

SHORT COMMUNICATIONS

Specificity of the Thiomethylation of 1,2-Diamines with Formaldehyde and Hydrogen Sulfide

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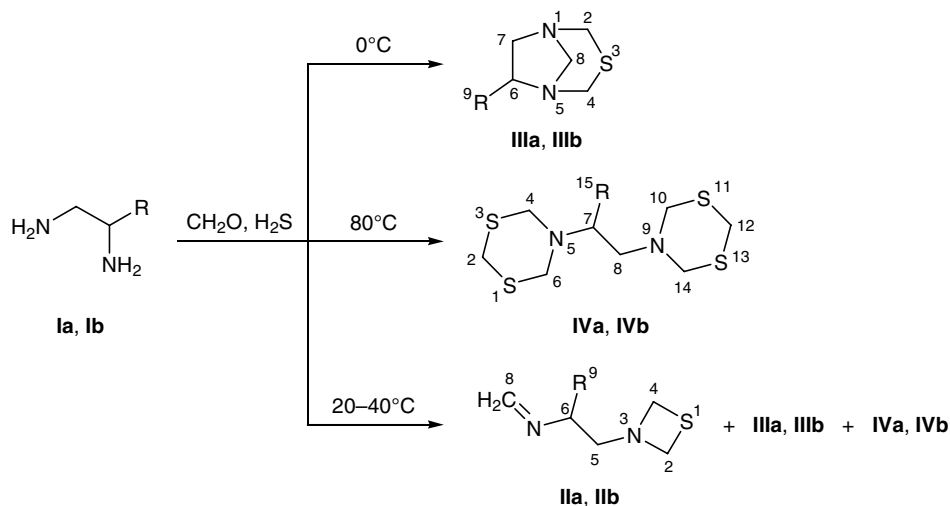
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We recently showed [1] that thiomethylation of ethylenediamine (**Ia**) with formaldehyde and hydrogen sulfide is accompanied by cyclization to give *N*-methylidene-2-(1,3-thiazetidin-3-yl)ethanamine (**IIa**) and 5,5'-ethylenebis(1,3,5-dithiazinane) (**IVa**), the latter possessing a high sorption ability toward gold and silver ions [2]. While studying this reaction in more detail, we have found that its direction and selectivity strongly depend on the temperature and reactant ratio. The present communication reports our new results on the heterocyclization of ethylenediamine (**Ia**) and propane-1,2-diamine (**Ib**) by the action of CH₂O and H₂S, which leads to the formation of difficultly accessible thiadiazabicyclooctanes in one step.

Thus the reaction of ethylenediamine (**Ia**) with CH₂O and H₂S at a ratio of 1:6:4 at 0°C in 3 h gave ~85% of 3-thia-1,5-diazabicyclo[3.2.1]octane (**IIIa**). Under analogous conditions, from propane-1,2-diamine (**Ib**) we obtained 6-methyl-3-thia-1,5-diazabicyclo[3.2.1]octane (**IIIb**) in ~87% yield. When the concentration of CH₂O and H₂S was reduced so that the ratio diamine **I**–CH₂O–H₂S was 1:3:2, the yields of compounds **IIIa** and **IIIb** decreased to 54 and 70%, respectively (see table).

Raising the temperature to 80°C changes the reaction direction. At a **I**–CH₂O–H₂S ratio of 1:6:4 we obtained exclusively 5-[2-(1,3,5-dithiazinane-5-yl)ethyl]-1,3,5-dithiazinane (**IVa**) and 5-[2-(1,3,5-dithiazinane-5-



yl)-1-methylethyl]-1,3,5-dithiazinane (**IVb**). The reaction performed in the temperature range from 20 to 40°C was characterized by considerably lower selectivity, and the products were mixtures of the corresponding bis-dithiazinanes **IV**, 1,3-thiazetidines **II**, and 3-thia-1,5-diazabicyclo[3.2.1]octanes **III**. The data in table show that cyclothiomethylation of propane-1,2-diamine (**Ib**) is more effective and selective.

The structure of 3-thia-1,5-diazabicycloheptanes **IIIa** and **IIIb** was confirmed by the data of elemental analysis and ^1H and ^{13}C NMR and mass spectra. The ^{13}C NMR spectrum of symmetric product **IIIa** contained a signal at δ_{C} 75.80 ppm from the C^8 atom located between two nitrogen atoms and two signals at δ_{C} 50.07 and 57.20 ppm, corresponding to the C^6/C^7 and C^2/C^4 methylene carbon atoms. In the spectrum of unsymmetrical compound **IIIb**, four signals were present in the δ_{C} range from 57.24 to 59.00 ppm (C^2 , C^4 , C^6 , C^7) and one signal appeared at δ_{C} 73.97 ppm (C^8). Bis-dithiazinane **IVb** showed signals at δ_{C} 33.76 and 33.83 ppm due to nonequivalent methylene carbon atoms in the SCH_2S fragment and two signals at δ_{C} 53.23 and 56.72 ppm from the NCH_2S carbon atoms. Protons of the methylene group on C^8 resonated in the ^1H NMR spectrum as an AB pattern (δ 3.08, 3.13 ppm; J = 16 Hz).

The mass spectra of the products contained the molecular ion peaks with m/z 130 (**IIa**, **IIIa**), 144 (**IIb**, **IIIb**), 268 (**IVa**), and 282 (**IVb**), as well as characteristic fragment ion peaks corresponding to elimination of HS, CH_2S , and CH_2SH groups from the molecular ions $[M]^+$ of thiazetidines **IIa** and **IIb**.

General procedure for the thiomethylation of diamines Ia and Ib with formaldehyde and hydrogen sulfide. Hydrogen sulfide prepared from required amounts of Na_2S and hydrochloric acid was bubbled over a period of 30 min through a 37% solution of formaldehyde to obtain a mixture of CH_2O and H_2S at a ratio of 3:2 or 6:4. Diamine **Ia** or **Ib** was then added dropwise, and the mixture was stirred at a specified temperature (for reaction conditions and reactant ratios, see table). Compounds **IIIa**, **IIIb**, **IVa**, and **IVb** were isolated by column chromatography on silica gel using hexane–ethyl acetate (4:3) as eluent.

N-Methylidene-2-(1,3-thiazetidin-3-yl)ethanamine (IIa) [1]. Yield 7%. Mass spectrum, m/z (I_{rel} , %): 130 (56) $[M]^+$, 98 (8) $[M - \text{S}]^+$, 84 (8) $[M - \text{SCH}_2]^+$, 56 (45) $[M - \text{SCH}_2\text{NCH}_2]^+$.

3-Thia-1,5-diazabicyclo[3.2.1]octane (IIIa). Initial amount of **Ia** 1.2 g (0.02 mol); yield 1.32 g (54%)

Thiomethylation of ethane-1,2-diamine (**Ia**) and propane-1,2-diamine (**Ib**) with CH_2O and H_2S

Temperature, °C	Ratio diamine– $\text{CH}_2\text{O}-\text{H}_2\text{S}$	Yield, %					
		IIa	IIIa	IVa	IIb	IIIb	IVb
0	1:3:2	–	54	–	–	70	–
0	1:6:4	–	85	–	–	87	–
20	1:6:4	7	21	42	5	46	3
40	1:6:4	6	8	44	3	33	30
80	1:6:4	–	–	65	–	–	73

(reactant ratio **Ia**– CH_2O – H_2S 1:3:2) or 2.21 g (85%) (1:6:4); yellow oily substance, R_f 0.24 (hexane–ethyl acetate, 4:3). IR spectrum, ν , cm^{-1} : 770, 1140, 1410, 2850, 2900. ^1H NMR spectrum, δ , ppm: 2.43 br.s (4H, 6-H, 7-H), 3.76 br.s (4H, 2-H, 4-H), 4.45 s (2H, 8-H). ^{13}C NMR spectrum, δ_{C} , ppm: 50.07 t (C^6 , C^7), 57.20 t (C^2 , C^4), 75.80 t (C^8). Mass spectrum, m/z (I_{rel} , %): 130 (100) $[M]^+$, 97 (95) $[M - \text{SH}]^+$, 56 (77) $[\text{CH}_2\text{CH}_2\text{NCH}_2]^+$, 42 (80) $[\text{CH}_2\text{NCH}_2]^+$. Found, %: C 45.57; H 7.59; N 20.47; S 25.29. $\text{C}_5\text{H}_{10}\text{N}_2\text{S}$. Calculated, %: C 46.10; H 7.74; N 21.51; S 24.63. M 130.21.

N-Methylidene-3-(1,3-thiazetidin-3-yl)propan-2-amine (IIb). Yield 5%. Mass spectrum, m/z (I_{rel} , %): 144 (27) $[M]^+$, 111 (67) $[M - \text{SH}]^+$, 97 (27) $[M - \text{CH}_2 - \text{SH}]^+$, 69 (51) $[\text{CH}_2\text{NCHCH}_3]^+$, 61 (28) $[\text{CH}_2\text{CH}_2\text{SH}]^+$, 56 (93) $[\text{CH}_2\text{NCHCH}_3]^+$, 42 (100) $[\text{CH}_2\text{NCH}_2]^+$.

6-Methyl-3-thia-1,5-diazabicyclo[3.2.1]octane (IIIb). Initial amount of **Ib** 1.5 g (0.02 mol); yield 2.02 g (70%) (reactant ratio **Ib**– CH_2O – H_2S 1:3:2) or 2.54 g (87%) (1:6:4); dark yellow oily substance, R_f 0.17 (hexane–ethyl acetate, 2:5). IR spectrum, ν , cm^{-1} : 750, 1100, 1400, 1450, 2850, 2900. ^1H NMR spectrum, δ , ppm: 1.08 d (3H, 9-H, J = 7.4 Hz), 2.37 m (2H, 7-H), 2.8 m (1H, 6-H), 3.81 s (2H, 2-H), 3.91 s (2H, 4-H), 4.47 s (2H, 8-H). ^{13}C NMR spectrum, δ_{C} , ppm: 19.57 q (C^9), 57.24 d (C^6), 57.36 t (C^4), 57.67 t (C^2), 59.00 t (C^7), 73.97 t (C^8). Mass spectrum, m/z (I_{rel} , %): 144 (64) $[M]^+$, 111 (100) $[M - \text{SH}]^+$, 69 (36) $[\text{CH}_2\text{CHNCH}_2\text{N}]^+$, 56 (60) $[\text{CH}_2\text{CHN}(\text{CH}_2)]^+$, 42 (90) $[\text{CH}_2\text{CHCH}_3]^+$. Found, %: C 50.31; H 8.07; N 18.11; S 23.17. $\text{C}_6\text{H}_{13}\text{N}_2\text{S}$. Calculated, %: C 49.96; H 8.39; N 19.42; S 22.23. M 145.25.

5-[2-(1,3,5-Dithiazinan-5-yl)ethyl]-1,3,5-dithiazinane (IVa). Yield 65%, colorless crystals, mp 179–180°C [1].

5-[2-(1,3,5-Dithiazinan-5-yl)-1-methylethyl]-1,3,5-dithiazinane (IVb). Yield 3.50 g (87%), from 1.5 g (0.02 mol) of **Ib**. Colorless crystals, mp 94–

95°C, R_f 0.78 (hexane–ethyl acetate, 2:5). IR spectrum, ν , cm^{-1} : 700, 1120, 1440, 1450, 2850, 2900. ^1H NMR spectrum, δ , ppm: 1.30 d (3H, 15-H, $J = 6.4$ Hz), 3.08 d (2H, 8-H_b, $J = 16$ Hz), 3.13 d (2H, 8-H_a, $J = 16$ Hz), 3.74 m (1H, 7-H), 4.15 s (4H, 2-H, 12-H), 4.48 s (4H, 10-H, 14-H), 4.58 m (8H, 4-H, 6-H). ^{13}C NMR spectrum, δ_c , ppm: 16.99 q (C^{15}), 33.76 t (C^2), 33.83 t (C^{12}), 48.67 d (C^7), 53.23 t (C^8), 56.72 t (C^4 , C^6), 59.42 t (C^{10} , C^{14}). Mass spectrum, m/z (I_{rel} , %): 282 (6) $[M]^+$, 235 (36) $[M - \text{CH}_2 - \text{SH}]^+$, 203 (6) $[M - \text{SCH}_2\text{SH}]^+$, 148 (100) $[M - \text{CH}_2\text{NCH}_2\text{SCH}_2\text{SCH}_2]^+$, 134 (8) $[\text{CH}_2\text{NCH}_2\text{SCH}_2\text{SCH}_2]^+$, 102 (13) $[\text{CH}_2\text{SCH}_2\text{NCH}_2\text{CH}_2]^+$, 70 (12) $[\text{NCH}_2\text{CHNCH}_3]^+$, 56 (29) $[\text{NCH}_2\text{CH}_2\text{CH}_2]^+$, 46 (8) $[\text{SCH}_2]^+$, 42 (24) $[\text{CH}_2\text{CHCH}_3]^+$. Found, %: C 37.91; H 6.23; N 9.62; S 45.37. $\text{C}_9\text{H}_{18}\text{N}_2\text{S}_4$. Calculated, %: C 38.26; H 6.42; N 9.92; S 45.4. M 144.24.

The ^1H NMR spectra were recorded on a Tesla BS-487 spectrometer (80 MHz); the ^{13}C NMR spectra were measured on a Jeol FX 90Q instrument (22.50 MHz); tetramethylsilane was used as internal

reference, and CDCl_3 , as solvent. The IR spectra were obtained on a Specord 75IR spectrometer from samples dispersed in mineral oil. The mass spectra were run on a Finnigan-4021 GC–MS system (HP-5 glass capillary column, 50000 $\times$ 0.25 mm, carrier gas helium, oven temperature programming from 50 to 300°C at a rate of 5 deg/min, injector temperature 280°C, ion source temperature 250°C, energy of ionizing electrons 70 eV). The purity of the isolated compounds was checked by TLC on Silufol UV-254 plates using hexane–ethyl acetate (4:3) as eluent; development with iodine vapor.

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