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Water-Soluble Heteroligand Complexes of 2-Methyl-4-oxo-4*H*-pyran-3-olatoneodymium(III) with Amino Acids

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Abstract—New water-soluble heteroligand complexes of 2-methyl-4-oxo-4*H*-pyran-3-olatoneodymium(III) with aliphatic amino acids (glycine, *N*-methylglycine, and alanine) have been prepared. Within the biological "transparency window" (700–900 nm) of their electronic absorption spectra, narrow bands of Nd^{3+} are found: $^4F_{7/2} \leftarrow {}^4I_{9/2}$; $^4F_{5/2} \leftarrow {}^4I_{9/2}$; $^4F_{3/2} \leftarrow {}^4I_{9/2}$ (750, 810, and 880 nm). Such complexes can be used as markers for biological tissues visualization.

Keywords: neodymium(III) complex, maltol, glycine, sarcosine, alanine, absorption spectrum

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Preparation of metal complexes with natural compounds as ligands is an important branch of bioinorganic chemistry [1]. Rare earth 4*f* elements possess unique optical properties making them promising for application in living systems diagnostics [2]. The interest towards studies of interaction of lanthanide ions with proteins, peptides, nucleotides, and nucleic acids has recently emerged, the obtained results being important for development of the lanthanide complexes applications in microscopy, cytofluorimetry, and immune analysis as well as for construction of DNA probes [3]. The two groups of compounds have been mainly studied so far: lanthanide polyaminocarboxylates based on ethylenediaminetetraacetic acid, diethylenetriaminepentaacetic acid, and 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid [4, 5]; and lanthanide β-diketonates [6, 7]. The latter group application in bioanalysis is limited due to the compounds instability.

Lanthanide complexes based on heterocyclic ligands with various pharmacophores can serve as biomarkers as well; however, they have been scarcely studied [8]. One of the promising non-toxic heterocyclic compounds that is permitted to use in food industry worldwide is 3-hydroxy-2-methyl-4*H*-pyran-4-one (maltol), revealing a wide spectrum of biological activity [9]. Maltol is an interesting chelating agent for preparation of complexes with various metal ions [10].

In this work we prepared a series of heteroligand compounds of neodymium based on maltol ($C_6H_6O_3$) and aliphatic amino acids (AA): glycine (Gly), sarcosine (Sar), and alanine (Ala), and studied some properties of the prepared complexes.

Heteroligand compounds **I–III** were prepared via interaction of aqueous solution of neodymium complexes with amino acids and ethanolic solution of maltol (1 : 1 ratio).

Alternation of the reactants ratio did not lead to change in the products composition or yield; the highest yield achieved under the synthesis conditions did not exceed 50%. Basing on the elemental analysis results, the composition of the complexes was elucidated as of $(AA)_2Nd(C_6H_5O_3)(H_2O)_3$. The prepared compounds were pale-violet solids, insoluble in diethyl ether and ethanol, but soluble in dimethylformamide and dimethylsulfoxide, and readily soluble in water.

Complexes **I–III** were stable up to 55°C, upon further heating they were dehydrated. The corresponding mass loss was of: **I** – 14.0% (exp.), 11.5% (calc.);

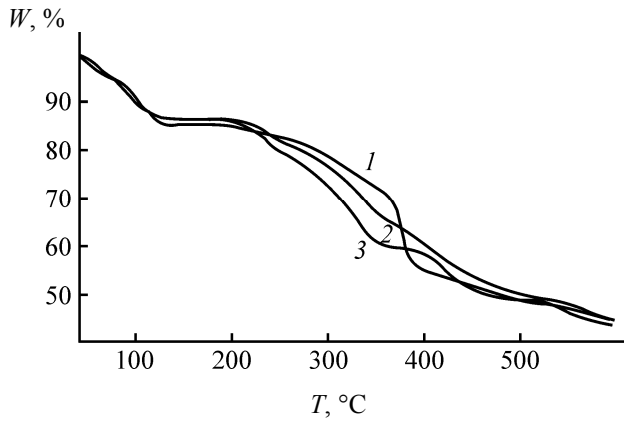

Fig. 1. TGA traces of complexes **I**–**III** (*1*–*3*) in air.

II – 12.0% (exp.), 10.8% (calc.); **III** – 12.0% (exp.), 10.8% (calc.). TGA traces of the complexes **I**–**III** are shown in Fig. 1. The anhydrous complexes were stable up to 200°C; at 200–650°C the complexes decomposed due to degradation of their organic part.

In contrast to IR spectra of the free amino acids and maltol (ν_{CO} 1653 cm^{-1}), those of the complexes **I**–**III** did not contain any bands assigned to vibrations of C=O bond. Instead, strong bands appeared at somewhat lower frequency, 1614–1520 cm^{-1}, reflecting coordination of neodymium ions with carboxylic groups of amino acids and the bidentate coordination of maltol. Assignment of IR spectra of the complexes was complicated due to overlap of the ligands absorption bands. At 580–470 cm^{-1}, the bands assigned to the Nd–O bond vibrations were observed. The presence of coordinated water molecules in the prepared complexes was confirmed by appearance of the band at 3470 cm^{-1} (stretching of the bound O–H).

Electronic absorption spectra of the complexes in visible and near-IR ranges are of particular interest, as they should reflect the *f*–*f* transition of Nd(III). In the spectra of neodymium compounds, sharp bands of variable intensity at 400–1000 nm are typical, reflecting the ground level ($^4I_{9/2}$ Nd^{3+}) electronic transitions. As seen from Fig. 2, strong bands of $^4F_{3/2} \leftarrow {}^4I_{9/2}$ (≈880 nm), $^4F_{5/2} + {}^2H_{9/2} \leftarrow {}^4I_{9/2}$ (≈810 нм), $^4F_{7/2} + {}^4S_{3/2} \leftarrow {}^4I_{9/2}$ (≈750 nm) fall into the biological "transparency window" (700–900 nm); hence, the studied complexes can be used as biomarkers for visualization of biological tissues.

According to the Judd-Ofelt theory, the $^4G_{5/2} + {}^2G_{7/2} \leftarrow {}^4I_{9/2}$ (580 nm) electronic transitions are hypersensitive, and these of $^4F_{7/2}$, $^4F_{5/2}$, $^4F_{3/2} \leftarrow {}^4I_{9/2}$ (750, 810, and 880 nm) are pseudosensitive [11, 12]. As was expected, the hypersensitive transitions $^4G_{5/2} + {}^2G_{7/2} \leftarrow {}^4I_{9/2}$ of the aminocarboxylate and pyranolate (**I**–**III**) complexes were the most sensitive to the ligand surrounding. Comparison of the homoligand (based on amino acids) and the heteroligand **I**–**III** complexes revealed the increase of integral intensity of the hypersensitive band by 1.7 times in the latter case. At 700–900 nm, the bands intensity was almost constant, whereas the band assigned to the $^4F_{3/2} \leftarrow {}^4I_{9/2}$ transition in the spectra of heteroligand complexes was split into two components (870 and 865 nm).

As a model of biological medium, 20 wt % gelatin matrix was used. As gelatin is similar to the biological tissues, it can be used in order to determinate the influence of laser irradiation on oncology objects [13].

Absorption spectra of the prepared complexes **I**–**III** embedded into the gelatin matrix are shown in Fig. 3. Within the biological "transparency window," the bands assigned to neodymium ion were observed: $^4F_{7/2} \leftarrow {}^4I_{9/2}$, $^4F_{5/2} \leftarrow {}^4I_{9/2}$, $^4F_{3/2} \leftarrow {}^4I_{9/2}$ (750, 810, and 880 nm), thus confirming the complexes promise to be used with biological objects.

EXPERIMENTAL

Electronic absorption spectra were recorded with the Perkin Elmer Lambda 25 UV/Vis spectrophotometer at room temperature, at 200–1100 nm. IR spectra were registered with the FSM 1201 spectrometer (Vaseline oil). Elemental analysis was performed with the Euro Vector EA 3000 CHN-analyzer; neodymium content was determined from the amount of solid residue after pyrolysis. TGA studies were performed using the Pyris 6 TGA instrument in air at 5 deg/min heating rate.

Homoligand complexes of neodymium(III) with glycine, sarcosine, and alanine were prepared as described elsewhere [14]. Heteroligand complexes of neodymium(III) with maltol, glycine, alanine, and sarcosine were prepared similarly.

Bis(glycinato)(2-methyl-4-oxo-4*H*-pyran-3-olato)-neodymium trihydrate (I). Yield 0.23 g (49%). IR spectrum, ν, cm^{-1}: 3477 m, 2953 m, 1614 m, 1580 s, 1555 m, 1521 s, 1465 s, 1426 m, 1411 m, 1343 w, 1304 w, 1267 s, 1233 m, 1192 s, 1051 w, 1026 m, 957 w, 925 m, 837 m, 677 m, 611 w, 575 m, 539 m, 528 m, 509 w, 470 m. Found, %: C 26.02; H 4.02; N 5.89; Nd 29.99. $C_{10}H_{19}N_2NdO_{10}$. Calculated, %: C 25.47; H 4.06; N 5.94; Nd 30.59.

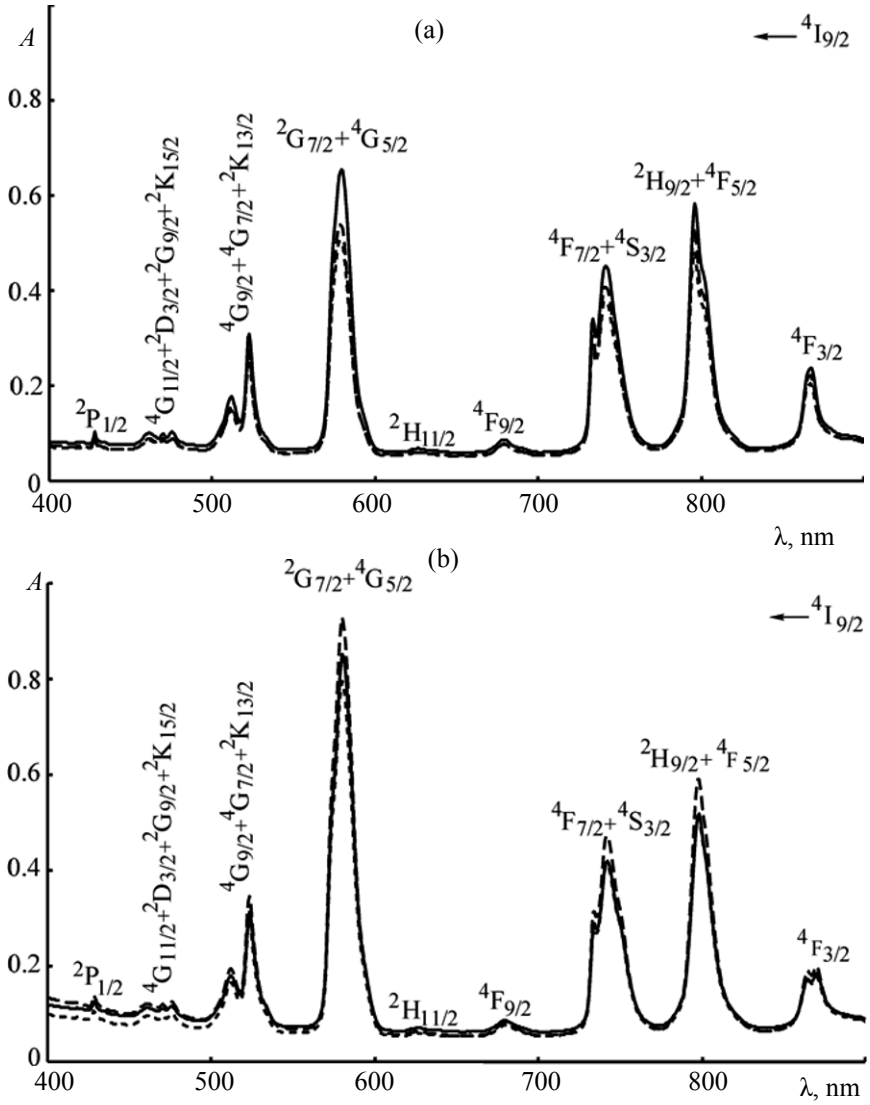

Fig. 2. Absorption spectra of aqueous solutions (0.05 mol/L) of homoligand complexes (a): $(NH_2CH_2COO)_3Nd$ (dashed line), $[NH_2CH(CH_3)COO]_3Nd$ (dotted line), and $[(CH_3)NHCH_2COO]_3Nd$ (solid line); of the heteroligand complexes (b): **I** (dashed line), **II** (dotted line), and **III** (solid line).

Bis(alaninato)(2-methyl-4-oxo-4*H*-pyran-3-olato)-neodymium trihydrate (II). Yield 0.22 g (44%). IR spectrum, ν, cm^{-1}: 3474 w, 2957 m, 1612 m, 1579 s, 1544 m, 1523 s, 1465 s, 1430 m, 1401 m, 1345 w, 1309 w, 1268 s, 1231 m, 1195 s, 1050 w, 1031 m, 962 w, 922 m, 846 m, 680 m, 653 m, 613 w, 577 m, 539 m, 527 m, 508 w, 474 w. Found, %: C 28.77; H 4.55; N 5.35; Nd 28.59. $C_{12}H_{23}N_2NdO_{10}$. Calculated, %: C 28.85; H 4.64; N 5.61; Nd 28.87.

Bis[2-(methylamino)acetato](2-methyl-4-oxo-4*H*-pyran-3-olato)neodymium trihydrate (III). Yield 0.25 g (50%). IR spectrum, ν, cm^{-1}: 3476 m, 2957 m, 1615 m, 1581 s, 1520 s, 1466 s, 1430 m, 1410 m, 1354 w, 1343 w, 1302 w, 1267 s, 1233 m, 1193 s, 1053 w,

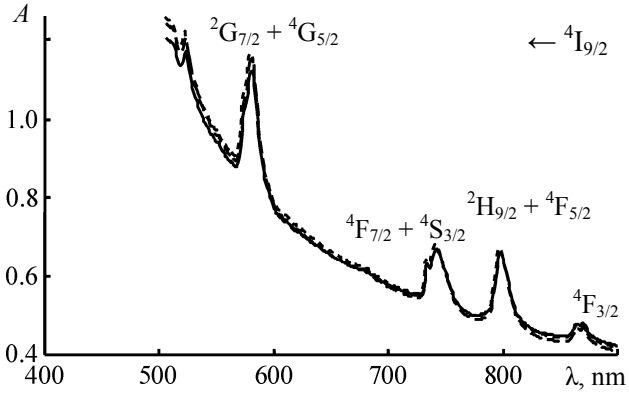

Fig. 3. Absorption spectra of the complexes in 20 w t% gelatin matrix (complexes concentration of 0.05 mol/L): **I** (dashed line), **II** (dotted line), and **III** (solid line).

1042 w, 1025 m, 958 w, 925 m, 836 m, 675 m, 611 w, 575 m, 539 m, 528 m, 509 w, 470 w. Found, %: C 28.72; H 4.61; N 5.25; Nd 28.71. $C_{12}H_{23}N_2NdO_{10}$. Calculated, %: C 28.85; H 4.64; N 5.61; Nd 28.87.

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