NITROALKYL DERIVATIVES OF SOME HETEROCYCLIC COMPOUNDS

I. Synthesis from Methyl γ-Methyl-γ-nitrovalerimidate Hydrochloride

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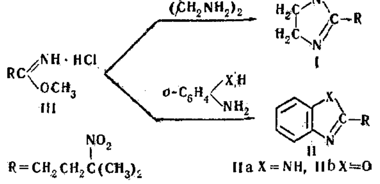
The 2-(γ-methyl-γ-nitrobutyl) derivatives of 2-imidazoline, benzimidazole, and benzoxazole and 2,4,6-tris-(γ-methyl-γ-nitrobutyl)-1,3,5-triazine have been synthesized. The nitroalkyl derivatives of 2-imidazoline and benzimidazole have been reduced to the corresponding 2-aminoalkyl derivatives.

Nitroalkyl derivatives of 2-imidazoline, benzimidazole, and benzoxazole and methods for their synthesis have been studied comparatively little [1].

In this paper we describe the preparation of 2-(γ-methyl-γ-nitrobutyl)-2-imidazoline (I), 2-(γ-methyl-γ-nitrobutyl)benzimidazole (IIa), and 2-(γ-methyl-γ-nitrobutyl)benzoxazole (IIb) by the condensation of methyl γ-methyl-γ-nitrovalerimidate hydrochloride (III) with ethylenediamine, o-phenylenediamine, and o-aminophenol, respectively.



2,4,6-Tris(γ-methyl-γ-nitrobutyl)-1,3,5-triazine (IV) was synthesized by heating methyl γ-methyl-γ-nitrovalerimidate (IIIa) in the presence of a small amount of its hydrochloride (III).

The reduction of I and II by the action of zinc and hydrochloric acid in ethanol gave, respectively, 2-(γ-methyl-γ-aminobutyl)-2-imidazoline (V) and 2-(γ-methyl-γ-aminobutyl)benzimidazole (VI).

EXPERIMENTAL

Methyl γ-methyl-γ-nitrovalerimidate hydrochloride (III). Dry hydrogen chloride was slowly passed into a solution of 7.1 g (0.05 mole) of γ-methyl-γ-nitrovaleronitrile [2] and 1.6 g (0.05 mole) of anhydrous methanol in 20 ml of absolute ether at 0 to 5° C until a white crystalline precipitate of III had deposited. The reaction mixture was left overnight at 0° C, and then the precipitate was filtered off, washed with ether, and dried over caustic soda. Yield 10.15 g (96.4%) of III with mp 96–96.5° C (from a mixture of acetic acid and ether). Found, %: Cl 16.85, 16.90; N 13.21, 13.24. Calculated for $C_7H_{14}N_2O_3 \cdot HCl$, %: Cl 16.83; N 13.30.

Methyl γ-methyl-γ-nitrovalerimidate (IIIa) was obtained by the action of aqueous caustic soda on III at –5 to –10° C; yield 82%, bp 81–83° C (0.5–1 mm); d_4^{20} 1.086; n_D^{20} 1.4590. Found, %: N 15.82, 15.88. MR_D 43.84. Calculated for $C_7H_{14}N_2O_3$%: N 16.08. MR_D 44.22.

2,4,6-Tris(γ-methyl-γ-nitrobytyl)-1,3,5-triazine (IV). A mixture of 1.74 g (0.01 mole) of IIIa and 0.05 g of III was heated in a distillation flask until methanol ceased to distil over. The yield of IV was 1.3 g (94%), mp 123.5–124° C (from ethanol). Found, %: C 50.54, 50.58; H 7.01, 7.02; N 19.88, 19.84. Calculated for $H_{30}N_6O_6$, %: C 50.69; H 7.09; H 19.71.

2-(γ-Methyl-γ-nitrobutyl)-2-imidazoline (I). Over 20 min with stirring at 0° C, 10.52 g (0.05 mole) of III was added to a solution of 3 g (0.05 mole) of ethylenediamine in 50 ml of absolute ethanol. The reaction mixture was stirred at 0° C for 1 hr and then an ethanolic solution of 1.9 g of dry hydrogen chloride was added in drops. After the mixture had reached room temperature, the ammonium chloride was filtered off and part of the ethanol was distilled off from the filtrate, which then, on cooling, deposited 8.4 g of the hydrochloride of I. The addition of ether to the mother solution furnished another 0.6 of the hydrochloride of I. Yield 90%, mp 191–192° C (from a mixture of ethanol and ether). Found, %: C 43.50, 43.46; H 7.26, 7.28; Cl 16.17, 16.20; N 18.83, 18.88. Calculated for $C_8H_{15}N_3O_2 \cdot HCl$, %: C 43.34; H 7.28; Cl 15.99; N 18.96. Compound I was obtained in the form of the free base by the action of caustic soda in ethanolic solution on its hydrochloride, mp 78–79° C (from a mixture of benzene and hexane).

2-(γ-Methyl-γ-nitrobutyl)benzimidazole (IIa). With stirring at room temperature, 4.21 g (0.02 mole) of III was added to a solution of 2.16 g (0.02 mole) of o-phenylenediamine in 20 ml of absolute ethanol. Then the reaction mixture was heated at 50–55° C for 1 hr, cooled, and treated with 30 ml of water. The precipitate of IIa that deposited was filtered off, washed with water, and dried over phosphorus pentoxide. Yield 3.97 g (86%), mp 218–219° C (from a mixture of ethanol and water). Found, %: C 61.98, 61.90; H 6.50, 6.46; N 17.81, 17.87. Calculated for $C_{12}H_{15}N_3O_2$, %: C 61.79; H 6.48; N 18.01.

2-(γ-Methyl-γ-nitrobutyl)benzoxazole (IIb). Compound IIb was prepared from III and o-aminophenol by the procedure described for IIa. After the addition of water to the reaction mixture, the oil formed was extracted with ether, and the ethereal solution was dried over magnesium sulfate. After the ether had been driven off, the IIb crystallized; yield 97%, mp 53–54° C (from hexane). Found, %: C 61.56, 61.50; H 5.98, 5.97; N 11.87, 11.90. Calculated for $C_{12}H_{14}N_2O_3$, %: C 61.53; H 6.02; N 11.96.

2-(γ-Methyl-γ-aminobutyl)-2-imidazoline (V). With stirring at 40–50° C, 10.5 g of zinc dust was added to 5.5 g (0.025 mole) of the hydrochloride of I and 50 ml of conc HCl in 50 ml of ethanol. Then the reaction mixture was boiled for 1 hr, cooled, filtered, and made alkaline by the addition of caustic soda. Then it was filtered again and the filtrate was evaporated to dryness. The compound was extracted with ether, the ethereal solution was dried with caustic soda, and the ether was distilled off; the residual oil crystallized after several days over caustic soda in a vacuum desiccator. The yield of V was 2.85 (72%), mp 68–69° C (from petroleum ether). The **dihydrochloride** obtained by passing dry hydrogen chloride into an ethereal solution of V, melted at 209–210° C (from a mixture of ethanol and ether). Found, %: C 41.86, 41.80, H 8.17, 8.23, Cl 31.30, 31.32, N 18.18, 18.26. Calculated for $C_8H_{17}N_3 \cdot 2HCl$, %: C 42.11; H 8.39; Cl 31.08; N 18.42.

2-(γ-Methyl-γ-aminobutyl)benzimidazole (VI) was prepared by reducing IIa by the method described for V. Extraction was carried out with isopropanol. Yield 83%. The dipicrate of VI had mp 215–216° C (from ethanol). Found, %: C 43.44, 43.40, H 3.48, 3.48, N 19.32, 19.36. Calculated for $C_{12}H_{17}N_3 \cdot 2C_6H_3N_3O_7$, %: C 43.58; H 3.50; N 19.06.

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