A Convenient Preparation of Acetamididine

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Surprisingly, no satisfactory procedure for the preparation of crystalline acetamidine seems to exist in the literature. Contrary to a previous report, we have found that deprotonation of acetamidinium chloride with sodium methoxide in methanol, followed by vacuum distillation and recrystallization, affords a satisfactory yield of acetamidine, stable at room temperature, but undergoing decomposition to ammonia and acetonitrile at 95 °C.

Experimental. A solution of acetamidine hydrochloride (9.4 g) in methanol (35 ml) was added in one portion to a sodium methoxide solution, prepared from sodium (2.3 g) and methanol (25 ml). The suspension was stirred and cooled in ice water for 10 min, filtered through Celite, concentrated in vacuo, and distilled. Yield 4.1 g (70%), b.p. 82 – 85 °C/10 mmHg, m.p. 59 – 66 °C. The distillate did not crystallize spontaneously at room temperature (20 °C), but crystallization took place at 0 °C. Recrystallization from methylene chloride (10 ml) at 0 °C gave colourless needles. Yield 3.53 g (61%), m.p. 65 – 67 °C. Repeated recrystallization raised the m.p. 66 – 67 °C. Standard microanalysis gave erratic results due to the very hygroscopic character of the compound. Titration with nitric acid to pH 7 in water gave equivalent weight 58.5 (M = 58.0). MS [IP 70 eV; m/z (% rel. int.)]: 58 (100, M), 43 (79), 42 (75) 41 (28). CI (isobutane) MS [m/z]: 59. 1H NMR (90 MHz, CDCl3): δ 1.97, 5.7 (s, variable δ, H on N), 7.38 (CHCl3, due to exchange of deuterium with hydrogen. The sum of integrals at δ 5.7 and 7.38 is equal to the integral at δ 1.97). After 2 h at 20 °C a triplet appeared. δ 1.96, J(D,H) 2 Hz. 13C NMR (CDCl3, 22.93 MHz, 1H decoupled): δ 23.2, 165.4, 77.6 (CHCl3 from deuterium exchange). The product has a mousy odor.

The stability was evaluated by keeping acetamidine (100 mg) in an evacuated ampoule (10 ml) at 95 °C for 12 h. The ampoule was cooled (0 °C) and carefully opened (pressure, ammonia) and shown (NMR, G.C.) to contain acetamidine (30%) and acetonitrile (70%).

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