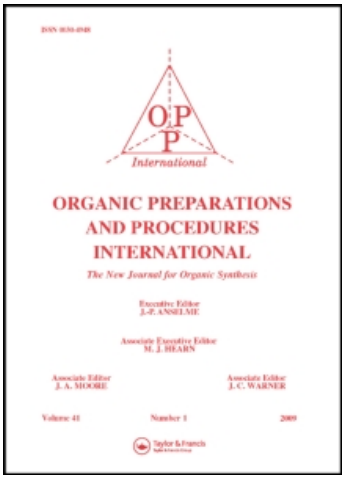

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IMPROVED SYNTHESIS OF 3-DIMETHYLAMINOPYRIDINE

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IMPROVED SYNTHESIS OF 3-DIMETHYLAMINOPYRIDINE

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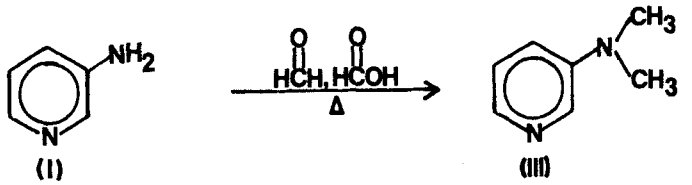
3-Dimethylaminopyridine was needed as a part of a study concerning structure-activity relationships in heterocyclic amines. The procedure of Binz and Schickh[1] gave a mixture of 3-methylaminopyridine (II) and the desired 3-dimethylaminopyridine (III), characterized by their proton NMR spectra and mass spectral analysis. The ^{1}H NMR spectrum of 3-methylaminopyridine exhibited a broad amino proton (δ = 4.50 ppm; 1H, exchangeable with D_2O). However, the work-up leads to an excessive amount of emulsion, which makes isolation of the products a tedious endeavor. Other procedures appeared either impractical[2,3] or were published without synthetic details[4]. We report a facile, good yield synthesis (64-70%) of 3-dimethylaminopyridine (III) using formaldehyde and formic acid[5].



(I) (III)

EXPERIMENTAL

Mps. were determined on a Buchi melting point apparatus with a calibrated thermometer and are corrected. Infrared spectra were measured with a Beckman Model IR-8 Grating Spectrometer. NMR spectra were recorded on a Varian Model EM-360 Spectrometer with TMS as an internal standard. Mass spectra were recorded on a CEC 21-104 Mass Spectrometer. Elemental analyses were performed by the TAMU Center for Trace Characterization, College Station, Texas.

3-Dimethylaminopyridine (III). - To the purple solution of 3-aminopyridine (18.8 g; 0.2 mole) in 90% formic acid (51.2 g; 1 mole) was added 40% formaldehyde (45 ml; 0.6 mole). The resulting mixture was heated at 100-105° for 8 hrs.; carbon dioxide evolution was noticeable after 5 minutes. The brown mixture was then treated with 4N HCl (100 ml) and taken to near dryness in vacuo (0.8 mm). The resulting yellow solid was dissolved in distilled water (75 ml) and made basic with 18N NaOH (50 ml). The dark brown organic layer was removed. The aqueous layer was extracted with benzene (3 x 50 ml). The combined organic and benzene layers were dried twice (K_2CO_3), filtered and the benzene removed in vacuo. The orange oil was distilled in vacuo giving 17.1 (70%) of III: bp. 58-60°/0.05 mm; lit.[1] 108-110°/12 mm, lit.[4] 95°/6 mm, lit.[6] 106-9°/6.5-7 mm; NMR ($CDCl_3$) δ 2.79 (s, 6, $-CH_3$), 6.95 (m, 2, ring protons 4 and 5), 8.00 (d, 1, ring proton 2), 8.15 (d, 1, ring proton 6); Mass Spec. M = 122(5.6%), M-1 = 121 (87.5%), M-2 = 120(100%). Its picrate was obtained by addition of a saturated solution of picric acid in 95% ethanol (5 ml) to a solution of 3-dimethylaminopyridine (III) (1.22g; 1 mmole) in 95% ethanol (5 ml). Yellow needles formed immediately. After two recrystallizations from methanol, the yellow picrate melted between 184-185°, lit.[4] 179-181°, lit.[6] 174-175°.

Anal. Calcd. for $C_{13}H_{13}N_5O_7$: C, 44.45; H, 3.73; N, 19.94; O, 31.88

Found: C, 44.16; H, 3.74; N, 19.54, O, 32.36

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