

Synthesis, Structure, and Properties of Co²⁺ and Ni²⁺ Complexes with the Product of Condensation of 2-(7-Bromo-2-oxo-5-phenyl-3H-1,4-benzodiazepin-1-yl)-acetohydrazide and 1H-Indole-2,3-dione

I. I. Seifullina^a, L. S. Skorokhod^{a,*}, A. V. Pulya^a, V. G. Vlasenko^b,
A. L. Trigub^c, and I. M. Rakipow^d

^a I.I. Mechnikov Odessa National University, Odessa, 65082 Ukraine

^b Research Institute of Physics, Southern Federal University, Rostov-on-Don, 344090 Russia

^c National Research Center “Kurchatov Institute,” Moscow, 123182 Russia

^d Odessa National Polytechnic University, Odessa, 65044 Ukraine

*e-mail: lborn@ukr.net

Received February 5, 2020; revised February 5, 2020; accepted February 16, 2020

Abstract—[Co(HydrHz)] and [Ni(HydrHz)]·2H₂O (M = Co, Ni) complexes have been obtained via the reaction of M(CH₃COO)₂ with 2-(7-bromo-2-oxo-5-phenyl-3H-1,4-benzodiazepin-1-yl)acetohydrazide (Hydr) and 1H-indole-2,3-dione (Hz). Structure and composition of the complexes have been confirmed by elemental analysis, thermogravimetry, IR spectroscopy, and mass spectrometry data. The electrical conductivity and magnetic susceptibility of the complexes have been determined. The local atomic structure of coordination centers has been established by X-ray absorption spectroscopy.

Keywords: coordination compounds, cobalt(II), nickel(II), 2-(7-bromo-2-oxo-5-phenyl-3H-1,4-benzodiazepin-1-yl)acetohydrazide, isatin

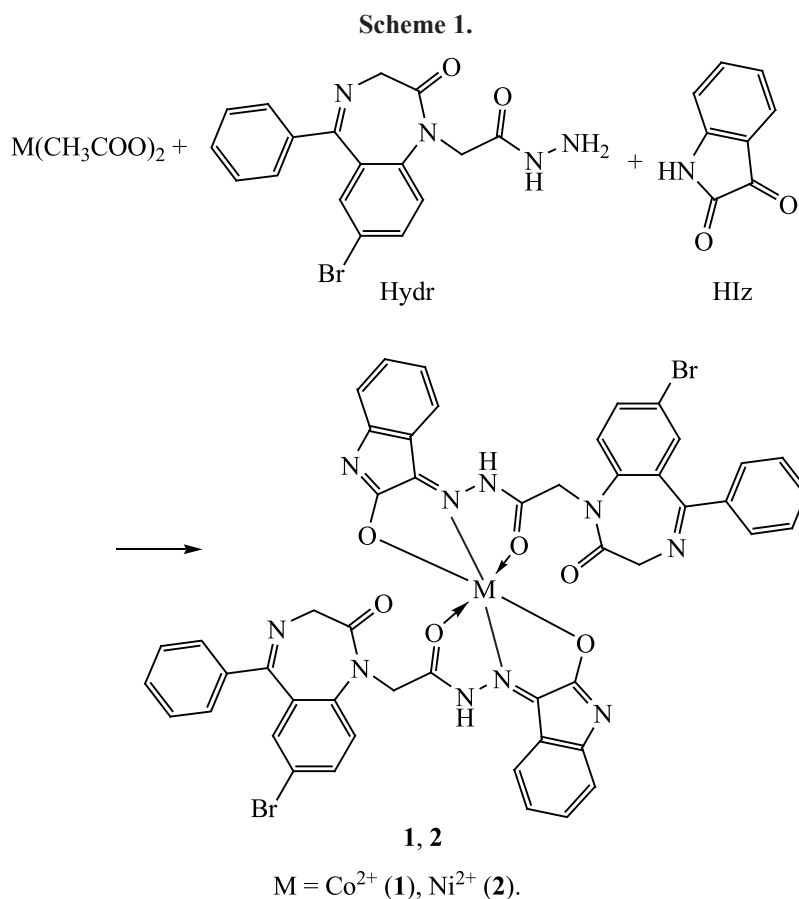
DOI: 10.1134/S1070363220070166

Synthesis of complexes of vital 3d-metals (manganese, cobalt, nickel, copper, or zinc) with biologically active polycyclic ligands is among important research fields in bioinorganic chemistry. A special class of these compounds are these based on nitrogen-containing heterocycles: they are involved in synthesis of nucleic acids as well as immunity and regeneration processes and are efficient in the clinical treatment of oncological and psychoneurological diseases or diverse traumatic states, exhibiting minimal range of side effects [1–3].

Pyridine, its analogs, and their coordination compounds with Co(II), Ni(II), and Cu(II) have been best studied so far. However, the data on benzodiazepine derivatives [daily sedative drug gidazepam—2-(7-bromo-2-oxo-5-phenyl-3H-1,4-benzodiazepin-1-yl)acetohydrazide (Hydr)—being an example] have been practically absent. In contrast to other benzodiazepine derivatives, gidazepam molecule contains a hydrazide moiety on top of several donor sites (N and O); being a peptide

group C(O)NH analog, the hydrazide moiety has been considered a source of gidazepam biological activity [4–7]. Coordination compounds of metals with a product of Hydr condensation with Hz (HydrHz, a benzodiazepine hydrazone ligand) are formed in the M(CH₃COO)₂–Hydr–Hz–isopropanol system [M = Co(II), Ni(II)]. The obtained complexes can exhibit synergetic biological activity of the components [8–16].

The [Zn(HydrHz)₂] complex has been earlier isolated from the Zn(CH₃COO)₂–Hydr–Hz system and characterized using a set of physico-chemical methods [17]. Extending that study, we isolated the [Co(HydrHz)₂] (**1**) and [Ni(HydrHz)₂] (**2**) complexes from the M(CH₃COO)₂–Hydr–Hz (M = Co, Ni) system. Complexes **1** and **2** were fine-crystalline substances insoluble in alcohols, chloroform, and acetonitrile and soluble in DMSO and DMF. Measurements of electrical conductivity of the 1×10^{−3} M solutions in DMSO



suggested that they were nonelectrolytes, molar electrical conductivity being 10.8 (**1**) and $6.2 \Omega^{-1} \text{cm}^2 \text{mol}^{-1}$ (**2**).

Thermal decomposition of complexes **1** and **2** occurred similarly. The thermograms revealed no low-temperature effects which could correspond to solvent elimination. The compounds were stable up to 300°C , revealing the endothermic effect accompanied by significant mass loss at 310 (**1**) and 330°C (**2**). Further heating of the complexes led to oxidative thermal decomposition of the organic part of the molecules reflected in a series of high-temperature exothermic effects. The final thermal decomposition product was CoO (**1**) or NiO (**2**), in line with the mass loss.

The studied complexes were poorly volatile under conditions of mass spectrometry (fast atoms bombardment), as reflected in weak peaks of the complex of fragmented ions in comparison with strong peaks of the matrix. The compounds spectra contained the peaks of the molecular ions $[M + 2L]^+$, with $M = \text{Co(II)}$, Ni(II) and $L = \text{HydrIz}$, confirming the presence of a new HydrIz ligand in complexes **1** and **2**, formed via template reaction with Co^{2+} and Ni^{2+} ions (Scheme 1).

The ligand coordination in the complexes was elucidated by means of IR spectroscopy, comparing the major absorption bands in the spectra of the starting compounds (Hydr and HIz) and complexes **1**, **2**. Assignment of the IR spectra in the range of $\nu(\text{C}=\text{O})$ stretching was complicated by the presence of the carbonyl groups both in the Hydr and HIz molecules. Therefore, the IR spectra were analyzed assuming the presence of a new ligand (HydrIz) in complexes **1** and **2**, as per mass spectroscopy data. Firstly, the $\nu(\text{NH}_2)$ band at 3429cm^{-1} observed in the IR spectrum of gidazepam was absent in the spectra of complexes **1** and **2**. Additional absorption bands appearing at 1613 (**1**), 1615cm^{-1} (**2**) [$\nu(\text{C}=\text{N})$] and 460 (**1**), 470cm^{-1} (**2**) [$\nu(\text{M}-\text{N})$] confirmed the condensation between the amino group of Hydr and the carbonyl group of HIz as well the participation of the formed $\text{C}=\text{N}$ bond in the coordination with the metal ions. In comparison with the IR spectra of the starting ligands Hydr and HIz, those of complexes **1** and **2** contained additional bands assigned to $\nu(\text{C}-\text{O})$ [1186 (**1**), 1187cm^{-1} (**2**)] and $\nu(\text{M}-\text{O})$ [549 (**1**), 550cm^{-1} (**2**)]. In view of the complexes composition (the absence of anion), the observed changes suggested that the complex

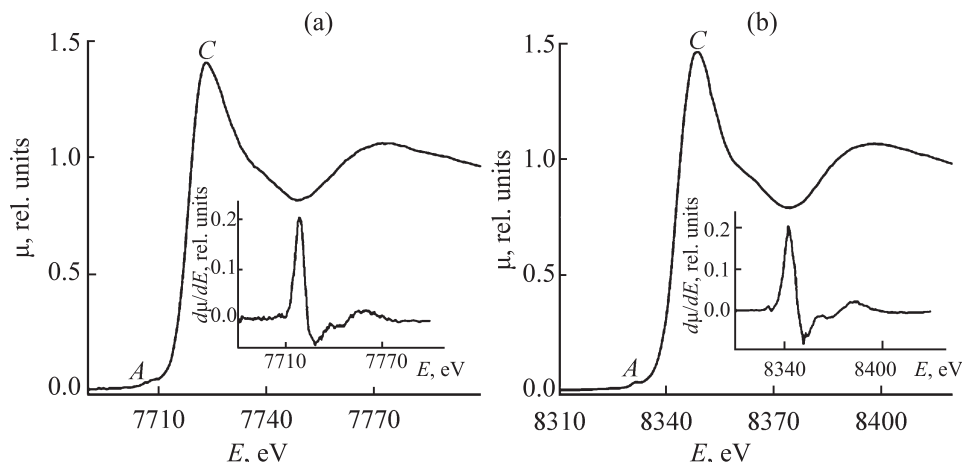


Fig. 1. Normalized XANES spectra of Co (a) and Ni (b) of the K -edges of absorption (the corresponding first derivatives $d\mu/dE$ are in the insets) of complexes **1** and **2**.

formation led to the HydrIZ keto form transformation into the enol one and binding of the latter with M^{2+} via the oxygen atom. Thus, the five-membered metallocycle was closed (involving the existing M–N bond). That conclusion coincided with the disappearance of the strong $\nu(\text{C}=\text{O})$ band (maximum at 1728 cm^{-1} and shoulder at 1748 cm^{-1}), typical of the starting ligand HIZ, in the spectra of complexes **1** and **2**. The $\nu(\text{C}=\text{O})$ range of IR spectra of complexes **1** and **2** contained pairs of bands at 1682 (**1**), 1678 cm^{-1} (**2**) and 1660 (**1**), 1663 cm^{-1} (**2**), likely due to the presence of one free and one coordinated carbonyl groups in the molecule. That suggestion was reasonable in view of the favorable closing of the second metallocycle in such case.

Detailed data on the structure of coordination nodes in complexes **1** and **2** was obtained by means of X-ray absorption spectroscopy (analysis of XANES and EXAFS of K -edges of the metals absorption). The normalized XANES spectra of Co and Ni absorption K -edges and their first derivatives are given in Fig. 1. The spectra of complexes **1** and **2** were similar and consisted of the major absorption maximum C and weak pre-edge maximum A . The nature of the pre-edge peak A is determined by the degree of the p – d mixing of the metal atomic orbitals, and its intensity depends on the symmetry of the coordination site surrounding, being the lowest for the octahedral surrounding. The latter type of surrounding is characterized by insignificant splitting of the vacant p^* -orbitals of the metal, which are the host of the electronic transitions from the $1s$ orbitals giving rise to the K -absorption spectra. The shape of the first derivatives of the K -edges ($d\mu/dE$) of complexes **1** and **2**

contained narrow single maximums. Qualitative analysis of the complexes XANES spectra suggested distorted octahedral surrounding of the metal ions in compounds **1** and **2**.

Local atomic structure of the coordination nodes in complexes **1** and **2** was elucidated by analysis of EXAFS of the corresponding K -edges of the X-ray absorption spectra. Parameters of the modules of Fourier transformant (MFT) of complexes **1** and **2** (Fig. 2) were close and contained the major peak at $r = 1.60$ – 1.65 \AA , assigned to the scattering of the photoelectron wave at the first coordination sphere consisting of nitrogen and oxygen complexes of the ligands. Further weaker peaks in the complexes MFT at $r = 2.35$ – 2.42 \AA were related to the coordination spheres containing different ligand atoms (mainly carbon).

The best fit of the theoretical EXAFS spectra to the experimental ones for complexes **1** and **2** was obtained for the model suggesting octahedral surrounding of the metal ion by six oxygen/nitrogen atoms in the first coordination sphere. The obtained mean $\text{Co}(\text{Ni})\cdots\text{N}/\text{O}$ distances (see Table 1) were practically identical within the measurement accuracy. The parameters of the local atomic structure of coordination nodes of complexes **1** and **2** determined from the EXAFS analysis confirmed the conclusion on octahedral surrounding of cobalt and nickel ions in the studied compounds, as made from the XANES analysis.

In summary, the results of the study of local atomic structure of complexes **1** and **2** by means of XANES and EXAFS analysis coincided with the data of elemental

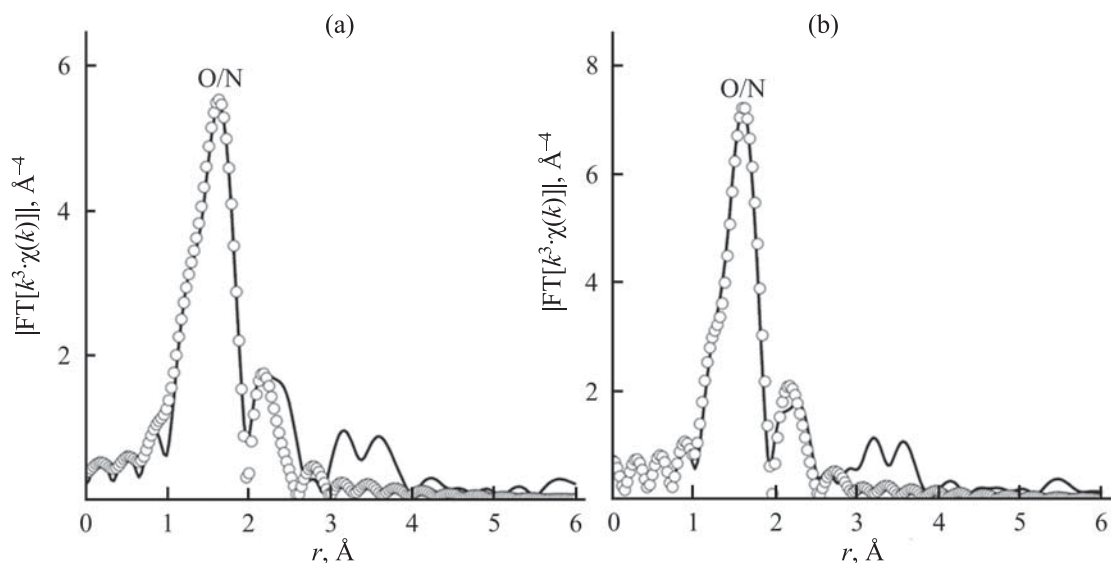


Fig. 2. MFT of EXAFS of Co and Ni K-edges of absorption of complexes **1** (a) and **2** (b); (solid line) experiments, (circles) theory.

and thermogravimetric analysis, IR spectroscopy, and mass spectrometry. Moreover, the effective magnetic moments [$\mu_{\text{eff}} = 5.16$ (**1**), 3.04 (**2**) μ_{B}] were typical of the mononuclear octahedral complexes of nickel and cobalt with the metal coordinated to two nitrogen and four oxygen atoms [19, 20]. Hence, the scheme of the complex formation and the obtained complexes structure were elucidated using a set of experimental methods.

EXPERIMENTAL

Thermogravimetric experiments were performed using a Q-derivatograph (Paulic–Paulic–Erdey system; specimen mass 60–80 mg, heating in air over 20–1000°C at 10 deg/min, specimen holder—open platinum crucible, reference—calcined alumina). Molar electrical conductivity of 1×10^{-3} M solutions of complexes **1** and **2** in DMSO was measured using an Ekonomiks–Ekspert digital instrument, the electrolyte type was determined using the tables in [21]. IR spectra were obtained using PerkinElmer Spectrum BX-II FI-IR and Shimadzu FTIR-8400S spectrophotometers (4000–400 cm^{-1} , KBr pellets). The mass spectra were recorded using a VG

7070 instrument (VG Analytical, Great Britain). The ions desorption from liquid matrix surface was performed using argon atoms beam (8 keV), *m*-nitrobenzyl alcohol was used as matrix. Specific magnetic susceptibility of complexes **1** and **2** was determined by means of relative Faraday method over 77.4–295 K with $\text{Hg}[\text{Co}(\text{CNS})_2]$ as reference. The molar magnetic susceptibility (χ_{M}) was calculated accounting for the atoms diamagnetism via the additive Pascal scheme [22]. The effective magnetic moment was calculated using Eq. (1).

$$\mu_{\text{ef}} = \sqrt{(3k/N\mu_{\text{B}}\chi T)} \approx \sqrt{8\chi T}, \quad (1)$$

with k —Boltzmann's constant, N —the Avogadro's number, and μ_{B} —the Bohr magneton.

X-ray absorption spectra of the solid complexes were recorded in the transmission mode using an EXAFS spectrometer of the station for Structural Materials Science, Kurchatov Synchrotron Center (Moscow) [23]. The electrons beam with energy of 2.5 GeV at current of 80–120 mA was used as the source of X-ray synchrotron radiation. The X-ray radiation was monochromatized using a two-crystal Si(111) monochromator. Processing of the recorded absorption spectrum involved standard

Table 1. Parameters of local atomic structure of complexes **1** and **2** obtained via two-sphere EXAFS fitting^a

Complex	N	R , Å	σ^2 , Å ²	Atom	\mathcal{R}^b , %
1	2	1.95	0.0045	O/N	1.0
	4	2.08	0.0045	O/N	
2	2	1.97	0.0040	O/N	1.2
	4	2.07	0.0040	O/N	

^a N —coordination number, R —interatomic distance, σ^2 —Debye–Waller factor, \mathcal{R} —goodness of fit factor.

^b Region of fitting in the r -space $\Delta r = 1.00$ – 1.9 Å

procedures of background subtraction, normalization by the K -edge jump value, and extraction of the atomic absorption μ_0 . After that, Fourier transformation of the obtained EXAFS (χ)-spectra was performed over the wave vector of the photoelectrons range k from 2.5 to 13.0 \AA^{-1} with the k^3 weighing function. The threshold ionization energy E_0 was chosen from the value of the maximum of the first derivative of the K -edge and then refined during fitting. The structural parameters of the nearest surrounding of cobalt and nickel ions in the compounds were determined via nonlinear fitting of

$$\mathcal{R} = \sum_{i=1}^{N_{\text{pts}}} \frac{\{\text{Re}[\chi_{\text{data}}(R_i) - \chi_{\text{th}}(R_i)]\}^2 + \{\text{Im}[\chi_{\text{data}}(R_i) - \chi_{\text{th}}(R_i)]\}^2}{\{\text{Re}[\chi_{\text{data}}(R_i)]\}^2 + \{\text{Im}[\chi_{\text{data}}(R_i)]\}^2},$$

with $\chi_{\text{data}}(R_i)$ and $\chi_{\text{th}}(R_i)$ being the EXAFS functions in the r -space, N_{pts} being the number of data points in the fitted spectral region.

Elemental analysis was performed using a CHN analyzer, bromine content was determined by means of mercurimetry [26], the content of cobalt and nickel was determined by means of atomic emission spectroscopy with inductively coupled plasma (ICP–AES) using an Optima–2100 DV PerkinElmer instrument.

Bis[N' -(2-oxido-3*H*-indol-3-ylidene)-2-(7-bromo-2-oxo-5-phenyl-3*H*-1,4-benzodiazepin-1-yl)-acetohydrazide]cobalt (nickel) (1, 2). 2 mmol of isatin (HIz) in 20 mL of propan-2-ol was added to a solution of 2 mmol of hydrazide (Hydr) in 20 mL of propan-2-ol. The reaction mixture was heated during 3 h on a water bath, and then 10 mL of a solution of $\text{Co}(\text{CH}_3\text{COO})_2 \cdot 6\text{H}_2\text{O}$ or $\text{Ni}(\text{CH}_3\text{COO})_2 \cdot 6\text{H}_2\text{O}$ in ethanol was added. The components molar ratio was $\text{M}(\text{CH}_3\text{COO})_2$: Hydr : HIz = 1 : 2 : 2. The mixture was refluxed during 1 h. After cooling, the formed precipitate was filtered off, washed with isopropanol, and dried to constant mass at 80°C.

Complex 1. Mass spectrum, m/z (I_{rel} , %): 1089 (7.5) $[2\text{L} + \text{M}]^+$, 516 (70.4) $[\text{L} + \text{H}]^+$, 575 (14.9) $[\text{L} + \text{M} + \text{H}]^+$, 315 (8.2) $[\text{C}_{15}\text{H}_{10}\text{BrN}_2\text{O} + \text{H}]^+$, 299 (99.8) $[\text{C}_{15}\text{H}_{10}\text{BrNO} + \text{H}]^+$. Found, %: C 54.84; H 3.00; Br 14.26; N 12.52; Co 5.08. $\text{C}_{50}\text{H}_{34}\text{Br}_2\text{CoN}_{10}\text{O}_6$. Calculated, %: C 55.00; H 3.12; Br 14.69; N 12.86; Co 5.42.

Complex 2. Mass spectrum, m/z (I_{rel} , %): 1088 (8.0) $[2\text{L} + \text{M}]^+$, 516 (20.8) $[\text{L} + \text{H}]^+$, 575 (10.7) $[\text{L} + \text{M} + \text{H}]^+$, 315 (28.0) $[\text{C}_{15}\text{H}_{10}\text{BrN}_2\text{O} + \text{H}]^+$, 299 (58.7) $[\text{C}_{15}\text{H}_{10}\text{BrNO} + \text{H}]^+$. Found, %: C 54.90; H 3.16; Br 14.32; N 12.36; Ni 5.04. $\text{C}_{50}\text{H}_{34}\text{Br}_2\text{Ni}_{10}\text{NiO}_6$. Calculated, %: C 55.99; H 3.128; Br 14.69; N 12.86; Ni 5.42.

the corresponding coordination spheres parameters by comparing the simulated EXAFS signal and the MFT of the total EXAFS spectrum. Nonlinear fitting was performed using IFFEFIT-1.2.11 software package [24]. The phases and amplitudes of the photoelectron scattering required for the simulation of the model spectrum were calculated using FEFF7 software [25] from atomic coordinated of the structurally similar compounds.

The goodness of fit function which was minimized to determine the structural parameters was calculated using Eq. (2).

FUNDING

X-ray spectral studies were financially supported by Southern Federal University (internal research grant of SFU, project no. VnGr/2020-01-IF).

CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

REFERENCES

1. Kogan, V.A., Zelentsov, V.V., Larin, G.M., and Lukov, V.V., *Kompleksy perekhodnykh metallov s gidrazonami* (Complexes of Transition Metals with Hydrazones), Tsivadze, A.Yu., Ed., Moscow: Nauka., 1990.
2. Albert, A., *Selective Toxicity—The Physicochemical Basis of Therapy*, New York: Chapman & Hall, 1985.
3. Garnovskii, A.D., Vasil'chenko, I.S., and Garnovskii, D.A., *Sovremennye aspekty sinteza metallokompleksov. Osnovnye ligandy i metody* (Modern Aspects of the Synthesis of Metal Complexes. Basic Ligands and Methods), Rostov-on-Don: LaPO, 2000.
4. Karbuj, R., El-Dissouky, A., Jeragh, B., and Al-Saleh, E., *J. Coord. Chem.*, 2010, vol. 63, no. 5, p. 868. <https://doi.org/10.1080/00958971003645946>
5. Bai, Y., Wang, J.-Li, Dang, D.-B., and Zheng, Y.-N., *Spectrochim. Acta (A)*, 2012, vol. 97, p. 105. <https://doi.org/10.1016/j.saa.2012.05.076>
6. Singh, J.V. and Singh, N.P., *Bioinorg. Chem. Appl.*, 2012, p. 1. <https://doi.org/10.1155/2012/104549>
7. Singh, N.P. and Singh, J.V., *E-J. Chem.*, 2012, vol. 9, no. 4, p. 1835. <https://doi.org/10.1155/2012/521345>
8. Ershov, P.V., Mezentsev, Y.V., Yablokov, E.O., Kaluzhsky, L.A., Florinskaya, A.V., Buneeva, O.A., Medvedev, A.E., and Ivanov, A.S., *Russ. J. Bioorg.*

- Chem.*, 2018, vol. 44, no. 2, p. 193.
<https://doi.org/10.1134/S1068162018010053>
9. Swathy, S.S., Joseyphus, R.S., Nisha, V.P., Subhadrambika, N., and Mohanan, K., *Arab. J. Chem.*, 2016, vol. 9, p. S1847.
<https://doi.org/10.1016/j.arabjc.2012.05.004>
10. Shebl, M., El-ghamry, M.A., Khalil, S.E., and Kishk, M.A., *Spectrochim. Acta (A)*, 2014, vol. 126, p. 232.
<https://doi.org/10.1016/j.saa.2014.02.014>
11. Khan, A., Jasinski, J.P., Smoleaski, V.A., Paul, K., Singh, G., and Sharma, R., *Inorg. Chim. Acta*, 2016, vol. 449, p. 119.
<https://doi.org/10.1016/j.ica.2016.05.013>
12. Tehrani, K.E., Hashemi, M., Hassan, M., Kobarfard, F., and Mohebbi, Sh., *Chin. Chem. Lett.*, 2016, vol. 27, no. 2, p. 221.
<https://doi.org/10.1016/j.cclet.2015.10.027>
13. Muralisankar, M., Sujith, S., Bhuvanesh, N.S.P., and Sreekanth, A., *Polyhedron*, 2016, vol. 118, p. 103.
<https://doi.org/10.1016/j.poly.2016.06.017>
14. Lian, Z.-M., Sun, J., and Zhu, H.-L., *J. Mol. Struct.*, 2016, vol. 1117, p. 8.
<https://doi.org/10.1016/j.molstruc.2016.03.036>
15. Teng, Y.-O., Zhao, H.-Y., Wang, J., Liu, H., and Yu, P., *Eur. J. Med. Chem.*, 2016, vol. 112, p. 145.
<https://doi.org/10.1016/j.ejmech.2015.12.050>
16. Sobhani, S., Asadi, S., Salimi, M., and Zarifi, F., *J. Organomet. Chem.*, 2016, vol. 822, p. 154.
<https://doi.org/10.1016/j.jorganchem.2016.08.021>
17. Pulya, A.V., Seifullina, I.I., Skorokhod, L.S., Vlasenko, V.G., Trigub, A.L., and Rakipov, I.M., *Russ. J. Gen. Chem.*, 2018, vol. 88, no. 2, p. 277.
<https://doi.org/10.1134/s1070363218020135>
18. Nakamoto, K., *Infrared Spectra of Inorganic and Coordination Compounds*, New York: Wiley, 1963.
19. Pulya, A.V., Seifullina, I.I., Skorokhod, L.S., Vlasenko, V.G., Trigub, A.L., Zubavichus, Y.V., and Levchenkov, S.I., *Russ. J. Gen. Chem.*, 2017, vol. 87, no. 1, p. 86.
<https://doi.org/10.1134/S1070363217010145>
20. Pulya, A.V., Seifullina, I.I., Skorokhod, L.S., Vlasenko, V.G., Trigub, A.L., and Levchenkov, S.I., *Russ. J. Gen. Chem.*, 2018, vol. 88, no. 7, p. 1451.
<https://doi.org/10.1134/S1070363218070162>
21. Geary, W.I., *Coord. Chem. Rev.*, 1971, vol. 7, p. 81.
[https://doi.org/10.1016/S0010-8545\(00\)80009-0](https://doi.org/10.1016/S0010-8545(00)80009-0)
22. Rakitin, Yu.V. and Kalinnikov, V.T., *Sovremennaya magnetokhimiya* (Modern Magnetochemistry), St. Petersburg: Nauka, 1994.
23. Chernyshov, A.A., Veligzhanin, A.A., and Zubavichus, Ya.V., *Nucl. Instr. Meth. Phys. Res. (A)*, 2009, vol. 603, p. 95.
<https://doi.org/10.1016/j.nima.2008.12.167>
24. Newville, M., *J. Synchrotron Rad.*, 2001, vol. 8, p. 96.
<https://doi.org/10.1107/S0909049500016290>
25. Zabinski, S.I., Rehr, J.J., Ankudinov, A., and Alber, R.C., *Phys. Rev.*, 1995, vol. 52, p. 2995.
<https://doi.org/10.1103/PhysRevB.52.2995>
26. Cheng, F.W., *Microchem. J.*, 1959, vol. 24, no. 6, p. 989.
[https://doi.org/10.1016/0026-265x\(59\)90085-02](https://doi.org/10.1016/0026-265x(59)90085-02)