85-14825) is gratefully acknowledged. We thank Dr. Chang S. Hsu of Corporate Research, Analytical Science Laboratory of Exxon Research and Engineering Company, Annadale, NJ, for his helpful discussions of mass spectrometric data.

Registry No. 1, 66946-48-3; 2, 31366-25-3; 4, 51501-77-0; 5, 108666-51-9; 6, 96913-57-4; 7, 108666-52-0; 8, 108666-53-1; 9, 108666-54-2; 10, 96913-58-5; MeI, 74-88-4; Se, 7782-49-2; PhSSPh, 882-33-7; MeSSMe, 624-92-0; $C_3H_7SeSeC_3H_7$, 7361-89-9; C_3H_7I, 107-08-4; $C_4H_9SeSeC_4H_9$, 20333-40-8; C_4H_9I, 542-69-8; $C_5H_{11}SeSeC_5H_{11}$, 52056-07-2; $C_5H_{11}I$, 628-17-1; PhSeSePh, 1666-13-3.

Kinetics and Mechanism of the Zn(II)-Catalyzed Hydrolysis of 2-Acetylpyridine Oxime Phenyl Sulfite[†]

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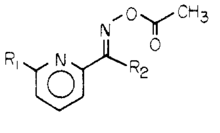
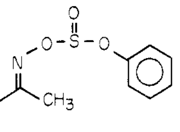
Previously, we have performed kinetic studies on the metal ion catalyzed hydrolysis of several acetyl esters of pyridine oximes **1a–d**,[1] disclosing several new catalytic features of metal ions which act as Lewis acids in organic reactions. The information obtained from such studies with small molecules makes significant contributions to the understanding of the mechanisms of not only organic and inorganic reactions but also metalloenzyme–catalyzed reactions.[2-4]



1a: R_1 = H, R_2 = H
1b: R_1 = H, R_2 = CH_3
1c: R_1 = COOH, R_2 = H
1d: R_1 = H, R_2 = 2-py

In the present study, the investigation of the catalytic effects of metal ions was extended to the hydrolysis of a sulfite ester analogue (**2**) of **1a–d**. The central sulfur atom of sulfite esters, to which three oxygen atoms are attached, contains a nonbonding electron pair and its configuration is tetrahedral.[5] Nucleophilic reactions on carboxyl esters proceed through the formation of tetrahedral intermediates.[6] On the other hand, the nucleophilic reactions on sulfite esters would occur through either a stepwise or a concerted mechanism.[5] In either mechanism of the reactions of sulfite esters, trigonal bipyramidal transition states are involved in which both the leaving group and the attacking group occupy the apical positions.[5] The differences in kinetic behavior between carboxyl and sulfite esters caused by the different structural and chemical properties of the ground states and the transition states will be discussed in this report.



2

Scheme I

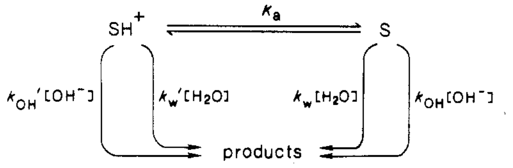


Table I. Kinetic Parameters for the Spontaneous and the Zn(II)-Catalyzed Hydrolysis of 2

reacn	parameter	value
spontaneous	k_{OH}	2.1×10^4 M^{-1} s^{-1}
	k_w'	4.7×10^{-6} M^{-1} s^{-1}
	$k_{OH}'K_w/K_a + k_w$ $[H_2O]$	6.5×10^{-5} s^{-1} [a]
Zn(II)-catalyzed	k_{OH}^{M} [b]	3.3×10^8 M^{-2} s^{-1}
	k_w^{M} [c]	1.3×10^{-3} M^{-2} s^{-1}

[a] If this value is contributed to solely by the k_w $[H_2O]$ term, k_w (the attack of water molecule at the unprotonated substrate) is 1.2×10^{-6} M^{-1} s^{-1} being only four times smaller than k_w' (the attack of water molecule at the protonated substrate). Therefore, the contribution of k_w $[H_2O]$ to this value should be negligible, $k_{OH}'K_w/K_a$ being the major part of the observed value. This leads to the k_{OH}' value of 8.2×10^6 M^{-1} s^{-1}, which is 4×10^2 times greater than the k_{OH} value. [b] Parameter k_{cat}^{OH} is much greater than 6.6×10^7 M^{-1} s^{-1} (see text). [c] Parameter k_{cat}^{w} is much greater than 2.6×10^{-4} M^{-1} s^{-1} (see text).

Experimental Section

Materials. 2-Acetylpyridine oxime phenyl sulfite **2** was prepared by the dropwise addition of phenyl chlorosulfinate[7] (0.71 g) dissolved in 2 mL of diethyl ether to a diethyl ether solution (20 mL) containing 2-acetylpyridine oxime (0.55 g) and triethylamine (0.50 g) at 4 °C. Precipitates of the hydrochloride salt of triethylamine were removed, and the resulting solution was washed with a 0.1 N hydrochloric acid solution and then with a 5% sodium bicarbonate solution followed by water. After drying with magnesium sulfate, the solvent was removed and the resulting residue was recrystallized from chloroform–hexane, producing white crystals of **2**, mp 73 °C.

Cupric chloride and zinc chloride solutions were prepared by dissolving corresponding oxides (Aldrich, Gold Label) with hydrochloric acid.

Kinetic Measurements. Reaction rates were measured with a Beckman 5260 or a Beckman 25 UV–vis spectrophotometer at wavelengths (~280–340 nm) which afforded maximal absorbance changes during the reaction. Temperature was controlled at 25 ± 0.1 °C with a Haake E52 or a Lauda Brinkman T-2 circulator. The reactions were carried out in the presence of 0.8% (v/v) dimethyl sulfoxide at ionic strength 1.0, which was adjusted with sodium chloride. Buffers (0.005–0.04 M) used were chloroacetic acid (pH 2.5–3.5), acetic acid (pH 4–5), 2-*N*-morpholinoethanesulfonic acid (Mes) (pH 5.5–7), and 2-[1-(2-hydroxyethyl)piperazin-4-yl]ethanesulfonic acid (pH 7.5–8). pH measurements were performed with a Fisher Accumet Model 525 pH meter. The concentration of **2** employed in kinetic studies was $(0.5\text{–}1) \times 10^{-4}$ M. The pseudo-first-order rate constants were calculated from the slopes of the linear plots (correlation coef-

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[†] Dedicated to Professor Sae-Hee Chang on the occasion of his 60th birthday.

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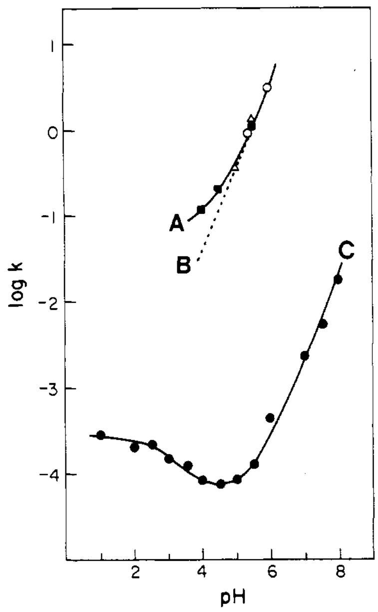


Figure 1. The pH dependence of log $k_o/[\mathrm{Zn(II)}]$ (curve A) for the Zn(II)-catalyzed hydrolysis of **2** and log k_o (curve C) for the spontaneous hydrolysis of **2**. The unit of k_o is s^{-1}. The points of curve A were obtained in the presence of 0.01 M Mes (○), 0.01 M acetic acid (△), and 0.02 M acetic acid (■). Curve B represents the pH dependence expected when the water path of eq 2 is not operative.

ficients were greater than 0.99) of ln $(A_i - A_\infty)$ againt time. The product spectra obtained at various pHs in the presence or absence of Zn(II) ion indicated that phenol and 2-acetylpyridine oxime were formed in quantitative yields as the hydrolysis products.

Results and Discussion

Spontaneous Hydrolysis of 2. The pseudo-first-order rate constants (k_o) measured for the spontaneous hydrolysis of **2** at various pHs are illustrated in Figure 1. When the buffer concentration was varied over 0.005–0.04 M at pH 2.5, 7.0, or 7.5, no noticeable change in k_o was observed. The pH dependence of k_o was analyzed in terms of Scheme I, whose rate expression is eq 1. In this

$$k_o = (k_{OH}K_w/[H^+] + k_w[H_2O] + k_{OH}'K_w/K_a + k_w'[H_2O][H^+]/K_a)/([H^+]/K_a + 1) \quad (1)$$

equation, K_w is the ion product of water. Spectral titration of the substrate (not shown) disclosed the pK_a value of 2.9 for SH^+. The parameter values used in the construction of curve C of Figure 1 are summarized in Table I.

Diaryl sulfite esters are subjected to nucleophilic reactions.[8] In this process, the expulsion of the better leaving group between the two aryloxy residues must occur to transfer the sulfinyl group to the entering nucleophile. In the spontaneous hydrolysis of the neutral form (S) of **2**, however, it is not clear whether the better leaving segment is the phenolate (pK_a = 10)[9] or the 2-acetylpyridine oxime (pK_a = 10.8).[1c] This is because of the small difference in their pK_a values. Thus, whether phenolate is cleaved prior to the oxime during the spontaneous hydrolysis of the neutral form of **2** is not known at present. On the other hand, the oxime portion would be cleaved first in the hydrolysis of the protonated form (SH^+) of **2** since protonation of the pyridyl group would lower the pK_a of the leaving oxime significantly. In Table I, the bimolecular rate constants for the attack of hydroxide ion or water molecule at SH^+ are listed.[10]

Zn(II) Ion Catalyzed Hydrolysis of 2. At a constant pH, k_o for the Zn(II)-catalyzed hydrolysis of **2** was proportional to [Zn(II)] when [Zn(II)] was raised up to 0.2 M, and the rates of the spontaneous reaction were negligible compared with those of the metal-catalyzed reaction under these conditions. The bimolecular rate constant (k_2^M), therefore, was calculated as the average value of $k_o/[\mathrm{Zn(II)}]$, and its pH dependence is illustrated in Figure 1. The pH profile was analyzed in terms of eq 2, and the parameter values used in the construction of curve A of Figure 1 are summarized in Table I.

$$k_2^M = k_o/[M] = k_w^M[H_2O] + k_{OH}^M[OH^-] \quad (2)$$

The metal ion catalyzed hydrolysis of **1a–d** involves complex formation.[1a,b,f] In the hydrolysis of diphenyl sulfite, the addition of Zn(II) ion did not result in appreciable rate increases. Therefore, it is very likely that the Zn(II) ion catalyzed hydrolysis of **2** also occurs through complex formation as indicated in eq 3. The corresponding rate expression is eq 4, which becomes eq 5 under the conditions of $K_a \gg [H^+]$, as in the present study. These

$$SH^+ \overset{K_a}{\rightleftharpoons} S \overset{K_f[M]}{\rightleftharpoons} MS \xrightarrow{k_{cat}^w[H_2O] + k_{cat}^{OH}[OH^-]} \text{products} \quad (3)$$

$$k_o = (k_{cat}^w[H_2O] + k_{cat}^{OH}[OH^-])\,[M]/\{([H^+]/K_a + 1)/K_f + [M]\} \quad (4)$$

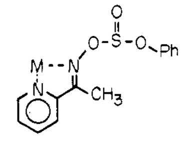
$$k_o = (k_{cat}^w[H_2O] + k_{cat}^{OH}[OH^-])[M]/(1/K_f + [M]) \quad (5)$$

equations predict saturation behavior of k_o with respect to [M]. Under the conditions of $1/K_f \gg [M]$; however, eq 5 is converted to eq 6, resulting in the k_o values proportional to [M] as observed in the present study. The k_w^M

$$k_o = (k_{cat}^w[H_2O] + k_{cat}^{OH}[OH^-])K_f[M] \quad (6)$$

and k_{OH}^M values (eq 2, Table I) estimated in the present study, therefore, correspond to $k_{cat}^wK_f$ and $k_{cat}^{OH}K_f$, respectively. The fact that k_o was proportional to [Zn(II)] up to 0.2 M [Zn(II)] indicates that $K_f \ll 5\ M^{-1}$ (eq 5) for the formation of the Zn(II)–**2** complex. The lowest limits of k_{cat}^w and k_{cat}^{OH} indicated in Table I are calculated on the basis of this limiting value of K_f.

The simpliest mechanism consistent with the complex formation is mechanism A, which assumes the increase in the leaving ability of the oxime anion as the sole catalytic factor. The plot of the logarithmic values of k_{OH} (bimolecular rate constants for alkaline hydrolysis) against pK_a of leaving phenols for various diaryl sulfite esters is plotted in Figure 2.[11] The data point for the Zn(II)–**2** complex represents the lowest limit of k_{cat}^{OH} mentioned above. If only the decrease in the pK_a of the leaving group is involved in the Zn(II)-catalyzed hydrolysis of **2**, the data point for Zn(II)–**2** would not deviate greatly from the straight line. The large deviation seen in this figure,



A

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(10) When the value of k_{OH}' of Table I is compared with the k_{OH} values illustrated in Figure 2, the k_{OH}' value (attack of hydroxide ion at the protonated form of **2**) corresponds to the k_{OH} for an aryl phenyl sulfite ester for which the pK_a of the leaving phenol is 5.6.

(11) Suh, J.; Koh, D.; Min, C. H., to be published.

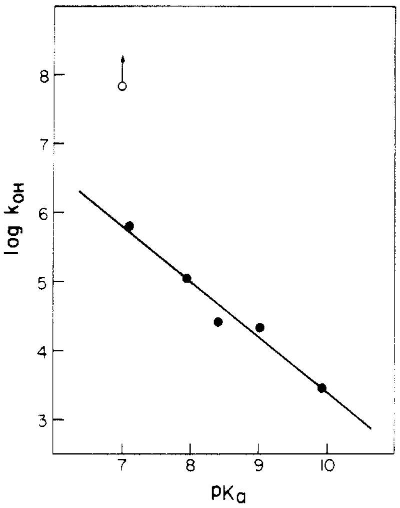
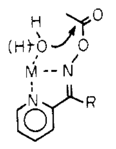


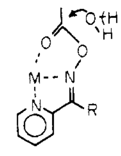
Figure 2. The plot of log k_{OH} (●) against pK_a of leaving phenol for the alkaline hydrolysis of aryl phenyl sulfite (ArOSOOPh) esters. The unit of k_{OH} is $M^{-1}\ s^{-1}$. The aryl groups employed are *p*-NO_2, *p*-CN, *m*-NO_2, *m*-Cl, and unsubstituted phenyls (in the order of increasing pK_a values). The data point for Zn(II)-2 (○) represents the lowest limit as discussed in the text. The pK_a of the leaving group of Zn(II)-2, i.e., the Zn(II) complex of 2-acetylpyridine oxime, is 7.0.[1c]

therefore, can be taken to indicate that additional catalytic factors are needed to explain the fast rate for Zn(II)-2.[12]

In the case of the acetyl esters, extra catalytic roles were also needed in addition to the decrease in the pK_a of leaving oxime in order to explain the observed rate data.[1a,b] The catalytic factors involved in B (nucleophilic attack by the metal bound water molecule or hydroxide ion) or C (polarization of the carbonyl group) were proposed,[1a] and the detailed analysis of kinetic data chose B as the correct mechanism.[1b,c] For the sulfite ester, D and E contain the extra catalytic roles proposed in B and C, respectively. In the hydrolysis of sulfite esters, both the entering and the leaving groups should occupy apical positions in trigonal bipyramidal intermediates or transition states. This is not possible in the mechanism of D. Therefore, the mechanism of E, which assumes both an increase in the leaving ability of the oxime anion and the polarization of the sulfinyl group, is the most probable mechanism for the Zn(II)-catalyzed hydrolysis of 2.



B



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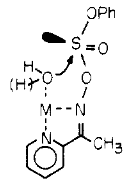
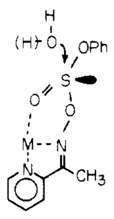


D



E

It is noteworthy that two five-membered chelate rings (E) are formed in the case of the Zn(II) complex of sulfite ester 2, while only one chelate ring (B) is formed in that of the corresponding acetyl esters. In the metal ion catalyzed hydrolysis of other esters in which coordination of the carbonyl oxygen atoms to metal ions is facilitated, the metal ion catalysis can proceed through mechanisms analogous to C.[1h,2] Therefore, it appears that the mechanism of C does not operate because of the strain involved in the chelate rings.[1h] The formation of the two-chelate-ring system (E) in the Zn(II)-2 complex in contrast to B can be attributed to the differences in the bond lengths and bond angles between the sulfite and acetyl esters. Thus, the longer bond lengths of sulfur-oxygen double and single bonds compared with carbon-oxygen double and single bonds can relieve the ring strain. In addition, the configuration of sulfur in sulfite esters is tetrahedral, while that of carbonyl carbon of acetyl esters is trigonal. On the other hand, the sulfinyl sulfur becomes trigonal bipyramidal and the carbonyl carbon tetrahedral in transition states. The consequent differences in bond angles around these atoms may also contribute to the relief of the ring strain.

Acknowledgment. This work was supported by a grant from Korea Science and Engineering Foundation.

Registry No. 2, 108711-91-7; Zn^{II}, 23713-49-7.

Supplementary Material Available: Derivation of eq 1 (2 pages). Ordering information is given on any current masthead page.

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[12] The catalytic effect of the decrease in the pK_a of the leaving oxime caused by metal complexation is best estimated by using the linear plot of log k_{OH} against pK_a of oximes for various oxime phenyl sulfite esters. For this purpose, the oxime anions of the sulfite esters should have greater leaving ability than phenolate ion. Such oxime phenyl sulfite esters, however, are not readily accessible. On the other hand, the high efficiency of the Zn(II) catalysis in the sulfite ester hydrolysis may be emphasized by k_{cat}^{OH} (the bimolecular rate constant for the attack of OH^- at MS) which is much greater than k_{OH}' (the bimolecular rate constant for the attack of OH^- at SH^+).

The Induced Decomposition of *S*-*tert*-Butyl Benzenethioseleninate[1a]

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Thiols react with benzeneseleninic acid ($PhSeO_2H$) with the overall stoichiometry shown in eq 1.[2] The reaction

$$3RSH + PhSeO_2H \rightarrow RSSePh + RSSR + 2H_2O \qquad (1)$$

takes place in several steps (eq 2a-c), the first (eq 2a) being reaction of the seleninic acid with the thiol to form a thioseleninate, PhSe(O)SR (1).[2] When R = *n*-Bu reaction of PhSe(O)SBu-*n* (**1a**) with thiol (eq 2b) is faster than its formation. However, when R = *t*-Bu, eq 2b is much slower

$$PhSeO_2H + RSH \rightarrow PhSe(O)SR + H_2O \qquad (2a)$$

$$\textbf{1a}, R = n\text{-Bu}$$

$$\textbf{1b}, R = t\text{-Bu}$$

$$PhSe(O)SR + RSH \rightarrow RSSR + PhSeOH \qquad (2b)$$

$$PhSeOH + RSH \rightarrow PhSeSR + H_2O \qquad (2c)$$

than eq 2a, especially in weakly acid solution. As a consequence, when $PhSeO_2H$ was allowed to react with an approximately equimolar amount of *t*-BuSH in aqueous dioxane Kice and Lee[2] were able to isolate the first known example of a thioseleninate, PhSe(O)SBu-*t* (**1b**). Isolation of a thioseleninate and investigation of its chemistry was of particular interest because of the suggestion[3] that an Se(O)S functionality may be an intermediate in the reaction cycle for the important enzyme glutathione peroxidase.

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[1] (a) This research was supported by the National Science Foundation (Grant CHE-82-15140). (b) Present address: Department of Chemistry, University of Denver, Denver CO 80208.

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