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Selective interactions of 18-crown-6 with D-glucose and D-galactose in aqueous solutions: Titration calorimetry, densimetry, viscosimetry

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Abstract

Titration calorimetric, densimetric and viscosimetric measurements have been combined to study the interactions of 18-crown-6 with D-glucose and D-galactose in water. The crown ether forms a thermodynamically stable 1:1 complex with D-galactose but not with D-glucose. These observations are explained in terms of the stereochemistry of the monosaccharide molecules.

Keywords: Monosaccharide; Crown ether; Aqueous solution; Selective interaction; Titration calorimetry; Densimetry; Viscosimetry

1. Introduction

Selective interactions of saccharides play an important role in a wide range of biochemical processes such as antigen–antibody interactions [1,2] and enzymatic reactions [1,3,4]. Cell surface oligosaccharides are the receptors of biologically active compounds (i.e. drugs) [5,6].

Literature data shows that selective binding of monosaccharides in solution depends on their stereochemical structure [7–9]. Each monosaccharide molecule has a unique stereo arrangements of OH-groups (axial and equatorial), which determine solute–solvent interactions and reactivity with other molecules. This is associated with hydrogen bonding and in some cases with multiple binding in the complex [7]. That requires steric complementarity of the OH-groups of the saccharide and the active centers of the complexing molecule. Moreover, because monosaccharide molecules are amphiphilic, the ratio of hydrophilicity to hydrophobicity depends on their stereochemical configuration [10,11].

A number of studies on interactions of monosaccharides with macrocyclic compounds in aqueous solutions indicate that some cyclodextrins [12–14] and cyclophanes [8,15] stereoselectively interact with monosaccharides through noncovalen, weak hydrogen bonding and hydrophobic and CH-π interactions. The macrocyclic compounds are often considered as models of enzymes and antibiotics [16,17]. Therefore, the studies of interactions between saccharides and macrocyclic compounds are of particular interest from the point of view of biochemistry, pharmacology and medicine.

The aim of the present work is to determine interactions of D-galactose and D-glucose with 18-crown-6 in water. D-Galactose and D-glucose differ only by steric orientation of the hydroxyl group at the fourth carbon atom. Both monosaccharides are in the pyranose form in aqueous solution [18]. Titration calorimetry, densimetry, and viscosimetry provide a comprehensive picture of the interactions under study.

2. Materials and methods

2.1. Materials

18-Crown-6 (1,4,7,10,13,16-hexaoxacyclooctadecane) (MP Biomedicals), D-glucose and D-galactose (Fluka) (>99% pure) were used without further purification. All chemicals were dried in vacuum at 323 K (crown ether) and 343 K (monosaccharides) during several days before

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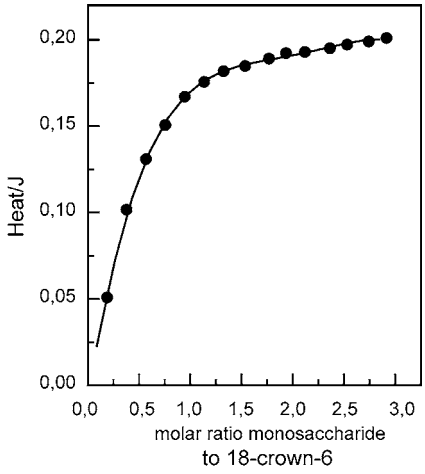

Fig. 1. Calorimetric titration curve of aqueous solution of 18-crown-6 (2.281 mM) by aqueous solution of D-galactose (0.20911 M) at 298.15 K.

use. Solutions were prepared by weight in doubly distilled degassed water.

2.2. Titration calorimetry

Heat measurements were made at 298.15 K with a differential titration calorimeter. The detailed description of the calorimeter and check of its reliability have been reported earlier [19]. In a typical run, a solution of monosaccharide (0.2–0.25 M) was incrementally titrated with crown ether solution (2–3 mM) in the calorimeter cell ($V \sim 40$ mL). The volume of an injection was 7.64×10^{-2} mL. All measurements were run in triplicate. The measurement technique and the procedure of treatment of the experimental data were as described earlier [20]. The calorimetric titration curve for the 18-crown-6–D-galactose–water system is presented in Fig. 1.

2.3. Densimetry

Density (ρ) measurements were performed with a magnetic float densimeter. Its construction is similar to that described elsewhere [21,22]. The volume of the glass cell was 30 cm^3. The float volume and solenoid constant were determined by calibration with water at 298.15 ± 0.005 K with a set of platinum weights. The current in the solenoid was varied from 0.05 to 0.13 A. The current was measured with an accuracy of $\pm 2 \times 10^{-5}$ A. The density values of the solution under study were calculated as:

$$\rho = \frac{W + w + fi^2}{V + \frac{w}{\rho_{Pt}}} \quad (1)$$

where W and V are the weight and the volume of the float, respectively; w the mass of the platinum weights; f the constant of the solenoid; i the current strength; ρ_{pt} the density of platinum. The instrumental uncertainty in ρ was estimated to be $\pm 1.2 \times 10^{-2}$ kg m^{-3}. The statistical uncertainty in ρ as result of 10 measurements was estimated to be $\pm 0.5 \times 10^{-2}$ kg m^{-3}.

2.4. Viscosimetry

Viscosities were measured with an Ubbelohde suspended-level viscosimeter equipped with a photo-optic system to register flow time. The flow time of water at 298.15 ± 0.005 K was 142 s. The viscosimeter had a volume of 8 cm^3, the radius and length of the capillary were 0.38 mm and 13 cm, respectively. The dynamic viscosities were calculated according to:

$$\eta = \nu\rho = A\tau - \frac{B}{\tau} \quad (2)$$

where ν is the kinematic viscosity; τ the flow time; A and B are the constants of the viscosimeter. A and B values were calculated from calibration data on water at different temperatures. The uncertainty in the flow time was ± 0.01 s, and the total uncertainty in η was estimated to be 0.03%.

The viscosities and densities of the three component solutions 18-crown-6–monosaccharide–water were measured at fixed concentration of crown ether ($m_{18\text{-cr-}6} = 0.04$ mol kg^{-1}). The concentration of monosaccharide was varied from 0 to 0.08 mol kg^{-1}.

3. Results

Apparent molar volumes of the monosaccharides studied were calculated with the equation

$$\phi_{vs} = \frac{M}{\rho} - \frac{1000(\rho - \rho_0)}{m_s \rho \rho_0} \quad (3)$$

where M is the molar mass of the monosaccharide; m_s the molality; ρ the density of the three component solution; ρ_0 the density of the aqueous solution of the crown ether ($m_{18\text{-cr-}6} = 0.04$ mol kg^{-1}). For binary solutions ρ and ρ_0 are the densities of aqueous monosaccharide solution and water, respectively. Taking into account that for given solution ρ_0 is constant and uncertainty in m_s is usually not greater than 0.03%, the calculated uncertainties in ϕ_{vs} at $m_s = 0.02$, 0.04 and 0.08 mol kg^{-1} were estimated to be 1, 0.5 and 0.3 cm^3 mol^{-1}, respectively. Variation of the ϕ_{vs} values of the monosaccharides with their concentration at fixed concentration of 18-crown-6 at 298.15 K is presented in Fig. 2.

The limiting partial molar volumes of the monosaccharides $\bar{V}_s^0$ in water and aqueous solution of 18-crown-6 were calculated by the method proposed elsewhere [23]. The volumes of transfer of the monosaccharides from water to aqueous crown ether solution were obtained as

$$\Delta \bar{V}_{trs}^0 = \bar{V}_s^0(H_2O + 18\text{-cr-}6) - \bar{V}_s^0(H_2O) \quad (4)$$

The volume data are summarized in Table 1.

The concentration dependence of relative viscosities ($\eta_r = \eta/\eta_0$) of the solutions of nonelectrolytes can be

Table 1
B-coefficient of viscosity and limiting partial molar volume, $\bar{V}_s^0$, of D-glucose and D-galactose in water and water–18-crown-6 solutions at 298.15 K

	D-Glucose		D-Galactose	
	$m_{18\text{-cr-}6} = 0.00000$[a]	$m_{18\text{-cr-}6} = 0.04010$[a]	$m_{18\text{-cr-}6} = 0.00000$[a]	$m_{18\text{-cr-}6} = 0.03996$[a]
B (mol kg^{-1})	0.462 ± 0.006	0.477 ± 0.006, 110.6 ± 0.2	0.439 ± 0.002	0.45 ± 0.01
$\bar{V}_s^0$ (cm^3 mol^{-1})	111.2 ± 0.5, 111.7[b]	111.5 ± 0.1	110.5 ± 0.3[c], 110.7[d]	109.8 ± 0.3
$\bar{V}_{trs}^0$ (cm^3 mol^{-1})	–	$\cong 0$	–	-0.8

[a] Units: mol kg^{-1}.
[b] Ref. [40].
[c] Ref. [39].
[d] Ref. [41].

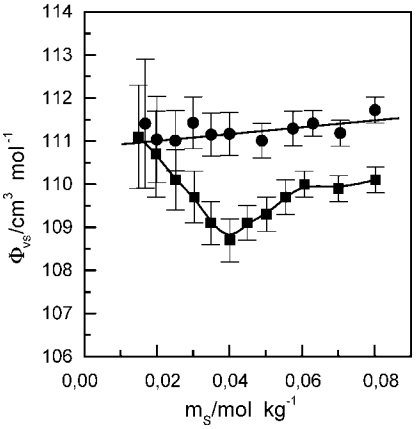

Fig. 2. Dependence of ϕ_{vs} on the concentration of D-glucose (●) and D-galactose (■) in aqueous solution of 18-crown-6 ($m_{18\text{-cr-}6} = 0.04$ mol kg^{-1}) at 298.15 K.

expressed as [24,25]

$$\eta_r = 1 + Bc_s \quad (5)$$

However, in dilute solutions the molar concentration, c_s, can be replaced by the molal concentration, m_s. *B*-coefficients usually reflect the structure effects induced by solute–solvent interactions [26]. The values of *B*-coefficients of the monosaccharides were calculated for the binary and three component solutions and are presented in Table 1.

4. Discussion

4.1. Calorimetric results

The calorimetric titration curve presented in Fig. 1 shows that 18-crown-6 forms a thermodynamically stable 1:1 complex with D-galactose. The calculated thermodynamic parameters of binding are $K = 2619(\pm 397)$; $\Delta H_{bind} = 3.40(\pm 0.52)$ kJ mol^{-1}; $\Delta S_{bind} = 77$ J mol^{-1} K^{-1}. These data are slightly different from those obtained earlier [27], but this has no influence on further conclusion. For D-glucose, no difference between the titration heat effects and heat effects of dilution was detected.

Complex formation between D-galactose and 18-crown-6 is endothermic. A positive binding enthalpy may be caused by (i) heat effects of dehydration of the reacting molecules and (ii) hydrophobic interactions. Numerous thermodynamic, spectroscopic and theoretical studies [28–31] show that monosaccharide molecules are extensively hydrated in aqueous solutions, but the extent of hydration depends on stereochemical structure. In particular, steric orientation of the OH-groups at the second (C2) and fourth (C4) carbon atoms is of crucial importance. D-Glucose with equatorial OH-groups at C2 and C4 is more compatible with the three-dimensional water structure then D-galactose having an equatorial OH-group at C2 and an axial group at C4 [28]. Moreover, the monosaccharide molecules are amphiphilic. D-Glucose is more hydrophobic than D-galactose [10,32]. However, D-galactose has a larger hydrophobic region on its surface than D-glucose [10,11]. Thus, their hydration cospheres are due to both hydrogen bonding of the OH-groups with water molecules and hydrophobic hydration of nonpolar fragments.

18-Crown-6 molecules are also amphiphilic and strongly hydrated in aqueous solution. Specific interactions with water are determined by oxygen lone pairs of electrons [33,34]. However, a number of studies [35–37] have concluded that hydrophobic hydration of $-CH_2$-groups gives a significant contribution to the hydration of crown ethers.

The interactions between the monosaccharides and 18-crown-6 should be accompanied by a significant endothermic effect of dehydration. The stronger the hydration of the monosaccharide molecules, the weaker the complex. It is likely that stronger hydration of D-glucose as compared with D-galactose is one of the factors that prevents formation of a complex between 18-crown-6 and D-glucose.

A large, positive ΔS_{bind} value for the complex formation indicates structural reorganization of the solvent which is the major contribution to the stability of the complex.

4.2. Volumetric properties

Fig. 2 shows the ϕ_{vs} values as a function of the monosaccharide concentration at a fixed concentration of 18-crown-6. This function exhibits a minimum at $m_s = 0.04$ mol kg^{-1} for D-galactose corresponding 1:1 complex. This minimum may be due to complex formation, similar to that shown by Bakshi [38]. D-Glucose exhibits no such minimum.

The limiting partial molar volumes $\bar{V}_s^0$ of the monosaccharides in water and in aqueous crown ether solution (Table 1)

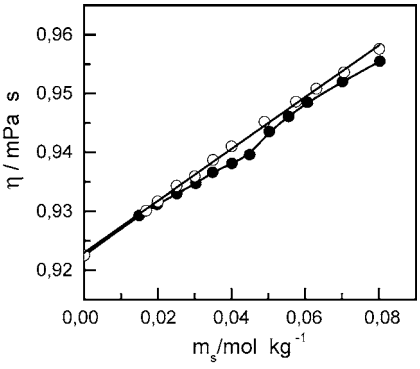

Fig. 3. Dependence of η of 18-crown-6–monosaccharide–water solutions on the concentration of monosaccharide at 298.15 K: (◯) D-glucose and (●) D-galactose ($m_{18\text{-cr-6}} = 0.04\,\text{mol kg}^{-1}$).

reflect the true volume of the solute and the volume change arising from the solute–solvent interactions. The $\bar{V}_s^0$ values of the monosaccharides in water are in good agreement with literature data. Table 1 shows that $\Delta V_{trs}^0 < 0$ for D-galactose while for D-glucose $\Delta V_{trs}^0 \cong 0$. According to the cosphere overlap model [42,43], the overlap of the cospheres of two hydrophobic groups or a hydrophobic group with that of a hydrophilic group produces negative volume changes. $\Delta V_{trs}^0 < 0$ means that hydrophobic–hydrophobic or hydrophobic–hydrophilic interactions are dominant in this system. These results are in agreement with those obtained from the calorimetric study.

4.3. Viscosimetric study

Fig. 3 shows the η values plotted against the monosaccharide concentration at a fixed concentration of 18-crown-6. The function $\eta = f(m_s)$ for D-glucose is linear while this function for D-galactose exhibits an inflexion point at $m_s = 0.04\,\text{mol kg}^{-1}$. The *B*-coefficients of the monosaccharides are positive in all the systems studied (Table 1). This corresponds to the structure making properties of the solutes [44]. The *B*-coefficient values of D-glucose and D-galactose in aqueous crown ether solution are slightly greater than that in pure water. This means that the monosaccharides have more structured surroundings in 18-crown-6 solution. However, the structure making behavior of D-galactose in aqueous crown ether decreases as compared with D-glucose. This may be due to disruption of the more structured region around the nonpolar fragments of D-galactose on complex formation and movement of the water molecules to the less structured bulk resulting in a decrease in viscosity *B*-coefficient.

5. Conclusion

The calorimetric, densimetric and viscosimetric studies show that there is a remarkable selectivity in the binding of these monosaccharides by 18-crown-6. A thermodynamically stable 1:1 complex forms between 18-crown-6 D-galactose in contrast to D-glucose. The complex formation is characterized by a small positive ΔH_{bind}, by a large positive ΔS_{bind}, and by a large stability constant. The transfer of D-galactose from water to aqueous 18-crown-6 solution is accompanied by a decrease of the limiting partial molar volume of the monosaccharide. For D-glucose ΔV_{trs}^0 is near zero. We suppose hydrophobic interactions between 18-crown-6 and D-galactose differs from D-glucose because of the orientation of the OH-group at the fourth carbon atom. Because of this difference, D-galactose is less hydrated and has a more accessible fragment to form the complex. Thus, a selectivity in the interaction of 18-crown-6 with the monosaccharides is affected by their steric configurations. This study may provide insight into carbohydrate binding specificity of drugs at the molecular level.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at 10.1016/j.tca.2005.05.002.

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