Effect of α-Cyclodextrin on the Hydration of Aliphatic Aldehydes in Water

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Synopsis. The ^{1}H NMR spectrometry of aliphatic aldehydes in D_2O showed that the addition of α-cyclodextrin (α-CD) causes a marked change in the hydration equilibrium of ethanal in favor of the unhydrated aldehyde. The inhibitory effect of α-CD on hydration was smaller in propanal than in ethanal and negligible in butanal, pentanal, and hexanal.

It is well-known that cyclodextrins (CD's) catalyze a variety of organic reactions.[1,2a] In contrast, the effect of CD's on chemical equilibria has been studied to a less extent. The dissociation equilibria of organic acids and indicator dyes,[2b,3] the keto–enol tautomerism of α-hydroxyketones,[4] the azo-azonium tautomerism of azo dyes,[5] and the conformational isomerism of a few compounds[6] are typical examples in which CD's affect the chemical equilibria.

The present work deals with the effect of α-CD on the hydration equilibria of straight-chain aliphatic aldehydes in water. Aliphatic aldehydes are partially hydrated in aqueous solution according to[7]

$$\text{R-CHO} + \text{H}_2\text{O} \rightleftharpoons \text{R-CH(OH)}_2.$$

The half-life of the reaction is on the order of 1 min in neutral solutions at room temperature.[8] In the present study, the hydration equilibria were examined by ^{1}H NMR spectrometry, which was advantageous for the direct observation of free and hydrated species of aldehydes.[9]

Experimental

The α- and β-CD's used were kindly supplied by Nihon Shokuhin Kako Co., Ltd. and Ensuiko Seito Co., Ltd. They were dried overnight in vacuo at 383 K. Straight-chain aliphatic aldehydes such as ethanal, propanal, butanal, pentanal, and hexanal were of reagent grade and used without further purification. D_2O (Isotec Inc., 99.8 atom%) was also commercially available for NMR use. The ^{1}H NMR spectra were recorded using a JEOL (Model JNM-GX270) FT NMR spectrometer (270 MHz) for D_2O solutions containing 10—20 mmol dm^{-3} aldehydes and various concentrations of α-CD at 298 K. Acetonitrile (δ=2.00) was used as an internal reference. The standard deviations of the observed chemical shifts were less than 0.005 ppm.

Results

Hydration of Aliphatic Aldehydes. Ethanal in D_2O gave ^{1}H NMR signals at δ=9.61 (q, J=2.9 Hz, CHO) and 2.17 (d, J=2.9 Hz, CH_3) due to free ethanal and at δ=5.18 (q, J=5.1 Hz, $CH(OH)_2$) and 1.26 (d, J=5.1 Hz, CH_3) due to the hydrate of ethanal. The ratio (R) of the peak area for the hydrate CH_3 to that for ethanal CH_3 was 1.45±0.01. The addition of α-CD to the solution caused a decrease in R (Fig. 1), indicating that α-CD causes a change in the hydration equilibrium of ethanal in favor of unhydrated aldehyde. The R ratio of the hydrate $CH(OH)_2$ proton to the ethanal CHO proton was similarly changed upon the addition of α-CD. However, it became inaccurate at high α-CD concentrations, due to an overlapping of the hydrate $CH(OH)_2$ signal with the α-CD C(1)–H signal. The addition of β-CD up to its saturated concentration (0.0125 mol dm^{-3}) had virtually no effect on R for ethanal.

The hydration equilibrium of propanal was also affected by α-CD: The aldehyde in D_2O gave well-separated ^{1}H NMR signals due to the CH_3 groups of free propanal (δ=0.98, t, J=7.3 Hz) and its hydrate (δ=0.84, t, J=7.6 Hz). The R ratio of the hydrate CH_3 to the aldehyde CH_3 was 1.30±0.01 in the absence of α-CD and decreased upon the addition of α-CD, as shown in Fig. 1.

Since the CH_3 groups of butanal and its hydrate gave overlapped triplet signals at δ=0.86 (J=7.5 Hz) and 0.85 (J=7.3 Hz), respectively, the R value for butanal could not be determined by means of these signals. The R value for butanal was estimated by means of the peak areas for the α-CH_2 signal (δ=2.44, double t, J=1.8 and 7.2 Hz) of butanal and the β-CH_2 signal (δ=1.31, sextet, J=7.5 Hz) of the hydrate. The observed R value was 0.86±0.01 in the absence of α-CD and 0.80±0.01 in

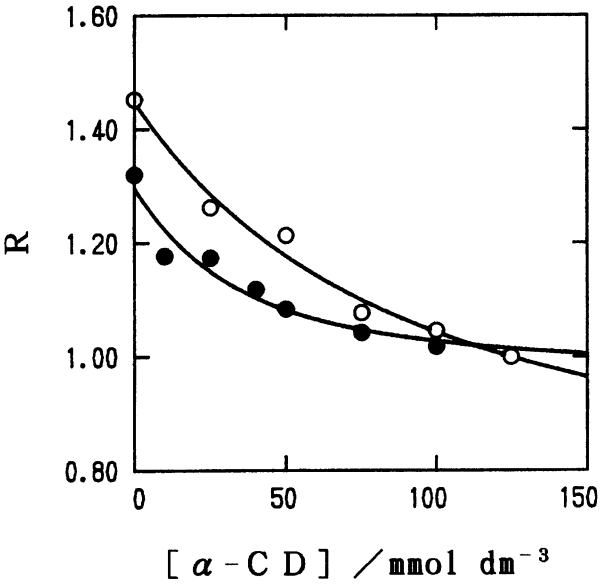

Fig. 1. Plots of R vs. the concentration (h) of added α-CD for ethanal (○) and propanal (●).

Table 1. Equilibrium Constants, K_1 and K_2, for the Hydration of Aldehydes Uncomplexed and Complexed with α-CD, Respectively, and Dissociation Constants, K_3 and K_4/mol dm^{-3}, for the α-CD Complexes with Free and Hydrated Species of Aldehydes, Respectively, in D_2O at 298 K

Guest	K_1	K_2	K_3	K_4
Ethanal	1.45±0.01	0.68±0.02	0.081±0.002	0.17 ±0.01
Propanal	1.30±0.01	0.96±0.03	0.022±0.001	0.030±0.002

the presence of 0.075 mol dm^{-3} α-CD. The change in R was too small to be accurately analyzed by a curve-fitting method. The effect of α-CD on the R values for the pentanal and hexanal was also very small.

Determination of Dissociation Constants for Complexes of α-CD with Aldehydes and Their Hydrates. The dissociation constants for the complexes of α-CD with the aldehydes and their hydrates were determined by a nonlinear least-squares curve-fitting analysis of the changes in R with the addition of α-CD: Upon assuming that the aldehydes and their hydrates form 1:1 complexes with α-CD, the chemical equilibria in a D_2O solution were expressed by

$$A + D_2O \rightleftharpoons B, \quad (1)$$

$$AC + D_2O \rightleftharpoons BC, \quad (2)$$

$$A + C \rightleftharpoons AC, \quad (3)$$

and

$$B + C \rightleftharpoons BC, \quad (4)$$

where A and B refer to an aldehyde and its hydrate, respectively; C to α-CD; AC and BC to 1:1 complexes of α-CD with A and B, respectively. When the equilibrium concentrations of A, B, C, AC, and BC are designated as a, b, c, x, and y, respectively, the equilibrium constants for the reactions of Eqs. 1, 2, 3, and 4 are expressed by:

$$K_1 = b/a, \quad (5)$$

$$K_2 = y/x, \quad (6)$$

$$K_3 = ac/x, \quad (7)$$

and

$$K_4 = bc/y. \quad (8)$$

A combination of Eqs. 5, 6, 7, and 8 gives $K_4 = K_1K_3/K_2$. The K_1 value is equal to R at $c=0$, and can be experimentally determined. On the other hand, the R values at $c>0$ are expressed by

$$R = (b+y)/(a+x). \quad (9)$$

Combining Eqs. 5, 6, 7, and 9 leads to

$$R = (K_1K_3 + K_2c)/(K_3 + c). \quad (10)$$

Upon designating the total concentrations of the host and guest as h and g, respectively, the equilibrium concentration of the free host, c, can be derived from Eqs. 5, 6, and 7 as

$$c = (1/2)(h - g - K) + (1/2)[(h - g - K)^2 + 4Kh]^{1/2}, \quad (11)$$

where

$$K = K_3(1 + K_1)/(1 + K_2). \quad (12)$$

Equations 10, 11, and 12 give a relationship between R and h. The best-fit values of K_2 and K_3 were determined by nonlinear least-squares curve-fitting analyses of the observed R–h data. The obtained curves (solid lines in Fig. 1) were well fitted to the observed data with correlation coefficients greater than 0.97. The determined K_1 to K_4 values are summarized in Table 1. The observed K_1 values for the hydration of ethanal and propanal were approximately equal to those thus-far reported.[7c]

Discussion

The equilibrium constant, K_2, for the hydration of ethanal in a 1:1 complex with α-CD was determined to be 0.68±0.02 (Table 1), which was about half that (1.45±0.01) for hydration in a bulk solution. This result indicates that the hydration of ethanal is significantly inhibited by complexation with α-CD. Ethanal and its hydrate are sufficiently small in size to be accommodated as a whole within the α-CD cavity. The CD cavity is hydrophobic in nature, whereas ethanal may be more hydrophobic than its hydrate. It is thus reasonable that ethanal is more stable in a hydrophobic cavity than its hydrate.

The K_2 value for the hydration of propanal in an α-CD complex was 0.96±0.03, which is about 3/4 of the corresponding K_1 value (1.30±0.01) in a bulk solution. Thus, the inhibitory effect of α-CD on the hydration equilibrium was smaller in propanal than in ethanal. Propanal and its hydrate are larger in size than ethanal and its hydrate. It is thus presumable that the propanal CHO group is located at the rim of the CD cavity, where the hydration of the CHO group may be inhibited to a less extent than in the interior of the CD cavity. The addition of α-CD had only slight influences on the hydration equilibria of butanal, pentanal, and hexanal. In such higher aliphatic aldehydes, the hydrophobic alkyl groups are included within the CD cavity, whereas the hydrophilic CHO groups may be extruded from the cavity to a bulk solution, where hydration is little affected.

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