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Structure and Molecular Lability of *N*-(Thio)phosphoryl(thio)amides: XVII.[1] Intramolecular Transformations of *N,N'*-Bis(thio)phosphoryl(thio)ureas with the Open-Chain Fragment in DMSO Solution

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Abstract—By means of the ^{1}H, ^{13}C, and ^{31}P NMR spectroscopy structure and intramolecular transformations of *N,N'*-bis[diisopropoxythiophosphorylaminothiocarbonyl]-1,7-diaminoheptane in 3–10% DMSO solutions were studied. High lability of molecule with the realization of two conformers (linear and pincer-like) of macromolecule, of the proton imide-imide exchange, and of different tautomeric forms was proved.

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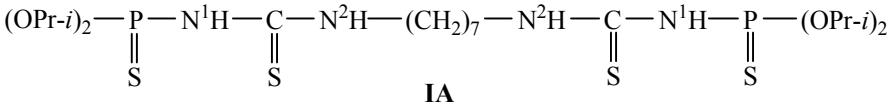
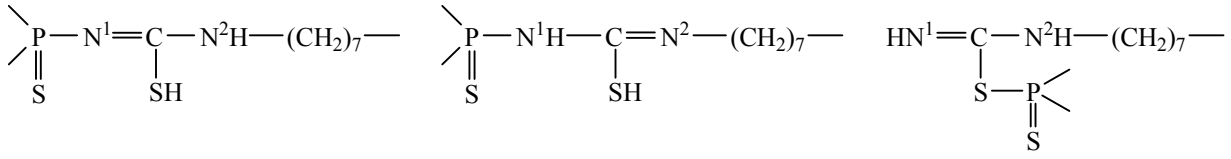
In extension of the studies of the structure and intramolecular transformations of thioureas in solutions [1, 2] the analysis of variable-temperature NMR spectra of *N,N'*-bis[*N*-diisopropoxythiophosphoryl-aminothiocarbonyl]-1,7-diaminoheptane **I** in DMSO was carried out. As known, this solvent can influence the location of NH proton in intramolecular bond due to polar properties (ε 50) as well as to the specific interactions. Besides, the possibility of investigation of dynamic properties of compound **I** in the sufficiently broad high temperature range (298–373 K) was also considered.



IA

In the ^{1}H NMR spectra of thioureas existing in the state of complex chemical exchange the range of the amide proton signals is the most informative where the signals of NH protons of the amide form **IA**, of the prototropic forms **B** ($N^{2}H$) or **C** ($N^{1}H$), and of the phosphorylotropic form **D** are usually located. Their chemical shifts strongly depend on temperature and on the concentration of solutions [1, 2].



B **C** **D**

For example, in the ^{1}H NMR spectrum of 5% solution of compound **I** at 298 K the signals of the amide protons form a doublet ($N^{1}H$) and a broad singlet ($N^{2}H$) (Fig. 1). In the temperature range 298–373 K NH signals broaden but do not change their location. In the spectrum of 10% solution at 298 K two

[1] For communication XVI, see [1].

broad signals of different intensity at δ 8.22 and 6.54 ppm are observed (Fig. 1). The first, more intense of them, is attributed to the protons of the amide form (N^1H and N^2H) characterizing fast amide-amide exchange $N^1H \leftrightarrow N^2H$. The second one belongs to the $=N^1H$ proton of the form **D**. Additional weak signal at δ 3.1 ppm is attributed to the SH proton of the form **B** or C (or both of them). At the increase in temperature to 353 K the averaged NH signal does not alter its location and form, but in the range 353–373 K two signals at δ 8.23 ppm (N^2H) and 8.35 ppm (N^1H) are observed (Table 1). At the reversed temperature motion each of the signals $N^{1,2}H$ also forms two signals with the intensity ratio 80:20% (Fig. 1). Signal of the $=N^1H$ proton (**D**) undergoes significant downfield shift (Δδ 1.3 ppm) while the SH signal (**B** or **C**) increases with temperature but does not alter its location. In the range 373–298 K additional broadened signals appear of the isopropyl group protons. Detailed information concerning temperature evolution of the ^1H NMR spectra is summarized in the Table 1.

While considering such significant and irreversible changes (Fig. 1, Table 1) in the ^1H NMR temperature spectra of thiourea the following circumstances must be taken into consideration.

Signals of N^1H and N^2H protons in the temperature range 373–298 K transform into the well resolved doublet and poorly resolved triplet respectively. Signal of N^1H proton is shifted downfield by 0.57 ppm (Table 1) while the signal of N^2H`proton practically does not change its position (Table 1). Together with the large difference in chemical shifts of these protons at *T* 298 K (reversed temperature moving) [$\Delta\delta(N^1H\ N^2H)$ 0.82 ppm] indicates the "freezing" of the $N^1H \leftrightarrow N^2H$ exchange. N^1H doublet firstly characterizes amide structure in the C–N^1–P triade. Secondly, the retention of the coupling between the N^1H proton and phosphorus ($^3J_{PNH}$ −11.73 Hz) shows the intramolecular character of transformations of molecule with the participation of this proton.

It was noted that the signal of second amide proton N^2H practically does not change its position. It is a strongly broadened and poorly resolved triplet [coupling with the protons of α-CH_2 group of $(CH_2)_7$ fragment, Table 1] which could be probably attributed to the simple participation of this proton in the formation of intramolecular hydrogen bond of N^2–H···S=C type (form **B**). But the problem of belonging of the SH proton signal (δ 3.1–3.3 ppm, see Table 1) to the form **B** or **C** cannot be solved unambiguously.

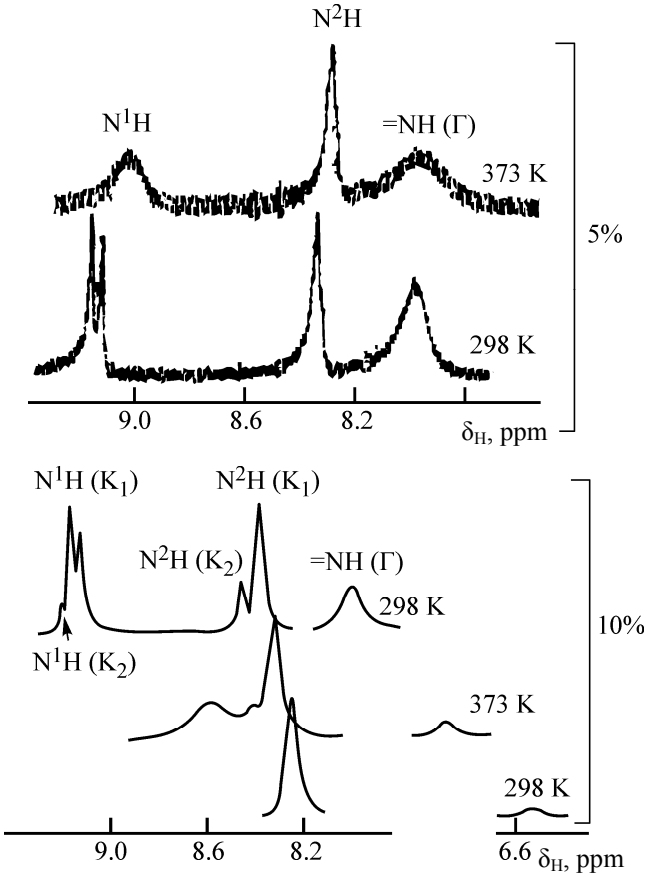


Fig. 1. ^1H NMR temperature spectra in the range of resonance of BH protons of compound **I**, 5% and 10% solutions in DMSO.

Another explanation is possible including the formation and temporary cleavage of N^2–H···S=C intramolecular bond in strongly solvating DMSO with the formation of analogous intramolecular hydrogen bond within the frames of macrostructure of thiourea under study, but with participation of C=S group of the second thiourea fragment. In the result of alternative (and probably the simultaneous) formation of intramolecular hydrogen bonds (considering the identity of two N^2H protons) the lifetime of N^2–H chemical bond occurs to be so short that the coupling can be averaged, but the amide form of compound by itself can remain. The last assumption can be considered within the frames of the realization of second conformation of macromolecule having the nonlinear form (the molecule can fold by itself to form a "pincer"). It is directly connected with the third circumstance.

(3) At the reversed temperature movement in the ^1H NMR spectrum the second less intense set of signals related practically to all the structural elements of

Table 1. ^{1}H NMR spectra [δ, ppm (J_{HH}, J_{HP}, Hz)] of *N,N'*-bis-[*N*-diisopropoxythiophosphorylaminothiocarbonyl]-1,7- diaminoheptane in DMSO-d_6

T, K	O<u>CH</u>$(CH_3)_2$	$(\underline{CH_3})_2CH$	N^1H	N^2H	α-CH_2	CH_2	Additional signals (shape)
298	4.8 (6.3, 10.9)	1.36 (6.3)	8.22 br.s	8.22 br.s	3.48 br.s	1.22–1.67	3.1 (**B, C**), 6.54 br.s (**D**)
353	4.83 br.s	1.4 br.d	8.35 br.s	8.23 br.s	3.5 br.s	1.3–1.63	C_2: 4.6 br.s, ~1.2 (*i*-PrO), 3.4 br.s, 1.18–1.62 [$(CH_2)_7$], 3.2 (**B, C**) br.s, 7.0 br.s (**D**)
373	4.84 br.s	1.4 d (6.0)	8.57 br.s	8.3 br.s	3.5 br.s	1.3–1.63	C_2: 8.38 (NH^1), 8.33 (NH^2), ~4.6 br.s, ~1.38 (*i*-PrO), 3.3 br.s, 1.2–1.6 [$(CH_2)_7$], 3.2 (**B, C**), 7.2 br.s (**D**)
353[a]	4.84 br.m	1.4 br.d (6.3)	9.0 br.s	8.3 br.s	3.5 br.d.t	1.6 (β) 1.1–1.3 m	C_2: 8.4 br.s (NH^1), 8.35 br.s (NH^2), 4.63 br.s, ~1.35 (*i*-PrO), 3.3br.s, 1.2–1.7 [$(CH_2)_7$], 3.2 (**B, C**), 7.0 br.s and 7.83 br.s (**D**, C_1 and C_2)
333[a]	4.83 br.m	1.39 d (6.0)	9.0 br.d (–9.75)	8.3 br.t (4.2)	3.5 d.t (~6.2)	1.2–1.7	C_2: ~9.1 br.d (NH^1), 8.39 br.t (NH^2), 4.64 br.m, ~1.35 (*i*-PrO), 3.4, 1.2–1.7 [$(CH_2)_7$], 3.2 (**B, C**), 7.0 br.s and 7.8 br.s (**D**, C_1 and C_2)
313[a]	4.83 m	1.38 (6.3)	9.0 d (–9.93)	8.32 br.t	3.5 br.d.t (~6.0)	1.2–1.7 m	C_2: 9.1 br.d (NH^1), 8.39 br.t (NH^2), 4.63 m, ~1.36 (*i*-PrO), 3.8, 1.2–1.7 br.m [$(CH_2)_7$], 3.2 (**B, C**), 7.0 and 8.82 br.s (**D**, C_1 and C_2)
298[a]	4.81 m	1.37 (6.0)	9.14 (–11.73)	8.32 br.t	3.5 br.s	1.1–1.8 br.m	C_2: 9.1 br.d (NH^1), 8.34 br.t (NH^2), 4.61, ~1.36 (*i*-PrO), 3.6, 1.26–1.6 [$(CH_2)_7$], 3.2 (**B, C**), 7.84 br.s (**D**)

[a] Reversed temperature motion.

Table 2. ^{13}C NMR spectra [δ_c, ppm (J_{PC}, Hz)] of *N,N'*-bis(*N*-diisopropoxythiophosphorylaminothiocarbonyl)-1,7-diaminoheptene in 10% DMSO-d_6 solution

T, K	C=S	*i*-PrO		$(CH_2)_7$		Additional signals (shape)
		OCH	$(CH_3)_2$	$(NCH_2)_2$	$(CH_2)_5$	
298	180.68 (1.89)	72.52	23.12, 23.40 (3.7)	44.18	27.9 (β), 26.35 (γ), 28.4 (δ)	C_2: C=S 180.83; β 27.37, γ 26.2, δ 28.22
333	180.38	72.68	22.5, 22.8 (3.1)	44.07	27.7 (β), 26.15 (γ), 28.18 (δ)	C_2: $(CH_3)_2$ 23.34, β 27.96, γ 26.0, δ 28.37; 140.69 (**B, C**); 156.1 (**D**)
373	–	72.65 (6.2) 70.1 (4.97)	22.98	–	25.1–28.5 br.s	C_2: 72.21 (OCH), 22.72 [$(CH_3)_2$]; 25.1–28.5 br.s (β, γ, δ); 130.8 [**B** (**C**)]
333[a]	–	70.13 (3.2)	23.33	–	25.2–28.7	C_2: 69.15 (6.86) (OCH), 25.2–28.7 br.s (β, γ, δ); 131.09, 140.66 (**B, C**)
298[a]	–		23.5	–	26.9 (β), 25.68 (γ), 28.04 (δ)	C_2: 69.21 (5.6) (OCH), 25.4–28.9 br.s (β, γ, δ); 136.09, 142.42 (**B, C**); 158.42, 145.6 (**D**)

[a] Reversed temperature motion.

macromolecule is formed. It may belong to thioamide in the C_2 conformation (Table 1). Ratio of integral intensities of the signals C_1/C_2 ~ 80:20%.

The assumption on the realization of the second conformation is confirmed by the data of ^{13}C NMR variable-temperature spectra where two sets of signals of carbon nuclei of β,γ,δ-methylene groups of the open-chain $(CH_2)_7$ fragment and C=S groups with the ratio of integral intensities in each pair of signals ~80:20% is observed (Table 2, Fig. 2).

At the increase in temperature and its reversed movement a second set of signals of carbon nuclei of *i*-PrO groups is formed (similarly to the case of ^{1}H NMR spectrum) as well as of the forms **B**(**C**) and **D**. The important indication of the appearance of the second non-linear conformation C_2 in the ^{13}C NMR spectra is

the disappearance of signals of carbon atoms of C=S and α-CH_2 groups in the range 373–298 K. These groups take part in prototropic transformations as well as in the formation of C_2 conformation. Simultaneously additional signals naturally appear in the resonance range of C=N groups belonging to **B,C**, and **D** forms (130.8–145.6 ppm, Table 2). The disappearance of signal of C=S group shows additionally the formation of intramolecular hydrogen bond of N^2–H···S=C type stabilizing C_2 conformation while in CD_2Cl_2 solution in the course of folding of molecule **I** at low temperatures the rapprochement of N^2H proton with β-CH_2 group of $(CH_2)_7$ fragment is observed [1].

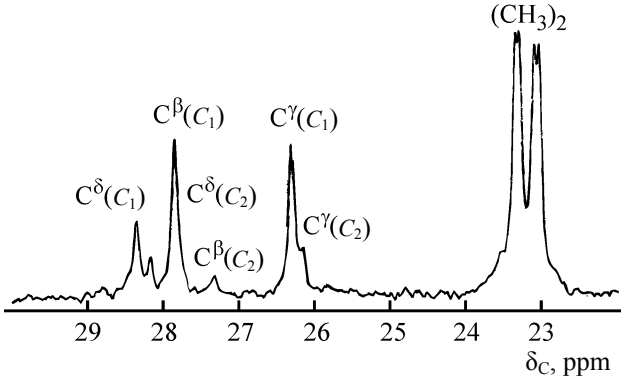


Fig. 2. ^{13}C NMR spectrum of compound **I** in the resonance range of $C_{αβγ}$-methylene groups.

Structural transformations of thioamide in DMSO solution cause also the changes in the ^{31}P NMR spectra. At 298 K in the resonance range of the amide and prototropic forms δ_P 56.9–58.2 ppm two intense signals of the imide form and weak signals of the forms **B**(**C**) (δ_P 57.4 and 58.2 ppm) and **D** are located (Table 3).

Ratio of integral intensities in each pair of signals coincides approximately with those obtained from the ^1H and ^{13}C NMR spectra. Attribution of signals to the forms **B**(**C**) in each conformation is carried out with the consideration of further transformations in ^{31}P NMR variable-temperature spectra. At the increase in temperature to 353 K more intense signal of **B**(**C**) form in the conformation C_1 broadens and undergoes small downfield shift. At 333 K in comes to the resonance range of the amide form **A** in the conformations C_1 and C_2. The intensity of signal of the form **B**(**C**) in the second conformation grows simultaneously, and at the reversed temperature movement it reaches 10% at 33 K. It may be presumed that due to solvating action of DMSO step-by-step occurs the cleavage of intramolecular hydrogen bonds. At first the rupture of intramolecular H-bond with the participation of N^1H proton leads to formation of **B** form. Due to that the equilibrium is shifted to the side of form **C** which is more stable under these conditions. Then the cleavage of intramolecular hydrogen bond with the participation of N^2H proton providing the existence of the form **C** is observed (in the temperature range 313–298 K the signal of the form **C** overlaps with the signals of amide form). Finally the formation of intramolecular hydrogen bond of N^2H proton with the sulfur atom of C=S group of the second thiourea fragment takes place that stabilizes the C_2 conformation. These assumptions agree with the fact of broadening of signal of N^2H in the whole temperature range and with the presence of C=N signals of prototropic forms **B**(**C**) in the ^{13}C NMR spectra (Table 2).

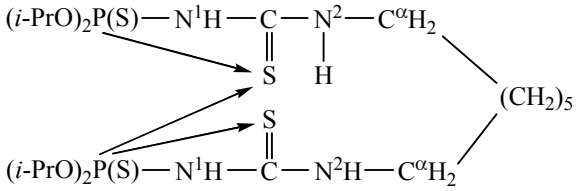
The temperature changes of ^{31}P NMR spectrum in the resonance range of the form **D** require a detailed discussion. In the linear conformation C_1 both thiophosphoryl groups are equivalent and may

Table 3. Temperature dependence of ^{31}P NMR spectra [δ_P, ppm (%)][a,b] of *N,N'*-bis(*N*-diisopropoxythiophosphoryl-aminothiocarbonyl)-1,7-diaminoheptane in DMSO-d_6 solution

T, K	C_1 (**A**)	C_2 (**A**)	**B** (**C**), **D** Shapes
298	57.2 (72.91)	56.9 (20.98)	57.4, 58.2 (0.27) [**B** (**C**), C_1 and C_2], 66.74 (5.84) (**D**, C_1)
333	57.24 (75.09)	57.02 (18.88)	58.24 (0.88) [**B** (**C**), C_2], 66.09 (4.25), 62.3 (0.9) br.s (**D**, C_1)
353	57.66 (91.76)		58.27 (5.85) [**B** (**C**), C_2], 62.32 (2.39) br.s (**D**, C_2)
373	57.72 (93.11)		58.31 (6.89) [**B** (**C**), C_2]
353[a]	57.83 (86.65)		58.3 (8.17) [**B** (**C**), C_2], 61.2, 61.61 (5.18) br.s (**D**, C_2)
333[a]	57.96, 58.04	(84.22)	58.27 (10.0) [**B** (**C**), C_2], 61.55, 61.7 (5.78) br.s (**D**, C_2)
298[a]	58.2 (96.63)		61.62, 61.96 (3.37) br.s [**B** (**C**), C_1 at **A**; **D**, C_2]

[a] Reversed temperature motion.

simultaneously take part in phosphorylotropic rearrangement with the formation of identical forms **D**. Therefore the broadened signal at δ_P 66.74 ppm (298 K, Table 3) is attributed just to this form. Additional broadening of the signal **D** in the range 290–353 K is accompanied by the formation of a new broadened signal at δ_P 62.32 ppm which doubles at the reversed temperature movement (Table 3). It is important to note that in the same temperature range the signals of carbon atoms of C=N (δ_C 156.1 ppm) and C=S groups disappear (Table 2). These changes in ^{31}P NMR spectrum are evidently also connected with the conformational transformations of molecule **I**. But it must be considered that in the "picer" conformation C_2 principally three possibilities exist for intramolecular migration of thiophosphoryl groups to the sulfur atom of C=S group as it is schematically shown below.



But the migration of $(i\text{-PrO})_2P(S)$- group to its own C=S group in the lower thiourea fragment seems hardly probable because of participation of the latter in formation of intramolecular H-bond with N^2H proton of the second thiourea fragment. Evidently it is the reason of doubling and not of tripling of signals of the form **D** (353–373–298 K) in the second conformation (Table 3).

Hence, by means of joint analysis of data of variable-temperture ^{1}H, ^{13}C, and ^{31}P NMR spectra it was established that *N,N'*-bis(*N*-diisopropoxythiophosphorylaminothiocarbonyl)-1,7-diaminoheptane **I** in DMSO solution exists in complex dynamic equilibrium. It is shown that on the background of conformational transformations of the molecule from the linear structure to the folded one there exists fast amide proton-proton exchange (298–373 K), prototropism with the participation of two amide protons and phosphorylotropism in each of conformations in the high temperature range. Comparative spectral analysis of tautomeric equilibrium of thiourea **I** in different media [1, 2] permits to conclude that in the course of increase in the solvating ability of solvent in the series $CD_3CN > CD_2Cl_2 > (CD_3)_2CO > (CD_3)_2SO$ the step-by step cleavage of intramolecular hydrogen bonds is facilitated, and the equilibrium shifts to the side of the form more stable under these conditions. Analogous tendencies of changes in NMR spectra on all three nuclei are found for low temperature measurements in CD_2CN, CD_2Cl_2, and $(CD_3)_2CO$ solutions and at high temperature in $(CD_3)_2SO$ solutions.

EXPERIMENTAL

^{1}H (300 MHz), ^{13}C (75.43 MHz), and ^{31}P (121.42 MHz) NMR spectra at different temperatures and concentrations of solutions were taken on a Varian UNITY-300 spectrometer in the regime of internal stabilization by the ^{2}H resonance line. The spectrometer was equipped with variable-temperature probe. While recording ^{31}P NMR spectra 10°–15° impulses and the retentions between impulses *RD* 1–2 s were used. Spectral width *SW* up to 100 ppm. Number of accumulations *NT* from 10 to 100, digital filtration was not used. While recording ^{13}C NMR spectra 20°–30° impulses were used with the wide band decoupling from protons, *RD* 0, *SW* 200 ppm, *NT* 400–1000. Digital exponential filtration with *LB* 2-4 Hz was used.

^{1}H NMR spectra were taken for the samples with the concentration 3–5 wt %, and ^{13}C and ^{31}P NMR spectra, for 10–15 wt % solutions. Chemical shifts were measured against the internal standards.

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