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β-Cyclodextrin hydration: a calorimetric and gravimetric study

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Abstract

The standard heat of solvation of β-cyclodextrin (βCD) with one mole of water is determined as -10.50 kJ per mol βCD, after measurement of the heat of dissolution of βCD samples containing various amounts of water. This value is constant in the composition range $\beta\text{CD}\cdot n\text{H}_2\text{O}$, with $0 < n < 11$ (n is the number of water molecules attached).

The thermogravimetric study of the kinetics of water absorption by βCD does not show a definite hydrate. The water content of the hydrate is controlled by the vapour pressure and temperature alone. Under ambient conditions, the number of water molecules bound to one βCD molecule lies between 10 and 12.

Keywords: Cyclodextrin; DSC; Heat of solvation; Thermodynamics; Water

1. Introduction

α-, β-, γ-Cyclodextrins are cyclic oligosaccharides composed of 6, 7, and 8 D-glucose units, respectively. They are known to form many inclusion compounds with organic and inorganic molecules, both in the solid state and in solution [1-5].

This paper is a contribution to the understanding of the thermal decomposition of the β-cyclodextrin-water complex. Many physico-chemical studies [6-8] have concluded in favour of a βCD hydrate with about 11 water molecules. In a previous

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paper, [9], we discussed a possible two-step dehydration of βCD. Here we discuss the eventuality of a distinct hydrate with 4 water molecules and the thermodynamic parameters of βCD–water bonding. Many studies [10–12] describe the removal of water molecules as a driving step in the formation of complexes with βCD.

The gravimetric study also contributes to the knowledge of βCD hydration states under atmospheric water pressure conditions.

2. Materials and methods

2.1. Apparatus

The heats of dissolution of βCD hydrates were determined using an isoperibolic calorimeter (LKB 8700) with a 100-ml cell [13]. The variations in the cell temperature were followed with a thermistor in contact with the reaction medium. A specific treatment of the data allowed us to calculate directly the enthalpy of dissolution, comparatively to an electric calibration.

Measurements of the βCD hydration ratio were made by thermogravimetric analysis, using a Mettler TG 50 thermobalance.

A MacBain-type thermobalance [14,15] was used to follow the hydration of βCD versus water vapour pressure. The weight increase of the samples was calculated from the lengthening of a silica spring, determined with a cathetometer. This apparatus allowed us to work under vacuum or controlled atmosphere. The temperatures of the sample and of the spring were controlled independently (Fig. 1).

2.2. Materials

β-Cyclodextrin was supplied by Roquette under reference βCD-16. The hydration ratio was found to be 14%. Samples of βCD with various water ratios, βCD(x% H_2O), were obtained by two distinct methods:

(1) For $0 < x < 5\%$, by slow rehydration of anhydrous βCD [9], in contact with ambient atmosphere or in a closed vessel containing small quantities of air and water vapour.

(2) For $5 < x < 14\%$, by slow and controlled dehydration of βCD(14% H_2O) at 50°C.

All samples were stored in a glove box under a dry argon atmosphere before the experiments were performed.

3. Calorimetric study

3.1. Results

Each value of $\Delta_{\text{diss}}H(298\ \text{K})$βCD($x$% H_2O) given in Table 1 is the average of ten measurements for a fixed water ratio. For every sample of βCD(x% H_2O), x was

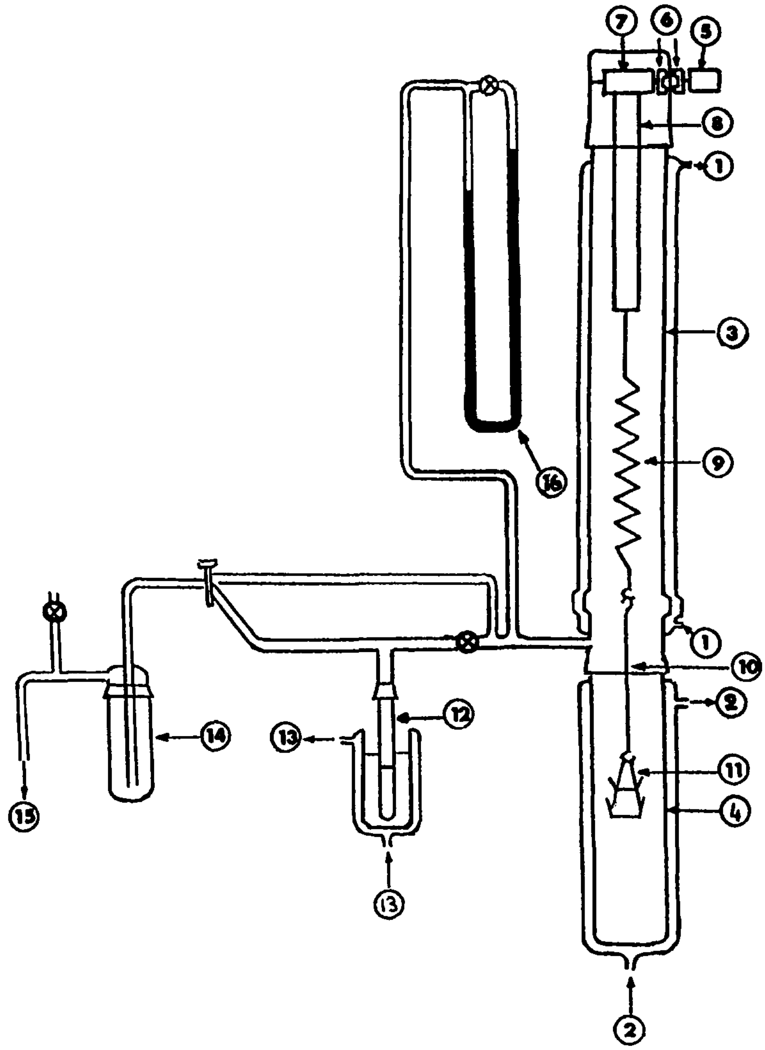

Fig. 1. MacBain-type thermobalance. Key: 1, 50°C thermostated oil circulation; 2, 29°C thermostated oil circulation; 3, double-wall spring chamber; 4, double-wall sample chamber; 5, engine; 6, magnets; 7, drum; 8, Ni/Cr wire; 9, silica spring; 10, silica stem; 11, double-plate crucible; 12, water tank (coldest point); 13, thermostated oil circulation; 14, trap; 15, vacuum pump; 16, manometer.

obtained from TGA measurements before calorimetric experiments were made, and were checked after the last dissolution on a sample stored in the glove box. In our storing conditions, the absolute uncertainty of the water ratio does not exceed 0.5%.

The number of water molecules n for one βCD molecule was calculated from the values of x.

The absolute uncertainty of n is about 0.3 for the values given in Table 1. The relative uncertainty of the measured heats of dissolution was estimated by chemical

Table 1
Enthalpy of dissolution of βCD samples with various water ratios

x [a]	1.0	2.0	5.0	6.9	7.3	10.4	12.8	13.9
n [b]	0.6	1.3	3.3	4.7	5.0	7.3	9.3	10.2
$\Delta_{\mathrm{diss}}H$ in J per g βCD	−75.6	−68.4	−48.9	−32.5	−26.3	−11.9	4.0	10.4
$\Delta_{\mathrm{diss}}H$ in J per g anh. βCD	−76.4	−69.8	−51.5	−34.9	−28.4	−13.3	4.6	12.1

[a] x%, water ratio.
[b] n, number of water molecules fixed on one molecule of βCD.

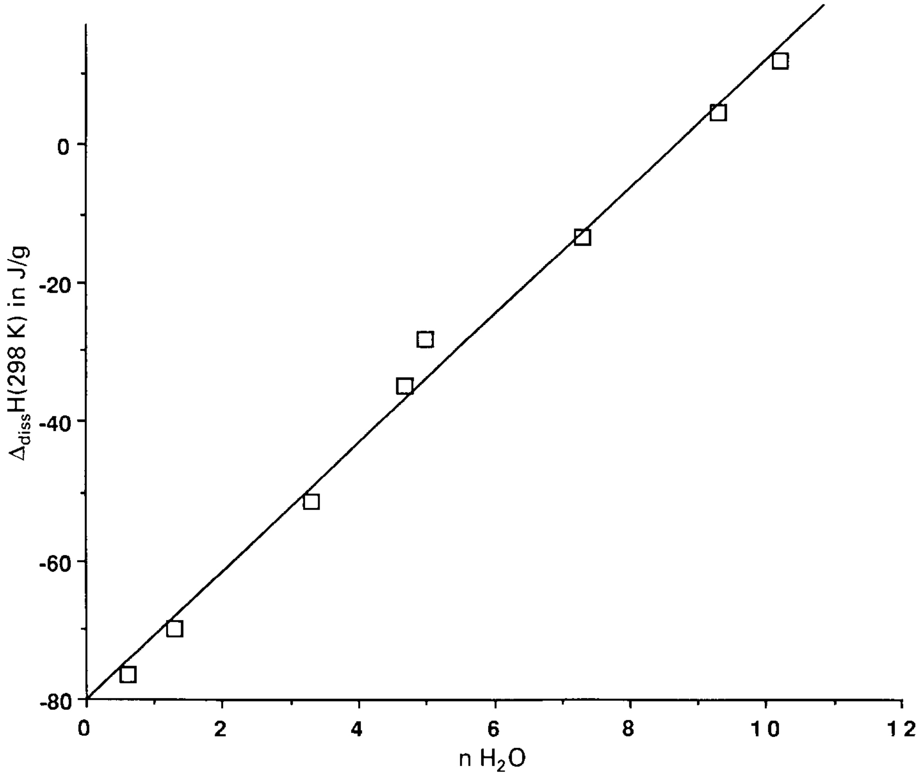

Fig. 2. Enthalpy of dissolution of βCD · nH$_2$O versus n at 298 K. ($\Delta_{\mathrm{diss}}H$(298 K)βCD · nH$_2$O is given in J per g anh. βCD.)

calibration (dissolution of tris-hydroxyaminomethane in HCl 0.1 mol l^{-1}). From our results it is estimated to be under 3%.

The evolution of $\Delta_{\mathrm{diss}}H$(298 K)βCD · nH$_2$O (J per g anh. βCD) versus n is plotted in Fig. 2. Taking into account the uncertainties, both of the values of n and of the calorimetric results, we can consider that $\Delta H = f(n)$ is linear in the range $n = 0$–12 water molecules.

In this composition range, $\Delta_{\mathrm{diss}}H(298\ \mathrm{K})\beta\mathrm{CD}\cdot n\mathrm{H_2O} = -91.22 + 10.50n$ (kJ per mol anh. βCD). This linear evolution does not indicate the existence of a possible intermediate hydrate.

3.2. *The thermodynamic consequences of the βCD inclusion process*

The driving force in the case of complex formation is the removal of high-energy water molecules by guest molecules from the cavity of βCD [10–12]. It is interesting to develop the calculation of the enthalpy "cost" of the dehydration step during the inclusion process.

3.3. *Hypothesis*

During the dissolution of solid βCD in water, the final state is always the same [10], even when the initial hydration of solid βCD is different. It will be denoted: $(\beta\mathrm{CD}\cdot n_{\mathrm{sol}}\mathrm{H_2O})(\mathrm{sln})$.

(1) Dissolution of $(\beta\mathrm{CD}\cdot n_1\mathrm{H_2O})(\mathrm{s})$ in water

$$(\beta\mathrm{CD}\cdot n_1\mathrm{H_2O})(\mathrm{s}) + (n_{\mathrm{sol}} - n_1)\mathrm{H_2O}(\mathrm{l}) \xrightarrow{\Delta H_1} (\beta\mathrm{CD}\cdot n_{\mathrm{sol}}\mathrm{H_2O})(\mathrm{sln})$$

$(n_{\mathrm{sol}} - n_1)\mathrm{H_2O}(\mathrm{l})$ brought by the solvent

(2) Dissolution of $(\beta\mathrm{CD}\cdot n_2\mathrm{H_2O})(\mathrm{s})$ in water

$$(\beta\mathrm{CD}\cdot n_2\mathrm{H_2O})(\mathrm{s}) + (n_{\mathrm{sol}} - n_2)\mathrm{H_2O}(\mathrm{l}) \xrightarrow{\Delta H_1} (\beta\mathrm{CD}\cdot n_{\mathrm{sol}}\mathrm{H_2O})(\mathrm{sln})$$

$(n_{\mathrm{sol}} - n_2)\mathrm{H_2O}(\mathrm{l})$ brought by the solvent

(3) Partial dehydration of $(\beta\mathrm{CD}\cdot n_2\mathrm{H_2O})(\mathrm{s})$

$$(\beta\mathrm{CD}\cdot n_2\mathrm{H_2O})(\mathrm{s}) \xrightarrow{\Delta H} (\beta\mathrm{CD}\cdot n_1\mathrm{H_2O})(\mathrm{s}) + (n_2 - n_1)\mathrm{H_2O}(\mathrm{l})$$

with $n_2 > n_1$

Application of Hess's law to these reactions enables us to write $\Delta H = \Delta H_2 - \Delta H_1$. The same result is found if we consider the following thermodynamic cycle

$$\begin{tikzcd}
(\beta\mathrm{CD}\cdot n_2\mathrm{H_2O})(\mathrm{s}) \arrow[rr, "\Delta H"] \arrow[dr, "\Delta H_2"'] & & (\beta\mathrm{CD}\cdot n_1\mathrm{H_2O})(\mathrm{s}) + (n_2 - n_1)\mathrm{H_2O}(\mathrm{l}) \arrow[dl, "\Delta H_1"] \\
& (\beta\mathrm{CD}\cdot n_{\mathrm{sol}}\mathrm{H_2O})(\mathrm{sln}) \quad \text{(same final state)} &
\end{tikzcd}$$

It is easy then, knowing the initial (n_2) and final (n_1) hydration states of βCD, to calculate the dehydration enthalpy.

Using the relation between the enthalpy of dissolution of βCD and the number of hydrating water molecules, we can write $\Delta H = 10.50\ (n_2 - n_1)$ (kJ per mol anh. βCD). To remove one mole of water from one mole of βCD ($n_2 - n_1 = 1$), $\Delta H = 10.50$ kJ per mol anh. βCD.

The enthalpic effect associated with βCD dehydration is endothermic. It is one of the thermodynamic parameters we may take into account when studying the inclusion processes in βCD.

4. Gravimetric experiments

4.1. Results

The experiments were carried out on only one sample of βCD-16 that had been dehydrated under vacuum (1.3×10^{-6} bar) and then hydrated at 29 ± 1°C, under various vapour pressures of water. The vapour pressure is controlled by the temperature of a water tank which represents the coldest point of the installation. The sample is placed in a double-plate crucible to increase the exchange area between solid and gas.

Table 2 shows the results obtained at equilibrium during experiments under vapour pressures of water varying between 0.013 and 0.031 bar, while the temperature of the sample is kept constant at 29 ± 1°C.

The data of Table 2 are plotted in Fig. 3. The estimation of the absolute uncertainty of the pressure is 2.5×10^{-4} bar and the relative uncertainty of the weight percentage of water is 1%.

In accordance with the experimental data shown in Fig. 3, and regarding the uncertainties, we have assumed that there is a linear relation between the weight percentage of water fixed at equilibrium by an anhydrous sample of βCD and the vapour pressure of water.

Fig. 4 shows the hydration kinetics of an anhydrous sample of βCD under various pressures of water. None of the curves representing the percentage of water fixed versus time exhibit a step or a break in slope that may indicate the existence of a definite hydrate. The curves show that the higher the water pressure, the faster the equilibrium is reached.

Table 2

Percentage of water fixed during hydration under various vapour pressures of water, at 29 ± 1°C, of a 214.7-mg sample of anhydrous β-cyclodextrin

Cold point in °C	P_{H_2O} in bar	Δm_{water} in %
11.48	0.01355	13.61
14.10	0.01608	13.88
16.34	0.01857	14.42
19.8	0.02309	14.88
21.33	0.02537	15.28
23.14	0.02833	15.49
25.08	0.03183	16.12

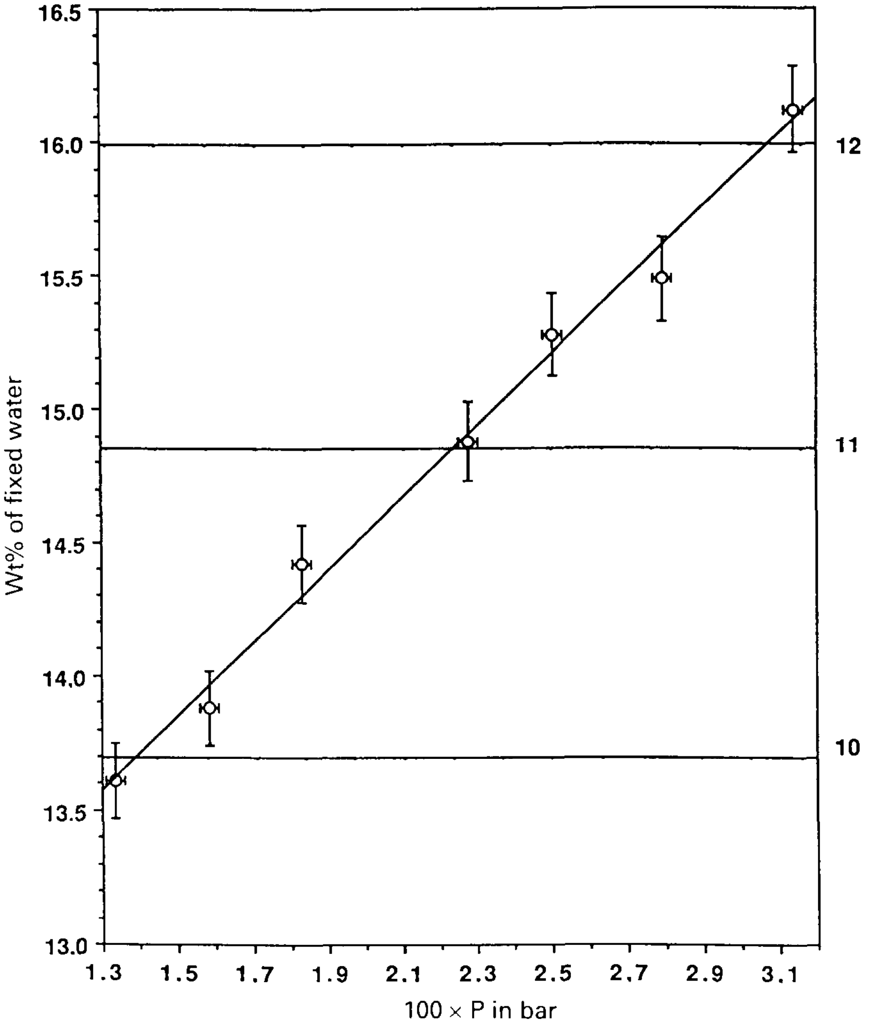

Fig. 3. Weight percentage of water fixed at 29 ± 1°C by an anhydrous sample of βCD at equilibrium, versus vapour pressure of water.

5. Discussion

To confirm the results obtained by isoperibolic calorimetry at 298 K, we have tried to calculate the enthalpy of dehydration of βCD from differential scanning calorimetry (DSC) measurements.

A Mettler TA2000B apparatus controlled by an HP85 computer was used. The apparatus was calibrated using the temperatures and enthalpies of high purity metals (or compounds). Argon circulation (5 l h^{-1}) was used because of the inertia, density and low thermal conductivity of this gas.

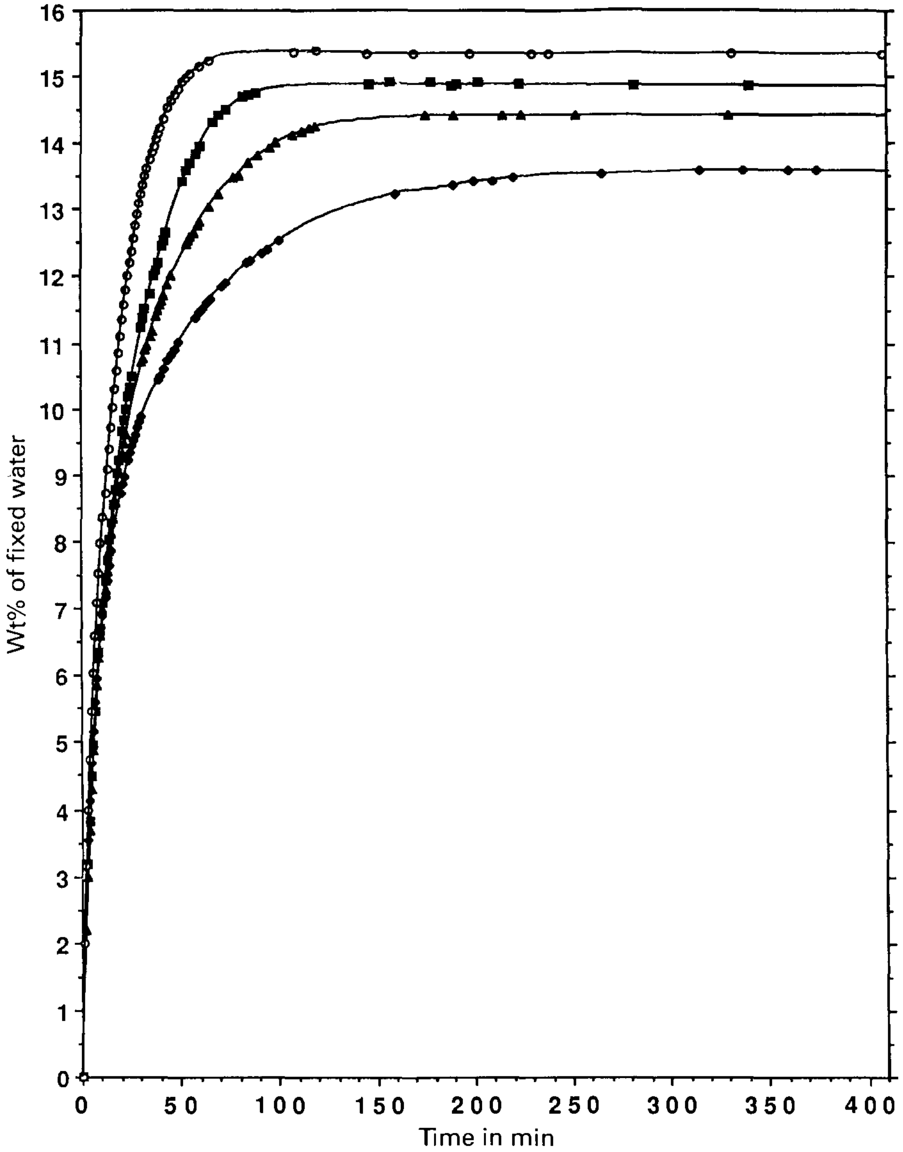

Fig. 4. Weight percentage of water fixed at 29 ± 1°C by an anhydrous sample of βCD and under various vapour pressures of water, versus time: ◆, $P_{H_2O} = 0.01355$ bar; ▲, $P_{H_2O} = 0.01857$ bar; ■, $P_{H_2O} = 0.02309$ bar; ○, $P_{H_2O} = 0.02537$ bar.

Samples (10–15 mg) of βCD were transferred into 40-μl aluminium crucibles which were sealed and weighed. The crucible covers had calibrated orifices to allow the vaporization of water. All experiments were performed with a heating rate of 5 K min^{-1} in the temperature range −100°C to +250°C.

Table 3
Enthalpy of the endothermic effect measured in the temperature range 20–150°C by differential scanning calorimetry (DSC) during dehydration of βCD

Sample	H_2O in %	ΔH_{mes} in J per g βCD	$\Delta H_{mes}/H_2O$ in kJ per mol H_2O
1 [a]	13.5	371	49.5
2 [a]	11.3	331	52.7
3 [a]	11.6	312	48.4
4 [a]	10.1	271	48.1
5 [a]	9.5	278	52.6
6 [a]	11.4	335	52.9
7 [a]	10.4	302	52.4
8 [b]	14.0	395	50.8
9 [c]	13.8	387	50.4
10 [d]	14.1	363	46.3
11 [d]	13.5	365	48.6

Key: ΔH_{mes} is the enthalpy of the measured effect for one gram of hydrated βCD. $\Delta H_{mes}/H_2O$ is the enthalpy of the measured effect according to the calculated amount of water initially present in the sample. Source: [a] Roquette; [b] Fluka; [c] Sigma; [d] Aldrich.

Eleven samples of βCD from various sources and of various water ratios were studied. The thermal effects for which the enthalpies are given in Table 3 take place in the 20–150°C temperature range.

In our hypothesis, this thermal effect corresponds to the dehydration of βCD samples according to the reaction

$$(\beta\text{CD}\cdot n\text{H}_2\text{O})(\text{s}) \xrightarrow{\Delta H_{\text{mes}}} (\beta\text{CD})(\text{s}) + n(\text{H}_2\text{O})(\text{g})$$

This reaction can be considered as two steps.

Dehydration $(\beta\text{CD}\cdot n\text{H}_2\text{O})(\text{s}) \rightarrow (\beta\text{CD})(\text{s}) + n(\text{H}_2\text{O})(\text{l})$

Vaporization of water $n(\text{H}_2\text{O})(\text{l}) \rightarrow n(\text{H}_2\text{O})(\text{g})$

The water ratio of the βCD samples is calculated from the weight before and after total dehydration at 250°C in the calorimeter. Table 3 gives the enthalpy ΔH_{mes} per mol H_2O of the measured effect according to the calculated amount of water initially present in the sample. From the results, the average value for ΔH_{mes} per mol H_2O can be deduced: ΔH_{mes} per mol $H_2O = 50.2$ kJ per mol H_2O. As indicated above $\Delta H_{mes} = \Delta_{dehydr}H + \Delta_{vap}H$.

According to handbook data [16]

$$\Delta_{\text{vap}}H\text{H}_2\text{O}\ (\text{at } 100°\text{C}) = 40.6\ \text{kJ mol}^{-1}$$

$$\Rightarrow \Delta_{\text{dehydr}}H = 9.6\ \text{kJ per mol H}_2\text{O}$$

Considering a 3% accuracy on enthalpic effects with the DSC method, the calculated accuracy on $\Delta_{dehydr}H$ is about 15%. This result is less reliable than the one obtained with dissolution enthalpy measurements at 25°C ($\Delta H = 10.50$ kJ per mol

H_2O). Nevertheless, it confirms the order of 10 kJ needed to remove one mole of water from one mole of βCD. This result is in agreement with our previous paper [9]. Contrary to Marini et al.'s comment [17], there are no contradictions with the results of Szafranek [11] who calculated the activation enthalpy of the βCD dehydration reaction. Marini et al. have confused the enthalpy of activation and the enthalpy of reaction, which are obviously different from physical and thermodynamics point of view.

6. Conclusions

Our previous hypothesis, based on the shape of some DSC thermograms for hydrated βCD samples, is not confirmed in the present work. It seems that a $4H_2O$ hydrate of βCD does not exist.

The enthalpy of dissolution of hydrated βCD has a linear evolution versus the number of fixed water molecules and no change in the slope of gravimetric evolution versus water ratio is found.

This study confirms that no definite hydrate of βCD exists and that the maximum hydration state is in direct relation with the temperature and water vapour pressure of the surrounding atmosphere.

For a sample maintained at $29 \pm 1°C$, the number of water molecules fixed on one βCD molecule ranges between 10 and 12, under normal atmospheric conditions of moisture.

The determination of the dehydration enthalpy is an important step in the understanding and in the thermodynamic forecast of inclusion reactions in βCD molecules.

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