI

EXPERIMENTAL

Melting points were taken on a Mel-temp apparatus (Laboratory Devices, Cambridge, Mass.) and corrected. Analytical work was done by Schwarzkopf Microanalytical Laboratory.

β-Carboline.

This compound was prepared by the procedure of Speitel and Schlittler and had a melting point of 199-200° (lit. (5) m.p. 199-200°). The methiodide was prepared in benzene-methanol solution and isolated as yellow needles, m.p. 234-236° (lit. (5) m.p. 239-241°).

β-Carboline anhydronium base was obtained by treating the methiodide with aqueous sodium hydroxide and had a melting point of 212-214° (lit. (1a, 5) m.p. 212-214°).

2-Methyl-1,2,3,4-tetrahydro-β-carboline. (a) By Reduction of β-Carboline Methiodide.

The methiodide salt (0.8 g.) in aqueous methanol (25 ml.; 1:1 V/V) was treated with sodium borohydride (0.4 g.). The solution deepened in color to orange, and within a minute a colorless solid began to separate. After 10 minutes the mixture was warmed on a steam bath for 10 minutes and cooled. The tetrahydro-β-carboline (0.41 g., 89%) was obtained as colorless needles, m.p. 216-217° (lit. (6) m.p. 217-218°).

Anal. Calcd. for $C_{12}H_{14}N_2$: C, 77.38; H, 7.58; N, 15.04. Found: C, 77.47; H, 7.47; N, 14.86.

A methiodide of *N*-methyltetrahydro-β-carboline was prepared in benzene, m.p. 260-262° (lit. (6) m.p. 265°). A picrate, isolated from methanol, had a melting point of 197-198° (lit. (6) m.p. 197-198°).

(b) Reduction of *N*-Methyl β-Carboline Anhydronium Base.

The anhydronium base (0.5 g.) in a mixture of methanol (10 ml.) and water (5 ml.) was treated with sodium borohydride (0.3 g.). After about one minute a slow evolution of gas began, the solution became slightly warm and the color slowly disappeared. A colorless solid precipitated, and the mixture was heated for 5 minutes on a steam bath. The product was isolated as small glistening crystals, 0.35 g., m.p. 212-216°. Recrystallization from aqueous methanol raised the melting point to 216-217°. The mixture melting point with 2-methyl-1,2,3,4-tetrahydro-β-carboline was not depressed and the infrared spectra of the two were identical.

REFERENCES

(1) For a summary of the chemistry of β-carboline anhydronium bases and references see: (a) I. D. Spenser, *J. Chem. Soc.*, 3659 (1956). (b) W. O. Kermack and J. E. McKail, "Heterocyclic Compounds," Vol. 7, R. C. Elderfield, Ed., John Wiley and Sons, Inc., New York, N. Y., 1961, p. 273.

(2) B. Witkop, *J. Am. Chem. Soc.*, 75, 3361 (1953); B. Witkop and J. B. Patrick, *ibid.*, 75, 4475 (1953).

(3) A. P. Gray, E. E. Spinner and C. J. Cavallito, *ibid.*, 76, 2792 (1954).

(4) Water seems to be essential for clean reductions of enamines by sodium borohydride; R. Mirza, *J. Chem. Soc.*, 4400 (1957).

(5) R. Speitel and E. Schlittler, *Helv. Chim. Acta*, 32, 860 (1949).

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