Thiocarbamoylation of amine-containing compounds

5.* The mechanism of reactions of tetramethylthiuram disulfide with aliphatic amines

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Thiocarbamoylation of aliphatic amines with tetramethylthiuram disulfide (TMTD) was studied. The reactions were established to proceed according to a two-stage mechanism. In the first stage, *S*-(thiocarbamoyl)thiohydroxylamines and dimethyl dithiocarbamates are formed. The latter exist in equilibrium with dimethyldithiocarbamic acid, which can undergo decomposition to give dimethylamine and carbon disulfide. In the second stage, several competitive transformations of these intermediates into the final products occur, *viz.*, (1) the reactions of CS_2 with primary amines on heating (70—110 °C) yield mixed and symmetrical thioureas and the reactions of CS_2 with secondary amines give symmetrical dithiocarbamates, and (2) insertion of CS_2 into *S*-(thiocarbamoyl)thiohydroxylamines affords thiuram disulfides. Thiuram disulfides formed from primary amines decompose to give isothiocyanates, which are converted into thioureas by condensation with amines, whereas thiuram disulfides which are obtained in the reactions with secondary amines and which cannot form thioureas react with amines analogously to TMTD.

Key words: tetramethylthiuram disulfide, aliphatic amines, dialkyl(cycloalkyl)ammonium dialkyl(cycloalkyl)dithiocarbamates, *S*-(*N*,*N*-dimethylthiocarbamoyl)-*N*-alkyl(dialkyl)-(cycloalkyl)thiohydroxylamines, mixed *N*′-alkyl(dialkyl)(cycloalkyl)-*N*,*N*-dimethylthiuram disulfides, dialkyl(dicycloalkyl)thioureas, benzyl and cyclohexyl isothiocyanates.

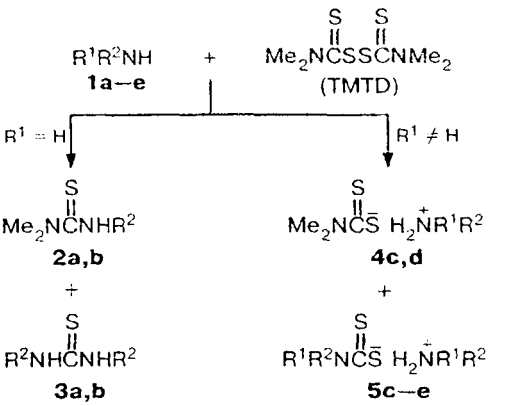
Previously, we have demonstrated[2—11] that one of the best procedures for the introduction of the thiocarbonyl group into organic compounds involves the reactions of tetramethylthiuram disulfide (TMTD) with amines, which had been poorly studied. We have established[1] that primary amines (**1a,b**) react with TMTD at temperatures below 110 °C to form mixtures containing mixed (**2a,b**) and symmetrical (**3a,b**) thioureas, while secondary amines (**1c—e**) give mixtures of dialkyl(cycloalkyl)ammonium dimethyldithiocarbamates (**4a,b**) and "symmetrical" dialkyl(cycloalkyl)ammonium dialkyl(cycloalkyl)dithiocarbamates (**5c—e**) with the latter predominating (Scheme 1).

The present work is devoted to studies of the character of the processes resulting in these products.

Hypothetical schemes of the reactions of TMTD with amines have been proposed previously. It was suggested[12] that TMTD initially decomposes to give sulfur and tetramethylthiuram monosulfide, which undergoes nucleophilic replacement with amines to form one mole of substituted thiourea and dimethyldithiocarbamic acid. The latter reacts with amines yielding the same thiourea with elimination of H_2S[12] (Scheme 2).

This scheme cannot explain many facts observed by us, for example, the formation of symmetrical thioureas

Scheme 1



$R^1 = H$, $R^2 = C_6H_{11}$ (**a**); $R^1 = H$, $R^2 = PhCH_2$ (**b**); $R^1 + R^2 = (CH_2)_2O(CH_2)_2$ (**c**); $R^1 + R^2 = (CH_2)_5$ (**d**); $R^1 = R^2 = Me$ (**e**)

3a,b, which were detected among the products of the reactions of TMTD with primary amines **1a,b**.

Based on the results of the synthesis and kinetic studies, a radical-ionic mechanism of the reactions of TMTD with aliphatic amines **1** was suggested.[13,14] At 20 °C, these reactions afford *S*-(*N*,*N*-dimethylthiocarbamoyl)thiohydroxylamines (**6**) and dimethyldithiocarbamic acid (**7**), which reacts with amines **1** to give the

* For Part 4, see Ref. 1.

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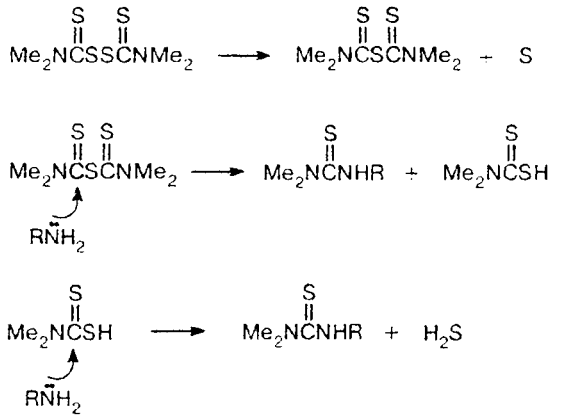
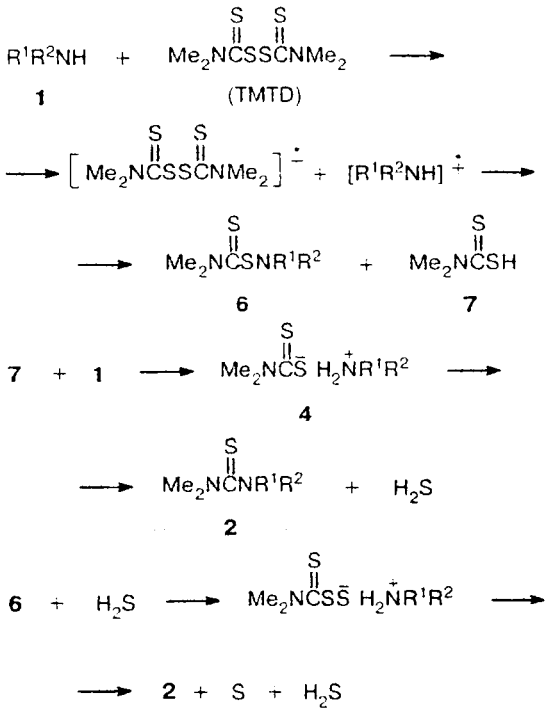
Scheme 2



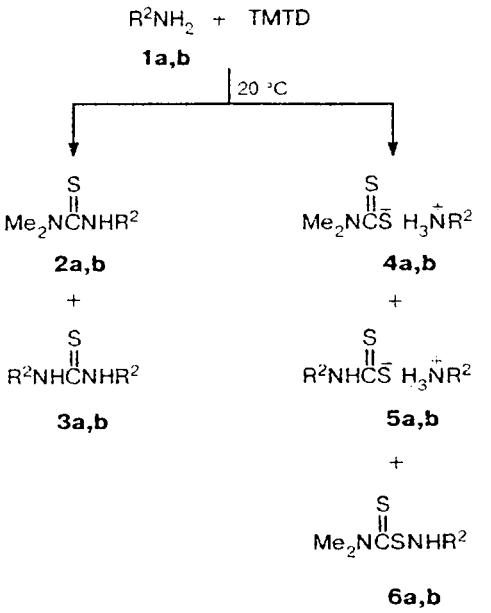
corresponding salts **4**. When the temperature is increased to 70 °C, salts **4** are converted into mixed *N'*,*N'*-dialkyl(*N'*-cycloalkyl)-*N*,*N*-dimethylthioureas **2** with elimination of H_2S, which serves as a catalyst of decomposition of *S*-(thiocarbamoyl)thiohydroxylamines **6** to form an additional amount of thiourea **2** (Scheme 3).

Scheme 3



The kinetics was studied with the use of high-frequency titration of dithiocarbamic acid **7** that formed[13,14] with $CuSO_4$. However, there are reasons to cast doubts on the reliability of this method because $CuSO_4$ reacts not only with dithiocarbamic acid **7**, but also with amines[15] and thiuram disulfides.[16] Moreover, the structures of a number of the resulting compounds[13] were not confirmed. Nevertheless, the idea of the formation of radical ions is of interest and will be specially investigated and discussed elsewhere.[17] Previously, we have demonstrated[1] that the reaction is much more complex. Actually, the reactions of TMTD with amines **1a—e** at 20 °C afforded *S*-(thiocarbamoyl)thiohydroxylamines **6a—e**. However, a mixture of salts **4a—d** and **5a—e** rather than individual salts **4a—e**, as has been reported previously,[13,14] was formed along with **6a—e**. In the case of primary amines **1a,b**, small amounts of thioureas **2a,b** and **3a,b** were also detected (Scheme 4) (see also Ref. 1).

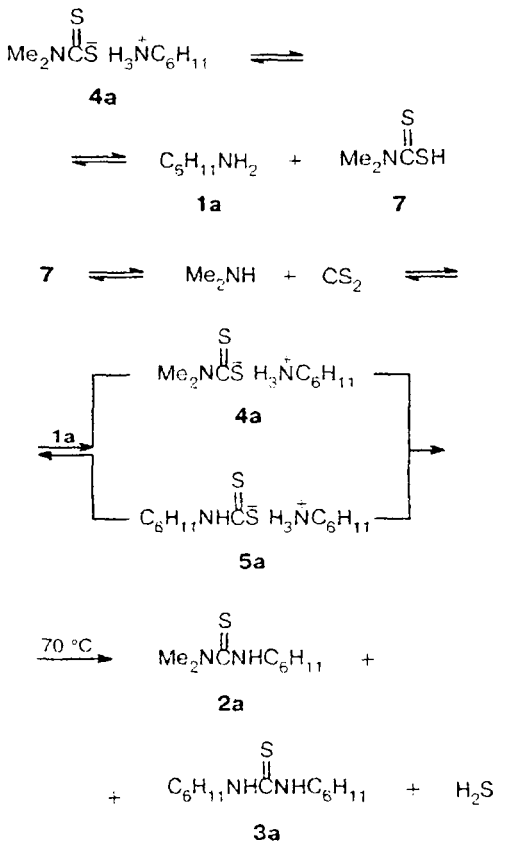
Scheme 4



To elucidate the pathways of formation of the final products, it was necessary to disclose the ways of "symmetrization" of dithiocarbamates, the formation of symmetrical thioureas, and transformations of thiohydroxylamines.

These problems were studied in most detail using the reaction of TMTD with cyclohexylamine **1a** as an example. The "symmetrization" of the salts can be explained as follows: the reaction of TMTD with **1a** affords *N*-cyclohexyl-*S*-(*N*,*N*-dimethylthiocarbamoyl)thiohydroxylamine **6a** and salt **4a**. Compound **4a** is a salt of a weak acid. In solutions, this salt dissociates into the amine and acid **7**. It is known that the latter readily decomposes to give dimethylamine and carbon disulfide.[18] This process occurs most rapidly at elevated temperature. Apparently, the reactions of CS_2 with amines which are present in the mixture afford mixtures of salts **4a** and **5a** (mixture A). Since this is an equilibrium process, interconversions of dithiocarbamates af-

Scheme 5



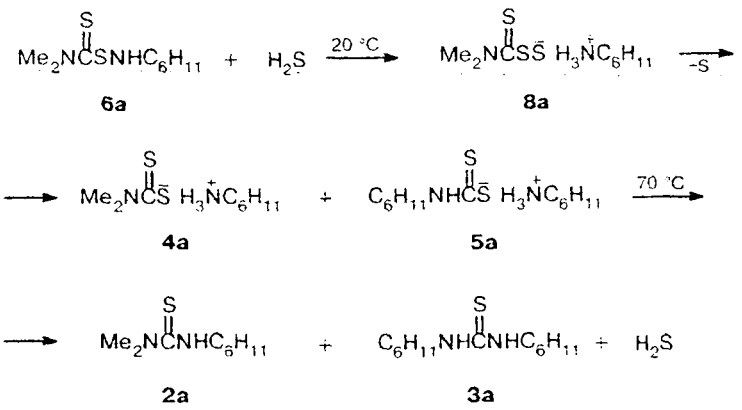
ford predominantly more stable "symmetrical" salt **5a** as the final product. This fact was confirmed experimentally. Thus when heated in toluene or dioxane at 80—110 °C for 5 min, mixture **A** (the initial composition was as follows: **4a**, ~85%; and **5a**, ~15% (see Ref. 1)) was converted into a mixture of salts **4a** and **5a** (17 and 83%, respectively; see the Experimental section). Prolonged heating resulted in further conversion of salts **4a** and **5a** into a mixture of thioureas **2a** and **3a** in 10 and 90% yields, respectively (Scheme 5).

Heating afforded also dimethylammonium *N,N*-dimethyldithiocarbamate, which is additional evidence for decomposition of acid **7** to form dimethylamine and carbon disulfide.

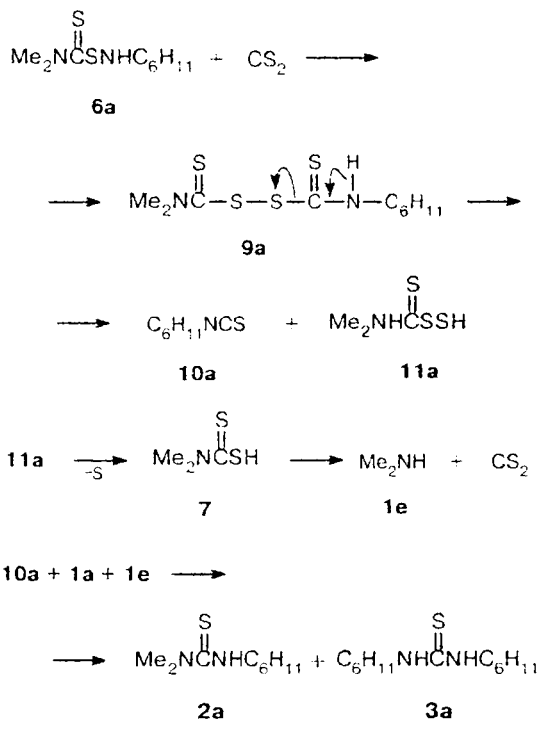
Several pathways of transformations of thiohydroxylamine **6a** under the reaction conditions are theoretically possible. The first pathway involves the conversion of compound **6a** under the action of hydrogen sulfide at 70 °C to form a mixture of thioureas **2a** and **3a**. In this case, symmetrization of the products is also observed. This process occurs in several stages. First, H_2S is inserted into molecule **6a** to give cyclohexylammonium *N,N*-dimethyldithiocarbamate hydrosulfide (**8a**),[19] which readily decomposes to yield sulfur and a mixture of salts **4a** and **5a**. We succeeded in isolating the latter even at room temperature by passing H_2S through a toluene (benzene) solution of compound **6a**. Then, according to Scheme 5, a mixture of salts **4a** and **5a** is converted on heating (70—110 °C) into thioureas **2a** and **3a** (70 and 30% yields, respectively; see Scheme 6).

However, this scheme leaves unexplained the formation of thioureas at 20 °C, when thermolysis of salts of *N,N*-dimethyldithiocarbamic acid with elimination of H_2S is impossible. It can be suggested that compound **6a** also spontaneously decomposes to give sulfur and thioureas. However, this pathway was not confirmed experimentally. Thioureas were not detected in a boiling benzene solution of compound **6a**. As was demonstrated above, thiohydroxylamine **6a** was formed together with CS_2 and amines **1a** and **1e**. Therefore, thioureas can apparently be formed in the reactions of **6a** with amines. However, according to the published data,[19,20] this reaction yielded transamination products. Note that heating of equimolar amounts of compounds **1a** and **6a** in benzene afforded a mixture of nearly equal amounts of thioureas **2a** and **3a**, but their yields were insignificant (~12—13% each). Our results are consistent with the published data.[19,20] Apparently, compounds **2a** and **3a** are the reaction products of **1a** with TMTD, which is generated upon thermal decomposition of thiohydroxylamine **6a**, rather than the direct reaction products of compounds **1a** and **6a**. Actually, TMTD was isolated in

Scheme 6



Scheme 7



46% yield by HPLC from a benzene solution of **6a** subjected to refluxing for 30 min. The formation of thiuram disulfides upon thermal decomposition of *N,N*-substituted thiohydroxylamines, whose structures are similar to that of compound **6a**, was reported in the literature.[21] Thus, one has to consider the last pathway. This pathway, which may afford thioureas in satisfactory yields, involves the insertion[22,23] of CS_2 into the N—S bond to form mixed *N'*-cyclohexyl-*N,N*-dimethylthiuram disulfide (**9a**). Due to the presence of the H atom at the N atom adjacent to the disulfide group, compound **9a** can undergo decomposition to give cyclohexyl isothiocyanate (**10a**) and *N,N*-dimethyl(trithio)peroxycarbamic acid (**11**). The latter is converted into *N,N*-dimethyldithiocarbamic acid **7** with elimination of sulfur. Acid **7**, in turn, decomposes to produce dimethylamine (**1e**) and CS_2. The reaction of isothiocyanate **10a** with a mixture of amines **1a** and **1e** is yet another source of thioureas **2a** and **3a** (Scheme 7).

The suggested scheme was confirmed by the following experiment. Thiuram disulfide **9a** was obtained in 48% yield by slow addition of carbon disulfide to a benzene solution of compound **6a** at 0—5 °C (Table 1). In dioxane, compound **9a** decomposed even at 30 °C to form acid **11** and isothiocyanate **10a**, which was also isolated by extraction with hexane and identified as thiourea **3a** by addition of amine **1a** (m.p. 178—180 °C). Note that *N'*-benzyl-*N,N*-dimethylthiuram disulfide **9b** decomposed so readily that thiourea **2b** (~40%) was always formed even when the reaction of thiohydroxylamine **6b** with carbon disulfide was performed with cooling.

Decomposition of thiuram disulfide **9a** yielding isothiocyanate **10a** was studied by IR spectroscopy, considering a change in the intensity of the ν(NCS) stretching vibration band at 2112—2116 cm^{-1} in different solvents. It was demonstrated that compound **9a** in dioxane decomposed even at room temperature, while decomposition in toluene or chloroform occurred more slowly. Judging from the optical density (*D*) of the absorption band of the NCS group at temperatures below 50 °C, a change in the concentration of compound **10a** with time passes through a maximum. Consequently, a preliminary conclusion can be drawn that the elimination of isothiocyanate **10a** is accompanied by

Table 1. The yields and selected physicochemical characteristics of thiuram disulfides **9a—d** and **13d**

Compound	Yield (%)	M.p. /°C	Found / Calculated (%) C	H	N	Molecular formula	^{1}H NMR ($CDCl_3$), δ (*J*/Hz)	Mass spectrum (EI, 70 eV), *m/z* (I_{rel} (%))
9a	48	98 (decomp.)	41.05 / 40.78	6.21 / 6.16	9.62 / 9.51	$C_{10}H_{18}N_2S_4$	1.60 (m, 10 H, CH_2 cycl); 3.02 (m, 1 H, CH cycl); 3.60 (s, 6 H, $N(CH_3)_2$); 4.55 (br.s, 1 H, NH)	294 [M]$^+$ (2), 141 [M − 153] (2), 121 [M − 173] (22), 98 [M − 196] (100), 88 [M − 206] (68)
9b	38	80 (decomp.)	43.59 / 43.69	4.61 / 4.67	9.17 / 9.26	$C_{11}H_{14}N_2S_4$	3.55 (s, 6 H, $N(CH_3)_2$); 3.90 (d, 2 H, CH_2, ^3J = 8.5); 5.20 (d, 1 H, NH, J = 8.5); 7.30 (m, 5 H, Ar)	302 [M] (1), 149 [M − 153] (10), 121 [M − 181] (42), 106 [M − 196] (100), 88 [M − 214] (72)
9c	78	114—116 (112—113)[24]	34.12 / 34.03	5.08 / 5.00	9.96 / 9.91	$C_8H_{14}N_2OS_4$	3.60 (s, 6 H, $N(CH_3)_2$); 3.83 (m, 4 H, CH_2N); 4.30 (m, 4 H, CH_2O)	282 [M] (12), 162 [M − 120] (10), 130 [M − 152] (60), 120 [M − 162] (15), 88 [M − 194] (100)
9d	58	99—101 (98—99)[24]	38.23 / 38.55	5.65 / 5.75	9.82 / 9.98	$C_9H_{16}N_2S_4$	1.78 (m, 6 H, CH_2 cycl); 3.61 (s, 6 H, $N(CH_3)_2$); 4.23 (m, 4 H, $(CH_2)_2N$)	280 [M] (8), 160 [M − 120] (10), 128 [M − 152] (54), 120 [M − 160] (12), 88 [M − 192] (100)
13d	18	127—129 (129—130)[23]	44.81 / 44.96	6.17 / 6.29	8.74 / 8.74	$C_{12}H_{20}N_2S_4$	1.78 (m, 12 H, CH_2 cycl); 4.23 (m, 8 H, CH_2N)	320 [M] (11), 160 [M − 160] (12), 128 [M − 192] (50), 84 [M − 236] (100)

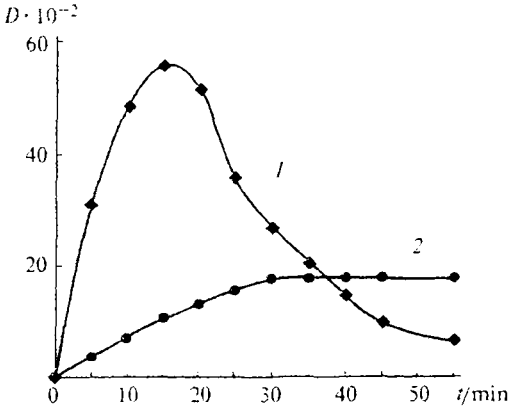


Fig. 1. Change in the optical density (D) of the absorption band of the NCS group of isothiocyanate **10a** formed upon decomposition of thiuram disulfide **9a** (10 mmol L^{-1}) at 40 °C in dioxane (*1*) and $CHCl_3$ (*2*).

its consumption leading to thiourea **2a** as a result of addition of the dimethylamine that is eliminated from acid **7** (see Scheme 7), the rate of the first process being higher than that of the second one. The difference in the rates of these two processes in chloroform at 40 °C is so large that the D value which corresponds to the maximum concentration of isothiocyanate **10a** remains unchanged for 1 h (Fig. 1).

The direct detection of isothiocyanate **10a** in the reaction of TMTD with amine **1a** would be a convincing proof of the suggested mechanism and, in particular, of symmetrization processes yielding a mixture of thioureas. Studies of a mixture of TMTD and amine **1a** by IR spectroscopy at different temperatures (30, 40, and 50 °C) in various solvents (toluene, chloroform, or dioxane) and using different reagent ratios unambiguously confirmed the formation of isothiocyanate **10a**. Changes in the optical density of the absorption band corresponding to vibrations of the NCS groups as the temperature was changed (Fig. 2) demonstrated that the formation of compound **10a** at temperatures below 40 °C started after a particular induction period

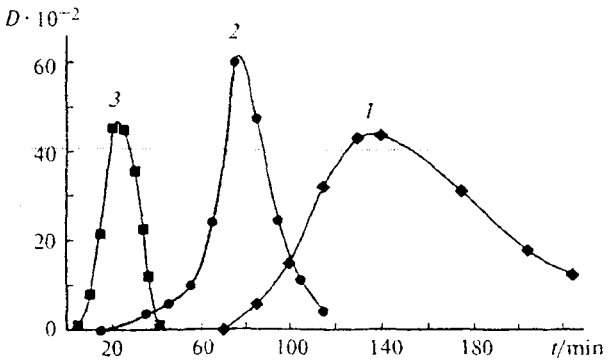


Fig. 2. Change in the optical density (D) of the absorption band of the NCS group of isothiocyanate **10a** formed in the reaction of amine **1a** (15 mmol L^{-1}) with TMTD (15 mmol L^{-1}) in dioxane at 30 (*1*), 40 (*2*), and 50 °C (*3*).

(~60 min at 30 °C and ~20 min at 40 °C). According to the D value, the time of attainment of the maximum concentration and the time of complete consumption of **10a** at 30 °C were 150—300 min. Consequently, compound **10a** and thioureas **2a** and **3a** were formed even at moderate temperature (30 °C), which agrees with the results of the synthesis.

The effect of the concentration of amine **1a** on the rates of formation of isothiocyanate **10a** and thioureas **2a** and **3a** is ambiguous. When **1a** and TMTD were taken in molar ratios of 0.4—2, the rate of formation of **10a** increased (an increase in D) proportionally to the concentration of compound **1a**. However, the larger the concentration of **1a** the sharper the decrease in the D value, *i.e.*, the higher the rate of addition of amine **1a** to isothiocyanate **10a** and the greater amount of symmetrical thiourea **3a** that formed (Fig. 3). When the **1a** : TMTD ratio became equal to 4, the rate of formation of **3a** was higher than the rate of formation of **10a** to such an extent that the ν(NCS) absorption band in the IR spectra was virtually absent (see Fig. 3). Under these conditions, thiourea **3a** was isolated in 80% yield (see Ref. 1).

The nature of the solvents affects substantially the rates of formation of isothiocyanate **10a** (an increase in D) and thioureas **2a** and **3a** (a decrease in D). The dipolar aprotic solvent dioxane forms a hydrogen bond with the NH group of thiuram disulfide **9a** or **1a** and simultaneously accelerates the formation of **10a** and addition of amine **1a** to **10a**. As a result, both branches of the curve of the change in D with time have a virtually symmetrical shape (Fig. 4). In toluene, the rate of formation of **10a** is so much lower than the rate of its consumption that a sharp decrease in the concentration of **10a** is observed after the maximum is smoothly

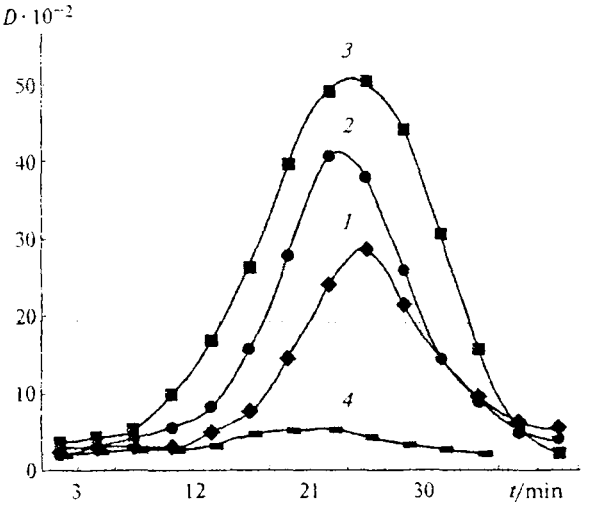


Fig. 3. Change in the optical density (D) of the absorption band of the NCS group of isothiocyanate **10a** formed in the reaction of amine **1a** (15 mmol L^{-1}) with TMTD (15 mmol L^{-1}) at 50 °C in dioxane when **1a** and TMTD were taken in a ratio of 0.4 (*1*), 1 (*2*), 2 (*3*), and 4 (*4*).

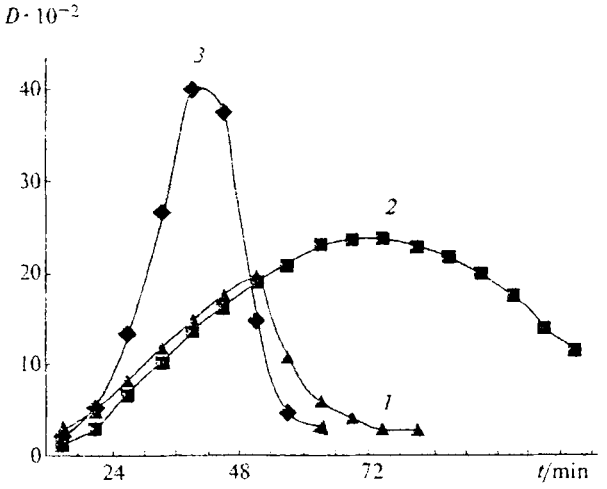


Fig. 4. Change in the optical density (D) of the absorption band of the NCS group of isothiocyanate **10a** formed in the reaction of amine **1a** (15 mmol L^{-1}) with TMTD (15 mmol L^{-1}) at 50 °C in toluene (*1*), $CHCl_3$ (*2*), and dioxane (*3*).

reached (see Fig. 4). These processes occur most slowly in chloroform. Apparently, the latter forms a complex with the amine, which not only slows down the formation of **10a**, but also substantially hinders the addition of the amine (see Fig. 4).

The use of secondary amines instead of primary amines does not lead to a change in the direction of the first stages of the process. The reactions of the secondary amines with TMTD at 20 °C also afford thiohydroxylamines **6c—e** and mixtures of salts **4c,d** and **5c—e** (mixture **B**) (Scheme 8).

Scheme 8

$$R^1R^2NH \xrightarrow[20\ ^\circ C]{TMTD} Me_2NC(=S)SNR^1R^2 + Me_2NC(=S)\bar{S}\,H_2\overset{+}{N}R^1R^2 + R^1R^2NC(=S)\bar{S}\,H_2\overset{+}{N}R^1R^2$$

1c—e **6c—e** **4c,d** **5c—e**

When the temperature is increased to 110 °C, these intermediates are converted into mixtures of salts (with "symmetrical" dithiocarbamates **5c—e** predominating) rather than thioureas.

Apparently, symmetrization of the salts (mixture **B**) follows a pathway identical with that of conversions of salts of primary amines (see Scheme 5). At temperatures below 110 °C, equilibrium interconversions of the salts of secondary amines afford more stable "symmetrical" salts **5c—e**. Thus heating of a toluene solution of salts **4d** and **5d** afforded salt **5d** in 64% yield.

Using compound **6d** as an example, decomposition of *S*-(carbamoylthio)thiohydroxylamines, which were obtained from secondary amines, was performed by passing hydrogen sulfide through a solution of compound **6d** in toluene at room temperature. After completion of the reaction, sulfur and a mixture of salts **4d** and **5d** (Scheme 9) were isolated. As expected, refluxing of the mixture in toluene gave salt **5d** in ~60% yield.

Scheme 9

$$Me_2NC(=S)SNR^1R^2 + H_2S \xrightarrow[-S]{110\ ^\circ C} Me_2NC(=S)\bar{S}\,H_2\overset{+}{N}R^1R^2 + R^1R^2NC(=S)\bar{S}\,H_2\overset{+}{N}R^1R^2$$

6c—e **4c,d** **5c—e**

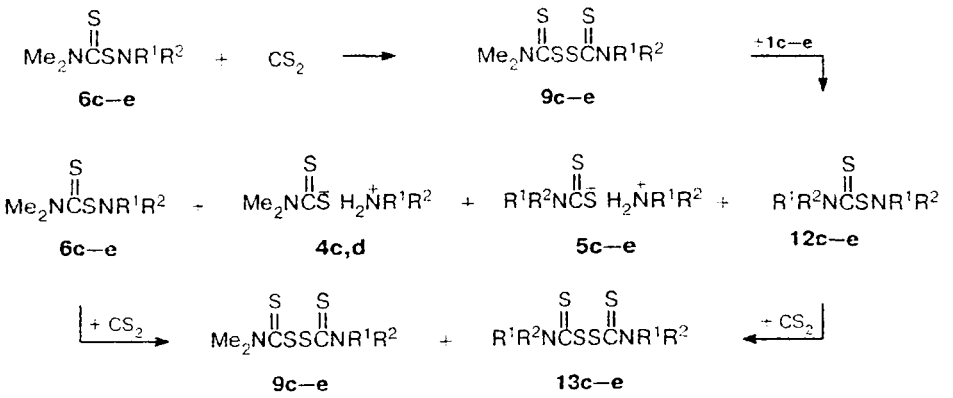
Compounds **6c—e** also react with carbon disulfide to form thiuram disulfides **9c—e**, but the reactions proceed less vigorously than those with compounds **6a,b**. In the case of **6d**, three thiuram disulfides were isolated (TMTD, *S*-(*N,N*-dimethylthiocarbamoyl)-*S'*-(piperidinothiocarbonyl) disulfide (**9d**), and *S,S'*-bis(piperidino)thiocarbonyl disulfide (**13d**) (see Table 1)). Due to the absence of H atoms at the N atoms, thiuram disulfides **9c—e** cannot be decomposed to give isothiocyanates; they are recycled and react with amines analogously to TMTD to form "symmetrical" *N,S*-substituted thiohydroxylamines (**12c—e**) and symmetrical thiuram disulfides (**13c—e**). This process occurs over and over as a "chain" reaction until thiohydroxylamines are completely consumed (Scheme 10). It can be suggested that in each new cycle, the molar amount of symmetrical thiuram disulfide **13c,d** increases by 50% compared to the amount of the preceding mixed thiuram disulfide **9c—e**. Apparently, when the reaction is performed for a long period of time, compounds **6c—e** are transformed into "symmetrical" salts **5c—e**. Therefore, the mechanism of the process agrees well with the practical results of the synthesis.

To summarize, the overall scheme, which illustrates the general mechanism of the reactions of TMTD with aliphatic amines, can be represented by Scheme 11.

According to the suggested mechanism, the reactions of TMTD with aliphatic amines proceed through two successive stages (1 and 2). According to the published data,[13] the first stage involves the attack of the amino group of amines **1a—e** on the disulfide group of TMTD to form *N,S*-disubstituted thiohydroxylamines **6a—e** and dithiocarbamic acid **7** (Eq. (1)).

In the second stage, several competitive processes occur. The first process involves decomposition of acid **7** to give dimethylamine and carbon disulfide, which serves as a source of "symmetrical" salts **5a—e** (2.1). At

Scheme 10



high temperatures (70—110 °C), salts of primary amines **4a,b** and **5a,b** are converted into thioureas **2a,b** and **3a,b** with elimination of hydrogen sulfide (2.1a), which catalyzes decomposition of thiohydroxylamines **6a,b** yielding the same thioureas, while thiohydroxylamines **6c—e** give a mixture of salts **4c,d** and **5c—e** (2.1b). In the second process, thiohydroxylamines **6a—e** are converted into mixed thiuram disulfides **9a—e** in reactions with carbon disulfide (2.2). Then thiuram disulfides **9a,b** formed from primary amines are converted into isothiocyanates **10a,b**. The latter are consumed in the formation of thioureas **2a,b** and **3a,b** upon addition of dimethylamine or amines **1a,b** (2.2a). Thiuram disulfides of secondary amines **9c—e**, which cannot undergo decomposition to give isothiocyanates, are recycled and react with amines analogously to TMTD. This process occurs over and over until thiohydroxylamines **6c—e** are completely converted into "symmetrical" salts **5c—e** (2.2b).

The suggested mechanism, which is confirmed by the abundant experimental data, adequately explains all complex processes that occur in the course of the reaction.

Based on the results of studies of the mechanism, the following important practical conclusion can be made: the reactions of primary aliphatic amines with TMTD taken in a molar ratio of ≥4 afford symmetrical thioureas in 80% yields. To obtain mixed thioureas in satisfactory yields, the molar ratio should be ≤2.

Experimental

The IR spectra were recorded on Specord M-80 and Perkin—Elmer 577 spectrometers. The ^{1}H NMR spectra were obtained on a Bruker AM-250 instrument. The chemical shifts were measured relative to Me_4Si as the internal standard. The mass spectra were obtained on an INCOS-50 instrument (EI, 70 eV). TLC was carried out on Silufol UV-254 plates; the spots were visualized with UV light. HPLC was performed on a Bruker LC-21 instrument.

A sample of TMTD was recrystallized from $CHCl_3$, m.p. 154—156 °C (*cf.* the literature data[24]: m.p. 156 °C). Amines **1a—d** were distilled *in vacuo* before use. Dimethylamine was used as a 33% aqueous solution of chemically pure grade.

N,S-Disubstituted thiohydroxylamines **6a—e** and ammonium dithiocarbamates **4a—d** and **5a—e** were prepared according to a procedure reported previously.[1]

Transformation of a mixture of salts 4a and 5a. *A.* A mixture of salts **4a** and **5a** (0.5 g, **4a** : **5a** ≈ 85 : 15) was refluxed in benzene (2 mL). Within 5 min after complete dissolution of the mixture, a colorless precipitate was formed. Heating was terminated and the reaction mixture was cooled. The precipitate was filtered off, washed with ether, and dried in air. A mixture of salts **4a** and **5a** was obtained in a yield of 0.42 g (17 : 83, NMR). MS, *m/z*: 121 $[Me_2NCS_2H]^+$ and 175 $[C_6H_{11}NHCS_2H]^+$. The same ions were detected in the mass spectra of the known salts synthesized according to a procedure reported previously.[25] ^{1}H NMR ($CDCl_3$), δ: 3.55 (Me_2N); 4.30 (CH).

B. A solution of a mixture of salts **4a** and **5a** (1.0 g) (see method *A*) in toluene (or benzene) (3 mL) was refluxed for 1 h. After cooling, the precipitates that formed were filtered off. After evaporation of toluene, an additional small amount of the precipitate was obtained from the mother liquor. The combined precipitates were washed with water, dried, and chromatographed on a column with silica gel or using HPLC. Thioureas **2a** and **3a** were obtained in yields of 0.06 g (10%) and 0.52 g (90%), respectively.

The reaction in dioxane gave thioureas **2a** and **3a** in yields of 0.04 g (~6%) and 0.48 g (94%), respectively.

The transformations of a mixture of salts **4c,d** and **5c,d** were performed analogously. The precipitates of **5c,d** were recrystallized from hot water. Salts **5c** and **5d** were prepared in yields of 0.20 g (65%) and 0.20 g (64.4%), respectively.

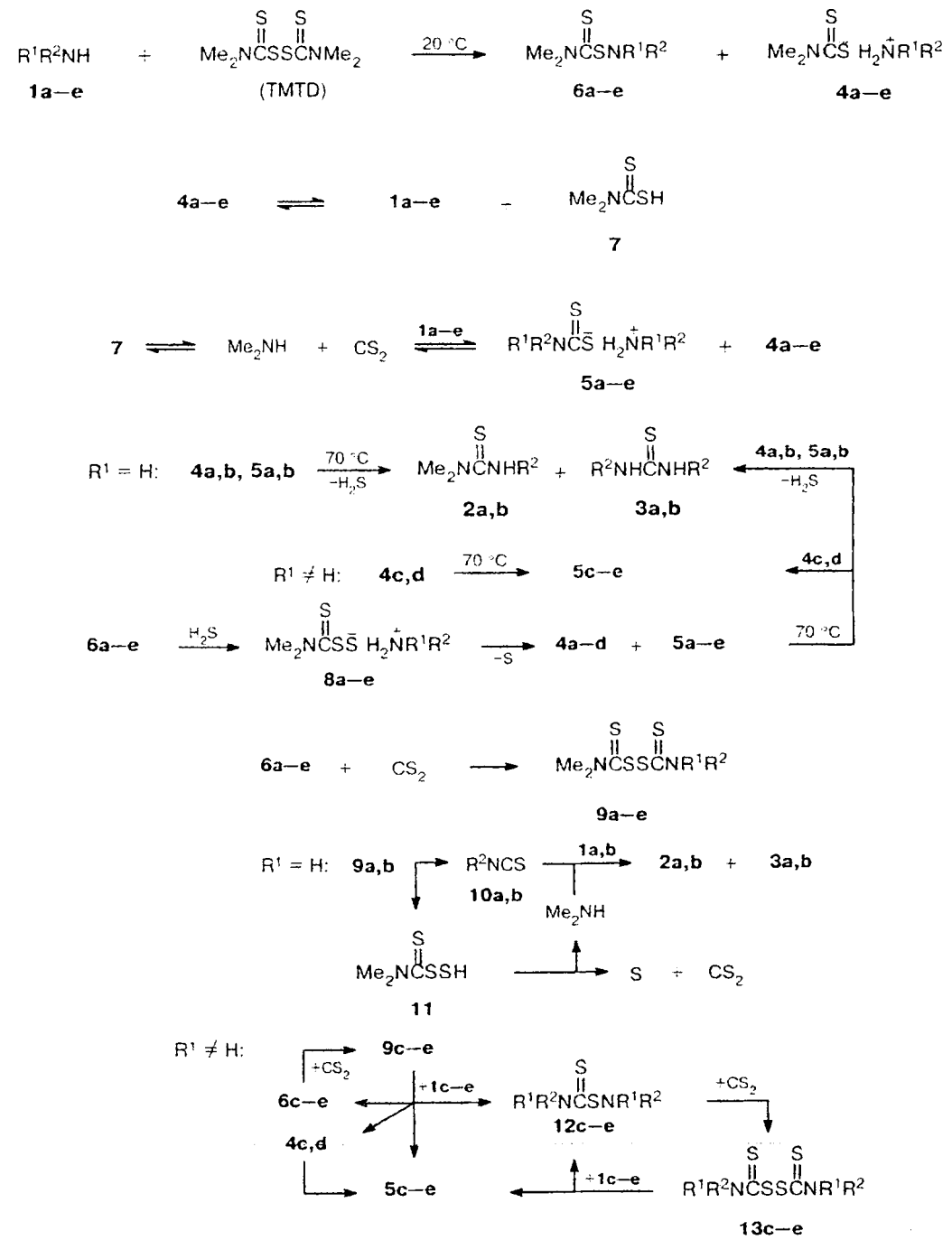
Decomposition of thiohydroxylamine 6a with hydrogen sulfide. *A.* H_2S was passed through a benzene solution of thiohydroxylamine **6a** (0.44 g, ~2 mmol) at 20 °C for 1 h. The precipitate that formed was filtered off and sulfur was separated by washing with light petroleum. A mixture of salts **4a** and **5a** (73 : 27) was obtained in a yield of 0.40 g.

B. H_2S was passed through a solution of compound **6a** (5 mmol) in toluene (1 mL) heated to 70 °C for 1 h. After cooling, toluene was distilled off *in vacuo* and the precipitate was treated as described above. Thioureas **2a** and **3a** were obtained in yields of 0.37 g (70.7%) and 0.16 g (29.3%), respectively.

Decomposition of thiohydroxylamine **6d** was performed analogously. The salts were obtained in a yield of 0.91 g. Recrystallization from water afforded salt **5d** in a yield of 0.45 g (~60%).

Thermal decomposition of thiohydroxylamine 6a. A benzene solution of compound **6a** (0.44 g) was refluxed for 30 min. After cooling, the crystals that precipitated were filtered off and washed first with ether and then with light petroleum. TMTD was obtained in a yield of ~0.11 g (~46%) (m.p. 154—156 °C).

Scheme 11



Reaction of thiohydroxylamine 6a with cyclohexylamine 1a. A mixture of thiohydroxylamine **6a** (0.44 g, 2 mmol) and cyclohexylamine **1a** (0.20 g, 2 mmol) in benzene (2 mL) was refluxed for 1 h. Then the solvent was evaporated *in vacuo* and the precipitate was washed on a filter with water, dried, and separated by HPLC (a 7 : 3 light petroleum—ethyl acetate mixture as the eluent). Thioureas **2a** and **3a** were obtained in yields of 48 mg (~13%) and 58 mg (~12%), respectively.

Reaction of thiohydroxylamine 6a with carbon disulfide. *A.* A solution of CS_2 (0.46 g, 0.38 mL) in benzene (2 mL) was slowly added with stirring to a solution of compound **6a** (1.1 g, 5 mmol) in benzene (2 mL) (the exothermic reaction). The precipitate that

formed was filtered off, washed with hexane, and separated by HPLC (a 7 : 3 light petroleum—ethyl acetate mixture as the eluent). Thiourea **2a** and thiuram disulfide **9a** were obtained in yields of 0.33 g (35.5%) and 0.12 g (8.2%), respectively.

After evaporation of the solvents, the filtrate containing cyclohexyl isothiocyanate was passed through a column with silica gel (hexane as the eluent). The eluent was evaporated, amine **1a** (25 mg) was added to isothiocyanate **10a** (32 mg), and the reaction mixture was slightly warmed on a water bath. Thiourea **3a** was obtained in a yield of 43 mg, m.p. 178—180 °C (*cf.* the literature data[1]: m.p. 178—180 °C).

B. An analogous experiment was carried out with preliminary cooling (~0—5 °C) of solutions of both initial reagents. Thiuram disulfide **9a** was obtained in a yield of 0.7 g (~48%).

The reactions of compounds **6b—d** with carbon disulfide were performed according to analogous procedures.

The results of the synthesis and selected characteristics of the resulting thiuram disulfides **9a—d** and **13d** are given in Table 1.

Studies of the processes of formation of isothiocyanate 10a by IR spectroscopy. ***A.*** A dioxane solution of compound **9a** (10 mmol L^{-1}) was placed into a 0.5-mm cell and the spectra were recorded every 3—6 min with the use of a temperature-controlled attachment.

The IR spectra of solutions of compound **9a** in $CHCl_3$ were recorded analogously.

The results of IR spectral studies of decomposition of **9a** are shown in Fig. 1.

B. A mixture of amine **1a** (15 mmol L^{-1}) and TMTD (15 mmol L^{-1}) in dioxane was placed into a 0.5-mm cell and the spectra were recorded with the use of a temperature-controlled attachment as described above. To compensate for absorption by the solvents, which appeared at high concentrations of the amine, a variable-width cell filled with the solvent was used.

The results of the studies of the effects of the temperature, the reagent ratio, and the nature of the solvents on the reaction of compound **1a** with TMTD are represented in Figs. 2—4

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