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# Thermodynamics of Inclusion complexes in Water: β-Cyclodextrin–Alkyl halides Adducts at 303.15 and 313.15 K

**Abstract**

The interaction in water of tetra ethyl ammonium bromide ($(C_2H_5)_4N(Br)$), tetra propyl ammonium bromide ($(CH_3CH_2CH_2)_4N(Br)$) and tetrabutylammonium bromide ($(CH_3CH_2CH_2CH_2)_4N(Br)$) with β –cyclodextrin (β -CD, cyclomaltose) ($C_{42}H_{70}O_{35}$ ) for dilute solutions has been studied calorimetrically at the temperature 303.15 and 313.15 K. The values of enthalpy of mixing, Q, of two binary aqueous solutions of β -CD with alkyl halides at all temperatures have been fltted by the method of least squares to the equatlon $Q = x_1x_2 [Ao + A_1(x_2 – x_1) + A_2(x_2 – x_1)^2 + A_3(x_2 – x_1)^3]$, where $x_2$ refers to the mole fraction of the alkyl halide. The results obtained have been interpreted in terms of host-guest interaction.

**Keywords**: β -cyclodextrin, tetra ethyl ammonium bromide, Calorimetry, host–guest complex, enthalpy of mixing, hydrophobic cavity.

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## 1. Introduction

$\beta - cyclodextrin$ (cyclomaltoses) ($\beta CD$) is cyclic oligosaccharides composed of seven glucopyranose units linked by α- (1,4) bonds, it is the mainly available, the lowest-priced and generally the most valuable cyclodextrins. Cyclodextrins are frequently used as building blocks. Up to 20 substituents have been linked to $\beta - cyclodextrin$ in a regioselective manner. Cyclodextrins are mainly applied in the separation of enantiomers by high performance liquid chromatography (HPLC) or gas chromatography (GC). The stationary phases of these columns contain immobilized cyclodextrins or derived supra molecular architectures. $\beta$ -CD as a molecular encapsulant allows the flavor quality and quantity to be preserved to a greater extent and longer period compared to other encapsulants and provides longevity to the food.

It contains a lipophilic central cavity and a hydrophilic outer surface. Due to the chair conformation of the glucopyranose units, the cyclodextrins are shaped like a truncated cone rather than perfect cylinders. The hydroxyl functions are orientated to the cone exterior with the primary hydroxyl groups of the sugar residues at the narrow edge of the cone and the secondary hydroxyl groups at the wider edge. The central cavity is lined by the skeletal carbons and ethereal oxygens of the glucose residues, which gives it a lipophilic character. The cavity diameter of β-cyclodextrins has been found to be the most appropriate size for hormones, vitamins, and other compounds frequently used in tissue and cell culture applications. The polarity of the cavity has been estimated to be similar to that of an aqueous ethanolic solution. Waste waters containing environmentally unacceptable aromatic compounds such as phenol, p-chlorophenol and benzene after treating with β-CD have considerably

reduced levels of these aromatic hydrocarbons from their initial levels. The most notable feature of cyclodextrins is their ability to form solid inclusion complexes (host–guest complexes) with a very wide range of solid, liquid and gaseous compounds by a molecular complexation[1]. In these, a guest molecule is held within the cavity of the cyclodextrin host molecule. Complex formation is a dimensional fit between host cavity and guest molecule[2].

The lipophilic cavity of cyclodextrin molecules provides a microenvironment into which appropriately sized non-polar moieties can enter to form inclusion complexes[3]. No covalent bonds are broken or formed during formation of the inclusion complex[4].

The main driving force of complex formation is the release of enthalpy-rich water molecules from the cavity. Water molecules are displaced by more hydrophobic guest.

Molecules present in the solution to attain an apolar–apolar association and decrease of cyclodextrin ring strain resulting in a more stable lower energy state[5]. The natural cyclodextrins, in particular βCD, are of limited aqueous solubility meaning that complexes resulting from interaction of lipophiles with these cyclodextrin can be of limited solubility resulting in precipitation of solid cyclodextrin complexes from water and other aqueous systems. Not all guests are readily solubilised in water, making complexation either very slow or impossible. In such cases, the use of an organic solvent to dissolve the guest is desirable. The solvent should not complex well with cyclodextrin and be easily removed by evaporation. Ethanol and diethylether are good examples of such solvents. Earlier we have reported data on calorimetric measurements of tetraethyl ammonium bromide(TEAB), tetrapropyl ammonium bromide(TPAB) and tetra butyl ammonium bromide (TBAB)with α-cyclodextrin (α-CD, cyclohexaamylose)[6]. In the present study, calorimetric study of $\beta$ –CD ($C_{42}H_{70}O_{35}$) with TEAB, TPAB, and TBAB have been made at the temperature 303.15 and 313.15 K and the data obtained have been reported and interpreted.

**2. Experimental**

$\beta$ –CD ($C_{42}H_{70}O_{35}$**)** was a crystalline sigma product (**≥**97%**),** was purified twice by recrystallization in redistilled water and dried under a reduced pressure at 353 K for 48 h prior to use. Water used in the preparation of solutions was obtained by redistillation in the presence of alkaline potassium permanganate. Tetra ethyl ammonium bromide (TEAB), tetra propyl ammonium bromide (TPAB) and tetra butyl ammonium bromide (TBAB) (All Fluka products) were of the highest purity commercially available and were used without further purification. Chromatographic analysis showed no organic impurities and the water content did not exceed 0.01%.

Calorimetric measurements were carried out using microcalorimeter ((C-80 model from seta ram, France))[7] at 303.15 and 313.15 K, whose temperature was controlled to within ±0.003K. The weights of the sample of the salts were chosen so as to result in a calorimeter solution of about $10^{-4}$ to $10^{-3}$ molarity. A dry box was used for preparing solutions, so that there were no contact between substances and air moisture. Fresh solutions were prepared to keep away from any decomposition on standing. The densities of various compounds and solutions have been determined using with a vibrating-tube densimeter from Anton Paar Co. Ltd. (Model DMA 602/60) in a manner as given elsewhere[7].

Experiments were carried out by batch method on C-80 calorimeter, which is composed of a reference and experimental vessel. These vessels are surrounded by two symmetrical thermal flux meters composed of thermocouples in series. The whole assembly is kept in an aluminium block and allowed to reach thermal equilibrium. If there is any heat liberated or absorbed in the experimental vessel during mixing of $\beta$ -cyclodextrin and alkyl halide, it leads to change in temperature which is allowed and this persists till same temperature is attained in both the vessels. The experimental cell has two chambers separated by tilting lid. The samples are separately introduced into the vessel by equilibrium. The mixing is performed by inverting the whole calorimeter by $180^0$C. The amount of heat, q evolved during an experiment can be calculated by determining the area under the curve

obtained during the experiment. The concentration of $\beta$ -cyclodextrin was 0.01M and 0.5M for alkyl halide throughout the experiment.

The heat of dilution of the guest was measured separately, for which appropriate corrections were made throughout the work.

**3. Results and Discussion**

If the initial concentrations of β-cyclodextrin and alkyl halide are $a0$ and $b0$ respectively and $v1$ and $v2$ are their volumes and the heat evolved denoted by q , then mole fraction of $\beta$ -cyclodextrin, $x1$ is given by

$$\boldsymbol{x1} = \frac{\boldsymbol{a0v1}}{\boldsymbol{a0v1+bov2}} \qquad \textbf{(1)}$$

and $\boldsymbol{x2} = \mathbf{1} - x1$ (2)

enthalpy of reaction , Q, is given by

$$\mathbf{10}\boldsymbol{Q} = \frac{qx10^3}{a0v1+b0v2}$$

The values of $Q$, obtained in the present investigation for the mixtures of {$x_1$ β -cyclodextrin +$x_2$ TEAB}, {$x_1$ β-cyclodextrin +$x_2$ TPAB}and {$x_1$ β-cyclodextrin +$x_2$ TBAB} have been given in the Table1. The values of Q for the various mixtures have been fitted by the method of least-squares to the Redlich–Kister type equation:

$$Q\ (J.mol^{-1}) = x_1x_2\,[A_o + A_1(x_2 - x_1) + A_2(x_2 - x_1)^2] + A_3\,(x_2 - x_1)^3 \qquad (3)$$

The resulting values of the coefficients $A_0$, $A_1$ and $A_2$ of Eq. (3), and the standard deviations σ(Q) of the fits for the different mixtures are given in Table 2. The precision in the values of Q is of the order of±0.5 $J.mol^{-1}$. The present Q values are observed to be positive throughout the entire range of $x_2$ for the mixtures of {$x_1$ β-cyclodextrin +$x_2$ TEAB} at both the temperatures, whereas negative and positive both for binary mixtures of {$x_1$ β-cyclodextrin +$x_2$ TPAB} at 303.15 K and positive values of Q observed at the temperature 313.15 K. For the system of {$x_1$ β-cyclodextrin +$x_2$ TBAB}, the values of Q are positive at both the temperatures.

At all temperatures, the values of Q decrease in the order
TEAB> TPAB> TBAB

It clearly suggests that interaction become stronger with increasing length of alkyl chain. β-cyclodextrin exhibit a hydrophobic cavity delimited by two rims, a wide and a narrow one, composed of secondary and primary hydroxy groups. By virtue of this structure, CDs are able to generate inclusion complexes with a wide variety of hydrophobic organic compounds in aqueous solution. The driving forces leading to complexation are numerous, varying from van der Waals to hydrophobic and to dipole–dipole interactions. The main factors acting as driving force to form complexes and also responsible for the stability of these complexes are hydrophobic forces, the sizes of molecules/cavity and the guest properties[8]. When a certain length of hydrophobic chain of alkyl bromide enters a molecular hole of β-CD, a number of water molecules will be driven to the bulk aqueous phase from the hydrophobic hole. The longer the hydrophobic chain of surfactant molecule that gets into the molecular cavity of β-CD, the more water molecules are driven from the hole and a larger amount of energy is released. Second, the magnitude of the force between the hydrophobic inner face of the hole of β-CD and the non-polar chain of an alkyl bromide is related to the size of the enclosed hydrophobic chain.

The glucopyranosides units are in C1 conformation, where the OH groups are linked to the carbon atoms C2 and C3 around the bigger edge and the more reactive OH group (linked to C6) is in the smaller edge. The cavity is delined by the hydrogens atoms and by the glucosidal bridge. The electron pairs of the oxygen atoms are inner of cavity, leading to a high electron density and resulting in an environment similar to that of Lewis bases[9].

Simultaneously, some energy must be consumed by the destruction of the "iceberg" structure formed by water molecules around the hydrophobic group of each surfactant ion[10], but this energy change should be much smaller in comparison with the amount of energy released by formation of the host–guest complex.

The signs of Q, positive or negative for above mentioned systems suggest that for β-cyclodextrin complexes, the hydrophobic interactions do not always play the major role in the formation of these inclusion complexes. Dipole-induced dipole, host-guest interactions and the decrease in the activation energy when a hydrophobic residue fills the cavity must also be considered as important effects. The positive value indicates that the formation of complexes implies squeezing out water molecules entrapped in the cavity, and then the guest molecule can penetrate the cavity with a modification of the solvent in its hydration cosphere. The negative values are the result of all types of interactions involved as above-mentioned.

**Table1: Reaction Enthalpies (Q) of ($C_{42}H_{70}O_{35}$) (1) + TEAB (2), or + TPAB(2), or + TBAB (2 ), at 303.15 and 313.15 K.**

| **β-cyclodextrin + TEAB at 303.15K** | |
|---|---|
| $x2$ | $Q$**(J.mol$^{-1}$)** |
| 0.9966 | 21 |
| 0.9945 | 32 |
| 0.9933 | 39 |
| 0.9901 | 54 |
| 0.9846 | 76 |
| 0.9837 | 79 |
| 0.9799 | 91 |
| 0.971 | 114 |
| 0.9668 | 121 |
| 0.9564 | 131 |
| 0.9502 | 139 |
| 0.9433 | 143 |
| 0.9412 | 148 |
| 0.9388 | 147 |
| 0.9212 | 167 |
| 0.9181 | 173 |

| **β cyclodextrin +TEAB at 313.15K** | |
|---|---|
| $x2$ | $Q$**(J.mol$^{-1}$)** |
| 0.9901 | 78 |
| 0.9886 | 89 |
| 0.98 | 129 |
| 0.9797 | 130 |
| 0.9734 | 151 |
| 0.9686 | 158 |
| 0.9581 | 170 |
| 0.9512 | 175 |
| 0.9482 | 176 |

| | |
|---|---|
| 0.9442 | 179 |
| 0.9365 | 184 |
| 0.9312 | 190 |
| 0.9212 | 212 |
| 0.9112 | 248 |

| **β- cyclodextrin(0.01) +TPAB) at 303.15K** | |
|---|---|
| $x2$ | $Q$(J.mol$^{-1}$) |
| 0.9967 | -3 |
| 0.9960 | -3 |
| 0.9952 | -4 |
| 0.9938 | -4 |
| 0.9924 | -5 |
| 0.9845 | -4 |
| 0.9823 | -3 |
| 0.9789 | -1 |
| 0.9732 | 3 |
| 0.9619 | 12 |
| 0.9511 | 18 |
| 0.9445 | 20 |
| 0.9395 | 21 |
| 0.9308 | 18 |
| 0.9266 | 15 |
| 0.9198 | 9 |

| **β-CD+TPAB at 313.15K** | |
|---|---|
| $x2$ | $Q$(J.mol$^{-1}$) |
| 0.9983 | 3 |
| 0.9971 | 4 |
| 0.9961 | 7 |
| 0.9954 | 9 |
| 0.9931 | 11 |
| 0.9911 | 13 |
| 0.9893 | 15 |
| 0.9887 | 16 |
| 0.9867 | 19 |
| 0.9849 | 21 |
| 0.9746 | 28 |
| 0.9665 | 30 |
| 0.9569 | 32 |
| 0.9593 | 33 |
| 0.9501 | 34 |
| 0.9471 | 35 |

| | |
|---|---|
| 0.9398 | 33 |
| 0.9332 | 36 |
| 0.9112 | 45 |

| **β -CD+TBAB at 303.15K** | |
|---|---|
| $x2$ | $Q$(J.mol$^{-1}$) |
| 0.9958 | -61 |
| 0.9954 | -65 |
| 0.9947 | -74 |
| 0.9889 | -142 |
| 0.9839 | -188 |
| 0.9773 | -235 |
| 0.9739 | -254 |
| 0.9630 | -290 |
| 0.9535 | -297 |
| 0.9511 | -296 |
| 0.9481 | -292 |
| 0.9479 | -293 |
| 0.9474 | -292 |
| 0.9234 | -235 |
| 0.9187 | -213 |

| **β-CD+TBAB at 313.15 K** | |
|---|---|
| $x2$ | $Q$(J.mol$^{-1}$) |
| 0.9962 | -79 |
| 0.9948 | -106 |
| 0.9932 | -131 |
| 0.9919 | -152 |
| 0.9884 | -199 |
| 0.9874 | -212 |
| 0.9834 | -254 |
| 0.9778 | -287 |
| 0.9611 | -326 |
| 0.9603 | -327 |
| 0.9558 | -328 |
| 0.9436 | -329 |
| 0.9402 | -332 |
| 0.9326 | -354 |
| 0.9275 | -388 |
| 0.9213 | -447 |
| 0.9145 | -542 |

**Table 2: Least Squares Coefficients of Eq 1 for the Enthalpies of solution, Q, and the standard deviations, σ, of β-cyclodextrin + TEAB, + TPAB, and + TBAB at 303.15 and 313.15 K**

| System | $A_0$ | $A_1$ | $A_2$ | $A_3$ | σ/ (J mol$^{-1}$) |
|---|---|---|---|---|---|
| **T=303.15K** | | | | | |
| β -cyclodextrin(1) + TEAB(2) | 109451 | -256292 | 153255 | --- | 1.1 |
| β -cyclodextrin(1) + TPAB(2) | 196333 | -746679 | 934028 | -384760 | 0.3 |
| β -cyclodextrin(1) + TBAB(2 | -1335248 | 350590 | -232370 | --- | 1.4 |
| **T=313.15 K** | | | | | |
| β -cyclodextrin(1) + TEAB(2) | 210586 | -490252 | 289312 | --- | 1.1 |
| β -cyclodextrin(1) + TPAB(2) | 36540 | -85500 | 50762 | --- | 0.8 |
| β -cyclodextrin(1) + TBAB(2) | -707201 | 1622052 | -937624 | --- | 1.9 |

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