



Determinations of the Inclusion Complex of Methylated β -Cyclodextrin with Styrene

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Inclusion complex of styrene with methylated β -cyclodextrin was prepared in aqueous media. NMR, TGA and UV-vis spectroscopy were used to characterize the complex. It was testified that the inclusion complex was formed between cyclodextrin and styrene and the stoichiometry tested was to be 1:1. It was found that the thermal stability of styrene encapsulated in cyclodextrin was much higher than that of free one. Then the association constants at different temperatures were determined using Benesi-Hildebrand linear regression. Thermodynamic parameters showed that the inclusion process was a spontaneous and exothermic one.

Key Words: Cyclodextrin, Styrene, Inclusion complex, Stoichiometry, Stability constant.

INTRODUCTION

Cyclodextrins (CDs) are cyclic oligoamyloses, consisting of 6(α), 7(β), 8(γ) units of 1,4-linked glucose. Because of their hydrophobic cavity and hydrophilic outer side, they are able to enclose suitable hydrophobic molecules to form host-guest compounds. The inclusion complexation of these host-guest systems occurs through various interactions, such as hydrogen bonding, van der Waals' forces, electrostatic or hydrophobic interactions. The formation of these complexes leads to significant changes of the solubility and reactivity of the guest molecules, but without any chemical modification, because there are no covalent bonds formed by the host-guest interaction of the CD and the water-insoluble molecule. β -Cyclodextrin is the most accessible, the lowest-priced and generally the most useful, which is capable of forming stable, supramolecular structures with various molecules^{1,2}.

The inclusion ability of CDs for organic substrates has been widely used in many fields, such as separation technology, food chemistry and pharmaceutical industries, *etc.*^{3,4}. In recent years, the utility of CDs in polymer synthesis has attracted many interests⁵⁻⁸. It is shown that water insoluble monomers, such as styrene or acrylates, may become water soluble just simply by mixing with aqueous solutions of CDs and it is turned out that the complexed hydrophobic monomers can be successfully polymerized directly in water without any organic solvent or surfactant, which is thought a new green way to polymer preparation^{9,10}. Our group has also focused on the CD-mediated polymerization for some years and observed many interesting phenomena¹¹⁻¹⁴. It is found that in presence

of CDs, both the reaction rate and the monomer conversion are markedly elevated. It is believed that there are important effects of the supermolecular structure of the host-guest inclusion complexes on the polymerization. The inclusion of the monomers into the CD cavities may be a key element in the understanding of the differences between the traditional polymerization and this new method. There are a few published articles about the structures of CD/reactive monomer complexes¹⁵⁻¹⁷, in which β -CD is the most used because of the most accessibility and the lowest price. Nevertheless, the solubility of β -CD in water (only 1.85 g/100 mL, 25 °C) is not satisfying because of the intramolecular strong hydrogen bond between HO-2 and O-3, which limits its application in this new polymerization. The utility of some more water-soluble chemically modified β -CDs, *e.g.*, randomly methylated β -CD (80-200 g/100 mL depending on different substituting degree, 25 °C), are necessary. It is essential to perform extensive characterization and modeling of reactive monomer/methylated β -CD inclusion complex, so the rules of this CD-mediated polymerization can be better interpreted.

In the present paper, the inclusion complex of methylated β -CD with guest styrene, a commonly used monomer in polymer synthesis, was obtained by mixing both the CD and styrene in water. The inclusion complex was characterized by thermogravimetric analysis, nuclear magnetic resonance and UV-vis spectroscopy. The association constants at different temperatures were determined using Benesi-Hildebrand linear regression and the thermodynamical parameters of the inclusion were calculated, while the polymerization of styrene inside the methylated β -CD will be the subject of a future paper.

EXPERIMENTAL

Methylated β -CD was purchased from Zibo Qianhui Fine Chemical Co. Ltd. (China, Zibo). Styrene (99.9 %) was obtained from Shantou Xilong Chemical Company (China Shantou). All the other chemicals used in this study were reagent grade and used without further purification. The water used in this study was deionized water.

Formation of styrene/cyclodextrin inclusion compound:

The accurately weighed methylated β -CD (1.31 g, 0.001 mol) was dissolved in 30 mL of deionized water at room temperature. Then, styrene (0.1 g, 0.001 mol) was added drop-wise to the clear aqueous solution of CD. The solution was stirred at room temperature for 24 h. Not like the inclusion of natural β -CD with hydrophobic substrates, there was no precipitate formed in this case, which is favourable in the next polymerization. Then the solution was evaporated in a vacuum oven to obtain solid complexes for further characterization.

^1H Nuclear magnetic resonance: The ^1H NMR spectra of the samples were recorded on a Bruker Avance AM 400 spectrometer at 30 °C. The δ scale relative to tetramethylsilane was calibrated by the deuterium signal of the solvent as internal standard.

Thermogravimetric analyses (TGA): Experiments were performed in the temperature range from 50-400 °C on a NETZSCH STA449C thermal analyzer (NETZSCH, German). The heating rate was of 5 °C/min and the nitrogen flow was 10 mL/min.

Determination of the stoichiometry of the inclusion complex: The most probable stoichiometry of the complexes was evaluated by monitoring UV absorbance of styrene with different concentration of CD. Different volumes of the host and the guest are mixed such that the volume of the styrene remains constant every time while CD concentration varies in small steps. In brief, a quantity of styrene (0.52 g, 0.005 mol) was added to 50 mL of aqueous solution containing various amounts of methylated β -CD (0-0.0075 mol). The solutions were stirred at room temperature for 24 h. The UV absorption of resulting solutions was performed at an Shimadzu UV-2550 at 290 nm. The relative UV-vis spectroscopic intensities (ABS) of these mixtures are a linear function of the mole fraction of each species under these conditions. A plot of these parameters yields a curve which determines the complex stoichiometry.

Determination of host/guest association constant: The Benesi-Hildebrand equation was employed to quantitatively describe the interaction between CD and styrene at different temperatures. 1.182 mg (1.74×10^{-2} mmol) styrene was added into 50 mL methylated β -CD solution with different CD concentrations ($0, 2.02 \times 10^{-2}, 4.04 \times 10^{-2}, 6.06 \times 10^{-2}, 8.08 \times 10^{-2}$ mol/L). Afterward, the solutions were stirred for 24 h in a water bath at a given temperature. Variations thus occurred in UV absorbance of the solutions were monitored on a UV-vis spectrophotometer. Then, association constant K_a could be readily obtained from a linearized Benesi-Hildebrand equation. The process mentioned above was repeated at each given temperature to determine the temperature dependence of K_a .

RESULTS AND DISCUSSION

NMR is a powerful technique to determine the presence of guest molecules in CD inclusion complexes. The presence of styrene in the styrene/methylated β -CD inclusion complex was confirmed by solution ^1H NMR. Fig. 1 illustrated characteristic ^1H NMR spectra of styrene/CD complex in comparison with the single methylated β -CD. The spectrum Fig. 1(b) showed highly resolved signals for the phenyl group in higher field, which indicated the inclusion of styrene in the CD cavity.

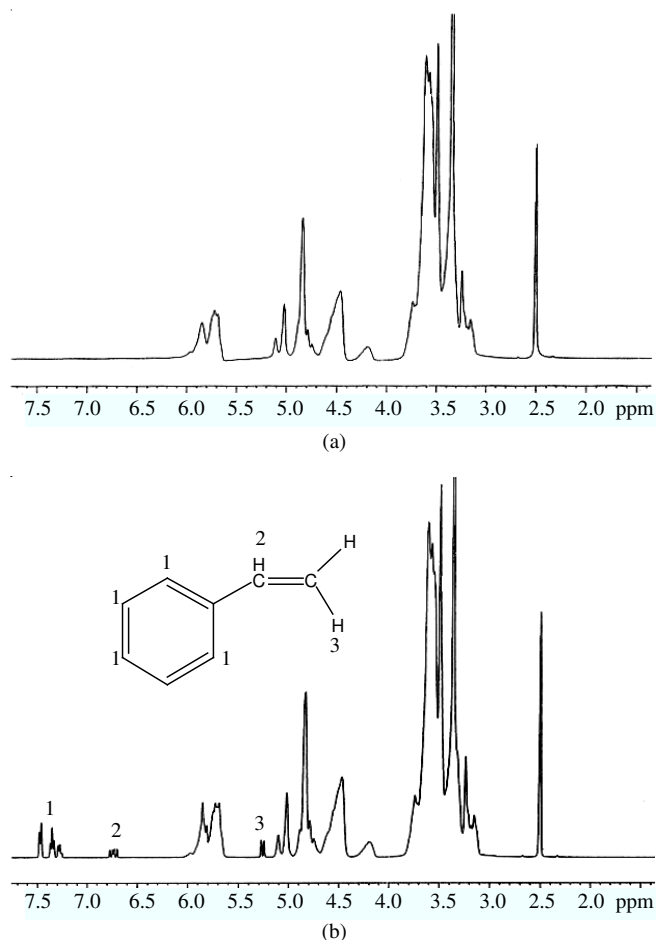


Fig. 1. ^1H NMR spectrum of (a) methylated β -CD and (b) styrene/methylated β -CD complex (measured in $\text{DMSO}-d_6$ at 30 °C)

The thermal stability of the styrene/methylated β -CD complex was evaluated using TGA analysis and compared with pure methylated β -CD and the physical mixture of styrene with the CD. Just as shown in Fig. 2, thermogravimetric results observed from pure methylated β -CD indicated two weight loss stages [Fig. 2(a)]. The one below 120 °C was attributed to the removal of water. The another one, with a beginning temperature at about 300 °C and corresponding to the major weight loss, was associated with the main degradation of the CD molecules. In the case of the physical mixture of styrene and methylated β -CD [Fig. 2(c)], there were also two weight loss phases. The high temperature weight loss stage was similar to that of pure CD which begin at about 300 °C, whereas the ending temperature of the low temperature one was unto 140 °C, about 20 °C increased compared to that of pure CD,

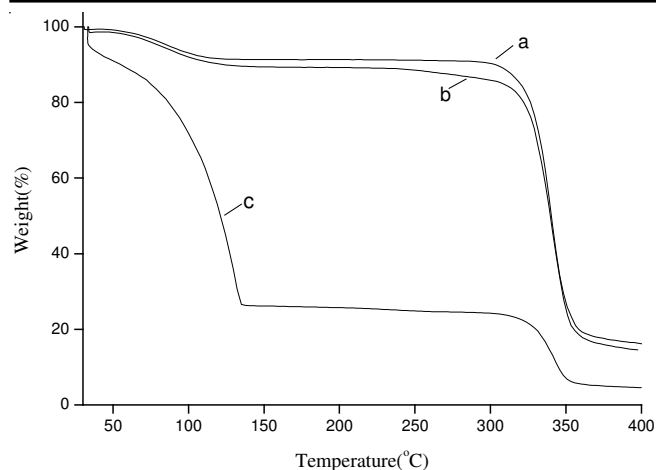


Fig. 2. TGA thermograms of (a) pure methylated β -CD, (b) styrene/methylated β -CD complex and (c) physical mixture of styrene and methylated β -CD

which is reasonable considering the boiling point of styrene (styrene $T_b \approx 138$ °C). The TGA thermogram of inclusion complex [Fig. 2(b)] was different from the thermogram of the physical mixture. The stability of a volatile guest molecule would be expected to increase due to guest-host interaction, which was the case for styrene/methylated β -CD inclusion complex. It was found that below 150 °C, the TGA thermogram of the complex was almost identical with the curve of pure methylated β -CD. However, up from about 150 °C, there was a continuous weight loss for the inclusion complex up to the main degradation of CD, suggesting the presence of styrene and its stability at temperature much higher than its boiling point, which may be valuable for polymerization of styrene at high temperature. The higher thermal stability of styrene at elevated temperature is further strong evidence for the complexation of styrene with methylated β -CD.

Stoichiometry of the inclusion complex: The complex formation of methylated β -CD with styrene was quantitatively studied. Fig. 3 showed plots of the UV absorbance versus different ratio of CD concentration and styrene concentration. It was clear indicated that the increase of CD concentration

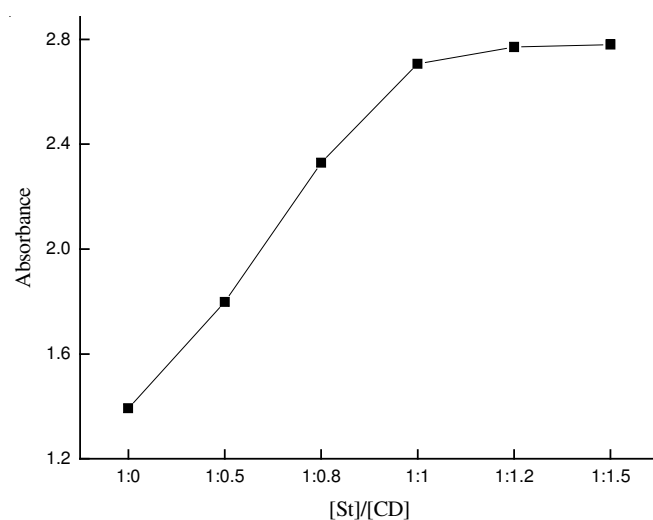


Fig. 3. Evolution of the UV absorbance of styrene with different concentration of CD [St]: concentration of the styrene, [CD]: concentration of the methylated β -CD

led a drastic increase in the UV absorbance which corresponded the concentration of the inclusion complex. When the ratio of the host/guest was above 1/1, hardly change in the absorbance was observed. These results suggested that the stoichiometry of the methylated β -CD/styrene complex was 1:1. It meant that each styrene molecule associated with one methylated β -CD to form a sufficiently water-soluble guest/host complex.

Association constant of the inclusion complex: For an analysis based on complexation, knowledge of the association constants for the CD complex is necessary in order to predict and better understanding of the interactions between the CDs and the guest in solution. The association constant can provide a measure of the complex stability and an understanding of the factors affecting the complexation. Benesi-Hildebrand linear regression¹⁸ was utilized to determine the association constant of styrene with methylated β -CD through UV spectrophotometry.

For a 1:1 stoichiometry, the inclusion complexation of methylated β -CD (CD) with styrene (S) could be expressed by eqn. 1:



So, the association constant K_a is given as follows:

$$K_a = \frac{[\text{CD}\cdot\text{S}]}{[\text{CD}][\text{S}]} \quad (2)$$

Under the condition of the present work, the initial concentration of CD was much higher than that of styrene, *i.e.*, $[\text{CD}]_0 \gg [\text{S}]_0$. Furthermore, there is no absorbance for methylated β -CD in the UV spectrum test. Styrene is the only contribution to UV absorbance. Therefore, any variation in UV absorbance could be presumably resulted from the complexation of methylated β -CD with styrene.

When reaching complexation equilibrium, association constant could be described as eqn. 3:

$$K_a = \frac{[\text{CD}\cdot\text{S}]}{[\text{CD}][\text{S}]} = \frac{[\text{CD}\cdot\text{S}]}{([\text{CD}]_0 - [\text{CD}\cdot\text{S}])([\text{S}]_0 - [\text{CD}\cdot\text{S}])} \quad (3)$$

Because of $[\text{CD}]_0 \gg [\text{S}]_0$, eqn. 3 could be further expressed as following equation:

$$K_a = \frac{[\text{CD}\cdot\text{S}]}{[\text{CD}][\text{S}]} = \frac{[\text{CD}\cdot\text{S}]}{[\text{CD}]_0([\text{S}]_0 - [\text{CD}\cdot\text{S}])} \quad (4)$$

According to the discussion above, the change in UV absorbance ΔA upon the complexation with CD could be expressed:

$$\Delta A = \epsilon[\text{CD}\cdot\text{S}] \quad (5)$$

where ϵ = molar extinction coefficient.

Then a substitution of eqn. 5 into eqn. 4 gives the form of the extended Benesi-Hildebrand equation as shown by eqn. 6:

$$K_a = \frac{\Delta A/\epsilon}{[\text{CD}]_0([\text{S}]_0 - \Delta A/\epsilon)} \quad (6)$$

Another form of the above equation:

$$\frac{1}{\Delta A} = \frac{1}{K_a[\text{S}]_0\epsilon} \cdot \frac{1}{[\text{CD}]_0} + \frac{1}{[\text{S}]_0\epsilon} \quad (7)$$

From the equation above, it is implied that a plot between $1/\Delta A$ versus $1/[\text{CD}]_0$ should give a straight line and from the slope and intercept, the value of K_a can be calculated.

Fig. 4 illustrated the double-reciprocal plot for styrene included with methylated β -CD at 20 °C. Just as seen, the plot was well described as a single straight line ($R^2 = 0.9988$), from which the value of the association constant was determined $K_a = 79.53 \text{ mol/L}^{-1}$. Furthermore, the excellent linearity of this double-reciprocal plot confirmed that each styrene complexed with only one methylated β -CD to form an inclusion compound, which was in accord with the result of stoichiometry tested last part.

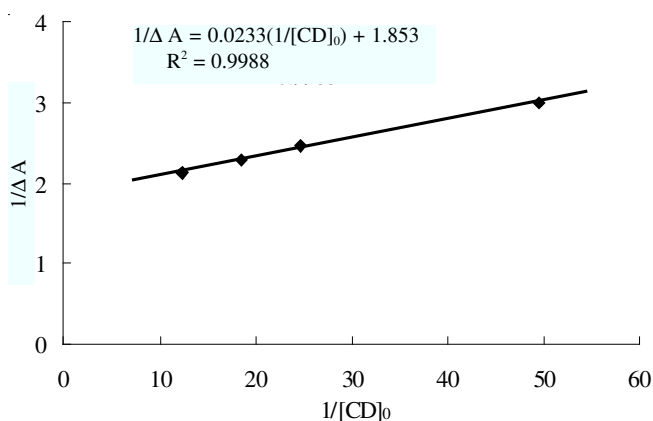


Fig. 4. Double-reciprocal plot for styrene complexed to methylated β -CD at 20 °C following the application of eqn. 1

Similarly, association constants at other different temperatures were determined, which was shown in Fig. 5. It was obvious that the K_a decreased with increasing temperature, which indicated that the complexation between styrene and methylated β -CD was an exothermic process.

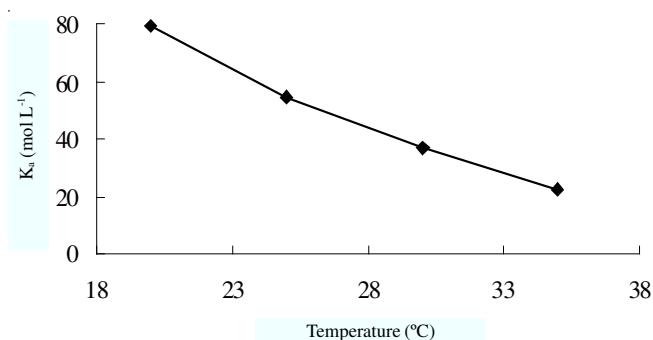


Fig. 5. Evolution of the association constants at different temperatures

Thermodynamic consideration of the complexation:

It is well known that thermodynamics is an efficient method in investigating a chemical or physical process. It can give much additional information involved in the process. According to the variation of association constants at different temperatures, the thermodynamic parameters involved in the complex formation were studied.

For CD binding with some guest compound, we know:

$$\Delta G_{\text{binding}} = -RT \ln K_a \quad (8)$$

$$\Delta G_{\text{binding}} = \Delta H - T\Delta S \quad (9)$$

As a result from the above eqns. 8 and 9, one can obtain:

$$\ln K_a = \frac{-\Delta H}{RT} + \frac{\Delta S}{R} \quad (10)$$

Generally speaking, there is little change for ΔH and ΔS at different temperatures for many chemical and physical processes. So in this case, it was hypothesized that ΔH and ΔS were constant in the temperature range tested (20-35 °C). Therefore, a plot $\ln K_a$ versus $1/T$ should be a straight line and from the slope and intercept, the values of ΔH and ΔS could be calculated.

As shown in Fig. 6, the fitting plot could be well expressed as a straight line ($R^2 = 0.9937$). The resulted thermodynamic parameters, ΔH and ΔS calculated from Fig. 6 and ΔG from eqns. 8 and 9 were listed in Table-1.

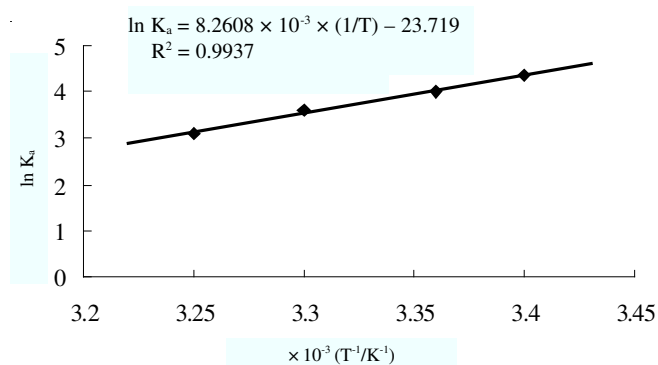


Fig. 6. Plot for styrene complexed to methylated β -CD at different temperatures following the application of eqn. 10

TABLE-1
THERMODYNAMIC PARAMETERS OF STYRENE
INCLUDED WITH METHYLATED β -CD

Temperature (°C)	ΔG^* (kJ mol ⁻¹)	ΔG^{**} (kJ mol ⁻¹)	ΔH (kJ mol ⁻¹)	ΔS (J mol ⁻¹ K ⁻¹)
20	-10.66	-10.9		
25	-9.91	-9.91		
30	-9.07	-8.93	-68.68	-197.2
35	-7.94	-7.94		

*Calculated from eqn. 8; **Calculated from eqn. 9.

From Table-1, ΔG values calculated from K_a were almost equal to that from ΔH and ΔS . It denoted that the hypothesis of ΔH and ΔS being constant in this case was reasonable. The negative values of ΔG indicated that the inclusion process between styrene with methylated β -CD was spontaneous. The negative value of ΔH showed that the formation of complex was an exothermic process. Some secondary bonds, such as van der Waals forces, hydrophobic interaction, may be play important roles in the inclusion. In the complexation process, the release of the water originally bonded in the cavity of the CD would induce the increase of ΔS value, whereas the inclusion of styrene molecule into CD cavity would decrease ΔS value. The negative ΔS calculated indicated that the decrease in motion degrees of freedom of the encapsulated styrene molecules is beyond the increase caused by the water molecules released, which gave a more ordered system.

Conclusion

The inclusion complex of styrene with methylated β -CD was studied by various techniques. ¹H NMR and TGA

measurements indicated that methylated β -CD could form inclusion complex. Furthermore, it was found that the thermal stability of styrene encapsulated in CD was much higher than that of free one, which would be valuable for the polymerization of styrene especially at high temperature. It was shown from the UV absorbance tested that the stoichiometry of the inclusion complex was 1:1. The association constants at different temperatures were determined using Benesi-Hildebrand linear regression. It was found that the value of K_a decreased with increasing temperature. Thermodynamic consideration showed that the inclusion process was a spontaneous and exothermic one.

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