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Experimental evidences for some unusual divalent cation complexes of valinomycin

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Abstract From extraction experiments and γ-activity measurements, the exchange extraction constants corresponding to the general equilibrium M^{2+} (aq) + $\mathbf{1}\cdot\mathrm{Sr}^{2+}$ (nb) $\rightleftarrows$ $\mathbf{1}\cdot M^{2+}$ (nb) + Sr^{2+} (aq) taking place in the two-phase water-nitrobenzene system ($M^{2+} =$ Cu^{2+}, Zn^{2+}, Cd^{2+}, Pb^{2+}, UO_2^{2+}, Fe^{2+}, Co^{2+}, and Ni^{2+}; $\mathbf{1}$ = valinomycin; aq = aqueous phase, nb = nitrobenzene phase) were evaluated. Moreover, the stability constants of the $\mathbf{1}\cdot M^{2+}$ complexes in water saturated nitrobenzene were calculated; they were found to increase in the order $\mathrm{Fe}^{2+} < \mathrm{Cd}^{2+}$, $\mathrm{Co}^{2+} < \mathrm{Ni}^{2+} < \mathrm{UO}_2^{2+}$, $\mathrm{Zn}^{2+} < \mathrm{Cu}^{2+} < \mathrm{Pb}^{2+}$.

Keywords Antibiotics; Macrocycles; Complexation; Stability constants; Valinomycin.

Introduction

Valinomycin is one of the antibiotics facilitating the transport of cations across a biological membrane [1, 2]. The ability of valinomycin (see Scheme 1) to carry ions is primarily due to its forming a molecular complex with them. As revealed in particular for the K^+ complex by NMR [3–9], infrared spectra [3–7] and X-ray diffraction [10–13], the complex formation requires a change in the conformation of the depsipeptide ring after which the six peptide units fortify a bracelet-like form of the molecule by intramolecular hydrogen bonds and the six carbonylic groups adopt a hexadentate formation binding the metal cation by a polycentric dipolar bond. The change is more dramatic in polar media, where valinomycin has a propeller-like conformation [14] due to intermolecular hydrogen bonds with the solvent. Recently, experimental evidence for a valinomycin-proton complex has been reported [15].

The dicarbollylcobaltate anion and some of its halogen derivatives are very useful reagents for the extraction of alkali metal cations (especially Cs^+), and also – in the presence of polyoexyethylene compounds – for the extraction of Sr^{2+} and Ba^{2+} from aqueous solutions into an organic high-polar phase, both under laboratory conditions for purely theoretical or analytical purposes [16], and on the technological scale for the separation of some high-activity isotopes in reprocessing of spent nuclear fuel and acidic radioactive waste [17–19].

Up to now, complex species of copper, zinc, cadmium, lead, uranyl, iron, cobalt, and nickel with valinomycin have not been proved. In the present work, stability constants of Cu^{2+}, Zn^{2+}, Cd^{2+}, Pb^{2+}, UO_2^{2+} Fe^{2+}, Co^{2+}, and Ni^{2+} complexes of valinomycin in the organic phase of the water-nitrobenzene extraction system are determined.

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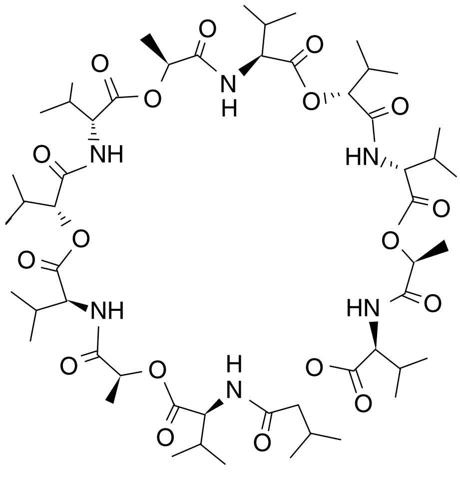

Scheme 1 Formula of valinomycin

Results and discussion

With regard to the previous results [20–23], the two-phase water- $M(NO_3)_2$ ($M^{2+} = Cu^{2+}$, Zn^{2+}, Cd^{2+}, Pb^{2+}, UO_2^{2+}, Fe^{2+}, Co^{2+}, and Ni^{2+})/nitrobenzene-$Sr(DCC)_2$ extraction system can be described by the following equilibrium (1) with the corresponding exchange extraction constant $K_{ex}(M^{2+}, Sr^{2+})$; aq and nb denote the presence of the species in the aqueous and nitrobenzene phases.

$$M^{2+}\ (aq) + Sr^{2+}\ (nb) \rightleftarrows M^{2+}\ (nb) + Sr^{2+}\ (aq) \quad (1)$$

For the constant $K_{ex}(M^{2+}, Sr^{2+})$ one can be write Eq. (2) where $K^i_{M^{2+}}$ and $K^i_{Sr^{2+}}$ are the individual extraction constants for M^{2+} and Sr^{2+} in the water – nitrobenzene system [20].

$$\log K_{ex}(M^{2+}, Sr^{2+}) = \log K^i_{M^{2+}} - \log K^i_{Sr^{2+}} \quad (2)$$

Knowing $\log K^i_{Cu^{2+}} = -11.5$, $\log K^i_{Zn^{2+}} = -11.6$, $\log K^i_{Cd^{2+}} = -11.5$, $\log K^i_{Pb^{2+}} = -10.6$, $\log K^i_{UO_2^{2+}} = -11.8$, $\log K^i_{Fe^{2+}} = -11.1$, $\log K^i_{Co^{2+}} = -11.4$, $\log K^i_{Ni^{2+}} = -11.6$ [22], and $\log K^i_{Sr^{2+}} = -10.7$, inferred from Refs. [20] and [23], the single exchange extraction constants $K_{ex}(M^{2+}, Sr^{2+})$ were simply calculated on the basis of Eq. (2). The corresponding data are given in Table 1.

In terms of previous papers [24, 25], the two-phase water-$M(NO_3)_2$ ($M^{2+} = Cu^{2+}$, Zn^{2+}, Cd^{2+}, Pb^{2+}, UO_2^{2+} Fe^{2+}, Co^{2+}, and Ni^{2+})/nitrobenzene-**1** (**1** = valinomycin)-$Sr(DCC)_2$ extraction system, chosen for determination of stability of the complex $\mathbf{1} \cdot M^{2+}$ in water saturated nitrobenzene, can be characterized by the main chemical equilibrium (3) to which the equilibrium extraction constant as shown by Eq. (4) corresponds.

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

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

It is necessary to emphasize that **1** is a considerably hydrophobic ligand, practically present in the nitrobenzene phase only, where this ligand forms relatively stable complexes $\mathbf{1} \cdot M^{2+}$ and $\mathbf{1} \cdot Sr^{2+}$ with the mentioned divalent cations.

Taking into account the conditions of electroneutrality in the organic and aqueous phases of the system under study, the mass balances of the considered divalent cations 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 obtain the final expression for the exchange extraction constant (Eq. (5)); $C^{in,aq}_{M(NO_3)_2}$ is the initial concentration of $M(NO_3)_2$ ($M^{2+} = Cu^{2+}$, Zn^{2+}, Cd^{2+}, Pb^{2+}, UO_2^{2+} Fe^{2+}, Co^{2+}, and Ni^{2+}) in the aqueous phase and $C^{in,nb}_{Sr(DCC)_2}$ denotes the initial concentration

Table 1 Equilibrium data for the M^{2+} and $\mathbf{1} \cdot M^{2+}$ cations in the two-phase water/nitrobenzene extraction system at 25°C ($M^{2+} = Sr^{2+}$, Cu^{2+}, Zn^{2+}, Cd^{2+}, Pb^{2+}, UO_2^{2+} Fe^{2+}, Co^{2+}, and Ni^{2+}; **1** = valinomycin; for the meaning of the constants see text)

Quantity	Sr^{2+}	Cu^{2+}	Zn^{2+}	Cd^{2+}	Pb^{2+}	UO_2^{2+}	Fe^{2+}	Co^{2+}	Ni^{2+}
$\log K^i_{M^{2+}}$	-10.7^a	-11.5^b	-11.6^b	-11.5^b	-10.6^b	-11.8^b	-11.1^b	-11.4^b	-11.6^b
$\log K_{ex}(M^{2+}, Sr^{2+})^c$	–	−0.8	−0.9	−0.8	0.1	−1.1	− 0.4	−0.7	−0.9
$\log K_{ex}(M^{2+}, \mathbf{1} \cdot Sr^{2+})^d$	–	0.2	−0.1	−0.4	1.7	−0.3	−0.4	−0.3	−0.2
$\log \beta_{nb}(\mathbf{1} \cdot M^{2+})^e$	5.4^f	6.4	6.2	5.8	7.0	6.2	5.4	5.8	6.1

[a] Inferred from Refs. [20] and [23]; [b] Ref. [22]; [c] calculated from Eq. (2) using data from Refs. [20], [22], and [23]; [d] calculated from Eq. (5); [e] calculated from Eq. (6) using data from Refs. [20], [22], [23], and [26]; [f] Ref. [26]

of $Sr(DCC)_2$ in the organic phase of the system under consideration.

$$K_{ex}(M^{2+}, \mathbf{1}\cdot Sr^{2+}) = \frac{1}{D_{Sr}} \frac{C^{in,nb}_{Sr(DCC)_2}}{(1+D_{Sr})C^{in,aq}_{M(NO_3)_2} - C^{in,nb}_{Sr(DCC)_2}} \qquad (5)$$

In this study, from the extraction experiments and γ-activity measurements by using Eq. (5), the logarithms of the constants $K_{ex}(M^{2+}, \mathbf{1}\cdot Sr^{2+})$ were determined and given in Table 1.

Furthermore, with respect to Refs. [24] and [25], for the extraction constants $K_{ex}(M^{2+}, Sr^{2+})$ and $K_{ex}(M^{2+}, \mathbf{1}\cdot Sr^{2+})$ defined above, as well as for the stability constants of the complexes $\mathbf{1}\cdot M^{2+}$ and $\mathbf{1}\cdot Sr^{2+}$ in nitrobenzene saturated with water, denoted by $\beta_{nb}(\mathbf{1}\cdot M^{2+})$ and $\beta_{nb}(\mathbf{1}\cdot Sr^{2+})$, one obtains Eq. (6).

$$\begin{aligned}\log \beta_{nb}(\mathbf{1}\cdot M^{2+}) = {} & \log \beta_{nb}(\mathbf{1}\cdot Sr^{2+}) \\ & + \log K_{ex}(M^{2+}, \mathbf{1}\cdot Sr^{2+}) \\ & - \log K_{ex}(M^{2+}, Sr^{2+}) \qquad (6)\end{aligned}$$

Using the constants log $K_{ex}(M^{2+}, Sr^{2+})$ and $\log K_{ex}(M^{2+}, \mathbf{1}\cdot Sr^{2+})$ given in Table 1, $\log \beta_{nb}(\mathbf{1}\cdot Sr^{2+}) = 5.4$ [26], and applying Eq. (6), we obtain the stability constants of the complexes $\mathbf{1}\cdot M^{2+}$ ($M^{2+} = Cu^{2+}, Zn^{2+}, Cd^{2+}, Pb^{2+}, UO_2^{2+}$ Fe^{2+}, Co^{2+}, and Ni^{2+}) in nitrobenzene saturated with water. These data are also summarized in Table 1.

In conclusion, it should be noted that the stability constant of the complex species $\mathbf{1}\cdot Ba^{2+}$ ($\mathbf{1}$ = valinomycin) in water saturated nitrobenzene is $\log \beta_{nb}(\mathbf{1}\cdot Ba^{2+}) = 6.5$ [27]. This value and the data reviewed in Table 1 indicate that the stability of the complex cation $\mathbf{1}\cdot M^{2+}$ in the mentioned medium increases in the series Sr^{2+}, $Fe^{2+} < Cd^{2+}$, $Co^{2+} < Ni^{2+} < UO_2^{2+}$, $Zn^{2+} < Cu^{2+} < Ba^{2+} < Pb^{2+}$.

Experimental

Valinomycin was purchased by Fluka, Buchs, Switzerland. Cs dicarbollylcobaltate, Cs*DCC*, was supplied by Katchem, Řež, Czech Republic. A nitrobenzene solution of hydrogen dicarbollylcobaltate (H*DCC*) was prepared from Cs*DCC* by the method described elsewhere [28]. The other chemicals used (Lachema, Brno, Czech Republic) were of reagent grade purity. The equilibration of the nitrobenzene solution of H*DCC* with stoichiometric $Sr(OH)_2$, which was dissolved in an aqueous solution of $Sr(NO_3)_2$ ($0.2 M$), yielded the corresponding $Sr(DCC)_2$ solution in nitrobenzene. The radionuclide $^{85}Sr^{2+}$ (DuPont, Belgium) was of standard radiochemical purity.

The extraction experiments were carried out in 10 cm³ glass test-tubes covered with polyethylene stoppers: 2 cm³ of an aqueous solution of $M(NO_3)_2$ ($M^{2+} = Cu^{2+}, Zn^{2+}, Cd^{2+}, Pb^{2+}, UO_2^{2+}$ Fe^{2+}, Co^{2+}, and Ni^{2+}) of the concentration in the range from 1×10^{-3} to $1\times 10^{-2} M$ and microamounts of $^{85}Sr^{2+}$ were added to 2 cm³ of a nitrobenzene solution of valinomycin and $Sr(DCC)_2$, whose initial concentrations varied also from 1×10^{-3} to $1\times 10^{-2} M$ (in all experiments, the initial concentration of valinomycin in nitrobenzene, $C_1^{in,nb}$, was always equal to the initial concentration of $Sr(DCC)_2$ in this medium, $C^{in,nb}_{Sr(DCC)_2}$). The test-tubes filled with the solutions were shaken for 2 h at 25 ± 1°C using a laboratory shaker. Under these conditions, the equilibria in the system under study were established after approximately 15 min of shaking. Then the phases were separated by centrifugation. Afterwards, 1 cm³ samples were taken from each phase and their γ-activities were measured using a well-type NaI(Tl) scintillation detector connected to a γ-analyzer NK 350 (Gamma, Budapest, Hungary).

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

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