SYNTHESIS OF SOME sym-TRIAZOLE DERIVATIVES

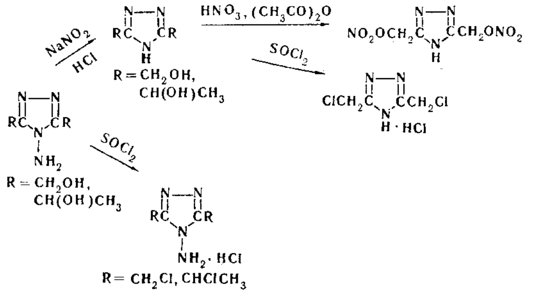
S. S. Novikov, V. M. Brusnikina, and V. A. Rudenko

Khimiya Geterotsiklicheskikh Soedinenii, Vol. 5, No. 1, pp. 157–158, 1969

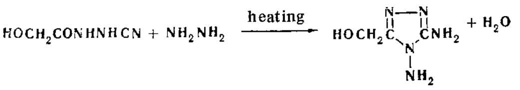
UDC 547.792.1.3.07

3, 5-Di(hydroxyalkyl) derivatives of 4-amino-1, 2, 4-triazole and the corresponding derivatives of 1, 2, 4-triazole obtained by diazotizing them are converted by reaction with $SOCl_2$ into the hydrochlorides of 4-amino-3, 5-di(chloroalkyl)-1, 2, 4-triazoles and 3, 5-di(chloroalkyl)-1, 2, 4-triazoles. The dinitrate of 3, 5-di(hydroxymethyl)-1, 2, 4-triazole has been prepared. When the cyanohydrazide of glycolic acid is heated with hydrazine hydrate, 4, 5-diamino-3-hydroxymethyl-1, 2, 4-triazole is formed.

During a study of the behavior of heterocyclic amines in the Mannich reaction, we obtained 4-amino-3, 5-di(hydroxymethyl)-1, 2, 3-triazole and 4-amino-3, 5-di(α-hydroxyethyl)-1, 2, 4-triazole [1]. In accordance with the known deamination of N-amino heterocyclic compounds under diazotization conditions, these 4-amino-1, 2, 4-triazole derivatives have been converted into 3, 5-di(hydroxymethyl)- and 3, 5-di(α-hydroxyethyl)-1, 2, 4-triazoles, respectively. The action of $SOCl_2$ on 3, 5-di(hydroxymethyl)-, 3, 5-di(α-hydroxyethyl)-, and 4-amino-3, 5-di(hydroxymethyl)- and 4-amino-3, 5-di(α-hydroxyethyl)-1, 2, 4-triazoles forms the hydrochlorides of the corresponding dichloro derivatives of sym-triazole (These substances actively attack the skin, and therefore the work must be carried out using rubber gloves in a hood):



Nitration of 3, 5-di(hydroxymethyl)-1, 2, 4-triazole with a mixture of nitric acid and acetic anhydride forms 3, 5-di(hydroxymethyl)-1, 2, 4-triazole dinitrate. Action of cyanogen bromide on glycolic hydrazide gives the cyanohydrazide of glycolic acid, heating which with hydrazine hydrate leads to the formation of 4, 5-diamino-3-hydroxymethyl-1, 2, 4-triazole:



EXPERIMENTAL

3, 5-Di(hydroxymethyl)-1, 2, 4-triazole. With cooling (5–10° C), 0.0105 mole of sodium nitrite in 10 ml of water was added to a solution of 0.01 mole of 4-amino-3, 5-di(hydroxymethyl)-1, 2, 4-triazole in 10 ml of water. The resulting solution was evaporated on the water bath and the solid residue (1.65 g) was extracted with n-butanol, to give 0.9 g of 3, 5-di(hydroxymethyl)-1, 2, 4-triazole, yield 75%, mp 139–140° C (from acetonitrile or nitromethane). Found, %: C 37.05, 36.74; H 5.58, 5.64; N 32.45, 32.67. Calculated for $C_4H_7N_3O_2$, %: C 37.21; H 5.43; N 32.59. Picrate, mp 92–93° C. Found, %: C 32.20, 32.40; H 3.21, 3.13; N 22.89, 23.03. Calculated for $C_4H_7N_3O_2 \cdot C_6H_3N_3O_7$, %: C 32.61; H 2.72; N 22.82.

3, 5-Di(α-hydroxyethyl)-1, 2, 4-triazole. Hydrogen chloride was passed into a solution of 0.01 mole of 4-amino-3, 5-di(α-hydroxyethyl)-1, 2, 4-triazole in 25 ml of ethanol to saturation, and then the ethanol was distilled off and the residue was dissolved in 15 ml of water and, with cooling (~10° C) and stirring, 0.0105 mole of sodium nitrite in 10 ml of water was carefully added. Then the mixture was evaporated to dryness on the water bath and extracted with n-butanol, and the solvent was driven off to give 3, 5-di(α-hydroxyethyl)-1, 2, 4-triazole, yield 73%, mp 124–124.5° C (from acetonitrile). Found, %: C 46.19, 46.19; H 7.16, 7.25; N 26.98, 27.24. Calculated for $C_6H_{11}N_3O_2$, %: C 45.86; H 7.00; N 26.75.

4-Amino-3, 5-di(chloromethyl)-1, 2, 4-triazole hydrochloride. In small portions, 0.044 mole of 4-amino-3, 5-di(hydroxymethyl)-1, 2, 4-triazole was added to 10 ml of $SOCl_2$, the mixture was left overnight, and the crystals that had precipitated (~10.5 g) were recrystallized from ethanol or water to give 8.1 g of 4-amino-3, 5-di(chloromethyl)-1, 2, 4-triazole hydrochloride, yield 84%, mp 138–139° C. Sometimes an oil deposited, for the crystallization of which it was necessary to add a small amount of ethanol, cool, and rub with a glass rod. Found, %: C 22.05, 22.25; H 3.61, 3.61; Cl 37.39, 48.55. Calculated for $C_4H_6Cl_2N_4 \cdot HCl$, %: C 22.08; H 3.24; Cl 48.90.

4-Amino-3, 5-di(α-chloroethyl)-1, 2, 4-triazole hydrochloride. A solution of 0.029 mole of 4-amino-3, 5-di(α-hydroxyethyl)-1, 2, 4-triazole in 40 ml of ethanol was saturated with HCl, and then the ethanol was driven off and the residue was treated with 15 ml of $SOCl_2$ and left overnight. The excess of $SOCl_2$ was distilled off in vacuum, giving an oil which chrystallized on standing; the yield of 4-amino-3, 5-di(α-chloroethyl)-1, 2, 4-triazole hydrochloride was 75%, mp 153–153.5° C (from acetonitrile). Found %: C 30.01, 30.06; H 4.67, 4.67; N 22.86, 22.79. Calculated for $C_6H_{10}Cl_2N_4 \cdot HCl$, %: C 29.34; H 4.51; N 22.81.

3, 5-Di(chloromethyl)-1, 2, 4-triazole hydrochloride. With stirring, 0.015 mole of 3, 5-di(hydroxymethyl)-1, 2, 4-triazole was added to 15 ml of $SOCl_2$ and the mixture was boiled for 1 hr and left overnight, after which the crystals that had deposited were separated off and recrystallized from acetonitrile to give 1.57 g (61%) of 3, 5-dichloromethyl-1, 2, 4-triazole hydrochloride, mp 113–114° C. Found, %: C 23.25, 23.33; H 2.73, 2.61; N 21.07, 21.20. Calculated for $C_4H_5Cl_2N_3 \cdot HCl$, %: C 23.21; H 2.96; N 20.73.

3, 5-Di(hydroxymethyl)-1, 2, 4-triazole dinitrate. With cooling (~0° C), 5 ml of HNO_3 (d 1.5) and then 0.5 g of ammonium chloride were added to 5 ml of acetic anhydride and these were followed by 0.0075 mole of 3, 5-di(hydroxymethyl)-1, 2, 4-triazole. The mixture was kept at 0° C for 30 min and at 30–35° C for 1 hr and was then poured onto crushed ice (~50 g). On standing, a precipitate deposited which was filtered off, washed, and dried to give 0.45 g (26.9%) of 3, 5-di(hydroxymethyl)-1, 2, 4-triazole dinitrate, mp 118–118.5° C. Found, %: C 22.23, 22.36; H 2.66, 2.70; N 31.70, 31.98. Calculated for $C_4H_5N_5O_6$, %: C 21.96; H 2.28; N 31.96.

4, 5-Diamino-3-hydroxymethyl-1, 2, 4-triazole. A solution of 35 g (0.33 mole) of cyanogen bromide in 450 ml of water was added to a solution of 31.5 g (0.35 mole) of glycolic hydrazide and 35 g of $KHCO_3$ in 100 ml of water, and the mixture was left overnight. The following day it was evaporated in vacuum at a temperature not exceeding 45° C, the residue was treated with 200 ml of boiling ethanol, the ethanolic solution was evaporated, and the residue was extracted with boiling acetone to give 28.6 g (71%) of glycolic cyanohydrazide, mp 140–141° C. Found, %: C 31.19, 31.10; H 4.45, 4.61; N 36.46, 36.22. Calculated for $C_3H_5N_3O_2$, %: C 31.31; H 4.38; N 36.51.

A mixture of 10 g (0.087 mole) of glycolic cyanohydrazide and 10 ml of hydrazine hydrate was boiled for 5 hr and the excess of hydrazine hydrate was distilled off with the water liberated in the reaction, giving a viscous mass which was treated with ethanol to yield 4.8 g (42.8%) of 4, 5-diamino-3-hydroxymethyl-1, 2, 4-triazole, mp 179–180° C (from ethanol). Found, %: C 28.54, 28.33; H 5.76, 5.66; N 53.96, 53.96. Calculated for $C_3H_7N_5O$, %: C 27.90; H 5.46; N 54.24.

REFERENCE

1. V. M. Brusnikina, S. S. Novikov, and V. A. Rudenko, Izv. AN SSSR, OKhN, 1681, 1963.

12 October 1966

Zelinskii Institute of Organic
Chemistry AS USSR,
Moscow