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A KINETIC STUDY ON THE PROTON-TRANSFER REACTIONS OF m- AND p-NITROPHENYLAZOSALICYLIC ACIDS COUPLED WITH INCLUSION REACTIONS WITH β-CYCLODEXTRIN IN AQUEOUS SOLUTIONS[1]

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A kinetic study on the proton-transfer reactions of the title compounds coupled with inclusion reactions with β-cyclodextrin in aqueous solutions is carried out by means of a temperature-jump method. The forward rate constants for the inclusion reactions are in the order of magnitude 10^6 mol^{-1} dm^3 s^{-1}. The rate constants for the recombination of the title compounds with OH^- ion increase in the concentrations of β-cyclodextrin.

β-Cyclodextrin forms inclusion compounds in aqueous solution with azo dyes and many other inorganic or organic molecules.[2] The main binding forces in the inclusion compounds are said to be hydrogen bonding,[3] van der Waals forces,[4] and hydrophobic interactions.[5] In general the acid dissociation of azo dyes is facilitated or retarded by forming inclusion compounds with β-cyclodextrin. This behavior is explained by the Raumalkalität (space alkalinity) of β-CD,[6] dipole-ion interaction,[7] and hydrophobic microenvironment of the β-CD cavity.[2]

On the other hand, the importance of the microenvironment at the periphery of the reaction site has been pointed out from the standpoint of solute-solvent interactions in the proton-transfer reactions of o-hydroxy azo compounds in a mixed solvent system.[8] In the present study the authors aimed to elucidate the microenvironmental effect in the proton-transfer reactions of m- and p-NPAS.

The absorption maxima (λ_{max}^{HA} = 376 and λ_{max}^{A} = 495 nm) of p-NPAS in aqueous solution show a red shift ($\lambda_{max}^{HA-\beta CD}$ = 382 and $\lambda_{max}^{A-\beta CD}$ = 507 nm) in the presence of a large excess of β-CD, and the absorbances A_{376} and A_{495} decrease with increasing β-CD concentrations (Fig. 2). Figure 3 shows the absorption spectra of m-NPAS which shows no appreciable red shift (λ_{max}^{HA} = 354 and λ_{max}^{A} = 453 nm in water ; $\lambda_{max}^{HA-\beta CD}$ = 356 and $\lambda_{max}^{A-\beta CD}$ = 453 nm) in the presence of a large excess of β-CD and A_{354} and A_{453} decrease with increasing β-CD concentrations.[1]

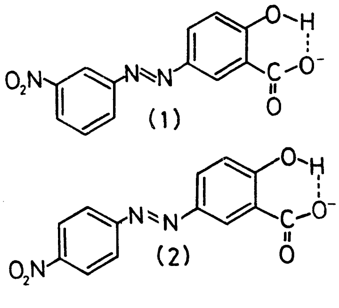
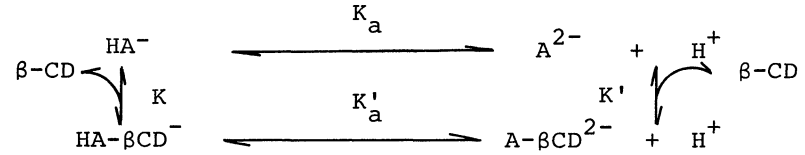


Fig. 1. Structural formulae of m-NPAS (1) and p-NPAS (2).

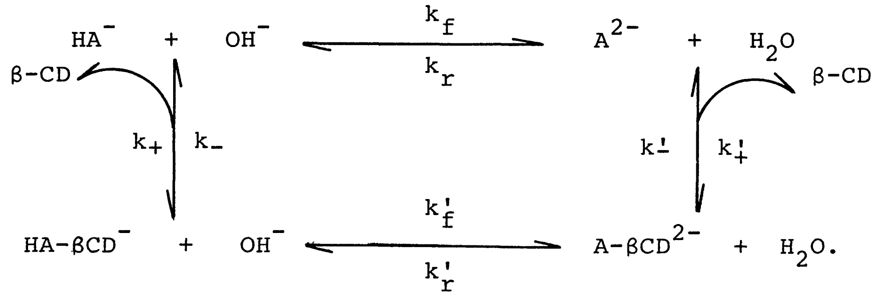
The formation of 1 : 1 inclusion compounds (HA-βCD$^-$ and A-βCD^{2-}) of these azo dyes with β-CD is confirmed by the presence of isosbestic points in the spectral change (Figs. 2 and 3) and by the plot as shown in Fig. 4. In 50%(v/v) dioxane-water media λ_{max}^{HA} of m- and p-NPAS are 365 and 387 nm and λ_{max}^{A} 464 and 506 nm, respectively.

The equilibria for the acid dissociation and the inclusion are expressed as follows,



where K_a = [A][H]/[HA], K'_a = [A-βCD][H]/[HA-βCD], K = [HA][β-CD]/[HA-βCD] and K' = [A][β-CD]/[A-βCD]. The values of K and K' were found to be 9.22×10^{-4} and 2.16×10^{-3} mol dm^{-3} for m-NPAS, and 1.37×10^{-3} and 1.12×10^{-3} mol dm^{-3} for p-NPAS. The changes in K_a with increasing β-CD concentrations are summarized in Table 1. In the case of p-NPAS, the change in K_a is quite a little.

The kinetic data were obtained under pseudo-first-order conditions using a large excess of β-CD. The inclusion of HA$^-$ proceeds in the time region of 20-50 μs div^{-1} and that of A^{2-} 0.1-0.5 ms div^{-1} in the case of m-NPAS. The kinetic data are interpreted in terms of the following scheme



The observed relaxation time, τ, for the inclusion reaction can be expressed as

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

The plot of τ^{-1} against [β-CD] gave a straight line with a slope k_+ and an intercept k_- (Fig. 5). In Table 2 the rate constants k_+, k_-, k'_+, and k'_- are summarized. The values of k_-/k_+ and k'_-/k'_+ for m- and p-NPAS are in agreement with the equilibrium constants K and K' determined spectrally. The values of k_+ or k'_+ for m- and p-NPAS are almost the same, which suggests that the process of inclusion is not hindered by the nitro group (Fig. 1). Cramer et al. have pointed out that the value of k_+ is about 2-3 orders of magnitude larger than that of k'_+ when a hydrophilic group such as a hydroxyl group is included into the α-CD cavity.2) In the present kinetic study the values of k_+ and k'_+ were found to be in the same orders of magnitude (10^6 mol^{-1} dm^3 s^{-1}; $k_+ > k'_+$), which suggests that the process of inclusion takes place at the hydrophobic site i.e. the nitro group.9)

The rate constants, k_f and k_r, are obtained from the following equation.

$$\tau^{-1} = k_f[OH^-] + k_r \qquad (2)$$

Table 1. Acid-dissociation constants, K_a/mol dm^{-3}

$C_{\beta\text{-CD}}$/mol dm^{-3}	p-NPAS obsd	p-NPAS calcd$^{a)}$	m-NPAS obsd	m-NPAS calcd$^{a)}$
0	2.06×10^{-11}	—	1.59×10^{-11}	—
6.36×10^{-4}	2.14×10^{-11}	2.21×10^{-11}	1.20×10^{-11}	1.21×10^{-11}
3.18×10^{-3}	2.29×10^{-11}	2.38×10^{-11}	1.05×10^{-11}	8.81×10^{-12}
∞	—	2.52×10^{-11}	—	6.77×10^{-12}

a) See Ref. 10.

Table 2.

Rate constants for the proton-transfer and inclusion reactions

Rate constants	p-NPAS	m-NPAS
k_+/mol^{-1} dm^3 s^{-1}	3.2×10^6	3.3×10^6
k_-/s^{-1}	1.1×10^4	4.0×10^3
k'_+/mol^{-1} dm^3 s^{-1}	1.5×10^6	1.4×10^6
k'_-/s^{-1}	4.0×10^3	2.2×10^3
k_f/mol^{-1} dm^3 s^{-1}	2.1×10^7	2.0×10^7
k_r/s^{-1}	1.9×10^4	3.5×10^4

The plot of τ^{-1} against [OH$^-$] gave a straight line at each β-CD concentration. Because of the strong intramolecular hydrogen-bond the values of k_f are three orders of magnitude smaller as compared with those of diffusion-controlled reactions. If the reaction site of the proton-transfer reaction is included into the hydrophobic β-CD cavity, where the dielectric constant is probably small, the rate constant k_f should decrease.$^{8)}$ However the values of k_f and k_r were found to increase with the increase in the β-CD concentrations, i.e., for m-NPAS k_f = 2.5×10^7 and 2.7×10^7 mol^{-1} dm^3 s^{-1} and k_r = 4.8×10^4 and 5.5×10^4 s^{-1} at [β-CD] = 1.60×10^{-3} and 8.02×10^{-3} mol dm^{-3}, respectively, and for p-NPAS k_f = 3.0×10^7 mol^{-1} dm^3 s^{-1} and k_r = 2.5×10^4 s^{-1} at [β-CD] = 3.26×10^{-3} mol dm^{-3}. This fact suggests that the reaction site (-COO$^-$···HO-) of m- and p-NPAS in the proton-transfer reaction is situated at the outside of the hydrophobic β-CD cavity.$^{9)}$

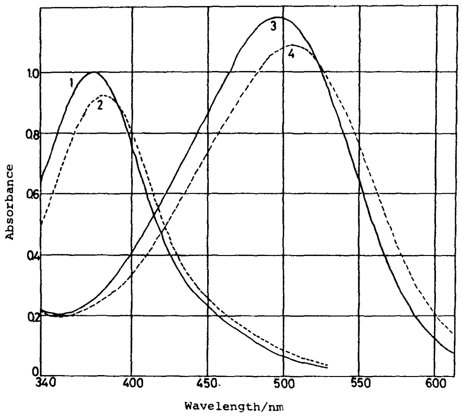


Fig. 2. Absorption spectra of HA^- (1), $HA\text{-}\beta CD^-$ (2), A^{2-} (3), and $A\text{-}\beta CD^{2-}$ (4) of p-NPAS at 25 °C and I = 0.1 mol dm^{-3} (KNO_3). $C_{dye} = 4.22 \times 10^{-5}$ mol dm^{-3}. $C_{\beta\text{-}CD} = (0\text{-}5.65) \times 10^{-3}$ mol dm^{-3} at pH = 7.19 for (1) and (2). $C_{\beta\text{-}CD} = (0\text{-}3.14) \times 10^{-3}$ mol dm^{-3} at pH = 11.74 for (3) and (4).

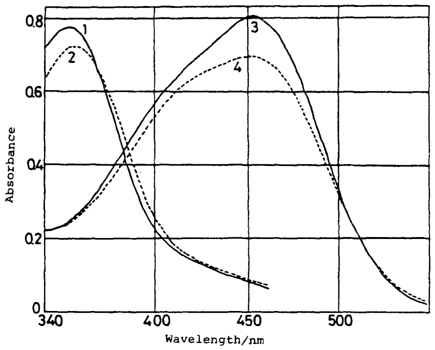


Fig. 3. Absorption spectra of HA^- (1), $HA\text{-}\beta CD^-$ (2), A^{2-} (3), and $A\text{-}\beta CD^{2-}$ (4) of m-NPAS at 25 °C and I = 0.1 mol dm^{-3} (KNO_3). $C_{dye} = 4.83 \times 10^{-5}$ mol dm^{-3}. $C_{\beta\text{-}CD} = (0\text{-}5.70) \times 10^{-3}$ mol dm^{-3} at pH = 7.43 for (1) and (2). $C_{\beta\text{-}CD} = (0\text{-}5.65) \times 10^{-3}$ mol dm^{-3} at pH = 11.76 for (3) and (4).

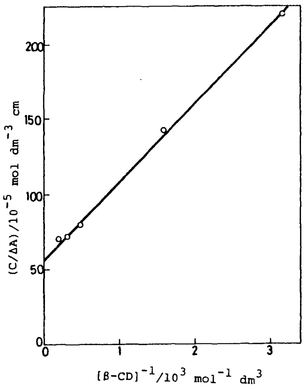


Fig. 4. Plot of $C/\Delta A$ against $[\beta\text{-}CD]^{-1}$ at pH = 7.43 for m-NPAS. ΔA and C are the change in absorbance and the total dye concentration, respectively.

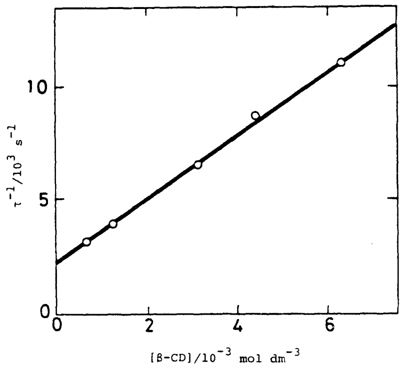


Fig. 5. Plot of Eq. 1 at pH = 11.80 for m-NPAS.

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9) As for the structure of the inclusion compounds formed in solution the ^{1}H and ^{13}C NMR spectroscopic studies are now in progress.

10) From the relationship, $K' \cdot K_a' = K \cdot K_a$, the equation $\bar{K}_a = K_a(1 + C°/K')/(1 + C°/K)$ is obtained, where $\bar{K}_a$ and C° denote the acid-dissociation constant at each β-CD concentration and the analytical β-CD concentrations, respectively. See K. A. Connors and J. M. Lipari, J. Pharm. Sci., 65, 379 (1976) and T. Miyaji, Y. Kurono, K. Uekame, and K. Ikeda, Chem. Pharm. Bull., 24, 1155 (1976).

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