CHEMISTRY LETTERS, pp. 963-966, 1976. Published by the Chemical Society of Japan

KINETIC STUDY ON THE FORMATION OF A BINUCLEAR COMPLEX BETWEEN COPPER(II) AND CYCLODEXTRIN

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The formation of a 2:1 complex between copper(II) and α- or β-cyclodextrin was examined in an alkaline solution by means of a stopped-flow spectrophotometer. The reaction involves a first-order rate process corresponding to the cross-linking of a cyclodextrin ring by a $Cu(OH^-)_2Cu$ or $Cu(OH^-)(O^{2-})Cu$ ion bridge.

Cyclodextrins (CD's) are cyclic oligomers composed of six (α-CD), seven (β-CD), or more α-D-glucopyranose units linked 1→4 as in amylose.[1)] We previously reported[2)] that copper(II) forms 2:1 complexes with CD's in an alkaline solution. It was suggested[2b)] that the two pairs of C_2 and C_3' secondary hydroxyl groups of contiguous glucose units are cross-linked by the $Cu(OH^-)_2Cu$ ion bridge in the α-CD complex and by the $Cu(OH^-)(O^{2-})Cu$ ion bridge in the β-CD complex with the distortion of the circular rings of CD's to the ellipsoidal forms. The present study was undertaken to elucidate the mechanism of the complex formation by means of kinetics. The rate of the complex formation is slow enough to be followed with a stopped-flow method.

An alkaline CD solution was rapidly mixed with an aqueous $CuSO_4$ solution containing Na_2SO_4 as a salt for the adjustment of the ionic strength (I_c) of a reaction mixture to be 0.50 M, and the resulting change in absorbance of the mixture was followed at 670 nm with an Union Giken stopped-flow reaction analyzer, Model RA-1100. Figure 1 shows a typical change in absorbance (A) with time (t) and the corresponding logarithmic plot. In every run examined, the plot of log (A_∞ - A) vs. t gave a good straight line after t exceeded 0.5 s, but it deviated upward from the straight line before t reached 0.5 s. This fact indicates that the reaction consists of at least two steps; a rapid process which is completed within 0.5 s and a subsequent slower process. Our attention was focused on the latter in the present study.

Table 1 gives the observed first-order rate constants (k_{obsd}'s) for the slower step at various CD and Cu(II) concentrations in 0.485 M NaOH (I_c = 0.50 M) at 25°C. The k_{obsd} values

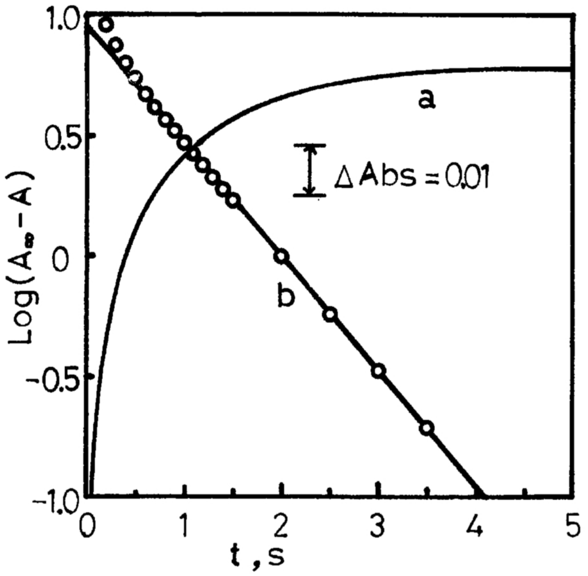


Fig. 1. Change in absorbance at 670 nm (a) and the corresponding log plot (b) for the formation of a Cu(II)-β-CD complex in 0.485 M NaOH at 25°C.
[Cu] = 6.25 mM, [β-CD] = 12.5 mM

Table 1. First-Order Rate Constants for the Formation of a 2:1 Cu(II)-CD complex in 0.485 M NaOH (I_c = 0.50 M) at 25°C

[CD], mM	[Cu(II)], mM	k_{obsd}, s^{-1}
	α-Cyclodextrin	
12.5	5.00	1.16 ± 0.01
25.0	5.00	1.17 ± 0.01
37.5	5.00	1.16 ± 0.01
50.0	3.75	1.20 ± 0.03
50.0	5.00	1.15 ± 0.02
50.0	6.25	1.09 ± 0.03
50.0	7.50	1.25 ± 0.04
	β-Cyclodextrin	
5.0	5.00	1.11 ± 0.02
12.5	3.75	1.12 ± 0.02
12.5	5.00	1.03 ± 0.01
12.5	6.25	1.07 ± 0.02
12.5	7.50	1.12 ± 0.01
20.0	5.00	1.02 ± 0.01
30.0	5.00	1.08 ± 0.01

were virtually constant, independent of the CD and Cu(II) concentrations. The k_{obsd} values for a Cu(II)-α-CD system were slightly larger than those for a Cu(II)-β-CD system.

To learn the role of OH^-, the effect of the OH^- concentration on k_{obsd} was examined. The k_{obsd} value increased with decreasing $[OH^-]$, and the plot of log k_{obsd} vs. log $[OH^-]$ gave a straight line with a slope of ca. - 1.0 for each of the Cu(II)-α- and β-CD systems (Fig. 2).

Methyl α-D-glucopyranoside (MG) also forms a Cu(II) complex with the mole ratio of 1:1 in an alkaline solution.2) However, the rate of the complex formation was too fast to be followed with a stopped-flow method. Margerum, et al.3) have reported similar phenomena, in which a macrocyclic ligand forms metal complexes much more slowly than the corresponding noncyclic ligands.

Figure 3 shows the temperature dependence of k_{obsd} measured in 0.485 M NaOH (I_c = 0.50 M). The activation enthalpy ($\Delta H^{\ddagger}$) and the activation entropy ($\Delta S^{\ddagger}$) were determined from the plots

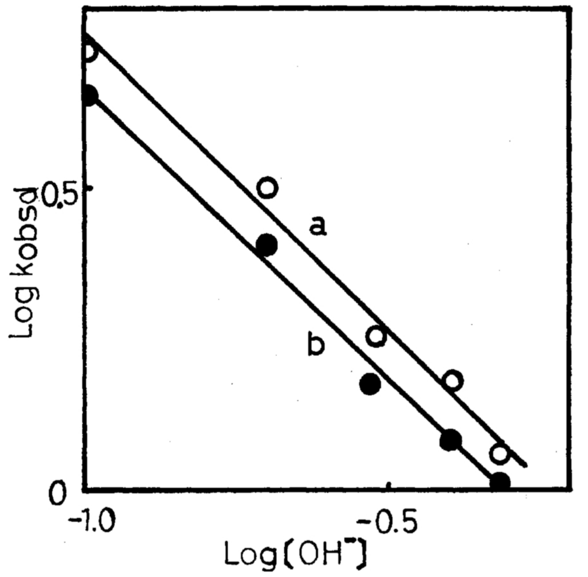


Fig. 2. Plots of log k_{obsd} vs. log $[OH^-]$ for the α- (a) and β-CD (b) systems at 25°C.

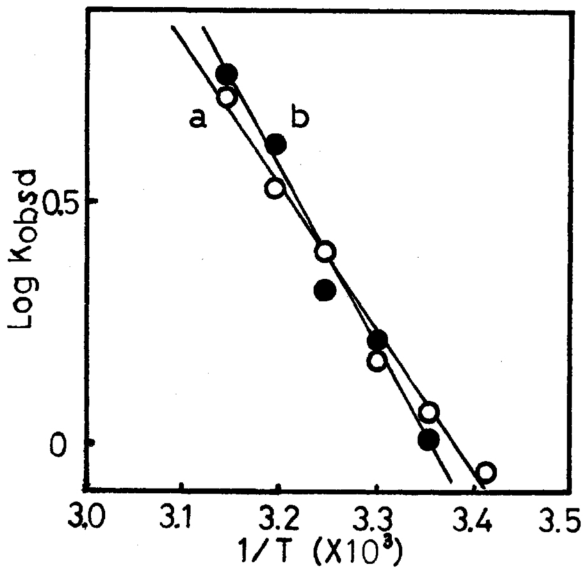


Fig. 3. Plots of log k_{obsd} vs. 1/T for the α- (a) and β-CD (b) systems in 0.485 M NaOH.

to be 13.5 $kcal\cdot mol^{-1}$ and - 13.0 e.u. for the α-CD complex and 16.6 $kcal\cdot mol^{-1}$ and - 2.7 e.u. for the β-CD complex respectively. Since the activation energies ($\Delta G^{\ddagger}$'s) for the α- and β-CD complexes are 17.3 and 17.4 $kcal\cdot mol^{-1}$ respectively at 25°C, the complex formation reactions are mainly governed by the enthalpy term.

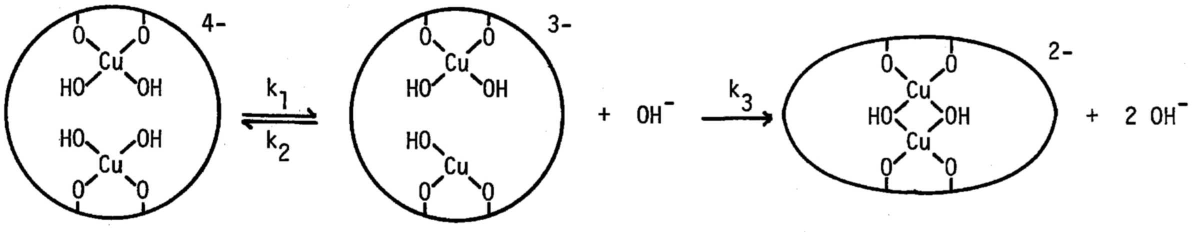
Taking into account the above observations, we posturated the reaction scheme for the formation of a Cu(II)-α-CD complex as shown below.$^{4)}$ The addition of two moles of Cu(II) to α-CD, yielding a complex $\underset{\sim}{\mathrm{I}}$, may be very fast, since a similar process for a Cu(II)-MG system is very fast. One mole of OH^- may be reversibly eliminated from $\underset{\sim}{\mathrm{I}}$ to form an unstable intermediate $\underset{\sim}{\mathrm{II}}$, which is then converted to the cross-linked complex $\underset{\sim}{\mathrm{III}}$ in a rate-determining step. The last process may accompany the large change in the CD conformation from circular to ellipsoidal. By the use of the method of stationary state with regard to the species $\underset{\sim}{\mathrm{II}}$, we obtain Eq. (1) for the rate (v) of the formation of $\underset{\sim}{\mathrm{III}}$.

$$v = \left\{k_1k_3/(k_3 + k_2[OH^-])\right\}\cdot[\underset{\sim}{\mathrm{I}}] \qquad (1)$$

In this equation, k_1, k_2, and k_3 are the rate constants for the reactions specified in the reaction scheme. Since the sum of $[\underset{\sim}{\mathrm{I}}]$ and $[\underset{\sim}{\mathrm{III}}]$ is virtually equal to $(1/2)[Cu]_0$ ($[Cu]_0$ is the initial concentration of Cu(II) added), and if we assume that $k_3 \ll k_2[OH^-]$, we obtain:

$$v = (k_1k_3/k_2[OH^-])\cdot\left\{(1/2)[Cu]_0 - [\underset{\sim}{\mathrm{III}}]\right\} \qquad (2)$$

$$2\ \mathrm{Cu(II)} + \alpha\text{-CD} + 8\ \mathrm{OH^-} \xrightarrow[-\ 4\ \mathrm{H_2O}]{\text{fast}}$$



I　　II　　III

This equation is consistent with the observations that the rate of the complex formation follows the first-order kinetics, regardless of the CD and Cu(II) concentrations, and increases linearly with decreasing OH^- concentration. The fact that the $\Delta H^{\ddagger}$ value for the β-CD complex is larger than that for the α-CD complex may be related to the need of a larger conformational change for the formation of the β-CD complex compared with that of the α-CD complex.

References and Notes

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   b) F. P. Hinz and D. W. Margerum, Inorg. Chem., **13**, 2941 (1974).

4) The reaction scheme for the formation of a Cu(II)-β-CD complex may be similar to that for a Cu(II)-α-CD complex except that the β-CD ring is cross-linked by the $Cu(OH^-)(O^{2-})Cu$ ion bridge instead of the $Cu(OH^-)_2Cu$ ion bridge for the α-CD complex.[2b]

(Received July 19, 1976)