Experimental and Theoretical Study on the Complexation of Beauvericin with the Ammonium Cation

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Abstract

From extraction experiments and γ-activity measurements, the extraction constant corresponding to the equilibrium $NH_4^+(aq) + NaL^+ (nb) \Leftrightarrow NH_4L^+(nb) + Na^+ (aq)$ taking place in the two-phase water–nitrobenzene system (L = beauvericin; aq = aqueous phase, nb = nitrobenzene phase) was evaluated as log K_{ex} (NH_4^+, NaL^+) = 1.5 ± 0.1. Further, the stability constant of the NH_4L^+ complex in water-saturated nitrobenzene was calculated for a temperature of 25 °C as log β_{nb} (NH_4L^+) = 4.6 ± 0.2. Finally, by using quantum mechanical DFT calculations, the most probable structure of the NH_4L^+ cationic complex species was derived. In this complex having C_3 symmetry, the ammonium cation NH_4^+ is bound by three strong linear hydrogen bonds to the three corresponding oxygen atoms of the parent beauvericin ligand L. The interaction energy of the resulting complex NH_4L^+ was found to be –828.8 kJ/mol, confirming the formation of the considered complex NH_4L^+.

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

1. Introduction

Beauvericin (abbrev. L; see Scheme 1) is a cyclic hexadepsipeptide with alternating methyl-phenylalanyl and hydroxyl-iso-valeryl residues.[1] For the first time, beauvericin was isolated from the fungus *Beauveria bassiana*. It was further found that the antibiotic beauvericin was produced by many other fungi (e. g., by some *Fusarium* species) so that this compound, which belongs to the enniatin family, can occur very often in grain contaminated with these fungi.[2–4]

The dicarbollylcobaltate anion (DCC⁻)[5] and some of its halogen derivatives are very useful reagents for the extraction of various metal cations (especially Cs⁺, Sr²⁺, Ba²⁺, Eu³⁺ and Am³⁺) from aqueous solutions into a polar organic phase, both under laboratory conditions for purely theoretical or analytical purposes,[6–22] and on the technological scale for the separation of some high-activity iso-
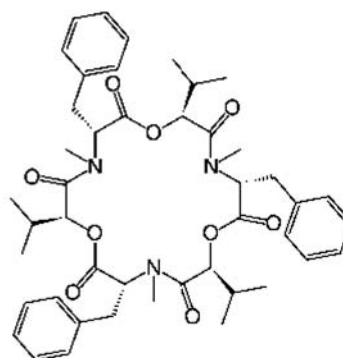
Scheme 1. Structural formula of beauvericin (abbrev. L).

topes in the reprocessing of spent nuclear fuel and acidic radioactive waste.[23,24]

Recently, the complexation of the ammonium cation with valinomycin has been investigated in methanolic

medium.[25] On the other hand, in the current work, the stability constant of the beauvericin complex with NH_4^+ (i. e., NH_4L^+) was determined in the organic phase of the water-nitrobenzene extraction system. Moreover, applying quantum mechanical DFT calculations, the most probable structure of the NH_4L^+ cationic complex species was predicted.

2. Experimental

Beauvericin (L; see Scheme 1) was purchased from Aldrich. Cesium dicarbollylcobaltate (CsDCC) was synthesized by means of the method published by Hawthorne et. al.[26] 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.[27] The equilibration of the nitrobenzene solution of HDCC with stoichiometric NaOH, which was dissolved in an aqueous solution of NaCl (0.20 mol/L), yielded the corresponding NaDCC solution in nitrobenzene. The radionuclide $^{22}Na^+$ (DuPont, Belgium) was of standard radiochemical purity.

The extraction experiments were carried out in 10 mL polypropylene test-tubes with polypropylene stoppers: 2 mL of an aqueous solution of NH_4Cl (1×10^{-2} to 3×10^{-2} mol/L) and microamounts of $^{22}Na^+$ were added to 2 mL of a nitrobenzene solution of L and NaDCC, whose initial concentrations varied also from 1×10^{-2} to 3×10^{-2} mol/L (in all experiments, the initial concentration of L in nitrobenzene, $C_L^{in,nb}$, was equal to the initial concentration of NaDCC in this medium, $C_{NaDCC}^{in,nb}$). 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 sodium, D_{Na}, were determined as the ratios of the measured radioactivities of $^{22}Na^+$ in the nitrobenzene and aqueous samples.

3. Results and Discussion

With respect to the results of previous papers,[5,28,29] the two–phase water–NH_4Cl–nitrobenzene–sodium dicarbollylcobaltate (NaDCC) extraction system can be described by the following equilibrium
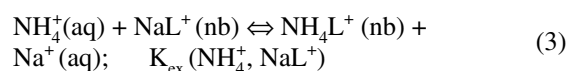
$$NH_4^+(aq) + Na^+(nb) \Leftrightarrow$$
$$NH_4^+(nb) + Na^+(aq); \quad K_{ex}(NH_4^+, Na^+) \quad (1)$$
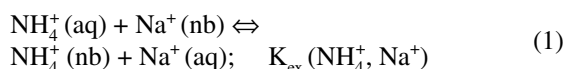
with the c,orresponding exchange extraction constant K_{ex} (NH_4^+, Na^+); aq and nb denote the presence of the species

in the aqueous and nitrobenzene phases, respectively. For the constant K_{ex} (NH_4^+, Na^+) one can write[5,28,29]

$$\log K_{ex}(NH_4^+, Na^+) = \log K_{NH_4^+}^i - \log K_{Na^+}^i \quad (2)$$

where $K_{NH_4^+}^i$ and $K_{Na^+}^i$ are the individual extraction constants for NH_4^+ and Na^+, respectively, in the water-nitrobenzene system.[28] Knowing the values $\log K_{NH_4^+}^i = -4.7$ [28] and $\log K_{Na^+}^i = -6.0$,[28] the exchange extraction constant K_{ex} (NH_4^+, Na^+) was simply calculated from Eq. (2) as $\log K_{ex}$ (NH_4^+, Na^+) = 1.3.

Previous results[30–33] indicated that the two–phase water–NH_4Cl–nitrobenzene–NaDCC–L (beauvericin) extraction system (see Experimental), chosen for determination of the stability constant of the complex NH_4L^+ in water-saturated nitrobenzene, can be characterized by the main chemical equilibrium

$$NH_4^+(aq) + NaL^+(nb) \Leftrightarrow NH_4L^+(nb) +$$
$$Na^+(aq); \quad K_{ex}(NH_4^+, NaL^+) \quad (3)$$

with the respective equilibrium extraction constant K_{ex} (NH_4^+, NaL^+):

$$K_{ex}(NH_4^+, NaL^+) = \frac{[NH_4L^+]_{nb}[Na^+]_{aq}}{[NH_4^+]_{aq}[NaL^+]_{nb}} \quad (4)$$

It is necessary to emphasize that L is a considerably hydrophobic ligand, practically present in the nitrobenzene phase only, where this ligand forms – with NH_4^+ and Na^+ – the relatively stable complexes NH_4L^+ and NaL^+.

Taking into account the conditions of electroneutrality in the organic and aqueous phases of the system under study, the mass balances of NH_4^+ and Na^+ cations at equal volumes of the nitrobenzene and aqueous phases, as well as the measured equilibrium distribution ratio of sodium, $D_{Na} = [NaL^+]_{nb} / [Na^+]_{aq}$, combined with Eq. (4), we get the final expression for $K_{ex}(NH_4^+, NaL^+)$ in the form

$$K_{ex}(NH_4^+, NaL^+) = \frac{1}{D_{Na}} \frac{C_{NaDCC}^{in,nb}}{(1 + D_{Na}) C_{NH_4Cl}^{in,aq} - C_{NaDCC}^{in,nb}} \quad (5)$$

where $C_{NH_4Cl}^{in,aq}$ is the initial concentration of NH_4Cl in aqueous phase and $C_{NaDCC}^{in,nb}$ denotes the initial concentration of NaDCC 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. (5), the following value of the constant K_{ex} (NH_4^+, NaL^+) was determined as $\log K_{ex}$ (NH_4^+, NaL^+) = 1.5 ± 0.1.

Furthermore, with regard to previous papers,[30–33] for the extraction constants K_{ex} (NH_4^+, Na^+) and K_{ex} (NH_4^+, NaL^+) defined above, as well as for the stability constants of the complexes NH_4L^+ and NaL^+ in nitrobenzene saturated with water, denoted by β_{nb} (NH_4L^+) and β_{nb} (NaL^+), respectively, one can formulate

$$\log \beta_{nb}(NH_4L^+) = \log \beta_{nb}(NaL^+) + \\ \log K_{ex}(NH_4^+, NaL^+) - \log K_{ex}(NH_4^+, Na^+) \tag{6}$$

Using the constants $\log K_{ex}(NH_4^+, Na^+)$ and $\log K_{ex}(NH_4^+, NaL^+)$ given above, the value $\log \beta_{nb}(NaL^+) = 4.4 \pm 0.1$,[34] and applying Eq. (6), we obtain the stability constant of the NH_4L^+ complex in water-saturated nitrobenzene at 25 °C as $\log \beta_{nb}(NH_4L^+) = 4.6 \pm 0.2$. This means that the stability constants of the cationic complex species NH_4L^+ and NaL^+ in the mentioned nitrobenzene medium are comparable. In this context it should be noted that the stability constant of the complex NH_4L^+, where L is valinomycin, in nitrobenzene saturated with water is $\log \beta_{nb}(NH_4L^+) = 8.4 \pm 0.1$.[35] Thus, in this medium, the stability of the NH_4L^+ complex (L = valinomycin) is substantially higher than that of the species NH_4L^+ (L = beauvericin) under study.

The quantum mechanical calculations were carried out at the density functional level of theory (DFT, B3LYP functional) using the Gaussian 03 suite of programs.[36] 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 keywords "Int = UltraFine".

Although a possible influence of a polar solvent on the detailed structures of L and NH_4L^+ 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.[37–44]

In the model calculations, we optimized the molecular geometries of the parent beauvericin ligand L and its complex species with NH_4^+. The optimized structure of the free ligand L with C_3 symmetry is illustrated in Figure 1.

In Figure 2, the structure obtained by the full DFT optimization of the NH_4L^+ complex having also C_3 symmetry is depicted, together with the lengths of the corresponding hydrogen bonds (in Å ; 1Å = 0.1 nm). As follows from this figure, the complexation with the NH_4^+ cation changes the overall shape of the parent ligand L only slightly. In the resulting NH_4L^+ cationic complex species, which is most energetically favoured, the "central" cation NH_4^+ is bound by three strong linear hydrogen bonds to the corresponding carbonyl oxygen atoms (1.72, 1.72 and 1.72 Å) of the parent beauvericin ligand L.
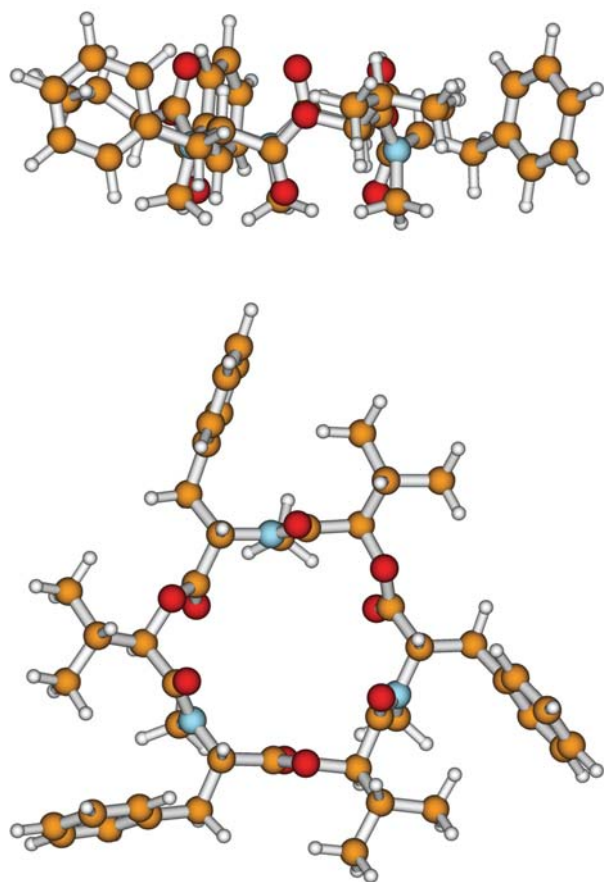

Figure 1. Two projections of the DFT optimized structure of free beauvericin ligand L [B3LYP/6–31G(d)].
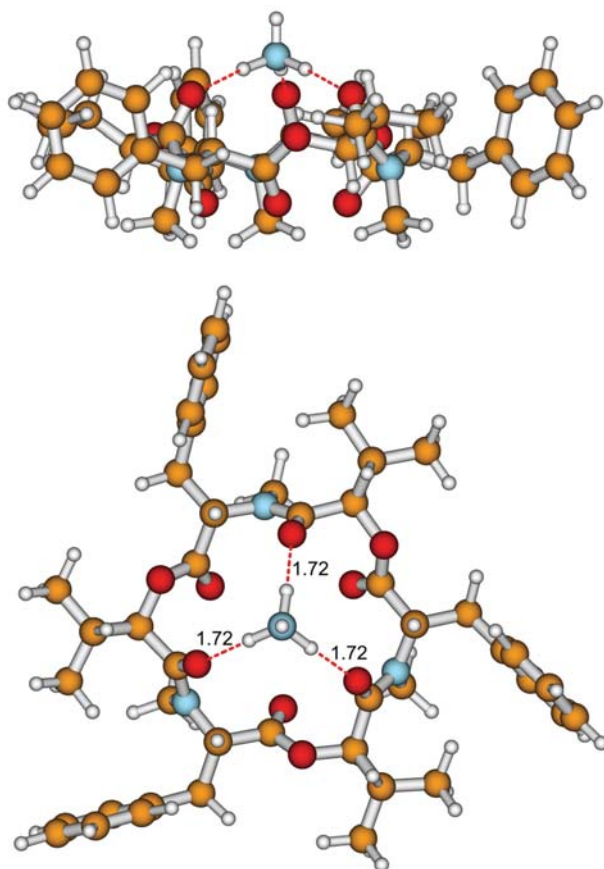

Figure 2. Two projections of the DFT optimized structure of the NH_4L^+ complex [B3LYP/6-31G(d)]. Hydrogen bond lengths of NH_4^+ to the three corresponding carbonyl oxygens of L are 1.72, 1.72 and 1.72 Å.

Finally, the interaction energy, E(int), of the NH_4L^+ complex [calculated as the difference between the pure electronic energies of the complex NH_4L^+ and isolated L and NH_4^+ species: E(int) = $E(NH_4L^+)$ − E(L) − $E(NH_4^+)$] was found to be –828.8 kJ/mol, which confirms the formation of the cationic complex NH_4L^+.

4. Conclusions

In summary, we have demonstrated that a complementary experimental and theoretical approach can provide important information on the beauvericin ligand L complexation with the ammonium cation. From the experimental investigation of the resulting complex NH_4L^+ in the two–phase water–nitrobenzene extraction system, the strength of the considered NH_4L^+ cationic complex species in nitrobenzene saturated with water was characterized quantitatively by the stability constant, log β_{nb} (NH_4L^+) = 4.6 ± 0.2 (for a temperature of 25 °C). By using the theoretical quantum mechanical DFT calculations, the structural details of the NH_4L^+ complex, such as position of the NH_4^+ cation with regard to the parent beauvericin ligand L as well as the significant interatomic distances within the complex species under study, were obtained.

5. Acknowledgements

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Povzetek

Z raziskavami ekstrakcije in meritvami γ-aktivnosti smo določili konstanto ekstrakcije za ravnotežje $NH_4^+(aq) + NaL^+$ (nb) $\Leftrightarrow NH_4L^+(nb) + Na^+ (aq)$ v dvofaznem sistemu voda-nitrobenzen (L = beauvericin; aq = vodna, nb = nitrobenzen), ki znaša $K_{ex} (NH_4^+, NaL^+) = 1.5 \pm 0.1$. Nadalje smo v vodi, nasičeni z nitrobenzenom, pri 25 °C določili konstanto stabilnosti kompleksa NH_4L^+, log $\beta_{nb} (NH_4L^+) = 4.6 \pm 0.2$. Z uporabo kvantno mehanskih DFT računov smo predvideli najbolj verjetno strukturo NH_4L^+ kationskega kompleksa.