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CHEMISTRY

Luminescence of Terbium Ions in Aqueous Solutions of Sodium Styrene Sulfonate Copolymers with 4-Methacrylamidosalicylic Acid

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Abstract—Water-soluble copolymers of sodium styrene sulfonate and 4-methacrylamidosalicylic acid of 93.7 mol % composition have been synthesized, and their interaction with terbium and gadolinium ions has been investigated to fabricate luminescent probes promising for their visualization in biomedical research. It has been shown that, in aqueous solutions in the copolymer concentration range 0.15–1.7 mg mL^{-1} and at the ratio $[Tb^{3+}]/[COO^-] = 1$, water-soluble luminescent metal polymer complexes with a luminescence lifetime of 823 μs are formed. When Tb^{3+} ions are partially replaced in the complex by Gd^{3+} ions, bimetallic complexes with intense luminescence are formed.

Keywords: luminescent metal–polymer complexes, lanthanides, sodium polystyrene sulfonate, 4-methacrylamidosalicylic acid

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The currently developing coronavirus pandemic stimulates the search for new antiviral agents, both among low-molecular-weight and water-soluble high-molecular-weight substances. Among polymers, of great interest to researchers are polyanions, in particular, sulfo-containing polymers, for example, sodium poly(styrene sulfonate) (poly-SSNa), sodium polyvinylsulfonate, etc., which are active against various viruses (influenza, HIV, herpes, rabies, etc.) [1, 2]. For biovisualization of cells, viruses, tissues, and biological processes, metal–polymer complexes of Eu^{3+} and Tb^{3+} lanthanides have recently been used [3–6].

To study the interaction of sodium poly(styrene sulfonate) (**I**) with viruses and cells, in this work we synthesized copolymer **II** of sodium styrene sulfonate (SSNa) with 4-methacrylamidosalicylic acid (MASA). The objects of study are shown in Fig. 1. For them, the conditions for the formation of luminescent complexes of Tb^{3+} ions in aqueous solutions were studied. 4-Aminosalicylic acid is an antituberculosis drug, and its polymeric derivatives form luminescing complexes with Eu^{3+} and Tb^{3+} [7, 8]. That is, the synthesized copolymer has polyfunctional biological activity.

The copolymer and homopolymers were obtained by radical (co)polymerization in solutions (DMF, DMSO) in the presence of azobisisobutyronitrile (AIBN) as an initiator at 65°C for 24 h. The resulting polymers were isolated by dialysis against water followed by freeze drying. The molecular weights were calculated from the intrinsic viscosity values according to the formula $[\eta] = 1.17 \times 10^{-2} \times M^{0.69}$ for sodium poly(styrene sulfonate) [9]: the molecular weight was 31×10^3 for **I** and for 84×10^3 for copolymer **II**. The content of MASA, used as a chelate label to obtain a luminescent probe, determined by UV spectrophotometry in the copolymer was 7 mol %.

Aqueous solutions with copolymer concentrations of 1.5 and 0.12 mg mL^{-1} and pH 8–9 were studied. The $[COO^-]/[Tb^{3+}]$ ratio was varied by adding a $TbCl_3$ solution ($c = 5 \times 10^{-4}$ mol L^{-1}) to the copolymer solution.

The absorption spectra of the solutions were recorded on an SF256 UVI spectrophotometer (OOO LOMO Phototonika, Russia). The excitation and luminescence spectra of the solutions were recorded on a PTI LS100 spectrofluorimeter. The lifetime of the excited state of the Tb^{3+} complex with copolymer **II** (τ_{phosph}) was determined from the kinetic phosphorescence decay curve. The measurements were carried out in a thermostated cell at 25°C in a quartz cuvette with an optical path length of 1 cm.

Figure 2a shows the absorption spectra of aqueous solutions of (co)polymers **I**–**III** in the wavelength range 220–400 nm. The absorption spectra of a solu-

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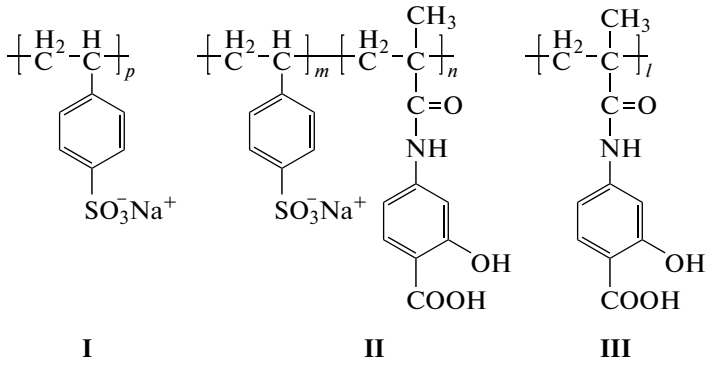

I II III

Fig. 1. Structural schemes of the objects of study. Sodium poly(styrene sulfonate) (**I**), sodium styrene sulfonate–4-methacrylamidosalicylic acid copolymer (**II**), and poly(4-methacrylamidosalicylic acid) (**III**).

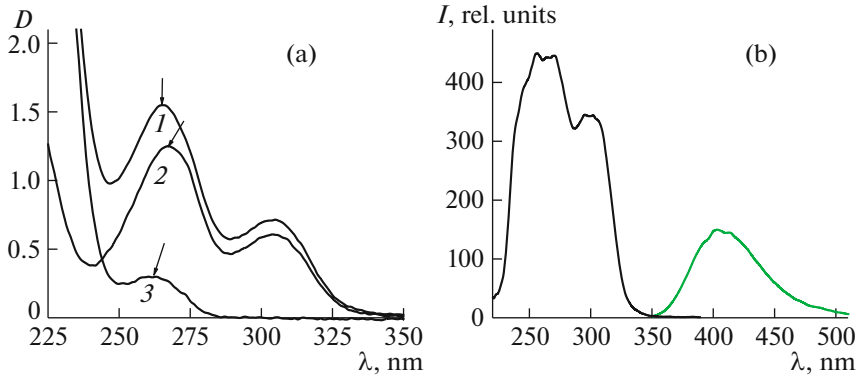

Fig. 2. (a) UV spectra of aqueous solutions of co(polymers): (*1*) (SSNa–MASA), (*2*) poly-MASA, and (*3*) poly-SSNa; (b) excitation spectra (black curve), λ_{em} = 402 nm and luminescence spectra (green curve) of the (SSNa–MASA) copolymer, λ_{exc} = 302 nm, pH 8.5.

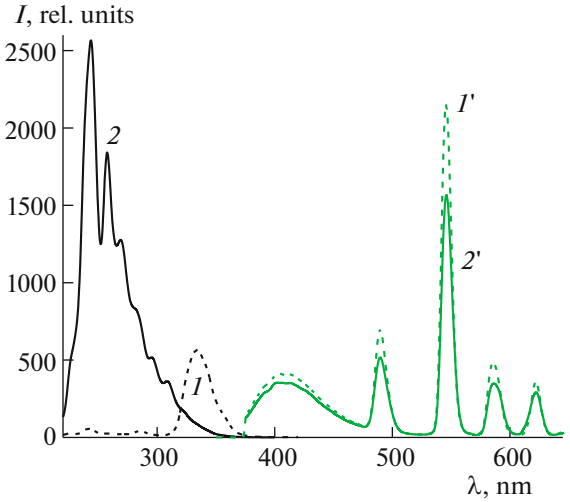

Fig. 3. Excitation spectra (black curves), λ_{em} = 544 nm, and luminescence spectra of Tb^{3+} (green curves) in a solution of (SSNa–MASA) copolymer at its concentrations (*1*) 1.57 and (*2*) 0.12 mg mL^{-1}. $[Tb^{3+}]/[COO^-] = 1$; λ_{exc} = (*1*) 335 and (*2*) 310 nm. The *I* values for curves *1*' and *2*' were multiplied by 5.0.

tion of copolymer **II** (Fig. 2a, spectrum *1*) show a band at λ_{max} = 265 nm due to π–π^* electronic transitions in the aromatic ring. This band is a superposition of two bands of **I** (λ_{max} = 262 nm, Fig. 2a, spectrum *2*) and **III** (λ_{max} = 267 nm, Fig. 2a, spectrum *3*). Figure 2b shows the excitation and luminescence spectra of copolymer **II**.

Figure 3 shows the excitation and luminescence spectra of Tb^{3+} ions in a solution of copolymer **II** at different concentrations of the copolymer.

Comparison of Figs. 2a and 3 shows that the excitation and absorption spectra of solutions of the Tb^{3+}/**II** complex and the initial solution of copolymer **II** differ in shape and, in addition, unlike the absorption spectra of solutions of **II**, change significantly with a change in the concentration of the copolymer. In lanthanide complexes, the ratio between the bands due to the absorption of the ligand and the absorption of the lanthanide ion depends not only on their molar absorption coefficients, but also on the efficiency of luminescence sensitization [6]. A significant change in the shape of the excitation spectra with a decrease in the concentration of the copolymer indicates a rear-

rangement of the inner sphere of the complex, associated with a change in the number of COO^- groups and water molecules coordinated by Tb^{3+}.

The excitation spectra at $c = 1.57$ mg mL^{-1} show one band with $\lambda_{max} = 335$ nm, while at $c = 0.12$ mg mL^{-1} bands with maxima at 227, 258, 268, 296, and 310 nm appear in the spectra (Fig. 3, spectra *1* and *2*). The observed effect of concentration is due to competition in the binding of Tb^{3+} ions by styrene sulfonate and MASA units. Styrene sulfonate, being a strong acid anion, weakly coordinates Tb^{3+} ions; therefore, at the concentration of copolymer **II** $c_{II} \geq 1.5$ mg mL^{-1}, they are mainly bound by MASA units. But since the constants of formation of lanthanide complexes with carboxyl groups are in the range (1×10^4)–(1×10^6) [10], when the solution is diluted, the equilibrium shifts towards the formation of "coordinatively unsaturated" complexes $Tb^{3+}(COO^-)_{3-n}$ ($n = 1, 2$).

The lifetimes τ_{phosph} of the excited state of Tb^{3+} complexes with copolymer **II** were determined from the kinetic phosphorescence decay curves. The kinetic curves are described by a two-exponential dependence with $\tau_{phosph} = 823$ and 157 μs, the pre-exponential factor is 0.92 and 0.08, respectively. Based on the calculations performed in [11], it can be assumed that the Tb^{3+}/**II** polymer complex can contain up to about four water molecules.

The photoluminescence spectra of solutions of Tb^{3+} with copolymer **II** for the studied concentrations (Fig. 3) show, along with the bands at 495, 545, 587, and 622 nm characteristic of Tb^{3+} due to the $^5D_4 \rightarrow {}^7F_j$ ($j = 6, 5, 4, 3$) transitions, there is a MASA luminescence band at $\lambda = 402$ nm, which indicates incomplete energy transfer from the ligand triplet level to the Tb^{3+} resonance level. It is known that, if the intrasystem transfer is not efficient enough, then the partial replacement of luminescent ions by Gd^{3+} ions can contribute to an increase in the luminescence intensity of lanthanide ions [12–14]. Macromolecular Gd^{3+} complexes, in addition to being used in MRI, are promising for simultaneous MRI and targeted therapeutic procedures [15] and can also be combined with other imaging methods.

Figure 4 shows the change in the luminescence intensity of the Tb^{3+}/**II** complex normalized to 1 at $[Tb^{3+}] = 4 \times 10^{-5}$ mol L^{-1} upon the addition of Gd^{3+} ions (black squares). The $[Tb^{3+}]/[Gd^{3+}]$ ratio was changed from 0.6 to 16, decreasing the concentration of Tb^{3+}, but keeping the total concentration of Tb^{3+} and Gd^{3+} ions constant and equal to 4×10^{-5} mol L^{-1}. For comparison, the dependence for Tb^{3+}/**II** without Gd^{3+} is shown in the same coordinates (solid curve).

It can be seen from Fig. 4 that the addition of Gd^{3+} does not affect the luminescence of Tb^{3+} at all $[Tb^{3+}]/[Gd^{3+}]$ ratios. This may be due to the fact that

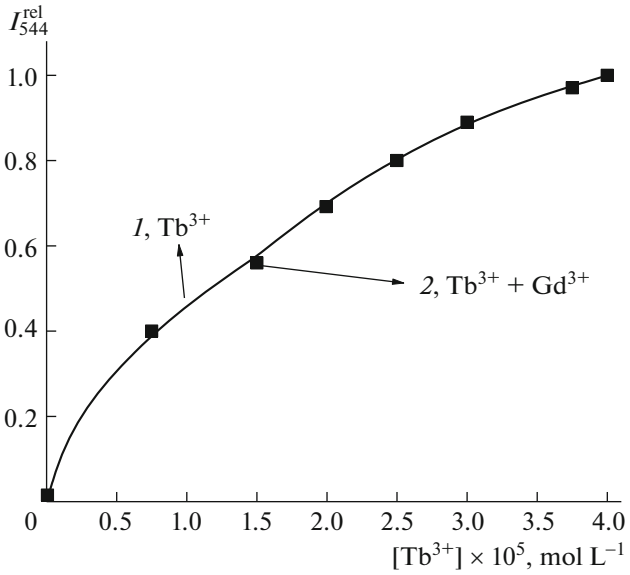

Fig. 4. Change in luminescence intensity (I_{544}^{rel}) normalized to 1 at $[Tb^{3+}] = 4 \times 10^{-5}$ mol L^{-1} of a solution of the Tb^{3+}/**II** complex induced by adding Gd^{3+} ions (black squares *2*) and analogous dependence in the absence of Gd^{3+} (solid line *1*) when Tb^{3+} concentration is changed.

either Gd^{3+} is bound by styrene sulfonate units, or Gd^{3+}, replacing Tb^{3+} in the complex with **II**, creates an additional step in the electron excitation energy transfer to the emitting Tb^{3+} level, which enhances luminescence, compensating for the decrease in the concentration of Tb^{3+}/MASA complexes in the copolymer.

Thus, the formation of complexes of the (SSNa–MASA) copolymer with Tb^{3+} ions, as well as bimetallic complexes of Tb^{3+} and Gd^{3+} with copolymer **II**, opens up prospects for the creation of water-soluble polymeric polyfunctional biologically active substances with antiviral activity containing probes with optical and magnetic resonance properties, for diagnostics and imaging of cells, organs, and tissues.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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