ISSN 1070-3632, Russian Journal of General Chemistry, 2012, Vol. 82, No. 11, pp. 1764–1769. © Pleiades Publishing, Ltd., 2012.
Original Russian Text © V.A. Dobysh, N.V. Koktysh, V.A. Tarasevich, V.E. Agabekov, V.N. Makatun, L.I. Antonovskaya, N.A. Belyasova, 2012, published in Zhurnal Obshchei Khimii, 2012, Vol. 82, No. 11, pp. 1772–1777.

Synthesis and Study of Properties of the Polyhexamethyleneguanidine Complexes with the Ions Cu^{2+}, Zn^{2+}, and Ni^{2+}

V. A. Dobysh[a], N. V. Koktysh[a], V. A. Tarasevich[a], V. E. Agabekov[a],
V. N. Makatun[b], L. I. Antonovskaya[c], and N. A. Belyasova[c]

[a] *Institute of Chemistry of New Materials, National Academy of Sciences of Belarus,*
ul. Skaryny 36, Minsk, 220141 Belarus
e-mail: dobusch.w@mail.ru

[b] *Institute of Physical Organic Chemistry, National Academy of Sciences of Belarus, Minsk, Belarus*

[c] *Belarus State Technological University, Minsk, Belarus*

Received February 6, 2012

Abstract—The reaction products of polyhexamethyleneguanidine hydrochloride with the Cu^{2+}, Zn^{2+}, and Ni^{2+} ions, which are the polyligand coordination compounds formed by polyguanidine and hydroxyl ligands, were studied using IR, UV, and ESR spectroscopy. The influence of the nature of the chelating agent on the structure of the complexes formed was revealed. Antibacterial properties of the synthesized complexes were assessed.

DOI: 10.1134/S1070363212110035

Guanidine derivatives are known as broad-spectrum biocides [1, 2]. However, the inevitable emergence and spread of the microorganisms resistant toward polyguanidine preparations requires the development of the methods for chemical modification of the active substance molecules, aimed at creating new drugs. The ability of guanidine groups in polyhexamethyleneguanidine to coordinate with transition metal cations is appropriate for such modifications. There are only few published data on the complex compounds of guanidine derivatives as the most promising biocides of low toxicity [3, 4].

The aim of this work was to synthesize and study the physicochemical and biocidal properties of the polyhexamethyleneguanidine hydrochloride complexes with ions Cu^{2+}, Zn^{2+}, Ni^{2+}, included as a structural unit into the oligomeric matrix.

The IR spectra of the polyhexamethyleneguanidine hydrochloride complexes of Cu^{2+}, Zn^{2+} and Ni^{2+} were compared with the spectrum of the free ligand [5, 6]. Secondary amino groups are known [7] to give one NH absorption band, but due to the formation of hydrogen bonds, a second absorption band may appear at lower frequency. The stretching vibrations of the NH group are in the range of 3500–3050 cm^{-1} [7].

In the spectra of the Cu^{2+} and Zn^{2+} complexes the stretching vibrations of NH groups are shifted to the longer wavelengths by 13 cm^{-1} for copper complex and by 30 cm^{-1} for the zinc complex compared with the ligand, indicating that the amino group is involved in the formation of coordination bonds with the respective metal ion and not involved in the formation of hydrogen bonds [8]. In addition, the spectra contain strong absorption bands with the maxima at 1048 and 1113 cm^{-1} (Table 1) characterizing the Cu–OH and Zn–OH bending vibrations, respectively [9]. The bands at 615 and 616 cm^{-1} can be attributed to the Cu–O and Zn–O stretching vibrations, respectively [10].

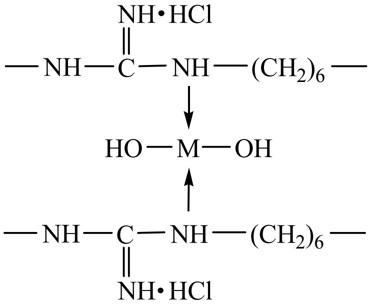
The IR spectrum of Ni^{2+} complex is characterized by the shift of stretching vibrations of NH groups from 3418 cm^{-1} (ligand) to 3348 cm^{-1} (complex). Also the Ni–OH bending vibrations were observed at 1101 cm^{-1}. These data suggest the participation of amino groups of the guanidine ligand in the formation of covalent bonds with metal ions in the complex by the donor–acceptor mechanism.

The process of dissociation of coordinated water in complexes of *d*-elements in the presence of a proton acceptor group may result in the appearance of

Table 1. Characteristic absorption bands in the IR spectra of polyhexamethyleneguanidine hydrochloride complexes

Comp. no.	Metal salt	ν(NH)	ν(CH)	ν(C=N)	δ(M–OH)	ν(M–O)
I	–	3418, 3196	2929, 2854	1636	–	–
II	$CuSO_4$	3416, 3210	2936, 2860	1634	1113	616
IIa	$Cu(CH_3COO)_2$	3416, 3212	2935, 2860	1635	1114	617
IIb	$CuCl_2$	3417, 3209	2935, 2860	1634	1112	616
III	$Zn(CH_3COO)_2$	3411, 3226	2929, 2855	1631	1048	615
IV	$NiBr_2$	3384	2929, 2856	1634	1101	–

hydroxyl surrounding [11]. In our case, the proton acceptors are the highly basic guanidine fragments of the polymer. The coordination node of the complex has a structure shown below.



$$\begin{array}{c} \text{NH}\cdot\text{HCl} \\ \| \\ \text{—NH—C—NH—(CH}_2)_6\text{—} \\ \downarrow \\ \text{HO—M—OH} \\ \uparrow \\ \text{—NH—C—NH—(CH}_2)_6\text{—} \\ \| \\ \text{NH}\cdot\text{HCl} \end{array}$$

In the IR spectra of copper complexes (Table 1) there are no absorption bands corresponding to the anions of metal salts (sulfate, acetate, chloride), which confirms the interaction of metal ions with the polyguanidine ligand by the donor–acceptor mechanism rather than through the formation of double salts [12].

Electronic spectra of the copper complexes with the polyhexamethyleneguanidine hydrochloride are characterized by the appearance of three absorption bands, at 205, 228, and 271 nm (Fig. 1), in contrast to the spectra of the free ligand, which has a maximum at 213 nm, and the spectrum of copper sulfate, which absorbs at 207 and 259 nm. The shift of the maximum to the region of 205 nm compared with the maximum absorption of the free ligand, as well as the appearance of the bands in the region of 228 nm can be attributed to the formation of the different-ligand complexes of the $M[X_2Y_2]$ composition. It was noted [8, 12] that the formation of such complexes leads to a distortion of the structure, lowering its symmetry, and therefore to the splitting of electronic levels, which increases the number of absorption bands. The appearance of a maximum at 271 nm can be attributed to the Cu–N bonding [13].

The complex of polyhexamethyleneguanidine hydrochloride with Zn^{2+} is characterized by the appearance

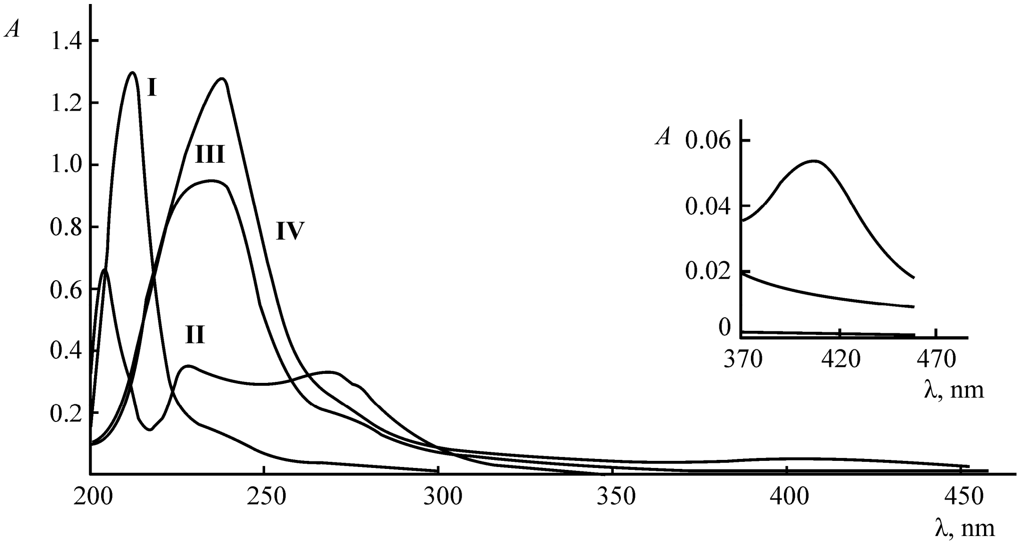


Fig. 1. Electronic spectra of the ligand **I** complexes with Cu^{2+} (**II**), Zn^{2+} (**III**), and Ni^{2+} (**IV**). [**I**] = 1×10^{-3} M, [**II**] = 4×10^{-5} M, [**III**] = [**IV**] = 2.7×10^{-3} M, the ratio metal:ligand = 1:2.

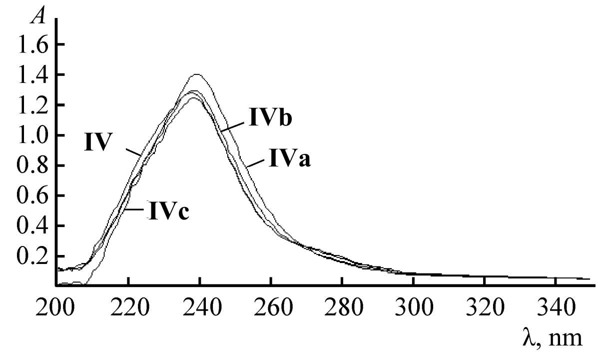


Fig. 2. Electronic spectra of ligand **I** (2.7×10^{-2} M) with Ni^{2+} (2.7×10^{-2} M). The metal–ligad ratios are 2:1 (**IVa**), 1:1 (**IVb**), 1:2 (**IV**) , and 1:3 (**IVc**).

of a maximum at 238 nm, whereas in the spectrum of zinc acetate this band is absent [14]. The maximum at 238 nm indicates a metal–ligand coordination [13, 14], taking into account the effect of the blue shift of the OH^- ligands. The appearance of a broad band in the spectra of these complexes is obviously due to the amorphous state of the product and, consequently, the random orientation of the coordination polyhedrons in the viscous matrix. It is also well known [13] that in a series of d_3–d_{10} complexes the complexes of the d_4–d_{10} ions (Fe^{2+}, Co^{2+}, Ni^{2+}, and Cu^{2+}) have a lower symmetry.

Complexes of the polymer with Ni^{2+} are characterized by the appearance of absorption bands with maxima at 238 nm and 406 nm. UV spectrum of nickel(II) bromide is characterized by the absorption band at 244 nm. The absorption band at 238 nm can be attributed to the formation of a coordination bond, as in the zinc complex. The presence of the bands of low intensity at 406 nm can be attributed to the vibrations of lone electrons of the metal ions [13]. The appearance of two absorption bands in the studied area are characteristic of Ni^{2+} complexes with other organic ligands, for example, the spectrum of the complex of nickel(II) with diethyldithiocarbaminate contains bands at 328 and 395 nm [15].

Figure 2 shows the electronic spectra of the synthesized complexes of Ni^{2+} with various metal to ligand ratios. The constant presence of the characteristic absorption band (238 nm) indicates that the obtained coordination compounds have similar structures regardless of the molar ratio of metal ions and ligands. This is typical also for the complexes of Cu^{2+} and Zn^{2+}.

ESR spectra of the polyhexamethyleneguanidine hydrochloride copper complex have the signals characteristic of low-spin complexes of Cu^{2+} with axial symmetry and the hyperfine structure of the central ion (^{63}Cu and ^{65}Cu, $I = 3/2$) on the line of the parallel orientation, which is resolved in the spectrum at the liquid nitrogen temperature. The g-factors at room temperature are as follows: $g_{\|} = 2.268$ and $g_{\perp} = 2.044$, and at liquid nitrogen temperature $g_{\|} = 2.327$ and $g_{\perp} = 2.047$. It is seen that the values of $g_{\perp}$ are almost the same at different temperatures of registration. The following parameters of the spin Hamiltonian should be accepted for this complex: $g_{\|} = 2.327$ and $g_{\perp} = 2.047$, $A_{II} = 118$ Gs. It is known that the square-planar environment of the metal ion leads to a characteristic anisotropy of the g-tensor: $g_{\|} > g_{\perp} > 2$. The values obtained from the observed ESR spectra satisfy this requirement ($g_{\|} = 2.327$; $g_{\perp} = 2.047$). Thus, it can be stated that the copper(II) ion in this complex is in a square-planar environment, or very near to it.

The geometric parameter G characterizing the exchange interaction between Cu^{2+} centers in polycrystalline compounds can be estimated by the ratio $G = (g_{\|}-2.0023)/(g_{\perp}-2.0023)$ [20]. When $G > 4$, the exchange interactions are negligible, while in the case of $G < 4$ they are essential. The geometric parameter G for the complex $Cu[(I)_2(OH)_2]$ is 7.3, which indicates the absence of a magnetic exchange interaction between the Cu^{2+} sites, that is, the system is magnetically diluted, the metal polyhedra are distributed in the polymer chain relatively evenly and do not form a phase-isolated clusters.

The study of viscosity of the solutions of polyhexamethyleneguanidine hydrochloride complexes with Cu^{2+}, Zn^{2+}, and Ni^{2+} ions showed that the formation of the copper complexes leads to an increase in the intrinsic viscosity from 0.052 dl g^{-1} (ligand) to 0.064 dl g^{-1} (copper complex), and the formation of complexes with Zn^{2+} and Ni^{2+} is accompanied by a decrease in viscosity to 0.021 and 0.022 dl g^{-1}, respectively. It can be assumed that the increase in intrinsic viscosity of the copper complexes is due to the cross-linking of the ligand molecules through the metal ion (Fig. 3a). It is also known [17] that intramolecular complex formation causes a decrease in the maximum size of the polymer random coil and the corresponding decrease in the viscosity of the solution. Thus, the copper complexes most likely are intermolecular ones (Fig. 3a), while zinc and nickel complexes are of the intramolecular structure (Fig. 3b).

The stability constants for complexes of copper, zinc, and nickel calculated by the method of [18] are 3.7×10^{6}, 1.45×10^{8}, and 1.16×10^{7} respectively.

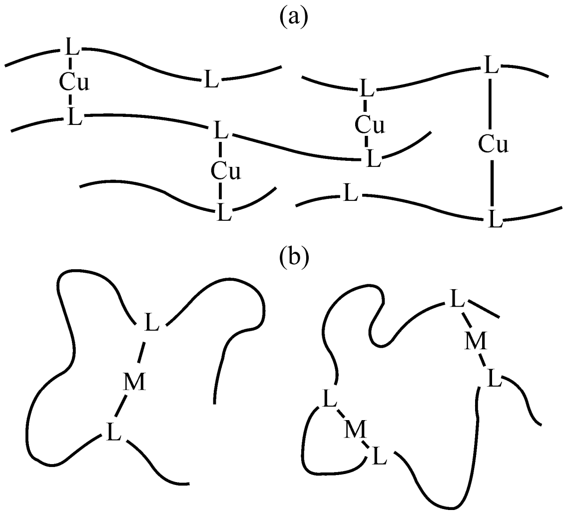


Fig. 3. Schematic structures the complexes of **I** with Cu^{2+} (a), Zn^{2+}, and Ni^{2+} (b), L is guanidine fragment.

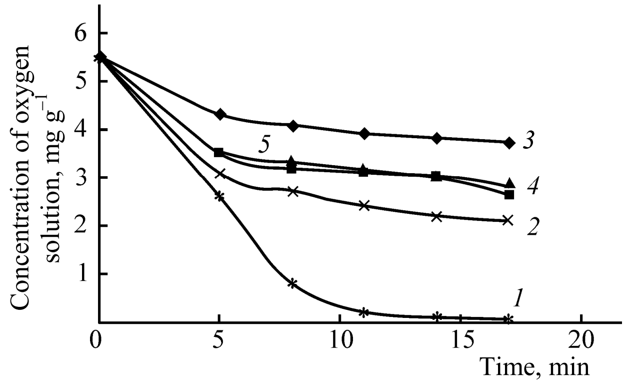


Fig. 4 The kinetics of absorption of molecular oxygen by bacteria *P. fluorescens* B2, before and after treatment with aqueous solutions of complexes. (*1*) control, (*2*) ligand **I**, (*3*) complex **II**, (*4*) complex **III**, and (*5*) complex **IV**.

Antibacterial properties of the macrocomplexes and metal salts against the test bacterium *Lactococcus lactis* subsp. *lactis* 411 were evaluated using 0.01 wt % aqueous solutions.

The polymeric ligand **I** and complexes with copper, zinc and nickel (**II, III**, and **IV**, respectively) exhibited antibacterial properties. Among the metal salts, the antibacterial activity at concentrations of 0.01 wt % was found in copper sulfate, while zinc acetate and nickel bromide do not have antibacterial properties (Table 2).

Table 2. Antibacterial properties of the ligand, metal complexes, and metal salts (adsorption–titrimetric method)

Sample	Concentration of accumulated lactic acid, mmol dm^{-3}	DS^a, rel. units	Evaluation of antibacterial properties
I	3.5	0.46	+
II	1.8	0.72	+
III	2.7	0.58	+
IV	2.8	0.57	+
$CuSO_4 \cdot 5H_2O$	3.2	0.50	+
$Zn(CH_3COO)_2 \cdot H_2O$	6.2	0.04	–
$NiBr_2 \cdot 3H_2O$	4.1	0.36	–
Water	6.5	–	–

[a] $DS = 1 - c_{add}/c_{acid}$, where c_{add} is the concentration of lactic acid accumulated in the lactococci cultural fluid with the sample treated with biocidal agent, mmol dm^{-3}, c_{acid} is the concentration of lactic acid accumulated in the lactococci cultural fluid with the control (water), mmol dm^{-3}. The presence of antibacterial properties in a sample (+ in the last column) was suggested at the $DS \geq 0.45$.

In parallel the antibacterial activity of the complexes was studied by measuring the respiration rate of bacteria *Pseudomonas fluorescens* B2 (Fig. 4, Table 3).

The data obtained suggest that the inclusion of metal ions in the polyhexamethyleneguanidine hydrochloride matrix by the considered mechanism provides a much more pronounced suppression of metabolic activity of the test organisms in comparison with the free ligand, which is especially evident in the copper-containing systems.

In the presence of the copper complex **II** (Table 3) a decrease in respiratory activity of the test bacteria is the sreongest: The reduction in the oxygen consumption rate by the culture fluid was three-fold compared

Table 3. The rate of absorption of molecular oxygen by bacteria *P. fluorescens* B2 treated with aqueous solutions of polyhexamethyleneguanidine hydrochloride complexes of Cu^{2+}, Zn^{2+}, and Ni^{2+}

Sample	Oxygen consumption rate, mg l^{-1} min^{-1}
I	0.21
II	0.12
III	0.17
IV	0.17
Control	0.32

to control. Note that this system also provides the achievement of the highest values of the relative rate of antibacterial activity *DS* by the adsorption–titrimetric method.

Thus, the work showed a possibility of synthesis of stable polyhexamethyleneguanidine hydrochloride complexes with the ions Cu^{2+}, Zn^{2+}, and Ni^{2+} with high biocidal activity. The inner sphere of the complexes is formed by two ligand molecules and two hydroxy groups, therewith, the ligand forms coordination bonds by free electron pair of amine nitrogen atom of the guanidine group.

EXPERIMENTAL

We used the polyhexamethyleneguanidine hydrochloride **I** described in [9], with the average molecular weight 6400, containing mainly linear oligomers with three monomer units, which was obtained by the improved method [20].

The IR spectra of complexes in the form of tablets with KBr were recorded on a spectrophotometer TENSOR 27. The stability constants of complexes were determined by calculation as described in [18] based on the optical density of solutions. The ESR study of copper complexes was performed on the X-band, operating frequency 9.45 GHz in a H_{102} rectangular resonator. The spectra were recorded at room temperature (298 K) and liquid nitrogen temperature (77 K).

The intrinsic viscosity of dilute aqueous solutions of the ligand and its complexes with transition metal ions was determined in a 0.5 molar solution of sodium chloride on a VPZh-2 viscometer with a capillary diameter 0.34 mm, at 25°C.

The assessment of antibacterial properties of synthesized complexes was carried out in two ways, by a modified adsorption-titrimetric method and by respiration rate of the obligate aerobic bacteria [21]. As a test cultures were used lactic acid bacteria *Lactococcus lactis* subsp. *lactis* 411 and obligate aerobic bacteria *Pseudomonas fluorescens* B2.

The complexes of the polymer with transition metal ions (Cu^{2+}, Zn^{2+}, and Ni^{2+}) were synthesized using methanol as a solvent. The metal ions as complexing agents were added to methanol solutions of the polymer as the alcoholic solutions of the corresponding salts in quantities not exceeding 1.0 wt %. Preliminary experiments showed that at this amount of a metal salt the full solubility of the compounds in methanol was retained and we were able to obtain a homogeneous reaction systems.

For the synthesis of the metal derivatives of polyhexamethyleneguanidine hydrochloride, to its 10% methanol solution were added dropwise with stirring the methanol solutions of copper sulfate, acetate, or chloride, zinc acetate, or nickel bromide at concentrations from 0.3 to 0.4 wt %. Salt solutions were added at a rate of 0.5 ml min^{-1} for 10 min and further the solution was stirred for 1 h at 40°C. The resulting solution was evaporated on a rotary evaporator, the residue was dried in a desiccator over sulfuric acid. The resulting products were waxy substances of yellow (zinc complex) of green (complexes of copper and nickel) color.

REFERENCES

1. Vointseva, I.I. and Gembitskii, P.A., *Poliguanidiny – dezinfektsionnye sredstva i polifunktsional'nye dobavki v kompozitsionnye materialy* (Polyguanidines: Disinfection Means and Polyfunctional Additives to the Composite Materials), Moscow: LKM-press, 2009.
2. Mashkovskii, M.D., *Lekarstvennye sredstva* (Pharmaceuticals), Khar'kov: Torsing, 1997.
3. Owsik, I. and Kolarz, B., *Polymers,* 2001, vol. 48, p. 169.
4. Nizhnik, V.V. and Nizhnik, T.Yu., *Vopr. Khim. Khim. Tekhn.*, 2006, no. 6, p. 120.
5. Zhang, Y., Jiang, J., and Chen, Y., *Polymers,* 1999, vol. 40, p. 6189.
6. Tarasevich, V.A. and Makatun, V.N., *Vesti Nats. Akad. Nauk Bel., Ser. Khim. Nauk*, 2010, no. 3, p. 78.
7. Kukushkin, V.Yu. and Kukushkin, Yu.N., *Teoriya i praktika sinteza koordinatsionnykh soedinenii* (Theory and Practice of the Synthesis of Coordination Compounds), Leningrad: Nauka, 1990.
8. Skopenko, V.V. and Zub, V.Ya., *Koordinationnaya khimiya* (Coordination Chemistry), Kiev: Kiev Univ., 2002.
9. Shevelenko, S.V., Kuchko, A.A., and Belyasova, N.A., *Trudy Bel. Gos. Tekh. Univ.*, 2010, vol. 18, no. 4, p. 290.
10. Zhang, L., Yao, S., and Guan, Y., *Process Biochemistry*, 2005, vol. 40, p. 189.
11. Bellamy, L.J., *Infrared Spectra of Complex Molecules*, Moscow: Inostrannaya Literatura, 1963.
12. Zheligovskaya, N.N. and Chernyaev, I.I., *Khimiya kompleksnykh soedinenii* (Chemistry of Complex Compounds), Moscow: Vysshaya Shkola, 1966.
13. Nakamoto, K., *Infrared and Raman Spectra of Inorganic and Coordination Compounds*, Moscow: Mir, 1991.

14. Kauffman, J.W., Hauge, R.H., and Margrave, J.L., *J. Phys. Chem*., 1985, vol. 89, no. 16, p. 3541.
15. Makatun, V.N., *Khimiya neorganicheskikh gidratov* (Chemistry of Inorganic Hydrates), Minsk: Nauka i Tekhnika, 1985, p. 82.
16. *Spektroskopicheskie metody v khimii kompleksnykh soedinenii* (Spectroscopic Methods in the Chemistry of Complex Compounds), Vdovenko, V.M., Ed., Moscow: Khimiya, 1964.
17. Beilar, J., *The Chemistry of Coordination Compounds*, Moscow: Inostrannaya Literatura, 1960.
18. Zhivopistsev, V.P. and Selezneva, E.A., *Analiticheskaya khimiya tsinka* (Analytical Chemistry of Zinc), Moscow: Nauka, 1975.
19. Peshkova, V.M. and Savostina, V.M., *Analiticheskaya khimiya nikelya* (Analytical Chemistry of Nickel), Moscow: Nauka, 1966.
20. Rakitin, Yu.V., Larin, G.M., and Minin, V.V., *Interpretatsiya spektrov EPR koordinatsionnykh soedinenii* (Interpretation of ESR Spectra of Coordination Compounds), Moscow: Nauka, 1993.
21. Rosthauser, J.W. and Winston, A., *Macromolecules*, 1981, vol. 14, p. 538.