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A New Method for Determining Cyclodextrin Complex Formation Constants with Electrolytes in Aqueous Medium

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Synopsis. By making use of the volatilization rate of iodine from aqueous into gaseous phase, association constants of α-cyclodextrin with electrolytes (chlorides, nitrates, and perchlorates) have been determined at 25 °C; the counter cations are found to be largely responsible for the association.

Among several methods so far available for determining cyclodextrin (CyD) complex formation constants, four techniques, i.e., conductometry,[1-3] calorimetry,[4] kinetic inhibition,[5] and spectral competitive inhibition[6-9] have been used for the systems where electrolytes having neither absorption nor fluorescence are involved.

We have studied CyD associations with volatile guests such as iodine, benzene, alkylbenzenes, naphthalenes.[10-12] The present work is concerned with a further development of the study; iodine is used as a volatile guest which serves as an indicator and α-CyD is used as a host.

By introducing an inert gas at a constant flow rate into aqueous solutions, iodine molecules are driven out into the gaseous phase. The volatilization rate is reduced in the presence of CyD owing to the host–guest association. The decrease in rate gives the complex formation constant. Now consider the presence of an electrolyte which does not interact with iodine, but does associate with CyD. Under such a circumstance, the iodine volatilization rate is expected to be accelerated as a result of competition with the electrolyte.

Associations of some inorganic electrolytes with CyD have been well demonstrated and anions are thought to be responsible for the association. Is there any contribution of the counter cation? It is another object of this work to elucidate the effect of counter cation.

Experimental

Distilled deionized water was used throughout this work. Electrolytes, NaCl, KCl, HNO_3, $NaNO_3$, $HClO_4$, $LiClO_4$, $NaClO_4$, $KClO_4$, and $(CH_3)_4NClO_4$, of analytical reagent grade were used as purchased and each stock solution was, when necessary, standardized by alkalimetry after passing a suitable portion of the stock solution through H^+-form cation-exchange resin. Preparations of α-CyD (Nakarai Chemical Co.) and iodine aqueous solutions, the iodine standardization method, experimental procedures, and apparatus were described in the previous paper.[10]

A brief statement of the experimental procedure will be made here. A 50 cm³ portion of the sample solution in which both iodine and electrolyte to be studied are present with or without CyD, was transferred into a 2.5ϕ×25 cm cylindrical glass tube immersed in a bath thermostated at 25.0±0.1 °C. N_2 gas was blown in the sample solution through a capillary glass tube at a constant flow rate of 600 cm³ min⁻¹. The I_2 concentration in this work was lower than that used in our previous study, and N_2 gas was blown at a much higher flow rate to expel I_2 effectively. The N_2 gas flow rate was kept the same irrespective of the presence of CyD. The iodine carried out of the solution by N_2 gas stream was trapped in a 5×10^{-4} M $Na_2S_2O_3$ solution of 20 cm³ and the amount of I_2 expelled during a fixed time, ΔQ_{I_2}, was determined.

The concentration in M unit (M≡ mol dm⁻³) used in most of the runs was as follows; iodine (1.57×10^{-5}), α-CyD (1.57×10^{-4}), NaCl (2.12×10^{-2}), KCl (1.00×10^{-2}), HNO_3 (5.00×10^{-2}), $NaNO_3$ (5.00×10^{-2}), $HClO_4$ (5.04×10^{-2}), $LiClO_4$ (4.24×10^{-2}), $NaClO_4$ (5.00×10^{-2}), $KClO_4$ (5.45×10^{-2}), and $(CH_3)_4NClO_4$ (3.51×10^{-2}). The association constants were determined on average of three or four measurements.

Results and Discussion

It is well established that both the molecular iodine and the electrolyte used in this study form 1:1 complex with α-CyD. Then, the reactions that should be taken into account are:

$$\mathrm{CyD} + \mathrm{I_2} \rightleftharpoons \mathrm{CyD\cdot I_2}, \quad K_{\mathrm{I_2}}, \tag{1}$$

$$\mathrm{CyD} + \mathrm{X} \rightleftharpoons \mathrm{CyD\cdot X}, \quad K_{\mathrm{X}}, \tag{2}$$

and

$$\mathrm{I_2(aq)} \longrightarrow \mathrm{I_2(gas)}, \quad k, \tag{3}$$

where K_{I_2} and K_X are association constants with iodine and electrolyte (X), respectively, and k is the rate constant for the transfer of iodine molecules from aqueous to gaseous phase. The iodine molecules expelled into the gaseous phase are collected successively by the absorbent, and the total amount, Q_{I_2}, which is the sum of ΔQ_{I_2}, is measured as a function of aeration time, t. The iodine volatilization rate at a constant N_2 gas flow rate is of the first-order with respect to the concentration of free iodine species in the solution as follows:

$$\mathrm{d}Q_{\mathrm{I_2}}V^{-1}/\mathrm{d}t = k[\mathrm{I_2}], \tag{4}$$

where V is the volume of the aqueous solution.

The mass-balance equations are:

$$\begin{aligned} C_{\mathrm{CyD}} &= [\mathrm{CyD}] + [\mathrm{CyD\cdot I_2}] + [\mathrm{CyD\cdot X}] \\ &= [\mathrm{CyD}](1 + K_{\mathrm{I_2}}[\mathrm{I_2}] + K_{\mathrm{X}}[\mathrm{X}]), \end{aligned} \tag{5}$$

and

$$\begin{aligned} C_{\mathrm{I_2}} &= [\mathrm{I_2}] + [\mathrm{CyD\cdot I_2}] + Q_{\mathrm{I_2}}V^{-1} \\ &= [\mathrm{I_2}](1 + K_{\mathrm{I_2}}[\mathrm{CyD}]) + Q_{\mathrm{I_2}}V^{-1} \end{aligned} \tag{6}$$

where C_{CyD} and $C_{\mathrm{I_2}}$ denote the total concentration of CyD and that of iodine, respectively. Substituting Eq.

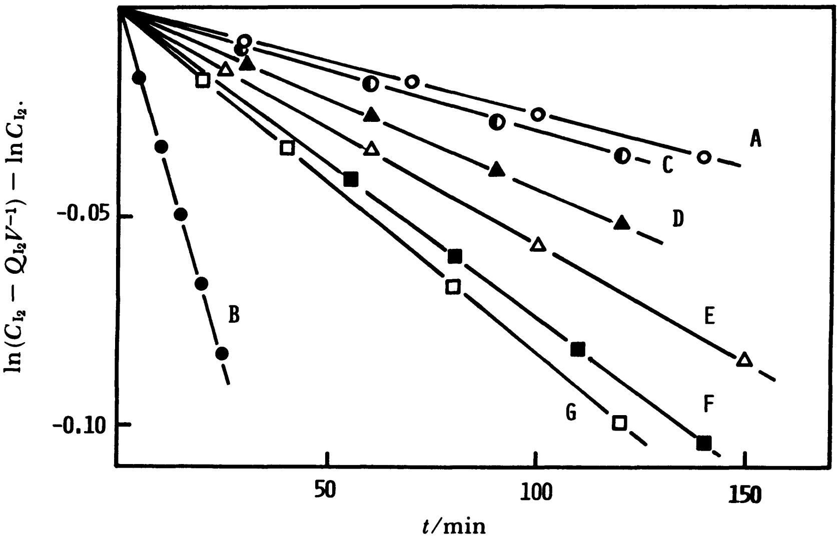

Fig. 1. The plots of $\ln(C_{I_2}-Q_{I_2}V^{-1})-\ln C_{I_2}$ vs. t in the presence (A) and absence (B) of CyD. N_2 flow rate: 600 cm^3 min^{-1}; C_{I_2}: 1.57×10^{-5} M, C_{CyD}: 7.99×10^{-4} M; Electrolyte ($C_X/10^{-2}$ M): (C) $(CH_3)_4NClO_4$ (3.51), (D) $LiClO_4$ (4.24), (E) $NaClO_4$ (5.00), (F) $KClO_4$ (5.45), (G) $HClO_4$ (5.04).

6 into Eq. 4 and integration ($Q_{I_2}=0$ at $t=0$) yield

$$\ln(C_{I_2}-Q_{I_2}V^{-1}) = -kt/(1+K_{I_2}[CyD]) + \ln C_{I_2}. \quad (7)$$

Here we set experimental conditions as follows: the equilibrium concentration of iodine is sufficiently low so that the product $K_{I_2}[I_2]$ can be neglected and that of electrolyte is so large that [X] can be taken as its total concentration, C_X. Then, Eq. 7 becomes

$$\ln(C_{I_2}-Q_{I_2}V^{-1}) = -kt/\{1+K_{I_2}C_{CyD}(1+K_XC_X)^{-1}\} + \ln C_{I_2}. \quad (8)$$

Plots of $\ln(C_{I_2}-Q_{I_2}V^{-1})$ vs. t (Fig. 1) gave straight lines over the aeration time investigated; the slope corresponds to $-k$ in the absence of CyD, to $-k/(1+K_{I_2}C_{CyD})$ in the absence of the associating electrolyte, and to $-k/\{1+K_{I_2}C_{CyD}(1+K_XC_X)^{-1}\}$ in the presence of both CyD and electrolyte. The K_{I_2} value thus determined was 1.5×10^4 M^{-1}, which agrees with our previous result.[10] The association constants of CyD with the electrolytes studied here are given in Table 1 together with literature values available.

The association constants determined in this work seem to be significantly larger than the literature data. It is not clear at present whether or not the present results are reasonable, because the data so far available are limited and, moreover, considerable disagreement exists among them.

It is generally accepted that the CyD association constant decreases in the order, $ClO_4^- > SCN^- > I^- > Br^- > NO_3^-$.[7] As for the cation, on the other hand, little attention has been paid. For instance, K_X was reported for α-CyD-ClO_4^- system without specifying the counter cation.[6] In spite of different cation being used, the relative magnitude of K_X value of a given anion was compared for α- and β-CyDs.[7] Based on the data obtained by the spectral competitive inhibition method, Buvári and Barcza pointed out the importance of the counter cation: potassium salts associate more strongly with β-CyD than the sodium salts.[8]

Table 1. Association Constants for the Complex Formation between Electrolytes and α-Cyclodextrin at 25 °C

Electrolyte	Association constant/M^{-1}	
	This work[a]	Literature
NaCl	3	negligible[4]
KCl	5	
HNO_3	11	
$NaNO_3$	4	1.4 (KNO_3)[1]
$HClO_4$	60	39.8[4]
$LiClO_4$	22	
$NaClO_4$	35	20.4,[4] 30.6[2]
$KClO_4$	48	28.9,[1] 37[9]
$(CH_3)_4NClO_4$	8	

a) The relative standard deviation is roughly estimated to be 30% for the association constant lower than 5 and 15% for that higher than 10.

The present study indicates that the counter cation plays an important role in the α-CyD association with electrolytes; the association constant decreases in the order, $H^+ > K^+ > Na^+ > Li^+ > (CH_3)_4N^+$. In light of the order of anions, this order of alkali ions is understandable: counter cation with less affinity with water is favorable to association with CyD. The behavior of H^+ is particular and should be ascribed to hydrogen bonding to CyD; H^+ bound to primary or secondary alcohol group of the CyD rim attracts its counter anion and holds it inside the CyD cavity, when the anion has low affinity with water. The small K_X observed for $(CH_3)_4N^+$ ion may be attributable to that this ion cannot enter into the α-CyD cavity.[3] The counter cation effect is thus explainable on the assumption that electrolyte exists as ion-pair inside or in the entrance of CyD cavity with anion preferentially included in the cavity, although there has been no direct experimental evidence supporting this idea.

There are two essential requirements for the present method to be successufully applied. One is that the difference between the tow slopes, $-k$ at $C_{CyD}=0$ and $-k/(1+K_{I_2}C_{CyD})$ at $C_X=0$, be as large as possible. Any volatile guest substance with sufficiently large association constant can be used as an indicator; iodine is suitable for α-CyD, but not for β-CyD; in the latter case different guest should be used. Another requirement is that the product, K_XC_X, should not be too small compared with unity. When K_X is small, as is the present case, C_X should be made large. In such a case, care must be taken for the so-called salt effect.

The spectral competitive inhibition method makes use of the fact that the presence of electrolyte shifts the CyD association equilibrium with a certain guest substance as an indicator, usually, azo dye. Our method resembles this spectral method with respect to competing the electrolyte with the indicator guest for the CyD bonding site. It should be noted that, as was pointed out by Mochida et al.,[13] the presence of electrolyte does not always inhibit the indicator guest association with CyD, but, on the contrary, promotes the association by reducing the activity of water surrounding the indicator guest molecule. It depends on the nature of both cation and anion constituting the electrolyte which governs promotion or inhibition. The spectral method usually needs electrolyte of high concentration to cause measurable absorbance changes of the indicator guest. If a counter ion has more or less a promoting effect, the K_X value for this electrolyte is to be underestimated. These situations hold for the present method. It is, however, easy to study the salt effect by our method. The volatilization rate of the indicator guest is measured in the presence of salt of desired concentration and is compared with that in the absence of salt. If there is no change between them, the salt effect can be ignored. The salt concentration used in this work did not affect the iodine volatilization rate constant, k.

When iodine is used as an indicator guest, association constants of such electrolytes as SCN^-, I^-, and Br^- cannot be determined by the present method.

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