

Short communication

Extraction and DFT Study on the Complexation of Zn²⁺ with Beauvericin

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Abstract

From extraction experiments and γ -activity measurements, the exchange extraction constant corresponding to the equilibrium $\text{Zn}^{2+}(\text{aq}) + \mathbf{1} \cdot \text{Sr}^{2+}(\text{nb}) \rightleftharpoons \mathbf{1} \cdot \text{Zn}^{2+}(\text{nb}) + \text{Sr}^{2+}(\text{aq})$ taking place in the two-phase water–nitrobenzene system ($\mathbf{1}$ = beauvericin; aq = aqueous phase, nb = nitrobenzene phase) was evaluated as $\log K_{\text{ex}}(\text{Zn}^{2+}, \mathbf{1} \cdot \text{Sr}^{2+}) = -0.3 \pm 0.1$. Further, the stability constant of the beauvericin – zinc complex (abbrev. $\mathbf{1} \cdot \text{Zn}^{2+}$) in nitrobenzene saturated with water was calculated for a temperature of 25 °C: $\log \beta_{\text{nb}}(\mathbf{1} \cdot \text{Zn}^{2+}) = 9.1 \pm 0.2$. Finally, by using quantum mechanical DFT calculations, the most probable structure of the $\mathbf{1} \cdot \text{Zn}^{2+}$ complex species was predicted.

Keywords: Beauvericin, zinc cation, complexation, extraction and stability constants, water – nitrobenzene system, DFT, complex structure

1. Introduction

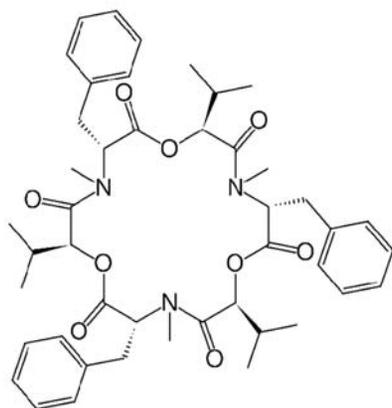
Beauvericin (abbrev. $\mathbf{1}$; see Scheme 1) is cyclic hexadepsipeptide with alternating methyl-phenylalanyl and hydroxy-iso-valeryl residues.¹ It was isolated from the fungus *Beauveria bassiana*, but it is also produced by other fungi, including several *Fusarium* species;² it may therefore occur in grain (such as corn, wheat, or barley) contaminated with these fungi.^{2–4} Its ion-complexing capability allows beauvericin to transport alkaline earth metal and alkali metal ions across cell membranes evidently in the same way as in the case of other related antibiotics.⁵

The dicarbollylcobaltate anion (DCC^-)⁶ and some of its halogen derivatives are very useful reagents for the 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 purely theoretical or analytical purposes,^{7–20} and on the technological scale for the separation of some high-activity isotopes in the reprocessing of spent nuclear fuel and acidic radioactive waste.^{21–23}

In the current work, the stability constant of the beauvericin · Zn²⁺ complex ($\mathbf{1} \cdot \text{Zn}^{2+}$) in nitrobenzene saturated with water was determined. Moreover, applying quantum mechanical DFT calculations, the most probable structure of this cationic complex species was derived. It is apparent that the considered structure may be an important contribution to the theoretical study of antibiotics.

2. Experimental

Beauvericin ($\mathbf{1}$; see Scheme 1) was purchased from Aldrich and it was employed as received. Cesium dicarbollylcobaltate (CsDCC) was synthesized by means of the method published by Hawthorne et al.²⁴ The other chemicals used (Lachema, Brno, Czech Republic) were of reagent grade purity. A nitrobenzene solution of hydrogen dicarbollylcobaltate (HDCC)⁶ was prepared from CsDCC by the method described elsewhere.²⁵ The equilibration of the nitrobenzene solution of HDCC with stoichiometric $\text{Sr}(\text{OH})_2$, which was dissolved in an aqueous solution of

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

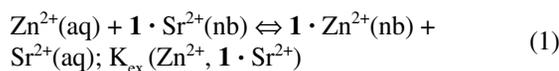
$\text{Sr}(\text{NO}_3)_2$ (0.20 mol/L), yielded the corresponding $\text{Sr}(\text{DCC})_2$ solution in nitrobenzene. The radionuclide $^{85}\text{Sr}^{2+}$ was supplied by DuPont, Belgium; its radionuclidic purity was 99.9%.

The extraction experiments were carried out in 10 mL polypropylene test-tubes with polypropylene stoppers: 2 mL of an aqueous solution of $\text{Zn}(\text{NO}_3)_2$ of a concentration in the range from 1×10^{-3} to 5×10^{-3} mol/L and 10 kBq of $^{85}\text{Sr}^{2+}$ were added to 2 mL of a nitrobenzene solution of **1** and $\text{Sr}(\text{DCC})_2$, the initial concentrations of which varied also from 1×10^{-3} to 5×10^{-3} mol/L (in all experiments, the initial concentration of **1** in nitrobenzene, $C_1^{\text{in,nb}}$, was equal to the initial concentration of $\text{Sr}(\text{DCC})_2$ in this medium, $C_{\text{Sr}(\text{DCC})_2}^{\text{in,nb}}$). The test-tubes filled with the solutions were shaken for 2 h at 25 ± 1 °C, using a laboratory shaker. Then the phases were separated by centrifugation. Afterwards, 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 NK 350 (Gamma, Budapest, Hungary).

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

3. Results and Discussion

Previous results^{26–29} indicated that the two-phase water– $\text{Zn}(\text{NO}_3)_2$ –nitrobenzene – **1** (beauvericin) – $\text{Sr}(\text{DCC})_2$ (strontium dicarbollylcolbaltate) extraction system (see Experimental), chosen for determination of the stability constant of the complex $\mathbf{1} \cdot \text{Zn}^{2+}$ in water-saturated nitrobenzene, can be characterized by the main chemical equilibrium



with the respective equilibrium extraction constant

$$K_{\text{ex}}(\text{Zn}^{2+}, \mathbf{1} \cdot \text{Sr}^{2+}):$$

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

It is necessary to emphasize that **1** is a considerably hydrophobic ligand, practically present in the nitrobenzene phase only, where it forms – with Zn^{2+} and Sr^{2+} – the very stable complexes $\mathbf{1} \cdot \text{Zn}^{2+}$ and $\mathbf{1} \cdot \text{Sr}^{2+}$, as given below.

Taking into account 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, $D_{\text{Sr}} = [\mathbf{1} \cdot \text{Sr}^{2+}]_{\text{nb}} / [\text{Sr}^{2+}]_{\text{aq}}$, combined with Eq. (2), we gain the final expression for $K_{\text{ex}}(\text{Zn}^{2+}, \mathbf{1} \cdot \text{Sr}^{2+})$ in the form

$$K_{\text{ex}}(\text{Zn}^{2+}, \mathbf{1} \cdot \text{Sr}^{2+}) = \frac{1}{D_{\text{Sr}}} \frac{C_{\text{Sr}(\text{DCC})_2}^{\text{in,nb}}}{(1 + D_{\text{Sr}}) C_{\text{Zn}(\text{NO}_3)_2}^{\text{in,aq}} - C_{\text{Sr}(\text{DCC})_2}^{\text{in,nb}}} \quad (3)$$

where $C_{\text{Zn}(\text{NO}_3)_2}^{\text{in,aq}}$ is the initial concentration of $\text{Zn}(\text{NO}_3)_2$ in the aqueous phase and $C_{\text{Sr}(\text{DCC})_2}^{\text{in,nb}}$ denotes the initial concentration of $\text{Sr}(\text{DCC})_2$ in the organic phase of the system under consideration.

In this study, from the extraction experiments and γ -activity measurements (see Experimental) by means of Eq. (3), the following value of the constant $K_{\text{ex}}(\text{Zn}^{2+}, \mathbf{1} \cdot \text{Sr}^{2+})$ was determined as $\log K_{\text{ex}}(\text{Zn}^{2+}, \mathbf{1} \cdot \text{Sr}^{2+}) = -0.3 \pm 0.1$.

Furthermore, with respect to previous results,^{26–29} for the extraction constant $K_{\text{ex}}(\text{Zn}^{2+}, \text{Sr}^{2+})$ corresponding to the equilibrium $\text{Zn}^{2+}(\text{aq}) + \text{Sr}^{2+}(\text{nb}) \rightleftharpoons \text{Zn}^{2+}(\text{nb}) + \text{Sr}^{2+}(\text{aq})$ and for the extraction constant $K_{\text{ex}}(\text{Zn}^{2+}, \mathbf{1} \cdot \text{Sr}^{2+})$ defined above, as well as for the stability constants of the complexes $\mathbf{1} \cdot \text{Zn}^{2+}$ and $\mathbf{1} \cdot \text{Sr}^{2+}$ in nitrobenzene saturated with water, denoted by $\beta_{\text{nb}}(\mathbf{1} \cdot \text{Zn}^{2+})$ and $\beta_{\text{nb}}(\mathbf{1} \cdot \text{Sr}^{2+})$, respectively, one gets

$$\log \beta_{\text{nb}}(\mathbf{1} \cdot \text{Zn}^{2+}) = \log \beta_{\text{nb}}(\mathbf{1} \cdot \text{Sr}^{2+}) + (\text{Zn}^{2+}, \mathbf{1} \cdot \text{Sr}^{2+}) - \log K_{\text{ex}}(\text{Zn}^{2+}, \text{Sr}^{2+}) \quad (4)$$

$$\log K_{\text{ex}}(\text{Zn}^{2+}, \mathbf{1} \cdot \text{Sr}^{2+})$$

Using the value $\log K_{\text{ex}}(\text{Zn}^{2+}, \text{Sr}^{2+}) = -0.9$ inferred from Reference 26, the constant $\log K_{\text{ex}}(\text{Zn}^{2+}, \mathbf{1} \cdot \text{Sr}^{2+})$ given above, $\log \beta_{\text{nb}}(\mathbf{1} \cdot \text{Sr}^{2+}) = 8.5 \pm 0.1$,³⁰ and applying Eq. (4), we obtain the stability constant of the $\mathbf{1} \cdot \text{Zn}^{2+}$ complex in water-saturated nitrobenzene as $\log \beta_{\text{nb}}(\mathbf{1} \cdot \text{Zn}^{2+}) = 9.1 \pm 0.2$. This means that in the mentioned nitrobenzene medium, the stability of the $\mathbf{1} \cdot \text{Zn}^{2+}$ complex under study is somewhat higher than that of the cationic complex species $\mathbf{1} \cdot \text{Sr}^{2+}$ with the same beauvericin ligand **1**.

The quantum mechanical calculations were carried out at the density functional level of theory (DFT, B3LYP functional)^{31,32} using the Gaussian 03 suite of programs.³³

The 6–31G(d) basis set was used and the optimizations were unconstrained. In order to increase the numerical accuracy and to reduce oscillations during the molecular geometry optimization, two-electron integrals and their derivatives were calculated by using the pruned (99,590) integration grid, having 99 radial shells and 590 angular points per shell, which was requested by means of the Gaussian 03 keyword “Int=UltraFine”.

Although a possible influence of a polar solvent on the detailed structures of **1** and the $\mathbf{1} \cdot \text{Zn}^{2+}$ complex species could be imagined, our quantum mechanical calculations in similar cases, performed in an analogous way, showed very good agreement of experiment with theory.^{34–41}

In the model calculations, we optimized the molecular geometries of the parent beauvericin ligand **1** and its complex with Zn^{2+} . The optimized structure of the free ligand **1** with C_3 symmetry is illustrated in Figure 1.

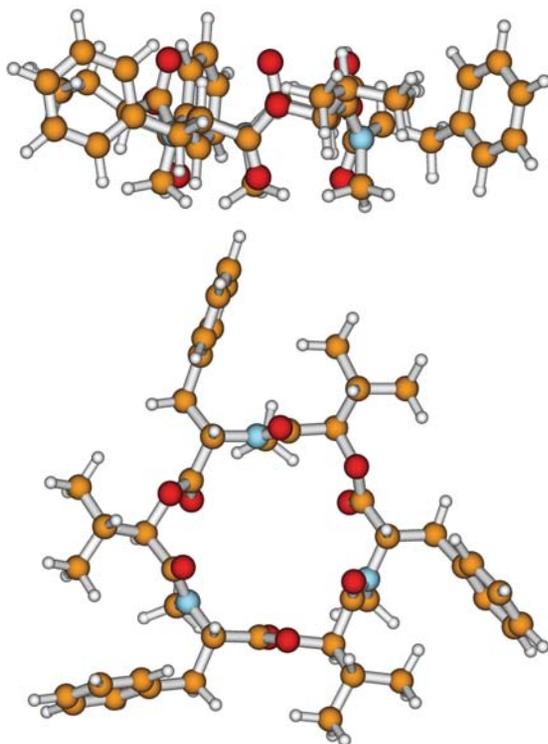


Figure 1. Two projections of the DFT optimized structure of free ligand **1** [B3LYP/6-31G(d)].

In Figure 2, the structure obtained by the full DFT optimization of the $\mathbf{1} \cdot \text{Zn}^{2+}$ complex having also C_3 symmetry is depicted, together with the lengths of the corresponding bonds (in Å; 1 Å = 0.1 nm). As follows from this figure, the complexation with the Zn^{2+} cation changes the overall shape of the parent ligand **1** only slightly. In the resulting $\mathbf{1} \cdot \text{Zn}^{2+}$ cationic complex species, which is most energetically favoured, the “central” cation Zn^{2+} is bound by nine bond interactions to nine oxygen atoms (2.22, 2.07, 3.62, 2.22, 2.07, 3.62, 2.22, 2.07 and 3.62 Å) of the parent beauvericin ligand **1**.

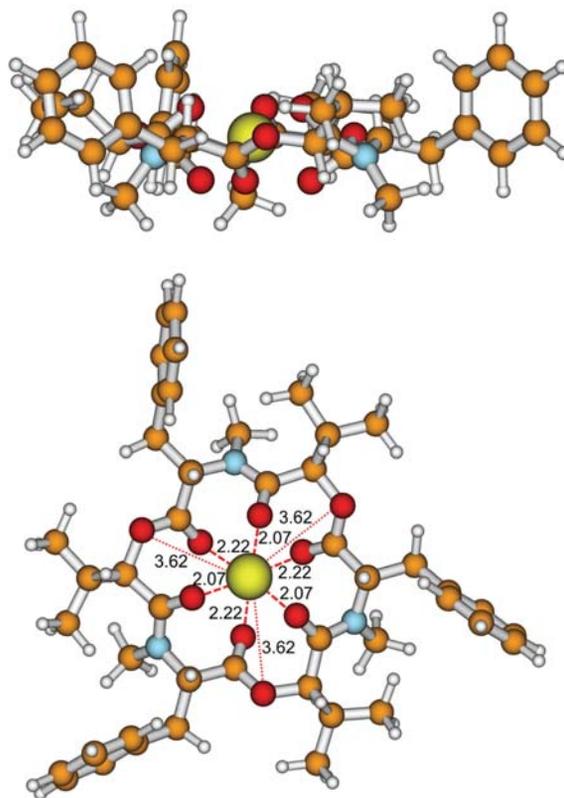


Figure 2. Two projections of the DFT optimized structure of the $\mathbf{1} \cdot \text{Zn}^{2+}$ complex [B3LYP/6-31G(d)].

Finally, the interaction energy, $E(\text{int})$, of the $\mathbf{1} \cdot \text{Zn}^{2+}$ complex [calculated as the difference between the electronic energies of $\mathbf{1} \cdot \text{Zn}^{2+}$ and isolated **1** and Zn^{2+} species: $E(\text{int}) = E(\mathbf{1} \cdot \text{Zn}^{2+}) - E(\mathbf{1}) - E(\text{Zn}^{2+})$] was found to be -1652.3 kJ/mol, which confirms the formation of the cationic complex $\mathbf{1} \cdot \text{Zn}^{2+}$.

4. Conclusions

In summary, we have demonstrated that a complementary experimental and theoretical approach can provide important information on the beauvericin (**1**) ligand complexation with the zinc cation. From the experimental investigation of the resulting complex $\mathbf{1} \cdot \text{Zn}^{2+}$ in the two-phase water–nitrobenzene extraction system, the strength of the considered $\mathbf{1} \cdot \text{Zn}^{2+}$ cationic complex species in nitrobenzene saturated with water was characterized quantitatively by the stability constant, $\log \beta_{\text{nb}}(\mathbf{1} \cdot \text{Zn}^{2+}) = 9.1 \pm 0.2$ (for a temperature of 25 °C). By using theoretical quantum mechanical DFT calculations, the structural details of the $\mathbf{1} \cdot \text{Zn}^{2+}$ complex, such as position of the Zn^{2+} cation with regard to the parent beauvericin ligand **1** as well as the significant interatomic distances within the complex species under study, were obtained.

5. Acknowledgements

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Povzetek

S pomočjo ekstrakcijskih eksperimentov in meritev γ -aktivnosti smo določili konstanto ravnotežja $\text{Zn}^{2+}(\text{aq}) + \mathbf{1} \cdot \text{Sr}^{2+}(\text{nb}) \Leftrightarrow \mathbf{1} \cdot \text{Zn}^{2+}(\text{nb}) + \text{Sr}^{2+}(\text{aq})$ v dvofaznem sistemu voda-nitrobenzen ($\mathbf{1}$ = beauvericin; aq = vodna faza, nb = faza nitrobenzena), $\log K_{\text{ex}}(\text{Zn}^{2+}, \mathbf{1} \cdot \text{Sr}^{2+}) = -0.3 \pm 0.1$. Pri temperaturi 25 °C smo ocenili konstanto stabilnosti kompleksa beauvericin – cink ($\mathbf{1} \cdot \text{Zn}^{2+}$) v nitrobenzenu, nasičenem z vodo, $\log \beta_{\text{nb}}(\mathbf{1} \cdot \text{Zn}^{2+}) = 9.1 \pm 0.2$. Z uporabo kvantno mehan-
skih DFT izračunov smo predvideli najbolj verjetno strukturo kompleksa $\mathbf{1} \cdot \text{Zn}^{2+}$.