

Kinetics of Hydrolysis of Phenyl Acetates Catalyzed by the Zinc(II) Complex of 1,5,9-Triazacyclododecane. Evidence for Attack of Water or Hydroxide Ion at the Coordinated Ester

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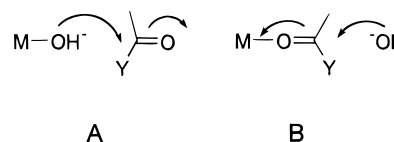
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Rates for hydrolysis of substituted phenyl acetates were measured in the presence of the Zn(II) complex of 1,5,9-triazacyclododecane. The kinetic data are incompatible with the mechanism in which the water and hydroxide ion coordinated to the metal center makes a nucleophilic attack at the ester linkage. Instead, the results support the mechanism in which the ester is first complexed to the metal center and then water or hydroxide ion makes a nucleophilic attack at the complexed ester. The kinetic data further indicate that the electrostatic interaction between the cationic metal center and the anionic hydroxide ion facilitates the attack of hydroxide ion at the complexed ester. In addition, the C–O bond of the ester is not cleaved significantly in the rate-determining transition state for attack by both water and hydroxide ion.

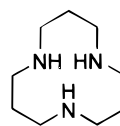
Introduction

Currently, there is much interest in catalysis of organic reactions by complexes of transition metal ions acting as Lewis acid catalysts.^{1,2} In particular, catalysis of hydrolysis of carboxyl^{3–10} or phosphoric^{11–15} acid derivatives has been investigated in relation to metalloproteinases or metallophosphoesterases. For many synthetic catalysts based on transition metal complexes, metal-bound hydroxide ions are proposed to act as nucleophiles that attack the carbonyl carbon or phosphoryl phosphorus atoms. In many cases, however, assignment of the nucleophilic role of the metal-bound hydroxide ions lacks rigorous mechanistic analysis.

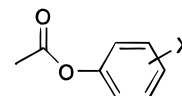
The attack (A) by metal-bound hydroxide ion at the carbonyl or phosphoryl group is kinetically equivalent to the attack (B) of hydroxide ion at the carbonyl or phosphoryl group coordinated to the metal ion. It is difficult to distinguish these two mechanisms solely on the basis of kinetic data. In the case of substitutionally inert complexes of Co(III), ¹⁸O-tracer experiments revealed that both of the two mechanisms occur in the



hydrolysis of the bound amino acid esters or amides.^{21–23} So far, experimental evidence has seldom been rigorously presented to distinguish the two mechanisms of A and B for hydrolysis of carboxyl or phosphoryl derivatives catalyzed by complexes of substitutionally labile metal ions. In this paper, we report that catalysis of hydrolysis of phenyl acetates 1–4 by the Zn(II) complex of 1,5,9-triazacyclododecane (L) proceeds through the mechanism of B on the basis of kinetic analysis. The Zn-



L



- 1: X = *p*-NO₂
- 2: X = *p*-CN
- 3: X = *m*-Cl
- 4: X = H

(II) complex of L is chosen in view of availability of detailed

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Table 1. Parameter Values Estimated from pH Titration of L in the Presence and Absence of L at 25 °C

| | pK_{a1} | pK_{a2} | pK_{a3} | $\log K_f$ | pK_a^M |
|----------------------------|-----------------|-----------------|------------------|-----------------|-----------------|
| present study ^a | 2.24 ± 0.01 | 7.59 ± 0.04 | 12.60 ± 0.01 | 8.70 ± 0.04 | 7.53 ± 0.04 |
| reported ^b | 2.4 ± 0.1 | 7.50 ± 0.02 | 12.6 ± 0.1 | 8.41 ± 0.04 | 7.30 ± 0.02 |

^a Measured in the presence of 10.2% (v/v) acetonitrile. ^b Measured in the absence of acetonitrile.⁹

structural information as well as a variety of catalytic features reported recently for its analogues.^{16–20}

Experimental Section

1,5,9-Triazaacyclododecane (L). The trihydrochloric acid salt of L was prepared according to the literature.²⁴ The trihydrochloric acid salt was converted into the corresponding perchloric acid salt by mixing with an equivalent of $\text{AgClO}_4 \cdot \text{H}_2\text{O}$ and by separating the resulting AgCl by filtration. Absence of a trace amount of Ag^+ or Cl^- ion was confirmed by checking with HCl or acidic AgNO_3 , respectively. The solution of perchloric acid salt of L was used in thermodynamic and kinetic measurements directly.

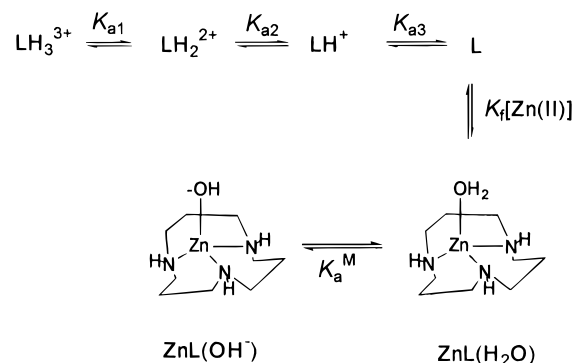
Other Materials. Esters **1–4** were prepared and purified according to the literature,^{25–29} and their purity was checked by comparing melting points with the reported values or through elemental analysis. Zinc perchlorate hexahydrate was purchased from Aldrich and used after recrystallization from water–acetone and titration with ethylenediaminetetraacetate. Water was distilled and deionized and acetonitrile was purified according to the literature¹⁶ prior to use in kinetic and thermodynamic measurements.

Measurements. Reaction rates were measured spectrophotometrically with a Beckman DU 68 UV/vis spectrophotometer equipped with a temperature controller. Rates of ester hydrolysis were followed at wavelengths (400, 283, 279, and 270 nm, respectively, for **1–4**) which were the λ_{max} for the phenols obtained by hydrolysis. At these wavelengths, the absorbance of the ester substrates was negligible. The solutions used in kinetic and thermodynamic measurements contained 10.2% (v/v) acetonitrile, and their ionic strength was maintained at 0.1 M with NaClO_4 . For kinetic studies, 0.05 M *N*-2-hydroxyethylpiperazine-*N'*-ethansulfonate (pH 7–7.7) and *N*-tris(hydroxymethyl)methyl-3-aminopropanesulfonate (pH 8–8.6) were used as the buffer. pH measurements were carried out with a Dongwoo Medical System DP 880 pH/ion meter. All the measurements were performed at 25 ± 0.1 °C. Temperature for the pH titration experiments was controlled with a Fisher Scientific Isotherm Circulator model 70. Results of the thermodynamic and the kinetic measurements could be duplicated within $\pm 3\%$. As indicated in the literature,^{16,18} the pH value measured under these conditions was determined by subtracting 0.03 units from the pH meter reading and a K_w ($= [\text{H}^+][\text{OH}^-]$) value of $10^{-13.97}$ was used.

Results

The ionization constants (K_{a1} , K_{a2} , and K_{a3} of Scheme 1) for L as well as the formation and the ionization constants (K_f and K_a^M of Scheme 1) for $\text{ZnL}(\text{H}_2\text{O})$ were previously measured by titration of L in the presence and absence of $\text{Zn}(\text{II})$ ion.¹⁶ Since kinetic studies were conducted in the presence of 10.2% (v/v) acetonitrile in the present study, the titration experiment was repeated under the conditions of the kinetic studies. Data of the titration experiment are summarized in Figure S1 of the Supporting information, and the parameter values estimated therefrom are summarized in Table 1 together with the values measured previously in the absence of acetonitrile.

Scheme 1



Rates of hydrolysis of phenyl acetates (**1–4**) in the presence of the $\text{Zn}(\text{II})$ complex of L were measured spectrophotometrically by following the release of the phenols. The buffer solution used for the kinetic measurements contained 10.2% (v/v) acetonitrile due to the limited solubility of **1–4** in water. The $\text{Zn}(\text{II})$ complex of L was generated in situ by adding $\text{Zn}(\text{ClO}_4)_2$ and L in 1:1 molar ratio. When either $\text{Zn}(\text{II})$ or L was added alone to the reaction mixture containing the substrate, the hydrolysis rate was similar to that of the spontaneous reaction. Considerable rate enhancement was observed when both $\text{Zn}(\text{II})$ and L were added. This demonstrates that $\text{ZnL}(\text{H}_2\text{O})$ and/or $\text{ZnL}(\text{OH}^-)$ are responsible for the acceleration. The kinetic data were collected at pH 7–8.6. At pH higher than 8.6, rates for the ester hydrolysis catalyzed by ZnL reached plateau values whereas that for the spontaneous hydrolysis increased considerably. Consequently, the rate contributed by ZnL was not much greater than the spontaneous path. When pH was lowered below 7, absorbance increase accompanying the release of phenols was diminished to low levels due to the protonation of phenols.

By following the absorbance increases up to 2% of the reactions, initial velocities (v_{in}) were measured. Since the substrate concentration ($S_0 = (1-4) \times 10^{-3}$ M) was essentially kept constant during the measurement, the absorbance increased linearly (correlation coefficient > 0.99) with the slope being v_{in} . Initial rate constant k_{in} was calculated as v_{in}/S_0 . When S_0 was varied, v_{in} changed proportionally with v_{in}/S_0 being unaffected. This indicates that the rate is first order with respect to the substrate. At a given pH, k_{in} was measured in the presence of various concentrations of $\text{Zn}(\text{II})$ and L ($[\text{Zn}(\text{II})]_0 = [\text{L}]_0$ and $[\text{Zn}(\text{II})]_0/S_0 = 0.1-10$).³⁰ For each kinetic run, $[\text{Zn}(\text{II})]$, $[\text{ZnL}(\text{H}_2\text{O})]$, and $[\text{ZnL}(\text{OH}^-)]$ were calculated by using the ionization constants estimated above for Scheme 1. The value of k_{in} was linearly related to $[\text{Zn}(\text{II})]_0$ ($= [\text{Zn}(\text{II})] + [\text{ZnL}(\text{H}_2\text{O})] + [\text{ZnL}(\text{OH}^-)]$) as illustrated in Figure 1, and the slopes ($k_{\text{bi}}^{\text{app}}$) of the linear plots were estimated for each substrate at various pH values. When the concentration of buffer was varied as 0.01, 0.03, and 0.05 M for the hydrolysis of **1** in the presence of $(0-1) \times 10^{-3}$ M $\text{Zn}(\text{II})$ and L ($[\text{Zn}(\text{II})]_0 = [\text{L}]_0$) at pH 7.05,

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(30) Addition of acetate and/or the leaving phenolate ions (concentration: 2% of S_0) to the reaction mixture did not affect the reaction rate appreciably.

Table 2. Parameter Values Estimated from the Kinetic Data for Hydrolysis of 1–4 in the Presence of Zn(II) Complex of L at 25 °C

| | 1 | 2 | 3 | 4 |
|---|----------------------------------|----------------------------------|----------------------------------|----------------------------------|
| $a, \text{s}^{-1} \text{M}^{-1}$ | $(2.59 \pm 0.29) \times 10^{-2}$ | $(2.45 \pm 0.80) \times 10^{-2}$ | $(0.85 \pm 0.26) \times 10^{-2}$ | $(1.07 \pm 0.13) \times 10^{-2}$ |
| b, s^{-1} | $(1.39 \pm 0.06) \times 10^{-9}$ | $(1.70 \pm 0.20) \times 10^{-9}$ | $(1.51 \pm 0.12) \times 10^{-9}$ | $(0.43 \pm 0.02) \times 10^{-9}$ |
| $(k_{\text{bi}}^{\text{w}}/k_{\text{bi}}^{\text{OH}^{\text{a}}})^{\text{a}}$ | $(4.0 \pm 0.5) \times 10^{-9}$ | $(3.1 \pm 1.1) \times 10^{-9}$ | $(1.2 \pm 0.4) \times 10^{-9}$ | $(5.3 \pm 0.7) \times 10^{-9}$ |
| $(k_{\text{bi}}^{\text{M}}/k_{\text{bi}}^{\text{MOH}^{\text{b}}})^{\text{b}}$ or $(k_{\text{bi}}^{\text{MS}}/k_{\text{bi}}^{\text{MSOH}^{\text{c}}})(K_{\text{a}}^{\text{M}}/K_{\text{a}}^{\text{MS}^{\text{c}}})^{\text{c}}$ | 0.55 ± 0.06 | 0.43 ± 0.15 | 0.17 ± 0.05 | 0.73 ± 0.09 |

^a For Scheme 2. ^b For Scheme 3. ^c For Scheme 4.

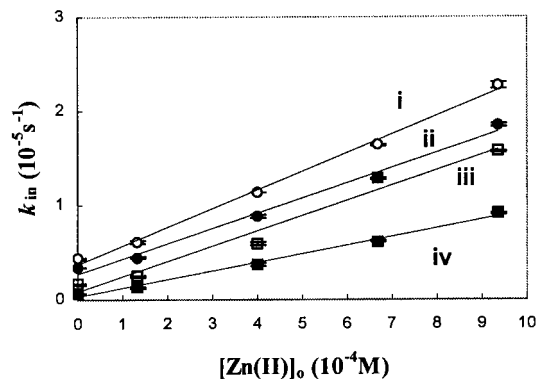


Figure 1. Dependence of k_{in} on $[\text{Zn(II)}]_0$ measured for 1 (line i, \circ), 2 (line ii, \bullet), 3 (line iii, \square), and 4 (line iv, \blacksquare) at pH 7.42, ionic strength 0.1 M, and 25 °C in the presence of 10.2% (v/v) acetonitrile. Slopes of the straight lines illustrated in this figure are denoted as $k_{\text{bi}}^{\text{app}}$. In Figures 1–4, the bars indicate standard deviations.

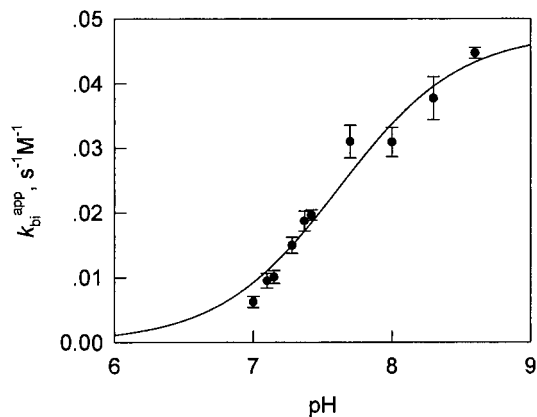


Figure 2. pH dependence of $k_{\text{bi}}^{\text{app}}$ for 1 catalyzed by Zn(II) complex of L at ionic strength 0.1 M and 25 °C in the presence of 10.2% (v/v) acetonitrile. The curve is obtained by fitting the data to a scheme in which the basic form of a monoprotic acid is assumed to be catalytically active.

7.20, 7.35, 8.00, and 8.35, no significant buffer effects were observed for $k_{\text{bi}}^{\text{app}}$. The pH dependence of $k_{\text{bi}}^{\text{app}}$ for 1 (Figure 2) shows a sigmoid with the inflection point of $\text{pH } 7.62 \pm 0.07$ which agrees with the $\text{p}K_{\text{a}}^{\text{M}}$ value estimated by the titration experiment. Since $[\text{Zn(II)}]_0$ contains various concentration terms which vary as pH changes, the pH profiles of $k_{\text{bi}}^{\text{app}}$ do not directly produce useful mechanistic information.

To analyze the kinetic data further, k_{in} obtained at each pH was plotted against $[\text{ZnL(H}_2\text{O)}]$. The slope of the linear plot (correlation coefficient > 0.98) for k_{in} against $[\text{ZnL(H}_2\text{O)}]$ was designated as k_{bi} . The k_{bi} was linearly related to $[\text{OH}^-]$ as illustrated in Figure 3, and, thus, its pH dependence was analyzed in terms of eq 1. When the kinetic data obtained at high pH values were included, reliable values of intercepts of the straight lines were not obtained although slopes were accurately estimated (Figure 3a). Instead, the intercepts were estimated by using the kinetic data obtained up to pH 7.4 (Figure 3b). The values of a estimated from the plot illustrated in Figure

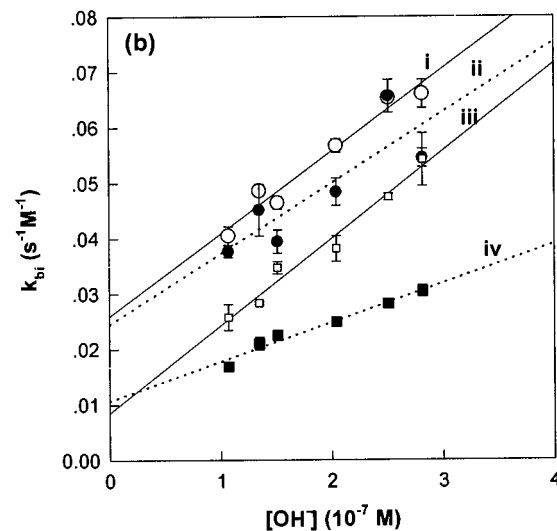
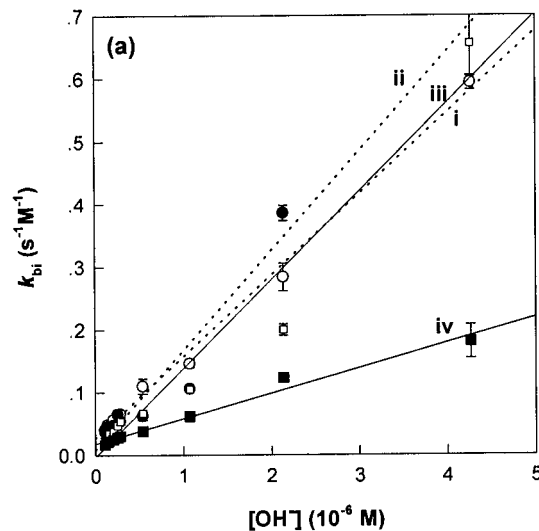


Figure 3. pH dependence of k_{bi} for 1 (curve i, \circ), 2 (curve ii, \bullet), 3 (curve iii, \square), and 4 (curve iv, \blacksquare) catalyzed by Zn(II) complex of L at ionic strength 0.1 M and 25 °C in the presence of 10.2% (v/v) acetonitrile. The lines are obtained by linear regression of the data according to eq 1.

3b and those of b estimated from the plot illustrated in Figure 3a are summarized in Table 2. In Figure 4, $\log a$ or $\log b$ is plotted against $\text{p}K_{\text{LG}}$ ($\text{p}K_{\text{a}}$ of leaving phenol³¹). The slopes (β_{LG}) of the straight lines of Figure 4 are -0.173 ± 0.074 for $\log a$ and -0.169 ± 0.107 for $\log b$.

$$k_{\text{bi}} = a + b/[\text{H}^+] \\ = a + b[\text{OH}^-]/K_{\text{w}} \quad (1)$$

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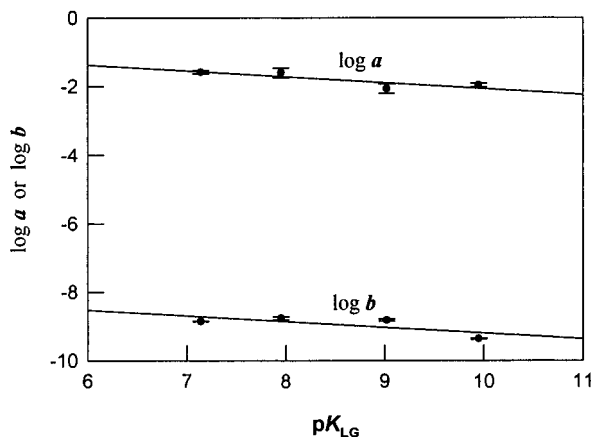
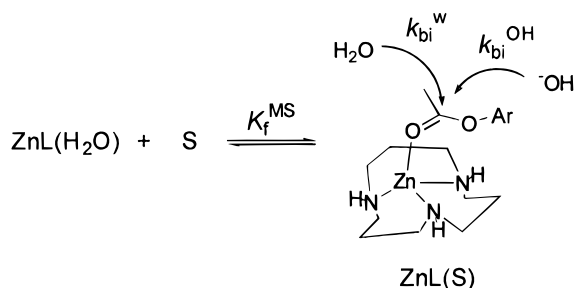
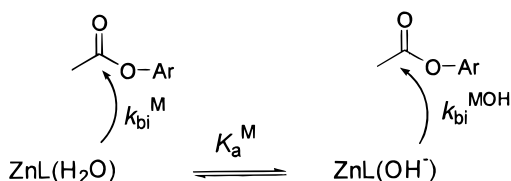


Figure 4. Plot of $\log a$ or $\log b$ against pK_{LG} . The lines are obtained by linear regression of the data.

Scheme 2



Scheme 3



Discussion

In the hydrolysis of **1–4** catalyzed by the Zn(II) complex of L, the carbonyl oxygen of the ester may be bound to the metal ion and water or hydroxide ion can make nucleophilic attack at the activated carbonyl group as summarized in Scheme 2. Alternatively, the Zn(II)-bound water or the Zn(II)-bound hydroxide ion can attack the ester linkage as illustrated in Scheme 3. Another possible mechanism is illustrated in Scheme 4, in which the metal center binds the carbonyl oxygen and the metal-bound water or hydroxide ion attacks the bound ester.

The rate expressions for the mechanisms of Schemes 2–4 are eqs 2–4, respectively. These equations are consistent with eq 1 and, therefore, the observed kinetic data may be analyzed in terms of Schemes 2–4.

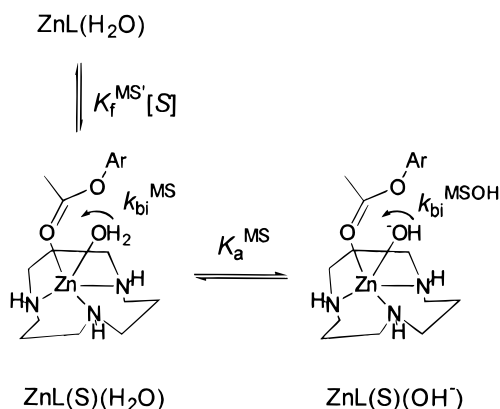
$$k_{bi} = k_{bi}^w K_f^{MS} [H_2O] + k_{bi}^{OH} K_f^{MS} K_w / [H^+] \quad (2)$$

$$k_{bi} = k_{bi}^M + k_{bi}^{MOH} K_a^M / [H^+] \quad (3)$$

$$k_{bi} = k_{bi}^{MS} K_f^{MS'} + k_{bi}^{MSOH} K_f^{MS'} K_a^{MS} / [H^+] \quad (4)$$

Parameters a and b are $k_{bi}^w K_f^{MS} [H_2O]$ and $k_{bi}^{OH} K_f^{MS} K_w$, respectively, for Scheme 2, k_{bi}^M and $k_{bi}^{MOH} K_a^M$, respectively, for Scheme 3, and $k_{bi}^{MS} K_f^{MS'}$ and $k_{bi}^{MSOH} K_f^{MS'} K_a^{MS}$, respectively, for Scheme 4. Values of k_{bi}^w / k_{bi}^{OH} for Scheme 2, k_{bi}^M / k_{bi}^{MOH} for Scheme 3, and $(k_{bi}^{MS} / k_{bi}^{MSOH}) (K_a^M / K_a^{MS})$ for Scheme 4 are

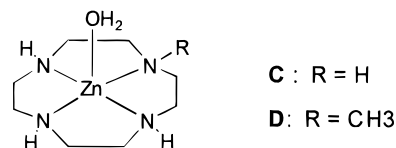
Scheme 4



calculated by using the values of a/b and K_a^M estimated in the present study and by using pK_w of 13.97 as mentioned in the Experimental Section. Values of k_{bi}^w / k_{bi}^{OH} , k_{bi}^M / k_{bi}^{MOH} , and $(k_{bi}^{MS} / k_{bi}^{MSOH}) (K_a^M / K_a^{MS})$ thus estimated are summarized in Table 2.

The value of k_{bi}^M / k_{bi}^{MOH} is evaluated as 0.2–0.7 (Table 2) from the experimental data on the basis of the mechanism of Scheme 3. This indicates comparable reactivities of $ZnL(H_2O)$ and $ZnL(OH^-)$ toward **1–4** despite the large difference in basicity of the hydroxide ion of $ZnL(OH^-)$ and the water molecule of $ZnL(H_2O)$. Nucleophilicity of oxygen bases toward aryl acetates is sensitive to their basicity. The slope for the plot of $\log k_2$ (k_2 : bimolecular rate constant for the nucleophilic attack at **1**) against pK_a of various nucleophiles is about 0.8.³² The hydroxide ion of $ZnL(OH^-)$ is about 10^9 times more basic than water, which in turn is considerably more basic than the water of $ZnL(H_2O)$. The difference in the basicity between the hydroxide of $ZnL(OH^-)$ and water of $ZnL(H_2O)$ is much greater than 10^9 -fold and k_{bi}^{MOH} should be, therefore, at least 10^7 times greater than k_{bi}^M . Almost identical reactivities predicted for $ZnL(H_2O)$ and $ZnL(OH^-)$ toward **1–4**, therefore, are not reasonable. This precludes the mechanism of Scheme 3. Koike and Kimura proposed¹⁷ the mechanism of Scheme 3 for the hydrolysis of **1** by the Zn(II) complex of L without rigorous mechanistic analysis. On the basis of Scheme 3, they estimated¹⁷ k_{bi}^{MOH} as $4.1 \times 10^{-2} \text{ s}^{-1} \text{ M}^{-1}$, which agrees well with that ($4.7 \times 10^{-2} \text{ s}^{-1} \text{ M}^{-1}$) estimated in this study (b/K_a^M as well as the limiting value of k_{bi}^{app} plotted in Figure 2).

For the mechanism of Scheme 4, $(k_{bi}^{MS} / k_{bi}^{MSOH}) (K_a^M / K_a^{MS})$ is evaluated as 0.2–0.7 (Table 2). The ionization constant (K_a^{MS}) for the Zn(II)-bound water of pentacoordinate complex $ZnL(S)(H_2O)$ cannot be measured. Instead, the pK_a for the Zn(II)-bound water of pentacoordinate complexes C or D has been



reported as 8.0 or 7.7, respectively.^{17,19} It is highly likely, therefore, that K_a^M is comparable to K_a^{MS} . Then, the kinetic data obtained in the present study suggest that k_{bi}^{MS} is also comparable to k_{bi}^{MSOH} . This is unreasonable as discussed above for the mechanism of Scheme 3. The mechanism of Scheme 4, therefore, is also precluded and that of Scheme 2 is chosen

as the mechanism for hydrolysis of **1–4** in the presence of the Zn(II) complex of L.

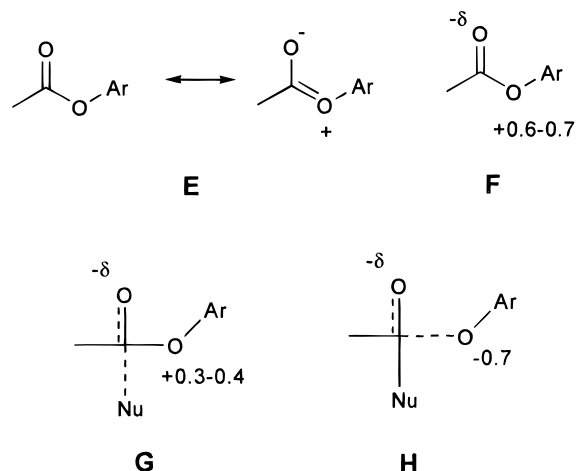
Since the mechanism of Scheme 2 is operative, $a/[H_2O]$ ($= 5.2 \times 10^{-4} \text{ s}^{-1} \text{ M}^{-2}$ for **1**) stands for $k_{bi}^w K_f^{MS}$ whereas b/K_w ($= 1.3 \times 10^5 \text{ s}^{-1} \text{ M}^{-2}$ for **1**) represents $k_{bi}^{OH} K_f^{MS}$. For esters without chelating sites, complexation to metal ions is so weak that the complexation has not been detected in any kinetic or spectroscopic studies performed in water. Thus, K_f^{MS} can be approximated as $\leq 1 \text{ M}^{-1}$. Then, k_{bi}^w and k_{bi}^{OH} are $\geq 5.2 \times 10^{-4} \text{ s}^{-1} \text{ M}^{-1}$ and $\geq 1.3 \times 10^5 \text{ s}^{-1} \text{ M}^{-1}$, respectively. The values of bimolecular rate constants previously measured for attack of water and hydroxide ion at **1** at 25 °C in the absence of any added catalyst were 1×10^{-8} and $15 \text{ s}^{-1} \text{ M}^{-1}$, respectively.³² The degree of activation of **1** toward water and hydroxide ion upon coordination to the Zn(II) complex of L, therefore, appears to be more than 10^4 – 10^5 .

When the experimental data are analyzed in terms of the mechanism of Scheme 2, attack (k_{bi}^{OH}) of hydroxide ion at **1–4** complexed to ZnL is $(2\text{--}8) \times 10^8$ times faster than that (k_{bi}^w) of water molecule (Table 2). This can be compared with value of 1.5×10^9 reported as the reactivity ratio of hydroxide attack against water attack at **1** in the absence of any added catalyst.³³ When **1** is bound by the Zn(II) complex of L, its reactivity is enhanced. The increased reactivity would be accompanied by decreased selectivity. Selectivity of **1** toward hydroxide ion and water is lowered by 6 times upon complexation of **1** to the Zn(II) complex.

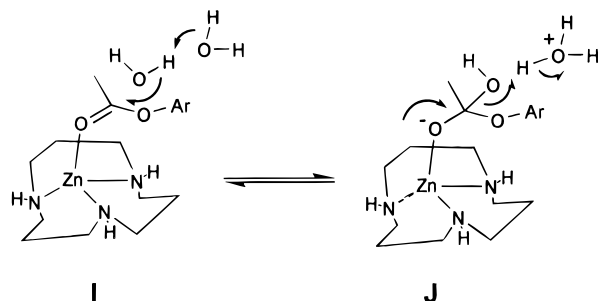
Compared with **1**, acetic anhydride is about 100 times more reactive toward hydroxide ion.³³ On the other hand, the selectivity ($k_{bi}^{OH}/k_{bi}^w = 2.0 \times 10^7$)³³ of acetic anhydride toward hydroxide ion and water molecule is about 75-times smaller than that ($k_{bi}^{OH}/k_{bi}^w = 1.5 \times 10^9$)³² of **1** in accordance with the reactivity–selectivity principle. Upon coordination of **1** to the Zn(II) complex of L to form ZnL(**1**) of Scheme 2, the reactivity expressed in terms of k_{bi}^{OH} is increased by at least 10^4 times, but selectivity expressed in terms of k_{bi}^{OH}/k_{bi}^w is decreased by only 6 times. Thus, ZnL(**1**) is over 100 times more reactive than acetic anhydride in terms of k_{bi}^{OH} , and yet 12 times more selective than acetic anhydride in terms of k_{bi}^{OH}/k_{bi}^w (2.0×10^7 for acetic anhydride and 2.5×10^8 for ZnL(**1**)). The inconsistency of the results with the reactivity–selectivity principle is attributable to electrostatic attraction between hydroxide anion and the cationic complex of ZnL(S). Due to the electrostatic interaction, k_{bi}^{OH} of Scheme 2 would be enhanced, leading to an increased ratio of k_{bi}^{OH}/k_{bi}^w .

Linear free energy relationship is obtained for the plot of $\log a$ or $\log b$ against pK_{LG} (Figure 4). The slope (β_{LG}) of such a plot gives information on effective charges on the leaving phenol oxygen in the transition state and the reactant.^{34–37} For alkaline hydrolysis of substituted phenyl esters of cinnamic acid, β_{LG} of -0.35 was observed.³⁶ For aminolysis of substituted diphenyl carbonates, β_{LG} of -0.2 or -1.3 was observed when the rate-determining step was formation or breakdown, respectively, of the tetrahedral intermediate.³⁵ Due to resonance (E) of the ester linkage, the leaving oxygen of ester possess a positive partial charge in the ground state. An effective charge of $0.6\text{--}0.7$ has been ascribed to the leaving oxygen (F) on the basis of various values of β_{LG} and related parameters obtained from kinetic studies on transacylation reactions.^{34,35} In the

transition states for formation (G) or the breakdown (H) of the tetrahedral intermediate, effective charges of $0.3\text{--}0.4$ or -0.7 , respectively, have been assigned to the oxygen. The difference in the effective charge on the leaving oxygen atom between the rate-determining transition state and the reactant is reflected by β_{LG} . The value of β_{LG} is between -0.2 and -0.4 when the formation of tetrahedral intermediate is rate-determining and is about -1.3 when the breakdown step is rate-determining.^{34–37}



For the hydrolysis of **1–4** catalyzed by the Zn(II) complex of L, β_{LG} was -0.173 ± 0.074 for $\log a$ and -0.169 ± 0.074 for $\log b$. These values indicate that C–O bond cleavage is not significant in the rate-determining transition state for the reaction paths represented by both a and b . Thus, the rate-determining step appears to be formation of the tetrahedral intermediate. For the formation step to be rate-determining, the expulsion of nucleophile from the tetrahedral intermediate should be much slower than that of the leaving phenolate. When hydroxide ion is the nucleophile, it should resist expulsion much more than phenolates in view of the greater basicity of hydroxide ion. When water is attached to the carbon in the tetrahedral intermediate, it would leave the intermediate more readily than the phenolates and the rate-controlling step would be the breakdown of the intermediate. The small β_{LG} values observed for a is attributable to general base assistance by another water molecule in the formation of the tetrahedral intermediate (I), which is considered to be a general phenomenon in ester hydrolysis.³⁸ Then, the expulsion of phenolate from the tetrahedral intermediate at neutral pHs would be faster than that (conversion of J to I) of hydroxide ion with assistance of hydronium ion.



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Supporting Information Available: Figure S1 illustrating titration curves for $\text{L}(\text{HClO}_4)_3$ (1.08×10^{-3} M) in the absence and presence of $\text{Zn}(\text{ClO}_4)_2$ (1.08×10^{-3} M) at 25 °C and ionic strength 0.1 M in the

presence of 10.2% (v/v) acetonitrile is available (1 page). Ordering information is given on any current masthead page.
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