ISSN 1070-3632, Russian Journal of General Chemistry, 2009, Vol. 79, No. 3, pp. 482–487. © Pleiades Publishing, Ltd., 2009.
Original Russian Text © E.V. Rumyantsev, I.E. Kolpakov, Yu.S. Marfin, E.V. Antina, 2009, published in Zhurnal Obshchei Khimii, 2009, Vol. 79, No. 3, pp. 493–497.

# Coordination Interactions of Alkyl-Substituted 2,2'-Dipyrrolylmethene Derivatives with Copper(II) Aminoacid Complexes

**E. V. Rumyantsev[a], I. E. Kolpakov[a], Yu. S. Marfin[a], and E. V. Antina[b]**

[a] *Ivanovo State Chemical Technological University, pr. Engelsa 7, Ivanovo, 153000 Russia*
*fax: (4932)417995*
*e-mail: evr@isuct.ru*

[b] *Institute of Solution Chemistry, Russian Academy of Sciences, Ivanovo, Russia*

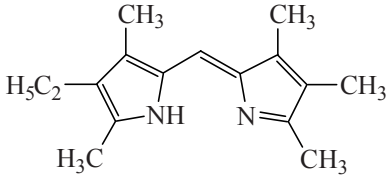
Received September 6, 2008

**Abstract—**Using the method of electron spectroscopy we showed that reaction of alkyl-substituted 2,2'-dipyrrolylmethene derivatives with copper(II) aminoacid complexes led to the formation of heteroligand complexes with two chelated metallocycles forming their coordination sphere. Formation constants of the heteroligand complexes were established and their interrelations with the structure of the aminoacid residue side group were elucidated. It was found that alongside the ability to the primary solvolytic dissociation of aminoacid complex, the main effect on the formation of combined coordination sphere of the chelate is defined by the steric factor depending on the structure of substituent in the aminoacid.

**DOI:** 10.1134/S1070363209030232

An important branch of the modern coordination chemistry is the investigation of features of formation of metallocomplexes containing a metal atom in a heteroligand environment. Such complexes, in particular, are structural models of active centers of metalloenzymes whose basis is mainly constituted by donor atoms of aminoacids and heterocyclic compounds [1, 2]. Varying the nature of ligands involved into the combined coordination sphere provides a fine control over physicochemical properties of the metallocomplex moieties. Therefore attention of researchers is more and more attracted by the heteroligand complexes that combine in one molecule the fragments of compounds of different nature imparting them principally new properties that are not inherent to the respective homoligand analogs.

Unlike the relatively well studied homoligand dipyrrolylmethene complexes [3–5], an information concerning their heteroligand complexes is restricted to the results of the study of coordination interactions of dipyrrole ligands (Hdpm) with several simple cheated Cu(II) and Co(II) salts [6]. It was shown that under the conditions of excess of Cu(II) acetate or acetylacetonate a heteroligand complex formed in the reaction mixture, while an excess of the ligand led to the formation of homoligand complex $[Cu(dpm)_2]$. Therefore at the synthesis of heteroligand complexes [CuL(dpm)] (L = $AcO^-$, $Acac^-$ and $Hfacac^-$) yield is 40% or less [7, 8]. Nevertheless, we found [6] that in the reactions with Cu(II) and Co(II) valinates only the heteroligand complexes [MVal(dpm)] were formed. This obviously is defined by high stability of the macrocyclic system containing aminoacid cheated ligand toward substitution and solvolysis reactions. Thus a possibility appears for predefined synthesis of dipyrrolylmethene heteroligand complexes containing coordinated anion of an aminoacid.




Hdpm

The purpose of this work was the study of the reaction between 3,3',4,5,5'-pentamethyl-4'-ethyl-2,2'-dipyrrolylmethene (Hdpm) and Cu(II) aminoacid complexes with glycine-like structure of the

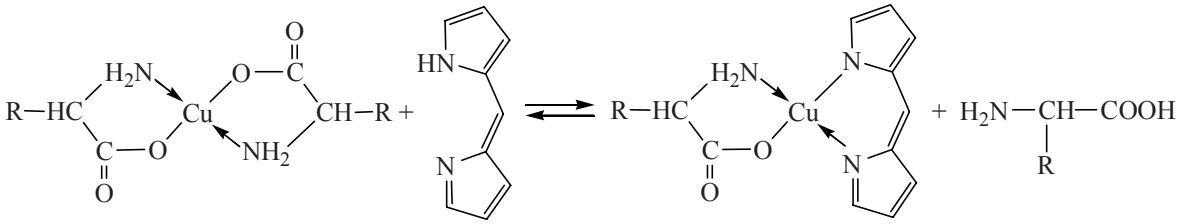
coordination node ([$CuL_2$], L = $Val^-$, $Tre^-$, $Leu^-$, $Asp^-$, $Trp^-$, $Arg^-$, β-$Ala^-$, $Phe^-$, $Lys^-$) in dimethylformamide (DMF).

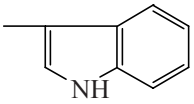
Figures 1–3 show changes in electron absorption spectra of solutions of chelate salts [$CuL_2$] observed on the addition of Hdpm. Increase in Hdpm concentration leads to the appearance and regular increase in the intensity of absorption band in the region of 497–499 nm with simultaneous a growing intensity of the band of the parent Hdpm (438 nm).

The curves of spectrophotometric titration (Fig. 4) reflect the growth of optical density of the formed coordination compound due to uniform increase in concentration of the chromophor ligand in the system. In the point of equivalence that corresponds to the concentration ratio [Hdpm]/[$CuL_2$] = 1.0 occurs a sharp bend on the titration curve followed by the region where the curve is practically parallel to the horizontal axis, the zone of saturation. Thus, the results obtained confirm the substitution of one aminoacid anion in the parent chelate complex $CuL_2$ by the $dpm^-$ anion with the formation of the respective heteroligand complexes [CuL(dpm)] according to the following scheme (for simplicity the substituents in Hdpm are omitted) (Scheme 1).

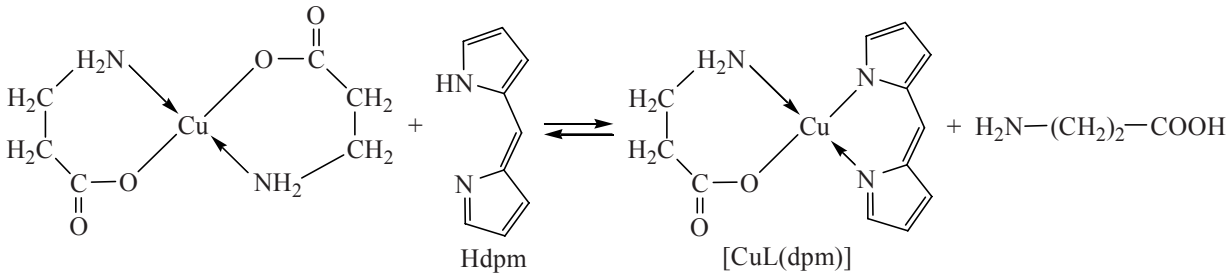
For the reaction with Cu(II) β-alaninate (Scheme 2).

**Scheme 1.**




$Cu(Val)_2$: R = $CH(CH_3)_2$; $Cu(Leu)_2$: R = $CH_2CH(CH_3)_2$; $Cu(Tre)_2$: R = $CH(CH_3)(OH)$; $Cu(Lys)_2$: R = $(CH_2)_3NH_2$; $Cu(Arg)_2$: R = $(CH_2)_3NHC(NH)(NH_2)$; $Cu(Asp)_2$: R = $CH_2COOH$; $Cu(Phe)_2$: R = $CH_2C_6H_5$; $Cu(Trp)_2$: R =  .

**Scheme 2.**




Comparison of the obtained electron spectra with the data published for the homoligand complex [$Cu(dpm)_2$] ($\lambda_{max}$ = 460, 512 nm [9]) shows a significant (13–15 nm) hypsochromic shift of the maximum of the strong band in the spectra of the heteroligand complexes [CuL(dpm)] as compared with the homoligand ones. The hypsochromic shift of the absorbtion maximum in going from [$Cu(dpm)_2$] to [CuL(dpm)] indicates the lower polarization of the π-electron system of the dipyrrole ligand by the Cu(II) atom when the latter is in a heteroligand environment. This obviously is a result of a decrease in the residual positive charge on the $Cu^{2+}$ owing to the effective electron transfer via M–O bonds between the cation and aminoacid anion.

It should be noted that [Cu(Phe)(dpm)] complex unlike the other ones possesses a strong charge transfer band in the region of 402 nm (Fig. 3). From the data [10] follows that enhanced stability of $Cu(Phe)_2$ as

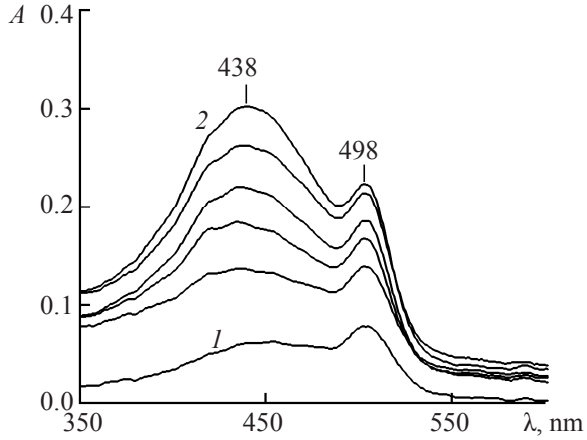



**Fig. 1.** Variations in electron absorption spectra of solutions at the titration of $Cu(Val)_2$ with Hdpm solution: [HL]/[$Cu(Val)_2$] = (*1*) 0.5 and (*2*) 2.5.

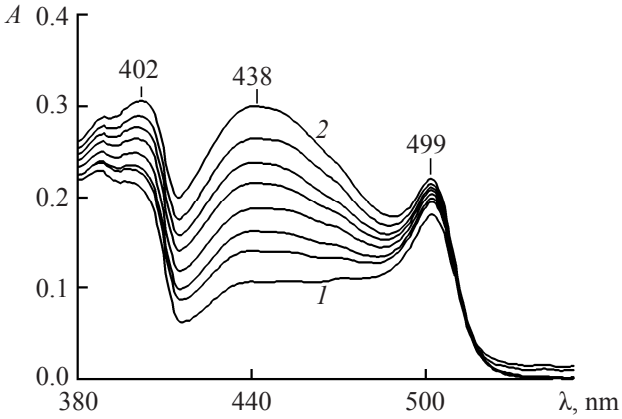



**Fig. 2.** Variations in electron absorption spectra of solutions at the titration of $Cu(Phe)_2$ with Hdpm solution: [HL]/[$Cu(Phe)_2$] = (*1*) 0.73 and (*2*) 2.91.

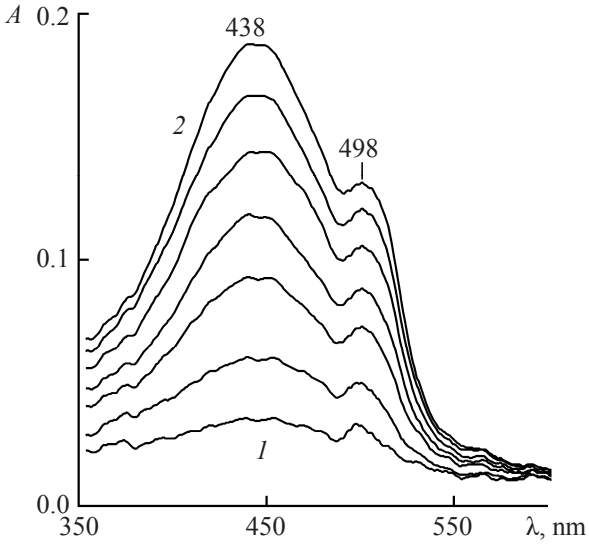



**Fig. 3.** Variations in electron absorption spectra of solutions at the titration of $Cu(Trp)_2$ with Hdpm solution: [HL]/[$Cu(Trp)_2$] = (*1*) 0.16 and (*2*) 3.00.

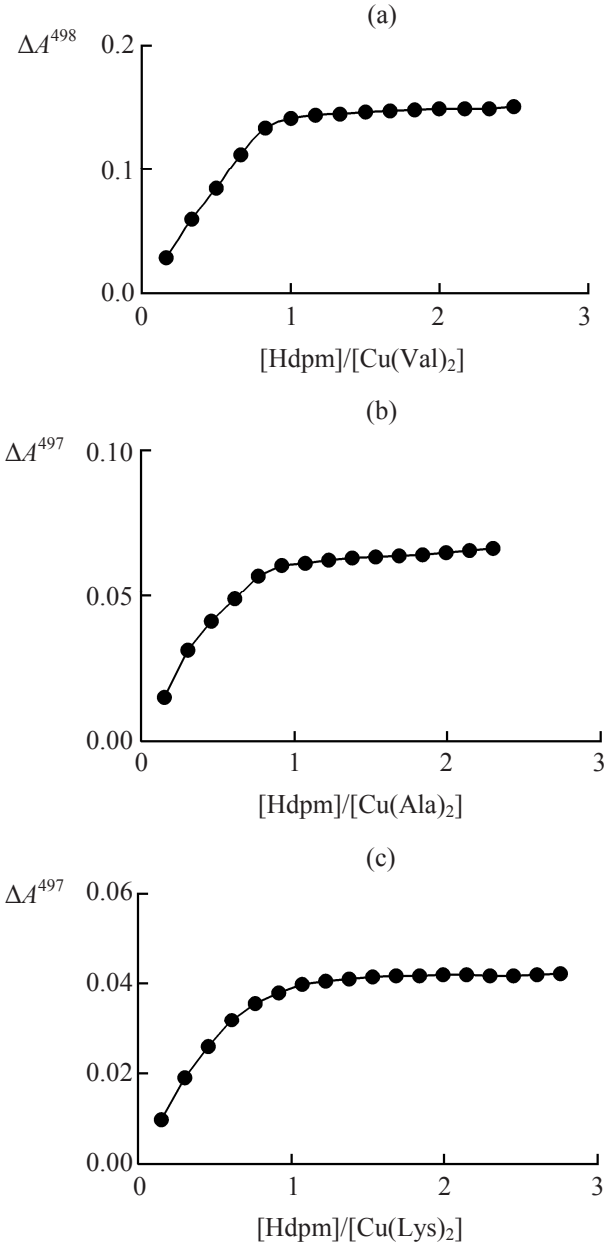


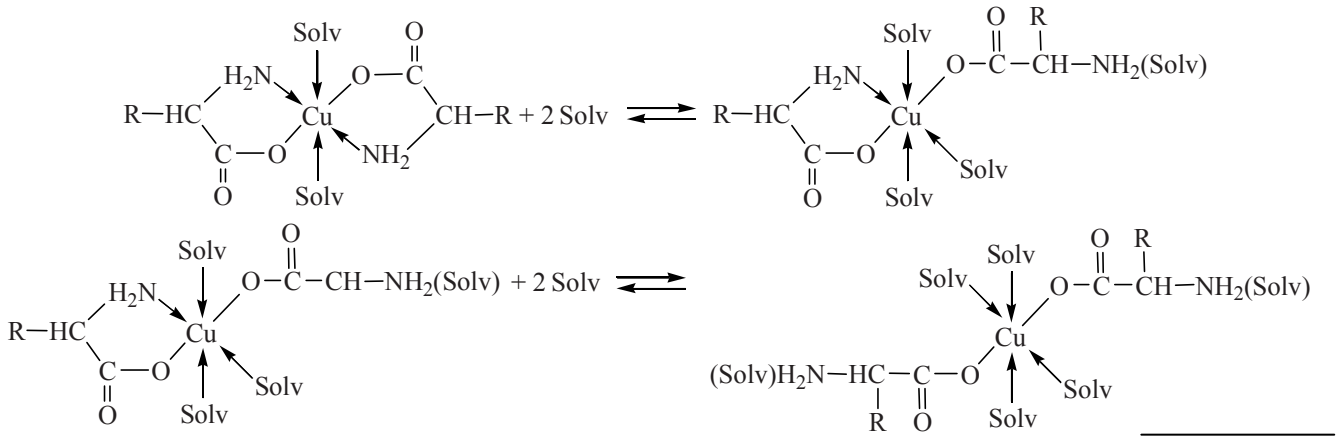

**Fig. 4.** Curves of spectrophotometric titration for systems: (a) $Cu(Val)_2$–Hdpm–DMF, (b) $Cu(\beta\text{-}Ala)_2$–Hdpm–DMF, and (c) $Cu(Lys)_2$–Hdpm– DMF.

compared with the complexes formed by aliphatic aminoacids is due to an additional interaction (back coordination) of $Cu^{2+}$ ion with the π-electron system of the phenyl group of the $Phe^-$ anion that possesses a negative inductive effect. This leads to enhanced coordination interactions of the aminoacid ligand with the central ion and to increased residual positive charge on the latter that promotes more effective transfer of electron density from the orbitals of dipyrrole ligand ($dpm^-$) on the orbitals of $Cu^{2+}$.

From the data of electron absorption spectra of the studied systems in the region of the ratio [Hdpm]/[$CuL_2$] > 1.0 we elucidated the apparent molar extinction coefficients and the constants of complex formation for the complexes [CuL(dpm)] (see the table). The formation constants are calculated along the equation:

$$K = \frac{[\mathrm{CuL(dpm)}][\mathrm{HL}]}{[\mathrm{CuL(dpm)}]^2} = \frac{[\mathrm{CuL_2}][\mathrm{Hdpm}]}{\{c^0_{\mathrm{CuL2}} - [\mathrm{CuL(dpm)}]\}[\mathrm{Hdpm}]},$$

where [CuL(dpm)] and [Hdpm] are equilibrium concentrations of the heteroligand complex and ligand (mol $l^{-1}$) obtained directly from the spectra, $c^0_{\mathrm{CuL2}}$ is the initial concentration of aminoacid complex (mol $l^{-1}$). The numerical K values for all the studied systems are practically independent of the concentration of the parent aminoacid complex. Actually, from the analysis of the data on solubility, solvation and chelate macrocyclic interaction of the aminoacid complexes of Cu(II) with tertaphenylporphyn [11, 12] follows that in the electron-donor solvents the following solvolysis reactions of [$CuL_2$] are possible:




Owing to the low ability of electron-donor solvents, DMF in particular, to solvation of anions (including $COO^-$ group) [13], the solvolysis of [$CuL_2$] complexes affects only the donor–acceptors Cu←N bonds retaining intact the electrical neutrality of the solution. Therefore we may assume that in the studied diluted solutions with [$CuL_2$] concentration below $1\times10^{-5}$ mol $l^{-1}$ the averaged log $K$ (see the table) are standard thermodynamic values.

The processes of formation of [CuL(dpm)] complexes by substitution of aminoacid ligand in the Cu (II) coordination sphere of aminoacid chelate complexes [$CuL_2$] are characterized by the constants by 8–10 orders of magnitude lower than those found for the substitution by $dpm^-$ of acetate ion in $Cu(AcO)_2$ [6]. Such difference results from the higher stability of aminoacid chelate complexes toward solvolytic and dissociation processes [11]. It is obvious that when the process of substitution should be preceded by thedissociation of the aminoacid complex with a loss of one ligand, then the stability of [$CuL_2$] should correlate with the constants characterizing substitution of the aminoacid ligand leading to the formation of heteroligand complex. Unfortunately, the absence of data on the stability of [$CuL_2$] in DMF currently does not allow the confirmation of the assumed dependence. Comparison of the final and stepwise stability constants of [$CuL_2$] in aqueous solutions does not lead to an unequivocal conclusion because of the difference in stability for the series of aminoacid complexes in water and in organic solvents [12] due to the difference in solvation of hydrophilic parts of the molecules. Nevertheless, the results obtained by us allow to state

Absorption maxima ($\lambda_{max}$, nm) and constants of formation (log $K^0$) of complexes [CuL(dpm)] in DMF at 298.15 K

| Complex | $\lambda_{max}$, nm | log $K^0$ |
|---|---|---|
| [Cu(Leu)(dpm)] | 498 | 0.52±0.03 |
| [Cu(Val)(dpm)] | 498 | 1.30±0.07 |
| [Cu(Trp)(dpm)] | 498 | 1.54±0.08 |
| [Cu(Asp)(dpm)] | 497 | 2.10±0.10 |
| [Cu(Phe)(dpm)] | 402, 499 | 2.14±0.10 |
| [Cu(Ala)(dpm)] | 497 | 2.32±0.12 |
| [Cu(Lys)(dpm)] | 498 | 2.40±0.14 |
| [Cu(Tre)(dpm)] | 498 | 2.41±0.13 |
| [Cu(Arg)(dpm)] | 498 | 2.46±0.15 |

certain regularities. Thus, the formation constants of heteroligand complexes with the anions $Leu^-$ and $Val^-$ whose side chains are branched alkyl groups, and $Trp^-$ that contain residue of aromatic indole ring are by 0.9–1.6 orders of magnitude less than the corresponding values for the other studied complexes. This is caused most probably by steric hindrances that restrict substitution of the aminoacid ligand by dipyrrole one. In the case of $Cu(Trp)_2$ the substitution reaction is hindered by stacking effect at the interaction of indole rings in the complex [14, 15]. Other aminoacid complexes enter easier into the substitution reactions. The highest value of log $K^0$ characterizes the reaction with $Cu(Arg)_2$ whose primary dissociation is promoted by strong interaction between acidic guanidine fragment of arginine with electron-donor DMF molecules [16].

Thus, we studied features of formation of nine copper(II) heteroligand complexes containing coordinated anions of an aminoacid and of alkyl-substituted 2,2'-dipyrrolylmethene in DMF. The obtained data on the electron absorption spectra and formation constants, and the revealed regularities allow to optimize conditions for the synthesis of the heterologand [CuL(dpm)] complexes and contribute to theoretical knowledge necessary for the creation of new coenzyme preparations, biocatalysts and drugs on the basis of oligopyrrole heteroligand complexes.

## EXPERIMENTAL

**3,3',5,5'-Tetramethyl-4,4'-diethyl-2,2'-dipyrrolylmethene** is synthesized and purified according to the procedure described in [17].

**Cu(II) aminoacid complexes** were synthesized and characterized by the data of elemental analysis, electronic and IR spectroscopy in keeping with procedures described in [18, 19]. Solid samples prior to the spectrophotometric investigations were ground and dried to constant weight in a vacuum.

DMF of the quality "extra purity" was dried over molecule sieves 4 Å and distilled under reduced pressure. Content of water in the solvent determined by Fisher method was not higher than 0.02 %.

Study of reactions between the Cu(II) aminoacid complexes and 2,2'-dipyrrolylmethene was carried out with the use of spectrophotometric method. The electron absorption spectra of the solutions of the reaction mixtures were registered in the range 350–800 nm on a SF-103 spectrophotometer (Akvilon, Russia) coupled with a personal computer by means of a program package "Spectr 1.0." For the measurements fused glass cells were used with the absorbing layer thickness 2 and 10 mm placed in a Peltier cell termostated at 298.15 K.

For measuring the composition, equilibrium concentration, and apparent molecular extinction coefficient of the metallocomplex moieties formed in solution a methodology was applied of spectrophotometric titration. The titration curves were obtained by plotting on the ordinate axis the absorption of the formed metallocomplex, minus the absorption of pure ligand at the same wavelength. Concentrations of reagents were varied in the range $10^{-5}$–$10^{-6}$ mol $l^{-1}$.

## REFERENCES


1. *Neorganicheskaya biokhimiya* (Inorganic Biochemistry), Eichgor, G., Ed., Moscow: Mir, 1979, vol. 1.
2. *Biologicheskie aspekty koordinatsionnoi khimii* (Biological Aspects of Coordination Chemistry), Yatsimirskii, K.B., Ed., Kiev: Naukova Dumka, 1979.
3. Murakami, Y., Matsuda, Y., and Sakata, K., *Inorganic Chemistry*, 1971, vol. 10, no. 8, p. 1728.
4. Wood, T.E. and Thompson, A., *Chem. Rev*., 2007, vol. 107, p. 1831.
5. Guseva, G.B., Antina, E.V., Berezin, M.B., and V'yugin, A.I., *Zh. Obshch. Khim*., 2004, vol. 74, no. 8, p. 1383.
6. Guseva, G.B., Antina, E.V., V'yugin, A.I., Mamardashvili, G.M., and Petrov, V.V., *Koord. Khim*., 2006, vol. 32, no. 2, p. 123.
7. Halper, S.R., Malachowski, M.R., Delaney, H.M., and Cohen, S.M., *Inorg. Chem*., 2004, vol. 43, p. 1242.
8. Hsieh, A.T.T., Rogers, C.A., and West, B.O., *Aust. J. Chem*., 1976, vol. 29, p. 49.
9. Antina, E.V., Rumyantsev, E.V., and Guseva, G.B., Abstracts of Papers, *XXIII Int. Chugaev Conf. on Coordination Chemistry*, Odessa, September 4–7, 2007, p. 68.
10. Van der Helm, D. and Lawson, M.B., *Acta Crystallogr*., 1971, vol. 27, no. 12, p. 2411.
11. Berezin, B.D. and Mamardashvili, G.M., *Koord. Khim*., 2002, vol. 28, no. 11, p. 822.
12. Mamardashvili, G.M. and Berezin, B.D., *Zh. Obshch. Khim*., 2000, vol. 70, no. 8, p. 1387.
13. Gutman, V., *Khimiya koordinatsionnykh soedinenii v nevodnykh rastvorakh* (Chemistry of Coordination Compounds in Non-Aqueous Solutions), Yatsimirskii, K.B., Ed., Moscow: Mir, 1971.
14. Britain, H.G., *Inorg. Chim. Acta*, 1983, vol. 70, no. 1, p. 71.

15. Bolotin, S.N., Bukov, N.N., Volynkin, V.A., and Panyushkin, V.T., *Koordinatsionnaya khimiya prirodnykh aminokislot* (Coordination Chemistry of Natural Amnoacids), Moscow: LKI, 2008.

16. Legler, E.V., Drivol'skaya, E.N., Kazbanov, V.I., Pashkov, G.L., and Kazachenko, A.S., *Zh. Neorg. Khim*., 2001, vol. 46, no. 8, p. 1404.

17. Semeikin, A.S., Syrbu, S.A., Berezin, M.B., and Lyubimova, T.V., *Izvestiya Vuzov, Khimiya i Khim. Tekhnol.,* 2004, vol. 47, no. 4, p. 10.

18. Ablov, A.V., Chapurina, L.F., D'yakon, I.A., and Ivanova, V.Ya., *Zh. Neorg. Khim*., 1966, vol. 11, no. 11, p. 2620.

19. Graddon, D.P. and Munday, L., *J. Inorg. Nucl. Chem*., 1961, vol. 23, nos. 3–4, p. 231.