

Influence of the Water Content on the Thermal Behaviour of β -Cyclodextrin at Low and Very Low Temperature

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Abstract. Heat capacities of β -CD·9.7H₂O were measured by adiabatic calorimetry in the temperature range 10–300 K. Differential scanning calorimetry was used to follow the evolution of the thermal behaviour versus hydration ratio between 170 and 300 K. At least three different behaviours were observed, according to the number, n , of water molecules: $0 < n < 7$, $7 < n < 10$, and $n > 10$. These macroscopic results are discussed in terms of organization differences between the most or the least hydrated β -CD. The structuring effect of the hydration water molecules is emphasised. The existence of two energetically distinct β -CD hydrates ($n < 10$ and $n > 10$) seems to be confirmed. This hypothesis is discussed in comparison with previous spectroscopic and structural studies.

Key words: β -cyclodextrin hydrates, thermodynamic, calorimetry, heat capacity, low temperature.

1. Introduction

A great number of scientific studies on the cyclodextrins, macrocycles formed by $\alpha(1-4)$ linked units of α -D-glucopyranose, have been published since their discovery, one hundred years ago. Despite these studies, many questions remain concerning the role of the water molecules of hydration during the inclusion process of a guest into the macrocycle cavity. The present paper is concerned with the β -cyclodextrin (β -CD) molecule. It is known [1, 2] that β -CD crystallises from water with 11 or 12 water molecules. However, recent studies indicate that β -CD does not exhibit defined hydrates [3–5]: the hydration rate depends directly on the humidity of the surrounding atmosphere. Under atmospheric storage conditions, the hydration water ratio may easily vary from 10 to 12 (or even more) water molecules per β -CD. Only a few studies have investigated the evolution of the β -CD physicochemical properties versus the hydration number [3–8].

In a previous paper [9], we have described the particular behaviour of anhydrous β -CD at very low temperature. This study seemed to confirm the existence of intramolecular hydrogen bond interactions (flip-flop type [10]) between the secondary hydroxyl groups. It is of interest to compare the low temperature behaviour

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of β -CD \cdot 9.7H₂O (this work) with that of anhydrous β -CD on the one hand and that of β -CD \cdot 10.9H₂O (Hanabata *et al.* [11]) on the other.

2. Experimental

2.1. MATERIALS

2.1.1. Adiabatic Calorimetry Experiments

β -Cyclodextrin was supplied by Roquette Frères and used without further purification. The sample hydration ratio was determined by thermogravimetric analysis (Mettler TG50 Thermobalance). The compound was found to be β -CD \cdot 9.7H₂O (± 0.3 H₂O). The molar mass is taken as 1310 g mol⁻¹ in the following calculation.

2.1.2. DSC Experiments

Samples with various hydration numbers were obtained by drying the β -CD \cdot 9.7H₂O between 50 to 80 °C for various durations or by hydrating it under water vapour pressure. However, the hydration numbers were measured by thermogravimetric analysis before each DSC run. The reproducibility of this determination is ± 0.2 wt%.

2.2. METHODS

Differential scanning calorimetry results were obtained using a Mettler TA 8000 apparatus. Weighed samples (10–15 mg) were conditioned into 40 μ L aluminium sealed crucibles. All the experiments were performed with a heating rate of 0.083 K s⁻¹ (5 K min⁻¹) in the temperature range 120–310 K.

The heat capacity determinations were performed between 10 and 300 K using a home built adiabatic calorimeter [9, 12]. The sample mass was 9.696 g corresponding to 7.402×10^{-3} mole. The thermal exchanges in the measurement cell are improved by addition of helium at a pressure of about 2×10^3 Pa (300 K). The heat capacity of the empty cell represents 40 to 70% of the total (measured) heat capacity according to the temperature range. The accuracy on the heat capacity values is about 5% at very low temperature (below 20 K) and 0.1% for temperatures above 200 K.

3. Results

The experimental values of heat capacities versus T are listed in Table I in chronological order and plotted in Figure 1. A heat capacity anomaly appears in the temperature range 230–290 K. The maximum of the observed peak is located at 273 K (Figure 1). The associated energy is found to be 3.0 ± 0.2 J mol⁻¹.

DSC curves, plotted with the same scale in Figure 3, show that the thermal behaviour of β -CD at low temperature depends on its hydration number.

Table I. Molar heat capacities of β -cyclodextrin \cdot 9.7H₂O.

T K	C_p J K ⁻¹ mol ⁻¹	T K	C_p J K ⁻¹ mol ⁻¹	T K	C_p J K ⁻¹ mol ⁻¹	T K	C_p J K ⁻¹ mol ⁻¹
<i>Series 1</i>		225.3	1478.7	27.8	117.7	166.1	1071.2
79.6	503.3	227.0	1495.3	29.5	134.2	168.5	1087.7
85.2	543.6	229.1	1512.6	31.5	151.9	172.5	1114.0
91.7	580.3	230.4	1532.2	34.1	172.6	174.9	1125.8
96.0	609.0	232.1	1532.8	36.9	195.4	176.6	1130.0
99.2	626.4	234.7	1550.8	39.7	218.1	178.6	1145.3
102.8	651.7	<i>Series 2</i>		42.6	243.2	180.6	1173.9
107.0	678.5	244.1	1645.6	46.0	270.0	183.0	1186.0
111.4	713.1	247.1	1679.6	49.9	299.7	184.6	1203.5
115.5	740.4	252.2	1742.5	53.9	329.4	188.6	1230.1
119.4	761.5	255.7	1798.9	57.7	356.1	190.5	1233.1
123.4	783.1	256.6	1798.7	61.4	381.6	202.5	1310.3
127.5	807.2	258.6	1832.8	64.4	401.4	205.7	1333.9
131.7	835.3	262.1	1898.3	67.1	424.7	207.2	1344.1
135.8	857.9	264.2	1941.2	71.5	450.2	208.2	1353.2
139.8	881.3	265.2	1975.8	75.8	474.3	210.9	1369.1
143.9	902.5	268.0	2026.4	81.6	515.7	213.4	1387.8
148.0	935.5	271.3	2109.6	88.2	561.5	215.9	1408.9
152.1	962.9	272.8	2139.8	92.5	589.0	219.0	1432.8
156.1	990.5	273.8	2157.0	95.71	601.6	224.8	1484.8
157.0	998.1	278.3	2114.8	99.22	634.1	236.3	1570.4
160.6	1028.6	282.1	2090.4	103.4	661.6	239.7	1601.3
163.7	1047.0	290.3	2099.5	107.7	690.1	250.2	1722.6
166.1	1066.1	294.6	2121.0	111.8	718.3	255.1	1775.0
170.9	1093.1	297.6	2147.1	115.8	740.9	260.4	1853.5
174.0	1120.1	<i>Series 3</i>		119.7	760.6	263.3	1920.2
177.9	1155.1	193.3	1247.7	123.8	792.4	266.4	2003.4
182.7	1178.2	196.8	1274.8	127.9	805.3	270.9	2090.3
188.3	1219.3	200.4	1297.5	132.1	841.4	273.2	2155.2
192.5	1240.6	204.6	1326.6	136.1	863.7	275.8	2143.7
195.4	1266.2	209.0	1361.1	140.2	880.5	276.8	2131.7
197.3	1281.2	213.2	1392.7	144.2	913.9	280.3	2103.0
200.5	1297.2	217.0	1421.0	148.3	939.5	281.2	2096.7
203.1	1320.2	221.0	1452.1	152.3	963.8	285.4	2070.7
209.6	1366.9	225.1	1481.8	154.2	975.8	287.2	2074.0
211.5	1378.3	229.3	1516.3	156.4	997.6	292.3	2104.5
213.9	1393.3	233.3	1550.6	158.9	1010.6	297.5	2140.2
217.5	1413.8	22.8	76.80	160.4	1023.6	300.5	2165.4
220.9	1459.3	24.3	89.00	162.7	1043.8	303.9	2188.7
223.6	1472.4	26.1	102.1	164.9	1063.7		

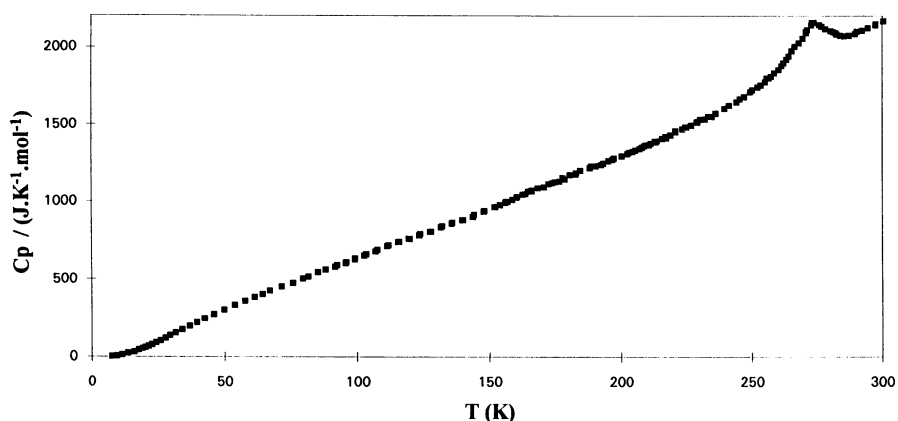


Figure 1. Molar heat capacities of β -cyclodextrin \cdot 9.7 H₂O.

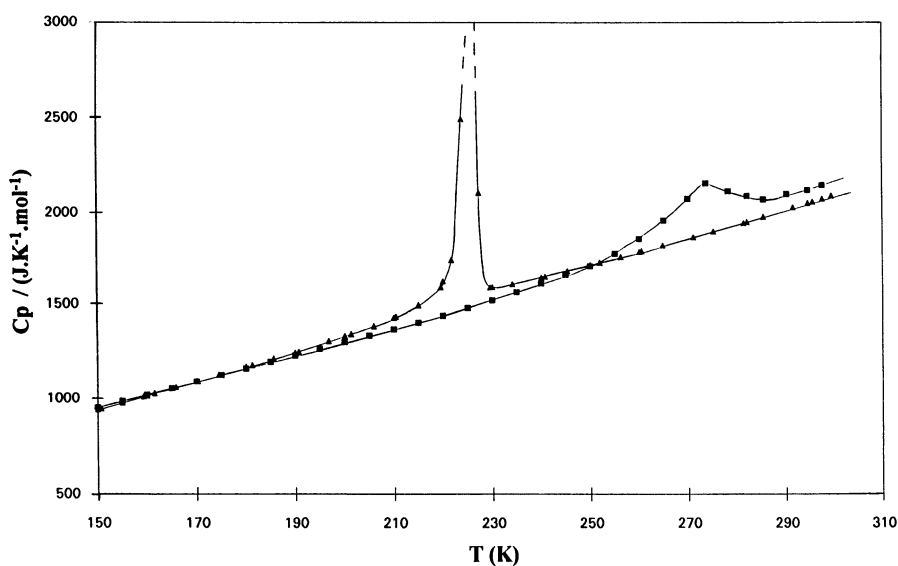


Figure 2. Molar heat capacities of ■: β -cyclodextrin \cdot 9.7H₂O, ▲: β -cyclodextrin \cdot 10.9H₂O [11].

4. Discussion

In previous paper [11], Hanabata *et al.* presented results of a similar adiabatic low temperature experiment. The studied compound was a sample of β -CD recrystallized from water. It was found to have the molecular composition β -CD \cdot 10.9H₂O \pm 0.1H₂O. Comparing our results with those of Hanabata *et al.* we found that both results agree well for temperatures lower than 200 K. At higher temperatures, Hanabata's compound exhibits a heat capacity anomaly with a maximum at 227 K, whereas it appeared at 273 K for our sample. The two curves, in the temperature

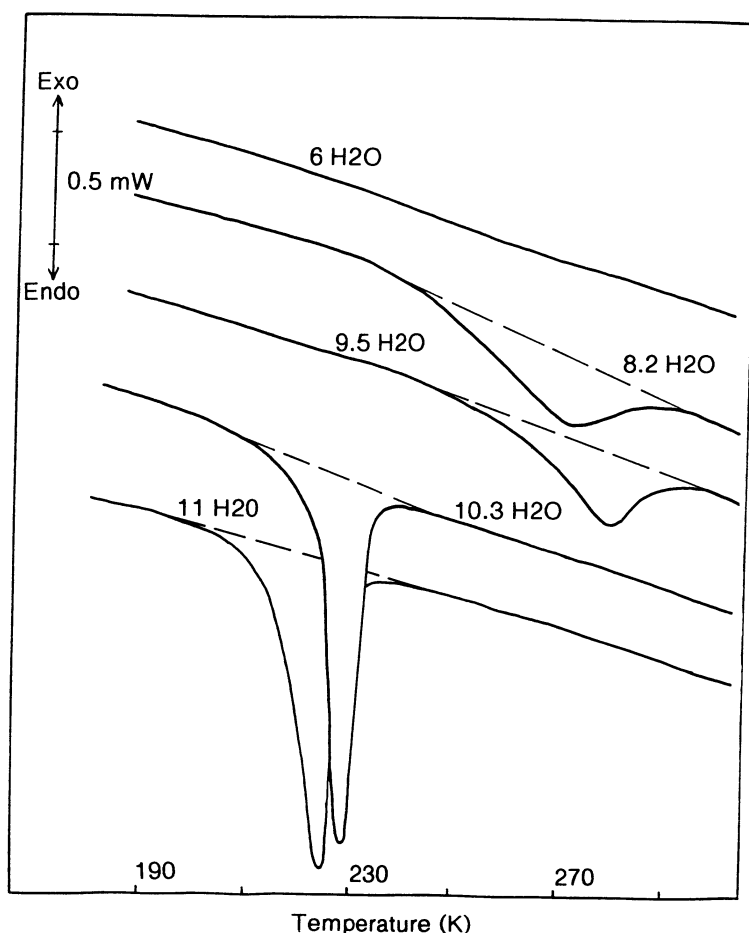


Figure 3. Thermal behaviour of β -cyclodextrin according to water content: DSC curves.

range 150–300 K, are reported in Figure 2. It seems very interesting to explain this surprising difference of behaviour. The first approach was to ascertain the difference in the two samples studied. The first difference was that Hanabata *et al.* had recrystallized β -CD, whereas we used a microcrystalline powder. The second difference was in the water content of the two hydrates.

In order to understand the reason for these two distinct behaviours, we performed a series of DSC experiments on differently hydrated β -CD microcrystalline powders. From the results of these DSC experiments (Figure 3) three types of thermal behaviour clearly appear. They can be related to three ranges of hydration of the macrocyclic compound.

From 0 to 7 H₂O per β -CD, no significant thermal event was detectable. Between 7 and 10 H₂O per β -CD, an endothermic effect occurred. The peak is broad and spread over a large temperature range (around 50 K). Depending on the water

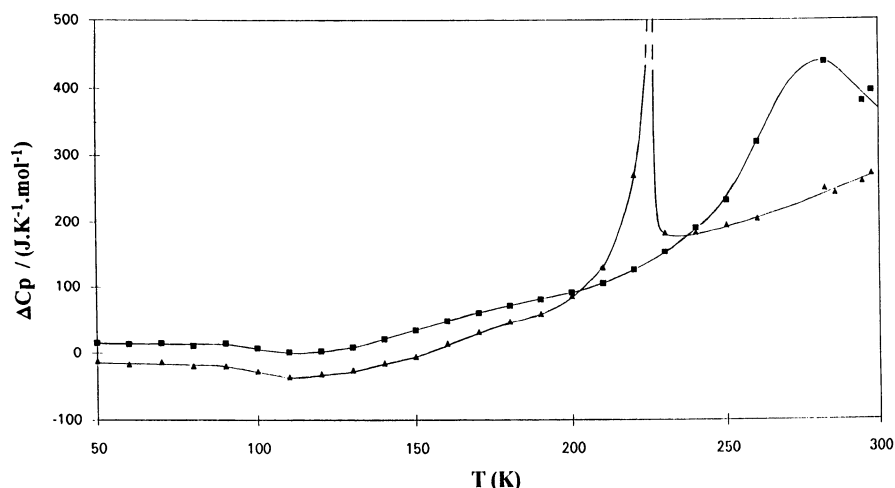


Figure 4. Calculated $\Delta C_p = f(T)$ curves: $\Delta C_p = C_p(\beta\text{-cyclodextrin}\cdot n \text{ H}_2\text{O}) - C_p(\text{anhydrous } \beta\text{-cyclodextrin}) - nC_p(\text{solid H}_2\text{O})$. ■: $n = 9.7 \text{ H}_2\text{O}$, ▲: $n = 10.9 \text{ H}_2\text{O}$ [11].

content, its maximum is observed around 277 K. This effect seems to be due to the same phenomenon that gives rise to a heat capacity anomaly in our adiabatic experiment. The associated enthalpy is low and calculation leads to $2.9 \pm 0.4 \text{ J g}^{-1}$.

Above 10 H_2O per $\beta\text{-CD}$, the broad transition rapidly disappeared to be replaced by a sharp, near first order transition, with a maximum at 227 K and a corresponding enthalpy change of $5.1 \pm 0.3 \text{ J g}^{-1}$. This transition is very similar to that previously found by Hanabata *et al.* [11].

These DSC experiments lead us to the hypothesis that the differences between Hanabata's results and ours are only due to the minor difference in the hydration numbers of the $\beta\text{-CD}$ samples in the critical range of hydration around 10 H_2O per $\beta\text{-CD}$.

In order to amplify the differences between the behaviours of the two samples which were observed in adiabatic calorimetry experiments, $\Delta C_p = f(T)$ was calculated for both samples and the resulting curves were plotted in Figure 4.

$$\Delta C_p = C_p(\beta\text{-CD} \cdot n\text{H}_2\text{O}) - C_p(\text{anhydrous } \beta\text{-CD}) - n \cdot C_p(\text{H}_2\text{O}).$$

Indeed, at each temperature, the measured value of the heat capacity is the sum of a number of particular contributions. If we assume that the contributions due to the macrocycle and to the water molecules are approximately the same for both hydrated forms ($n < 10$ and $n > 10$), ΔC_p will only represent the contributions due to water-macrocycle interactions.

The heat capacities of anhydrous $\beta\text{-CD}$ versus T have been reported in a recent paper [9]. The heat capacity of water is taken as C_p (solid H_2O) from reference [13].

Three temperature ranges appear in the evolution of the two β -CD hydrates' behaviour. From 50 to 120 K, the evolution of the two $\Delta C_p = f(T)$ curves is very similar and the calculated values of ΔC_p are quite constant. The relative positions of the two curves would seem to indicate a better organisation (lower values of ΔC_p) for the more hydrated compound. One hypothesis could be that, in this case, the number of water molecules induce a better long distance order between the macrocycles than in the case of β -CD \cdot 9.7H₂O. This first observation is surprising having regard to the small difference in the water contents between the two β -CD hydrates.

From 120 K, the slopes of the two curves increase in a similar way. The thermal behaviours of the two β -CD hydrates evolve identically. We assume that the same process begins at this temperature. From 200 K, this process accelerates but the evolution of ΔC_p versus temperature is significantly different for the two hydrates. The temperature of the anomaly's maximum appears to depend on the water content because it is 227 K for β -CD \cdot 10.9H₂O and 273 K for β -CD \cdot 9.7H₂O.

Hanabata *et al.* [9] explained the heat capacity peak at 227 K by the existence of a particular hydrogen bond network between β -CD hydroxyl groups and some external water molecules. This arrangement was described by Betzel [2] who performed a low temperature neutron diffraction study on the dodecahydrate. Assuming that the 273 K anomaly, pointed out in the present work, represents the same intermolecular phenomenon, the differences in the temperature of the maximum could be explained in terms of a more or less structuring effect of water, which depends on the hydration ratio. The structuring interactions between water molecules and macrocycles exist in both hydrates but in the less hydrated, they could be less important. Water molecules that are not engaged in the four membered flip-flop ring nearly behave as free water with high mobility. The confirmation of this hypothesis should be given by a complete structural study of the low β -CD hydrate in the same temperature range. The existence (or not) of external flip-flop hydrogen bond rings could be a determining factor in understanding the long distance arrangement between β CD-molecules. Another important point is the modification of the behaviours of the two hydrates at the same temperature of 120 K. It has been previously shown by neutron diffraction [14] that, at this temperature, water molecules and hydroxyl groups are fully ordered in β -CD \cdot 11 H₂O. We assume from our previous work on anhydrous β -CD, that the intramolecular interglucose hydrogen bond interactions between OH groups are all active above 120 K. Concerning the hydrated form, it seems that the intermolecular interactions depending on the presence of water molecules cannot begin before this activation takes place.

A recent ²H-NMR study of β -CD \cdot 11 H₂O [15] gives some information which support our hypothesis. The hydration water molecules are all equivalent at room temperature from a mobility point of view. Below 235 K, three relaxation components become discernible. One is probably associated with the β -CD hydroxyl groups, the two others are attributed to two sub-groups of water molecules for

which mobilities are very different. One sub-group of water molecules is involved in flip-flop chain interactions, the second sub-group includes relatively free water molecules or ones that are distributed over a large number of interaction sites. Another description of the water molecules organisation has been given by Steiner [4] from X-ray diffraction studies of crystalline β -CD hydrate at various humidities. The dehydration of β -CD is surprisingly fast in the range of hydration between 12 and 10 water molecules. In this range, dehydration does not affect the crystal structure. But when the water content becomes lower than 10, the crystal structure collapses irreversibly. One major conclusion of this study is the existence of two distinct networks of water molecules. The dehydration from 12 to 10 water molecules seems to affect one network to a larger extent than the other. The fast diffusion of water molecules has been explained by temporary opening of diffusion channels in the lattice.

Taking all this information into account, the large difference of the low temperature thermal behaviour between the low ($n < 10$) and the high ($n > 10$) β -CD hydrates is not surprising. The hypothesis of important modification in the long distance arrangement of the water molecules caused by the dehydration is not incoherent, but our calorimetric results could not give further information. From this work, at least two thermodynamic behaviours of β -CD have been detected, depending on the hydration rate. This fact must be kept in mind for the storage and the use of β -CD in inclusion reactions.

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