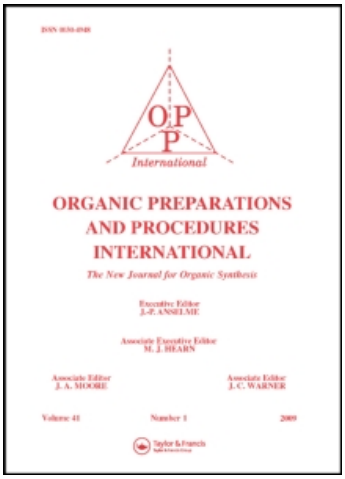


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# 4-NITROISOQUINOLINE

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# 4-NITROISOQUINOLINE

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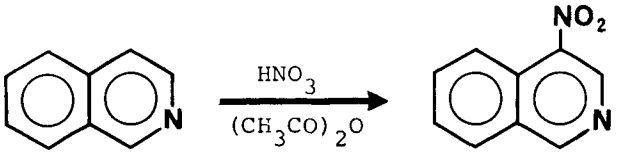


The only syntheses of 4-nitroisoquinoline from isoquinoline reported in the literature are multistep routes.[1,2] Although both quinoline and isoquinoline are most readily nitrated in the benzene ring under the usual nitrating conditions,[3] Dewar and Maitlis have shown that nitration of quinoline in acetic anhydride gives 3-nitroquinoline as the major nitration product, although only in 6% yield.[4] We have found that under similar conditions, the nitration of isoquinoline also occurs predominantly in the pyridine ring at a position meta to the ring-nitrogen atom (i.e. at C-4). Although the yield of purified material is only 14%, this is a more direct and more convenient route to this compound than either of the routes previously described.

## EXPERIMENTAL

Concentrated nitric acid (5 ml) was slowly added to a solution of 10g. (0.083 mole) isoquinoline in 100ml of

acetic anhydride. The solution was heated with stirring on a steam bath for 1 hr. then poured over 300g. of crushed ice. After neutralization with conc. aqueous ammonia, the resulting solution was extracted with chloroform (3 x 150 ml). The combined chloroform extracts were washed with hydrochloric acid (1N; 4 x 100 ml) to remove isoquinoline, and dried over anhydrous magnesium sulfate. Removal of the solvent gave a residue which was dissolved in anhydrous ether. After removing any insoluble material, the hydrochloride salt of 4-nitroisoquinoline was precipitated by bubbling hydrogen chloride through the ethereal solution. An aqueous solution of this hydrochloride salt in the minimum amount of water was extracted with chloroform (3 x 50ml), and after having been dried over magnesium sulfate, this extract was evaporated. The formation of the hydrochloride salt and its reconversion to the free base was repeated. The total yield of product obtained in this fashion was 1.5g, mp. 58-60°.

A further 0.4g. of 4-nitroisoquinoline may be obtained by neutralization of the original acid extracts to pH 2, extraction with chloroform, and isolation of the product via the hydrochloride salt as described above. Total yield of 4-nitroisoquinoline 1.9 g. (14%). Recrystallisation from aqueous ethanol gave pale yellow needles, mp. 63°, lit.[1,2] mp. 64°.

Nmr ($CDCl_3$): δ9.36(s, 1H), 9.19(s, 1H), 8.56(doublet of doublets, 1H, J = 9 and 1.5 cps), 7.6 - 8.1 (m, 3H).

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