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 \( \text{NH}_4^+(\text{aq}) + \text{NaL}^- (\text{nb}) \Leftrightarrow \text{NH}_4\text{L}^+ (\text{nb}) + \text{Na}^+ (\text{aq}) \) taking place in the two-phase water–nitrobenzene system (L = beauvericin; aq = aqueous phase, nb = nitrobenzene phase) was evaluated as \( \log K_{\text{ex}} (\text{NH}_4^+, \text{NaL}^+) = 1.5 \pm 0.1 \). Further, the stability constant of the \( \text{NH}_4\text{L}^+ \) complex in water-saturated nitrobenzene was calculated for a temperature of 25 °C as \( \log \beta_{\text{nb}} (\text{NH}_4\text{L}^+) = 4.6 \pm 0.2 \). Finally, by using quantum mechanical DFT calculations, the most probable structure of the \( \text{NH}_4\text{L}^+ \) cationic complex species was derived. In this complex having C3 symmetry, the ammonium cation \( \text{NH}_4^+ \) 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 \( \text{NH}_4\text{L}^+ \) was found to be \(-828.8 \text{ kJ/mol}\), confirming the formation of the considered complex \( \text{NH}_4\text{L}^+ \).

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. 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 isotopes 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. On the other hand, in the current work, the stability constant of the beauvericin complex with NH₄⁺ (i.e., NH₄L⁺) was determined in the organic phase of the water-nitrobenzene extraction system. Moreover, applying quantum mechanical DFT calculations, the most probable structure of the NH₄⁺–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. The other chemicals used (Lachema, Brno, Czech Republic) were of reagent grade purity. A nitrobenzene solution of hydrogen dicarbollylcobaltate (HDCC) was prepared from CsDCC by the procedure described elsewhere. The equilibrium 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 ²²Na⁺ (DuPont, Belgium) was of standard radiochemical purity.

The equilibrium distribution ratios of sodium, D Na⁺, were determined as the ratios of the measured radioactivities of ²²Na⁺ in the nitrobenzene and aqueous samples. In the aqueous and nitrobenzene phases, respectively. For the constant Ke(NH₄⁺, Na⁺) one can write

\[ \log K_{ex}(\text{NH}_4^+, \text{Na}^+) = \log K_{\text{Na}^+} - \log K_{\text{NH}_4^+} \]  

(2)

where \( K_{\text{NH}_4^+} \) and \( K_{\text{Na}^+} \) are the individual extraction constants for NH₄⁺ and Na⁺, respectively, in the water-nitrobenzene system. Knowing the values log \( K_{\text{NH}_4^+} = -4.7 \) and log \( K_{\text{Na}^+} = -6.0 \), the exchange extraction constant \( K_{ex}(\text{NH}_4^+, \text{Na}^+) \) was simply calculated from Eq. (2) as log \( K_{ex}(\text{NH}_4^+, \text{Na}^+) = 1.3 \).

Previous results indicated that the two-phase water–N₄Cl–nitrobenzene–NaDCC–L (beauvericin) extraction system (see Experimental), chosen for determination of the stability constant of the complex NH₄L⁺ in water-saturated nitrobenzene, can be characterized by the main chemical equilibrium

\[ \text{NH}_4^+(aq) + \text{NaL}^+(nb) \rightleftharpoons \text{NH}_4L^+(nb) + \text{Na}^+(aq); \quad K_{ex}(\text{NH}_4^+, \text{NaL}^+) \]  

(3)

with the respective equilibrium extraction constant \( K_{ex}(\text{NH}_4^+, \text{NaL}^+) \):

\[ K_{ex}(\text{NH}_4^+, \text{NaL}^+) = \frac{[\text{NH}_4L^+]}{[\text{NH}_4^+][\text{NaL}^+]} \]  

(4)

It is necessary to emphasize that L is a considerably hydrophobic ligand, practically present in the nitrobenzene phase only, while this ligand forms – with NH₄⁺ and Na⁺ – the relatively stable complexes NH₄L⁺ and NaL⁺.

Taking into account the conditions of electroneutrality in the organic and aqueous phases of the system under study, the mass balances of NH₄⁺ 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⁺] / [Na⁺], combined with Eq. (4), we get the final expression for \( K_{ex}(\text{NH}_4^+, \text{NaL}^+) \) in the form

\[ K_{ex}(\text{NH}_4^+, \text{NaL}^+) = \frac{1}{D_{\text{Na}^+}} \frac{C_{\text{NaCl}}^{\text{in}}}{(1 + D_{\text{Na}^+}) C_{\text{NaDCC}}^{\text{in}} 

(5)

where \( C_{\text{NaCl}}^{\text{in}} \) is the initial concentration of NH₄Cl in aqueous phase and \( C_{\text{NaDCC}}^{\text{in}} \) denotes the initial concentration of NaDCC in the organic phase of the system under consideration.

In this study, from the extraction experiments and activity measurements (see Experimental) by means of Eq. (5), the following value of the constant \( K_{ex}(\text{NH}_4^+, \text{NaL}^+) \) was determined as log \( K_{ex}(\text{NH}_4^+, \text{NaL}^+) = 1.5 \pm 0.1 \).

Furthermore, with regard to previous papers, the extraction constants \( K_{ex}(\text{NH}_4^+, \text{Na}^+) \) and \( K_{ex}(\text{NH}_4^+, \text{NaL}^+) \) defined above, as well as for the stability constants of the complex NH₄L⁺ and NaL⁺ in nitrobenzene saturated with water, denoted by \( \beta_{\text{nb}}(\text{NH}_4L^+) \) and \( \beta_{\text{nb}}(\text{NaL}^+) \), respectively, one can formulate

\[ \beta_{\text{nb}}(\text{NH}_4L^+) = K_{ex}(\text{NH}_4^+, \text{NaL}^+) \]

\[ \beta_{\text{nb}}(\text{NaL}^+) = K_{ex}(\text{NH}_4^+, \text{NaL}^+) \]

3. Results and Discussion

With respect to the results of previous papers, the two-phase water–N₄Cl–nitrobenzene–sodium dicarbollylcobaltate (NaDCC) extraction system can be described by the following equilibrium

\[ \text{NH}_4^+(aq) + \text{Na}^+(nb) \rightleftharpoons \text{NH}_4L^+(nb); \quad K_{ex}(\text{NH}_4^+, \text{Na}^+) \]  

(1)

with the corresponding exchange extraction constant \( K_{ex}(\text{NH}_4^+, \text{Na}^+) \); aq and nb denote the presence of the species.
log $\beta_{nb}^{\text{H}^{+}}$ (NH$_4$L$^+$) = log $\beta_{nb}^{\text{Na}^{+}}$ (NaL$^+$) + log $K_{ex}^{\text{H}^{+}}$ (NH$_4^+$,NaL$^+$) – log $K_{ex}^{\text{H}^{+}}$ (NH$_4^+$,Na$^+$) \quad (6)

Using the constants log $K_{ex}^{\text{H}^{+}}$ (NH$_4^+$,Na$^+$) and log $K_{ex}^{\text{H}^{+}}$ (NH$_4^+$,NaL$^+$) given above, the value log $\beta_{nb}^{\text{Na}^{+}}$ (NaL$^+$) = 4.4 ± 0.1, and applying Eq. (6), we obtain the stability constant of the NH$_4$L$^+$ complex in water-saturated nitrobenzene at 25 °C as log $\beta_{nb}^{\text{H}^{+}}$ (NH$_4$L$^+$) = 4.6 ± 0.2. This means that the stability constants of the cationic complex species NH$_4$L$^+$ and NaL$^+$ in the mentioned nitrobenzene medium are comparable. In this context it should be noted that the stability constant of the complex NH$_4$L$^+$, where L is valinomycin, in nitrobenzene saturated with water is log $\beta_{nb}^{\text{H}^{+}}$ (NH$_4$L$^+$) = 8.4 ± 0.1. Thus, in this medium, the stability of the NH$_4$L$^+$ complex (L = valinomycin) is substantially higher than that of the species NH$_4$L$^+$ (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. 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$_4$L$^+$ 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.

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$_4$L$^+$ 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$_4$L$^+$ 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.

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**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$_4$L$^+$ 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 NH4L+ complex [calculated as the difference between the pure electronic energies of the complex NH4L+ and isolated L and NH4+ species: E(int) = E(NH4L+) – E(L) – E(NH4+) was found to be ~828.8 kJ/mol, which confirms the formation of the cationic complex NH4L+.

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 NH4L+ in the two-phase water–nitrobenzene extraction system, the strength of the considered NH4L+ cationic complex species in nitrobenzene saturated with water was characterized quantitatively by the stability constant, log βab (NH4L+) = 4.6 ± 0.2 (for a temperature of 25 °C). By using the theoretical quantum mechanical DFT calculations, the structural details of the NH4L+ complex, such as position of the NH4+ 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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6. References

Z raziskavami ekstrakcije in meritvami $\gamma$-aktivnosti smo določili konstanto ekstrakcije za ravnotežje $\text{NH}_4^+(aq) + \text{Na}^+ L^+ (nb) \Leftrightarrow \text{NH}_4^+ L^+(nb) + \text{Na}^+ (aq)$ v dvo faznem sistemu voda-nitrobenzen (L = beauvericin; aq = vodna, nb = nitrobenzen), ki znaša $K_{ex} (\text{NH}_4^+, \text{Na}^+ L^+) = 1.5 \pm 0.1$. Nahajšo smo v vodi, nasičeni z nitrobenzenom, pri 25 °C določili konstanto stabilnosti kompleksa $\text{NH}_4^+ L^+$, $\log \beta_{nb} (\text{NH}_4^+ L^+) = 4.6 \pm 0.2$. Z uporabo kvantno mehanskih DFT računov smo predvideli najbolj verjetno strukturo $\text{NH}_4^+ L^+$ kationskega kompleksa.