Study of inclusion complex formation between a homologous series of \( n \)-alkyltrimethylammonium bromides and \( \beta \)-cyclodextrin, using conductometric technique

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Abstract

The behaviour of the inclusion complex based on a homologous series of \( n \)-alkyltrimethylammonium bromides and \( \beta \)-cyclodextrin (\( \beta \)-CD) were studied using conductometric technique. Association constants have been determined for \( S(\text{CD}) \) and \( S(\text{CD})_2 \) complexes. It has been found that DETAB and DOTAB form only the 1:1 complexes, while TTAB forms 1:1 1:2 TTAB/CD complexes. The results are explained in terms of the difference in chain length of surfactants and dimensions of the \( \beta \)-CD cavity. The experiments were carried out at different temperatures. The association constant values are used for evaluation of thermodynamic parameters of complexation, such as \( \Delta G^\circ \), \( \Delta H^\circ \) and \( \Delta S^\circ \).

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1. Introduction

Cyclodextrins are cyclic oligosaccharides with six, seven, or eight glucopyranose units linked by glycosidic bonds \( \alpha \)-1,4 (\( \alpha \)-, \( \beta \)-, and \( \gamma \)-cyclodextrins, respectively). They have a toroidal or hallow, truncated, cone shape, with an apolar, hydrophobic interior and two hydrophilic rims, formed by the primary (narrow rim) and secondary (wider rim) OH groups.

Cyclodextrins are known to form inclusion complexes with a variety of guest compounds [1]. In an aqueous solution, the slightly apolar cyclodextrin cavity is occupied by water molecules, which are energetically unfavored (polar–apolar interaction) and therefore can be readily substituted by appropriate guest molecules which are less polar than water. The driving force of the complex formation is the substitution of the high enthalpy water molecules by an appropriate guest molecule.

Generally, interaction of a cyclodextrin with an apolar guest molecule in water results in the formation of 1:1 molecular inclusion compounds, in which the guest is included within the cyclodextrin cavity. The inclusion is a thermodynamic equilibrium process with an association constant, \( K \), given by the usual relationship:

\[
CD + S \rightleftharpoons S(\text{CD}) \quad K = \frac{[S(\text{CD})]}{[S][\text{CD}]} \tag{1}
\]

More recently, a number of 2:1 cyclodextrin–substrate complexes have been characterized [2–7]. A wide variety of experimental methods have been employed for study of the complexation between CDs and guest molecules. These include microcalorimetry [7–9], UV–VIS spectroscopy [10–13], potentiometry [3,11,14–16] vapor pressure [17,18], surface tension [19], conductometry [20,21], etc. Conductometric technique is frequently employed to determine

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equilibrium constants of complexation between cyclodextrins and a variety of guest ions [22-25].

The object of the present study was to determine the complexation constants between the \( \beta \)-cyclodextrin and a homologous series of \( n \)-alkyltrimethylammonium bromides and to ascertain the effect of chain length of surfactant on the complexation. Conductometric measurements were undertaken to determine the stoichiometry and association constants of cyclodextrin-surfactant inclusion complexes in the pre-cmc region (cmc=critical micelle concentration) at different conditions. Also, thermodynamic quantities have been evaluated from the temperature dependence of complexation constants, using the van’t Hoff equation.

2. Experimental

Decyltrimethylammonium bromide (DETAB) was provided by Prof. Gharibii [26]. Dodecyltrimethylammonium bromide (DOTAB) and tetradecyltrimethylammonium bromide (TTAB) were obtained from Sigma and twice recrystallized using methanol/acetone mixture and water/ethanol mixture, respectively. \( \beta \)-cyclodextrin (\( \beta \)-CD) was obtained from Sigma and used as supplied. The water content of the cyclodextrin, determined by thermogravimetric analysis, was 13.0%. The hydration water of the \( \beta \)-CD was taken into account in the concentration of the solutions that were prepared by weight.

Specific conductivities of the solutions were measured using a Genway conductometer Model 4020, and a dipping cell with platinum electrode (cell constant=1 cm\(^{-1}\)). The conductivity cell was calibrated with KCl solution in the appropriate concentration range. The measuring cell was immersed in a thermostat bath keeping the temperature constant with \( \pm 0.1 \) °C.

3. Results and discussion

In the presence of \( \beta \)-CD, for a 1:1 complex formation one should be able to define the equilibrium for this reaction:

\[
S + CD \rightleftharpoons S(CD)
\]

The mass conservation law equations for the above equilibrium could be written for the total surfactant and cyclodextrin concentrations as:

\[
[S]_t = [S]_i + [S(CD)]
\]

\[
[CD]_t = [CD]_i + [S(CD)]
\]

where \([S]_i\) and \([CD]_i\) are total surfactant and cyclodextrin concentrations, respectively. In this case, the observed specific conductance could be expressed as:

\[
K_{obs} = K_S + K_{S(CD)}
\]

where \( K_{obs} \), \( K_S \) and \( K_{S(CD)} \) are observed, surfactant and complex (1:1) specific conductance, respectively. On the other hand, we can explain Eq. (5) based on molar conductivity as follows:

\[
K_{obs} = \lambda_S [S^+]_t + \lambda_C [C^-]_t + \lambda_{S(CD)} [S(CD)]
\]

where \([S(CD)]\) and \( \lambda_{S(CD)} \) are the concentration and ionic molar conductivity of the 1:1 complex, respectively.

If the second equilibrium proceeds, we should consider a 2:1 stoichiometry for complex formation. In this case, an amount of the complex \( S(CD)_2 \) is formed according to:

\[
S(CD) + CD \rightleftharpoons S(CD)_2
\]

\[
K_2 = \frac{[S(CD)_2]}{[S(CD)][CD]_t}
\]

Given the law of conservation of mass, it could be stated:

\[
[S]_i = [S]_t + [S(CD)] + [S(CD)_2]
\]

\[
[CD]_i = [CD]_t + [S(CD)] + 2[S(CD)_2]
\]

where \([S(CD)_2]\) is the concentration of 2:1 complex. Accordingly, the specific conductivity of solution could be written as:

\[
K_{obs} = K_S + K_{S(CD)} + K_{S(CD)_2}
\]

where \( K_{S(CD)_2} \) is the specific conductance of 2:1 complex. The molar conductance for each species can be defined in terms of the specific conductance as follows:

\[
A_i = \frac{10^{-3} K}{[C_i]}
\]

\[
\frac{A_i}{(\Omega^{-1} \text{ mol}^{-1})} \text{ is molar conductivity. By combining Eqs. (10) and (11):}
\]

\[
A_{obs} = \frac{A_S + A_{S(CD)} K_1 [CD] + A_{S(CD)} K_1 K_2 [CD]^2}{1 + K_1 [CD] + K_1 K_2 [CD]^2}
\]

The free cyclodextrin concentrations, \([CD]_t\), were calculated by means of a Newton–Raphson procedure. Once the value of \([CD]_t\) had been obtained, the concentrations of all other species involved were calculated by using the estimated values of the formation constants at the current iteration step of the program. Refinement of the parameters is continued until the sum-of-squares of the residuals between calculated and observed values of the conductance for all experimental points is minimized. The output of the program KINFIT [27] comprises refined parameters, the sum-squares and the standard deviation of the data. The program is based on the iterative adjustment of the calculated values of the conductance to the observed values by using either the Wentworth matrix technique [28] or the Powell procedure [29]. All the calculated formation constants are summarized in Table 1.
Table 1

<table>
<thead>
<tr>
<th>Surfactant</th>
<th>$t$ (°C)</th>
<th>$K_1$ (mol dm$^{-3}$)</th>
<th>$K_2$ (mol dm$^{-3}$)</th>
<th>Sum square</th>
</tr>
</thead>
<tbody>
<tr>
<td>DETAB</td>
<td>25</td>
<td>3843</td>
<td>–</td>
<td>1.77</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>2855</td>
<td>–</td>
<td>0.59</td>
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<td></td>
<td>35</td>
<td>1438</td>
<td>–</td>
<td>1.85</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>967</td>
<td>–</td>
<td>0.20</td>
</tr>
<tr>
<td>DOTAB</td>
<td>25</td>
<td>18,633</td>
<td>–</td>
<td>1.26</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>14,996</td>
<td>–</td>
<td>1.62</td>
</tr>
<tr>
<td></td>
<td>35</td>
<td>11,180</td>
<td>–</td>
<td>0.89</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>5794</td>
<td>–</td>
<td>1.30</td>
</tr>
<tr>
<td>TTAB</td>
<td>25</td>
<td>62,742</td>
<td>1226</td>
<td>0.14</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>48,396</td>
<td>964</td>
<td>0.21</td>
</tr>
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<td></td>
<td>35</td>
<td>44,334</td>
<td>1131</td>
<td>0.13</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>19,966</td>
<td>929</td>
<td>0.55</td>
</tr>
</tbody>
</table>

Figs. 1–3 show $A_{obs}$ as a function of $\beta$-CD concentration for DETAB, DOTAB and TTAB solutions at a constant concentration of each surfactant ($7.5 \times 10^{-4}$ mol dm$^{-3}$) and different temperatures. These plots show how $A_{obs}$ is affected by an increasing in the $\beta$-CD concentration. The molar conductance decreased sharply as $\beta$-CD was added presumably because the surfactant ions complexed by $\beta$-CD were less effective as a charge carrier. The counter ion ($Br^-$) is not thought to be complexed by $\beta$-CD to any extent. At a certain concentration in $\beta$-CD, this linear decrease of molar conductance with $\beta$-CD concentration shows a change in the gradient of slope. The stoichiometry at which this halt occurred were 1.1:1 for $\beta$-CD:TTAB, 1:1 for $\beta$-CD:DOTAB and $\beta$-CD:DETAB. This indicates that the inclusion complex of $\beta$-CD with DOTAB and DETAB is only 1:1, while in the case of TTAB the chief inclusion complex is 1:1 with possibly a little 2:1 complex also present.

The obtained results for TTAB showed that $K_1 \gg K_2$ which indicates that the formation of the 1:1 stoichiometric complex predominates rather than the 2:1 ones. The cyclodextrin structure is such that the inside of the cavity is covered with CH$_2$ groups thus providing a hydrophobic environment that is favorable to interact with the hydrocarbon chain of surfactant. X-ray crystallography shows that the depth and inner diameter of $\beta$-CD are 7.8 and 7.8 Å, respectively. The length, $l$, and
diameter, \( d \), of the structural alkyl group with formula \( \text{C}_n\text{H}_{2n+1} \) are calculated from the following equations [6]:

\[
l(\text{Å}) = 1.5 + 1.265(n - 1)
\]

\[
d(\text{Å}) = \left[ \frac{34.89 + 34.25(n - 1)}{1.5 + 1.265(n - 1)} \right]^{1/2}
\]

For DETAB, DOTAB and TTAB that have 10, 12 and 14 carbon atoms in their alkyl chain, Eq. (14) gives the length of the chain as 12.89, 15.42 and 17.95 Å, respectively. Also, using Eq. (15), give the diameter as approx. ≈ 5.17 Å for all surfactants. Comparison of these values with the structural characteristics of \( \beta \)-CD shows that there is a good match fitting between \( \beta \)-CD cavity and surfactant alkyl chain. On the other hand, there is the possibility for simultaneous entry of two \( \beta \)-CD molecules in the length of the TTAB chain, but this does not occur for DETAB and DOTAB.

The increment of temperature were also caused unstability of complexes, though refers to increasing of agitation energy. The obtained values of \( K_1 \) and \( K_2 \) from fitting of data have been used for the calculation of the thermodynamic parameters such as \( \Delta H^\circ \), \( \Delta G^\circ \) and \( \Delta S^\circ \). The Gibbs free energy of each step complex formation could be calculated from the following equation:

\[
\Delta G^\circ = -RT \ln K
\]

The enthalpy of complexation was obtained from the temperature dependence of the complexation constant \( K \) using the van’t Hoff relation:

\[
d(\ln K)/d(1/T) = - \Delta H^\circ / R
\]

and finally the \( \Delta S^\circ \) values could be obtained from the following equation:

\[
\Delta G^\circ = \Delta H^\circ - T \Delta S^\circ
\]

The obtained results are listed in Table 2. The negative values of \( \Delta H^\circ \) could be attributed to attraction between hydrocarbon chain of the surfactant and hydrophobic interior of the CD. Fig. 4 shows a plot of \( \Delta G^\circ_1 \) versus number of carbon atoms in the alkyl chain of the surfactant at various temperatures. As it was observed, the values of \( \Delta G^\circ_1 \) have been more negative with increasing chain length of the surfactant, which corresponded with hydrophobicity of cyclodextrin cavity.

The \( \Delta S^\circ \) values for the first step of complexation (1:1 stoichiometry) are negative. The value of \( \Delta S^\circ \) has been affected by several phenomena. One of the most important factors is the hydrophobic effect that could be mainly attributed to the hydrophobic interaction between the alkyl chain and the inner wall of the CD molecule and partly to the release of water molecules from the alkyl chain of the surfactant and the cavity of the CD during the penetration process.

We can represent \( \Delta S^\circ \) as a summation of several contributions, in which \( \Delta S^\circ = \Delta S^\circ_1 + \Delta S^\circ_2 + \Delta S^\circ_3 + \Delta S^\circ_4 \), where:

(I) \( \Delta S^\circ_1 \): refers to the disordering of the water structure around the hydrocarbon chain of the surfactant, in which \( \Delta S^\circ_1 > 0 \).

(II) \( \Delta S^\circ_2 \): according to the structure of CD in aqueous solution, the slightly apolar cyclodextrin cavity is

### Table 2

The calculated values of thermodynamic parameters for complexation between \( \text{C}_n\text{H}_{2n+1} \) and \( \beta \)-CD (7.5×10^{-4} mol dm^{-3}) at various temperatures

<table>
<thead>
<tr>
<th>Surfactant</th>
<th>( t ) (°C)</th>
<th>( K_1 ) (mol dm^{-3})</th>
<th>( \Delta G^\circ_1 ) (kJ mol^{-1})</th>
<th>( \Delta H^\circ_1 ) (kJ mol^{-1})</th>
<th>( \Delta S^\circ_1 ) (J mol^{-1} K^{-1})</th>
<th>( K_2 ) (mol dm^{-3})</th>
<th>( \Delta G^\circ_2 ) (kJ mol^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>DETAB</td>
<td>25</td>
<td>3843</td>
<td>-20.46</td>
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<td>-180.8</td>
<td>-182.5</td>
<td>-115.2</td>
</tr>
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<td>-20.05</td>
<td>-179.8</td>
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<td>-182.5</td>
<td>-115.2</td>
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<td>1438</td>
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<td>-182.5</td>
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<td>18,633</td>
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<td>-91.4</td>
<td>929</td>
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</table>
occupied by water molecules, which are energetically unfavored (polar–apolar interaction), and therefore can be readily substituted by appropriate “guest molecules” which are less polar than water (i.e. surfactant hydrocarbon chain). Therefore, the withdrawing of the water molecules from the CD cavity results in $\Delta S_c^b$.

(III) $\Delta S_c^b$: refers to association of species, i.e. CDs and surfactant molecules, in which $\Delta S_c^b$.

The resultant sum of these three $\Delta S^c$ ($\Delta S_{\text{tot}}^c = \Delta S_a^c + \Delta S_b^c + \Delta S_c^c$) determines the sign of $\Delta S^c$.

The value of $\Delta S^c$ is affected by several phenomena. Hydrophobic effects that can be mainly attributed to the hydrophobic interaction between the alkyl chain and the inner wall of the CD molecule, and partly to the release of water molecules from the alkyl chain of the surfactant and the cavity of the CD during the penetration process, is one of the most important factors.

4. Conclusion

According to Park and Song [5] on the geometric issues regarding entry of a hydrocarbon chain inside the cyclodextrin cavity, it is shown that $\beta$-cyclodextrin has placed four carbon atoms in the trans position and eight carbon atoms in a two node chain. In other words, entry of a hydrocarbon chain into the $\beta$-Cyclodextrin cavity is filled with a maximum of four carbon atoms for an open chain. Comparison of the length and volume surfactants with the structural parameters for $\beta$-cyclodextrin shows that there is the possibility for simultaneous entry of two $\beta$-cyclodextrin molecules in the length of the TTAB chain, but this does not occur for DETAB and DOTAB.

The larger value of $K_1$ with respect to $K_2$ predicts the preferable formation of 1:1 complex. The calculated thermodynamic parameters show that the hydrophobic effect has a very important role in complexation process. The more negative values of $\Delta G^c$ with increasing the hydrocarbon chain of surfactants indicate that the interaction between surfactant and $\beta$-cyclodextrin has hydrophobic characteristics.

References