Benzoheterocycles *via* Aryne C–C Cyclisation: 2-Methylisoindole

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Summary 2-Methylisoindole is obtained in high yield by the reaction of *N*-methyl-2-chlorobenzylaminoacetonitrile with potassamide in liquid ammonia.

METHODS used for the synthesis of isoindoles have recently been reviewed.[1] Most of those which involve simple stages rely upon prior formation and isolation of an isoindoline or a related cyclic compound, elimination from an isoindoline with the leaving group on nitrogen being an example.[1,2]

Treatment of *N*-methyl-2-chlorobenzylaminoacetonitrile† in liquid ammonia with potassamide (4 equiv.) over 0·5 h and quenching with ammonium nitrate gave 2-methylisoindole (89%). The m.p.,[3–5] u.v.,[6] and n.m.r. spectra, and the 1,3,5-trinitrobenzene adduct were consistent with 2-methylisoindole. Its identity was further confirmed by its reduction ($NaBH_4$–EtOH) to 2-methylisoindoline (identified by i.r.,[4] n.m.r., and analysis). Reduction was only efficient with an acid (HCl) work-up, suggesting that the reduction is actually of a protonated species.‡

In the formation of 2-methylisoindole it is considered that cyclisation to 1-cyano-2-methylisoindoline occurs first followed by hydrogen cyanide elimination to yield the isoindole. It is not known whether cyanide is eliminated from an anion following proton abstraction from C-1 and proton shift (or direct abstraction from C-3) or is eliminated first to give a cationic isoindolenine followed by proton loss and rearrangement.

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† Prepared by treating 2-chlorobenzyl chloride with methylaminoacetonitrile.

‡ Although acetic acid work-up of borohydride mixtures has been shown to cause generation of diborane (J. A. Marshall and W. S. Johnson, *J. Amer. Chem. Soc.*, 1963, **28**, 421, 595), because of the presence of ethanol and water in the reaction mixture we favour the suggestion made in the text.

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