Chemistry of Heterocyclic Compounds, Vol. 40, No. 7, 2004

CYCLIZATION OF N,N-BIS(2-CHLOROETHYL)-METHYLAMINE IN AQUEOUS HYDRAZINE

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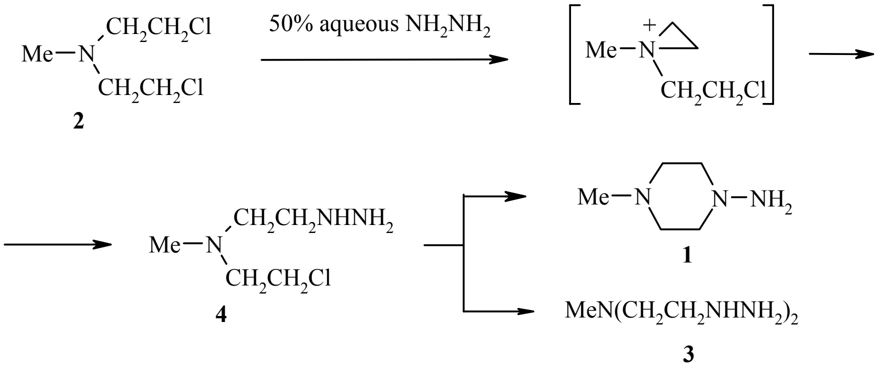
Keywords: 1-amino-4-methylpiperazine, haloalkylamines, N-(2-chloroethyl)-N-(2-hydrazinoethyl)-methylamine.

1-Amino-4-methylpiperazine (**1**) is widely used as an intermediate in synthesis of medicinal drugs [1]. Several methods for obtaining it are known. A method based on a two-step scheme has been used industrially, starting from piperazine and followed by its nitrosation and reduction [2, 3].

We have obtained compound **1** for the first time by reaction of N,N-bis(2-chloroethyl)methylamine (**2**) with an aqueous solution of hydrazine, and we have also developed an efficient method for its isolation. Analysis of the literature [3, 4] allowed us to determine the optimum ratio of the reagents when the dihalo derivative is used as the substrate. In the temperature range 40-50°C, the ratio of the reagents is substrate **1**:N_2H_4 (50%) 1:10.

Analysis of the reaction mass using GLC data, chromatography/mass spectrometry, and ^{13}C NMR showed that along with the target product **1**, a number of impurities are formed which we identified.



In particular, using chromatography/mass spectrometry, we observed formation of up to 2% N,N-bis(2-hydrazinoethyl)methylamine (**3**). For less than 80% conversion of substrate **2**, we identified N-(2-chloroethyl)-N-(2-hydrazinoethyl)methylamine (**4**) in the reaction mass.

Along with the identified compounds **1, 3, 4**, the compounds remaining in the vat after distillation of the target product **1** evidently can be assigned as quaternary ammonium bases [3, 4].

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1-Amino-4-methylpiperazine (1). N,N-bis(2-chloroethyl)methylamine hydrochloride (51.0 g, 0.265 mol) was added to a 50% aqueous solution of hydrazine (132 ml, 2.65 mol). The mixture was held for 2 h at 50°C. The reaction mass was evaporated under vacuum to dryness. A 1 M sodium hydroxide solution (100 ml) was added to the dry residue, and the mixture was stirred for 40 min. The precipitate was filtered out. The filtrate was distilled under vacuum. Yield 26.5 g (87%); bp 128-131°C (13 mm Hg). ^{13}C NMR spectrum (D_2O), δ, ppm: 57.51 (C(2), NCH_2); 54.15 (C(3), CH_2N); 45.01 (C(1), CH_3). Mass spectrum (electron impact, 70 eV), *m/z* (I_{rel}, %): 116 $[M+1]^+$ (5.5), 115 $[M]^+$ (79.5), 99 $[M–NH_2]^+$ (73.9), 98 $[M–NH_3]^+$ (21.3), 58 $[M–CH_3N(CH_2)_2]^+$ (20.6), 57 $[M–NH_2N(CH_2)_2]^+$ (24.5). Found, %: C 52.58; H 11.21; N 36.39. $C_5H_{13}N_3$. Calculated, %: C 52.14; H 11.38; N 36.48.

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