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A TEMPERATURE-JUMP STUDY OF INCLUSION REACTIONS OF m- AND p-NITROPHENYLAZOSALICYLIC ACID WITH α-CYCLODEXTRIN IN AQUEOUS SOLUTIONS

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Inclusion reactions of the title compounds with α-cyclodextrin were studied in aqueous solution by means of a temperature-jump method. The rate constants for inclusion reactions were found to be in the order of magnitude 10^6-10^7 mol^{-1} dm^3 s^{-1}.

Ring-shaped α and β-cyclodextrin molecules (α-CD and β-CD) form inclusion compounds with a large number of azo and triphenylmethane dyes.[1)] The driving force for inclusion has been attributed to hydrogen bonding,[2)] van der Waals forces,[3,4)] hydrophobic interactions,[5)] the relaxation of the conformational strain in the cyclodextrin,[6)] and the release of non-hydrogen bonding water molecules with high energy in the cyclodextrin cavity.[4)]

Linear shaped m- and p-nitrophenylazosalicylic acids (m-NPAS and p-NPAS) were found to form 1 : 1 inclusion compounds with β-CD from spectrophotometric and temperature-jump measurements.[7)] The rate constants for the inclusion process were in the order of magnitude 10^6 mol^{-1} dm^3 s^{-1}. ^1H and ^{13}C NMR studies showed that the nitrobenzene ring (hydrophobic portion of m- and p-NPAS) is situated in the β-CD cavity.[8)]

The present study was carried out to investigate inclusion reactions of m- and p-NPAS with α-CD by the use of a temperature-jump method. With regard to the rate constant for inclusion process of α-CD system two different expectations are proposed: (1) The rate constants for inclusion processes of α-CD system become much smaller than those of β-CD system, since the diameter of α-CD cavity (4.5 Å)[9)] is smaller than that of β-CD cavity (7.5 Å).[10)] (2) The rate constants for inclusion processes of α-CD system become much larger than those of β-CD system, since m- and p-NPAS molecules are rigidly located in close proximity to the smaller cavity of α-CD.

The absorption spectra of acid (HA^-) and base (A^{2-}) form of m- and p-NPAS at varying α-CD concentrations showed isosbestic points at constant pH and ionic strength (0.1 mol dm^{-3}; KNO_3) and at 25 °C. The wavelength of the absorption maximum (λ_{max}) was dependent on the concentration of α-CD except for A^{2-} of m-NPAS (Fig. 1), showing a red shift. A similar red shift was observed also in 50%(v/v) dioxane-water media, a less polar solvent (dielectric constant; D ≈ 35) than aqueous media (Fig. 1). The values of λ_{max} obtained from the plateau region in Fig. 1 are summarized in Table 1. It is worth while to mention that the wave-length of λ^A_{max} of m-NPAS was not virtually changed in α-CD system, and only the absorbance at λ_{max} decreased with increase in the concentration of α-CD. This was also observed in β-CD system.

A plot of $[NPAS]_T[\alpha\text{-CD}]_T/\Delta A$ against $[\alpha\text{-CD}]_T$ gave a straight line (Fig. 2), where ΔA denotes the change in absorbance of a solution of NPAS-αCD system on addition of α-CD and $[\ \ ]_T$ the total concentration.[7,11,12] The linear relation in Fig. 2 indicates the formation of a 1 : 1 inclusion compound between α-CD and the species HA^- and A^{2-} of m- and p-NPAS. The equilibria for inclusion reaction are expressed as follows,

$$HA^- + \alpha\text{-CD} \underset{K}{\rightleftharpoons} HA\text{-}\alpha CD \quad (1); \quad A^{2-} + \alpha\text{-CD} \underset{K'}{\rightleftharpoons} A\text{-}\alpha CD, \quad (2)$$

where $K = [HA^-][\alpha\text{-CD}]/[HA\text{-}\alpha CD]$ and $K' = [A^{2-}][\alpha\text{-CD}]/[A\text{-}\alpha CD]$. The values of K and K' were determined to be in the order of magnitude 10^{-4} mol dm^{-3} from Fig. 2. The m- and p-NPAS inclusion complexes with α-CD become 2-7 times more stable compared to those with β-CD. The relationship, K' < K, was found to hold also in α-CD system.

Table 1. Values of λ_{max} in absorption spectra of m- and p-NPAS

Conditions	λ_{max}/nm for p-NPAS		λ_{max}/nm for m-NPAS	
	HA^-	A^{2-}	HA^-	A^{2-}
(1) in water	376	495	354	453
(2) in 50%(v/v) dioxane-water	387 (11)	506 (11)	365 (11)	464 (11)
(3) included with β-CD	382 (6)	507 (12)	356 (2)	453 (0)
(4) included with α-CD	390 (14)	506 (11)	364 (10)	453 (0)[b]

a) Parentheses denote $\lambda_{max}(2, 3, 4) - \lambda_{max}(1)$.
b) A shoulder at 424 nm.

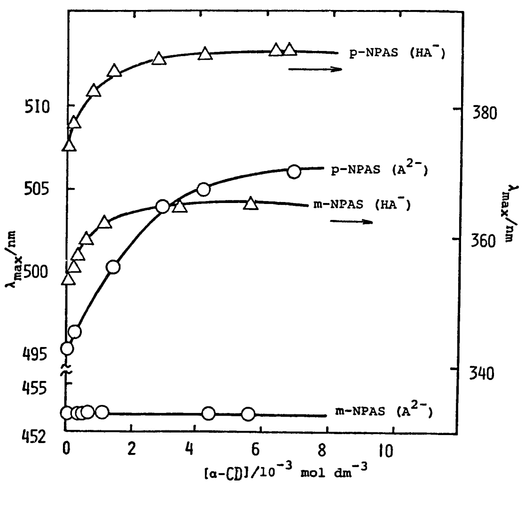

Fig. 1. Dependence on [α-CD] of λ_{max} of the absorption spectra of HA^- and A^{2-} of m- and p-NPAS.

Kinetic data were obtained under pseudo-first-order conditions using a large excess of α-CD. The rate for inclusion reaction was followed spectrophotometrically at λ_{max} of the inclusion species. The inclusion reaction in neutral region is

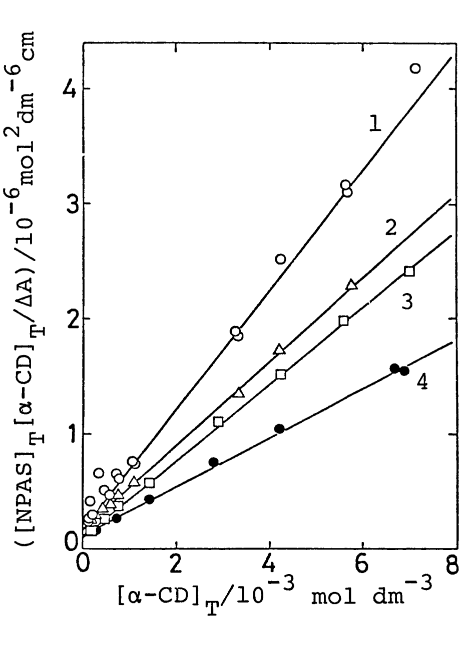

Fig. 2. Plots of $[NPAS]_T[\alpha\text{-CD}]_T/\Delta A$ against $[\alpha\text{-CD}]_T$. (1) A^{2-} of m-NPAS (454 nm). (2) HA^- of m-NPAS (370 nm). (3) A^{2-} of p-NPAS (490 nm). (4) HA^- of p-NPAS (400 nm).

$$HA^- + \alpha\text{-CD} \underset{k_-}{\overset{k_+}{\rightleftharpoons}} HA\text{-}\alpha CD \qquad (3)$$

and in basic region

$$A^{2-} + \alpha\text{-CD} \underset{k_-'}{\overset{k_+'}{\rightleftharpoons}} A\text{-}\alpha CD. \qquad (4)$$

The observed relaxation time, τ, for the reactions 3 and 4 can be expressed as

$$\tau^{-1} = k_+[\alpha\text{-CD}] + k_- \qquad (5)$$

and

$$\tau^{-1} = k_+'[\alpha\text{-CD}] + k_-', \qquad (6)$$

respectively. The plot of τ^{-1} against [α-CD] gave a straight line with a slope k_+ (k_+') and an intercept k_- (k_-') (Fig. 3). The values of rate constants, k_+, k_-, k_+', and k_-', are summarized in Table 2. The equilibrium constants, K and K', determined kinetically as the ratio of k_-/k_+ and k_-'/k_+', respectively, were in agreement with those determined spectrophotometrically (Table 2). In the inclusion of m- and p-NPAS with α-CD, one can expect that the rate constant, k_+ (k_+'), decreases owing to the smaller α-CD cavity. However, the higher stability of inclusion complex with α-CD may be attributed to the increase in k_+ (k_+'). Actually in our investigations the rate constant k_+ (k_+') of α-CD system was considerably larger than that of β-CD system.[13] The value of k_+ in α-CD system was found to depend on the position of the sustituent group (nitro

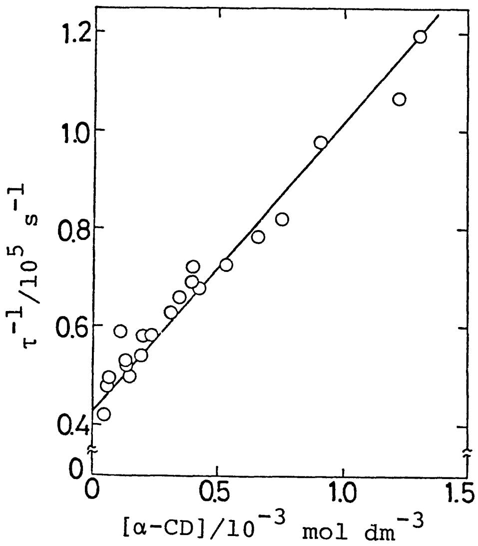

Fig. 3. A plot of Eq. 5 for HA^- of p-NPAS.

Table 2. Rate and equilibrium constants for the inclusion reactions of m- and p-NPAS in α-CD and β-CD systems

Equilibrium and Rate Constants	α-CD		β-CD[a)]	
	m-NPAS	p-NPAS	m-NPAS	p-NPAS
(1) k_+/mol^{-1} dm^3 s^{-1}	9.3×10^6	6.1×10^7	3.3×10^6	3.2×10^6
(2) k_-/s^{-1}	3.0×10^3	4.1×10^4	4.0×10^3	1.1×10^4
(3) K = (k_-/k_+)/mol dm^{-3}	3.2×10^{-4}	6.7×10^{-4}	1.2×10^{-3}	3.4×10^{-3}
(4) K(spectr)/mol dm^{-3}	4.95×10^{-4}	6.80×10^{-4}	9.22×10^{-4}	1.37×10^{-3}
(5) k_+'/mol^{-1} dm^3 s^{-1}	9.0×10^6	2.3×10^7	1.4×10^6	1.5×10^6
(6) k_-'/s^{-1}	2.0×10^3	8.0×10^3	2.2×10^3	4.0×10^3
(7) K' = (k_-'/k_+')/mol dm^{-3}	2.2×10^{-4}	3.5×10^{-4}	1.6×10^{-3}	2.7×10^{-3}
(8) K'(spectr)/mol dm^{-3}	3.07×10^{-4}	2.98×10^{-4}	2.16×10^{-3}	1.12×10^{-3}

a) Ref. 7.

group) on m- and p-NPAS, i.e., the values of k_+ of m- and p-NPAS was fairly different from each other compared to the case of β-CD system. Larger steric hindrance of the nitro group in m-NPAS contributes to decreasing the rate constants k_+ (k'_+). This indicates that the inclusion process takes place at the hydrophobic site (nitrobenzene moiety). Cramer et al. pointed out that the value of k_+ is almost 2-3 orders of magnitude larger than that of k'_+ when a hydrophilic group such as hydroxyl group is included into α-CD cavity.[14] In the present kinetic study, however, the values of k_+ and k'_+ were found to be in the same order of magnitude (10^6 mol^{-1} dm^3 s^{-1} for m-NPAS and 10^7 mol^{-1} dm^3 s^{-1} for p-NPAS).[15] This supports the inclusion of the hydrophobic site of a guest molecule into α-CD cavity.

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13) In α-CD system the rate constant k_+ for p-NPAS (6.1×10^7 mol^{-1} dm^3 s^{-1} at 25 °C) was in the same order of magnitude that for 4'-nitrophenylazo-1-naphthalene-4-hydroxy-5-sulfonate ion (5.2×10^7 mol^{-1} dm^3 s^{-1} at 14 °C). F. Cramer, W. Saenger, and H.-Ch. Spatz, J. Am. Chem. Soc., 89, 14 (1967).
14) For example, in the case of 3'-methyl-4'-hydroxyphenylazo-naphthalene-4-sulfonate, $k_+ = 1.2 \times 10^5$ mol^{-1} dm^3 s^{-1} and $k'_+ = 1.5 \times 10^2$ mol^{-1} dm^3 s^{-1}.
15) The relationship, $k'_+ < k_+$, was observed also in α-CD system (Table 2).

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