ISSN 1070-3632, Russian Journal of General Chemistry, 2011, Vol. 81, No. 3, pp. 488–492. © Pleiades Publishing, Ltd., 2011.
Original Russian Text © F.Kh. Karataeva, 2011, published in Zhurnal Obshchei Khimii, 2011, Vol. 81, No. 3, pp. 391–396.

Structure and Intramolecular Mobility of *N*-(Thio)phosphoryl(thio)amides: XVI.[1] ^{1}H, ^{13}C and ^{31}P NMR Study of Intramolecular Dynamics of *N*,*N*'-Bis(thio)phosphoryl(thio)urea Containing an Open-chain Fragment in CD_2Cl_2 and CD_3CN Solutions

F. Kh. Karataeva

Kazan State University, ul. Kremlevskaya 18, Kazan, Tatarstan, 420008 Russia
e-mail: farida.karataeva@ksu.ru

Received March 10, 2010

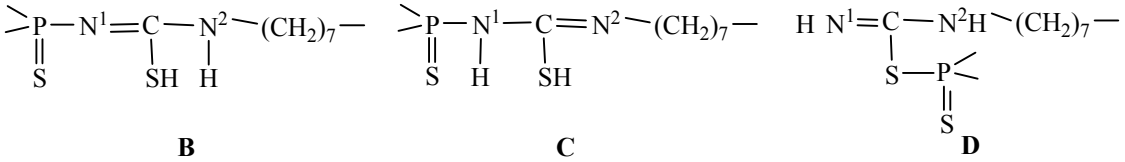
Abstract—The structure and intramolecular transitions of *N*,*N*'-bis[*N*-disopropoxythiophosphorylaminothiocarbonyl]-1,7-diaminoheptane in CD_2Cl_2 and CD_3CN 3–10% solutions were studied by means of ^{1}H, ^{13}C, and ^{31}P NMR spectroscopy. Combined analysis of the NMR data confirmed a high lability of the molecules with the realization of two conformational forms of the macromolecule, the amide–amide proton exchange, and existence of various tautomeric forms.

DOI: 10.1134/S1070363211030078

In the study of intramolecular transformations of *N*,*N*'-bis(thio)phosphoryl(thio)ureas of various structures existing in solution in the state of the complicated tautomeric and stereoisomeric equilibrium both poorly solvating (CD_2Cl_2 and CD_3CN) and polar solvating [$(CD_3)_2C=O$ and $(CD_3)_2S=O$] [1–4] solvents were used. The choice of solvent is determined by its ability to affect the position of tautomeric equilibrium, as well as by a substantial expansion of the temperature range (373–183 K).

Aiming at the study of structure and dynamic properties of the compounds of this type at the changes in temperature and solvent, we obtained the ^{1}H, ^{13}C and ^{31}P NMR spectra of *N*,*N*'-bis[*N*-disopropoxythiophosphorylaminothiocarbonyl]-1,7-diaminoheptane (i-PrO)$_2$P(S)N^{1}HC(S)N^{2}H(CH$_2$)$_7$N^{2}HC(S)N^{1}HP(S)(OPr-i)$_2$ (**I**, **A**) in CD_2Cl_2 and CD_3CN solutions (ε 8.9 and 36.2, respectively).

Study of intramolecular transformations of **I** in $(CD_3)_2C=O$ solution (ε 20.7) showed [4] that the amide form **A** is predominant [5]. In addition, amide–amide exchange and prototropy (leading to structures **B** and **C**) were observed occurring simultaneously with the conformational transformations of macromolecules, as well as the formation of phosphorylotropic structure **D** with the existence of *Z*,*E*-isomers relative to the C=N^1 bond:



B **C** **D**

Comparative analysis of the ^{1}H NMR spectra of compound **I** in CD_2Cl_2 and CD_3CN solutions (5%) at room temperature showed that the signals of the most important for the analysis amide protons N^{1}H and N^{2}H appeared as a broadened doublet and a singlet, respectively (Table 1). The signals assignment was done with accounting for the spin–spin coupling of the proton N^{1}H with the phosphorus nucleus (doublet) and of the

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

Table 1. ^{1}H NMR spectra [δ, ppm (J_{HH}, J_{HP}, Hz)] of *N*,*N*'-bis[*N*-disopropoxythiophosphorylaminothiocarbonyl]-1,7-diaminoheptane in CD_2Cl_2 and CD_3CN solutions

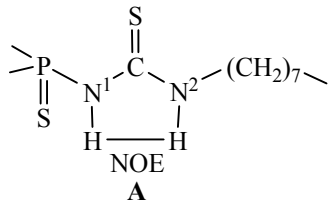
T, K	OCH (in *i*-PrO)	$(CH_3)_2$ (in *i*-PrO)	N^1H	N^2H	$(\alpha\text{-}CH_2)_2$ [in $(CH_2)_7$]	$(CH_2)_5$ [in $(CH_2)_7$]	Additive signals, form
293[a]	4.1 (6.0, 10.9)	0.7 (6.0)	8.9 br.d (~11.0)	10.2 br.s	3.2 s	0.4–0.9	K_2: 3.8, 0.7, 1.4 and 1.37, 10.5 br.s (**D**)
298[b]	4.7 (~6.0, ~11.0)	1.26 (~6.0)	6.9 d (–10.4)	7.7 br.s	3.5 d.t (~6.0, ~6.0)	1.4 (β) br.s, 1.3 (γ), 1.1 (δ)	K_2: 4.56 (~6.0, ~11.0), ~1.1 (*i*-PrO), 3.4 d.t (~6.0, ~6.0), 0.95–1.6 [$(CH_2)_7$], 2.8 br.s (**B**), 8.2 br.s (**D**)
263[b]	4.7 (~6.0, 10.6)	1.3 (6.0)	6.9 d (–11.84)	7.7 br.s	3.5 d.t (~6.0, ~6.0)	1.1.1–1.6 m	K_2: 4.5 (~6.0, ~11.0), ~1.2 (*i*-PrO), 3.37 d.t (~6.0, ~6.0), 0.95–1.6 [$(CH_2)_7$], 2.8 and 2.9 (**B** in K_1 and K_2), 8.2 br.s (**D**)
243[b]	4.75 (6.3, 10.6)	1.25 (6.3)	7.0 d (–12.3)	7.6 br.t	3.5 d.t (7.0)	1.6 (β) 1.1–1.3 m	K_2: 4.5 (~6.0, ~11.0), ~1.23 (*i*-PrO), 3.8 d.t (~6.0, ~6.0), 0.95–1.6 [$(CH_2)_7$], 2.8 and 2.9 (**B** in K_1 and K_2), 8.2 br.s (**D**)
223[b]	4.78 (6.3, 10.65)	1.25 (6.3)	7.1 d (–12.6)	7.6 br.t (4.2)	3.5 d.t	1.7 (β) 1.1–1.4 m	K_2: 4.58, ~1.25 (*i*-PrO), 3.4, 0.95–1.78 [$(CH_2)_7$], 2.8 and 2.9 (**B** in K_1 and K_2), 8.18 br.s (**D**)
203[b]	4.78 (6.3, 10.65)	1.25 (6.3)	7.2 d (–13.43)	7.5 br.t (4.2)	3.5 br.m	1.1–1.7 m	K_2: 4.7, ~1.3 (*i*-PrO), 3.8, 1.3–1.5 [$(CH_2)_7$], 2.8 (**B**), 8.18 br.s (**D**)
183[b]	4.78 br.m	1.3 (6.3)	7.38 (–13.7)	7.45 br.t (4.5)	3.5 br.s	1.1–1.8 br.m	K_2: 4.5, ~1.2 (*i*-PrO), 3.3, 1.3–1.5 [$(CH_2)_7$], 2.95 (**B**), 8.18 br.s (**D**)

[a] Solvent is CD_3CN. [b] Solvent is CD_2Cl_2.

proton N^2H with the α-methylene protons of the fragment $(CH_2)_7$ (triplet). The data of Table 1 show that in CD_3CN solution both protons resonate downfield compared with the solution in CD_2Cl_2 and with larger difference in the chemical shifts (Δδ 1.3 and 0.8 ppm, respectively, Table 1). This is likely due to the participation of the amide protons in the formation of the stronger intramolecular hydrogen bond of type NH···S=P or NH···S=C in the first solvent. For comparison, the Δδ value in $(CD_3)_2CO$ at room temperature equals 0.13 ppm [4]. The spectral characteristics of the remaining protons of **I** are summarized in Table 1. All signals are broadened.

Measuring the ^{1}H NMR spectra of compound **I** in CD_2Cl_2 solution at variable temperature showed that N^2H singlet is transformed into a broadened triplet with $^3J(HN^2CH)$ 4.5 Hz as the temperature is lowered to 183 K (Fig. 1, Table 1). The N^1H proton doublet is shifted downfield by 0.48 ppm, and the N^2H triplet, upfield by 0.25 ppm. At 183 K the chemical shifts of the two amide protons are almost identical (Table 1).

The presence of a single N^1H proton signal in both solvents which remains a doublet in the whole temperature range indicates the existence of a single *trans*-rotamer (N^1H and C=S relative to the bond C–N^1) [4]. The same applies to the N^2H proton. Thus, each of the amide protons has a *transoid* orientation with respect to the thiocarbonyl group realative to the bonds C–N^1 and C–N^2, and mutual *cis*-orientation, as shows the structure below (*Z*,*Z*-form):



A

The spatial proximity of the amide protons in the form **A** is confirmed by the presence of the NOE (nuclear Overhauser effect) between them in the NMR 2MOC NOESY spectrum of the solution in CD_3CN. Considering the lability of these protons, a fast amide–amide exchange $N^1H \rightleftarrows N^2H$ is not excluded.

However, the opposite direction in the δ_H change with temperature in CD_2Cl_2 solution (Table 1) indicates the participation of N^1H and N^2H protons in different intramolecular processes. At the same time, the rigid steric arrangement in the **A** form excludes

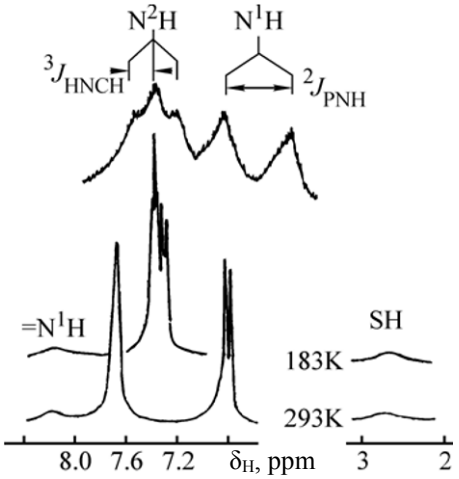


Fig. 1. Temperature dependence of the signals of amide protons N^1H, N^2H and =HN of *N,N′*-bis(*N*-diisopropoxythiophosphorylthiocarbonyl)-1,7-diaminoheptane **I** in CD_2Cl_2 solution.

from the consideration the process of rotation around the C–N^1 bond. However, in the ^1H NMR spectra in the range of 298–183 K there are some characteristics of the involvement of amide protons into the other intramolecular processes (Table 1): The broadening of the signals N^1H and N^2H while retaining their multiplicity, the instability of the values of $^2J(PN^1H)$ (–10.4 and –13.7 Hz) and $^3J_{HN^2CH}$ constants, the presence of additional broadened signals at δ 2.8, 2.9, and 8.2 ppm, the doubling of the proton signals of groups OPr-*i* and mobile fragment $(CH_2)_7$ with a ratio of integral intensities ~86:14% at 298 K.

The first three characteristics are related to the prototropy, i.e. migration of the amide protons to the reaction center C=S to give **B** or **C** forms (see scheme and Table 1), or both simultaneously (in this case, their chemical shifts are averaged). Taking into account the greater lability of the proton N^1H, the form **B** is preferred. The prototropy in the triad N^1–P=Y to form *N*-acylphosphazene >P(CH)=N^1–C(S)– was not considered, because such compounds, being products of intermediate stage of the synthesis of *N*-(thio)phosphoryl(thio)amides, are very unstable and easily converted into the corresponding amides [5, 6], which makes difficult their spectral registration. In any case, in the ^{13}C NMR spectrum (Fig. 2) the upfield signal of imine carbon atom C=N at δ 139 ppm was assigned to the form **B** and the second signal at δ 154 ppm to the C=N carbon atom of the phosphorylotropic form **D** formed at the migration of thiophosphoryl group $(OPr\text{-}i)_2P(S)$ to the sulfur atom C=S [7]. The broadened signal of the =NH proton of the form **D** also exists in the ^1H NMR spectrum (Fig. 1, Table 1).

Consider the fragment $(CH_2)_7$, which contains two α-CH_2 (directly attached to the group N^2H), β-CH_2 and γ-CH_2 groups, and one δ-CH_2 group: N^2H–$C^\alpha H_2C^\beta H_2C^\gamma H_2C^\delta H_2C^\gamma H_2C^\beta H_2C^\alpha H_2$–$N^2H$. The signals of these groups were identified taking into account the distance of each one from the nitrogen atom (chemical shift), the doubling of the relative integral intensities of the signals of the first three groups with respect to the fourth, and their multiplet structures. Thus, the signal of the two $C^\alpha H_2$ groups is a triplet of doublets, and of $C^{\beta,\gamma,\delta}H_2$ groups, the triplets of triplets.

The temperature evolution of the signals of labile fragment is shown in Table 1 which indicates that the $C^{\alpha,\gamma,\delta}H_2$ signals do not practically change the position

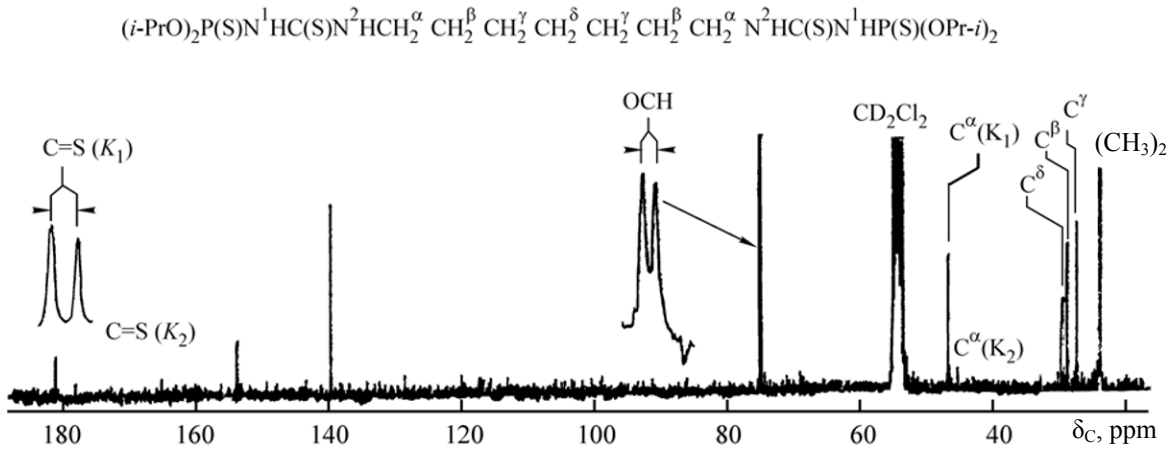


Fig. 2. The ^{13}C NMR spectrum of *N,N′*-bis(*N*-diisopropoxythiophosphorylthiocarbonyl)-1,7-diaminoheptane **I** in CD_2Cl_2 solution at 298 K.

Table 2. Temperature dependence of ^{31}P NMR spectra [δ_P, ppm (%)][a,b] of *N*,*N*′-bis[*N*-diisopropoxythiophosphoryl-aminothiocarbonyl]-1,7-diamino-heptane in CD_2Cl_2 and CD_3CN solutions

T, K	K_1 (**A**)	K_2 (**A**)	K_1 (**B**, **C**, **D**)	K_2 (**B**, **D**)
289[d]	59.92 (72.2)	60.05 (15.0)	60.2 (9.94), 63.52	60.7 (2.07)
296[c]	53.62 (64.15)	53.7 (14.2)	**B** 53.7 2 (9.65), **D** 58.4 (1.8), traces	**B** 53.8 (1.72), traces **D** 53.82 (2.23)
273	53.62 (61.55)	53.71 (21.1)	53.74 (7.2), 58.2 (1.52)	–
228	52.87 (74.9)	52.96 (22.0)	in **A** form region, 57.1, ~62.0 traces	56.8, ~62.0 traces
193	53.21 br.s (98.85)		56.9.0	–

[a] Integral intensities were determined approximately because of small differences in δ_P values. [b] There are additional signals in spectra at δ_P 44.7–46.2 ppm (4–8 wt %). [c] In CD_2Cl_2 solutions. [d] In CD_3CN solutions.

and remain well-resolved. The signal of $C^{\beta}H_2$ is broadened (as the signal of N^2H) and shifted downfield by 0.4 ppm, i.e. the signals of $C^{\beta}H_2$ and N^2H approach each other. The realization of the dynamic equilibrium of two conformations of macromolecules with different locations of the two equivalent substituents (*N*-thiophosphorylthioureas) in the sterically non-rigid open-chain fragment $(CH_2)_7$ is the most probable reason for the signals doubling [4]. A similar result was obtained in studying the structure of this compound in $(CD_3)_2C{=}O$ solution [4] and that of crown-containing *N*-thiophosphorylthioureas [3]. In turn, the approaching and broadening of the proton signals of $C^{\beta}H_2$ and N^2H indicate the spatial proximity of these groups at folding the molecule. This conformation is evidently advantageous.

In the ^{13}C NMR spectrum at 298 K the signals of the open-chain fragment are also doubled (Fig. 2). The ratio of integral intensities of the well-separated signals of the carbon atom $C^{\alpha}H_2$ in two conformations (δ 47 and 46 ppm) coincides similarly to the ^{1}H NMR spectrum. In addition, the doubled signals of thiocarbonyl and isopropyl groups are sensitive to the changes in molecular conformation [3, 4], and the doublet signal of C=S [$^2J(PN^1C)$ = –9.5 Hz] is a characteristic feature of the amide form **A**.

An essential supplement to the understanding of intramolecular processes in the compound **I** is the data of the temperature dependence of ^{31}P NMR spectra, which allow qualitative and quantitative monitoring the stereoisomeric and tautomeric forms in the equilibrium. Table 2 summarizes the results of determination of the chemical shifts and the percentage of each of the forms in the overall content. Figure 3 shows the temperature dependence of proton-coupled and proton-decoupled ^{31}P NMR spectra (upper spectrum at *T* 296 K) in CD_2Cl_2 solution. At 296 K the spectrum contains two pairs of the signals in the resonance region of amide and prototropic forms (δ_P 53.6–53.8 ppm, Table 2) with the ratio of integral intensities of ~82:12% in each of the pairs. In the range of 296–228 K this ratio changed to 77:23%, i.e. the fraction of the second conformation grows, while at 193 K there is a broadened singlet. The assignment of signals to the amide **A** and **B** prototropic forms in each of the two conformations was done taking into account the relevant ratio of the integral intensities C_1:C_2 in the spectra of all three nuclei [86:14% (^{1}H), 86:14% (^{13}C), 82:12%] indicates a significant advantage of the amide form **A** in both conformations and explains the signals multiplicity in the proton-decoupled spectrum. So, the downfield signals disappearing in the range of 296–

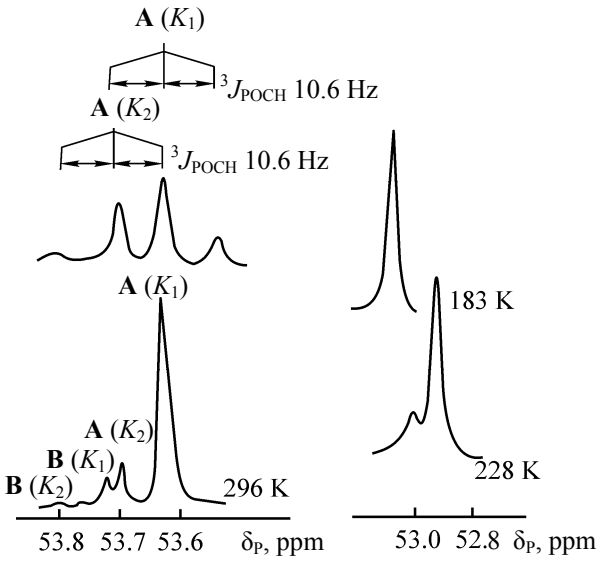


Fig. 3. The ^{31}P NMR spectra in the resonance region of the amide form of *N*,*N*′-bis[*N*-diisopropoxythiophosphoryl-aminothiocarbonyl]-1,7-diaminoheptane in CD_2Cl_2 solution.

228 K belong to the imidothiol form **B** (P–N^1=C). In addition, there is the downfield signal of phosphorylotropic form **D** (Table 2), whereas in CD_2Cl_2 solution the content of this form is no less than 7% [4].

In the temperature-controlled proton-decoupled ^{31}P NMR spectra (Fig. 3) each of the signals of amide forms is a triplet instead of the expected triplet of doublets characteristic of the stable amide form. It should be assumed that the averaging the value of geminal constant $^2J(PN^1H)$ to zero (in contrast to the ^1H NMR spectrum) is due, on the one hand, to the participation of this proton in several intramolecular processes, and, on the other hand, to the relaxation effects (different relaxation times for the ^1H and ^{31}P), depending on the temperature [8]. The signals of prototropic forms appear as triplets. Transformation of the signals in this resonance region as the temperature decreases firstly into the two signals with unequal intensities and then into the broadened singlet showed that the rate of proton and conformational exchange is reduced.

The above-stated changes in the temperature-controlled NMR spectra of all three nuclei indicate that in CD_3CN and CD_2Cl_2 solutions thiourea **I** is in an exchange state. Some intramolecular processes occurring simultaneously were identified: firstly, the conformational transformation of the macromolecule with the formation of two forms, Conf-1 and Conf-2. The predominant Conf-1 form has folded structure with the N^2H proton located spatially close to the β-CH_2 methylene group; secondly, the fast amide–amide exchange $N^1H \rightleftarrows N^2$; thirdly, the prototropy to form imidothiol form >P(S)–N^1=C(SH)–; fourthly, the phosphorylotropy.

EXPERIMENTAL

The ^1H NMR (300 MHz), ^{13}C (75.43 MHz), and ^{31}P (121.42 MHz) spectra at different temperatures and concentrations of solutions were taken on a Varian UNITY-300 spectrometer. The spectrometer operated in the internal stabilization on ^2H resonance mode and was equipped with a temperature control unit. For recording the ^{31}P NMR spectra typically 10–150º pulses and 1–2 s delays between the pulses were applied. The spectral width *SW* was 100 ppm. The scan number *NT* is from 10 to 100, digital filtering was not applied. The ^{13}C NMR spectra were usually obtained with 20°–300° pulses and broad band proton-decoupling, *RD* = 0, *SW* = 200 ppm, *NT* = 400–1000, digital exponential filtration with *LB* = 2–4 Hz.

For the recording two-dimensional NOESY spectrum the recommendations of the spectrometer manual were used, $NT \geq 8$. Iterations number *NI* in the time interval t_2 to obtain the second frequency axis was selected from the condition *NI* > *SW*. Phase-sensitive pulse sequence was used. For the construction of two-dimensional spectrum we used algorithms of the Fourier transform and of the linear prediction, for the recovery of the truncated FID the Gaussian weighting function was used as a digital filter. FID was added with zero to obtain the spectrum dimension 2048·2048 points.

The samples were prepared as 3–5 wt % solutions when recording the ^1H NMR spectra, and 10–15 wt % in the case of the ^{13}C and ^{31}P NMR spectra. The chemical shifts are reported relative to the internal references.

ACKNOWLEDGMENTS

The author is grateful to Prof. N.G. Zabirov for providing compound **I**.

This work was supported by the Russian Foundation for Basic Research (grant no. 09-03-007).

REFERENCES

1. Karataeva, F.Kh., Kopytova, N.I., Sokolov, F.D., Babashkina, M.G., and Zabirov, N.G., *Zh. Obshch. Khim.,* 2009, vol. 79, no. 11, p. 1775.
2. Karataeva, F.Kh., Galiullina, N.F., Aganov, A.V., and Zabirov, N.G., *Zh. Obshch. Khim.,* 1998, vol. 68, no. 5, p. 788.
3. Karatayeva, F.Kh., Aganov, A.V., and Klochkov, V.V., *Appl. Magn. Res*., 1998, vol. 14, no. 4, p. 545.
4. Karataeva, F.Kh., Galiullina, N.F., Aganov, A.V., and Zabirov, N.G., *Zh. Obshch. Khim.,* 2000, vol. 70, no. 8, p. 1303.
5. Zimin, M.G., Lazareva, G.A., Savel'eva, N.I., Islamov, R.G., Zabirov, N.G., and Cherkasov, R.A., *Zh. Obshch. Khim.,* 1982, vol. 52, no. 8, p. 1776.
6. Gilyarov, V.A., Tsvetkov, E.N., and Kabachnik, M.I., *Zh. Obshch. Khim.,* 1966, vol. 36, no. 2, p. 274.
7. Karataeva, F.Kh., *Zh. Obshch. Khim.,* 1999, vol. 69, no. 7, p. 1183.
8. Gunther, H., *Vvedenie v kurs spektroskopii YaMR* (Introduction into NMR Spectroscopy), Moscow: Mir, 1984.