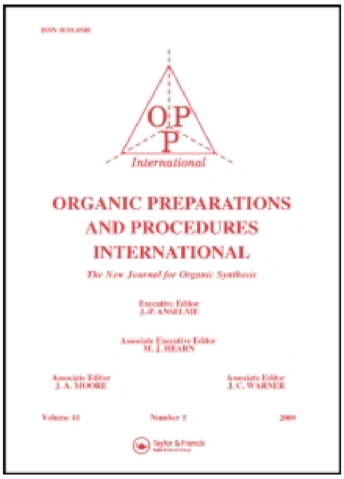

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PREPARATION OF 3-BROMO-4-NITROPYRIDINE 1-OXIDE

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PREPARATION OF 3-BROMO-4-NITROPYRIDINE 1-OXIDE

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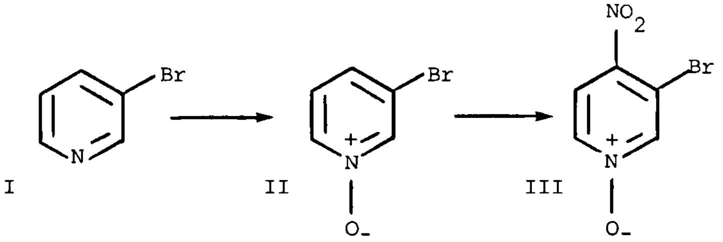
The preparation of 3-bromo-4-nitropyridine 1-oxide (III) from 3-bromopyridine (I) has been described by several workers.



In the initial synthesis,[1] the intermediate 3-bromopyridine 1-

oxide (II) was isolated as the hydrochloride salt which was then nitrated and assumed to give III; the overall yield was low. This route was modified by den Hertog et al.[2] who reported that the conversion of I to II took ten days using perphthalic acid and the phthalate salt was then nitrated using fuming nitric acid. The overall yield of III was only 30%, even after ether extraction of the mother liquor. Okuda et al.[3] improved the overall yield slightly by using peracetic acid for the oxidation step, isolating II as the hydrochloride and nitrating the hydrochloride salt. Matsumura[4] repeated the method of Okuda et al.[3] and obtained a 53% overall yield.

We now report a simplified one-pot method which gave consistent yields of III over 75%.

EXPERIMENTAL SECTION

CAUTION! *Because of the potential hazards associated with the use of hydrogen peroxide, protective clothing as well as eye goggles and gloves should be worn. All operations must be performed in an efficient hood behind a safety shield.*

A mixture of 3-bromopyridine (50.0 g, 0.316 mol), hydrogen peroxide solution (30% v/v, 117 ml) and glacial acetic acid (117 ml) was heated at 60° for 48 hrs. The resulting light yellow solution was carefully evaporated under reduced pressure using a rotary evaporator with the water bath maintained at 50° until the excess acetic acid and hydrogen peroxide was removed. The residue was cooled to between -5 and 0° and conc. sulphuric acid (63 ml) slowly added keeping the temperature at 0°. The resulting solution was then added carefully to a mixture of conc. nitric (94 ml) and sulphuric (83 ml) acids also at 0°. When the addition was complete, the mixture was heated slowly to 90° over 1 hr., kept at this temperature for a further 2 hrs. and then at 100° for another hr. The reaction mixture was then cooled to room temperature, poured onto ice (2 Kg) and the resulting mixture neutralized with sodium hydroxide solution (4N) to pH 4-5, the temperature not being allowed to rise above 20°. The crude precipitate was collected, dried and recrystallized from benzene to give 54.0 g (78%) of 3-bromo-4-nitropyridine 1-oxide (III) as long yellow needles, mp. 152-153°, lit.[2,4] mp. 152-153°; IR(KBr): 3060, 1590, 1550, 1500, 1440, 1340, 1290, 1255 cm^{-1};PMR ($CDCl_3$): δ 7.95 (d, 1H, J = 6.0 Hz, ring 5H), 8.13 (q, 1H, J = 6.0, 1.5 Hz, ring 6H); 8.44 (d, 1H, J = 1.5 Hz, ring H, 2H).

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