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Synthesis and Spectral Characteristics of the Combined Ligand Copper Complex with Proline and Corazole

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Abstract—Synthesis of the combined ligand complex of copper(II) prolinate bis(1,5-pentamethylenetetrazole) $[Cu(PMT)_2](Pro)_2$ was carried out. The product is interesting as a biologically active compound. It is obtained by reaction of copper carbonate with proline followed by further reaction with corazole. The composition and structure of the complex were confirmed by elemental analysis and data of UV, IR, and ^1H NMR spectroscopy. The complex was characterized in detail by the method of circular optical dichroism.

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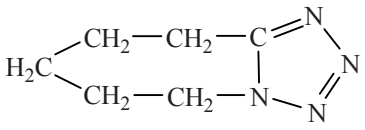
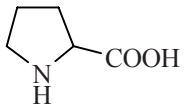
Coordination compounds of transition metals with biologically active ligands are of great interest. As far as transition metals often possess biological activity, a synergetic effect of biological actions of the organic ligand and the complex-forming metal is expectable.

The significance of copper derivatives in biological processes is well known. For the further development in this direction, in this work we prepared a combined ligand complex, copper(II) prolinate bis(1,5-pentamethylenetetrazole) $[Cu(PMT)_2](Pro)_2$, where PMT is corazole and Pro is prolinate anion.



Corazole
(PMT, 1,5-pentanethylenetetrazole)
I



Proline (ProH)
II

Corazole (**I**) has been widely applied in practical medicine and traumatology for treatment of a series of heavy diseases and traumas complicated by development of shock, weakening of cardiac and respiratory activity and at acute poisoning with soporifics and drugs of excitation effect on the respiratory and vasomotor centers of the brain [1].

Proline belongs to coded nonessential aminoacids and is a component of practically all proteins.

As far as both these ligand (**I** and **II**) possess a biological activity, it is presumable that the complexes obtained with them also will display biological activity. In this connection it seemed interesting to synthesize such complexes and to study their composition and structure.

Synthesis of the complex $[Cu(PMT)_2](Pro)_2$ was carried out in two steps according to the following scheme:

$$CuCO_3 + 2ProH \rightarrow Cu(Pro)_2 + CO_2\uparrow + H_2O,$$

$$Cu(Pro)_2 + 2PMT \rightarrow [Cu(PMT)_2](Pro)_2.$$

Initially a chelate complex copper prolinate was obtained by reaction of copper carbonate with proline. The reaction completion was indicated by end of carbon dioxide evolution. Then to the solution of copper prolinate corazole **I** was added in an equivalent amount. The target complex precipitated from the solution. The complex was purified by recrystallization from isopropyl alcohol.

The composition and the structure of the complex were proved by the data of elemental analysis, IR, UV, and ^1H NMR spectroscopy, and by the method of circular dichroism. The data of elemental analysis showed the agreement of elemental composition to the assumed formula. The data of IR spectroscopy confirm assumed composition of the compound and contain all characteristic absorption bands. Stretching and stretching–bending vibrations of the tetrazole ring appear at

1100–800 cm^{-1}; stretching and stretching–bending vibrations of methylene groups are at 1925 (ν_{as}), 2860 (ν_s) and 1470 (scissoring) cm^{-1}; vibration bands of amino group are observed at 3400–3000 (ν_s) and 1560 cm^{-1}; stretching vibrations of carboxy group give rise to a band at ~1600 cm^{-1}; bands of coordinated water appear at 3550–3200 (ν_s and ν_{as}) and 1640–1600 (δ_{as}) cm^{-1} [2].

The shift of absorption band of carboxy group in the studied complex to lower frequency compared to the proline copper salt (from 1612 to 1593 cm^{-1}) indicates that proline coordinates at the oxygen atom that is well consistent with the published data [3].

The insignificant change in intensity and the absence of shifts in the position of absorption bands characteristic of stretching–bending vibrations of the tetrazole ring (~1100 cm^{-1}) points to weak coordination of pentamethylenetetrazole with the central ion.

In the ^1H NMR spectrum appear signals of all protons of 1,5-pentamethylenetetrazole [δ, ppm: 4.5 (CH_2–N^1); 3.0 (CH_2–C^5); 1.87, 1.75. 1.65 (–CH_2–CH_2–CH_2–)] and proline [δ, ppm: 3.55 (CH); 3.0 2.30 (NH+CH_2); 1.64, 1.75 [(–CH_2–CH_2–), overlapping with the signals of three methylene groups of corazole]. Small upfield shift of the signals of two methylene groups protons [4.50 (CH_2–N^1), 3.0 (CH_2–C^5)] relatively to free ligand [4.51 (CH_2–N^1). 3.60 (CH_2–C^5)] suggests that the most probable point of coordination is N^4 atom of the tetrazole ring.

Proline is a chiral ligand, therefore the study of chirooptocal characteristics of the obtained complex is the most informative.

The curcular dichroism (CD) spectra of solutions of the complex [$CuPMT_2$ $(Pro)_2$] in water and in ethanol in the region of 50–12.5 kK (200–800 nm, 1 kK = 1000 cm^{-1}) are shown in Fig. 1. The spectra contain two broad absorption bands without a well defined structure. (The complex [$Cu(Pro)_2PMT_2$] is well soluble in water and less soluble in ethanol). The long-wave band characteristic of many copper(II) complexes defining the saturated blue color of this compound has maximum in the region of 16.7 kK (600 nm), half-width at half-height about 5000 cm^{-1} and ε ~100 $M^{-1}cm^{-1}$. The absorption band in UV region has maximum at 40 kK (250 nm), half-width about 8000 cm^{-1} and moderate intensity (ε ~ 6000 M^{-1} cm^{-1}). Both bands are asymmetrical ones and cannot be described

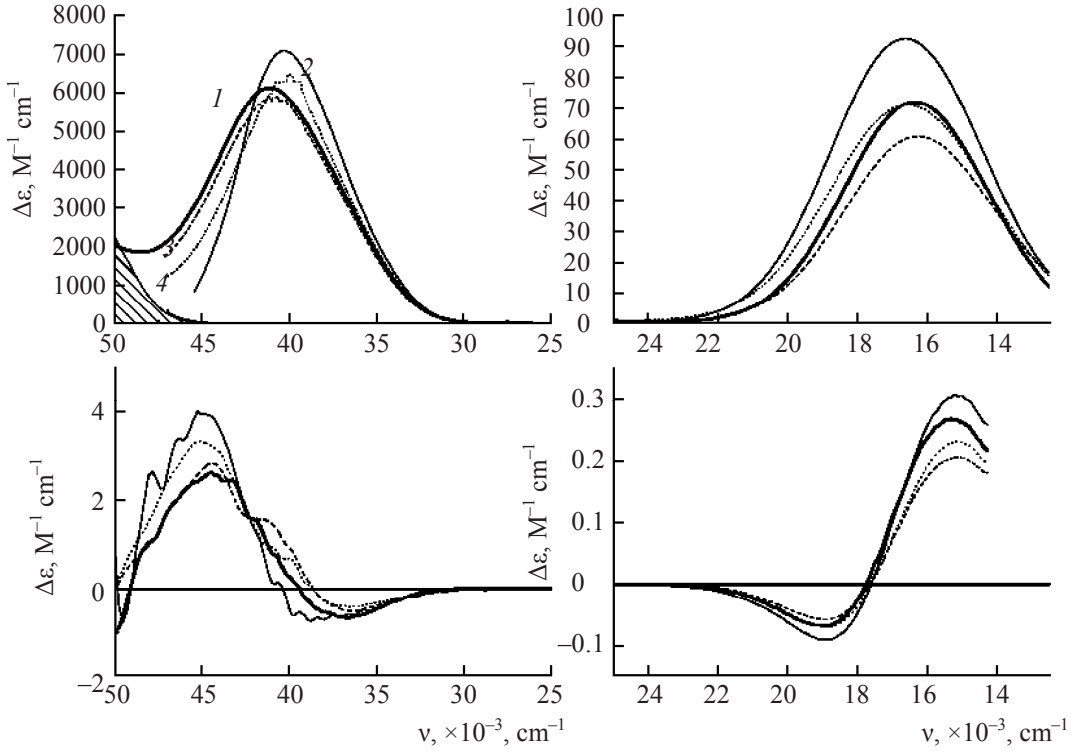


Fig. 1. Absorption spectra (top) and circular dichroism spectra (bottom) of solutions of the complex [$Cu(Pro)_2PMT_2$] (*1*) in water and (*2*) ethanol. Dashed lines depict the spectra of solutions of [$Cu(Pro)_2$] under the same conditions [(*3*) water and (*4*) ethanol]. Hatched area is the absorption spectrum of pentamethyleneterazole in water.

by canonical spectral profiles. The complex multicomponent nature of the absorption bands is clearly revealed in the circular dichroism (CD) spectra of the complex. In the CD spectra to the both absorption bands correspond pairs of the bands of optical activity with opposite signs. The band in the visible region has a longwave component with a positive sign of CD. The positive and negative CD maxima in visible region are located at 19 and 15 kK respectively, the point of compensation of optical activity is at 17.7 kK. In the UV region the CD maxima are at 36 kK (negative) and 44 kK (positive). In both pairs the maximum of positive CD is approximately 3.5-fold more intensive than negative. In going from ethanol to water solution both bands diminish in intensity and absorption maximum in visible region is shifted to longwave region from 16.6 kK to 16.4 kK (formally a bathochromic shift) while the maximum of absorption band in UV region, to shortwave region from 40.3 to 41.1 kK (formally, hypsochromic shift). Both components of UV band in the CD spectrum also are shifted to shortwave region. The behavior of CD bands in the visible region is rather complicated: at increase in the solvent polarity the CD maximum is shifted to the direction opposite to the shift of the absorption band. By this reason the shift is defined by redistribution of oscillator power and rotation power of the components contributing to the band rather than by purely polarization effects (Fig. 1).

Thus the shape of bands in absorption spectra of the complex $[CuPMT_2\ (Pro)_2]$ is typical of copper (II) complexes with α-*L*-aminoacids [3]. The CD spectra are close by the shape to the spectra of $[Cu(Pro)_2]$ solutions which are depicted for comparison by dashed lines in Fig. 1. The longwave band is defined by copper *d*–*d* transitions and is a superposition of 2–4 separate transitions. The observed position of this band is characteristic of tetragonal–screwed octahedral environment of the copper atom. The actual number of observed transitions in aqueous solutions is even larger due to dissociation, the acid–base equilibrium, and the presence of many charged forms. The presence of optically active ligands induces in *d*–*d* transitions the optical activity of different signs. The positive longwave component in CD spectrum of $[Cu(Pro)_2PMT_2]$ is much stronger than negative one as is characteristic just of the copper complexes with L-proline: in the majority of the other copper(II) complexes with L-aminoacids the negative component is much stronger then positive one. The band in the spectra of $[Cu(Pro)_2PMT_2]$ and $[Cu(Pro)_2]$ in UV region is due to the electronic transitions in the proline ligands. The broadening of this band and appearance of two bands of opposite signs in the CD spectrum instead of one in the spectrum of *L*-proline (at ~50 kK) is induced by strong exciton splitting due to interaction of two proline ligands. On the whole, it can be concluded that the coordination with PMT in $[Cu(Pro)_2PMT_2]$ complexes insignificantly affected the optical spectra as compared with the parent copper(II) diprolinate: small but not uniform increase in absorption and CD of all bands and decrease in their width. New bands in the spectra of $[Cu(Pro)_2PMT_2]$ did not appear that most probably was due to the absence of low energy electron transitions in the PMT ligand (a part of PMT absorption spectrum is shown in Fig. 1 by the hatched region). Effect of PMT coordination on the position of bands is very small, much weaker than the solvent effect. Thus, we can conclude that the coordination with PMT exerts little effect on the electron levels of copper as compared with the effect of two homochiral proline stereogenic ligands, and most likely the PMT ligands occupy in $[Cu(Pro)_2PMT_2]$ remote axial positions (Fig. 2).

The most probable geometry of $[Cu(Pro)_2PMT_2]$ complex in aqueous and ethanol solutions is tetragonal bipyramid (an octahedron screwed due to Jahn–Teller effect) whose plane is formed by two strongly bound (N,O)-coordinated proline ligands. The complex undergoes a fast enough isomerization, but predominantly has *trans*-N,N-arrangement (this arrangement

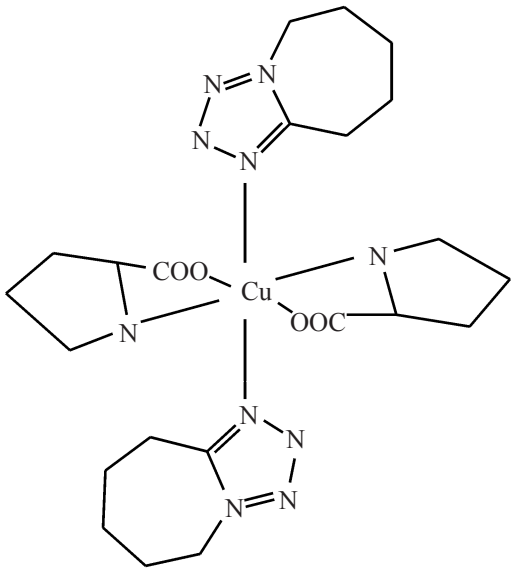


Fig. 2. Possible structure of combined ligand copper(II) complex $[Cu(Pro)_2PMT_2]$.

is preferable for the bis-aminoacid complexes with the same chirality of the stereogenic center). Two axial positions are occupied by tetrazole ligands. In aqueous solutions of $[Cu(Pro)_2]$ these position for the most time are occupied by water molecules. In such geometry only two of four potential *d*-transitions are allowed, and just for them should be observed optical activity of opposite signs. Effect of axial ligands on the optical spectra is much less significant than of chelate equatorial ones, in agreement with the observed picture. The decrease in the width and the increase in the intensity of bands in the spectra of $[Cu(Pro)_2PMT_2]$ can be assigned to the decrease in mobility and isomerization of proline ligands. Also, a possibility of equilibrium exchange PMT–water existing in 96% ethanol solutions should not be excluded.

EXPERIMENTAL

Synthesis of copper(II) bis(1,5-pentamethylenetetrazole) prolinate. Freshly prepared copper carbonate (0.42 g) was poured over with 20 ml of distilled water. To the obtaned suspension was poured at stirring an aqueous solution of proline (0.78 g). The reaction end was indicated by the ceased CO_2 evolution. To the obtained solution of copper prolinate was added a calculated amount of pentamethylenetetrazole (0.49 g). In this work we used commercial pentamethylenetetrazole from ACROS ORGANICS of 98% purity with mp 58.5°C. The reaction mixture was heated for 2 h at 60°C and then cooled to 17°C, the precipitate was filtered off, washed with ethyl acetate (20 ml), and recrystallized from isopropyl alcohol. Yield 52%. The IR spectrum, cm^{-1}: 1100–800 (Tz), 1925 (ν_{as} CH_2); 2860 (ν_s CH_2); 1470 (scissoring CH_2), 3259.5 (ν_s NH); 1593.1 (COO^-). The ^1H NMR spectrum (DMSO-d_6), δ, ppm: 4.5 (CH_2–N^1); 3.55 (CH); 3.0 (CH_2–C^5); 2.30 (NH+CH_2); 1.87, 1.75, 1.65 (–CH_2–CH_2–CH_2–). Found, %: C 46.42; H 5.61; N 24.67. $C_{22}H_{34}CuN_{10}O_4$. Calculated, %: C 46.50; H 6.40; N 24.66.

The IR spectra of crystalline substances were registered from films or suspensions in mineral or fluorinated oil placed on KBr tablets on Perkin-Elmer M-457 and UR-20 spectrophotometers and on IFS-113V instrument at analytical concentration 10^{-1}–10^{-2} mol l^{-1}. The ^1H NMR spectra were registered on a Bruker AC instrument with operating frequency 400 MHz. The spectra of isotropic absorption in UV and visible regions were obtained on a double-beam scanning spectrophotometer Specord-M40 (Karl Zeiss, Germany). Rectangular quartz cells were used with the optical route length 0.5 cm.

The spectra of circular dichroism were registered on a dichrograph Mark–V (Jobin–Yvon, France). The measurements were carried out using cylindrical quartz cells with the optical route length 1 cm (400–700 nm) and 0.1 cm (200–400 nm) from the solutions of three different concentrations. The instrument was calibrated with reference aqueous solutions of (+)10-D-camphorsulfonic acid (1 mg ml^{-1}) at 190 and 290 nm [4].

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