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Molecular recognition of crown ethers by β-lactose in aqueous solutions

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Densimetric and viscosimetric measurements have been combined to conform the associate formation of β-lactose with 15-crown-5 but not with 18-crown-6 in dilute aqueous solution.

The cellular molecular recognition of physiologically active compounds (hormones, toxins, drugs, *etc.*) is of considerable interest. Oligosaccharides located at cell membrane surfaces are the receptors of molecular ligands.[1–3] This trend is true of natural and artificial macrocyclic ligands.[4–6] They are often considered as models for studying enzymes and cyclic antibiotics. 15-Crown-5 and 18-crown-6 and the disaccharide β-lactose were used as test materials.

Recently,[7] we found that β-lactose forms a thermodynamically stable 1:1 associate with 15-crown-5. For 18-crown-6, associate formation has not been found. The aim of this work is not only to confirm these results but to obtain information on the nature of the interacting molecules and factors having influence on the molecular recognition in these systems. The results of densimetric and viscosimetric studies[†] are presented in Figures 1–3. The apparent molar volumes of β-lactose (ϕ_{vlac}) in water and aqueous solutions of 15-crown-5 and 18-crown-6 were calculated according to a known equation.[8] The limiting partial molar volumes of β-lactose ($\overline{V}^0_{\mathrm{lac}}$) were calculated from the molar volumes of solution[9]

$$V_{\mathrm{s}} = (1000 + mM_2)/\rho,$$

where M_2 is the molar mass of the solute, m is its molality, and ρ is the density of solution. The molar volumes were adequately represented by the linear equation

$$V_{\mathrm{s}} = V_1 + \overline{V}^0_{\mathrm{lac}} m_{\mathrm{lac}},$$

where V_1 is the molar volume of binary solvent (aqueous crown ether, $m_{\mathrm{cr}} = 0.04$ mol kg^{-1}).

Note that the $\overline{V}^0_{\mathrm{lac}}$ value in water equal to $(207.5\pm0.2)\times\times10^{-6}$ m^3 mol^{-1} agrees well with published data.[10] On the basis of the above values, the volumes of transfer of β-lactose (V^0_{trlac}) from water to aqueous solutions of the crown ethers were determined.[8]

The volumetric data suggest different behaviours of the crown ether in relation to β-lactose. As can be seen in Figure 1, the $\phi_{\mathrm{vlac}} = f(m_{\mathrm{lac}})$ dependence for 15-crown-5 exhibits a maximum at $m_{\mathrm{lac}}:m_{\mathrm{cr}} = 1:1$. In water and the aqueous solution of 18-crown-6 similar extrema have not been found. Such a maximum may be due to a rearrangement of water molecules in the hydration cospheres of the disaccharide and crown ether at 1:1 associate formation. Because this process is accompanied by a positive volume change ($V^0_{\mathrm{trlac}} = 0.8\times10^{-6}$ m^3 mol^{-1}), according to the cosphere overlap model,[12,13] the interactions between β-lactose and 15-crown-5 involving hydrophilic groups are dominant. Water molecules from the hydration cospheres of these groups are forced out to the bulk. Therefore, the associate formation should be accompanied by a significant solvent reorganization. The resultant volume change is determined by difference between the structure of water in the hydration cospheres and in the bulk. The relaxation of the electrostricted water molecules from the cospheres of polar groups to more structured bulk results in a positive volume changes. The V^0_{trlac} value in aqueous 18-crown-6 is also positive and equal to 0.6×10^{-6} m^3 mol^{-1}. This means that the mechanism of the interactions of β-lactose with both the crown ethers is the same but for 18-crown-6 such interactions do not lead to associate formation.

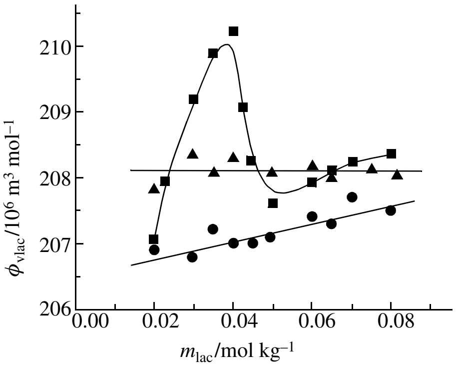

Figure 1 Dependence of the apparent molar volume of β-lactose (ϕ_{vlac}) on its concentration in water (●) and aqueous solutions of 15-crown-5 (■) and 18-crown-6 (▲) ($m_{\mathrm{cr}} = 0.04$ mol kg^{-1}) at 298.15 K.

The dependence of dynamic viscosity (η) for the β-lactose–crown-ether–water solutions on the concentration of β-lactose (Figure 2) also reflects associate formation between β-lactose and 15-crown-5 (an inflexion point at 1:1 composition) and its absence in the case of 18-crown-6 and the aqueous solution of β-lactose (linear plot). The first derivative of the viscosity with disaccharide concentration ($\mathrm{d}\eta/\mathrm{d}m_{\mathrm{lac}}$) is more revealing as far as structure is concerned than the simple viscosity curve (Figure 3). The rate of change of the viscosity with β-lactose concentration exhibits a minimum at m_{lac} corresponding to the stoichiometric composition of the associate. The minimum testifies about a

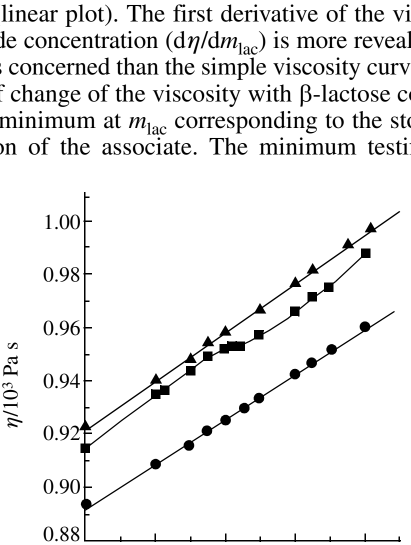

Figure 2 Dependence of the dynamic viscosity (η) of β-lactose–water (●), β-lactose–15-crown-5–water (■) and β-lactose–18-crown-6–water (▲) solutions ($m_{\mathrm{cr}} = 0.04$ mol kg^{-1}) on disaccharide concentration at 298.15 K.

[†] β-Lactose (Sigma, >99%) was used without further purification. The samples of the disaccharide were dried in a vacuum at 343 K during several days before use. 15-Crown-5 (Sigma) was treated with molecular 0.3 nm sieves and used without further purification. 18-Crown-6 (ICN Biomedicals Inc.) was vacuum dried at 308 K. Solutions were prepared by weight using doubly distilled degassed water.

Density measurements were performed with a magnetic float densimeter.[11] The estimated uncertainty in density was 2×10^{-2} kg m^{-3}. Viscosities were measured with an Ubbelode suspended-level viscosimeter equipped wit a photo-optic system. The uncertainty in the flow time was ±0.01 s. The total uncertainty in viscosity measurements was estimated to be 0.035%.The density and viscosity of the three component solutions were measured at fixed concentration of crown ether ($m_{\mathrm{cr}} = 0.04$ mol kg^{-1}). The concentration of β-lactose was varied from 0 to 0.08 mol kg^{-1}.

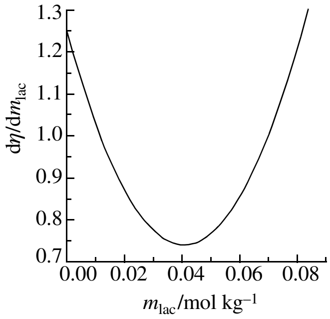

Figure 3 Dependence of $d\eta/dm_{lac}$ on β-lactose concentration in a β-lactose–15-crown-5–water solution (m_{cr} = 0.04 mol kg^{-1}).

minimal structure of the solution at the composition indicated.[14] Thus, the volumetric and viscosimetric data are in agreement with those obtained from the calorimetric study.[7]

Such different behaviours of the crown ethers in relation to β-lactose may be explained at least by two reasons. At first, molecular recognition is affected by the hydration state of interacting particles.[14] According to published data,[15,16] 18-crown-6 is comparatively more hydrated than 15-crown-5. It may be supposed that the stronger hydration of 18-crown-6 as compared with 15-crown-5 is one of the factors preventing associate formation. Moreover, the crown ethers have different macrocycle sizes and conformational states in solution. For 18-crown-6, a centrosymmetrical D_{3d} conformation is dominant in aqueous solution[17] while distorted conformation is typical of 15-crown-5.[18]

Thus, the volumetric and viscosimetric data and the calorimetric results[7] indicate that a 1:1 associate occurs between β-lactose and 15-crown-5 but no associate is formed with 18-crown-6. The associate formation is accompanied by a great solvent reorganization. The associate is formed mainly through hydrogen bonding. Molecular recognition of the crown ethers by β-lactose may be associated with their hydration and/or a steric complementary of the interacting particles.

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