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*To blessed memory of S.V. Larionov, famous scientist in the area of coordination chemistry*

# Complexes of Zn(II) and Cu(II) with the Amino Derivatives of Deoxycholic Acid: Syntheses, Structures, and Properties

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**Abstract**—Complexes $[Zn(L)Cl_2]$ (**I**), $Cu(L)Cl_2 \cdot H_2O$ (**II**), $Zn(L^1)Cl_2 \cdot 0.5H_2O$ (**III**), and $Cu(L^1)Cl_2 \cdot 0.5H_2O$ (**IV**) (where L and $L^1$ are the diaminopropylene and diaminoethylene derivatives of deoxycholic acid, respectively) are synthesized. The structure of mononuclear complex **I** is determined by X-ray structure analysis (CIF file CCDC no. 1875305). The coordination polyhedron of the Zn atom ($Cl_2N_2$) is a distorted tetrahedron. According to the X-ray diffraction data, the crystals of compounds **III** and **IV** are isostructural. It is shown by IR spectroscopy that the structures of complexes **II–IV** are similar to that of complex **I**. In the solid phase, compounds L and $L^1$ possess photoluminescence in the visible spectral range ($\lambda_{max}$ = 440 and 415 nm, respectively). Complex formation with $Zn^{2+}$ ions does not change the photoluminescence properties of L and $L^1$.

*Keywords:* deoxycholic acid, complexes, zinc, copper, synthesis, crystal structure
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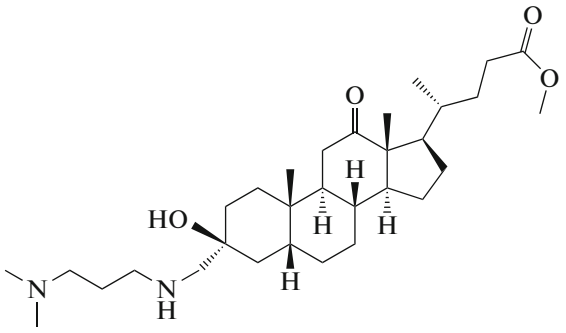
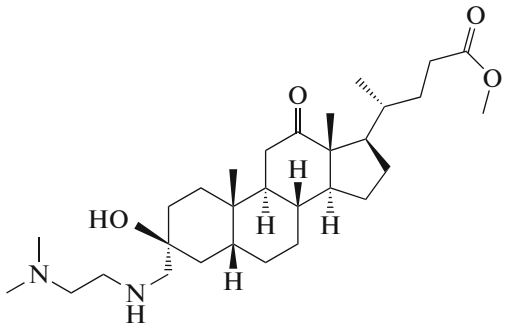
## INTRODUCTION

The study of the complex formation of metal ions with organic compounds based on substances of the plant and animal origin is among urgent trends of coordination and bioinorganic chemistry [1, 2]. In the recent decade, attention of researchers was focused on bile acids and products of their modification with antiproliferative, antitumor, antimicrobial, and biological activity of other types [3–6]. Bile acids being metabolites of the steroid series contain hydroxyl and carboxyl groups and can act as ligands to form metal complexes capable of manifesting valuable physicochemical and biological properties [7, 8]. For example, the Sn(IV) and Pt(II) complexes with the bile acid derivatives are characterized by antifungal and antitumor activity [9–11]. The introduction of additional functional groups into various positions of the steroid framework makes it possible to significantly extend the range of new substances: derivatives of bile acids, in particular, promising ligands for the preparation of coordination compounds with diverse structures. The synthesis of the deoxycholic acid derivatives containing the amino groups (aliphatic and cyclic) in the C(3) position was described [12], and the cytotoxic properties of these new compounds were studied. The results of the studies showed that some amino derivatives demonstrated an improved antiproliferative activity compared to that of the initial deoxycholic acid. The study of the possibility of complex formation with these derivatives of deoxycholic acid will enable one to obtain a new group of complexes with promising properties.

The purpose of this work is the synthesis of the Zn(II) and Cu(II) complexes with the amino derivatives of deoxycholic acid, namely, methyl 3β-hydroxy-3α-((3-(dimethylamino)propylamino)methyl)-12-oxo-5β-cholan-24-oate (L) and methyl 3β-hydroxy-3α-((2-(dimethylamino)ethylamino)methyl)-12-oxo-5β-cholan-24-oate ($L^1$), and the study of their structures and properties. The choice of the metals is due to the participation of these metal ions in physiological processes of living organisms. The Zn(II) complexes can exhibit luminescence properties, which makes them promising as fluorescent chemosensors.



(L)



($L^1$)

## EXPERIMENTAL

Reagents L and $L^1$ were synthesized using a known procedure [12]. Reagents $ZnCl_2$, $CuCl_2 \cdot 2H_2O$, *iso*-PrOH (analytical grade), and EtOH (rectificate) were used for the synthesis of the complexes.

**Synthesis of $[Zn(L)Cl_2]$ (I)**. A solution of $ZnCl_2$ (0.014 g, 0.1 mmol) in EtOH (1 mL) was gradually added with stirring to a solution of L (0.052 g, 0.1 mmol) in EtOH (4 mL). The resulting solution was stirred, and the solvent was evaporated to a possibly minimum volume (~1–2 mL). A white precipitate was filtered off with suction on a porous glass filter, washed with cooled *iso*-PrOH, and dried in a vacuum desiccator. The yield was 0.046 g (70%).

For $C_{31}H_{54}N_2O_4Cl_2Zn$

| | | | |
|---|---|---|---|
| Anal. calcd., % | C, 56.8 | H, 8.3 | N, 4.3 |
| Found, % | C, 57.1 | H, 8.0 | N, 4.1 |

**Synthesis of $[Cu(L)Cl_2] \cdot H_2O$ (II)**. A solution of $CuCl_2 \cdot 2H_2O$ (0.034 g, 0.2 mmol) in EtOH (3 mL) was gradually added with stirring to a solution of L (0.052 g, 0.1 mmol) in EtOH (4 mL). The resulting solution was stirred, and the solvent was evaporated to a possibly minimum volume (~1–2 mL). A blue precipitate was filtered off with suction on a porous glass filter, washed with cooled *iso*-PrOH, and dried in a vacuum desiccator. The yield was 0.030 g (45%).

For $C_{31}H_{56}N_2O_5Cl_2Cu$

| | | | |
|---|---|---|---|
| Anal. calcd., % | C, 55.5 | H, 8.4 | N, 4.2 |
| Found, % | C, 55.4 | H, 8.2 | N, 4.2 |

**Synthesis of $[Zn(L^1)Cl_2] \cdot 0.5H_2O$ (III)**. A solution of $ZnCl_2$ (0.014 g, 0.1 mmol) in EtOH (2 mL) was gradually added with stirring to a solution of $L^1$ (0.050 g, 0.1 mmol) in EtOH (2 mL). The resulting solution was stirred, and the solvent was evaporated to a possibly minimum volume (~1–2 mL). A white precipitate was filtered off with suction on a porous glass filter, washed with cooled *iso*-PrOH, and dried in a vacuum desiccator. The yield was 0.050 g (77%).

For $C_{30}H_{52}N_2O_4Cl_2Zn$

| | | | |
|---|---|---|---|
| Anal. calcd., % | C, 55.4 | H, 8.1 | N, 4.2 |
| Found, % | C, 55.6 | H, 8.1 | N, 4.2 |

**Synthesis of $[Cu(L^1)Cl_2] \cdot 0.5H_2O$ (IV)**. A solution of $CuCl_2 \cdot 2H_2O$ (0.034 g, 0.2 mmol) in *iso*-PrOH (2 mL) was gradually added with stirring to a solution of $L^1$ (0.050 g, 0.1 mmol) in an *iso*-PrOH–EtOH (1 : 1 vol/vol) mixture (4 mL). The resulting solution was stirred, and the solvent was evaporated to a possibly minimum volume (~1–2 mL). A blue precipitate was filtered off with suction on a porous glass filter, washed with cooled *iso*-PrOH, and dried in a vacuum desiccator. The yield was 0.040 g (60%).

For $C_{30}H_{53}N_2O_{4.5}Cl_2Cu$

| | | | |
|---|---|---|---|
| Anal. calcd., % | C, 55.6 | H, 8.2 | N, 4.3 |
| Found, % | C, 55.9 | H, 8.3 | N, 4.3 |

Single crystals of compound **I** suitable for X-ray structure analysis were grown by the slow evaporation of the solution obtained in the course of the synthesis of complex **I**.

Microanalyses to C, H, and N were carried out on a Euro EA 3000 analyzer. IR spectra were recorded in a range of 4000–80 $cm^{-1}$ on Scimitar FTS 2000 and Vertex 80 FT-IR spectrometers. Samples were prepared by pressing with KBr for a range of 4000–400 $cm^{-1}$ and with spectroscopic polyethylene for a range of 500–80 $cm^{-1}$.

**The X-ray diffraction analysis** of polycrystals of compound **I** was carried out on a Shimadzu XRD-7000 diffractometer (Cu$K_\alpha$ radiation, Ni filter, 5°–50° 2θ range, 0.03° 2θ increment, acquisition time 1 s). Samples for analysis were prepared as follows. Polycrystals were triturated in an agate mortar in the presence of heptane, and the obtained suspension was deposited on the polished side of a standard quartz

**Table 1.** Crystallographic characteristics and experimental and structure refinement details for complex **I**

| Parameter | Value |
|---|---|
| *FW* | 655.03 |
| Crystal system | Triclinic |
| Space group | $P\bar{1}$ |
| *a*, Å | 6.5682(7) |
| *b*, Å | 7.3866(7) |
| *c*, Å | 18.728(2) |
| α, deg | 99.495(3) |
| β, deg | 91.224(3) |
| γ, deg | 114.96(1) |
| *V*, Å$^3$ | 808.26(16) |
| *Z*; $\rho_{calcd}$, mg/cm$^3$ | 1; 1.346 |
| μ, mm$^{-1}$ | 0.962 |
| Crystal sizes, mm | 0.22 × 0.13 × 0.06 |
| Scan range over θ, deg | 4.44 –61.56 |
| Number of measured reflections | 15343 |
| Number of independent reflections | 9454 |
| $R_{int}$ | 0.0509 |
| Number of reflections with $I > 2\sigma(I)$ | 6544 |
| Number of refined parameters | 367 |
| GOOF for $F^2$ | 0.921 |
| *R* factor ($I > 2\sigma(I)$) | $R_1 = 0.0526$, $wR_2 = 0.0729$ |
| *R* factor (for all $I_{hkl}$) | $R_1 = 0.0955$, $wR_2 = 0.0849$ |
| Residual electron density (max/min) e/Å$^3$ | 0.60/–0.69 |
| Absolute structure parameter | 0.046(8) |

cell. After heptane was dried, the sample represented a thin smooth layer (thickness ~100 μm). The diffraction patterns were identified by the data of the single-crystal study.

**X-ray structure analysis.** The unit cell parameters and reflection intensities for single crystals of complex **I** were measured at low temperature (150 K) on a Bruker X8 Apex CCD automated diffractometer equipped with a two-coordinate detector using a standard procedure (Mo$K_\alpha$ radiation, λ = 0.71073 Å, graphite monochromator). The crystallographic characteristics and the details of X-ray diffraction experiment and structure refinement of compound **I** are presented in Table 1. The structure was solved by a direct method and refined by full-matrix least squares for $F^2$ in the anisotropic (for non-hydrogen atoms) approximation using the SHELXTL program package [13]. Positions of all hydrogen atoms were determined from the difference Fourier syntheses and included into the refinement in the isotropic approximation. The main interatomic distances and bond angles are presented in Table 2.

The full tables of atomic coordinates, bond lengths, and bond angles were deposited with the Cambridge Crystallographic Data Centre (CIF file CCDC no. 1875305) and are available at deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk/data_request/cif or can be obtained from the authors.

Photoluminescence (PL) and luminescence excitation (LE) spectra were measured on a Fluorolog-3 spectrofluorimeter (Horiba Jobin Yvon) with a 450 W xenon lamp and a double monochromator for absorption and emission. Excitation spectra were recorded in the range from 300 to 500 nm and corrected to the spectral range of the lamp intensity. Emission spectra were recorded in the range from 400 to 700 nm and corrected to the response of the monochromators and detector using the correction spectra presented by the producer. The first and second harmonics of the excitation source were blocked using the filters.

## RESULTS AND DISCUSSION

Complexes **I**–**IV** with the ratio M : L = 1 : 1 were synthesized by the reactions of Zn(II) and Cu(II)

**Table 2.** Selected interatomic distances ($d$, Å) and bond angles (ω, deg) in the structure of complex **I***

| Bond | $d$, Å | Bond | $d$, Å |
|---|---|---|---|
| Zn(1)–N(1) | 2.047(4) | C(3)–C(26) | 1.519(6) |
| Zn(1)–N(2) | 2.057(4) | C(10)–C(19) | 1.548(6) |
| Zn(1)–Cl(1) | 2.202(1) | C(13)–C(18) | 1.542(6) |
| Zn(1)–Cl(2) | 2.268(1) | C(17)–C(20) | 1.531(6) |
| N(1)–C(30) | 1.479(6) | C(20)–C(21) | 1.532(7) |
| N(1)–C(31) | 1.485(6) | C(20)–C(22) | 1.538(6) |
| N(1)–C(29) | 1.496(5) | C(22)–C(23) | 1.540(7) |
| N(2)–C(27) | 1.490(6) | C(23)–C(24) | 1.488(7) |
| N(2)–C(26) | 1.493(6) | C(27)–C(28) | 1.529(6) |
| O(1)–C(3) | 1.436(5) | C(28)–C(29) | 1.526(6) |
| O(2)–C(12) | 1.216(5) | O(3)–C(25) | 1.445(6) |
| O(3)–C(24) | 1.343(6) | O(4)–C(24) | 1.211(6) |
| Angle | ω, deg | Angle | ω, deg |
| N(1)Zn(1)N(2) | 101.0(2) | N(1)Zn(1)Cl(2) | 108.8(1) |
| N(1)Zn(1)Cl(1) | 115.2(1) | N(2)Zn(1)Cl(2) | 103.1(1) |
| N(2)Zn(1)Cl(1) | 110.3(1) | Cl(1)Zn(1)Cl(2) | 116.7(1) |

* The C–C bond lengths in three six-membered cycles vary from 1.507(7) to 1.557(6) Å, and those in the five-membered cycle range from 1.550(6) to 1.567(7) Å.

chlorides with L and $L^1$ in EtOH. The Zn(II) complexes were synthesized at the stoichiometric ratio of the starting reagents, and an excess of the metal salt is required for the synthesis of the Cu(II) complexes.

The crystal structure of complex **I** consists of isolated molecules of the mononuclear complex (Fig. 1). The Zn atom coordinates two N atoms of bidentate-chelate ligand L and also two Cl atoms in the *cis* position. As a result of the coordination of L, the six-membered $ZnN_2C_3$ chelate with the chair conformation undergoes ring closure: the Zn(1) and C(28) atoms deviate from the plane of four other C atoms by –0.786(4) and 0.732(5) Å, respectively. The $ZnCl_2N_2$ polyhedron is a distorted tetrahedron. The $\tau_4$ parameter characterizing the geometry of the coordination polyhedron (coordination number 4) is equal to 0.91 [14]. The values of the Zn–N and Zn–Cl bond lengths and bond angles in complex **I** are comparable with similar values in the Zn(II) complexes with the aliphatic diamine derivatives [15–20]. In a molecule of complex **I**, the steroid fragment consists of fused alicycles (three six-membered (A, B, C) and one five-membered). Three six-membered rings have common edges C(5)–C(10) and C(8)–C(9) (Fig. 1). These cycles exist in the chair conformation: the C(3) and C(10) atoms in A, C(5) and C(8) in B, and C(9) and C(13) in C deviate from the planes of four other C atoms by 0.646(5), –0.656(4), and 0.671(5) and –0.654(5), 0.631(5), and –0.780(5) Å, respectively. Cycles A and B in complex **I** exist in the *cis* conjunction (the hydrogen atom in position 5 has the β configuration). The five-membered alicycle (D) has the common edge C(13)–C(14) with six-membered ring C. The conformation of cycle D is an envelope with the deviation of the C(13) atom from the plane of four other C atoms by –0.651(5) Å.

The projection of the crystal structure of complex **I** onto the (010) plane is presented in Fig. 2. The molecule of complex **I** interacts with the translationally identical molecule by weak C···O contacts (C(31)···O(4") 3.404(7) Å) to form a zigzag chain along the *c* axis. An inflection is observed between two cycles A and B in which the planar fragments are arranged at a dihedral angle of 81.0(2)°. One this chain falls onto the unit cell. The next chain is translationally identical. In addition, the shortest distances between the adjacent molecules are at the level of van der Waals interactions: Cl(2)···O(1) 3.298(4) and Cl(2)···N(2) 3.371(4) Å. The Zn···Zn distances between the chains are 6.5682(7) Å along the *a* axis and 7.3866(7) Å along the *b* axis.

The X-ray diffraction analysis of compound **I** showed the identity of the single crystal and the synthesized polycrystalline phase. The powder sample is single-phase. A comparison of the powder diffraction patterns of complexes **III** and **IV** with the same composition showed the isostructural character of the crystals of these compounds (Fig. 3).

The IR spectra of compounds L and $L^1$ and complexes **I**–**IV** contain the bands corresponding to the ν(OH), ν(NH), and ν(C=O) vibrations (Table 3). As

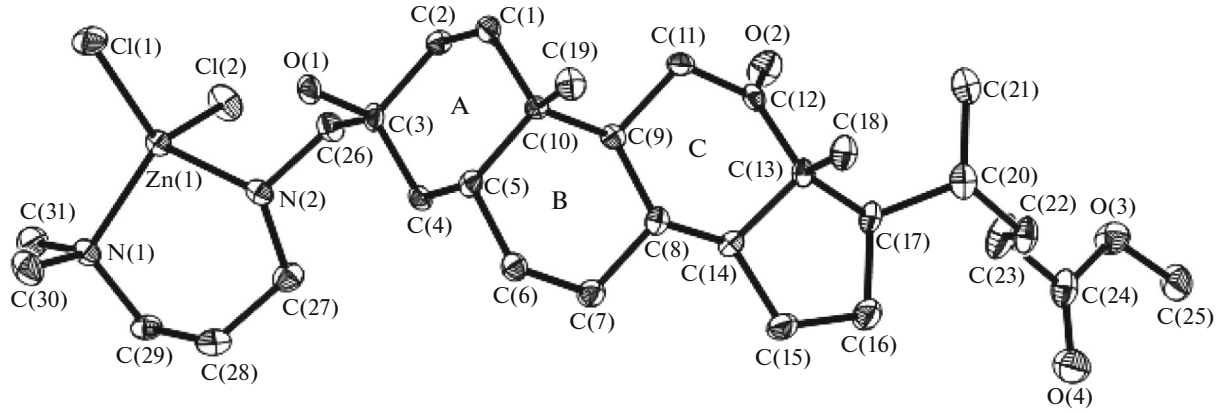



**Fig. 1.** Molecular structure of complex **I** with the enumerated non-hydrogen atoms. Hydrogen atoms are omitted for clarity. Ellipsoids are presented with 50% probability.

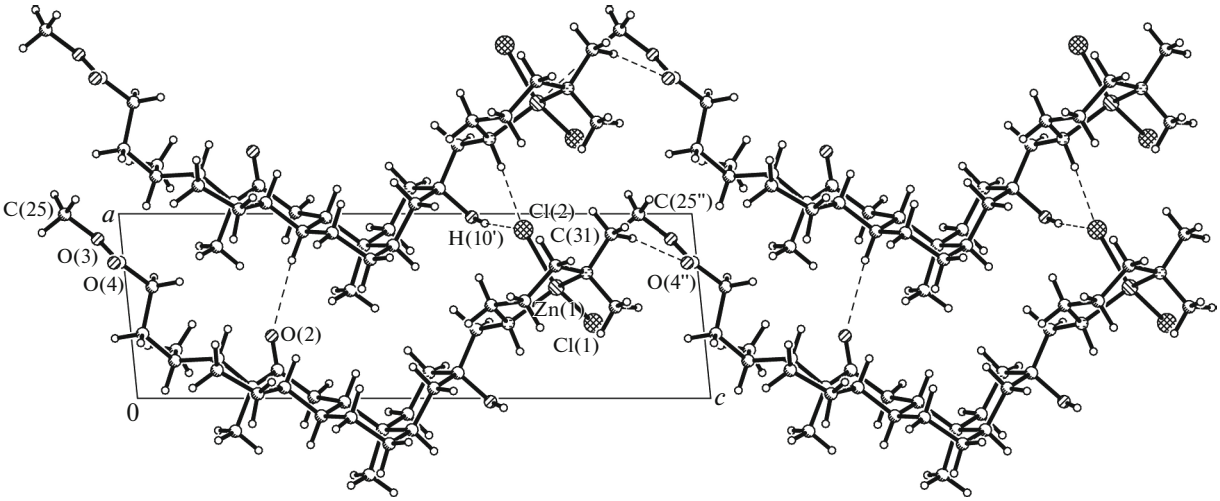



**Fig. 2.** Molecular packing in the crystal structure of complex **I** in the projection onto the (010) plane. Dashed lines show intermolecular contacts.

compared to the IR spectra of ligands L and $L^1$, the spectra of complexes **I**–**IV** exhibit a low-frequency shift of the ν(NH) band, indicating the coordination of the donor NH group. These data are consistent with the results of X-ray structure analysis for complex **I**. Insignificant changes in the positions of the ν(OH) and ν(C=O) bands show the absence of coordination bonds involving these functional groups in complexes **I**–**IV**, which is most likely caused by the presence of another system of intermolecular contacts in the structures of the complexes compared with L and $L^1$. The IR spectra of complexes **I**–**IV** exhibit bands in the 600–100 $cm^{-1}$ range assigned to ν(M–Cl) and ν(M–N) (Table 3). The positions of these bands are close to those of similar bands in the IR spectrum of the mononuclear Zn(II) chloride complex with 2,2'-dimethylpropane-1,3-diamine containing, according to the X-ray structure analysis data, the tetrahedral coordination polyhedron $ZnN_2Cl_2$ [15]. Therefore,

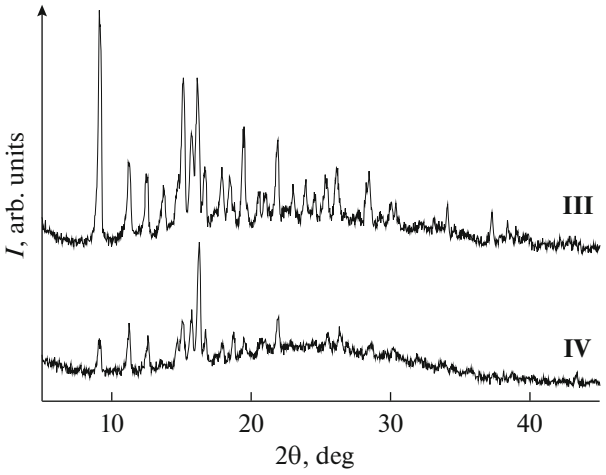



**Fig. 3.** Diffraction patterns of complexes $ZnL^1Cl_2 \cdot 0.5H_2O$ (**III**) and $CuL^1Cl_2 \cdot 0.5H_2O$ (**IV**).

**Table 3.** Main vibrational frequencies in the IR spectra of compounds L and $L^1$ and complexes **I**–**IV**

| Assignment | $cm^{-1}$ | | | | | |
|---|---|---|---|---|---|---|
| | L | **I** | **II** | $L^1$ | **III** | **IV** |
| ν(OH) | 3440 sh, 3375 sh | 3483 | 3450 sh, 3390 sh, 3325 sh | 3500, 3386 | 3442 | 3388 |
| ν(NH) | 3246 | 3241 | 3169 | 3278 | 3228 | 3168 |
| ν(C=O) | 1740, 1697 | 1737, 1670 | 1739, 1705 | 1737, 1699 | 1737, 1704 | 1736, 1704 |
| ν(M–N) | | 458 | 490 | | 466 | 474 |
| ν(M–Cl) | | 332, 282 | 367, 337 | | 331, 283 | 349, 311 |

the data of IR spectroscopy suggest that the structures of complexes **II**–**IV** are similar to the structure of mononuclear complex **I** with the $MN_2Cl_2$ coordination node, which is formed due to the coordination of the N atoms of the bidentate-cyclic amino derivatives of deoxycholic acid.

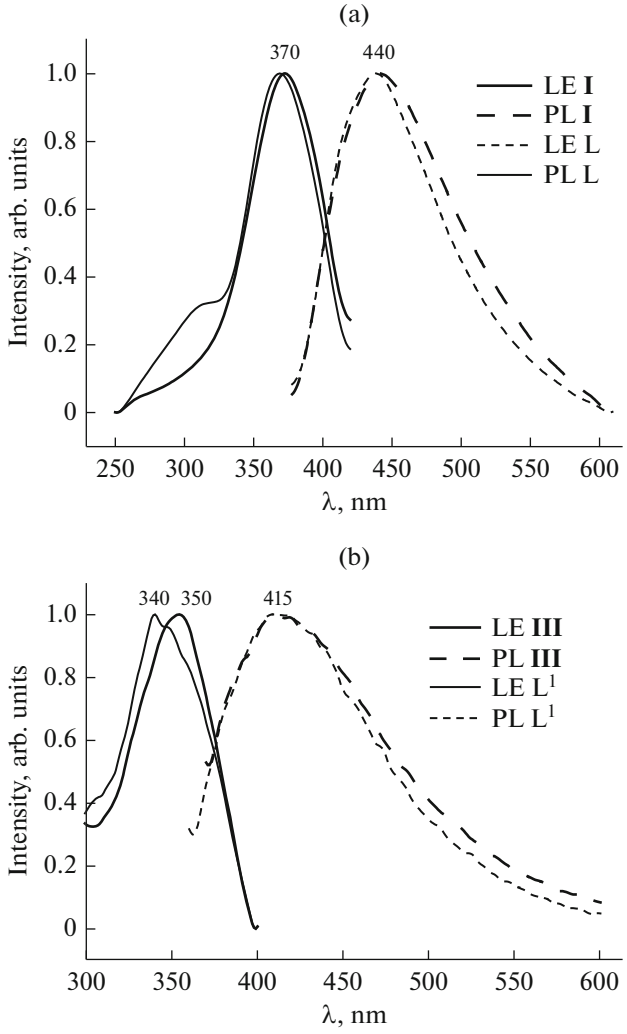



**Fig. 4.** Normalized LE and PL spectra of the solid phases for compounds (a) L, **I** and (b) $L^1$, **III** ($\lambda_{exc}$ = 370 and 350 nm, respectively).

The LE spectra of the solid samples of compounds L and **I** (Fig. 4a) exhibit the band in the visible spectra range at $\lambda_{max}$ = 370 nm. The LE spectra of compounds $L^1$ and **III** contain the band with the maxima at 340 and 350 nm, respectively (Fig. 4b). Based on these data, we chose the excitation wavelengths equal to 370 nm for recording the PL spectra of compounds L and **I** and to 350 nm for $L^1$ and **III**. The positions of band maxima in the PL spectra of free ligand L and complex **I** coincide and lie at 440 nm. A similar character of the PL spectra is also observed for compounds $L^1$ and **III** with $\lambda_{max}$ at 415 nm. The obtained data indicate no influence of complex formation with $Zn^{2+}$ ions on the luminescence spectra of L and $L^1$.

The possibility of preparing the coordination metal compounds with the amino derivatives of deoxycholic acid was shown in the result of this study. The mononuclear Zn(II) and Cu(II) complexes with the diaminopropylene and diaminoethylene derivatives of deoxycholic acid were synthesized. The structures of the new compounds were determined by X-ray structure analysis, X-ray diffraction analysis, and IR spectroscopy. The luminescence properties of compounds L, $L^1$, **I**, and **III** were studied.

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