

# Kinetic Deuterium Isotopic Effects in the Thermal Decomposition of $\beta$ -Cyclodextrin hydrates

A. SZAFRANEK

*Institute of Physics, University of Gdańsk, 80-952 Gdańsk, ul. Wita Stwosza 57, Poland.*

J. SZAFRANEK

*Department of Chemistry, University of Gdańsk, 80-952 Gdańsk, ul. Sobieskiego 18, Poland.*

Received: 8 January 1997; in final form: 1 May 1977

**Abstract.** The apparent kinetic parameters of the thermal decomposition of the  $\beta$ -cyclodextrin–heavy water complex were obtained from dynamic TG analysis. Various calculation methods were used and the results compared with those of the ordinary water complex. The processes of decomposition occur as zero order reactions with an activation energy of 65.7 and 69.7 kJ/mole respectively, calculated for one mole of water and heavy water. The parameters were used to estimate the kinetic deuterium isotopic effect.

**Key words:**  $\beta$ -Cyclodextrin hydrates and deuterates, thermal analyses, apparent kinetic parameters.

## 1. Introduction

$\beta$ -Cyclodextrin ( $\beta$ -CD) is composed of seven (1  $\rightarrow$  4) linked  $\alpha$ -D-glucopyranosyl residues and possesses a molecular cavity which is capable of including various guest molecules to form inclusion complexes [1]. Hydrogens of C—H groups and glycosidic oxygen atoms of  $\beta$ -cyclodextrin are oriented into the interior of the cavity. The cavity micropolarity is similar to that of neat methanol [2]. According to the results of X-ray [3, 4] and neutron [5] diffraction studies, 11 water molecules are distributed over 16 positions, eight in the cavity of  $\beta$ -CD (6.13 water molecules) and eight in interstices (4.88 water molecules). Cavity waters form only two hydrogen bonds to the enclosing  $\beta$ -CD and six contacts to neighbouring  $\beta$ -CD.

Considerable effort has been devoted to determining the mechanism of the inclusion complex formation process. It is generally believed that the driving force for complex formation on the molecular level is the removal of water molecules from the cavity by guest molecules, and the London dispersion intermolecular interactions [6, 7].

From thermodynamic studies of a wide range of cyclodextrins and guest molecules in solutions a linear relation between the entropy of complex formation ( $\Delta S$ ) and enthalpy ( $\Delta H$ ) changes was found [8–10]:

$$T \Delta S = \alpha \Delta H + E, \quad (1)$$

where  $E$  (energy) is of the order of 10 kJ/mol and  $\alpha$  is a coefficient in the range 0.6–1.

The parameter  $E$  has the same order as the heat of hydration of  $\beta$ -cyclodextrin by 1 mole of water (10.5 kJ/mole [11]). The relation describes the behaviour of a large group of similar complexes. This uniform behaviour is interpreted [9, 12] by the role hydration water played in the inclusion phenomenon followed by a conformational change.

Thermal decomposition of  $\beta$ -cyclodextrin hydrate provides a single peak on the DTA curve [13]. However, inclusion complexes show two distinguishable peaks in the same experiments [14]. We believe that comparative studies of the thermal decomposition of  $\beta$ -cyclodextrin hydrates and deuterates will help better understand the role of the water molecule in the inclusion phenomenon.

## 2. Experimental

$\beta$ -Cyclodextrin (Aldrich, Germany) was crystallised twice from glass distilled water, and dried at room temperature. For the heavy water complex preparation, a sample of  $\beta$ -cyclodextrin was vacuum dried at 65 °C for 24 h, recrystallized twice from deuterium oxide (Aldrich, Germany), dried at room temperature and stored for four weeks in a sealed vessel before the measurements. The samples were ground and sieved to the fraction of 170–200 mesh.

A derivatograph (MOM, Budapest, Hungary) was used for the thermal decomposition studies, in which 50 mg samples (measured at a scale of 0–100 divisions with 0.25 mg accuracy) were run against a standard of 50 mg  $\alpha$ -Al<sub>2</sub>O<sub>3</sub> in a nitrogen atmosphere. A platinum semimicro crucible was used for the thermogravimetry. Linear temperature programming of 4 °C/min to 14 °C/min was used. The basic galvanometer sensitivity of 10<sup>-10</sup> A/mm/m was reduced to 1/10 for DTG and 1/3 for DTA curves.

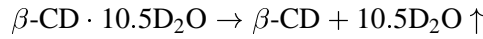
Linear regression methods were employed for calculations.

## 3. Results and Discussion

The thermal analysis curves of the  $\beta$ -cyclodextrin-heavy water complex show the low-temperature changes between 50 °C and 120 °C which correspond to the loss of heavy water molecules. These escape in one step from the complexes. The processes occur as endothermic ones with negative peaks in DTA curves.

The total weight loss of the  $\beta$ -cyclodextrin-heavy water complexes suggests 10.5 ± 0.5 molecules of heavy water. This figure is the average result of triplicate preparation experiments. The composition was found to be identical to that found in crystallographic studies [5]. The complexes of  $\beta$ -cyclodextrin break down according to reactions





with a solid ( $\beta$ -cyclodextrin) and vapours as the products.

The kinetics of the processes  $A \rightarrow B + C$  can be described by the expression

$$-\frac{dc_A}{dt} = \frac{dc_B}{dt} = \frac{dc_C}{dt} = f(c_A)k(T), \quad (2)$$

where the  $f(c_A)$  function represents a hypothetical reaction model.

The decomposition reaction proceeds as a process with an activation energy. Therefore the isothermal rate constant  $k(T)$  is described by the Arrhenius relation

$$k(T) = Z \exp(-E/RT), \quad (3)$$

where  $E$  is the apparent activation energy and  $Z$  is the pre-exponential factor.

Assuming the same  $f(c_A)$  function for hydrates and deuterates we obtain the kinetic effect of

$$\frac{dc_{\text{H}_2\text{O}}/dt}{dc_{\text{D}_2\text{O}}/dt} = \frac{k_{\text{H}_2\text{O}}f(c)_{\text{H}_2\text{O}}}{k_{\text{D}_2\text{O}}f(c)_{\text{D}_2\text{O}}} = \frac{Z_{\text{H}_2\text{O}} \exp(-E_{\text{H}_2\text{O}}/RT)}{Z_{\text{D}_2\text{O}} \exp(-E_{\text{D}_2\text{O}}/RT)}. \quad (4)$$

The change of composition can be expressed as the fractional conversion  $\alpha$

$$\frac{d\alpha}{dt} = k(T)f(\alpha). \quad (5)$$

For non-isothermal conditions this equation is modified to

$$\frac{d\alpha}{dT} = \frac{Z}{\Phi} \exp\left(-\frac{E}{RT}\right) f(\alpha), \quad (6)$$

where  $\Phi = dT/dt$  is a constant heating rate.

The function  $f(\alpha)$  has a simple form

$$f(\alpha) = (1 - \alpha)^n, \quad (7)$$

which enables calculation of only the reaction order  $n$ ; or the general form [15]

$$f(\alpha) = (1 - \alpha)^n \alpha^m [-\ln(1 - \alpha)]^P. \quad (8)$$

where  $n$ ,  $m$ , and  $P$  are the constants.

Here the function  $f(\alpha)$  distinguishes between the mechanisms involved.

Apparent activation energies of thermal decomposition of  $\beta$ -cyclodextrin hydrates were determined from thermal analysis curves (TG, DTG and DTA) according to the methods of Coats–Redfern [16, 17], Freeman–Carroll [18], Kissinger [19] and Piloyan *et al.* [20].

Table I. Activation energy  $E$  of the thermal decomposition of the  $\beta$ -cyclodextrin–heavy water complex computed according to Coats and Redfern [17].

$n$	$\Phi = 2.3^\circ/\text{min}$		$\Phi = 4.8^\circ/\text{min}$	
	$E$ kJ/mol	$r$	$E$ kJ/mol	$r$
0	75.8	0.997	58.1	0.993
0.1	83.8	0.996	60.5	0.994
0.5	102.7	0.995	71.0	0.998
0.9	129.9	0.994	83.9	0.998
1.0	137.9	0.994	86.4	0.998
1.1	146.0	0.993	89.7	0.998
1.5	181.3	0.988	103.2	0.996

The Coats and Redfern method [17] offers the possibility to determine the apparent activation energy from the TG curve and the differential equation

$$\int_0^\alpha \frac{d\alpha}{f(\alpha)} = \frac{Z}{\Phi} \int_0^T e^{-E/RT} dT. \quad (9)$$

Assuming  $f(\alpha) = (1 - \alpha)^n$ , they obtained

$$\log \left[ \frac{-\log(1 - \alpha)}{T^2} \right] = \log \frac{ZR}{\Phi E} \left[ 1 - \frac{2RT}{E} \right] - \frac{E}{2.3RT} \quad (10)$$

for  $n = 1$  and

$$\log \left[ \frac{1 - (1 - \alpha)^{1-n}}{T^2(1 - n)} \right] = \log \frac{ZR}{\Phi E} \left[ 1 - \frac{2RT}{E} \right] - \frac{E}{2.3RT} \quad (11)$$

for  $n \neq 1$ .

Assuming  $E \gg 2RT$ , the plots of the left side of the equation vs.  $1/T$  should give a straight line with a slope of  $-E/2.3R$ , if a correct  $f(\alpha)$  is employed. Reaction orders between 0 and +1.5 were checked. The results of calculations for heating rates  $\Phi = 2.3^\circ/\text{min}$  and  $\Phi = 4.8^\circ/\text{min}$  are included in Table I. One can see that the changes of linear correlation coefficients  $r$  for different reaction orders  $n$  are small (in the third decimal place) and are not the same for different heating rates. It makes the assignment of reaction order  $n$  for the thermal decomposition of the  $\beta$ -cyclodextrin complex with heavy water extremely difficult. But the best values of  $r$  for the heating rates used were found for  $n < 1$ .

Moreover, a significant influence of heating rates on activation energy values is observed. In order to obtain an activation energy more comparable to that under isothermal conditions, a linear extrapolation of  $E$  values to  $\Phi = 0$  was performed (Table II) for reaction order  $n = 0$ ,  $n = 0.5$  and  $n = 1$ .

Table II. Activation energy  $E$  of the thermal decomposition of the  $\beta$ -cyclodextrin-heavy water complex obtained by extrapolation to isothermal conditions for reaction order  $n = 0$ ,  $n = 0.5$  and  $n = 1$ .

$n$	$E$ kJ/mol	$r$
0	$69.16 \pm 0.5$	0.996
0.5	$82.88 \pm 1.4$	0.995
1	$99.08 \pm 2.7$	0.975

Table III. Activation energy  $E$  and reaction orders  $n$  of the thermal decomposition of the  $\beta$ -cyclodextrin-heavy water complex calculated according to Freeman and Carroll [18].

$\Phi$ °/min	$E$ kJ/mole	$n$	$r$
2.3	64.8	0.05	0.993
4.8	61.0	0.07	0.997
5.6	62.7	0.10	0.997
9.4	59.0	0.03	0.997
14.0	54.3	0.06	0.993

The best results were obtained for  $n = 0$ , the same reaction order as for the water complex. The activation energy of the process was found to be  $69.1 \pm 1.4$  kJ/mole as compared to  $65.7 \pm 3.1$  kJ/mole for the water complex [13].

Freeman and Carroll [18] assumed that  $f(\alpha) = (1 - \alpha)^n$  and, using Equations (3) and (5), obtained the relation which can be used to compute the activation energy  $E$  and reaction order  $n$  from TG and DTG curves

$$\frac{\Delta \log \frac{dw_t}{dt}}{\Delta \log w} = \frac{E}{-2.3R} \Delta \frac{1}{T} + n, \quad (12)$$

where  $w = w_\infty - w_t$ ;  $w_\infty$  is the weight loss on completion of reaction;  $w_t$  is the total loss in weight up to time  $t$ ; and  $n$  is the reaction order.

Activation energies calculated according to Freeman and Carrol are included in Table III.

The activation energy from extrapolation to  $\Phi = 0$  is  $66.6 \pm 1.1$  kJ/mole but the reaction order has to be  $n = 0$  again.

A few DTA curves were used to calculate the apparent activation energy according to Kissinger [19]. Kissinger assumed that the temperature of maximum reaction

Table IV. Activation energy  $E$  of the thermal decomposition of the  $\beta$ -cyclodextrin-heavy water complex calculated according to Piloyan *et al.* [20].

$\Phi$ °C/min	$E$ kJ/mole	$r$
2.3	107.5	0.969
4.8	100.3	0.991
5.6	61.8	0.993
14.0	57.8	0.994

rate,  $T_m$ , and the temperature at the maximum of the DTA curve are the same. For temperature  $T = T_m$ , when maximum rate occurs,

$$\frac{d}{dt} \left( \frac{d\alpha}{dt} \right) = 0.$$

Furthermore, assuming  $f(\alpha) = (1 - \alpha)^n$  and  $E \gg 2RT$ , he obtained the equation

$$\frac{E\Phi}{RT_m^2} = Ze^{-E/RT_m} \quad (13)$$

which no longer includes the reaction order  $n$ . For heating rates between 4 to 14°/min, the activation energy  $E$  of the thermal decomposition of the complex of  $\beta$ -cyclodextrin with heavy water was determined as  $87.1 \pm 1.3$  kJ/mole. But it is well known that the Kissinger method provides an overestimate of the activation energy value.

A simple equation of Piloyan *et al.* [20] was used for determination of the activation energy

$$\ln \Delta T = C - \frac{E}{RT} \quad (14)$$

from DTA curves, where  $C$  is a constant and  $\Delta T$  is the deviation from the baseline of the DTA curve.

For  $\Delta T$  values at different temperatures between the beginning and the minimum of the DTA curve for the decomposition of the complex (e.g. for reaction degree of 5–65%), the activation energy  $E = 57.9 \pm 1.2$  kJ/mole was calculated for the heating rate of 14°/min. Similarly to previous results (Tables I and III), activation energy decreases when the heating rate increases (Table IV).

All the above mentioned methods used the  $f(\alpha)$  function in the simplest form. Incorporation of a general form of  $f(\alpha)$  function (8) into Equation (9) enables a

search for other mechanisms involved. The linear relations were obtained only for three functions which describe the diffusions [15, 21, 22]:

$$f(\alpha) = \frac{1}{2}(\alpha)^{-1} \quad \text{one-dimensional diffusion } D_1 \quad (15)$$

$$f(\alpha) = [-\ln(1 - \alpha)]^{-1} \quad \text{two-dimensional diffusion } D_2 \quad (16)$$

cylindrical symmetry

$$f(\alpha) = \frac{3}{2}(1 - \alpha)^{1/3}[(1 - \alpha)^{-1/3} - 1]^{-1} \quad \text{three-dimensional diffusion } D_3 \quad (17)$$

spherical symmetry; Jander's  
function [25]

The activation energy of those diffusion models for  $E \gg 2RT$  were computed from the following relations, respectively

$$\ln \left[ \frac{\alpha^2}{T^2} \right] = C - \frac{E}{RT} \quad D_1 \quad (18)$$

$$\ln \left[ \frac{(1 - \alpha) \ln(1 - \alpha) + \alpha}{T^2} \right] = C - \frac{E}{RT} \quad D_2 \quad (19)$$

$$\ln \left[ \frac{1 - (1 - \alpha)^{1/3}}{T} \right]^2 = C - \frac{E}{RT} \quad D_3 \quad (20)$$

where

$$C = \ln \frac{AR}{\Phi R} \left[ 1 - \frac{2RT}{E} \right].$$

The values of activation energies of diffusion for three heating rates are included in Table V.

The changes of the correlation coefficients are negligible for the three diffusion models. This did not allow us to assign the model of diffusion. The extrapolated values of the activation energies to isothermal conditions are presented in Table VI.

#### 4. Conclusion

The composition of the complex of  $\beta$ -cyclodextrin with heavy water concluded from thermogravimetric curves is  $(C_6H_7D_3O_5)_7 \cdot 10.5D_2O$  similar to crystallographic studies [5]. According to the preparation procedure this complex differs from that of ordinary water in both guest and host molecules, as  $\beta$ -cyclodextrin was deuterated at hydroxyl groups. This should be kept in mind during the comparative studies.

Table V. Activation energies and correlation coefficients computed following the Coats and Redfern method according to Equations (18)–(20) for chosen heating rates  $\Phi$ .

Diffusion	$\Phi = 4.8$		$\Phi = 9.5$		$\Phi = 14$	
	°/min		°/min		°/min	
	$E$	$r$	$E$	$r$	$E$	$r$
	kJ/mole		kJ/mole		kJ/mole	
$D_1$	127.7	0.995	99.5	0.998	90.5	0.997
$D_2$	138.7	0.996	107.7	0.997	96.6	0.999
$D_3$	150.9	0.998	118.0	0.997	103.2	0.998

Table VI. Activation energy  $E$  of diffusion obtained by extrapolation of the results to  $\Phi = 0$ .

Diffusion	$f(\alpha)$	$E$	$r$
		kJ/mol	
One-dimensional	$\frac{1}{2}(\alpha)^{-1}$	140.2	0.953
Two-dimensional	$[-\ln(1 - \alpha)]^{-1}$	151.7	0.947
Three-dimensional	$\frac{3}{2}(1 - \alpha)^{1/3}[(1 - \alpha)^{1/3} - 1]^{-1}$	164.4	0.943

The activation energies of the thermal decomposition of the complex calculated according to various methods employed are collected in Table VII together with those of ordinary water complexes [13]. The apparent activation energies for both complexes (water and heavy water) are similar but that of heavy water is slightly greater. The activation energies of thermal decomposition of both complexes should be greater than the sum of the solvation enthalpy of cyclodextrin by one mole of heavy water and the vaporisation enthalpy of the guest molecule. The solvation enthalpy of  $\beta$ -cyclodextrin with water is 10.5 kJ/mole of guest molecule [11]. That of heavy water is unknown. The vaporization enthalpy of water is 40.66 kJ/mole [23] but that of heavy water is slightly greater at 41.69 kJ/mole. This 1 kJ/mole difference cannot account for ca. 4 kJ/mole differences in activation energies.

For the thermal decomposition of hydrates and deuterates of inorganic salts e.g. cupric sulphate, an insignificant isotopic effect was found and only in the second stage of dehydration. Even more important was the fact that the magnitude and sign of the isotopic effect was independent of the mechanism assumed [22].

Dehydration and hydration of  $\beta$ -cyclodextrin in the solid state is a very complicated process. The two processes, dehydration and hydration, show a hysteresis [24]. The molecules trapped in the complex do not leave the cavities easily and equilibrium is not reached. It can be assumed that similar to hydrates of inorganic salts, water or heavy water molecules behave as in ice. They are linked with hydrogen or deuterium bonding in the chain with a flip-flop arrangement as was identified by neutron diffraction studies of  $\beta$ -cyclodextrin [5]. The composition



Table VII. A comparison of activation energy  $E$ , linear correlation coefficient  $r$  and reaction order  $n$  for thermal decomposition of  $\beta$ -cyclodextrin with water and heavy water.

Method of	Eq. No.	$(C_6H_{10}O_5)_7 \cdot 11.1H_2O$ [13]		$(C_6H_7D_3O_5)_7 \cdot 10.5D_2O$	
		$E$ (kJ/mole)	$n$	$E$ (kJ/mole)	$n$
Kissinger [19]	13	$72.5 \pm 0.8$		$87.1 \pm 1.3$	
Piloyan <i>et al.</i> [20]	14	$59.1 \pm 0.9$		$57.9 \pm 1.2$	
Freeman and Carroll [18]	12	$61.5 \pm 3.1^*$	0.09*	$66.6 \pm 1.1^{***}$	0.06*
Coats and Redfern [16]	11	$65.7 \pm 3.1^{***}$	0	$69.1 \pm 1.4^{***}$	0
$f(\alpha) = (1 - \alpha)^n$					
Coats and Redfern [16]	19	$160.6 \pm 1.5$		$151.7 \pm 1.9^{***}$	
$f(\alpha) = [-\ln(1 - \alpha)]^{-1}$					

\* An average value from 6 runs at different heating rates.

\*\*  $r$  value of the run closest to the average activation energy  $E$ .

\*\*\* Value of  $E$  extrapolated to  $\Phi = 0$ .

of the hydrates and deuterates were found in the present study to be the same as from X-ray and neutron diffraction studies [3–5]. Diffraction studies [5] showed that the water (heavy water) molecules are distributed between the cavity and the interstices. Despite that the total water or heavy water was liberated in one step during thermal decomposition.

### Acknowledgement

Financial support for this work from the Polish State Committee for Scientific Research (Grant BS) is gratefully acknowledged.

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