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SPECTROSCOPIC STUDIES OF NEODYMIUM AND EUROPIUM PHOSPHORO-AZO β -DIKETONATES

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New complexes of lanthanides (Nd, Eu) with phosphoro-azo derivatives of β -diketones were synthesized. Optical properties of these compounds were investigated and confronted with the structure and single crystal spectra of different types of earlier reported lanthanide phosphoro-azo β -diketonates. The exchange of the N-P-O-Me ligand group by the N-P-NR₂ one plays only a minor role in binding character of lanthanide ions but strongly affects biological functions and properties of lanthanide systems. *In vitro* experiment on cytotoxicity of the samples was performed using 10T_{1/2}, L₁, MCF, DETA and Mew-132 cell lines.

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1. Introduction

Phosphoro-azo derivatives of β -diketone are applied in clinical practice as anticancer medicals [1, 2]. The role and function of chelating part of -CO-NH-PO< ligand are not known in this process. To our knowledge, lanthanide phosphoro-azo β -diketonates have not been examined as antitumor agents yet. Recently we undertook studies on physicochemical properties of two series of complexes with two kinds of β -diketones: *A* with CCL₃-C(O)N-P(O)(OCH₃)₂ derivatives, which were reported in [3], and *B* with CCL₃-C(O)N-P(O)[N(CH₂)₂]₂. The aim of this paper was to explain the structure and cytotoxicity of the latter type of compound.

2. Experimental

Lanthanides β -diketonates of *B* type were synthesized according to the procedure described in [3].

Absorption spectra at 293 K were measured by a Cary Varian 5 spectrophotometer. Excitation and emission spectra were recorded at 77 and 293 K using a SLM Aminco 500 spectrofluorometer. IR spectra were obtained using a Brüker FS 88 FTIR spectrometer, while the Raman ones — with a DFS 24 double monochromator equipped with photon counting system. An argon ion laser was used as an excitation source.

3. Results and discussion

As it was mentioned above, the phosphoro-azo derivatives of β -diketone are applied in anticancer medicine. However, cytotoxicity of these compounds is relatively high. Studies of lanthanide complexes were undertaken to explain the role of metal ion in enhancement or inhibition of the ligand properties. Moreover, the process of complexation could limit moiety of the C(O)-N-P(O)-N part of the ligand molecule, explaining the role of this part in biological activity. The main goal of our investigations was the synthesis of samples of excellent quality. Next, their spectroscopic properties throw light on the problem of structure of these systems. Finally, the effort has been made to test the cytotoxicity behaviour of the samples using four different cell lines (*in vitro* experiments).

Fig. 1. The absorption spectra of *a* — Na[NdWo₄] · H₂O single crystal, and *b* — Na[NdAz₄] · H₂O in the visible and UV region, *c* — these of Na[EuAz₄] (1), HAz (2), and Na[EuAz] vs. HAz (3).

Figure 1 shows the absorption spectrum of neodymium powder complex with *B*, and a single crystal spectrum of neodymium complex with *A* kinds of ligand in the range of NIR and hypersensitive transitions, which are the most sensitive to the changes of lanthanide ion environment. Both the splitting of bands and relative intensities of *f*-*f* transitions (Table I) are comparable to those observed in the spectra of sample *A*, whose structure was well-defined by X-ray method.

TABLE I

Oscillator strength values ($P_{\text{exp}} \times 10^8$) of $f-f$ transitions for simple crystal of $\text{Na}[\text{NdW}_4] \cdot \text{H}_2\text{O}$ and for $\text{Na}[\text{NdAz}_4] \cdot \text{H}_2\text{O}$ in powder.

$S' L' J'$	Spectral region [Å]	$\text{Na}[\text{NdW}_4] \cdot \text{H}_2\text{O}$		$\text{Na}[\text{NdAz}_4] \cdot \text{H}_2\text{O}$ ($C \cdot D = 1$)
		293 K	5 K	293 K
$^4F_{3/2}$	8400–9200	422.3	210.8	44.05
$^4F_{5/2}, ^2H_{9/2}$	7750–8450	949.2	651.1	85.40
$^4F_{7/2}, ^4S_{3/2}$	7100–7750	873.1	523.3	87.32
$^4F_{9/2}$	6610–7050	61.5	51.1	9.42
$^4G_{5/2}, ^2G_{7/2}$	5500–6100	1837.7	1458.2	287.31
$^2K_{13/2}, ^4G_{7/2}, ^4G_{9/2}$	4900–5500	788.0	542.2	118.85
$^2K_{15/2}, ^2G_{9/2},$ $(^2D, ^2F)_{3/2}, ^4G_{11/2}$	4500–4900	216.4	205.8	28.25
$^2P_{1/2}, ^2D_{5/2}$	4130–4400	57.9	38.6	6.83
$^4D_{3/2}, ^4D_{5/2}, ^2I_{11/2},$ $^4D_{1/2}, ^2L_{15/2}$	3380–3700	1206.2	899.4	65.19
$^2I_{13/2}, ^4D_{7/2}, ^2L_{17/2}$	3200–3380	267.5	260.4	—

Note that in *A* the sodium ions are encapsulated inside the structure of the complexes [3]. In the system presented here situation could be changed because of steric factors.

UV region of absorption of complexes is dominated by a charge-transfer (C-T) band (Fig. 1c); this region is also that of transitions inside ligand. Relative positions of bands are presented in Fig. 1c — 1, 2, 3. Their role in the emission process will be the subject of our future studies.

Let us confront the excitation spectra obtained at 293 and 77 K (Fig. 2) and compare them with the data of complex *A*. At room temperature, the $^7F_0 \rightarrow ^5D_2$ transition is the strongest line in the spectrum; similarly, strong $^7F_1 \rightarrow ^5D_1$ band shows significant population of the $^7F_1$ level.

When lowering temperature, a strong and broad UV band appears; moreover, relative intensities of $^7F_0 \rightarrow ^5L_6$, $^5D_2$ transitions change significantly. Splitting of the $^7F_0 \rightarrow ^5D_J$ transition is close to that in compound *A*, indicating similarity of structures. Moreover, the number of the Stark components in the emission spectra and shapes of bands remind those in the spectrum of single crystal of *A* (Fig. 3).

The above data confirm well similarities of the two kinds of compounds. Inspection of IR and Raman results in the range of modes which are most sensitive to the bonding of metal ion yields further evidence for analogies in the bonding. The IR and Raman spectra indicate that the structure of the complexes studied is composed of octacoordinated LnO_8 polyhedra. The stretching $\nu(\text{Ln}-\text{O})$ vibrations occur in the $170\text{--}360\text{ cm}^{-1}$ region and the bending modes appear below 150 cm^{-1} . The bands corresponding to these vibrations are split into distinct doublets. Such

Fig. 2. The excitation spectra $\text{Na}[\text{EuAz}_4] \cdot \text{H}_2\text{O}$ at 293 K (a) and at 77 K (b), and comparative data for $\text{Na}[\text{EuAz}_4] \cdot \text{H}_2\text{O}$ (1) and $\text{Na}[\text{EuWo}_4] \cdot \text{H}_2\text{O}$ (2) at 77 K in the range of ${}^7F_0 \rightarrow {}^5D_2$ transition (c).

Fig. 3. Comparative results for $\text{Na}[\text{EuAz}_4] \cdot \text{H}_2\text{O}$ (a) and $\text{Na}[\text{EuWo}_4] \cdot \text{H}_2\text{O}$ (b) in emission spectra at 77 K.

behaviour is characteristic of the case when the LnO_8 polyhedron contains two sets of the Ln–O distances with significantly different values. It means that the structure of the polyhedron, which occupies the general positions, could be described by the Archimedean antiprismatic symmetry.

Almost all bands observed have complex shapes composed of the two, three or four components, due to the crystal field effect. The structure of the crystal seems to be monoclinic with $Z = 4$.

Let us analyze now the results of *in vitro* cytotoxicity tests (Table II). Rather unexpected strong waste of tumor cells was observed. In fact, blocking of $-\text{C}(\text{O})-\text{N}-\text{P}(\text{O})-\text{N}$ part of ligand molecule changes almost nothing in biological activity of the system under consideration; its cytotoxicity is a little lower for lanthanide complexes, which seems to be confirmed by our preliminary *in vivo* cytotoxicity experiments [4]. Explanation of this phenomenon is not easy. Either the

ending part of molecule plays an important role in its biological properties (which is the most probable) or the exchange of Ca^{2+} by La^{3+} is so fast that the free ligand reacts like its complexes with a lanthanide. The mechanism of biological activity of the systems tested will be the subject of further studies.

TABLE II
The results of cytotoxical experiments of samples. The numbers are % of dead cells after incubation with the compound.

	$\text{NaEu}(\text{Az})_4$	$\text{H}(\text{Az})$	NaAz
$10\text{T}_{1/2}$	96.0	100	99.7
L_1	99.5	99.2	98.2
	99.3	100	100
MCF	91.7	100	100
	97.0	100	100
DETA	98.1	100	100
	95.2	99.5	100
Mew-132	89.9	100	100
	84.2	100	100

Cell lines:

$10\text{T}_{1/2}$ — line of normal cells (no-tumor),

L_1 — Sarcoma L_1 ,

MCF — Mammary Carcinoma Female,

DETA — Human Colon Carcinoma,

Mew-132 — Melanoma Human.

4. Conclusions

Comparison of relative intensities of the f - f transitions in the range of the hypersensitive one and of the IR spectral region, as well as the composition of the Stark level seem to indicate the similar structure of the system under study to that reported earlier for the compound A.

Substitution of the $\text{NP}(\text{O})(\text{OCH}_3)_2$ ligand group by $\text{NP}(\text{O})\text{N}(\text{CH}_2)_2$ changes biological function of the compound. Such an exchange plays only a minor role in binding of lanthanide ions.

In vitro cytotoxicity experiments on lanthanide complexes exhibit anticancer properties of the cell strains tested.

Acknowledgments

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