

Thiomethylation of Amino Alcohols Using Formaldehyde and Hydrogen Sulfide

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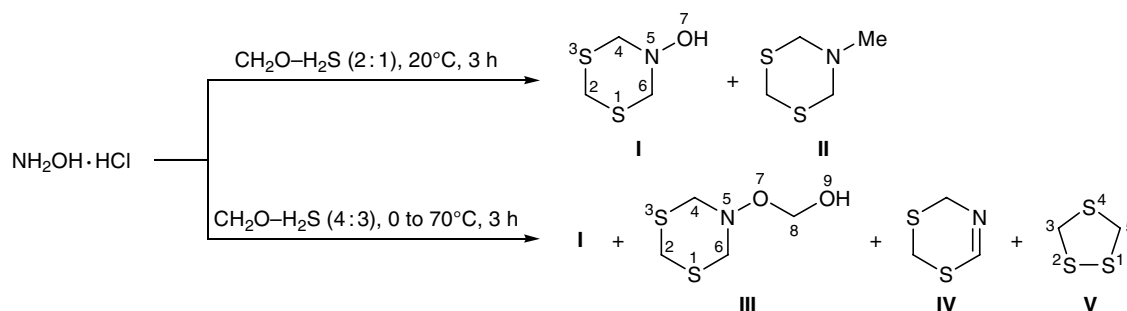
Abstract—Three-component condensations of formaldehyde with hydrogen sulfide and hydroxylamine or amino alcohols at a ratio of 3:2:1 give 47–73% of *N*-hydroxy(or hydroxyalkyl)-1,3,5-dithiazinanes. The reactions of CH₂O with H₂S and hydroxylamine or α -amino alcohols at a ratio of 4:3:1 involve both amino and hydroxy groups, leading to the corresponding dithiazinanes. 4-Aminobutan-1-ol reacts with CH₂O and H₂S under analogous conditions only at the amino group to form 4-(1,3,5-dithiazinan-5-yl)butan-1-ol.

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Thiomethylation of various amines with formaldehyde and hydrogen sulfide is known to give 1,3,5-dithiazinanes [1–3]. With a view to extend the scope of application of this method and elucidate the possibility of using difunctional amino- and hydroxy-containing monomers as substrates, in the present study we examined for the first time reactions of aliphatic amino alcohols with CH₂O and H₂S. As initial compounds we selected aqueous ammonia, hydroxylamine, 2-aminoethanol, *R*-(–)-2-aminobutan-1-ol, 2-amino-3-hydroxypropionic acid (serine), and 4-aminobutan-1-ol. According to [4], hydroxylamine reacts with formaldehyde to give exclusively 1,3,5-trihydroxy-1,3,5-triazine. We have found that three-component condensation of hydroxylamine with CH₂O and H₂S at a ratio of 1:2:1 or 1:3:2 at 20°C leads to the formation of

1,3,5-dithiazinan-5-ol (**I**) (Scheme 1). When the amount of the thiomethylating agent (CH₂O–H₂S) increases (reactant ratio 1:4:3), the hydroxy group of the substrate is also involved in the process. At a reactant ratio of 1:2:1, the yield of compound **I** is ~31%; also, 5-methyl-1,3,5-dithiazinane (**II**) is formed as minor product: its fraction does not exceed 1% (Table 1). In the presence of excess CH₂O and H₂S (NH₂OH–H₂O–H₂S ratio 1:4:3), the major product is 1,3,5-dithiazinan-5-yloxymethanol (**III**, ~56%). In addition, ~3% of 1,3,5-dithiazinane (**IV**) and ~2% of 1,2,4-trithiolane (**V**) are formed. Further raising of the amount of CH₂O–H₂S to a ratio of (5:3):1 with respect to hydroxylamine favors preferential formation of alcohol **III** which is likely to arise from compound **I** and formaldehyde.

Scheme 1.



The yield of dithiazine **I** is 46–47% at a stoichiometric reactant ratio ($\text{NH}_2\text{OH}-\text{CH}_2\text{O}-\text{H}_2\text{S}$, 1:3:2) in the temperature range from 20 to 70°C (Table 1). The formation of 5-methyl-1,3,5-dithiazinane (**II**) may be explained assuming that methylamine is generated during the process; its reaction with CH_2O and H_2S leads to dithiazinane **II**, which is consistent with the data of [5–7]. Dithiazinanes **I** and **III** were isolated as individual substances by column chromatography on silica gel using toluene–ethyl acetate–acetone (4:1:1) as eluent. The structure of compound **I** was proved by X-ray analysis.

According to the X-ray diffraction data, the crystal-line structure of **I** includes two independent molecules **IA** and **IB** (Fig. 1), each having *chair* conformation of the heteroring with axial orientation of the hydroxy group but different geometric parameters (Table 2). Molecules **IA** and **IB** in crystal are linked to give H-dimers via $\text{O}^2-\text{H}^2\cdots\text{O}^1$ hydrogen bonds with the following parameters: $\text{O}^1\cdots\text{O}^2$ 2.892(2), $\text{H}^2\cdots\text{O}^1$ 2.33 Å, $\angle\text{O}^2\text{H}^2\text{O}^1$ 124°. The hydroxy proton (H^1) in molecule **IB** is not involved in intermolecular hydrogen bond, but it gives rise to intramolecular hydrogen bond with the S^1 sulfur atom, which provides additional stabilization of the heteroring conformation. The distance from H^1 to S^1 (2.61 Å) is shorter than to S^2 (2.74 Å), while the distances $\text{H}^2\cdots\text{S}^3$ and $\text{H}^2\cdots\text{S}^4$ in molecule **IA** are approximately equal (2.72 and 2.75 Å, respectively). Analogous *chair* conformation of the dithiazinane ring was found previously for such compounds as 2,4,6-trimethyl-5-nitroso-5,6-dihydro-4*H*-1,3,5-dithiazine [9], 2-(6-methoxy-3,5,6-trimethyltetrahydro-2*H*-pyran-5-yl)-1,3,5-dithiazinane [10], and 2,4,6-trimethyl-1,3,5-dithiazinane [11].

The H-dimers are linked to zigzag chains (Fig. 2) via specific $\text{S}^2-\text{S}^{4'}$ dipole–dipole interaction, the $\text{S}^2\cdots\text{S}^{4'}$ distance being 3.530 Å. Packing of molecules **I** in crystal is largely determined by hydrogen bonding; as a result, stacks along the 0*a* crystallographic axis are

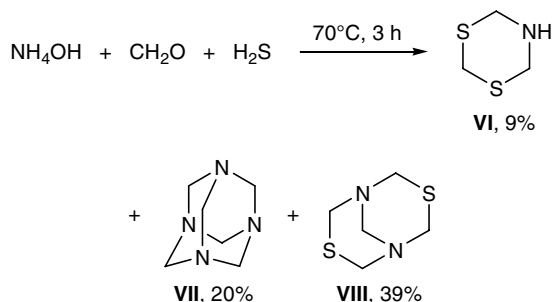
Table 1. Reaction of hydroxylamine with formaldehyde and hydrogen sulfide

Ratio $\text{NH}_2\text{OH}-\text{CH}_2\text{O}-\text{H}_2\text{S}$	Temperature, °C	Yield, %				
		I	II	III	IV	V
1 : 2 : 1	20	31	1	–	–	–
1 : 3 : 2	20	47	2	2	–	–
	40	46	5	7	–	–
	70	47	3	5	–	–
1 : 4 : 3	0	10	3	38	1	2
	40	5	1	56	3	2
	70	5	6	39	4	1
1 : 5 : 3	40	5	4	54	3	2

Table 2. Bond lengths (Å) and bond angles (deg) in molecules **IA** and **IB** in crystal

Parameter	Molecule IA	Molecule IB
N–O bond	N^2-O^2 1.408(2)	N^1-O^1 1.422(2)
N–C bond	N^2-C^5 1.457(2) N^2-C^6 1.451(2)	N^1-C^2 1.442(2) N^1-C^3 1.446(2)
S–C bond	S^3-C^5 1.823(2) S^4-C^6 1.824(2) S^3-C^4 1.804(2) S^4-C^4 1.801(2)	S^1-C^2 1.822(2) S^2-C^3 1.822(2) S^1-C^1 1.801(2) S^2-C^1 1.800(2)
Intramolecular O...S distance	$\text{O}^2\cdots\text{S}^3$ 3.163 $\text{O}^2\cdots\text{S}^4$ 3.169	$\text{O}^1\cdots\text{S}^1$ 3.107 $\text{O}^1\cdots\text{S}^2$ 3.135
Intramolecular S...H distance	$\text{S}^3\cdots\text{H}^2\text{O}$ 2.72 $\text{S}^4\cdots\text{H}^2\text{O}$ 2.75	$\text{S}^1\cdots\text{H}^1\text{O}$ 2.61 $\text{S}^2\cdots\text{H}^1\text{O}$ 2.74
Dihedral angle ONCS	$\text{O}^2\text{N}^2\text{C}^5\text{S}^3$ 62.1(2) $\text{O}^2\text{N}^2\text{C}^6\text{S}^4$ 61.5(2)	$\text{O}^1\text{N}^1\text{C}^2\text{S}^1$ 60.4(2) $\text{O}^1\text{N}^1\text{C}^3\text{S}^2$ 61.0(2)
Deviation from the C_2S_2 plane	ΔC^4 0.884 ΔN^2 0.650	ΔC^1 0.881 ΔN^1 0.634
Intermolecular S...S distance	$\text{S}^1\cdots\text{S}^3$ 3.756 $\text{S}^2\cdots\text{S}^4$ 3.530 $\text{S}^2\cdots\text{S}^3$ 3.800	$\text{S}^4\cdots\text{S}^4$ 3.492
Intermolecular S...O distance		$\text{S}^1\cdots\text{S}^2$ 3.924 $\text{S}^1\cdots\text{O}^2$ 3.427

Scheme 2.



formed. The chains are extended along the 0*b* axis and are linked with each other through specific $\text{S}^4-\text{S}^{4'}$ dipole–dipole interactions with a distance of 3.492 Å (Fig. 3).

The condensation of aqueous ammonia with CH_2O and H_2S at 70°C gave ~9% of 1,3,5-dithiazinane (**VI**), while the major products were urotropin (**VII**, ~20%) and 3,7-dithia-1,5-diazabicyclo[3.3.1]nonane (**VIII**, ~39%) (Scheme 2). It is known that analogous reaction

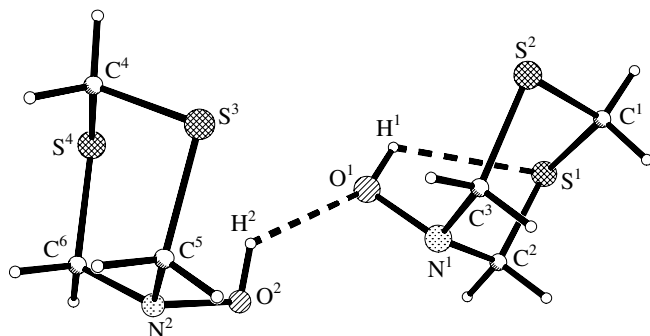


Fig. 1. Structure of two independent molecules **IA** and **IB** according to the X-ray diffraction data (the atoms are numbered according to SHELXTL PLUS 5 [8]).

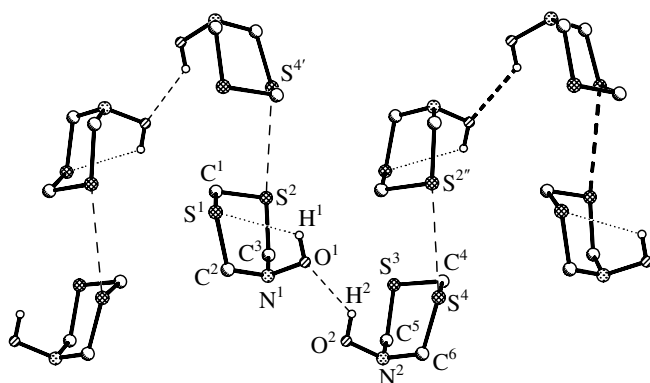


Fig. 2. Intermolecular contacts in the crystalline structure of 1,3,5-dithiazinan-5-ol (**I**).

of gaseous ammonia or ammonium sulfide leads to the formation of compounds **VII** and **VIII** exclusively [12]; the formation of 1,3,5-dithiazinanes from aqueous ammonia was observed only in reactions with formaldehyde alkyl acetals [13–15].

2-Aminoethanol (**IXa**), *R*-(–)-2-aminobutan-1-ol (**IXb**), 2-amino-3-hydroxypropionic acid (**IXc**), and 4-aminobutan-1-ol (**XII**) reacted with CH_2O – H_2S (3:2) to afford 2-(1,3,5-dithiazinan-5-yl)ethanol (**Xa**), (*R*)-2-(1,3,5-dithiazinan-5-yl)butan-1-ol (**Xb**), 2-(1,3,5-di-

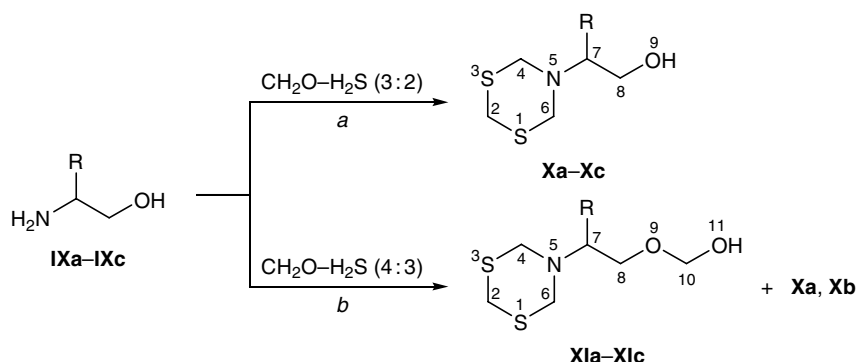
thiazinan-5-yl)-3-hydroxypropionic acid (**Xc**), and 4-(1,3,5-dithiazinan-5-yl)butan-1-ol (**XIII**), respectively (Schemes 3, 4). Increase in the concentration of CH_2O and H_2S (amine– CH_2O – H_2S ratio 1:4:3) leads to hydroxymethylation of the hydroxy group with formation of [2-(1,3,5-dithiazinan-5-yl)ethoxy]methanol (**XIa**), (*R*)-[2-(1,3,5-dithiazinan-5-yl)butoxy]methanol (**XIb**), and 3-(hydroxymethoxy)-2-(1,3,5-dithiazinan-5-yl)propionic acid (**XIc**) (Scheme 3).

Like α -amino alcohols, 4-aminobutan-1-ol (**XII**) reacted with CH_2O and H_2S at a ratio of 1:3:2, yielding ~51% of 4-(1,3,5-dithiazinan-5-yl)butan-1-ol (**XIII**). When the reaction was performed with increased amount of CH_2O – H_2S (reactant ratio 1:4:3), the yield of **XIII** was ~42%, and minor CH_2O – H_2S condensation products, 1,2,4-trithiolane (**V**, 5%) and 1,2,4,6,8-pentathionane (**XIV**, 3%) were also formed.

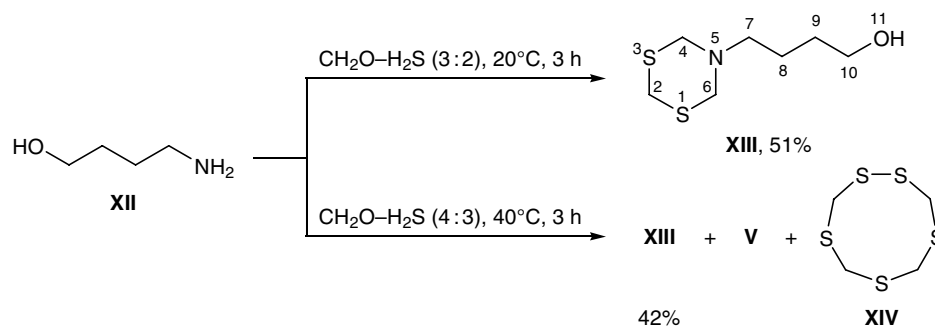
In all cases, no intramolecular cyclization products were detected, though examples of condensation of α -amino alcohols with CH_2O to 1,3-oxazolidines [16–20] and with epoxyethane to morpholine [20] were reported. Presumably, the reason is that the amino group in amino alcohols is more nucleophilic than the hydroxy group; therefore, the reaction with CH_2O and H_2S occurs stepwise. Initially, selective condensation at the amino group gives dithiazinanes **Xa–Xc** which then undergo hydroxymethylation with excess CH_2O to form compounds **XIa–XIc**. α -Amino alcohols **IXb** and **IXc** having a substituent at the carbon atom bearing the amino group give rise to greater yields of compounds **Xb**, **Xc** and **XIb**, **XIc**. The examined amino alcohols can be ranked as follows with respect to their reactivity in the thiomethylation with CH_2O and H_2S : 2-aminobutan-1-ol (**IXb**) > serine (**IXc**) > 2-aminoethanol (**IXa**).

In the condensation of *R*-(–)-2-aminobutan-1-ol with CH_2O and H_2S we obtained optically active dithiazinanes **Xb**, $[\alpha]_{\text{D}}^{18} = +5.4^\circ$ ($c = 0.38$, CHCl_3), and

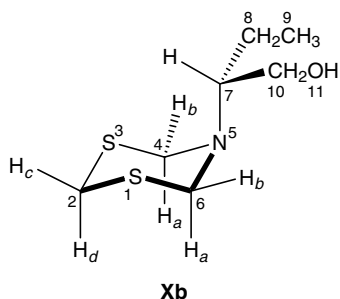
Scheme 3.



Scheme 4.



XIb, $[\alpha]_{\text{D}}^{17} = -61.4^\circ$ ($c = 1.00$, DMSO). Due to the presence of an asymmetric center, protons in the methylene groups located between the nitrogen and sulfur atoms in the dithiazinane rings of **Xb** and **XIb** are nonequivalent. In the ^1H NMR spectrum of **Xb**, diastereotopic protons in the methylene groups at the nitrogen atom appear as an AB spin system, δ 4.38 and 4.48 ppm ($^3J = 13.6$ Hz), while the corresponding protons in **XIb** resonate at δ 4.33 and 4.47 ppm ($^3J = 11.5$ Hz). With a view to determine the absolute configuration of these enantiomers we analyzed the ^1H and ^{13}C NMR spectra of **Xb**, recorded in the presence of a chiral lanthanide shift reagent, tris[3-(heptafluorobutyl)-*l*-camphorato]europium. No additional signals were observed, which indicated the presence of only one *R*-enantiomer [21–23]. We can conclude that the formation of 1,3,5-dithiazinane ring from *R*(–)-2-aminobutan-1-ol (**IXb**), CH_2O , and H_2S is stereoselective and that the configuration of the asymmetric carbon atom in 2-(*R*)-**Xb** is the same as in the initial chiral amino alcohol.



The mass spectra of all heterocyclic products **I**, **III**, **Xa–Xc**, **XIa–XIc**, and **XIII** contained strong molecular ion peaks. In the ^1H NMR spectra of these compounds, signals at δ 3.80–4.50 and 4.25–4.90 ppm had an intensity ratio of 1:2, which confirmed the presence of a 1,3,5-dithiazinane ring in their molecules. The corresponding carbon nuclei resonated in the ^{13}C NMR spectra at δ_{C} 30.44–33.82 and 53.96–58.78 ppm. Com-

pounds **III** and **XIa–XIc** also displayed signals in the region δ_{C} 82–90 ppm, which belong to side-chain methylene carbon atoms located between oxygen atoms.

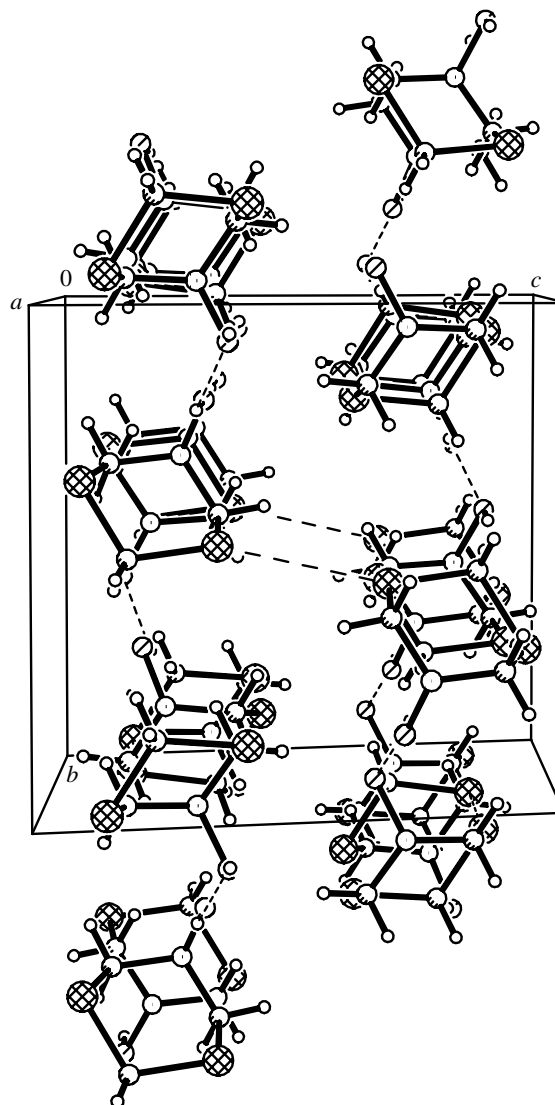


Fig. 3. Packing of molecules of 1,3,5-dithiazinan-5-ol (**I**) in crystal.

Table 3. Condensation of aqueous ammonia with formaldehyde and hydrogen sulfide

Ratio NH ₄ OH–CH ₂ O–H ₂ S	Temperature, °C	Yield, %			
		V	VI	VII	VIII
1:2:1	15	1	4	29	44
1:3:2	40	–	5	42	19
1:3:2	70	–	9	20	39

2-(2-Hydroxyethylamino)ethanol, being a secondary amine, failed to react with CH₂O and H₂S, i.e., both amino and hydroxy groups therein are inactive under the examined conditions.

Thus, the condensation of amino alcohols with formaldehyde and hydrogen sulfide can occur either at the amino group or at both nucleophilic centers (amino and hydroxy groups in hydroxylamine and α -amino alcohols), depending on the reactant ratio. Increase in the distance between the amino and hydroxy groups in going to 4-aminobutan-1-ol leads to increased reactivity of the amino group, while the reactivity of the hydroxy group becomes weaker; as a result, the product is dithiazinane **XIII** which does not undergo subsequent hydroxymethylation with formaldehyde. Presumably, the reactivity of the amino group increases due to reduction of $-I$ effect of the hydroxy group and weakening of intramolecular hydrogen bond typical of amino alcohols [24] (strong IR bands in the region 3350–3180 cm⁻¹ [25]). The condensation of *R*-(–)-2-aminobutan-1-ol with CH₂O and H₂S is enantioselective, and the configuration of the chiral center is retained; depending on the reactant ratio, (*R*)-2-(1,3,5-dithiazinan-5-yl)butan-1-ol (**Xb**) or (*R*)-[2-(1,3,5-dithiazinan-5-yl)butoxy]methanol (**XIb**) is formed in 73 and 52% yield, respectively.

EXPERIMENTAL

The thiomethylation products were analyzed by GLC on a Chrom-5 chromatograph equipped with a flame-ionization detector and a 2400×3-mm steel column packed with 5% of SE-30 on Chromaton N-AW-HMDS; carrier gas helium; oven temperature programming from 50 to 270°C at a rate of 8 deg/min. The ¹H NMR spectra of compounds **Xb** and **XIb** were recorded on a Bruker AM-300 spectrometer at 300 MHz, and of the other compounds, on a Tesla BS-487 instrument (80 MHz); the ¹³C NMR spectra were measured on a Jeol FX 90Q instrument at 22.50 MHz; tetramethylsilane was used as internal reference, and

CDCl₃ and DMSO-*d*₆ were used as solvents. The IR spectra were obtained on a Specord 75IR spectrometer from samples dispersed in mineral oil. Gas chromatography–mass spectrometry was performed on a Finnigan 4021 instrument (HP-5 glass capillary column, 50000×0.25 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; electron impact, 70 eV). The elemental compositions were determined on a Carlo Erba Model 1106 CHNS analyzer. The specific rotations were measured on a Perkin–Elmer-141 polarimeter. Hydrogen sulfide was bubbled using an ANP-10 peristaltic pump. The melting points were determined on an RNMK 80/2617 hot stage. The purity of the products was checked by TLC on Silufol UV-254 plates; development with iodine vapor.

X-Ray analysis of 1,3,5-dithiazinan-5-ol (I). A 0.60×0.45×0.35-mm single crystal of **I** was grown by crystallization from toluene–ethyl acetate–acetone (4:1:1). The X-ray diffraction data were acquired on an Enraf–Nonius CAD 4 diffractometer at 293 K (λ MoK α irradiation, $2\theta_{\max}$ = 29.99°). Colorless crystals; C₃H₇NOS₂, *M* 137.22; monoclinic crystal system, space group *P*2₁2₁2₁. Unit cell parameters (293 K): *a* = 10.672(5), *b* = 10.279(3), *c* = 10.916(4) Å; β = 103.73(2)°; *V* = 1163.2(8) Å³; *Z* = 8, *d*_{calc} = 1.567 g×cm⁻³. Averaging of equivalent reflections left 3373 independent reflections with *R*_{int} = 0.0397, which were used in the structure solution and refinement. The structure was solved by the direct method, and the positions of atoms were determined from the difference syntheses of electron density and were refined with respect to *F*² in anisotropic–isotropic approximation. The final divergence factors were *R*₁ = 0.0380 [calculated by *F*_{hkl} for 2800 reflections with *I* > 2σ(*I*)] and *wR*₂ = 0.1019 (calculated by *F*_{hkl}² for 3373 reflections involved in the final refinement step); GOOF 1.021; 127 refined parameters. All calculations were performed using SHELXTL PLUS 5 software package [8].

General procedure for thiomethylation of hydroxylamine hydrochloride, aqueous ammonia, 2-aminoethanol (IXa), *R*-(–)-2-aminobutan-1-ol (IXb), 2-amino-3-hydroxypropionic acid (IXc), and 4-aminobutan-1-ol (XII). A three-necked flask equipped with a stirrer, reflux condenser, and a gas-inlet tube was charged with a required amount of 37% formaldehyde solution, and hydrogen sulfide (generated from sodium sulfide and hydrochloric acid) was bubbled through the solution at a specified temperature over a period of 30 min to attain a CH₂O–H₂S ratio of

3:2 (method *a*) or 4:3 (method *b*) [2, 3]. A solution of 1 equiv of the corresponding amine (hydroxylamine hydrochloride dissolved in hot water, 10% aqueous ammonia, 2-aminoethanol, *R*-(–)-2-aminobutan-1-ol, or 2-amino-3-hydroxypropionic acid dissolved in hot water, or neat 4-aminobutan-1-ol) was added dropwise, and the mixture was stirred at a specified temperature (0 to 70°C). The product obtained from hydroxylamine hydrochloride was neutralized with a 10% solution of NaOH, and the precipitate was filtered off and dried. A mixture of compounds **I**–**V**, obtained at 0°C (method *b*), was separated by column chromatography on silica gel using toluene–ethyl acetate–acetone (4:1:1) as eluent.

1,3,5-Dithiazinan-5-ol (I). Yield 10%, colorless crystals, mp 86–87°C, R_f 0.63 (toluene–ethyl acetate–acetone, 4:1:1). IR spectrum, ν , cm^{-1} : 750, 1050, 1200–1180, 1480, 2880. ^1H NMR spectrum (DMSO- d_6), δ , ppm: 4.12 br.s (2H, 2-H), 4.58 br.s (4H, 4-H, 6-H). ^{13}C NMR spectrum, δ_C , ppm: 30.63 t (C^2), 58.78 t (C^4 , C^6). Mass spectrum, m/z (I_{rel} , %): 137 (47) [M] $^+$, 120 (6) [$M - \text{OH}$] $^+$, 104 (60) [$M - \text{CH}$] $^+$, 92 (29) [$M - \text{SCH}$] $^+$, 64 (17) [SS] $^+$, 59 (14) [$M - \text{SCH}_2\text{S}$] $^+$, 46 (100) [CH_2S] $^+$. Found, %: C 27.05; H 5.11; N 10.11; S 46.88. $\text{C}_3\text{H}_7\text{ONS}_2$. Calculated, %: C 26.26; H 5.14; N 10.21; S 46.73. M 137.21.

5-Methyl-1,3,5-dithiazinane (II). Mass spectrum, m/z (I_{rel} , %): 135 (67) [M] $^+$, 89 (40) [$M - \text{SH}_2\text{S}$] $^+$, 76 (10) [$M - \text{CH}_2\text{SCN}$] $^+$, 57 (62) [CSCH] $^+$, 46 (32) [CH_2S] $^+$, 44 (100) [CS] $^+$, 42 (86) [$\text{CS} - 2$] $^+$.

1,3,5-Dithiazinan-5-yloxymethanol (III). Yield 38%, white powder, mp 106–108°C, R_f 0.90 (toluene–ethyl acetate–acetone, 4:1:1). IR spectrum, ν , cm^{-1} : 740, 810, 1050, 1380, 1450, 2870, 3100–3300. ^1H NMR spectrum (DMSO- d_6), δ , ppm: 3.38 br.s (2H, 2-H), 4.30 br.s (4H, 4-H, 6-H), 4.79 br.s (2H, 8-H), 6.33 br.s (1H, OH). ^{13}C NMR spectrum, δ_C , ppm: 30.44 t (C^2), 57.22 t (C^4 , C^6), 89.98 t (C^8). Mass spectrum, m/z (I_{rel} , %): 167 (5) [M] $^+$, 135 (7) [$M - \text{S}$] $^+$, 121 (57) [$M - \text{SCH}_2$] $^+$, 110 (8) [$M - \text{CSCH}$] $^+$, 91 (10) [CHSCH_2S] $^+$, 75 (32) [$\text{HOCH}_2\text{ONHCH}_2$] $^+$, 57 (29) [ONCH_2CH] $^+$, 46 (76) [CH_2S] $^+$, 45 (100) [CHS] $^+$. Found, %: C 29.64; H 5.68; N 8.41; S 38.68. $\text{C}_4\text{H}_9\text{O}_2\text{NS}_2$. Calculated, %: C 28.72; H 5.42; N 8.37; S 38.34. M 167.25.

4H-1,3,5-Dithiazine (IV). Mass spectrum, m/z (I_{rel} , %): 119 (100) [M] $^+$, 92 (59) [$M - \text{NCH}$] $^+$, 86 (29) [$M - \text{S}$] $^+$, 73 (36) [$M - \text{SCH}_2$] $^+$, 64 (11) [SS] $^+$, 45 (90) [SCH] $^+$.

1,2,4-Trithiolane (V). R_f 0.92 (toluene–ethyl acetate–acetone, 4:1:1). ^{13}C NMR spectrum, δ_C , ppm:

32.7 s (C^3 , C^5). Mass spectrum: m/z 124 [M] $^+$. The melting point and IR, ^1H and ^{13}C NMR, and mass spectra of **V** were identical to those reported in [5].

In the reaction with aqueous ammonia (method *a*) we isolated compounds **VI**–**VIII**. Compound **VI** was purified by recrystallization from hexane, and compound **VIII** was recrystallized from chloroform as described in [26].

1,3,5-Dithiazinane (VI). Yield 9%, mp 96–98°C. Mass spectrum, m/z (I_{rel} , %): 121 (85) [M] $^+$, 92 (3) [$M - \text{CH}_2\text{NH}$] $^+$, 75 (45) [$M - \text{CH}_2\text{S}$] $^+$, 64 (4) [$M - \text{CSCH}$] $^+$, 57 (7) [CSCH] $^+$, 46 (58) [CH_2S] $^+$, 43 (100) [CH_2NHCH_2] $^+$.

1,3,5,7-Tetraazatricyclo[3.3.1.1^{3,7}]decane (VII). Yield 20%, mp 263°C [27]. Mass spectrum, m/z (I_{rel} , %): 140 (59) [M] $^+$, 112 (8) [$M - \text{NCH}_2$] $^+$, 85 (8) [$M - \text{NCH}_2\text{NCH}$] $^+$, 42 (100) [NCH_2N] $^+$.

3,7-Dithia-1,5-diazabicyclo[3.3.1]nonane (VIII). Yield 39%, mp 199–200°C [26]. Mass spectrum, m/z (I_{rel} , %): 162 (39) [M] $^+$, 129 (11) [$M - \text{SH}$] $^+$, 120 (17) [$M - \text{CH}_2\text{NCH}_2$] $^+$, 97 (14) [$M - \text{NCH}_2\text{NCC}$] $^+$, 89 (16) [$M - \text{SCH}_2\text{NCH}$] $^+$, 73 (6) [SCH_2NCH] $^+$, 57 (14) [CSCH] $^+$, 46 (31) [CH_2S] $^+$, 42 (100) [CH_2NCH_2] $^+$. The ^1H NMR spectrum of **VIII** was identical to that reported previously [26].

2-(1,3,5-Dithiazinan-5-yl)ethanol (Xa) was obtained according to method *a*; yield 56%, mp 47–48°C; published data: mp 44–45°C [2], 49°C [28]. IR spectrum, ν , cm^{-1} : 580, 650, 1050, 1170, 2850, 3610. Mass spectrum, m/z (I_{rel} , %): 165 (21) [M] $^+$, 133 (3) [$M - \text{S}$] $^+$, 119 (12) [$M - \text{SCH}_2$] $^+$, 87 (26) [$M - \text{SCH}_2\text{S}$] $^+$. The ^1H and ^{13}C NMR spectra were identical to those described in [2].

R-2-(1,3,5-Dithiazinan-5-yl)butan-1-ol (Xb). In the reaction with compound **IXb** according to method *a* we isolated a product which was passed through a column charged with silica gel (benzene–acetone–diethyl ether, 5:1:1) to obtain **Xb** as a transparent oily substance. Yield 73%, R_f 0.50 (benzene–acetone–diethyl ether, 5:1:1), $[\alpha]_D^{18} = +5.4^\circ$ ($c = 0.38$, CHCl_3). IR spectrum, ν , cm^{-1} : 680, 1070, 1270, 1380, 2950, 3400. ^1H NMR spectrum (CDCl_3), δ , ppm: 0.80 t (3H, 9-H, $J = 7.3$ Hz), 1.52 d.q (2H, 8-H, $J = 16.1$, 7.3 Hz), 3.00 s (1H, 7-H), 3.66 m (2H, 10-H), 4.11 s (2H, 2-H), 4.38 d (2H, part A of AB quartet, 4- H_A , 6- H_A , $^2J = 13.6$ Hz), 4.48 d (2H, part B of AB quartet, 4- H_B , 6- H_B , $^2J = 13.6$ Hz). ^{13}C NMR spectrum, δ_C , ppm: 9.99 q (C^9), 20.61 t (C^8), 33.47 t (C^2), 55.48 t (C^4 , C^6), 59.75 d (C^7), 62.25 t (C^{10}). Mass spectrum, m/z

(I_{rel} , %): 193 (6) $[M]^+$, 177 (13) $[M - \text{OH}]^+$, 149 (100) $[M - \text{CHCH}_2\text{OH}]^+$, 121 (21) $[\text{HNCH}_2\text{SCH}_2\text{SCH}_2]^+$, 104 (34) $[\text{CHSCH}_2\text{SCH}]^+$, 93 (32) $[\text{SCH}_2\text{SCH}_3]^+$. Found, %: C 43.45; H 7.80; N 7.31; S 33.05. $\text{C}_7\text{H}_{15}\text{ONS}_2$. Calculated, %: C 43.52; H 7.77; N 7.25; S 33.16. M 193.33.

3-Hydroxy-2-(1,3,5-dithiazinan-5-yl)propionic acid (Xc) was synthesized from compound **IXc** (method *a*), mp 158–159°C; published data [28]: mp 154–155°C. The spectral parameters of compound **Xc** were given in [3].

[2-(1,3,5-Dithiazinan-5-yl)ethoxy]methanol (XIa). The reaction with compound **IXa** according to method *b* gave a mixture of **Xa** and **XIa** (27 and 18%, respectively), which were separated by crystallization from chloroform. Yield 18%, mp 50–52°C. ^1H NMR spectrum ($\text{DMSO}-d_6$), δ , ppm: 1.95 t (2H, 7-H, $^3J = 7.1$ Hz), 3.60 t (2H, 8-H, $^3J = 7.1$ Hz), 4.50 br.s (2H, 2-H), 4.90 br.s (4H, 4-H, 6-H), 5.19 d (2H, 10-H, $^3J = 5.4$ Hz), 6.99 t (1H, OH, $^3J = 5.4$ Hz). ^{13}C NMR spectrum, δ_{C} , ppm: 31.52 t (C^2), 53.53 t (C^7), 57.11 t (C^4 , C^6), 63.37 t (C^8), 88.44 t (C^{10}). Mass spectrum, m/z (I_{rel} , %): 195 (13) $[M]^+$, 193 (89) $[M - 2]^+$, 148 (26) $[M - \text{SCH}_2]^+$, 147 (100) $[M - \text{SCH}_3]^+$, 134 (47) $[M - \text{CH}_2\text{OCH}_2\text{OH}]^+$, 115 (79) $[(\text{CH}_2)_2\text{NCH}_2\text{CH}_2\text{OCH}_2\text{OH}]^+$, 102 (97) $[\text{CHNCH}_2\text{CH}_2\text{OCH}_2\text{OH}]^+$, 73 (89) $[\text{CCH}_2\text{OCH}_2\text{OH}]^+$, 56 (79) $[\text{CSC}]^+$. Found, %: C 37.04; H 6.63; N 7.16; S 32.78. $\text{C}_6\text{H}_{13}\text{O}_2\text{NS}_2$. Calculated, %: C 36.92; H 6.67; N 7.18; S 32.82. M 195.31.

(R)-[2-(1,3,5-Dithiazinan-5-yl)butoxy]methanol (XIb) was obtained from compound **IXb** (method *b*). Yield 52%, colorless oily substance, $[\alpha]_{\text{D}}^{17} = -61.4^\circ$ ($c = 1.00$, DMSO). IR spectrum, ν , cm^{-1} : 730, 1010, 1170, 1370, 2940, 3400. ^1H NMR spectrum ($\text{DMSO}-d_6$), δ , ppm: 0.92 t (3H, 9-H, $J = 7.5$ Hz), 1.45 d.q (2H, 8-H, $J = 22.3, 7.0$ Hz), 3.06 m (1H, 7-H), 3.35 s (1H, OH), 3.92 s (2H, 12-H), 3.94 m (2H, 10-H), 4.02 s (2H, 2-H), 4.33 d (2H, part A of AB quartet, 4-H_A, 6-H_A, $^2J = 11.5$ Hz), 4.47 d (2H, part B of AB quartet, 4-H_B, 6-H_B, $^2J = 11.5$ Hz). ^{13}C NMR spectrum, δ_{C} , ppm: 10.38 q (C^9), 25.75 t (C^8), 32.07 t (C^2), 55.41 t (C^4 , C^6), 62.94 d (C^7), 69.74 t (C^{10}), 84.36 t (C^{12}). Mass spectrum, m/z (I_{rel} , %): 223 (7) $[M]^+$, 162 (20) $[M - \text{CH}_2\text{OCH}_2\text{OH}]^+$, 130 (8) $[M - \text{HSCH}_2\text{SCH}_3]^+$, 116 (7) $[M - \text{CH}_2\text{SCH}_2\text{SCH}]^+$, 84 (46) $[\text{CH}_2\text{CH}(\text{CH}_2\text{CH}_3)\text{NCH}]^+$, 70 (46) $[\text{CH}_2\text{CH}(\text{CH}_2\text{CH}_3)\text{N}]^+$, 45 (38) $[\text{CHS}]^+$, 42 (100) $[\text{CHCH}_2\text{CH}_3]^+$. Found, %: C 42.98; H 7.52; N 6.19; S 28.80. $\text{C}_8\text{H}_{17}\text{O}_2\text{NS}_2$. Calculated, %: C 43.05; H 7.62; N 6.28; S 28.70. M 223.36.

2-(1,3,5-Dithiazinan-5-yl)-3-(hydroxymethoxy)-propionic acid (XIc). The reaction with compound **IXc** (method *b*) gave a mixture of products **V** and **XIc**. Compound **XIc** was isolated by fractional crystallization from CHCl_3 . Yield 64%, mp 270°C (decomp.). IR spectrum, ν , cm^{-1} : 700, 1000, 1450, 1650, 2900, 3300. ^1H NMR spectrum ($\text{DMSO}-d_6$), δ , ppm: 3.20–3.80 m (9H, 2-H, 4-H, 6-H, 7-H, 8-H), 4.25 br.s (2H, 10-H). ^{13}C NMR spectrum, δ_{C} , ppm: 33.82 t (C^2), 53.96 t (C^4 , C^6), 60.27 d (C^7), 64.34 t (C^8), 82.23 d (C^{10}), 166.40 s (C^{12}). Found, %: C 35.58; H 5.22; N 5.51; S 26.83. $\text{C}_7\text{H}_{13}\text{O}_3\text{NS}_2$. Calculated, %: C 35.15; H 5.44; N 5.86; S 26.78.

4-(1,3,5-Dithiazinan-5-yl)butan-1-ol (XIII). The reaction with amino alcohol **XII** according to method *a* gave compound **XIII** in 51% yield; following method *b*, a mixture of compounds **V** (5%), **XIII** (42%), and **XIV** (3%) was obtained. Colorless oily substance. IR spectrum, ν , cm^{-1} : 680, 1050, 1270, 2900, 3350. ^1H NMR spectrum (CDCl_3), δ , ppm: 1.30–1.52 br.s (4H, 8-H, 9-H), 2.91 s (2H, 7-H), 3.48 s (2H, 10-H), 3.97 s (2H, 2-H), 4.30 s (2H, 4-H, 6-H). ^{13}C NMR spectrum, δ_{C} , ppm: 22.82 t (C^8), 29.72 t (C^9), 33.27 t (C^2), 47.96 t (C^7), 57.43 t (C^4 , C^6), 61.54 d (C^{10}). Mass spectrum, m/z (I_{rel} , %): 193 (17) $[M]^+$, 114 (100) $[M - \text{N}(\text{CH}_2)_4\text{OH}]^+$, 84 (11) $[\text{SCH}_2\text{NC}_2]^+$, 71 (16) $[\text{HO}(\text{CH}_2)_3\text{C}]^+$, 58 (31) $[\text{CH}_2\text{SC}]^+$, 42 (58) $[\text{SCH}_2]^+$. Found, %: C 43.75; H 7.78; N 7.47; S 33.25. $\text{C}_7\text{H}_{15}\text{ONS}_2$. Calculated, %: C 43.52; H 7.77; N 7.25; S 33.16. M 193.33.

1,2,4,6,8-Pentathiacyclononane (XIV). Yield 3%. Mass spectrum, m/z (I_{rel} , %): 216 (7) $[M]^+$, 170 (5) $[M - \text{SCH}_2]^+$, 124 (38) $[M - (\text{SCH}_2)_2]^+$, 78 (47) $[\text{SCH}_2\text{S}]^+$, 45 (100) $[\text{CHS}]^+$.

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