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SHORT COMMUNICATIONS

Heterocyclization of 3,5-Dibromo-1-(thiiran-2-ylmethyl)-1*H*-1,2,4-triazole into 5-Substituted 2-Bromo-5,6-dihydrothiazolo[3,2-*b*][1,2,4]triazoles

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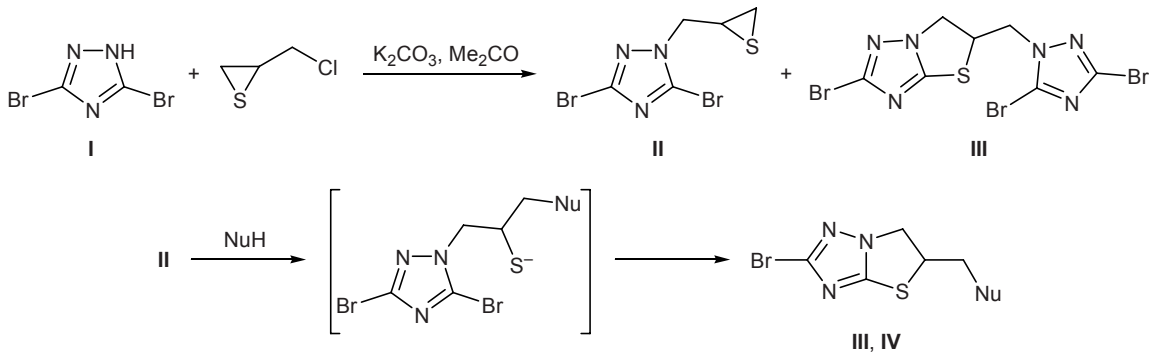
We previously found [1] that 3,5-dibromo-1*H*-1,2,4-triazole (**I**) reacts with 2-chloromethylthiirane in acetone in the presence of potassium carbonate to produce 2-bromo-5-(3,5-dibromo-1*H*-1,2,4-triazol-1-ylmethyl)-5,6-dihydrothiazolo[3,2-*b*][1,2,4]triazole (**III**). Our further studies showed that the reaction involves intermediate formation of 3,5-dibromo-1-(thiiran-2-ylmethyl)-1,2,4-triazole (**II**), and we succeeded in isolating the latter as individual substance by raising the amount of 2-chloromethylthiirane to 5 equiv. Some amount of thiazolotriazole **III** was also formed. Compound **II** was isolated by column chromatography in 29% yield.

The ^{1}H NMR spectrum of **II** contained multiplet signals from protons in the thiiranylmethyl fragment, which can be treated according to the first-order pattern. Protons in the endocyclic CH_2 group resonated at δ 2.20 and 2.31 ppm with a geminal coupling constant of 1.36 Hz. The SCH proton gave a multiplet at δ 2.93–3.03 ppm, and two doublets of doublets at δ 3.75 and 4.22 ppm were assigned to the exocyclic methylene group (NCH_2). In the ^{13}C NMR spectrum of **II** signals from carbon atoms in the thiiranylmethyl substituent and nonequivalent carbon atoms in the triazole ring (δ_C 129.32, 140.82 ppm) were observed. These data indicated that the alkylation of **I** occurred at the N^1 atom.

With a view to confirm intermediacy of thiirane **II** in the formation of thiazolotriazole **III**, compound **II** was brought into reaction with an equimolar amount of initial triazole **I** in acetone in the presence of potassium carbonate. As a result, we obtained 94% of **III**. A probable mechanism involves opening of the thiirane ring with formation of intermediate thiolate ion and subsequent intramolecular heterocyclization. Compound **III** thus obtained showed no depression of the melting point upon mixing with a sample prepared as described in [1], and their IR spectra were identical. It might be expected that other 5-substituted 5,6-dihydrothiazolo[3,2-*b*][1,2,4]triazoles could be synthesized by reaction of thiirane **II** with nucleophiles. In fact, the reaction of thiirane **II** with 3 equiv of morpholine afforded 2-bromo-5-(morpholinomethyl)-5,6-dihydrothiazolo[3,2-*b*][1,2,4]triazole (**IV**) in 52% yield.



III, Nu = 3,5-dibromo-1*H*-1,2,4-triazol-1-yl; **IV**, Nu = morpholino.

We can conclude that 3,5-dibromo-1-(thiiran-2-ylmethyl)-1,2,4-triazole is a promising building block for the synthesis of 5-substituted 2-bromo-5,6-dihydrothiazolo[3,2-*b*][1,2,4]triazoles via reactions with nucleophiles.

3,5-Dibromo-1-(thiiran-2-ylmethyl)-1,2,4-triazole (II). Triazole **I**, 7.26 g (32 mmol), was dissolved in 150 ml of acetone on heating, 4.41 g (32 mmol) of potassium carbonate and 17.38 g (160 mmol) of 2-chloromethylthiirane were added, and the mixture was heated for 3 h under reflux on a water bath. The mixture was cooled to room temperature and filtered, the filtrate was evaporated under reduced pressure, and the residue was treated with hexane. The hexane extract was evaporated, and the residue was subjected to column chromatography on silica gel using hexane–ethyl acetate (4:1) as eluent. Yield 2.80 g (29%), colorless oily substance, n_D = 1.6107, R_f = 0.71. ^{1}H NMR spectrum, δ, ppm: 2.20 d.d (1H, SCH_2, ^2J = 1.36, ^3J = 5.12 Hz), 2.31 br.d (1H, SCH_2, ^3J = 6.05 Hz), 2.93–3.03 m (1H, SCH), 3.75 d.d (1H, NCH_2, ^2J = 14.36, ^3J = 7.50 Hz), 4.22 d.d (1H, NCH_2, ^2J = 14.36, ^3J = 5.01 Hz). ^{13}C NMR spectrum, δ_C, ppm: 24.24 (SCH_2), 30.86 (SCH), 54.80 (NCH_2), 129.32 (C^3), 140.82 (C^5). Found, %: C 19.75; H 1.28; N 14.37. $C_5H_5Br_2N_3S$. Calculated, %: C 20.09; H 1.69; N 14.05.

2-Bromo-5-(3,5-dibromo-1*H*-1,2,4-triazol-1-ylmethyl)-5,6-dihydrothiazolo[3,2-*b*][1,2,4]triazole (III). *a*. The undissolved residue obtained after extraction with hexane in the synthesis of **II** was recrystallized from propan-2-ol. Yield 1.88 g (26%), mp 152–153°C, R_f 0.60.

b. Triazole **I**, 0.27 g (1.2 mmol), was dissolved in 20 ml of acetone on heating, 0.41 g (1.2 mmol) of potassium carbonate and 0.36 g (1.2 mmol) of thiirane **II** were added, and the mixture was heated for 3 h under reflux (on a water bath). The mixture was cooled to room temperature and filtered, the filtrate was evaporated under reduced pressure, the residue was treated with hexane, and the precipitate was filtered off. Yield 0.50 g (94%), mp 153–156°C (from butan-1-ol), R_f 0.60. IR spectrum, ν, cm^{-1}: 1451, 1431, 1286, 1261, 1224. Found, %: C 18.75; H 1.06; N 18.94. $C_7H_5Br_3N_6S$. Calculated, %: C 18.90; H 1.13; N 18.89.

2-Bromo-5-(morpholinomethyl)-5,6-dihydro-[1,3]thiazolo[3,2-*b*][1,2,4]triazole (IV). Morpholine, 0.26 g (3.0 mmol), was added to a solution of 0.29 g (1.0 mmol) of thiirane **II** in 10 ml of ethanol, and the mixture was heated for 3 h under reflux. The solvent was distilled off under reduced pressure, the residue was treated with water, and the precipitate was filtered off. Yield 0.18 g (52%), mp 162–163°C (from *i*-PrOH), R_f 0.56. ^{1}H NMR spectrum, δ, ppm: 2.45–2.64 m (4H, CH_2NCH_2), 2.77 d (2H, CH_2N, ^3J = 7.56 Hz), 3.62–3.78 m (4H, CH_2OCH_2), 4.18–4.28 m (1H, NCH_2), 4.32–4.42 m (1H, NCH_2), 4.55–4.67 m (1H, SCH). Found, %: C 35.42; H 4.29; N 18.36. $C_9H_{13}BrN_4OS$. Calculated, %: C 35.84; H 4.56; N 18.28.

The ^{1}H and ^{13}C NMR spectra were measured on a Bruker AM-300 instrument at 300 and 75 MHz, respectively, using CCl_4–C_6D_6 (**II**) or $CDCl_3$ (**IV**) as solvent; the chemical shifts were determined relative to signals from residual protons and carbon atoms in the solvents. The IR spectra were recorded in KBr on an Infralyum FT-02 instrument. The purity of the products was checked by TLC on Silufol plates using hexane–ethanol (1:4) as eluent; spots were visualized by treatment with iodine vapor.

REFERENCE

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