Experimental and theoretical study on interaction of the barium cation with antamanide

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HIGHLIGHTS

- Stability constant of the antamanide–Ba^{2+} cationic complex in water-saturated nitrobenzene was determined.
- Quantum mechanical DFT calculations were carried out.
- Structure of the resulting cationic complex species was predicted.

GRAPHICAL ABSTRACT
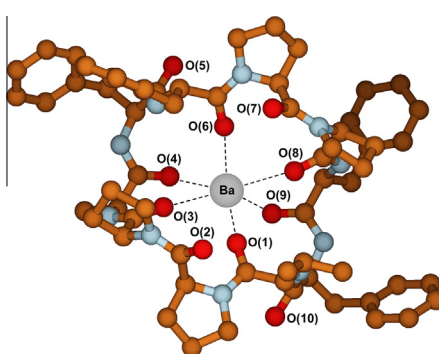
ABSTRACT

By using extraction experiments and γ-activity measurements, the extraction constant corresponding to the equilibrium $Ba^{2+}(aq) + \mathbf{1}\cdot Sr^{2+}(nb) \rightleftarrows \mathbf{1}\cdot Ba^{2+}(nb) + Sr^{2+}(aq)$ occurring in the two-phase water–nitrobenzene system ($\mathbf{1}$ = antamanide; aq = aqueous phase, nb = nitrobenzene phase) was determined as $\log K_{ex}$ ($Ba^{2+}, \mathbf{1}\cdot Sr^{2+}$) = 0.2 ± 0.1. Further, the stability constant of the $\mathbf{1}\cdot Ba^{2+}$ complex in nitrobenzene saturated with water was calculated for a temperature of 25 °C: $\log \beta_{nb}$ ($\mathbf{1}\cdot Ba^{2+}$) = 8.8 ± 0.2. Finally, applying quantum mechanical DFT calculations, the most probable structure of the cationic complex species $\mathbf{1}\cdot Ba^{2+}$ was derived. In the resulting complex, the "central" cation Ba^{2+} is bound by six bond interactions to the corresponding six carbonyl oxygen atoms of the parent ligand $\mathbf{1}$. The interaction energy of the considered $\mathbf{1}\cdot Ba^{2+}$ complex was found to be −964.9 kJ/mol, confirming the formation of this cationic species as well.

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1. Introduction

The cyclic decapeptide antamanide, *cycl*[-Val(1)-Pro(2)-Pro(3)-Ala(4)-Phe(5)-Phe(6)-Pro(7)-Pro(8)-Phe(9)-Phe(10)-], consisting entirely of L-amino acids (see Scheme 1), forms 1:1 complexes with a variety of metal cations [1,2]. Antamanide was isolated from the poisonous mushroom *Amanita phalloides* [3] and it has the unique property of counteracting the toxin phalloidin, produced by the mentioned mushroom. Furthermore, it is necessary to emphasize that antamanide prevents the inhibition of depolymerization of F-actin and G-actin in the liver cell membranes of mammals [4].

The dicarbollylcobaltate anion (DCC^-) [5] and some of its halogen derivatives have been applied very often for the solvent extraction of various metal cations (especially Cs^+, Sr^{2+}, Ba^{2+}, Eu^{3+}, and Am^{3+}) from aqueous solutions into a polar organic phase, both under laboratory conditions for theoretical or experimental purposes [6–13], and on the technological scale for the separation

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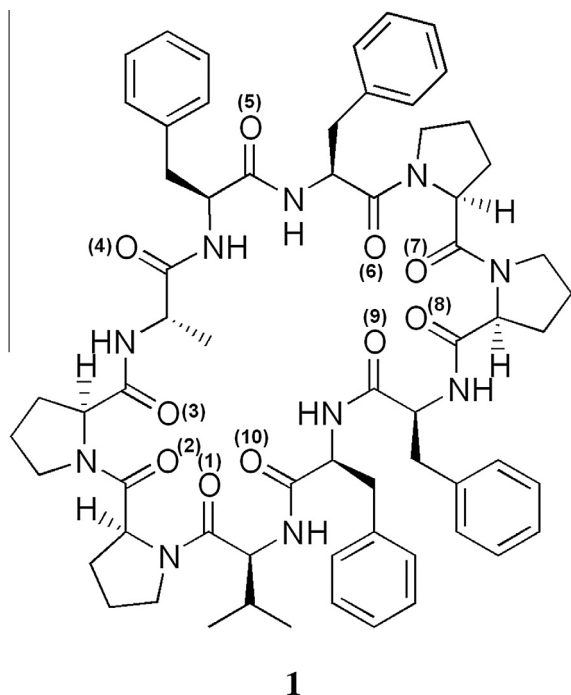
Scheme 1. Structural formula of antamanide (abbrev. **1**).

of some high-activity isotopes in the reprocessing of spent nuclear fuel and acidic radioactive waste [14–16].

In the current work, the solvent extraction of Ba^{2+} into nitrobenzene by means of a synergistic mixture of strontium dicarbollylcobaltate, $Sr(DCC)_2$, and antamanide (**1**; see Scheme 1) was investigated. At this point it should be noted that the Ba^{2+} ion is a typical one of the "heavy" divalent cations; therefore, this cation was chosen for the present study. Moreover, the stability constant of the proved $\mathbf{1} \cdot Ba^{2+}$ complex species in the organic phase of the water–nitrobenzene extraction system was evaluated. Finally, applying quantum mechanical DFT calculations, the most probable structure of this cationic complex species was predicted on the basis of the thorough conformational analysis (i.e., different initial mutual positions of the ligand **1** and the Ba^{2+} cation were considered during the geometry optimization) and the respective vibrational frequency calculations.

2. Experimental

Antamanide (**1**; see Scheme 1) was prepared by the method described in Ref. [17]; the corresponding spectroscopic data of antamanide and its analogs were reported by Ruzza et al. [2]. Cesium dicarbollylcobaltate (CsDCC) was synthesized by means of the method published by Hawthorne et al. [18]. The other chemicals used (Lachema, Brno, Czech Republic) were of reagent grade purity. A nitrobenzene solution of hydrogen dicarbollylcobaltate (HDCC) [5] was prepared from CsDCC by the procedure described elsewhere [19]. The equilibration of the nitrobenzene solution of HDCC with stoichiometric $Sr(OH)_2$, which was dissolved in an aqueous solution of $Sr(NO_3)_2$ (0.20 M), yielded the corresponding $Sr(DCC)_2$ solution in nitrobenzene. The radionuclide $^{85}Sr^{2+}$ was obtained from DuPont, Belgium; its radionuclidic purity was 99.9%.

The extraction experiments were carried out in 10 mL polypropylene test-tubes with polypropylene stoppers: 2 mL of an aqueous solution of $Ba(NO_3)_2$ of a concentration in the range from 1×10^{-3} to 3×10^{-3} M and 10 kBq of $^{85}Sr^{2+}$ were added to 2 mL of a nitrobenzene solution of **1** and $Sr(DCC)_2$, whose initial concentrations varied also from 1×10^{-3} to 3×10^{-3} M (in all experiments,

the initial concentration of **1** in nitrobenzene, $C_1^{in,nb}$, was equal to the initial concentration of $Sr(DCC)_2$ in this medium, $C_{Sr(DCC)_2}^{in,nb}$). The test-tubes filled with the solutions were shaken for 3 h at $25 \pm 1\ °C$, using a laboratory shaker. Under these conditions, the equilibria in the system under study were established after approximately 30 min of shaking. Then the phases were separated by centrifugation. Finally, 1 mL samples were taken from each phase and their γ-activities were measured by means of a well-type NaI(Tl) scintillation detector connected to a γ-analyzer Triathler (Hidex, Turku, Finland).

The equilibrium distribution ratios of strontium, D_{Sr}, were determined as the ratios of the corresponding measured radioactivities of $^{85}Sr^{2+}$ in the nitrobenzene and aqueous samples.

3. Results and discussion

3.1. Extraction experiments

In terms of previous papers [5,20,21], the two-phase water–$Ba(NO_3)_2$–nitrobenzene–$Sr(DCC)_2$ (strontium dicarbollylcobaltate) extraction system can be described by the following equilibrium

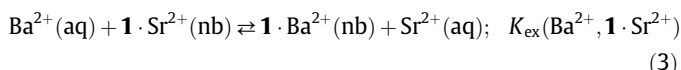$$Ba^{2+}(aq) + Sr^{2+}(nb) \rightleftarrows Ba^{2+}(nb) + Sr^{2+}(aq); \quad K_{ex}(Ba^{2+},\ Sr^{2+}) \quad (1)$$
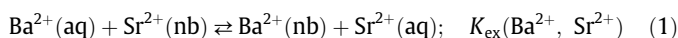
with the corresponding exchange extraction constant K_{ex} (Ba^{2+}, Sr^{2+}); aq and nb denote the presence of the species in the aqueous and nitrobenzene phases, respectively. For the constant K_{ex} (Ba^{2+}, Sr^{2+}) one can write [5,21]

$$\log K_{ex}(Ba^{2+},\ Sr^{2+}) = \log K_{Ba^{2+}}^i - \log K_{Sr^{2+}}^i \quad (2)$$

where $K_{Ba^{2+}}^i$ and $K_{Sr^{2+}}^i$ are the individual extraction constants for Ba^{2+} and Sr^{2+}, respectively, in the water–nitrobenzene system [21]. Knowing the values $\log K_{Ba^{2+}}^i = -10.5$ [21] and $\log K_{Sr^{2+}}^i = -10.7$ [21], the exchange extraction constant K_{ex} (Ba^{2+}, Sr^{2+}) was simply calculated from Eq. (2) as $\log K_{ex}$ (Ba^{2+}, Sr^{2+}) = 0.2.

From previous results [22,23] it follows that the two-phase water–$Ba(NO_3)_2$–nitrobenzene–**1** (antamanide)–$Sr(DCC)_2$ extraction system (see Section 2), chosen for determination of the stability constant of the $\mathbf{1} \cdot Ba^{2+}$ complex in nitrobenzene saturated with water, can be characterized by the main chemical equilibrium

$$Ba^{2+}(aq) + \mathbf{1} \cdot Sr^{2+}(nb) \rightleftarrows \mathbf{1} \cdot Ba^{2+}(nb) + Sr^{2+}(aq); \quad K_{ex}(Ba^{2+}, \mathbf{1} \cdot Sr^{2+}) \quad (3)$$

with the respective equilibrium extraction constant K_{ex} (Ba^{2+}, $\mathbf{1} \cdot Sr^{2+}$):

$$K_{ex}(Ba^{2+},\ \mathbf{1} \cdot Sr^{2+}) = \frac{[\mathbf{1} \cdot Ba^{2+}]_{nb}[Sr^{2+}]_{aq}}{[Ba^{2+}]_{aq}[\mathbf{1} \cdot Sr^{2+}]_{nb}} \quad (4)$$

At this point it should be noted that **1** is a considerably lipophilic ligand, practically present in the nitrobenzene phase only, where this ligand forms – with Ba^{2+} and Sr^{2+} – the very stable complexes $\mathbf{1} \cdot Ba^{2+}$ and $\mathbf{1} \cdot Sr^{2+}$, as given below.

Employing the conditions of electroneutrality in the organic and aqueous phases of the system under study, the mass balances of the divalent cations studied at equal volumes of the nitrobenzene and aqueous phases, as well as the measured equilibrium distribution ratio of strontium, $D_{Sr} = [\mathbf{1} \cdot Sr^{2+}]_{nb}/[Sr^{2+}]_{aq}$, combined with Eq. (4), we gain the final expression for K_{ex} (Ba^{2+}, $\mathbf{1} \cdot Sr^{2+}$) in the form

$$K_{ex}(Ba^{2+},\ \mathbf{1} \cdot Sr^{2+}) = \frac{1}{D_{Sr}} \frac{C_{Sr(DCC)_2}^{in,nb}}{(1 + D_{Sr})C_{Ba(NO_3)_2}^{in,aq} - C_{Sr(DCC)_2}^{in,nb}} \quad (5)$$

where $C_{Ba(NO_3)_2}^{in,aq}$ is the initial concentration of $Ba(NO_3)_2$ in the aqueous phase and $C_{Sr(DCC)_2}^{in,nb}$ denotes the initial concentration of $Sr(DCC)_2$ in the organic phase of the system under consideration.