

REDUCTIONS OF ACRIDINE BY METAL-AMMONIA SOLUTIONS

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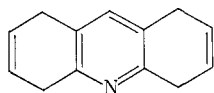
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Introduction

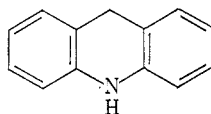
The pyridine ring readily takes up one or two electrons from metal-ammonia solutions. The products of protonation consist frequently of dimeric dihydro derivatives, but there is indirect evidence¹ of formation of some dihydropyridine. In the hope of obtaining more stable crystalline products to enable examination to be made of mechanisms, we have examined the reduction of acridine.

Reductions of Acridine

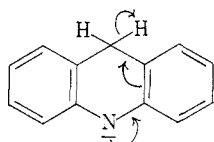
Using a large excess of reagent, acridine was converted by lithium and ethanol in ammonia into 1,4,5,8-tetrahydroacridine (I), the structure of which is based on reactions, analyses, and spectra. Oxidation with lead tetraacetate² regenerated acridine quantitatively, and hydrogenation using tris(triphenylphosphine)rhodium chloride gave 1,2,3,4,5,6,7,8-octahydroacridine.



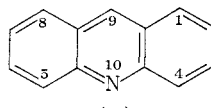
(I)



(II)



(III)



(IV)

Anthracene under similar reduction conditions gives 1,4,5,8,9,10-hexahydroanthracene (e.g.³) and the survival of the pyridine ring was puzzling. Reduction of acridine in an ammonia solution buffered with ammonium acetate (cf.⁴) gave 9,10-dihydroacridine in which the pyridine ring alone is reduced. To see whether this compound could be an intermediate in reduction to (I), its reaction with lithium and ethanol in ammonia was examined and (I) was indeed formed. No dimeric products were observed in either type of reaction, probably because of steric inhibition of dimerization through the 10-position.

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¹ Birch, A. J., *J. chem. Soc.*, 1947, 1270.

² Birch, A. J., Fogiel, A., and Harvey, G. J., *Aust. J. Chem.*, 1954, 7, 261.

³ Harvey, R. G., and Urberg, K., *J. org. Chem.*, 1968, 33, 2570.

⁴ Birch, A. J., Hextall, P., and Sternhell, S., *Aust. J. Chem.*, 1954, 7, 256.

Discussion of Results

The second reaction seems to indicate that the pyridine ring, as expected, readily takes up electrons, and this was further confirmed by reaction of acridine with lithium and methyl iodide to produce 9,10-dihydro-9,10-dimethylacridine. That a dihydropyridine ring has been re-aromatized by oxidation during work-up seems to be excluded by carrying this out under nitrogen with the same result. A possible explanation is the elimination of metal hydride, known to occur from dihydro-benzenes by the action of the metal amide.⁵ The ethoxide anion is probably basic enough to equilibrate with NH of a dihydropyridine to generate the anion and re-aromatize (III) \rightarrow (IV). The result indicates once again⁴ the importance of exact details of experimental conditions.

The method is a simple one for producing (I) which is a new compound.

Experimental

1,4,5,8-Tetrahydroacridine

Acridine (5 g) in tetrahydrofuran (100 ml) and ethanol (50 ml) was added to ammonia (500 ml) freshly distilled from sodium. Lithium (3 g) was added with stirring; water was added after 30 min and the crystalline precipitate removed by filtration. The product gave one peak on gas chromatography. It was passed through alumina in benzene to remove some yellow colour and crystallized from ethanol. The 1,4,5,8-tetrahydroacridine (3.1 g) had m.p. 130.5° (Found: C, 85.2; H, 7.3; N, 7.4. $C_{13}H_{13}N$ requires C, 85.2; H, 7.1; N, 7.6%). λ_{\max} (ethanol) 283 m μ ; m/e 183; ν_{\max} 1662, 1710 (CH=CH), 1601, 1573 (pyridine), and 888 cm⁻¹ (CH in tetrasubstituted pyridine); τ (CDCl₃) 2.89 (one proton, aromatic), 4.1 q (four protons, CH=CH), 6.55 and 6.60 (CH₂ groups).

Hydrogenation in benzene with tris(triphenylphosphine)rhodium chloride, followed by filtration through Florisil, gave 1,2,3,4,5,6,7,8-octahydroacridine, m.p. 70° (lit.⁶ m.p. 69°); τ 2.96 s (one proton), 7.25 m (eight protons), and 8.19 t (eight protons).

9,10-Dihydroacridine

Acridine (2.5 g) in tetrahydrofuran (50 ml) and acetic acid (15 ml) was added to ammonia (250 ml) followed by lithium (2 g). Dilution with water and crystallization of the product from ethanol gave 9,10-dihydroacridine, m.p. 170° undepressed by an authentic specimen.

Reductive Methylation

Acridine (1.5 g) in tetrahydrofuran (50 ml) and ammonia (300 ml) was treated with lithium (0.4 g) and methyl iodide (5 ml) added. The ammonia was evaporated, water was added, and the product crystallized from aqueous ethanol after chromatography on alumina (benzene-light petroleum), m.p. 139° (lit.⁷ 140°); τ 8.65 d (three protons), 6.65 s (three protons), 6.05 q (one proton), 2.90 m (eight protons).

Acknowledgment

One of us (H.H.M.) is indebted to the Romanian Academy of Science for leave of absence.

⁵ Birch, A. J., *J. chem. Soc.*, 1947, 1642.

⁶ Gill, N. S., James, K. J., Lions, F., and Potts, K. T., *J. Am. chem. Soc.*, 1952, 74, 4923.

⁷ Semon, W. L., and Craig, D., *J. Am. chem. Soc.*, 1936, 58, 1278.