ISSN 1070-3632, Russian Journal of General Chemistry, 2006, Vol. 76, No. 7, pp. 1178–1180. © Pleiades Publishing, Inc., 2006.
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LETTERS TO THE EDITOR

Synthesis of 8-Piperidino-5,6-dihydro-4*H*-thiazolo[5,4-*c*]azepines and 8-Amino-5,6-dihydro-4*H*-bis[1,3]thiazolo-[3,2-*a*: 5′,4′-*c*]azepin-7-ium Chlorides

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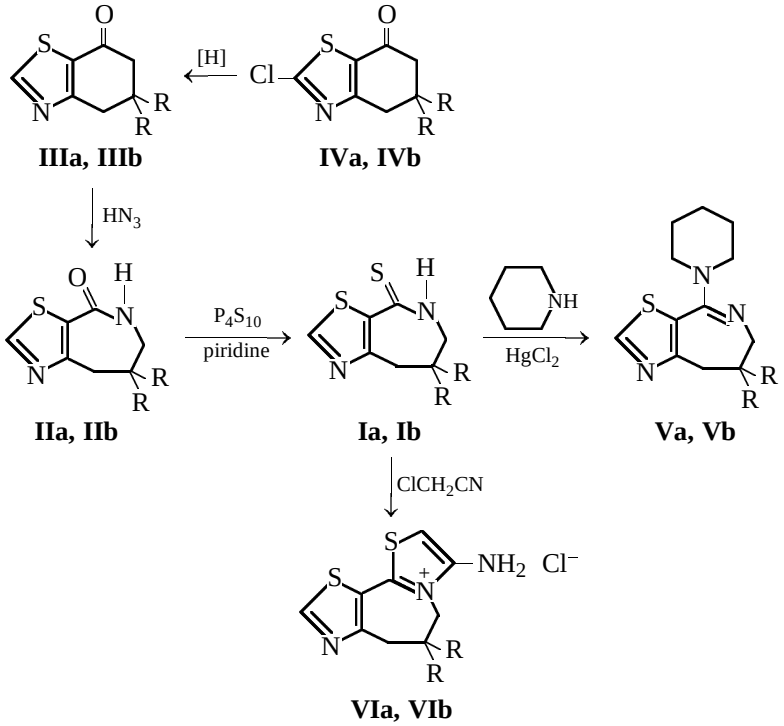
Received June 23, 2005

DOI: 10.1134/S1070363206070334

Continuing our studies in the field of thiazoloazepine chemistry [1] we synthesized thiazoloazepinethiones **Ia** and **Ib** by heating thiazoloazepinones **IIa** and **IIb** with P_4S_{10} in pyridine. The synthesis of compounds **IIa** and **IIb** having no substituent in the 2-position via reduction of the corresponding 2-chlorothiazoloazepinones was described previously [2]. Insofar as the yields of 2-chlorothiazoloazepinones [3] were relatively poor, we obtained ketones **IIIa** and **IIIb** by heating 2-chlorothiazolyl ketones **IVa** and **IVb** with reduced iron in a boiling solution of acetic acid in alcohol [3], and compounds **IIIa** and **IIIb** were then converted into thiazoloazepines **IIa** and **IIb** in 69–70% yield according to Schmidt under conditions similar to those given in [3]. Amidines **Va** and **Vb** were obtained by heating thiazoloazepinethiones



R = CH_3 (**a**), R = H (**b**).

Ia and **Ib** with piperidine in the presence of $HgCl_2$ to bind hydrogen sulfide liberated during the process. By reaction of thiazoloazepinethiones **Ia** and **Ib** with chloroacetonitrile were synthesized 8-amino-5,6-dihydro-4*H*-bis[1,3]thiazolo[3,2-*a*:5',4'-*c*]azepin-7-ium chlorides **VIa** and **VIb**.

5,5-Dimethyl-4,5,6,7-tetrahydrobenzothiazol-7-one (IIIa). Chlorothiazoloazepinone **IVa**, 4.95 g, was dissolved in 25 ml of ethanol, 5.2 g of reduced iron and 12.5 ml of acetic acid were added, and the mixture was heated for 40 h at the boiling point under stirring. The mixture was cooled and filtered, the solvent was distilled off from the filtrate, the residue was dissolved in diethyl ether, and the organic solution was washed with an aqueous solution of $NaHCO_3$ until neutral reaction and dried over Na_2SO_4. The product was purified by column chromatography on aluminum oxide using chloroform as eluent. Yield 3.62 g (87%). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.19 s (6H, Me_2C), 2.68 s (2H, 6-H), 3.01 s (2H, 4-H), 8.85 s (1H, 2-H). Found, %: C 59.66; H 6.14; N 7.71; S 17.67. *m/z* 181 $[M]^+$. $C_9H_{11}NOS$. Calculated, %: C 59.64; H 6.12; N 7.73; S 17.69. *M* 181.

4,5,6,7-Tetrahydrobenzothiazol-7-one (IIIb) was synthesized in a similar way from compound **IVb**. Yield 82%. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 2.06 m (2H, 5-H), 2.81 t (2H, 6-H, *J* = 6.5), 2.89 t (2H, 4-H, *J* = 6.2), 8.83 s (1H, 2-H). Found, %: C 54.85; H 4.63; N 9.42; S 20.90. *m/z* 153 $[M]^+$. C_7H_7NOS. Calculated, %: C 54.88; H 4.61; N 9.41; S 20.93. *M* 153. Compounds **IIIa** and **IIIb** were isolated as oily liquids.

5,5-Dimethyl-5,6,7,8-tetrahydro-4*H*-thiazolo[5,4-*c*]azepine-8-thione (Ia). Compound **IIa**, 1.96 g, was dissolved in 20 ml of pyridine, 3.7 g of P_4S_{10} was added, and the mixture was heated for 9 h under reflux. The solvent was distilled off, the residue was dissolved in chloroform, and the product was purified by column chromatography on aluminum oxide using chloroform as eluent. Yield 1.34 g (63%), mp 164C (from toluene). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.10 s (6H, Me2C), 2.94 s (2H, 4-H), 3.15 d (2H, 6-H, *J* = 6.7), 8.46 br.s (1H, 7-H), 8.77 s (1H, 2-H). Found, %: C 50.90; H 5.71; N 13.18; S 30.18. *m/z* 212 $[M]^+$. $C_9H_{12}N_2S_2$. Calculated, %: C 50.91; H 5.70; N 13.19; S 30.20. *M* 212.

5,6,7,8-Tetrahydro-4*H*-thiazolo[5,4-*c*]azepine-8-thione (Ib) was synthesized in a similar way from compound **IIb**. Yield 61%, mp 167°C (from toluene). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.97 m (2H, 5-H), 3.09 t (2H, 4-H, *J* = 6.0), 3.39 m (2H, 6-H), 8.59 br.s (1H, 7-H), 8.79 s (1H, 2-H). Found, %: C 45.60; H 4.39; N 15.18; S 34.77. *m/z* 184 $[M]^+$. $C_7H_8N_2S_2$. Calculated, %: C 45.62; H 4.38; N 15.20; S 34.80. *M* 184.

5,5-Dimethyl-8-piperidino-5,6-dihydro-4*H*-thiazolo[5,4-*c*]azepine (Va). Compound **Ia**, 100 mg, was dissolved in 2 ml of piperidine, 128 mg of $HgCl_2$ was added, and the mixture was heated for 2 h under reflux. It was then cooled and filtered, piperidine was distilled off, the residue was dissolved in benzene, and the solution was passed through a short column charged with aluminum oxide, followed by elution with benzene. The solvent was distilled off from the eluate, and the residue was dissolved in chloroform and purified by column chromatography on silica gel using first chloroform and then chloroform–ethanol as eluent. Yield 77 mg (62%), mp 170°C (from benzene–hexane). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.21 s (6H, Me_2C), 1.64 m (6H, CH_2, piperidine), 2.65 s (2H, 4-H), 3.40 s (2H, 6-H), 3.47 t (4H, NCH_2, piperidine, *J* = 6.3). Found, %: C 63.81; H 8.06; N 1.93; S 12.17. *m/z* 263 $[M]^+$. $C_{14}H_{21}N_3S$. Calculated, %: C 63.84; H 8.04; N 1.95; S 12.17. *M* 263.

8-Piperidino-5,6-dihydro-4*H*-thiazolo[5,4-*c*]-azepine (Vb) was synthesized in a similar way from compound **Ib**. Yield 60%, mp 172°C (from benzene–hexane). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.64 m (6H, CH_2, piperidine), 2.11 m (2H, 5-H), 2.88 t (2H, 4-H, *J* = 6.2), 3.48 t (4H, NCH_2, piperidine, *J* = 6.3), 3.51 t (2H, 6-H, *J* = 6.4). Found, %: C 61.22; H 7.29; N 17.84; S 13.60. *m/z* 235 $[M]^+$. $C_{12}H_{17}N_3S$. Calculated, %: C 61.24; H 7.28; N 17.85; S 13.62. *M* 235.

5,5-Dimethyl-5,6-dihydro-4*H*-bis[1,3]thiazolo-[3,2-*a*:5',4'-*c*]azepin-7-ium chloride (VIa). A mixture of 143 mg of thiazoloazepinethione **Ia** (finely powdered in a mortar) and 3 ml of chloroacetonitrile was heated for 2 h on a boiling water bath. The mixture was cooled and filtered, the precipitate was washed on a filter with diethyl ether and mixed with 3 ml of isobutyl alcohol, and the mixture was heated for 30 min under reflux, cooled, and filtered. The precipitate was washed on a filter with isobutyl alcohol, dried in air, and recrystallized twice from ethanol. Yield 140.62 mg (73%), mp 284°C (decomp., from toluene). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.02 s (6H, Me_2C), 3.18 s (2H, 4-H), 4.25 s (2H, 6-H), 6.75 s (1H, thiazole), 6.98 br.s (2H, NH_2), 9.36 s (1H, thiazole). Found, %: C 45.90; H 4.89; Cl 12.33; N 14.63; S 22.23. *m/z* 252 $[M - HCl]^+$. $C_{11}H_{13}N_3S_2 \cdot HCl$. Calculated, %: C 45.91; H 4.87; Cl 12.35; N 14.61; S 22.26. [*M* – HCl] 252.

5,6-Dihydro-4*H*-bis[1,3]thiazolo[3,2-*a*:5',4'-*c*]-azepin-7-ium chloride (VIb) was synthesized in a similar way from thiazoloazepinethione **Ib** and chlo-

roacetonitrile. Yield 75%, mp 280°C (decomp., from toluene). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 2.55 m (2H, 5-H), 3.21 t (2H, 4-H, *J* = 6.4), 4.30 t (2H, 6-H, *J* = 6.3), 6.79 s (1H, thiazole), 7.11 br.s (2H, NH_2), 9.38 s (1H, thiazole). Found, %: C 41.60; H 3.87; Cl 13.63; N 16.17; S 24.68. *m/z* 224 [*M* – HCl]$^+$. $C_9H_9N_3S_2 \cdot HCl$. Calculated, %: C 41.62; H 3.85; Cl 13.8; N 16.19; S 24.66. [*M* – HCl] 224.

The ^{1}H NMR spectra were recorded on a Varian-300 spectrometer (300 MHz). The mass spectra (electron impact, 70 eV) were obtained on an MKh-1321 spectrometer with direct sample admission into the ion source. The progress of reactions and the purity of products were monitored by TLC on Silufol UV-254 plates.

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