Cyclothiomethylation of aryl hydrazines with formaldehyde and hydrogen sulfide

V. R. Akhmetova,[a]★ G. R. Nadyrgulova,[a] T. V. Tyumkina,[a] Z. A. Starikova,[b] D. G. Golovanov,[b] M. Yu. Antipin,[b] R. V. Kunakova,[c] and U. M. Dzhemilev[a]

[a] *Institute of Petrochemistry and Catalysis, Russian Academy of Sciences, 141 prosp. Oktyabrya, 450075 Ufa, Russian Federation. Fax: +7 (347 2) 31 2750. E-mail: ink@anrb.ru*

[b] *A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 28 ul. Vavilova, 119991 Moscow, Russian Federation. Fax: +7 (495) 135 9271. E-mail: star@xray.ineos.ac.ru*

[c] *Ufa State Academy of Economics and Service, 145 ul. Chernyshevskogo, 450077 Ufa, Russian Federation. Fax: +7 (347 2) 52 0806. E-mail: nis_utis@bashnet.ru*

Cyclothiomethylation of phenyl hydrazine with CH_2O and H_2S in a ratio of 1 : 3 : 2 in an acidic medium (HCl) afforded previously unknown 3-phenyl-1,3,4-thiadiazolidine (35% yield) and *N*-phenyl(perhydro-1,3,5-dithiazin-5-yl)amine (35% yield). The analogous reaction in an alkaline medium (BuONa) produced *N*-phenyl(perhydro-1,3-thiazetidin-3-yl)amine (22% yield). The reaction of 1,2-diphenyl hydrazine with CH_2O and H_2S in an alkaline medium gave 1,2,4,5-tetraphenylhexahydro-1,2,4,5-tetrazine and previously unknown 3,4-diphenyl-1,3,4-thiadiazolidine and 5,6-diphenyltetrahydro-1,3,5,6-dithiadiazepine in 39 and 22% yields, respectively. Cyclothiomethylation of benzyl hydrazine afforded previously unknown bis[(6-benzyl-4,2,6-thiadiazolidin-2-yl)methyl] sulfide (60% yield) and *N*-benzyl(perhydro-1,3,5-dithiazin-5-yl)amine (19% yield). The reaction of tosyl hydrazine produced 3-[(*p*-tolyl)sulfonyl]-1,3,4-thiadiazolidine, *N*-(perhydro-1,3,5-dithiazin-5-yl)-*p*-tolylsulfonamide, and 3,7-bis(*p*-tolylsulfonylamino)-1,5-dithia-3,7-diazacyclooctane in 21, 38, and 41% yields, respectively.

Key words: cyclothiomethylation, aryl hydrazines, formaldehyde, hydrogen sulfide, 1,3,5-dithiazines, 1,3,4-thiadiazolidines, X-ray diffraction study.

Earlier,[1] we have performed cyclothiomethylation of hydrazine with formaldehyde and hydrogen sulfide and prepared annelated 1,3,4-thiadiazolidines and 1,3,5-thiadiazines. According to the available data,[2—4] 1,3,4-thiadiazole derivatives have found wide use as antibacterial and antiviral agents and as inhibitors of oxidation of cyanine dyes and metal complexing agents.[5] *N*-Phenyl-substituted nitrogen-containing heterocycles, in which the N atoms are conjugated with chromophoric groups, are of particular interest as photosensitive and photocontrolled molecular devices.[6]

The present study is a continuation of investigations on cyclothiomethylation of amines with CH_2O and H_2S.[7—9] Another aim was to develop efficient methods for the synthesis of aryl-substituted thiadiazoles. The latter compounds are of practical interest. We examined thiomethylation of phenyl, 1,2-diphenyl, benzyl, and tosyl hydrazines with the H_2S—CH_2O system under neutral, acidic, and alkaline conditions.

Results and Discussion

Recently,[10] we have found that the thiomethylation pathway of hydrazine with CH_2O and H_2S strongly depends on the starting component ratio, the heterocyclization temperature, and pH of the reaction mixture.

In the present study, we examined cyclothiomethylation of phenyl hydrazine hydrochloride (**1**·HCl) with CH_2O and H_2S in a ratio of 1 : 3 : 2 at pH 0.45—0.50 (method *A*). It was found that the reaction performed at 0 °C selectively produces 3-phenyl-1,3,4-thiadiazolidine (**2**), whereas *N*-phenyl(perhydro-1,3,5-dithiazin-5-yl)amine (**3**) and 6-phenylperhydro[1,3,4]thiadiazino[5,4-*d*][1,3,5]dithiazine (**4**) are generated along with compound **2** at higher temperature (20—70 °C) (Scheme 1). At 70 °C, the amount of minor product **4** derived under these conditions from compound **3** is at most 8%.

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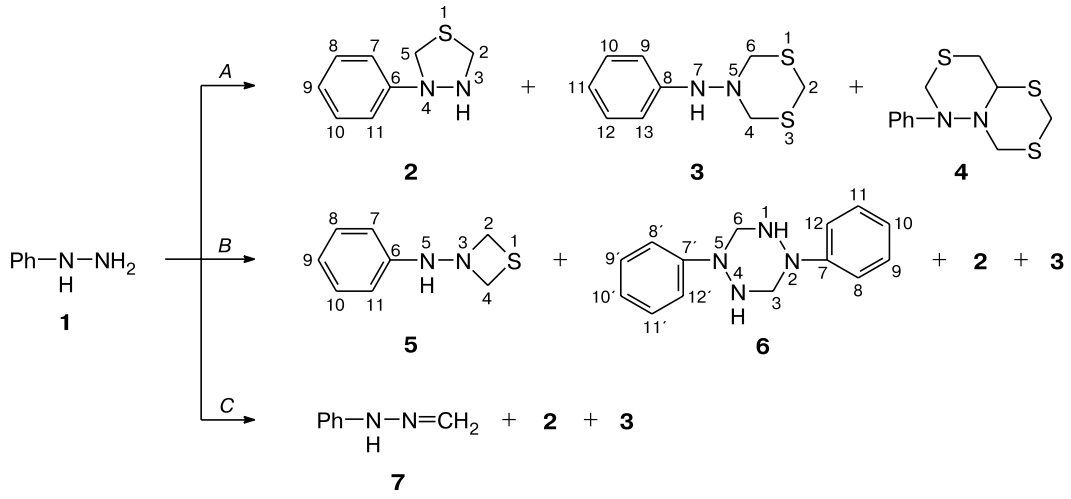
Scheme 1



Reagents and conditions: *A*. **1** · HCl : CH_2O : H_2S = 1 : 3 : 2, 0—70 °C, pH 0.45—0.50.
B. **1** : BuONa : CH_2O : H_2S = 1 : 3 : 3 : 2, 0—70 °C, pH 11.5—11.7.
C. **1** : CH_2O : H_2S = 1 : 3 : 2, 0—70 °C, pH 3.15—3.20.

Under alkaline (pH 11.5—11.7) or neutral (in the absence of acidic-alkaline additives, pH 3.15—3.20) conditions (methods *B* and *C*, respectively), compounds **2** and **3** were obtained as well. The reaction in an alkaline medium at 70 °C afforded *N*-phenyl(perhydro-1,3-thiazetidin-3-yl)amine (**5**) and 1,4-diphenylhexahydro-1,2,4,5-tetrazine (**6**) as the major products in 22 and 50% yields, respectively (Table 1). The reaction of phenyl hydrazine with CH_2O and H_2S in a neutral medium at 0—20 °C produced predominantly formaldehyde phenylhydrazone (**7**) in 76% yield.

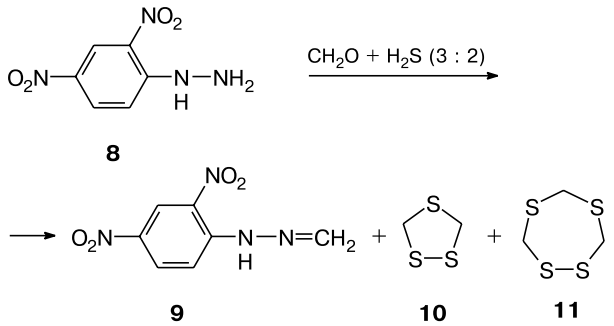
Table 1. Influence of the thiomethylation conditions of phenyl hydrazine (**1**) on the yield and composition of the reaction products

Method (pH)	*T* /°C	**1** : CH_2O : H_2S	Yields of products (%)					
			2	**3**	**4**	**5**	**6**	**7**
A	0	1 : 2 : 1	31	—	—	—	—	—
(0.45—0.50)	0	1 : 3 : 2	35	—	—	—	—	—
	20	1 : 3 : 2	26	30	—	—	—	—
	40	1 : 3 : 2	22	26	—	—	—	—
	70	1 : 3 : 2	20	35	8	—	—	—
B	0	1 : 3 : 2	20	—	—	18	23	—
(11.5—11.7)	20	1 : 3 : 2	11	13	—	15	19	—
	40	1 : 3 : 2	14	7	—	15	10	—
	70	1 : 3 : 2	—	—	—	22	50	—
C	0	1 : 3 : 2	17	6	—	—	—	76
(3.15—3.20)	20	1 : 3 : 2	12	5	—	—	—	74
	40	1 : 3 : 2	26	9	—	—	—	49
	70	1 : 3 : 2	14	8	—	—	—	72

These results can be attributed to the change in the electron density in the phenyl hydrazine molecule (**1**) depending on pH of the reaction mixture.[11]

Unlike the reaction of compound **1**, cyclothiomethylation of 2,4-dinitrophenyl hydrazine (**8**) does not afford sulfur-containing heterocycles. Apparently, this behavior of compound **8** in the reaction is associated with its low basicity[12] compared to phenyl hydrazine (**1**) due to which hydrazone **9** was obtained as the major product. In these experiments, 2,4-dinitrophenyl hydrazine (**8**) is not involved in cyclothiomethylation regardless of pH, and CH_2O and H_2S give cyclic sulfides **10** and **11**[13] (Scheme 2).

Scheme 2



By analogy with phenyl hydrazine, we carried out cyclothiomethylation of 1,2-diphenyl hydrazine (**12**) with an expectation to prepare 3,4-diphenyl-1,3,4-thiadiazolidine. However, under the conditions used

Scheme 3

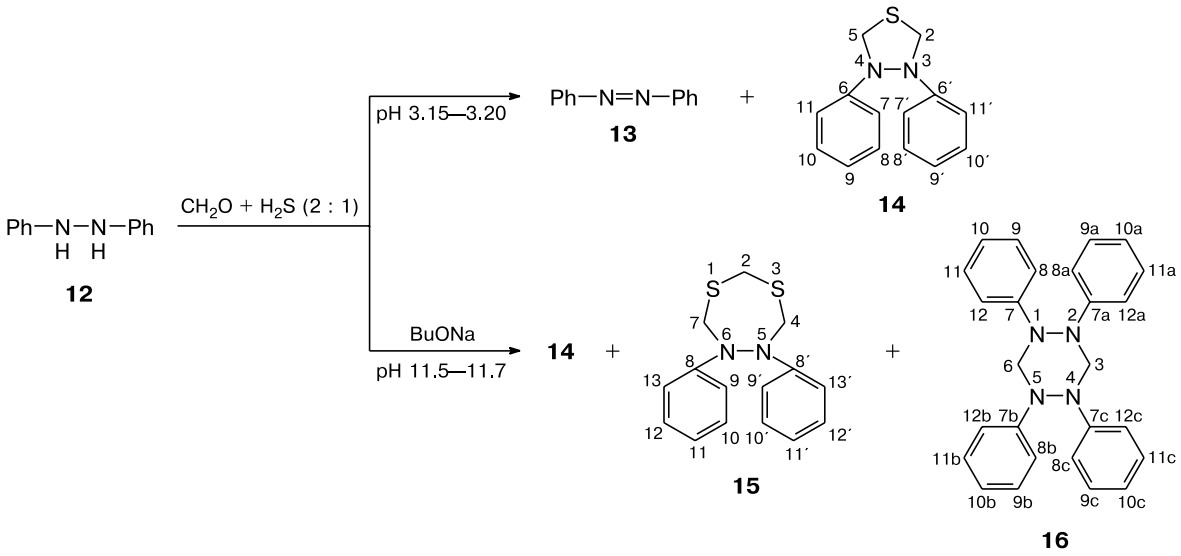


Table 2. Influence of the thiomethylation conditions of 1,2-diphenyl hydrazine (**12**) on the yield and composition of the reaction products

pH	*T*/°C	Yields of products (%)			
		13	**14**	**15**	**16**
3.15—3.20	0	17	5	—	—
	20	77	13	—	—
	40	46	2	—	—
	70	59	4	—	—
11.5—11.7	0	21	9	—	—
	20	14	39	10	6
	40	16	11	22	6
	70	31	—	—	—

(method *C*), the reaction gave (*Z*)-azobenzene (**13**) as the major product in ~77% yield. The latter reaction also produced 3,4-diphenyl-1,3,4-thiadiazolidine (**14**), but the yield of the latter was at most 13% (Scheme 3, Table 2).

The yield of compound **14** can be increased to 39% by performing cyclothiomethylation of diphenyl hydrazine **12** in the presence of BuONa at 20 °C. 5,6-Diphenyltetrahydro-1,3,5,6-dithiadiazepine (**15**) and 1,2,4,5-tetraphenylhexahydro-1,2,4,5-tetrazine (**16**)[14] were produced simultaneously in 22 and 6% yields, respectively. Under acidic conditions, diphenyl hydrazine **12** undergoes the benzidine rearrangement.[15]

Earlier,[16] it has been reported that configurational stability of the nitrogen atoms in 1,3,4-oxa(thia)diazolidines increases due to an increase in the volume of the substituents at the nitrogen atoms. According to the published data,[17,18] the inversion barrier of the adjacent nitrogen atoms in oxa(thia)diazolidines is higher due to steric destabilization of the monoplanar transition state. For example, the inversion barrier of the nitrogen atoms increases in the series of *N*,*N*′-dialkyl-substituted oxadiazolidines (Alk = Me, Pr^i, or Bu^i) and is 44.5, 81.5, and >88 kJ mol^{-1}, respectively.[19] The inversion barrier for 3,4-diisopropyl-1,3,4-thiadiazolidine (77.2 kJ mol^{-1}, $T = 66$ °C)[16] is close to that for the oxa analog. However, this compound is unstable and is transformed into a white powdered polymer at 20 °C, due to which conformational studies are difficult to perform. Unlike 3,4-diisopropyl-1,3,4-thiadiazolidine, phenyl-substituted thiadiazolidines **2** and **14** are more stable.

For compound **14**, we estimated $\Delta G^{\neq}$ by dynamic ^{1}H NMR spectroscopy. At −20 °C, the ^{1}H NMR spectrum of this compound shows splitting of the singlet for the methylene protons of the ring into two doublets ($\Delta\delta_{AB}$ = 55.8 Hz, ^2J = 10.0 Hz), which indicates that inversion processes become slower on the NMR time scale (Fig. 1). The experimental inversion barrier of the nitrogen atoms is ~51.5 kJ mol^{-1} ($T = -20$ °C),[20] which is

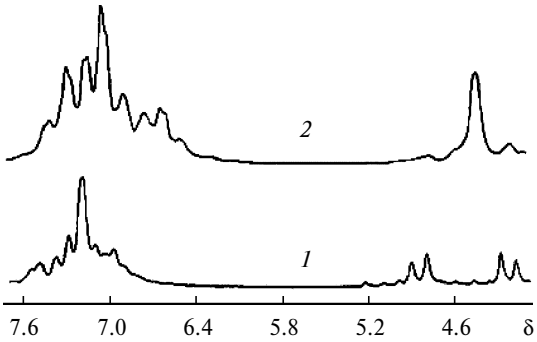


Fig. 1. ^{1}H NMR spectrum of compound **14** at −20 (*1*) and 25 °C (*2*).

evidence that configurational stability of the nitrogen atoms is insufficient for resolution of thiadiazolidine **14** into enantiomers under ambient conditions.

Heterocycles **2**, **3**, **5**, and **6** were isolated in individual state by column chromatography. The IR spectra of compounds **2—5** show stretching vibrations of the methylene groups at 2900 cm^{-1}. Intense absorption at 1600 cm^{-1} is characteristic of vibrations of the aromatic ring. The absorption band at 1020—1150 cm^{-1} belongs to C—N stretching vibrations. The C—S stretching vibrations are observed at 580—750 cm^{-1}.

The ^{13}C NMR spectra of isomeric compounds **2** and **5** differ in the number of signals. The ^{13}C NMR spectrum of compound **2** shows two resonances at δ_C 53.8 and 55.2 due to the presence of magnetically nonequivalent C atoms of the methylene groups, which is indicative of the presence of the thiadiazolidine ring. By contrast, the ^{13}C NMR spectrum of compound **5** contains the only signal in this region at δ_C 57.3, which is evidence for the formation of *N*-phenyl(perhydro-1,3-thiazetidin-3-yl)amine (**5**).

In the ^1H NMR spectra of compounds **2** and **5**, the signals are averaged due to high conformational flexibility of the heterocycles. The resonance of the magnetically equivalent methylene protons in thiazetidine **5** appears as a singlet at δ_H 4.63, and the shifts of the protons at the C(2) and C(5) atoms in compound **2** differ by 0.82 ppm.

The mass spectra of products **2** and **5** have the same molecular ions $[M]^+$ at *m/z* 166 and the characteristic fragment ions generated by loss of CH_2S (*m/z* 120) and CH_2SCH_2 (*m/z* 105) from $[M]^+$; however, the intensities of the signals are different.

The formation of the dithiazine ring in compound **3** is confirmed by two characteristic singlets in the ^1H NMR spectra at δ_H 4.79 and 5.20 with an integrated intensity ratio of 1 : 2. The aromatic protons of dithiazine **3** are observed at low field (δ_H 7.37—8.13).

The ^{13}C NMR spectrum of compound **6** has the only intense signal for the C atoms of the methylene groups (δ_C 63.3), which is indicative of spatial symmetry and the absence of the sulfur atom in molecule **6**. The geminal protons at the C(3) and C(6) atoms in the ^1H NMR spectrum are diastereotopic ($\Delta\delta_H = 0.55$), which also indicates that the molecule is symmetric.

The structures of compounds **7** and **9** were confirmed by comparison with the data published in the literature.[21,22]

Compounds **14** and **15** were isolated in individual state by column chromatography. In the ^1H NMR spectrum of compound **14**, the methylene protons of the thiadiazolidine ring appear as a broadened singlet at δ_H 4.65 ($\Delta\nu_{1/2}$ = 24 Hz) and a multiplet at δ 6.88—8.10. In the ^{13}C NMR spectrum of compound **14**, the signal at δ_C 53.0 belongs to the C(2) and C(5) atoms of the thiadiazolidine ring. The mass spectrum of product **14** has a molecular ion $[M]^+$ at *m/z* 242 and characteristic ion peaks at *m/z* 195 ($[M - CH_2S]^+$), 136 ($[C_6H_5NCH_2SH]^+$), 104 ($[C_6H_5NHN]^+$), 91 ($[C_6H_5N]^+$), 77 ($[C_6H_5]^+$), 51 ($[CN—NC]^+$), and 46 ($[CH_2S]^+$).

The formation of 5,6-diphenyltetrahydro-1,3,5,6-dithiadiazepine (**15**) is evidenced by the fact that the ^{13}C NMR spectrum has signals at δ_C 36.3 and 55.1 assigned to C atoms located between two S atoms and to magnetically equivalent C atoms located between the S and N atoms. The ^1H NMR spectrum of dithiadiazepine **15** shows a singlet for the methylene protons located between the S atoms (δ_H 4.00), an AB system of the protons of the NCH_2S fragments (δ_H 4.91 and 5.03, ^2J = 14.8 Hz), and a multiplet for the phenyl protons (δ_H 6.93—7.40); the intensity ratio is 2 : 2 : 2 : 10. In the mass spectrum of product **15**, the molecular ion peak is absent, but the spectrum has characteristic fragment ion peaks at *m/z* 136 ($[PhNHCH=S]^+$) and 164 ($[PhNNH(NCH_2)CH=S]^+$). The molecular weight determined cryoscopically[23] is 288±10, which corresponds to compound **15**. Based on the above-given physicochemical characteristics of product **15**, we assigned the structure of 5,6-diphenyltetrahydro-1,3,5,6-dithiadiazepine to this compound.

Recrystallization of a mixture of heterocycles **14—16** from DMSO afforded 1,2,4,5-tetraphenylhexahydro-1,2,4,5-tetrazine (**16**) in a yield of at most 6%. X-ray diffraction study demonstrated that the tetrazine ring

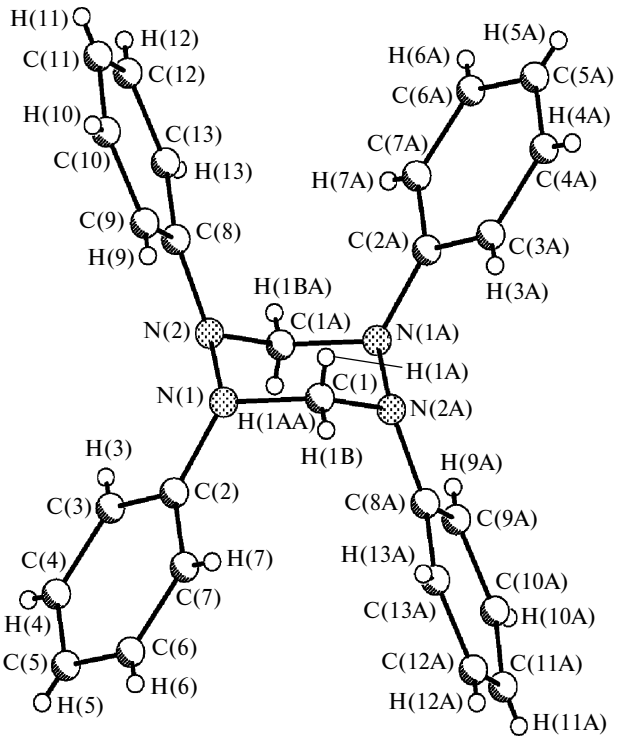


Fig. 2. Structure of 1,2,4,5-tetraphenylhexahydro-1,2,4,5-tetrazine (the atomic numbering scheme is given for crystallographically independent molecule **16A**).

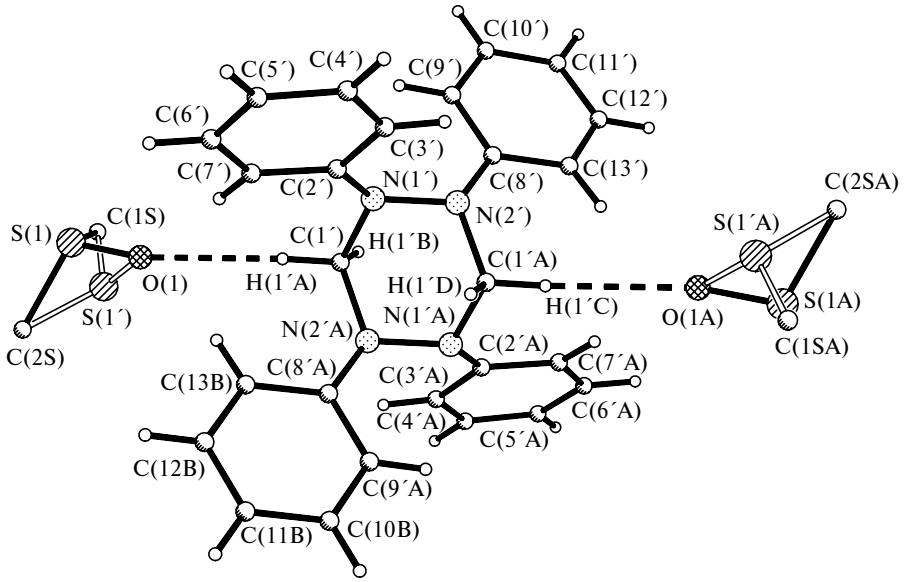


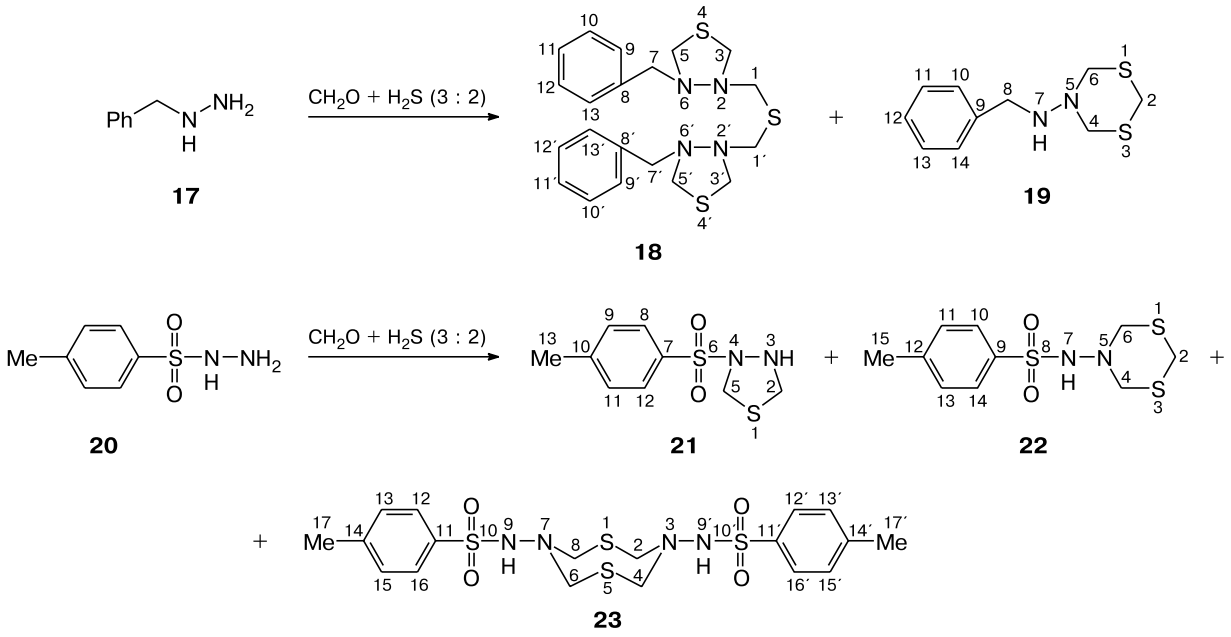
Fig. 3. Hydrogen bonds in the structure of 1,2,4,5-tetraphenylhexahydro-1,2,4,5-tetrazine (crystallographically independent molecule **16B**).

adopts a chair conformation with four benzene rings at the nitrogen atoms in axial positions and the rings at the adjacent nitrogen atoms in *trans* positions. The crystal structure contains two centrosymmetric independent molecules, **16A** (Fig. 2) and **16B** (Fig. 3), having similar structures. Molecule **16B** forms intermolecular bonds with the solvent (DMSO) molecules.

The deviation of the C(1) and C(1A) atoms from the plane formed by the nitrogen atoms is 0.590 Å. All phenyl substituents are in axial positions with respect to the mean plane of the ring. The bond lengths in the ring have typical values (N—N, 1.414(2) Å; C—N, 1.454(2) Å). The N—C_{Ph} bond length is 1.411(2) Å.

The sulfur atom in the DMSO molecule is disordered over two positions (S(1) and S(1´)) with occupancies of 0.7 and 0.3, respectively. The DMSO molecule is involved in the weak intermolecular C(1´)—H(1´A)...O(1) and C(1´A)—H(1´C)...O(1A) hydrogen bonds only with

Scheme 4



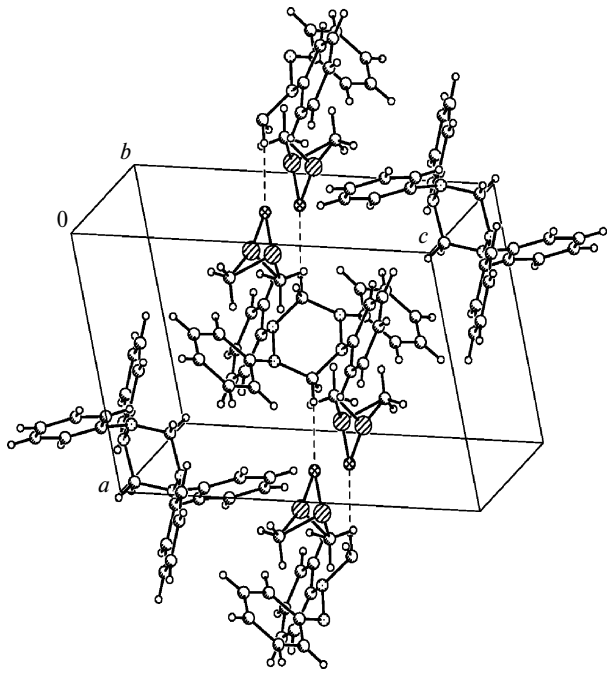


Fig. 4. Molecular packing of compound **16**. Intermolecular C—H...S hydrogen bonds are indicated by dashed lines.

independent molecule **16B** (Fig. 4). The H...O distance is 2.52(2) Å, and the C—H—O angle is 167°.

To extend the scope of cyclothiomethylation, we performed not only the reactions of phenyl hydrazines with CH_2O and H_2S but also the reactions of benzyl hydrazine (**17**) and tosyl hydrazine (**20**). In a neutral medium (the reagent ratio was 1 : 3 : 2, ~20 °C), the 1,3,4-thiadiazolidine and 1,3,5-dithiazine derivatives were obtained (Scheme 4).

It was found that benzyl hydrazine (**17**) reacts with CH_2O and H_2S to form bis[(6-benzyl-4,2,6-thiadiazolidin-2-yl)methyl] sulfide (**18**) and *N*-benzyl(perhydro-1,3,5-dithiazin-5-yl)amine (**19**) in 60 and 19% yields, respectively (see Scheme 4), whereas tosyl hydrazine (**20**) gives 3-[(*p*-tolyl)sulfonyl]-1,3,4-thiadiazolidine (**21**), *N*-(perhydro-1,3,5-dithiazin-5-yl)-*p*-tolylsulfonamide (**22**), and 3,7-bis(*p*-tolylsulfonylamino)-1,5-dithia-3,7-diazacyclooctane (**23**) in 21, 38, and 41% yields, respectively.

All our attempts to perform the selective synthesis of 1,3,4-thiadiazolidines starting from tosyl hydrazine (**20**) failed. Under the reaction conditions used, we obtained a mixture of the above-mentioned nitrogen- and sulfur-containing heterocycles **21—23** in all experiments.

According to the experimental data, benzyl and tosyl hydrazines are more reactive in reactions with CH_2O and H_2S in a neutral medium compared to mono- and 1,2-diphenyl-substituted hydrazines. In benzyl hydrazine, there is no p—π conjugation between the aromatic ring and the lone electron pairs on the nitrogen atoms, which is confirmed by the ease of addition of formaldehyde thio- and hemiacetals to the hydrazine group giving rise to heterocycles **18** and **19**, respectively.

Heterocycles **18**, **19**, and **21—23** were isolated in individual state by column chromatography. The structures of these compounds were confirmed by spectroscopic methods (^1H and ^{13}C NMR and IR spectroscopy and positive-ion mass spectrometry). In addition, the structures of compounds **18** and **23** were established by X-ray diffraction.

The ^{13}C NMR spectrum of sulfide **18** shows four signals (δ_C 55—60) assigned to the C atoms of the methylene groups, which are located between the N and S atoms and between the N atom and the Ph ring ($N\underline{C}H_2Ph$). The signals for the aromatic C atoms are observed at δ 127—137. It should be noted that the ^{13}C NMR spectrum of compound **21** shows only two high-field signals (δ 57.7 and 58.1) corresponding to the nonequivalent C atoms of the methylene groups of the thiadiazolidine ring. The mass spectrum of compound **18** is little informative due to instability of this compound. In the crystal structure, the bis[(6-benzyl-4,2,6-thiadiazolidin-2-yl)methyl] sulfide molecule (**18**) exists as a centrosymmetric dimer, in which two monomeric fragments are related by a twofold pseudoaxis passing through the S(1) atom (Fig. 5).

The mass spectrum of compound **19** has a low-intensity molecular ion peak at *m/z* 226; the higher-intensity peak at *m/z* 91 corresponds to the [$CHSCH_2S$] fragment.

The ^{13}C NMR spectra of dithiazines **19** and **22** show, in addition to the characteristic signals of the dithiazine ring (at δ_C 31.7, 58.2 and 31.9, 60.1, respectively), signals belonging to the C atoms of the aromatic ring (δ_C 127—138).

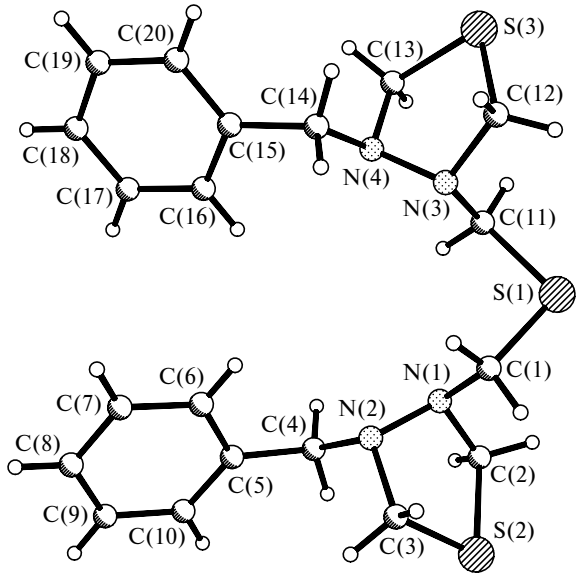


Fig. 5. Molecular structure of bis[(6-benzyl-4,2,6-thiadiazolidin-2-yl)methyl] sulfide (**18**).

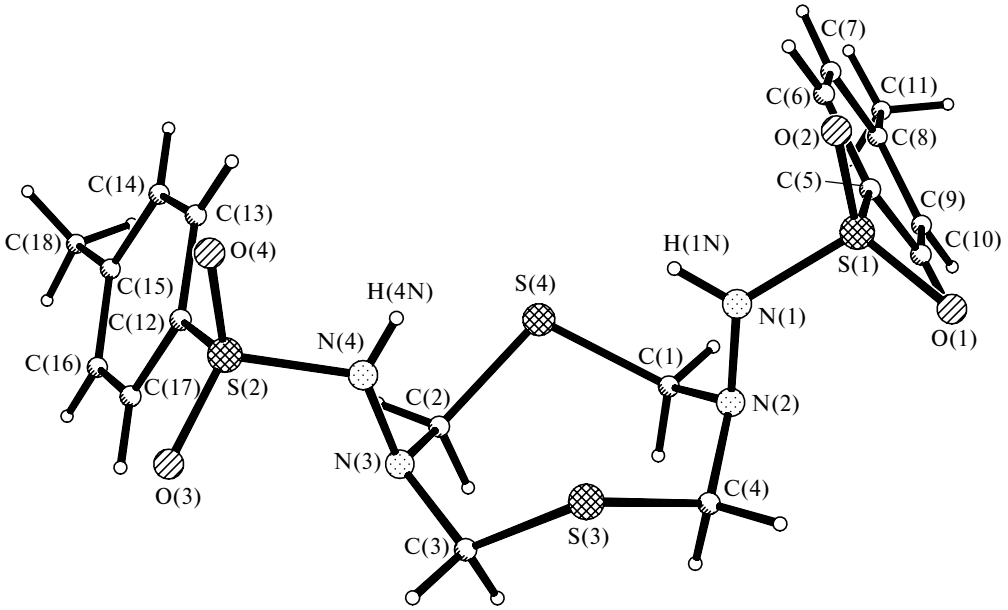


Fig. 6. Molecular structure of 3,7-bis(*p*-tolylsulfonylamino)-1,5-dithia-3,7-diazacyclooctane (**23**) in crystals.

The ^{13}C NMR spectrum of compound **23** has a high-field signal at δ_C 21.2 corresponding to the carbon atom of the Me group and one signal at δ_C 62.2, which is indicative of the equivalence of four C atoms of the methylene groups and, consequently, of the symmetric structure of 3,7-bis(*p*-tolylsulfonylamino)-1,5-dithia-3,7-diazacyclooctane (**23**). This is confirmed by ^1H NMR spectroscopic data. The methylene groups of the eight-membered heterocycle are equivalent, and their signals appear as an AB system (doublets at δ_H 4.04 and 4.16, $^3J_{AB}$ = 14.5 Hz).

According to X-ray diffraction data, the eight-membered heterocycle, *viz.*, 1,5-dithia-3,7-diazacyclooctane, in the crystal structure of compound **23** adopts a chair—chair conformation (a crown with the heteroatoms occupying the apical positions). The aromatic substituents are in axial positions at the nitrogen atom in the *cis* configuration (Fig. 6).

Similar conformations of the ring are also observed in 3,7-di[(*R*)-(+)-1′-methylbenzyl]-3,7-diaza-1,5-dithiacyclooctane[24] and 1,5,3,7-diazadiphosphacyclooctanes.[25,26] The nitrogen atoms in the latter compounds have a planar-trigonal coordination due to conjugation between the lone electron pairs and the π systems of the benzene rings. This conjugation fixes the conformations of the aromatic fragments at the nitrogen atoms.

In the crystal structure of compound **23**, there is one solvent ($CHCl_3$) molecule per asymmetric unit.

Studies of cyclothiomethylation of phenyl and 1,2-diphenyl hydrazines having p—π conjugation demonstrated that heterocyclization with CH_2O and H_2S more efficiently occurs in an alkaline medium, this reaction with phenyl hydrazine more efficiently proceeds under neutral or acidic conditions, whereas benzyl and tosyl hydrazines more actively react with CH_2O and H_2S in a neutral medium (without acidic or alkaline additives). All the hydrazines under study are characterized by the formation of 1,3,4-thiadiazolidines. Monosubstituted hydrazines give also perhydro-1,3,5-dithiazines. In addition, the reaction of phenyl hydrazine produces 1,3-thiazetidine and 1,2,4,5-tetrazine derivatives. The reaction of tosyl hydrazine affords also 1,5-dithia-3,7-diazacyclooctane.

To summarize, the thiomethylation pathway of aryl-substituted hydrazines is determined by the nature and the structures of the starting substrates as well as by the reaction conditions (pH and the temperature).

Experimental

Thiomethylation products **2—9** were analyzed by GLC on a Chrom-5 chromatograph (flame-ionization detector, SE-30 (5%) stationary phase on Chromaton N-AW-HMDS, 2400×3 mm steel packed column, temperature programming from 50 to 270 °C at a rate of 8 °C min^{-1}, helium as the carrier gas). Products **13—16** were analyzed by HPLC on an LKB chromatograph (photometric detector, the wavelength was 238 nm). The separation was carried out at room temperature on a metallic column (125×4 mm) packed with the Separon SGX C_{18} sorbent (grain size was 5 μm). The MeCN—H_2O mixture (60 : 40, v/v) was used as the mobile phase; the eluent flow rate was 0.2 mL min^{-1}. The ^1H NMR spectra of compounds **2**, **14—16**, **18**, and **23** were recorded on a Bruker spectrometer (300 MHz). The ^1H NMR spectra of the other compounds were measured on a Tesla BS-487 spectrometer (80 MHz). The ^{13}C NMR spectra were recorded on a Jeol FX 90Q spectrometer (22.50 MHz) in $CDCl_3$ with Me_4Si as the internal standard. The IR spectra were measured on a Specord 75 IR spectrophotometer in Nujol mulls. The GLC-mass spectrometry was carried out on a Finnigan 4021 instrument (50000×0.25 mm glass capil-

lary column, HP-5 stationary phase, helium as the carrier gas, temperature programming from 50 to 300 °C at a rate of 5 °C min^{-1}, the vaporizer temperature was 280 °C, the ion source temperature was 250 °C, 70 eV). Elemental analysis was performed on a Karlo Erba 1106 analyzer. Hydrogen sulfide was bubbled with the use of an ANP-10 peristaltic pump. The pH values of solutions were determined on a pH meter (pH-340). Column chromatography was performed with the use of silica gel; spots were visualized with iodine vapor. The TLC analysis was carried out on Silufol W-254 silica gel.

Thiomethylation of phenyl hydrazine (1). Method *A*. A 37% formaldehyde solution (2.21 mL, 0.03 mol) was saturated with hydrogen sulfide (0.02 mol) at 20 °C for 30 min. Then phenyl hydrazine hydrochloride (1.08 g, 0.01 mol) dissolved in EtOH was added dropwise. The reaction mixture was stirred at a specified temperature (0, 20, 40, or 70 °C) for 3 h and then neutralized with a KOH solution. The product was extracted with chloroform (2×30 mL), and the extract was dried with $CaCl_2$ and concentrated, after which a mixture of products **2—4** was obtained. The reaction product prepared at 40 °C was separated by column chromatography (C_6H_{14}—C_6H_6, 1 : 3, as the eluent). The reaction with the use of an analogous mixture of the reagents at 0 °C afforded individual compound **2**. The product was extracted with chloroform (2×30 mL), and the extract was dried with $CaCl_2$ and concentrated.

3-Phenyl-1,3,4-thiadiazolidine (2). The yield was 0.36 g (22%), pale-brown oil, R_f 0.27 (C_6H_{14}—C_6H_6, 1 : 3). Found (%): C, 58.15; H, 6.11; N, 16.93; S, 18.81. $C_8H_{10}N_2S$. Calculated (%): C, 57.83; H, 6.02; N, 16.87; S, 19.28. IR, ν/cm^{-1}: 750, 1020, 1300, 1600, 2920, 3050. ^{1}H NMR (25 °C), δ: 3.98 (d, 2 H, C(2)H_2, ^2J = 17.0 Hz); 4.70—4.90 (m, 2 H, C(5)H_2); 4.57 (br.s, 1 H, N(3)H); 7.00—7.25 (m, 5 H, H arom.). ^{13}C NMR, δ: 53.8 (t, C(2)); 55.2 (t, C(5)); 115.0 (d, C(7), C(11)); 121.2 (d, C(9)); 128.9 (d, C(8), C(10)); 148.4 (t, C(6)). MS, *m/z* (I_{rel} (%)): 166 $[M]^+$ (23); 120 $[M - CH_2S]^+$ (100); 105 $[M - NHCH_2S]^+$ (28); 91 $[M - NHCH_2SCH_2]^+$ (37); 77 $[C_6H_5]^+$ (49).

***N*-Phenyl(perhydro-1,3,5-dithiazin-5-yl)amine (3).** The yield was 0.55 g (26%), a dark-brown resinous substance, R_f 0.54 (C_6H_{14}—C_6H_6, 1 : 3). Found (%): C, 51.23; H, 5.47; N, 13.27; S, 30.03. $C_9H_{12}N_2S_2$. Calculated (%): C, 50.94; H, 5.66; N, 13.21; S, 30.19. IR, ν/cm^{-1}: 750, 1380, 1600, 2900, 3300—3400 br. ^{1}H NMR, δ: 4.79 (s, 2 H, C(2)H_2); 5.20 (s, 4 H, C(4)H_2, C(6)H_2); 7.37—8.13 (m, 5 H, H arom.). ^{13}C NMR, δ: 32.2 (t, C(2)); 58.6 (t, C(4), C(6)); 114.5 (d, C(9), C(13)); 120.3 (d, C(10), C(12)); 129.1 (d, C(11)); 145.9 (s, C(8)). MS, *m/z* (I_{rel} (%)): 212 $[M]^+$ (91); 166 $[M - CH_2S]^+$ (7); 134 $[M - SCH_2S]^+$ (48); 120 $[M - CH_2SCH_2S]^+$ (100).

6-Phenylperhydro[1,3,4]thiadiazino[5,4-*d*][1,3,5]dithiazine (4). The yield was 8%. MS, *m/z* (I_{rel} (%)): 270 $[M]^+$ (9); 224 $[M - CH_2S]^+$ (9); 179 $[M - SCH_2SCH]^+$ (56); 165 $[M - SCH_2SCHCH_2]^+$ (80); 133 $[M - SCH_2SCHCH_2S]^+$ (100); 119 $[M - SCH_2SCHCH_2SCH_2]^+$ (53); 105 $[M - CH_2SCH_2SCHCH_2SCH_2]^+$ (86); 91 $[M - NCH_2SCH_2SCHCH_2SCH_2]^+$ (23); 77 $[C_6H_5]^+$ (75); 59 $[CH_2SCH]^+$ (31).

Method *B*. A 37% formaldehyde solution (11.1 mL, 0.15 mol) was saturated with hydrogen sulfide (0.1 mol) for 30 min. Then a mixture of phenyl hydrazine (4.93 mL, 0.15 mol) and a solution of sodium butoxide in butanol, which was prepared according to a standard procedure from BuOH (27×2 mL) and sodium (6.9 g, 0.3 mol), was added dropwise. The resulting mixture was stirred at a specified temperature (0, 20, 40, or 70 °C) for 3 h, and then neutralized with a HCl solution. The organic phase was concentrated, and a mixture of compounds **2**, **3**, **5**, and **6** was isolated. The reaction product prepared at 0 °C was separated by column chromatography ($CHCl_3$—petroleum ether, 1 : 1, as the eluent).

***N*-Phenyl(perhydro-1,3-thiazetidin-3-yl)amine (5).** The yield was 0.3 g (18%), m.p. 128—129 °C, R_f 0.43 ($CHCl_3$—petroleum ether, 1 : 1). Found (%): C, 57.85; H, 6.13; N, 16.75; S, 19.52. $C_8H_{10}N_2S$. Calculated (%): C, 57.83; H, 6.02; N, 16.87; S, 19.28. IR, ν/cm^{-1}: 750, 1250, 1600, 2910, 3240. ^{1}H NMR, δ: 4.63 (s, 4 H, C(2)H_2, C(4)H_2); 6.88—7.10 (m, 5 H, H arom.). ^{13}C NMR, δ: 57.3 (t, C(2), C(4)); 114.3 (d, C(7), C(11)); 120.4 (d, C(9)); 129.2 (d, C(8), C(10)); 147.1 (t, C(6)). MS, *m/z* (I_{rel} (%)): 166 $[M]^+$ (2); 120 $[M - CH_2S]^+$ (10); 105 $[M - CH_2SCH_3]^+$ (40); 92 $[M - C_6H_5NH]^+$ (16); 77 $[C_6H_5]^+$ (100); 61 $[CH_2SCH_3]^+$ (36); 51 $[CN—NC]^+$.

1,4-Diphenylhexahydro-1,2,4,5-tetrazine (6). The yield was 0.55 g (23%), m.p. 164—166 °C (*cf.* lit. data[21]: m.p. 175 °C), R_f 0.68 ($CHCl_3$—petroleum ether, 1 : 1). IR, ν/cm^{-1}: 600, 660, 900, 1120, 1280, 1380, 1460, 1600, 2910. ^{1}H NMR, δ: 4.25 and 4.82 (both d, 2 H each, C(3)H_2, C(6)H_2, ^2J = 14.2 Hz); 6.01 (br.s, 2 H, N(1)H, N(4)H); 6.80—7.35 (m, 10 H, H arom.). ^{13}C NMR, δ: 63.3 (t, C(3), C(6)); 114.2 (d, C(8), C(12), C(14), C(18)); 120.3 (d, C(10), C(16)); 129.3 (d, C(9), C(11), C(15), C(17)); 145.6 (t, C(7), C(13)).

Method *C*. A mixture of compounds **2**, **3**, and **7** was prepared using an analogous mixture of the starting reagents at specified temperatures without the use of BuONa/BuOH. The product was extracted with chloroform (2×30 mL). The extract was dried with $CaCl_2$ and concentrated.

Formaldehyde phenylhydrazone (7). M.p. 26—27 °C (*cf.* lit. data[21]: m.p. 28—29 °C). MS, *m/z* (I_{rel} (%)): 120 $[M]^+$ (67); 92 $[M - NCH_2]^+$ (100); 77 $[M - NHNCH_2]^+$ (8).

Thiomethylation of 2,4-dinitrophenyl hydrazine (8). A 37% formaldehyde solution (2.2 mL, 0.03 mol) was saturated with hydrogen sulfide at 20 °C for 30 min. Then a solution of dinitrophenyl hydrazine **8** (1.98 g, 0.01 mol) in chloroform was added dropwise. The mixture was stirred at a specified temperature (0, 20, 40, or 70 °C) for 3 h. The product was extracted with chloroform (2×30 mL), dried with $CaCl_2$, and concentrated. Product **9** was obtained in a yield from 39 to 84% depending on the reaction temperature. In addition, products **10** and **11** were obtained.

Formaldehyde 2,4-dinitrophenylhydrazone (9). M.p. 165—166 °C (*cf.* lit. data[27]: m.p. 166—167 °C). ^{13}C NMR, δ: 115.6 (t, C(5)); 115.9 (d, C(9)); 121.7 (d, C(6)); 122.0 (d, C(8)); 128.8 (t, C(7)); 136.5 (t, C(1)); 144.2 (t, C(4)). MS, *m/z* (I_{rel} (%)): 210 $[M]^+$.

1,2,4-Trithiolane (10).[13] ^{13}C NMR, δ: 32.7 (s, C(3), C(5)). MS, *m/z* (I_{rel} (%)): 124 $[M]^+$.

1,2,4,6-Tetrathiepane (11).[13] MS, *m/z* (I_{rel} (%)): 170 $[M]^+$.

Thiomethylation of 1,2-diphenyl hydrazine (12). A 37% formaldehyde solution (1.5 mL, 0.02 mol) was saturated with hydrogen sulfide at 20 °C for 30 min. Then a solution of diphenyl hydrazine **12** (1.84 g, 0.01 mol) in chloroform was added dropwise, and the mixture was stirred at a specified temperature (0, 20, 40, or 70 °C) for 3 h. A mixture of products **13** and **14** was obtained.

Analogously to the above-described procedure, a mixture of products **13—16** was obtained upon predissolution of diphenyl hydrazine **12** (1.84 g, 0.01 mol) in a solution of sodium butoxide

in butanol, which was prepared from BuOH (1.8×2 mL) and sodium (0.46 g, 0.02 mol), at 20 °C. Compound **16** was isolated by recrystallization from DMSO. Products **13—15** were separated by silica gel column chromatography (CCl_4—petroleum ether, 9 : 1, as the eluent).

(*Z*)-Azobenzene (13). Orange-red crystals, m.p. 68 °C (*cf.* lit. data[28]: m.p. 68 °C). MS, *m/z* (I_{rel} (%)): 182 $[M]^+$.

3,4-Diphenyl-1,3,4-thiadiazolidine (14). The yield was 0.94 g (39%), bright-orange oil, R_f 0.26 (CCl_4—petroleum ether, 9 : 1). Found (%): C, 69.70; H, 5.69; N, 11.56; S, 13.17. $C_{14}H_{14}N_2S$. Calculated (%): C, 69.42; H, 5.79; N, 11.57; S, 13.22. IR, ν/cm^{-1}: 740, 1160, 1600, 2900, 3300. ^{1}H NMR (25 °C), δ: 4.65 (br.s, 4 H, C(2)H_2, C(5)H_2, $\Delta\nu_{1/2}$ = 24 Hz); 6.88—8.10 (m, 10 H, H arom.). ^{1}H NMR (–20 °C), δ: 4.23 (d, 2 H, C(2)H_A, C(5)H_A, ^2J = 10.0 Hz); 4.85 (d, 2 H, C(2)H_B, C(5)H_B, ^2J = 10.0 Hz); 6.88—8.10 (m, 10 H, H arom.). ^{13}C NMR, δ: 53.0 (t, C(2), C(5)); 115.1 (d, C(7), C(11), C(7′), C(11′)); 122.0 (d, C(9), C(9′)); 129.5 (d, C(8), C(10), C(8′), C(10′)); 148.2 (t, C(6), C(6′)). MS, *m/z* (I_{rel} (%)): 242 $[M]^+$ (62); 195 $[M - CH_2S]^+$ (100); 136 $[C_6H_5NCH_2SH]^+$ (12); 104 $[C_6H_5NHN]^+$ (38); 91 $[C_6H_5N]^+$ (16); 77 $[C_6H_5]^+$ (77); 51 $[CN—NC]^+$ (53); 46 $[CH_2S]^+$ (13).

5,6-Diphenyltetrahydro-1,3,5,6-dithiadiazepine (15). The yield was 0.29 g (10%), orange crystals, m.p. 123—125 °C, R_f 0.19 (CCl_4—petroleum ether, 9 : 1). Found (%): C, 62.44; H, 5.61; N, 9.33; S, 21.90. $C_{15}H_{16}N_2S_2$. Calculated (%): C, 62.50; H, 5.56; N, 9.72; S, 22.22. IR, ν/cm^{-1}: 740, 1200, 1450, 1590, 2900. ^{1}H NMR, δ: 4.00 (s, 2 H, C(2)H_2); 4.91 (d, 2 H, C(4)H_a, C(7)H_a, ^2J = 14.9 Hz); 5.03 (d, 2 H, C(4)H_b, C(7)H_b, ^2J = 14.9 Hz); 6.93—7.00 (m, 6 H, H arom.); 7.30—7.40 (m, 4 H, H arom.). ^{13}C NMR, δ: 36.3 (t, C(2)); 55.1 (t, C(4), C(7)); 113.6 (d, C(9), C(13), C(9′), C(13′)); 120.4 (d, C(11), C(11′)); 129.7 (d, C(10), C(12), C(10′), C(12′)); 145.3 (t, C(8), C(8′)). MS, *m/z* (I_{rel} (%)): 164 $[PhNNH(NCH_2)CH=S]^+$, 136 $[PhNHCH=S]^+$. M_{Cr} = 288±10.

1,2,4,5-Tetraphenylhexahydro-1,2,4,5-tetrazine (16). The yield was 0.27 g (6%), colorless crystals, m.p. 203—205 °C. ^{1}H NMR, δ: 5.42 (br.s, 4 H, C(3)H_2, C(6)H_2); 6.82 (t, 4 H, C(10)H, C(10a)H, C(10b)H, C(10c)H), ^3J = 7.3 Hz); 7.00 (d, 8 H, C(8)H, C(8a)H, C(8b)H, C(8c)H, C(12)H, C(12a)H, C(12b)H, C(12c)H, ^3J = 7.3 Hz); 7.20 (t, 8 H, C(9)H, C(9a)H, C(9b)H, C(9c)H, C(11)H, C(11a)H, C(11b)H, C(11c)H, ^3J = 7.3 Hz). ^{13}C NMR, δ: 60.4 (t, C(3), C(6)); 115.1 (d, C(8), C(8a), C(8b), C(8c), C(12), C(12a), C(12b), C(12c)); 120.2 (d, C(10), C(10a), C(10b), C(10c)); 129.3 (d, C(9), C(9a), C(9b), C(9c), C(11), C(11a), C(11b), C(11c)); 147.8 (t, C(7), C(7a), C(7b), C(7c)).

Thiomethylation of benzyl hydrazine (17). Analogously to the above-described procedure (method *C*), a mixture of products **18** and **19** was prepared from benzyl hydrazine (1.19 mL, 0.01 mol) at 20 °C; the starting reagents were taken in the ratio **17** : CH_2O : H_2S = 1 : 3 : 2. The mixture was separated by column chromatography (CCl_4—Et_2O, 5 : 1, as the eluent).

Bis[(6-benzyl-4,2,6-thiadiazolidin-2-yl)methyl] sulfide (18). The yield was 2.51 g (60%), colorless crystals, m.p. 100—106 °C, R_f 0.78 (CCl_4—Et_2O, 5 : 1). Found (%): C, 57.38; H, 6.26; N, 13.50; S, 23.00. $C_{20}H_{26}N_4S_3$. Calculated (%): C, 57.41; H, 6.22; N, 13.40; S, 22.97. IR, ν/cm^{-1}: 700, 1030, 1450, 1600, 2940. ^{1}H NMR, δ: 3.80 (br.s, 8 H, C(1)H_2, C(3)H_2, C(1′)H_2, C(3′)H_2); 4.15—4.54 (m, 8 H, C(5)H_2, C(7)H_2, C(5′)H_2, C(7′)H_2); 7.00—7.25 (m, 10 H, H arom.). ^{13}C NMR, δ: 55.7 (t, C(3)); 56.6 (t, C(5)); 57.7 (t, C(1)); 59.8 (t, C(7)); 127.5 (d, C(11), C(11′)); 128.4 (d, C(10), C(12), C(10′), C(12′)); 129.2 (d, C(9), C(13), C(9′), C(13′)); 138.0 (t, C(8), C(8′)).

***N*-Benzyl(perhydro-1,3,5-dithiazin-5-yl)amine (19).** The yield was 0.43 g (19%), a yellow resinous substance, R_f 0.28 (CCl_4—Et_2O, 5 : 1). Found (%): C, 53.07; H, 6.30; N, 12.38; S, 28.63. $C_{10}H_{14}N_2S_2$. Calculated (%): C, 53.10; H, 6.19; N, 12.39; S, 28.32. IR, ν/cm^{-1}: 700, 1030, 1450, 1600, 2940. ^{1}H NMR, δ: 4.25 (s, 2 H, C(2)H_2); 4.63 (s, 2 H, C(8)H_2); 4.72 (s, 4 H, C(4)H_2, C(6)H_2); 7.87—8.05 (br.s, 5 H, H arom.). ^{13}C NMR, δ: 31.7 (t, C(2)); 58.2 (t, C(4), C(6)); 59.0 (t, C(8)); 127.3 (d, C(12)); 128.4 (d, C(11), C(13)); 129.0 (d, C(10), C(14)); 138.15 (s, C(9)). MS, *m/z* (I_{rel} (%)): 226 $[M]^+$ (30); 192 $[M - H_2S]^+$ (5); 147 $[M - C_6H_5 - 2]^+$ (10); 131 $[C_6H_5CH_2NNC]^+$ (58); 118 $[C_6H_5CHNN]^+$ (23); 91 $[CHSCH_2S]^+$ (100); 77 $[C_6H_5]^+$ (58); $[SCH]^+$ (80).

Thiomethylation of tosyl hydrazine (20). A mixture of products **21—23** was prepared according to the above-described procedure (method *C*) from tosyl hydrazine (2.02 g, 0.01 mol) (**20**) and CH_2O (2.21 mL, 0.03 mol) at 0 °C. The mixture was separated by column chromatography. Compounds **21** and **22** were eluted with a 5 : 1 CCl_4—Et_2O mixture; product **23**, with $CHCl_3$.

3-[(*p*-Tolyl)sulfonyl]-1,3,4-thiadiazolidine (21). The yield was 0.51 g (21%), m.p. 134—135 °C, R_f 0.29 (CCl_4—Et_2O, 5 : 1). Found (%): C, 44.35; H, 5.00; N, 11.42; S, 26.43. $C_9H_{12}N_2S_2O_2$. Calculated (%): C, 44.24; H, 4.95; N, 11.47; S, 26.25. IR, ν/cm^{-1}: 720, 1150, 1300, 1600, 2900, 3200. ^{1}H NMR, δ: 1.73 (s, 3 H, C(13)H_3); 3.59 (d, 2 H, H_{ax}(2), H_{ax}(5), ^3J = 14.4 Hz); 4.50 (d, 2 H, H_{eq}(2), H_{eq}(5), ^3J = 14.4 Hz); 7.24 (br.s, 1 H, N(3)H); 7.47 (d, 4 H, H arom., ^3J = 8.1 Hz); 7.98 (t, 4 H, H arom., ^3J = 8.1 Hz). ^{13}C NMR, δ: 21.4 (q, C(13)); 57.7 (t, C(2)); 58.1 (t, C(5)); 127.8 (d, C(7), C(11)); 129.0 (d, C(8), C(12)); 134.9 (d, C(7)); 144.3 (s, C(10)). MS, *m/z* (I_{rel} (%)): 244 $[M]^+$ (70); 213 $[M - S - 2]^+$ (9); 182 $[M - SO_2 + 2]^+$ (12); 154 $[M - C_6H_5CH_2]^+$ (6); 123 $[CH_3C_6H_5S]^+$ (100); 89 $[HNCH_2SCH_2N]^+$ (6).

***N*-(Perhydro-1,3,5-dithiazin-5-yl)-*p*-tolylsulfonamide (22).** The yield was 1.1 g (38%), m.p. 145—146 °C, R_f 0.86 (CCl_4—Et_2O, 5 : 1). Found (%): C, 41.55; H, 4.85; N, 9.80; S, 33.58. $C_{10}H_{14}N_2S_3O_2$. Calculated (%): C, 41.36; H, 4.86; N, 9.65; S, 33.12. IR, ν/cm^{-1}: 750, 1140, 1320, 1600, 2900, 3210. ^{1}H NMR, δ: 2.59 (s, 3 H, C(15)H_3); 3.59 (d, 1 H, H_{eq}(2), ^2J = 13.7 Hz); 3.99 (d, 2 H, H_{eq}(4), H_{eq}(6), ^2J = 13.6 Hz); 4.50 (d, 1 H, H_{ax}(2), ^2J = 13.7 Hz); 4.71 (d, 2 H, H_{ax}(4), H_{ax}(6), ^3J = 13.6 Hz); 7.24 (br.s, 1 H, N(7)H); 7.47 (d, 2 H, H arom., ^3J = 8.1 Hz); 7.98 (t, 2 H, H arom., ^3J = 8.1 Hz). ^{13}C NMR, δ: 20.2 (d, C(15)); 31.9 (t, C(2)); 60.1 (t, C(4), C(6)); 128.3 (d, C(11), C(13)); 129.9 (d, C(10), C(14)); 131.2 (d, C(9)); 144.6 (s, C(12)). MS, *m/z* (I_{rel} (%)): 290 $[M]^+$ (6); 258 $[M - S]^+$ (6); 155 $[CH_3C_6H_4SO_2]^+$ (10); 135 $[CH_3C_6H_4SO]^+$ (100); 124 $[CH_3C_6H_4SH]^+$ (25); 91 $[CH_3C_6H_4]^+$ (96); 44 $[CS]^+$ (67).

3,7-Bis(*p*-tolylsulfonylamino)-1,5-dithia-3,7-diazacyclooctane (23). The yield was 1.66 g (41%), colorless crystals, m.p. 175—177 °C, R_f 0.09 (CCl_4—Et_2O, 5 : 1). Found (%): C, 44.24; H, 4.83; N, 11.48; S, 26.26. $C_{18}H_{24}N_4O_4S_4$. Calculated (%): C, 44.26; H, 4.92; N, 11.48; S, 26.23. IR, ν/cm^{-1}: 660, 1160, 1450, 1600, 2900, 3200. ^{1}H NMR, δ: 2.42 (s, 6 H, C(17)H_3, C(17′)H_3); 4.04 (d, 4 H, C(2)H_A, C(4)H_A, C(6)H_A, C(8)H_A, $^3J_{AB}$ = 14.5 Hz); 4.16 (d, 4 H, C(2)H_B, C(4)H_B, C(6)H_B, C(8)H_B, $^3J_{AB}$ = 14.5 Hz); 7.30 and 7.77 (both d, 4 H each, H arom., ^3J = 8.2 Hz); 8.50 (br.s, 2 H, N(9)H, N(9′)H).

^{13}C NMR, δ: 21.2 (q, C(17), C(17′)); 62.2 (t, C(2), C(4), C(6), C(8)); 127.3 (d, C(12), C(16), C(12′), C(16′)); 129.4 (d, C(13), C(15), C(13′), C(15′)); 136.6 (s, C(14), C(14′)); 143.6 (s, C(11), C(11′)).

X-ray diffraction study of compound 16, which was prepared by recrystallization from DMSO, was carried out on an Enraf-Nonius CAD4 diffractometer (Mo-Kα radiation, graphite monochromator, θ/2θ scanning technique, $2\theta_{max} = 54°$) at 293 K. Merging of 5713 observed reflections gave 5376 independent reflections ($R_{int} = 0.0603$), which were used in the structure solution and refinement. Colorless crystals of **16** ($C_{26}H_{24}N_4 \cdot \cdot C_2H_6OS$) are triclinic: $a = 9.172(2)$ Å, $b = 11.932(2)$ Å, $c = 13.087(3)$ Å, $\alpha = 66.65(3)°$, $\beta = 72.05(3)°$, $\gamma = 79.46(3)°$, $V = 1247.8(4)$ Å^3, $d_{calc} = 1.253$ g cm^{-3}, space group $P\bar{1}$, $Z = 2$. The structure was solved by direct methods and refined by the full-matrix least-squares method against F^2_{hkl} with anisotropic displacement parameters. The hydrogen atoms were located in difference electron density maps and refined using a riding model. The final R factors were as follows: $wR_2 = 0.1564$ (calculated based on F^2_{hkl} for all 5376 reflections), $R_1 = 0.0504$ (calculated based on F_{hkl} for 4102 reflections with $I > 2\sigma(I)$), GOF 0.973, 328 parameters were refined.

X-ray diffraction study of compound 18, which was prepared by recrystallization from a 5 : 1 CCl_4—Et_2O mixture, was carried out on a Bruker SMART 1000 CCD Area Detector diffractometer (Mo-Kα radiation, graphite monochromator, θ/2θ scanning technique, $2\theta_{max} = 54°$) at 120 K. Colorless crystals, $C_{20}H_{26}N_4S_3$ (M = 218.62), are orthorhombic: $a = 9.4221(15)$ Å, $b = 10.5469(17)$ Å, $c = 20.836(3)$ Å, $V = 2070.6(6)$ Å^3, space group $P2_12_12_1$, $Z = 8$, $d_{calc} = 1.343$ g cm^{-3}. Merging of 15240 observed reflections gave 3843 independent reflections ($R_{int} = 0.0699$), which were used in the structure solution and refinement. The structure was solved by direct methods and refined by the full-matrix least-squares method against F^2_{hkl} with anisotropic displacement parameters. The hydrogen atoms were placed in geometrically calculated positions and refined using a riding model. The final R factors were as follows: $wR_2 = 0.0968$ (calculated based on F^2_{hkl} for all 3843 reflections used in the final step), $R_1 = 0.0456$ (calculated based on F_{hkl} for 3117 reflections with $I > 2\sigma(I)$), GOF 1.010, 244 parameters were refined.

X-ray diffraction study of compound 23, which was prepared by recrystallization from $CHCl_3$, was carried out on a Syntex $P2_1$ diffractometer (Mo-Kα radiation, graphite monochromator, θ/2θ scanning technique, $2\theta_{max} = 54°$) at 163 K. Colorless crystals, $C_{19}H_{25}Cl_3N_4O_4S_4$ (M = 608.02), are monoclinic: $a = 10.528(4)$ Å, $b = 18.293(6)$ Å, $c = 14.916(6)$ Å, $\beta = 109.45°$, $V = 2708.6(17)$ Å^3, space group $P2_1n$, $Z = 4$, $d_{calc} = 1.491$ g cm^{-3}. A total of 6289 reflections were collected. Merging of equivalent reflections gave 5907 independent reflections ($R_{int} = 0.0182$), which were used in the structure solution and refinement. The structure was solved by direct methods and refined by the full-matrix least-squares method against F^2_{hkl} with anisotropic displacement parameters. The hydrogen atoms of the NH groups were located in difference electron density maps. The other hydrogen atoms were placed in geometrically calculated positions. All H atoms were refined using a riding model. The final R factors were as follows: $R_1 = 0.0430$ (calculated based on F_{hkl} with the use of 3786 reflections with $I > 2\sigma(I)$), $wR_2 = 0.1036$ (calculated based on F^2_{hkl} for all 5907 reflections), GOF 0.998, 307 parameters were refined.

All calculations were carried out with the use of the SHELXTL PLUS 5 program package.[29]

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References

1. S. R. Khafizova, V. R. Akhmetova, T. V. Tyumkina, L. M. Khalilov, R. V. Kunakova, and U. M. Dzhemilev, *Izv. Akad. Nauk, Ser. Khim.*, 2004, 1652 [*Russ. Chem. Bull., Int. Ed.*, 2004, **53**, 1717].
2. M. R. Stillings, A. P. Welbourn, and D. J. Walter, *Med. Chem.*, 1986, **29**, 2280.
3. M. Kidwai, N. Negi, and S. R. Chaudhary, *Acta Pharma*, 1995, **45**, 511.
4. US Pat. 4,246,126 (1981); *Chem. Abstrs*, 1981, **94**, 142505h.
5. *Heterocyclic Compounds*, Ed. R. C. Elderfield, Wiley, New York, 1961.
6. S. P. Gromov, S. N. Dmitrieva, A. I. Vedernikov, and M. V. Churakova, *Izv. Akad. Nauk, Ser. Khim.*, 2004, 1362 [*Russ. Chem. Bull., Int. Ed.*, 2004, **53**, 1417].
7. R. V. Kunakova, S. R. Khafizova, Yu. S. Dal´nova, R. S. Aleev, L. M. Khalilov, and U. M. Dzhemilev, *Neftekhimiya*, 2002, **42**, 382 [*Russ. Petroleum Chem.*, 2002, **42**, 347 (Engl. Transl.)].
8. S. R. Khafizova, V. R. Akhmetova, R. V. Kunakova, and U. M. Dzhemilev, *Izv. Akad. Nauk, Ser. Khim.*, 2003, 1722 [*Russ. Chem. Bull., Int. Ed.*, 2003, **52**, 1817].
9. S. R. Khafizova, V. R. Akhmetova, L. F. Korzhova, T. V. Khakimova, G. R. Nadyrgulova, R. V. Kunakova, E. A. Kruglov, and U. M. Dzhemilev, *Izv. Akad. Nauk, Ser. Khim.*, 2005, 423 [*Russ. Chem. Bull., Int. Ed.*, 2005, **54**, 432].
10. V. R. Akhmetova, G. R. Nadyrgulova, S. R. Khafizova, R. R. Khairullina, E. A. Paramonov, R. V. Kunakova, and U. M. Dzhemilev, *Zh. Org. Khim.*, 2006, **42**, 151 [*Russ. J. Org. Chem.*, 2006, **42** (Engl. Transl.)].
11. A. P. Grekov and V. Ya. Veselov, *Fizicheskaya khimiya gidrazina* [*Physical Chemistry of Hydrazine*], Naukova Dumka, Kiev, 1979, 264 pp. (in Russian).
12. *Comprehensive Organic Chemistry*, Eds S. D. Barton and W. D. Ollis, Pergamon Press, Oxford—New York—Toronto—Sydney—Paris—Frankfurt, 1979.
13. R. S. Aleev, Yu. S. Dal´nova, Yu. I. Popova, R. M. Masagutov, and S. R. Rafikov, *Dokl. Akad. Nauk SSSR,* 1988, **303**, 873 [*Dokl. Chem.*, 1988 (Engl. Transl.)].
14. B. Rassow, *J. Prakt. Chem.*, 1901, **64**, 136.
15. Weygand-Hilgetag, *Organisch-Chemische Experimentierkunst*, Leipzig, 1964.
16. R. G. Kostyanovskii, P. Rademakher, Yu. I. El´natanov, G. K. Kadorkina, G. A. Nikiforov, I. I. Chervin, S. V. Usachev, and V. R. Kostyanovskii, *Izv. Akad. Nauk, Ser. Khim.*, 1997, 1346 [*Russ. Chem. Bull.*, 1997, **46**, 1291 (Engl. Transl.)].

17. J. E. Anderson and J. M. Lehn, *J. Am. Chem. Soc.*, 1967, **89**, 81.
18. G. V. Shustov, A. Yu. Shibaev, Yu. V. Puzanov, and R. G. Kostyanovskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1988, 1869 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1988, **37**, 1671 (Engl. Transl.)].
19. V. J. Baker, A. R. Katritzky, and J.-P. Majoral, *J. Chem. Soc., Perkin Trans. 2*, 1975, 1191.
20. H. Günter, *NMR Spectroscopy, An Introduction*, Wiley, Chichester, 1980.
21. B. V. Ioffe and V. S. Stopskii, *Dokl. Akad. Nauk SSSR,* 1967, **175**, 1064 [*Dokl. Chem.*, 1967 (Engl. Transl.)].
22. Houben-Weyl, *Methoden der organischen Chemie*, Verlag Georg Tieme, Stuttgart, 1953.
23. *Analiz nefti i nefteproduktov* [*Analysis of Petroleum and Petroleum Products*], Ed. B. M. Rybak, Gostoptekhizdat, Moscow, 1962, **5**, 887 pp. (in Russian).
24. G. Cadenas-Pliego, M. J. Rosales-Hoz, R. Contreras, and A. Flores-Parra, *Tetrahedron Asymmetry*, 1994, **5**, 633.
25. R. M. Kuznetsov, A. S. Balueva, I. A. Litvinov, A. T. Gubaidullin, G. N. Nikonov, A. A. Karasik, and O. G. Sinyashin, *Izv. Akad. Nauk, Ser. Khim.*, 2002, 142 [*Russ. Chem. Bull., Int. Ed.*, 2002, **51**, 151].
26. B. A. Arbuzov, O. A. Erastov, G. N. Nikonov, I. A. Litvinov, D. S. Yufit, and Yu. T. Struchkov, *Dokl. Akad. Nauk SSSR,* 1981, **257**, 127 [*Dokl. Chem.*, 1981 (Engl. Transl.)].
27. N. D. Cheronis, *Micro and Semimicro Methods*, Intersci. Publ., New York, 1954.
28. *Spravochnik khimika* [*Chemist's Handbook*], Ed. B. P. Nikol´skii, Khimiya, Moscow—Leningrad, 1964, **3**, 1008 pp. (in Russian).
29. G. M. Sheldrick, *SHELXTL PLUS, PC Version, System of Computer Programs for the Determination of Crystal Structure from X-ray Diffraction Data, Rev. 502*, Siemens Analytical X-Ray Instruments, Inc., Germany, 1994.

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