afforded 286 g (90.5%), mp 66-68 ℃ (lit.[4] mp 66-67.5 ℃). The ^{1}H NMR spectrum was identical to those reported.[2]

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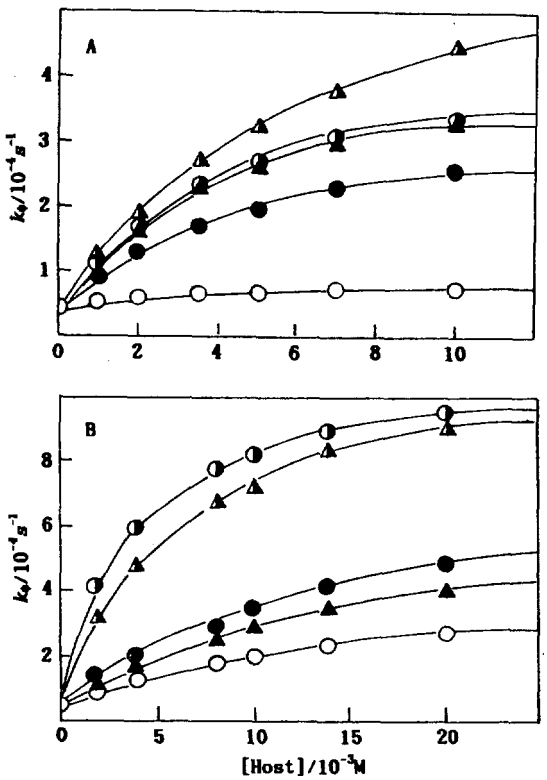

Figure 1. Variation of the pseudo-first-order rate constants for the deacylation reactions of *p*- (A) and *m*-carboxyphenyl acetate (B) as function of the concentration of hosts in the presence or absence of zinc ion: ○, β-CD; ▲, β-CDen; ●, β-CDdien; △, β-CDen/Zn^{2+}(4 : 1); ◑, β-CDdien/Zn^{2+}(4 : 3).

Deacylation Reaction of Carboxyl-Substituted Phenyl Acetate in the Presence of β-Cyclodextrin and Mono-(6-alkylamino)-β-Cyclodextrins : Effects of Carboxyl Group and Zinc Ion

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Cyclodextrins (CDs) have attracted great interest as enzyme mimics due to their ability to form inclusion complexes with a variety of substrates and to exhibit catalytic effects on various types of reactions.[1] The cleavage of phenyl esters in aqueous base is the most widely investigated of such CD-catalyzed reactions, and it is generally believed that the reactions take place from an ester-CD complexes in which the aryl group of the ester is included in the cavity of the CD.[2-6] We have been interested in the catalytic effects of β-CD and functionalized β-CDs on the cleavage of various aryl esters.[4-6] We now report the kinetic studies of the deacylation reactions of *p*- and *m*-carboxyphenyl acetates in β-CD (1), mono-6-deoxy-6-[N-(2-aminoethyl)]amino-β-CD (β-CDen, 2), and mono-6-deoxy-6-[N-(2-aminoethyl)-2-aminoethyl]-amino-β-CD (β-CDdien, 3) media. Carboxyphenyl acetates have a net charge on carboxyl group and can interact with the amine-derivatized β-CDs, electrostatically. In addition, the carboxyl group of the substrates and amine groups of β-CDen and β-CDdien could be binding sites for metal ions. The effects of the position of carboxyl group on phenyl ring and zinc ion on the stability and reactivity of the complexes between carboxyphenyl acetates and β-CDs are investigated.

β-CDen and β-CDdien were available from a previous study.[5,6] Carboxyphenyl acetates were prepared by a literature procedure.[2a] Deacylation reactions of carboxyphenyl acetates were initiated by adding 20 μL of 0.01 M solution of *p*-carboxyphenyl acetate in acetonitrile or 20 μL of 0.02 M solution of *m*-carboxyphenyl acetate in acetonitrile to 2.00 mL of the host solutions (0-20 mM) in 0.05 M pH 9.60 borate buffer (I=0.2 M) containing a desired amount of zinc ion in a cuvette pre-equilibrated at 25 ℃. The concentrations of zinc ion were adjusted such that [Zn^{2+}]/[host] ratio is 0.25 for β-CDen-containing media or 0.75 for β-CDdien-containing media. Reactions were followed spectrophotometrically by monitoring the formation of *p*-hydroxybenzoic acid at 279 nm or *m*-hydroxybenzoic acid at 289 nm. The reactions obeyed pseudo-first-order kinetics with respect to the esters, regardless of the presence of the hosts and zinc ion. The pseudo first-order rate constants (k_ψ) were determined in the presence of various concentrations of the hosts.

Figure 1 shows variation of k_ψ for the deacylation reactions

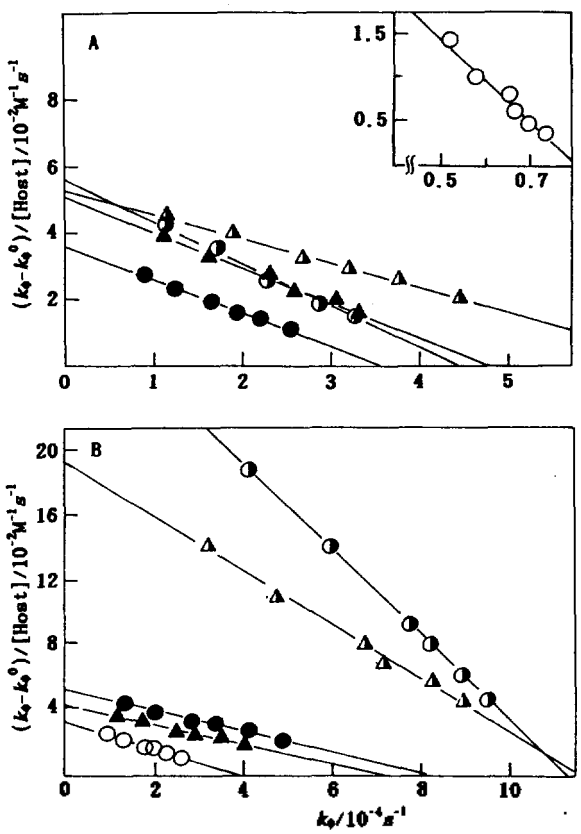


Figure 2. Plots of data of Figure 1 according to Eqn. (1). See Figure 1 for legends.

of *p*- and *m*-carboxyphenyl acetate as function of the concentration of hosts in the presence or absence of zinc ion.[7] Assuming 1 : 1 complexation between a substrate and host, k_ψ is related with the rate constants k_ψ^{CD} for the fully complexed substrate and the binding constant K of the substrate to the host by Eqn. (1).[2]

$$(k_\psi-k_\psi^0)/[\text{host}]=-Kk_\psi+Kk_\psi^{CD} \quad (1)$$

where k_ψ^0 is the rate constant observed in the absence of host.

By plotting the kinetic data shown in Figure 1 according to Eqn. (1), straight lines were obtained (Figure 2). K and k_ψ^{CD} values were calculated from the slopes and intercepts of the lines. The results are summarized in Table 1.

Table 1 shows that the stability of the complexes between carboxyphenyl acetate and β-CDs is much greater for the *p*-isomer than the *m*-isomer. The largest difference in stability of the complexes is observed with native β-CD of which *p*-isomer complex is about 6 times tighter than the *m*-isomer complex. The difference is much greater than that observed with nitrophenyl acetates: the binding constant of *p*-nitrophenyl acetate with β-CD was reported to be 160 M^{-1}, whereas that of *m*-nitrophenyl acetate is 130 M^{-1}.[2a] This indicates that far more selective binding for the *p*-isomer is exhibited in carboxyphenyl acetates than in nitrophenyl acetates.

It is known that the deacylation reaction of aryl esters complexed with β-CD proceeds through nucleophilic attack by a secondary hydroxyl group in its ionic state on the carbonyl atom of the substrates.[2b] Thus the *p*- or *m*-substituent

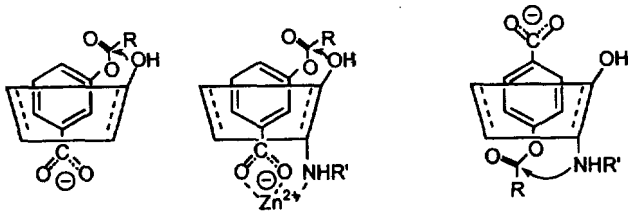
Table 1. Binding Constants and Kinetic Parameters for the Cleavage of *p*- and *m*-Carboxyphenyl Acetate in the Presence of β-CDs and Zinc Ion.[a]

Host	$[Zn^{2+}]/[Host]$	K/M^{-1}	$k_\psi^{CD}\times10^4/s^{-1}$	$(k_\psi^{CD}/k_\psi^0)^b$
	(A) *p*-Carboxyphenyl Acetate			
β-CD	0	480	0.8	2.1
β-CDen	0	210	4.8	13
β-CDen	0.25	140	7.3	19
β-CDdien	0	200	3.6	9.6
β-CDdien	0.75	260	4.4	12
	(B) *m*-Carboxyphenyl Acetate			
β-CD	0	84	3.9	9.5
β-CDen	0	61	7.0	17
β-CDen	0.25	160	12	28
β-CDdien	0	60	8.5	21
β-CDdien	0.75	260	11	27

[a] At 25 °C, in 0.05 M pH 9.60 borate buffer (I=0.2 M). [b] k_ψ^0 is 0.38×10^{-4} s^{-1} for the *p*-isomer and 0.41×10^{-4} s^{-1} for the *m*-isomer.

on phenyl ring of the esters in productive complexes is located toward the narrow primary hydroxyl side of β-CD cavity (mode A). Space-filling models of the complexes of carboxyphenyl acetate indicated that the carboxyl group of the *p*-isomer protrudes further from the cavity, while that of the *m*-isomer stays closer to the interior of β-CD. Since the carboxylate anion has a net charge and more solvated than a nitro group, the close proximity of the carboxylate group to the hydrophobic β-CD cavity requires higher energy. This would be a reason why the *m*-isomer forms less stable complex than the *p*-isomer. This agrees well with a quantum mechanical calculation. A structural optimization by MM+ calculation using *HyperChem* program showed that the energy of the *p*-isomer and β-CD is lowered by 18 kcal/mol upon complexation whereas the *m*-isomer and β-CD is stabilized by 11 kcal/mol and the carboxyl group of the *p*-isomer protrudes further.

The alkylamine displacements of the primary hydroxyl group of β-CD resulted in less tighter binding with carboxyphenyl acetates (see Table 1). This implies that the electrostatic interaction between the carboxyl group of the substrates and the amine group of the hosts is overwhelmed by the steric effect exerted by the substituents on β-CD. In a previous paper,[6] we demonstrated that the amine groups of β-CDen and β-CDdien participate in the deacylation reactions of *p*-substituted aryl esters. In this case, the complexes formed by insertion of the acetyl portion first into the cavity from the secondary hydroxyl side of β-CD (mode B),[8] which is nonproductive for native β-CD complexes, is productive. Also, the carboxyl and amine groups in the complexes might be too apart to interact effectively in the medium of high ionic strength. However, the complexes appear to undergo faster deacylation reactions than the complexes formed *via* mode A, because of greater nucleophilicity of the amine groups, compared to hydroxyl group. The rate enhancement by β-CDen and β-CDdien is much greater for *p*-nitrophenyl esters[6] than for *p*-carboxyphenyl acetate. This seems to indicate that the complexes of the former esters have better



Scheme. Schematic representation of the major 'productive' complexes of carboxyphenyl acetates with β-CDs. The mode B complexes with native β-CD are non-productive and mode A complexes of the *p*-isomer are less reactive than those of *m*-isomer.

geometry for the reaction than the latter. Difference in affinity of the *p*-substituents to β-CD cavity might be responsible for this.

Table 1. also shows that the rate constant k_o^{CD} of the deacylation of the fully complexed substrate is greater for the *m*-isomer than for the *p*-isomer. This result is in line with the general trend known as '*meta selectivity*'.[2] The *meta* selectivity is biggest in β-CD and least in β-CDen. The less pronounced *meta* selectivity in β-CDen and β-CDdien can be explained in terms of the afore-mentioned mode B complexation. To be attacked by the amine groups, acetyl portion of the substrates should locate close proximity to the amine groups.[6] For the *m*-isomer, the mode B complexation results in positioning of the carboxylate anion deep in the hydrophobic cavity and considerable steric hindrance. Thus the mode B complexation is less plausible for the *m*-isomer than for the *p*-isomer and the reaction of the *m*-isomer proceeds mainly through mode A complexation, whereas the major reaction route for the *p*-isomer is *via* mode A complexation with β-CD and mode A and B complexations with β-CDen and β-CDdien.

Addition of zinc ion causes tighter binding of the substrates with β-CDen and β-CDdien except for the case between the *p*-isomer and β-CDen, and resulted in greater reactivity of all the complexed substrates with the aminated β-CDs. The effects of zinc ion on the binding constant is much more pronounced for the *m*-isomer. Zinc ion can form ternary complexes with carboxylate anion of the substrate and amine groups of the hosts.[10] This is possible only when the complexes are formed *via* mode A fashion. Little dependence of K values of the *p*-isomer on zinc ion and large enhancement in K values of *m*-isomer can be taken as a further evidence of involvement of mode A complexation for *m*-isomer and little contribution of mode A complexation for the *p*-isomer for the deacylation reaction.

In conclusion, this work demonstrates that the *p*-isomer of carboxyphenyl acetate shows enhanced binding affinity than the *m*-isomer to β-CD, β-CDen and β-CDdien, and addition of zinc ion increases the reactivity of the complexed substrates. The reaction of the *p*-isomer also proceeds *via* attack by amine groups of β-CDen and β-CDdien, whereas the attack by secondary hydroxyl group is the major reaction route for the m-isomer even in the presence of the amine-derivatized β-CD.

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7. In agreement with a previous study,[6] control experiments with ethylenediamine and diethylenetriamine in the absence of β-CDs did not show significant effects of the amines on the reaction rate. The observation of saturation kinetics (Figure 1) also indicates that the reactions proceed mainly via complexation with the hosts.
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A Melt Processable Ethynylphenoxy Group Substituted Cyclotriphosphazene: Synthesis and Thermal Polymerization

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Cyclotriphosphazenes exhibit useful thermal properties such as self-extinguishibility and flame retardancy, which are imparted mainly by the presence of nitrogen and phosphorus atoms in the ring. Several research groups reported that cyclotriphosphazenes incorporated into organic polymeric systems as pendants improved thermal properties of the resulting polymers considerably.[1-10] The thermal polymerization of cyclotriphosphazenes containing thermally curable maleimido groups was also reported. The resulting polymers