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Cd^{2+}-Catalyzed Methanolysis of Phenyl Phosphatosulfate. Selectivity of Metal Ion in the Site of Cleavage of P–O and S–O Bond

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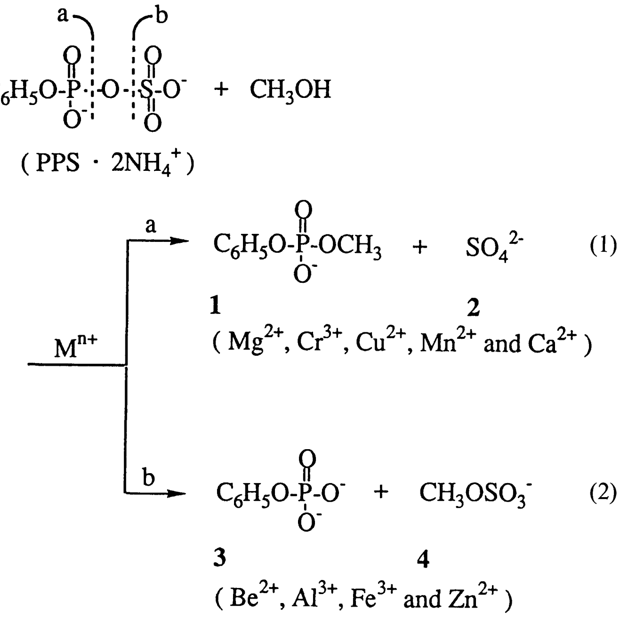
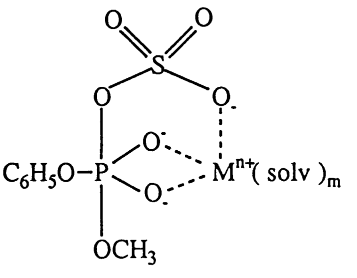
It was reported previously that metal ions such as Mg^{2+}, Cr^{3+}, Cu^{2+}, Mn^{2+}, and Ca^{2+} catalyzed selective P–O bond cleavage of P–O–S linkage in the methanolysis of phenyl phosphatosulfate (PPS), and in contrast, metal ions such as Zn^{2+}, Fe^{3+}, Al^{3+}, and Be^{2+} promoted selective S–O bond cleavage.[1] We have now found that Cd^{2+} catalyzes mixed cleavage of P–O and S–O bond in a ratio of 58 and 42%, respectively, in the methanolysis of PPS. The value of second-order-rate constant (k_2) for Cd^{2+} catalyzed P–O bond cleavage satisfied the correlation between values of k_2(P–O) and ionic radii of metal ions, but that for Cd^{2+} catalyzed S–O bond cleavage was considerably smaller than that expected from the rate correlation. The presence of chloride ion reduced the rate of Cd^{2+} catalyzed P–O bond cleavage to about one tenth of that in the absence of chloride ion, but inhibited completely the S–O bond cleavage catalyzed by Cd^{2+} or Zn^{2+}. The kinetic studies suggested that the inhibition by chloride ion occurred with the formation of ternary ($PPS \cdot Cd^{2+} \cdot Cl^-$) and tetramerous ($PPS \cdot Zn^{2+} \cdot 2Cl^-$) complexes of substrate, metal ion and chloride ion. On the basis of these results the selectivity of the metal ion in the site of bond cleavage was discussed.

An interesting subject in the biochemical reactions of 3′-phosphoadenosine-5′-phosphatosulfate (PAPS) and adenosine-5′-phosphatosulfate (APS) which are key intermediates in the sulfur methabolism is the role of a metal ion: How a metal ion affects the rate and the selectivity in the site of cleavage of P–O and S–O bond of P–O–S linkage.[2] But many aspects of mechanisms of metal ion catalysis have been left unclarified.

The easiest way to obtain detailed insight into the metal ion catalysis is to study effects of metal ion on the solvolysis of organic phosphatosulfate. It was reported previously that there were two groups of metal ions which catalyzed selectively either P–O (Eq. 1) or S–O (Eq. 2) bond cleavage in the methanolysis of phenyl phosphatosulfate (PPS).[1] The metal ion catalyzed P–O and S–O bond cleavages were different from one another in the mechanism. It was suggested that P–O bond cleavage occurred with dimolecular nucleophilic attack of methanol on phosphorus proceeding via the formation of pentavalent phosphorus intermediate as illustrated in **5** and S–O bond cleavage occurred with monomolecular elimination of sulfur trioxide involving a molecule of solvent in the transition state as illustrated in **6**. The correlation of second-order rate constants for metal ion catalyzed methanolysis with ionic radii of metal ions[3] showed two rate maxima in the vicinity of





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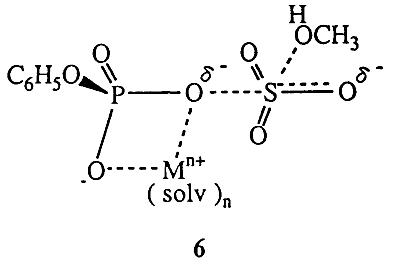

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0.5 and 0.7 Å corresponding to S–O and P–O bond cleavage, respectively. A small optimum ionic radius in the S–O bond cleavage suggested a small bond angle of chelating ∠O–P–O near 109° in **6**, and in contrast, a large optimum ionic radius in the P–O bond cleavage suggested a large bond angle of chelating ∠O–P–O near 120° in **5**. Thus ionic radii of metal ions seemed to play an important role not only in controlling the rate but also in the selectivity in the site of bond cleavage. But it was difficult to explain the selectivity only by the ionic radius, because Mg^{2+} with small ionic radius catalyzed selective P–O bond cleavage and Zn^{2+} with large ionic radius promoted selective S–O bond cleavage.

It is known that Be^{2+} and Al^{3+} with small ionic radii, and Fe^{3+} and Zn^{2+} with the electron configuration of 3d^{5} and 3d^{10}, respectively, favor generally tetrahedral coordination.4) On the other hand, metal ions such as Mg^{2+}, Cr^{3+}, Cu^{2+}, Mn^{2+}, and Ca^{2+} favor octahedral coordination. Accordingly, the selectivity appeared to relate closely with two different coordination.

Meanwhile, in aqueous media Zn^{2+} as well as Mg^{2+} 5) always catalyzed the selective P–O bond cleavage, e.g., in the hydrolysis of 2-pyridylphosphonosulfate,6) and in the reaction of PPS with 2-pyridinecarbaldehyde oxime.7) It was therefore considered that the change in the selectivity of Zn^{2+} in the site of cleavage from P–O bond in water to S–O bond in methanol was due to the change of the type of coordination, i.e., octahedral in water but tetrahedral coordination in methanol.

The purpose of this study is to test whether the selectivity of metal ion in the site of bond cleavage can always be explained only by the different coordination or not, and to approach better understanding of the selectivity. To explore this, the methanolysis of PPS catalyzed by Cd^{2+} with large ionic radius and the electron configuration of 4d^{10} has been studied in the absence and presence of chloride ion.

We report here that, if one accepts the different coordination and ionic radius of the metal ion, it appears easy to understand the findings.

Experimental

The diammonium salt of PPS was prepared by the reaction of phenyl phosphate with DMF–SO$_3$ complex in DMF at room temperature according to the previous method.8) Organic solvents and *N*-ethylmorpholine were distilled before use. Other organic and inorganic compounds were analytical grade and used without further purification.

Procedures of kinetics and product analyses were essentially the same as those used previously.1) The alcoholyses of PPS were followed by two monitoring techniques. Phenyl phosphate and methyl phenyl phoshate were analyzed by the UV method. Inorganic sulfates were analyzed colorimetrically by the barium chromate method.9) The analytical data of UV, NMR, and paper chromatography for product analysis were shown in the previous paper.1)

Results

Catalysis of Cd^{2+}. The methanolysis of PPS (1×10^{-2} mol dm^{-3}) was carried out in a mixed solvent of DMF–methanol (1 : 1, v/v) containing *N*-ethylmorpholine (0.25 mol dm^{-3}) and Cd^{2+} including hydrated water (0—0.1 mol dm^{-3}) at 55 °C. In this study the nitrate of Cd^{2+} was used for kinetics instead of the chloride, because the nitrate was more soluble in the mixed solvent than the chloride. It was reported that counter ions such as chloride, nitrate and perchlorate, hydrated water, *N*-ethylmorpholine, and DMF did not affect the selectivity.1)

Cd^{2+} was found to catalyze mixed cleavage of P–O bond to give methyl phenyl phosphate (**1**) and inorganic sulfate (**2**) (Eq. 1) and of S–O bond to give phenyl phosphate (**3**) and methyl sulfate (**4**) (Eq. 2) in a ratio of 58 and 42%, respectively. The pseudo-first-order rate constants (k_{obsd}) for Cd^{2+}-catalyzed methanolysis are plotted against the concentration of the metal ion in Fig.

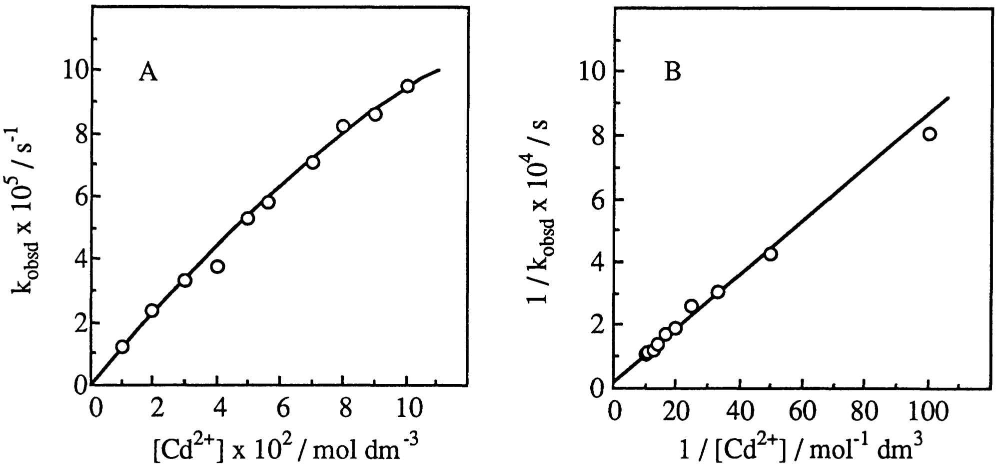
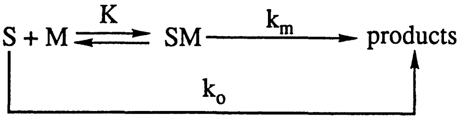


Fig. 1. (A). Plots of k_{obsd} vs. metal ion concentration. [PPS]=1.0×10^{-2} mol dm^{-3}, [*N*-ethylmorpholine]=2.5×10^{-1} mol dm^{-3} in CH$_3$OH · DMF (1 : 1, v/v) at 55 °C. (B). The reciprocal plots.



(3)

$$k_{obsd} - k_o = \frac{(k_m - k_o)K[M]_T}{1 + K[M]_T + K[S]_T\left(1 - \frac{k_{obsd} - k_o}{k_m - k_o}\right)} \tag{4}$$

$$k_{obsd} - k_o = \frac{(k_m - k_o)K[M]_T}{1 + K[M]_T} \quad ([M]_T > [SM]) \tag{5}$$

$$\frac{1}{k_{obsd} - k_o} = \frac{1}{(k_m - k_o)} + \frac{1}{(k_m - k_o)K} \cdot \frac{1}{[M]_T} \tag{6}$$

1A. The rates tend to saturate with increasing concentration of the metal ion. The observation can be explained by assuming a reaction scheme (Eq. 3) involving the preequilibrium formation of a binary complex (SM) of PPS (S) and the metal ion (M). Eq. 4 is formulated in accordance with the scheme,[1,6,10] where $[S]_T$ and $[M]_T$ are the initial stoichiometric concentration of PPS and the metal ion, respectively, k_o and k_m are the rate constants for the methanolysis of S and SM, respectively, and K is the formation constant for SM. When $[M]_T > [SM]$, Eq. 4 can be represented as Eq. 5, which gives Eq. 6. In practice, k_o value was negligibly small and neglected in the rate calculation. In accordance with Eq. 6, a plot of $1/k_{obsd}$ against $1/[M]_T$ is found to be linear as shown in Fig. 1B. Calculated curve in Fig. 1A is obtained by Eq. 5, using the evaluated values of k_m and K given in Table 1. The table shows that K value for the formation of PPS complex of Cd^{2+} is similar to that of Zn^{2+}, but considerably smaller than that of Mg^{2+} or Ca^{2+}.

Cd^{2+} alone among various metal ions tested in the studies catalyzed mixed cleavage of P–O and S–O bond, which were suggested to proceed by the mechanisms described early. The simplest one of the methods to ascertain the mechanism of S–O and P–O bond cleavage was to study the alcoholysis of PPS by 2-propanol in a mixed solvent of 2-propanol and DMF (1 : 1, v/v) under the same conditions as those used in the methanolysis. It was reported that Zn^{2+} promoted the alcoholysis to give quantitative yields of **3** and isopropyl sulfate (**7**) and Mg^{2+} catalyzed the alcoholysis to give quantitative yields of **2** and **3**.[1] Probably because of severe steric hindrance of 2-propanol, Mg^{2+} catalyzed hydrolysis by a trace of water contained in the mixed solvent to give **2** and **3**. On the other hand, such steric hindrance was less important in the S–O bond cleavage to give **7** and **3**. Cd^{2+} catalyzed alcoholysis by 2-propanol was observed to give **2** and **7** in a ratio of 46 and 54%, respectively, and quantitative yield of **3**. This suggested that Cd^{2+} assisted both dimolecular nucleophilic attack of water on phosphorus to give **2** and **3** and monomolecular elimination of sulfur trioxide to give **3** and **7**, and accordingly it was difficult to consider that another mechanism different from that described above affected the selectivity of Cd^{2+} in the site of bond cleavage.

The value of $k_mK/(1+K[S]_T)$ shown in Table 1 corresponds to the second-order-rate constant (k_2) for metal ion catalyzed methanolysis. In order to compare catalytic efficiency of Cd^{2+} with that of various metal

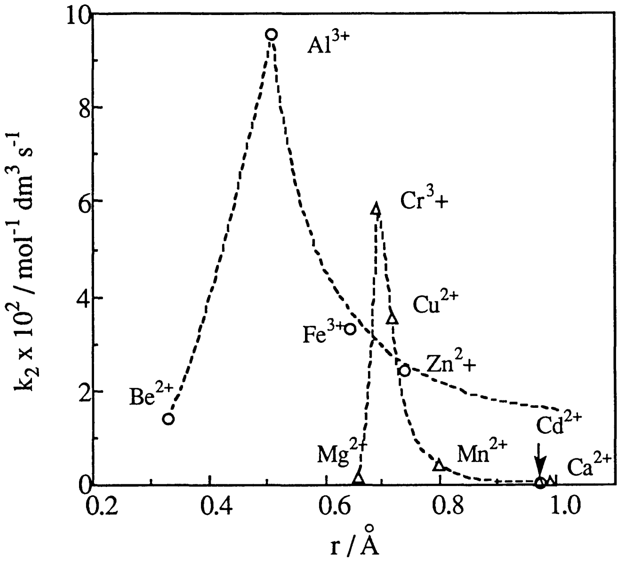


Fig. 2. Plots of the second-order rate constants (k_2) for metal ion catalyzed S–O (○) and P–O (△) bond cleavage vs. ionic radii of the metal ions. Cd^{2+}; present study, other metal ions; data taken from Ref. 1.

Table 1. Kinetic Parameters for the Metal Ion Catalyzed Methanolysis and Site of Bond Cleavage

Metal ion	Site	k_m/s^{-1}	K/mol^{-1} dm^3	$k_mK/(1+K[S]_T)$ mol^{-1} dm^3 s^{-1}
Cd^{2+} [a]	S-O, P-O	4.72×10^{-4}	2.54	1.16×10^{-3}
Zn^{2+} [b]	S-O	8.33×10^{-3}	3.03	2.45×10^{-2}
Mg^{2+} [b]	P-O	2.60×10^{-5}	102	1.31×10^{-3}
Ca^{2+} [b]	P-O	1.01×10^{-5}	38.6	2.81×10^{-4}

a) Nitrate, [PPS]=1.0×10^{-2} mol dm^{-3}, [*N*-ethylmorpholine]=2.5×10^{-1} mol dm^{-3} in CH$_3$OH/DMF (1 : 1, v/v), 55 °C. b) Data in Ref. 1.

ions reported in the previous paper, k_2 (P–O) and k_2 (S–O) values for Cd^{2+}-catalyzed P–O and S–O bond cleavage, respectively, obtained from k_2 value for the mixed cleavage and the ratio of mixed cleavage, are plotted as a function of ionic radius (r) of metal ion in Fig. 2. Value of k_2 (P–O) for Cd^{2+}-catalyzed P–O bond cleavage appears to satisfy the correlation between ionic radii of metal ions and the rates, but k_2 (S–O) value for Cd^{2+}-catalyzed S–O bond cleavage appears to be considerably smaller than that expected from the rate correlation. These observations will be discussed later.

Effects of Chloride Ion on Metal Ion Induced Spectral Change of PPS and on the Metal Ion Catalysis. Chloride ion inhibited Cd^{2+} or Zn^{2+}-catalyzed S–O bond cleavage, but not completely Cd^{2+}-catalyzed P–O bond cleavage, and this inhibition was suggested to occur with formation of a ternary complex of $PPS \cdot Cd^{2+} \cdot Cl^-$ and a tetramerous complex of $PPS \cdot Zn^{2+} \cdot 2Cl^-$ as described below.

The UV spectrum of PPS was changed by the addition of metal ion. The difference spectra induced by Cd^{2+}, Zn^{2+}, Mg^{2+}, and Ca^{2+} recorded at 25 °C are shown in Fig. 3A. There is almost no large difference in the shape among the difference spectra induced by these metal ions, but the difference absorbance increases in the order of $Ca^{2+}<Cd^{2+}<Mg^{2+}<Zn^{2+}$, which interest-

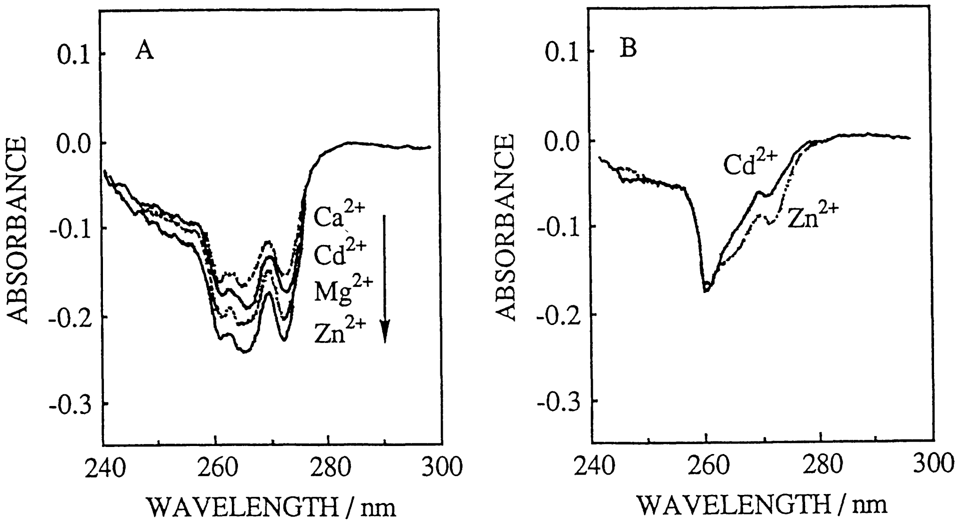


Fig. 3. Metal ion induced difference spectra of PPS in the absence (A) and presence (B) of tetrabutylammonium chloride (25 °C). $[M^{2+}]=5.0\times10^{-3}$ mol dm^{-3}, (chloride), $[PPS]=1.0\times10^{-3}$ mol dm^{-3}, $[Bu_4N^+Cl^-]=0$ and 2.0×10^{-2} mol dm^{-3}, [N-ethylmorpholine]$=1.5\times10^{-2}$ mol dm^{-3}, DMF-CH_3OH (1 : 1, v/v), $\mu=0.1$ ($Bu_4N^+ClO_4^-$).

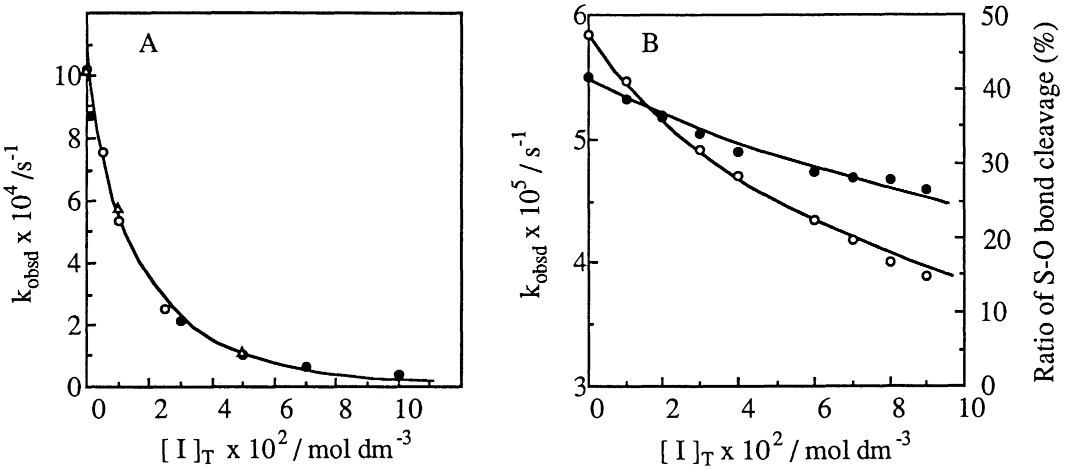


Fig. 4. (A). Plots of k_{obsd} vs. concentration of chloride ion (I) for Zn^{2+} promoted S–O bond cleavage. I: LiCl (○), $Me_4N^+Cl^-$ (●) and $Bu_4N^+Cl^-$ (△). $[ZnCl_2]=5.0\times10^{-2}$ mol dm^{-3}. (B). Plots of k_{obsd} (○) or the ratio of S–O bond cleavage (●) vs. concentration of chloride ion (I: LiCl) for Cd^{2+}-catalyzed mixed cleavage, $[Cd^{2+}]=5.6\times10^{-2}$ mol dm^{-3}. The other reaction conditions were essentially the same with those shown in Fig. 1. The ratio was determined by the barium chromate method and UV method (see Experimental).

ingly applies to the order of increasing $k_mK/(1+K[S]_T)$ values given in Table 1. An excess of tetrabutylammonium chloride over metal ion and PPS changes the shape of difference spectra induced by Cd^{2+} and Zn^{2+} as shown in Fig. 3B, but not by Mg^{2+} and Ca^{2+}. The change of the difference spectra brought about by chloride ion was considered due to the formation of complexes of PPS, Cd^{2+}, or Zn^{2+} and chloride ion, but not due to the inhibition of the metal ion from the complexation with PPS by chloride ion.

As expected, the presence of lithium chloride had almost no effect on Mg^{2+} or Ca^{2+}-catalyzed P–O bond cleavage, and lithium, tetramethylammonium, and tetrabutylammonium chlorides equally inhibited Zn^{2+}-promoted S–O bond cleavage. But P–O bond cleavage catalyzed by Zn^{2+} could not observed in the presence of the salts. Fig. 4A shows that pseudo-first-order rate constants for Zn^{2+}-promoted S–O bond cleavage decrease with increasing concentration of the salts.

Fig. 4B shows the inhibition of Cd^{2+}-catalyzed methanolysis by lithium chloride in a manner similar to that shown in Fig. 4A, but it is noticeable that a ratio of S–O bond cleavage against mixed cleavage decreases with increasing concentration of lithium chloride as shown in the same figure, indicating that chloride ion inhibits Cd^{2+}-catalyzed S–O bond cleavage, but not completely the metal ion-catalyzed P–O bond cleavage.

$$\begin{tikzcd} S + M \arrow[r, shift left, "K"] & SM \arrow[l, shift left] \arrow[r, "k_m"] \arrow[d, shift left] \arrow[d, shift right, "K_i, I"'] & 1+2+3+4 \\ & SMI \arrow[u, shift left=2] \arrow[r, "k_i"] & 1+2 \end{tikzcd} \tag{7}$$

$$k_{obsd} = \frac{k_mK[M]_T + k_iKK_i\,[M]_T[I]_T}{1 + K[M]_T + KK_i\,[M]_T[I]_T} \tag{8}$$

$$(\,[M]_T > [SM], [SMI];\ [I]_T >, [SMI]\,)$$

$$k_{obsd}\,(S\text{-}O) = \frac{k_m(S\text{-}O)K[M]_T}{1 + K[M]_T + KK_i\,[M]_T[I]_T} \tag{9}$$

$$\frac{1}{k_{obsd}\,(S\text{-}O)} = \frac{1}{k'_o} + \frac{K_i}{k_m(S\text{-}O)}\,[I]_T \tag{10}$$

$$\left(k'_o = k_m(S\text{-}O)K[M]_T/(\,1+K[M]_T)\right)$$

$$k_{obsd} - k' = \frac{k_iKK_i\,[M]_T[I]_T}{1 + K[M]_T + KK_i\,[M]_T[I]_T} \tag{11}$$

$$\left(\,k' = k_mK[M]_T/(\,1 + K[M]_T + KK_i\,[M]_T[I]_T)\,\right)$$

$$\frac{1}{k_{obsd} - k'} = \frac{1}{k_i} + \frac{1 + K[M]_T}{k_iKK_i[M]_T} \cdot \frac{1}{[I]_T} \tag{12}$$

The inhibitory curve for Cd^{2+}-catalyzed S–O bond cleavage can be analyzed by assuming a scheme (Eq. 7) involving the preequilibrium formation of the binary complex (SM) and a ternary complex (SMI) of PPS (S), Cd^{2+} (M) and chloride ion (I). Eq. 8 is formulated in accordance with the scheme, where $[I]_T$ is the initial stoichiometric concentration of lithium chloride, k_i and K_i are the rate constant for the methanolysis of the ternary complex (SMI) resulting in P–O bond cleavage and the formation constant for SMI, respectively, and $[S]_T$, $[M]_T$, k_m, and K are defined in Eq. 4. Eq. 8 gives Eq. 9 for Cd^{2+}-catalysed S–O bond cleavage and then Eq. 10, where k_{obsd} (S–O) and k_m(S–O) is pseudo-first-order rate constant and the rate constant of SM ($1.98 \times 10^{-4}\,s^{-1}$), respectively, which are evaluated from the ratio of S–O bond cleavage against mixed cleavage

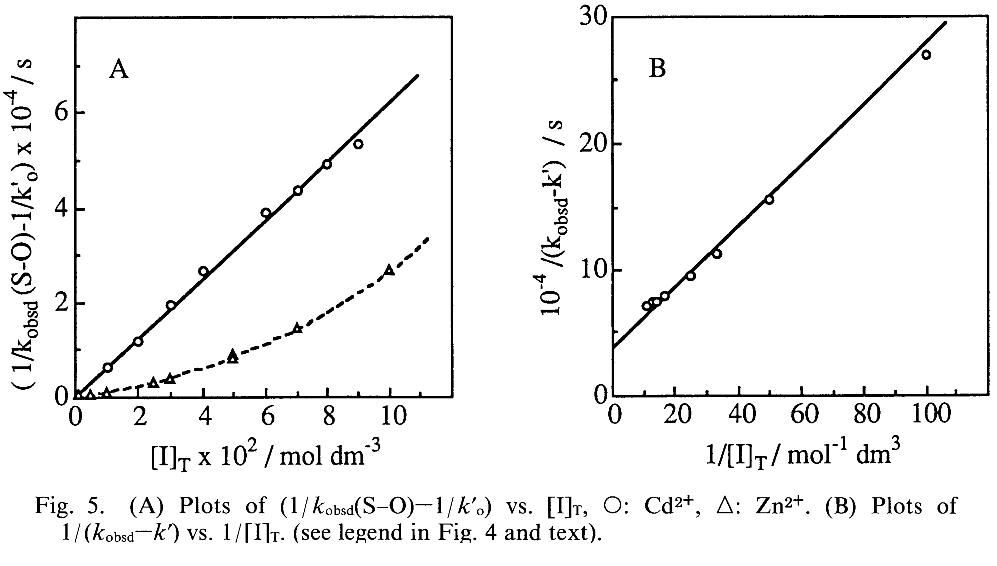


Fig. 5. (A) Plots of $(1/k_{obsd}(S\text{–}O)-1/k'_o)$ vs. $[I]_T$, ○: Cd^{2+}, △: Zn^{2+}. (B) Plots of $1/(k_{obsd}-k')$ vs. $1/[I]_T$. (see legend in Fig. 4 and text).

and the value of k_{obsd} for mixed cleavage shown in Fig. 4B, and k_{m} value given in Table 1, respectively. In accordance with Eq. 10, a plot of $1/k_{\mathrm{obsd}}$ (S–O) against $[\mathrm{I}]_{\mathrm{T}}$ is found to be linear as shown in Fig. 5A, and the value of K_i evaluated from the slope and k_{m} (S–O) value is 1.21×10^{2} ($\mathrm{mol^{-1}\,dm^{3}}$). Eq. 8 gives Eq. 11, and then Eq. 12. In accordance with Eq. 12, a linear correlation between $1/(k_{\mathrm{obsd}}-k')$ and $1/[\mathrm{I}]_{\mathrm{T}}$ is observed as shown in Fig. 5B. The calculated curves shown in Fig. 4B is obtained by Eq. 8, using evaluated values of k_i ($2.63\times10^{-5}\,\mathrm{s^{-1}}$), K_i determined above, k_{m} and K given in Table 1. The value of k_i for $\mathrm{Cd^{2+}}$-catalyzed P–O bond cleavage is about one tenth of the calculated value of k_{m}(P–O) for $\mathrm{Cd^{2+}}$ catalyzed P–O bond cleavage ($2.73\times10^{-4}\,\mathrm{s^{-1}}$) in the absence of chloride ion.

Meanwhile, it is difficult to explain the inhibitory curve for $\mathrm{Zn^{2+}}$-promoted S–O bond cleavage (Fig. 4A) by Eq. 10, because a linear rate correlation between $1/k_{\mathrm{obsd}}$ and $[\mathrm{I}]_{\mathrm{T}}$ can not be observed as shown in Fig. 5A. But it can readily be explained by assuming a scheme involving the preequilibrium formation of an inactive tetramerous complex ($\mathrm{SMI_2}$) of PPS (S), $\mathrm{Zn^{2+}}$ (M) and chloride ions (I) as well as the active SM and the inactive SMI complexes (Eq. 13). Eq. 14 is formulated in accordance with the scheme, where K_{1i} and K_{2i} are formation constants for SMI and $\mathrm{SMI_2}$, respectively, and k_{m}, K, $[\mathrm{S}]_{\mathrm{T}}$, $[\mathrm{M}]_{\mathrm{T}}$, and $[\mathrm{I}]_{\mathrm{T}}$ are defined in Eqs. 4 and 8. Eq. 14 gives Eq. 15. Fig. 6 illustrates linear plots of $(1/k_{\mathrm{obsd}}-1/k'_{\mathrm{o}})/[\mathrm{I}]_{\mathrm{T}}$ vs. $[\mathrm{I}]_{\mathrm{T}}$ in accordance with Eq. 15. The calculated curve shown in Fig. 4A is obtained by Eq. 14, using evaluated values of K_{1i} ($5.66\times10^{2}\,\mathrm{mol^{-1}\,dm^{3}}$), K_{2i} ($2.92\times10\,\mathrm{mol^{-1}\,dm^{3}}$), k_{m} and K given in Table 1.

$$\begin{tikzcd}
\mathrm{S}+\mathrm{M} \arrow[r, shift left, "K"] & \mathrm{SM} \arrow[l, shift left] \arrow[r, "k_{\mathrm{m}}"] \arrow[d, shift left, "{K_{1i},\,\mathrm{I}}"'] & 3+4 \\
 & \mathrm{SMI} \arrow[u, shift left] \arrow[r, shift left, "{K_{2i},\,\mathrm{I}}"] & \mathrm{SMI_2} \arrow[l, shift left]
\end{tikzcd} \tag{13}$$

$$k_{\mathrm{obsd}}=\frac{k_{\mathrm{m}}K[\mathrm{M}]_{\mathrm{T}}}{1+K[\mathrm{M}]_{\mathrm{T}}+K[\mathrm{M}]_{\mathrm{T}}[\mathrm{I}]_{\mathrm{T}}(K_{1i}+K_{1i}K_{2i}[\mathrm{I}]_{\mathrm{T}})} \tag{14}$$

$$([\mathrm{M}]_{\mathrm{T}}>[\mathrm{SM}],[\mathrm{SMI}],[\mathrm{SMI_2}];\ [\mathrm{I}]_{\mathrm{T}}>[\mathrm{SMI}],[\mathrm{SMI_2}])$$

$$\frac{(1/k_{\mathrm{obsd}}-1/k'_{\mathrm{o}})}{[\mathrm{I}]_{\mathrm{T}}}=\frac{1}{k_{\mathrm{m}}}(K_{1i}+K_{1i}K_{2i}[\mathrm{I}]_{\mathrm{T}}) \tag{15}$$

$$\left(k'_{\mathrm{o}}=k_{\mathrm{m}}K[\mathrm{M}]_{\mathrm{T}}/(1+K[\mathrm{M}]_{\mathrm{T}})\right)$$

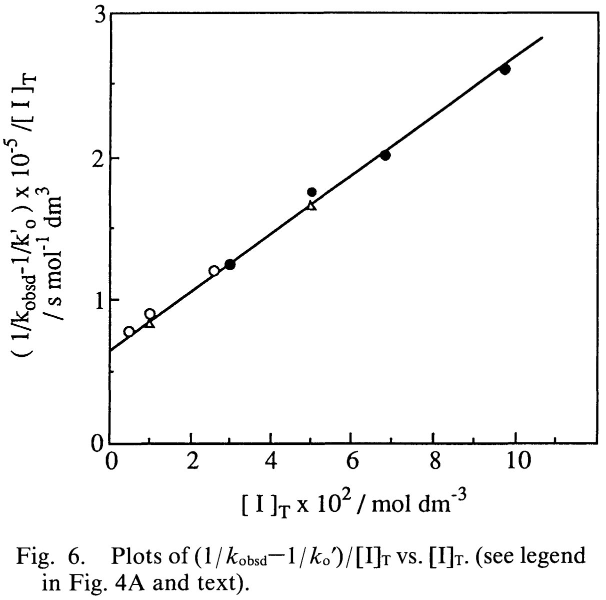


Fig. 6. Plots of $(1/k_{\mathrm{obsd}}-1/k_{\mathrm{o}}')/[\mathrm{I}]_{\mathrm{T}}$ vs. $[\mathrm{I}]_{\mathrm{T}}$. (see legend in Fig. 4A and text).

As described above, the inhibitory curve for $\mathrm{Zn^{2+}}$-promoted methanolysis by chloride ion could successfully be analyzed by Eq. 14, suggesting that probably because of neutralization of effective charge of $\mathrm{Zn^{2+}}$ required for an electrophilic catalysis by chloride ion, the ternary and tetramerous complexes were inactive. As discussed below, the inhibition of $\mathrm{Cd^{2+}}$-catalyzed S–O bond cleavage by chloride ion as well as the observations obtained from Fig. 2 is helpful in understanding the selectivity of the metal ion in the site of bond cleavage.

Discussion

As described early, it has been considered that metal ions with octahedral coordination such as $\mathrm{Mg^{2+}}$ and $\mathrm{Ca^{2+}}$ catalyze selective P–O bond cleavage in the methanolysis of PPS, and in contrast, metal ions with tetrahedral coordination such as $\mathrm{Zn^{2+}}$ promote selective S–O bond cleavage, and that the small optimum ionic radius of metal ion in the S–O bond cleavage reflects the bond angle of chelating ∠O–P–O near 109° in **6** which is smaller than that near 120° in **5** resulting in the P–O bond cleavage. However, interestingly $\mathrm{Cd^{2+}}$ catalyzed the mixed cleavage of P–O and S–O bond in the absence of chloride ion. The metal ion-catalyzed alcoholysis by 2-propanol suggested that the mechanism of P–O or S–O bond cleavage catalyzed by $\mathrm{Cd^{2+}}$ was the same as that catalyzed by $\mathrm{Mg^{2+}}$ or $\mathrm{Zn^{2+}}$, respectively, and the scheme and rate equation (Eqs. 3 and 4) used for the kinetic analysis of $\mathrm{Cd^{2+}}$-catalyzed methanolysis (Fig. 1A) were the same as those used for that of $\mathrm{Mg^{2+}}$ or $\mathrm{Zn^{2+}}$-catalyzed methanolysis.[1)] In addition, the shape of the difference spectrum of PPS induced by $\mathrm{Cd^{2+}}$ was almost comparable to that induced by $\mathrm{Mg^{2+}}$ or $\mathrm{Zn^{2+}}$ (Fig. 3A). Thus the catalytic action of $\mathrm{Cd^{2+}}$ was not essentially unusual, but it might be difficult to explain the selectivity of $\mathrm{Cd^{2+}}$ in the site of bond cleavage only by either tetrahedral or octahedral coordination. $\mathrm{Cd^{2+}}$ with large ionic radius was phenomenally similar to $\mathrm{Zn^{2+}}$ with small ionic radius in the inhibition of metal ion-catalyzed S–O bond cleavage by chloride ion (Fig. 4),

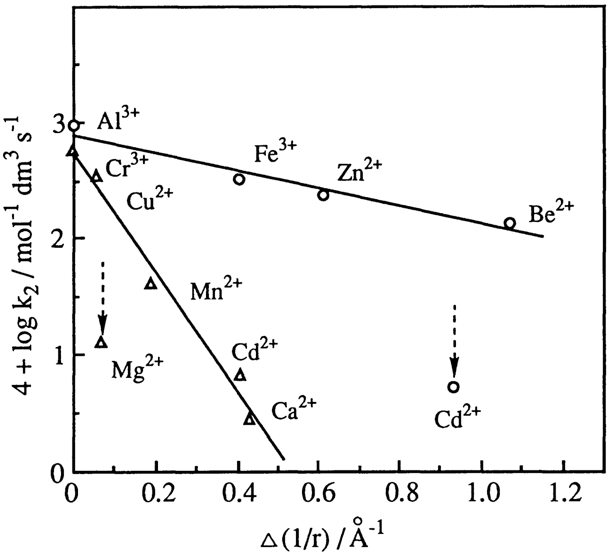


Fig. 7. Plots of log k_2 (S–O) (○) or log k_2 (P–O) (△) vs. Δ (1/r). (see Fig. 2 and text).

but different in the selectivity in the absence of chloride ion.

It is highly likely that large ionic radius of Cd^{2+} affects its selectivity in the site of bond cleavage. Figure 2 suggests that k_2(S–O) value for Cd^{2+} catalyzed S–O bond cleavage is considerably smaller than that expected from the interesting correlation of the rates with ionic radii of metal ions (r). Figure 7 shows that this deviation becomes clearer with approximately linear plots of log k_2(S–O) value against $\Delta(1/r)$, where $\Delta(1/r)$ is the difference in reciprocal of r between Al^{3+} with maximum rate as a standard and other metal ions such as Be^{2+}, Fe^{3+}, and Zn^{2+}. The figure also shows that with the exception of Mg^{2+} with small ionic radius, a linear correlation of k_2(P–O) with $\Delta(1/r)$ exists, using ionic radius of Cr^{3+} with rate maximum as a standard in a manner similar to that described above, and that k_2(P–O) value for Cd^{2+} catalyzed P–O bond cleavage satisfies the linear rate correlation. In Figs. 2 and 7 we use ionic radii of metal ions evaluated from both theoretical values by Pauling and experimental values by Goldschmidt.[3)] But ionic radius estimated by Shannon on the bases of both ionic and covalent bond character[11)] gave poor correlation with either log k_2(P–O) or log k_2(S–O) value, suggesting that the interaction between PPS and metal ion involves bonds of a highly polar bond.

It is considered in general that trivalent metal ions such as Al^{3+}, Fe^{3+}, and Cr^{3+} act as more effective electrophilic catalyst as in the present case than divalent metal ions. However there is almost no large difference in k_2 value for the trivalent metal ion-catalyzed methanolysis between the observed value and the expected value from rate correlation with ionic radii of divalent metal ions (Figs. 2 and 7). It is conceivable that the solvation to reduce effective charge required for the easy formation of SM complex (Eq. 3) and for the favorable stabilization of pentavalent phosphorus intermediate (**5**) or the transition state (**6**) is stronger for trivalent metal ions than for divalent metal ions, resulting in a smaller difference in their catalytic efficiency. It is interesting to note that, in spite of the unfavorable solvation, Cr^{3+} and Al^{3+} or Fe^{3+} catalyze selective P–O and S–O bond cleavage, respectively.

Figure 7 indicates that metal ion-catalyzed P–O and S–O bond cleavage are different from one another not only in the optimum ionic radius of metal ion but also in the slope of linear rate correlation, −5.1 and −0.60, respectively. The large difference in the slope of linear rate correlation suggests a chelate effect, i.e., the tridentate and bidentate coordination with strict geometrical requirements in **5** and **6**, respectively. Then it becomes more conceivable that ionic radius of Cd^{2+} with tetrahedral coordination is too large to stabilize favorably **6** for selective S–O bond cleavage. However it may be hard to appreciate that Cd^{2+} with tetrahedral coordination becomes favorable to catalyze P–O bond cleavage instead of S–O bond cleavage, because ionic radius of Zn^{2+} is also larger than the optimum ionic radius in S–O bond cleavage and near that in P–O bond cleavage, but Zn^{2+} promotes selective S–O bond cleavage, but not the mixed cleavage of P–O and S–O bond. Accordingly, the fit of log k_2(P–O) value for Cd^{2+}-catalyzed P–O bond cleavage to the linear rate correlation can be explained by assuming that the metal ion increases easily coordination number from four to six in order to form favorably **5**, by coordination with molecules of solvent, negatively charged oxygen atom of the sulfate moiety and that of phosphate moiety brought about by nucleophilic attack of methanol on phosphorus, resulting in P–O bond cleavage. In other words, Cd^{2+} with larger ionic radius becomes favorable to change the site of cleavage from S–O to P–O bond with changing the type of coordination from tetrahedral to octahedral coordination, so as to account for the mixed cleavage catalyzed by Cd^{2+}.

The change of the site of bond cleavage dependent on the change of the type of coordination may be demonstrated by Cd^{2+}-catalyzed S–O and P–O bond cleavage in the absence and presence of chloride ion, respectively, in the following way. Fig. 5 showed that the inhibition of Cd^{2+}-catalyzed S–O bond cleavage by chloride ion occurred with formation of the ternary complex of PPS, the metal ion and chloride ion (SMI), but chloride ion had almost no effect on the difference spectrum induced by Mg^{2+} or Ca^{2+} and on the methanolysis catalyzed by these metal ions, suggesting that chloride ion was difficult to form such a ternary complex with Mg^{2+} or Ca^{2+} with octahedral coordination and PPS, which was not a complex salt of chloride ion. It is therefore considered that Cd^{2+} with tetrahedral coordination in the binary complex (SM), which catalyzes S–O bond cleavage, increases coordination number from four to five by coordination with chloride ion to form the ternary complex, in which Cd^{2+} with trigonal bipyramidal coordination catalyzes P–O bond cleavage. But, because of partial neutralization of effective charge of Cd^{2+} required for an electrophilic catalysis by chloride ion, the rate of P–O bond cleavage is reduced to about one tenth of that in the absence of chloride ion.

In a manner similar to that described above, it is considered that the ternary (SMI) and tetramerous (SMI_2) complexes of PPS, Zn^{2+} and chloride ion shown in Eq. 13 are formed with changing the type of coordination, i.e., tetrahedral in SM complex, trigonal bipyramidal in SMI complex and octahedral coordination in SMI_2 complex.

Figure 7 also appears to indicate that Mg^{2+} is too small to stabilize **5** favorably. But Mg^{2+} could not change so easily the site of cleavage from P–O to S–O bond as Cd^{2+} changed that from S–O to P–O bond, suggesting that Mg^{2+} favors octahedral coordination alone in the present medium.

As discussed above, a convenient explanation of the findings was provided by the different coordination and ionic radius of Cd^{2+}, and it became more conceivable that the different coordination plays an essential role in the selectivity of metal ion in the site of bond cleavage, i.e., tetrahedral coordination in S–O bond cleavage and trigonal bipyramidal or octahedral coordination in P–O bond cleavage. However the catalysis of Mg^{2+} in the biochemical reactions of PAPS and that in the methanolysis of PPS are different from one another in the selectivity. Mg^{2+} catalyzes selective S–O bond cleavage in the biochemical sulfuryl group transfer from PAPS to numerous acceptors such as polysaccharides, phenols, steroids, and other nucleophiles,2) but the same metal ion catalyzes selective P–O bond cleavage in the solvolyses of PPS under neutral or basic conditions.1,5) We are interested in determining whether biochemically important Mg^{2+} catalyzes S–O bond cleavage in alcoholyses of PPS or not. Work along this line is in progress.

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