Alkali-Metal Ion Catalysis in Nucleophilic Substitution Reactions of 5-Nitro-8-quinolyl Picolinate with Alkali Metal Ethoxides: Effect of Modification of Nonleaving Group from Benzoyl to Picolinyl on Reactivity and Transition State Structure

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A kinetic study on nucleophilic substitution reaction of 5-nitro-8-quinolyl picolinate (**6**) with alkali-metal ethoxides (EtOM; M = K, Na, and Li) in anhydrous ethanol is reported. The plot of k_{obsd} *vs*. [EtOM] curves upward in the absence of crown ethers but is linear with significantly decreased reactivity in the presence of crown ethers. Dissection of k_{obsd} into k_{EtO^-} and k_{EtOM} (*i.e.*, the second-order rate constants for the reactions with the dissociated EtO⁻ and ion-paired EtOM, respectively) has revealed that the ion-paired EtOM is significantly more reactive than the dissociated EtO⁻ (*e.g.*, k_{EtOM}/k_{EtO^-} = 33.4-141). This indicates that the reaction of **6** is catalyzed by M⁺ ions in the order Na⁺ > Li⁺ > K⁺ and the catalytic effect disappears in the presence of a proper crown ether. Picolinate ester **6** is much more reactive and is more strongly catalyzed by M⁺ ions than 5-nitro-8-quinolyl benzoate (**5**). It has been concluded that M⁺ ions catalyze the reaction of **6** by increasing electrophilicity of the reaction center through a cyclic transition state, which is structurally not possible for the reaction of **5**.

Key Words : Metal-ion catalysis, Crown ether, Electrophilicity, Nucleofugality, Transition state

Introduction

Metal ions have often been reported to behave as a Lewis acid catalyst in nucleophilic substitution reactions of various esters.[1-10] Since Lewis acidity increases with increasing charge density of metal ions, most studies have focused on multivalent metal ions (*e.g.*, Mg²⁺, Co²⁺, Zn²⁺, La³⁺, Eu³⁺ *etc*.).[1-5] Effects of alkali-metal ions on nucleophilic substitution reactions of esters have been investigated much less intensively, although alkali-metal ions are ubiquitous in nature and play an important role in biological systems (*e.g.*, Na-K pump in mammalian cells).[6-10]

Buncel *et al*. carried out a systematic study on nucleophilic substitution reaction of 4-nitrophenyl diphenylphosphinate (**1a**) with alkali-metal ethoxides (EtOM; M = K, Na, Li) in anhydrous ethanol and found that M⁺ ions catalyze the reaction in the order Li⁺ > Na⁺ > K⁺.[6a] However, the catalytic effect shown by M⁺ ions disappeared in the presence of complexing agents such as 18-crown-6-ether (18C6) for K⁺ ion and 15-crown-5-ether (15C5) for Na⁺ ion.[6a] In contrast, we have shown that the reaction of 4-nitrophenyl diphenylphosphinothioate (**1b**) with EtOM is inhibited by Li⁺ ion but is catalyzed by K⁺ and 18C6-complexed-K⁺ ions.[7a] A similar result has been found for the reactions of paraoxon (**2a**) and parathion (**2b**) with EtOM, *e.g.*, the reaction of **2a** is catalyzed by M⁺ ions with a catalytic order Li⁺ > Na⁺ > K⁺, while the corresponding reaction of **2b** is inhibited by Li⁺ ion but is catalyzed by K⁺ and 18C6-complexed-K⁺ ions.[8] These results demonstrate convincingly that the role of M⁺ ions is strongly

dependent on the nature of the electrophilic center (*e.g.*, P=O *vs*. P=S). Thus, TS$_I$ has been suggested to be responsible for the contrasting M⁺ ion catalysis and inhibition on the basis of the contrasting M⁺ ion effects.[6-8]
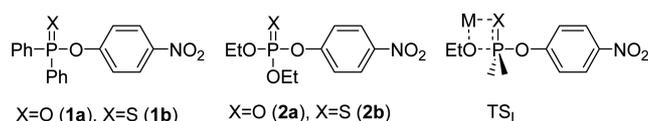

We have also reported that M⁺ ions strongly inhibit the reaction of 4-nitrophenyl salicylate (**3**) with EtOM in anhydrous ethanol (*e.g.*, k_{obsd} decreases as the concentration of M⁺ ions increases up to a certain concentration and then levels off thereafter).[9] The inhibitory effect of M⁺ ions has been found to be in the order K⁺ < Na⁺ < Li⁺. It has been suggested that formation of a stable 6-membered cyclic complex (*e.g.*, **3M**) is responsible for the inhibitory effect since **3M** would prevent the subsequent reaction (*i.e.*, an E1cb mechanism which yields an α-oxoketene).[9] The inhibitory effect of M⁺ ions was quite an unexpected result because M⁺ ions were expected to catalyze the reaction by increasing electrophilicity of the reaction center through a cyclic complex **3M**.
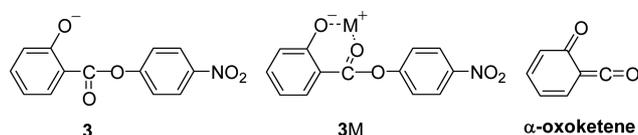
It has been reported that M^+ ions catalyze the reactions of 2-pyridyl benzoate (**4**) and 5-nitro-8-quinolyl benzoate (**5**) with EtOM in the order $Na^+ > K^+ > Li^+$, while the crown-complexed-M^+ ions (*e.g.*, 18C6-K^+ and 15C5-Na^+) do not exhibit any catalytic effect.[10a,b] Thus, the M^+ ion catalysis observed in the reactions of **4** and **5** has been attributed to an increase in nucleofugality of the leaving group through TS_{II} and TS_{III}.[10a,b]
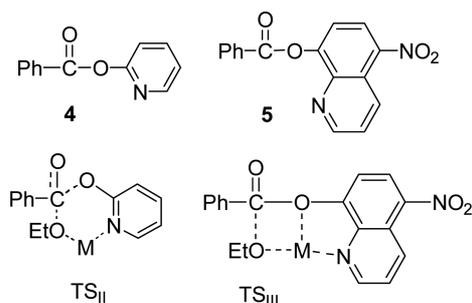
Our study has now been extended to nucleophilic substitution reaction of 5-nitro-8-quinolyl picolinate (**6**) with EtOM (M = K^+, Na^+, Li^+) in anhydrous ethanol to obtain further information on the role of M^+ ions (Scheme 1). The current kinetic results have been compared with those reported previously for the corresponding reaction of **5**[10b] to investigate the effect of modification of the nonleaving group from benzoyl to picolinyl on reactivity and TS structure.
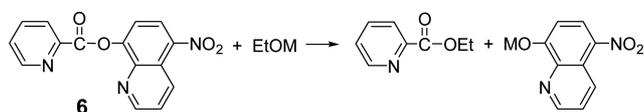
Scheme 1

Results and Discussion

The kinetic study was carried out spectrophotometrically under pseudo-first-order conditions in which the concentration of EtOM was in large excess over that of substrate **6**. All the reactions in this study obeyed pseudo-first-order

kinetics and proceeded with quantitative liberation of 5-nitro-8-quinolinolate ion. Pseudo-first-order rate constants (k_{obsd}) were calculated from the equation, $\ln (A_\infty - A_t) = -k_{obsd}t + C$. The kinetic conditions and results are summarized in Table 1. The uncertainty in the k_{obsd} values was estimated to be less than ± 3% from replicate runs. The second-order rate constants for the reactions of **6** with the dissociated EtO^- and ion-paired EtOM (*i.e.*, k_{EtO^-} and k_{EtOM}, respectively) were calculated from the ion-pairing treatment of the kinetic data and are summarized in Table 2 together with those reported previously for the corresponding reaction of **5** for comparison.

Effect of Alkali-Metal Ions on Reactivity. As shown in Figure 1, the reactivity of EtOM is strongly dependent on the nature of M^+ ion (*e.g.*, the reactivity of EtOM decreases in the order EtONa > EtOLi > EtOK). The plot of k_{obsd} *vs.* [EtOM] is linear for the reaction with EtOK in the presence of 18C6 ($k_{EtOK/18C6} = 52.7$ $M^{-1}s^{-1}$, inset of Figure 1). In contrast, the plots in the absence of the complexing agent curve upward with significantly enhanced k_{obsd} values. Such upward curvature is typical of reactions in which the ion-paired EtOM is more reactive than the dissociated EtO^-.[6-8] Thus, one can suggest that M^+ ions behave as a Lewis acid catalyst and the catalytic effect decreases in the order $Na^+ > Li^+ > K^+$.

Crown ethers are known to be a good complexing agent for M^+ ions (*e.g.*, 18C6 and 15C5 for K^+ and Na^+ ions, respectively). Thus, EtOM would exist as dissociated EtO^- and crown-complexed M^+ ion. To investigate the effect of crown ethers on reactivity, the reactions of **6** with a given concentration of EtONa and EtOK have been carried with varying concentrations of 15C5 and 18C6, respectively.

As shown in Figure 2, the k_{obsd} value for the reaction with EtONa decreases rapidly on initial addition of 15C5 up to
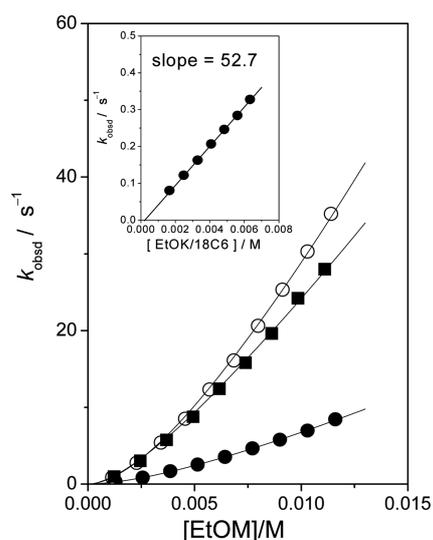
Table 1. Kinetic Data for the Reactions of 5-Nitro-8-quinolyl Picolinate (**6**) with EtOM in Anhydrous Ethanol at 25.0 ± 0.1 °C

[EtOK]/ mM	k_{obsd}/s^{-1}	[EtONa]/ mM	k_{obsd}/s^{-1}	[EtOLi]/ mM	k_{obsd}/s^{-1}
1.29	0.298	1.14	0.851	1.23	0.971
2.57	0.838	2.28	2.75	2.46	3.01
3.86	1.66	3.42	5.39	3.69	5.74
5.14	2.52	4.56	8.51	4.93	8.75
6.43	3.51	5.70	12.3	6.16	12.4
7.71	4.63	6.84	16.1	7.39	15.8
9.00	5.77	7.98	20.6	8.62	19.6
10.3	6.95	9.12	25.3	9.85	24.2
11.6	8.42	10.3	30.3	11.1	28.0
–	–	11.4	35.2	–	–

Figure 1. Plots of k_{obsd} *vs.* [EtOM] for the reactions of 5-nitro-8-quinolyl picolinate (**6**) with EtOK (●), EtONa (○) and EtOLi (■) in anhydrous ethanol at 25.0 ± 0.1 °C. The reaction with EtOK in the presence of 18C6 is illustrated in the inset. [18C6]/[EtOK] = 4.0.
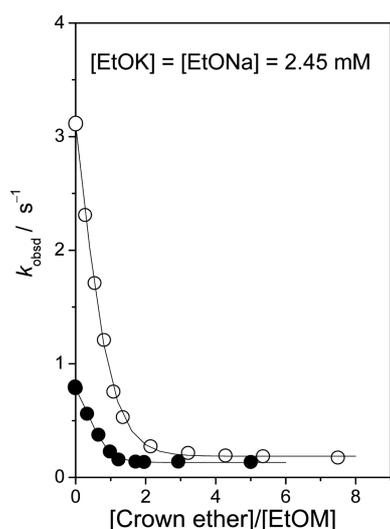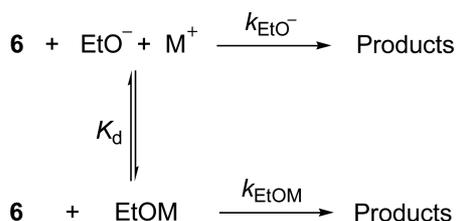
Figure 2. Effect of added crown ethers on reactivity of EtONa (○, 15C5) and EtOK (●, 18C6) for the reaction of 5-nitro-8-quinolyl picolinate (**6**) with a given concentration of EtOM at 25.0 ± 0.1 °C. [EtONa] = [EtOK] = 2.45 mM.

near [15C5]/[EtONa] = 5.0 and then modestly thereafter. A similar result is shown for the reaction with EtOK. It is noted that the reactions with EtONa and EtOK result in almost the same k_{obsd} value when the crown ethers are present in excess. This supports the preceding argument that M$^+$ ions catalyze the reaction of **6** and the catalytic effect disappears when M$^+$ ions are complexed by the crown ethers.

Dissection of k_{obsd} into k_{EtO^-} and k_{EtOM}. To quantify the catalytic effect shown by M$^+$ ion, the k_{obsd} values have been dissected into the second-order rate constants for the reactions with the dissociated EtO$^-$ ion and ion-paired EtOM (*i.e.*, k_{EtO^-} and k_{EtOM}, respectively). EtOM was reported to exist as dimers or other aggregates in a high concentration (*e.g.*, [EtOM] > 0.1 M).[11] However, EtOM would exist mainly as the dissociated and ion-paired species in a low concentration as in the current study (*e.g.*, [EtOM] < 0.1 M). Since both the dissociated EtO$^-$ and ion-paired EtOM would react with substrate **6** as shown in Scheme 2, one can derive a rate equation as in Eq. (1).

Under pseudo-first-order kinetic conditions (*e.g.*, [EtOM] >> [**6**]), k_{obsd} can be expressed as Eq. (2). It is noted that the dissociation constant K_d = [EtO$^-$]$_{eq}$[M$^+$]$_{eq}$/[EtOM]$_{eq}$, and [EtO$^-$]$_{eq}$ = [M$^+$]$_{eq}$ at equilibrium. Accordingly, Eq. (2) can be converted to Eq. (3). The [EtO$^-$]$_{eq}$ and [EtOK]$_{eq}$ values can be calculated from the reported K_d value for EtOM (*i.e.*, K_d =

Figure 3. Plots of k_{obsd}/[EtO$^-$]$_{eq}$ *vs.* [EtO$^-$]$_{eq}$ for the reactions of 5-nitro-8-quinolyl picolinate (**6**) with EtOK (●), EtONa (○) and EtOLi (■) in anhydrous ethanol at 25.0 ± 0.1 °C.

11.1 × 10^{-3}, 9.80 × 10^{-3} and 4.72 × 10^{-3} M for EtOK, EtONa and EtOLi, in turn)[12] and the initial concentration of EtOM using Eqs. (4) and (5).

$$\text{Rate} = k_{EtO^-}[\text{EtO}^-]_{eq}[\textbf{6}] + k_{EtOM}[\text{EtOM}]_{eq}[\textbf{6}] \tag{1}$$

$$k_{obsd} = k_{EtO^-}[\text{EtO}^-]_{eq} + k_{EtOM}[\text{EtOM}]_{eq} \tag{2}$$

$$k_{obsd}/[\text{EtO}^-]_{eq} = k_{EtO^-} + k_{EtOM}[\text{EtO}^-]_{eq}/K_d \tag{3}$$

$$[\text{EtOM}] = [\text{EtO}^-]_{eq} + [\text{EtOM}]_{eq} \tag{4}$$

$$[\text{EtO}^-]_{eq} = [-K_d + (K_d^2 + 4K_d[\text{EtOM}])^{1/2}]/2 \tag{5}$$

One might expect that the plot of k_{obsd}/[EtO$^-$]$_{eq}$ *vs.* [EtO$^-$]$_{eq}$ would be linear if the reaction proceeds as proposed in Scheme 2. In fact, the plots shown in Figure 3 exhibit excellent linear correlations, indicating that the derived equations based on the reactions proposed in Scheme 2 are correct. Accordingly, one can calculate the k_{EtO^-} and k_{EtOM}/K_d values from the intercept and the slope of the linear plot, respectively. The k_{EtOM} value can be calculated from the above k_{EtOM}/K_d values and the reported K_d value for EtOM. In Table 2 are summarized the calculated k_{EtO^-} and k_{EtOM} values for the reactions of **6**. The k_{EtO^-} and k_{EtOM} values reported previously for the corresponding reactions of **5** are also summarized in Table 2 for comparison.

Scheme 2. Reactions of **6** with the dissociated EtO$^-$ and ion-paired EtOM.

Table 2. Summary of Second-Order Rate Constants (k_{EtO^-} and k_{EtOM}) Calculated from Ion-Pairing Treatment of the Kinetic Data for the Reactions of 5-Nitro-8-quinolyl Picolinate (**6**) and Benzoate (**5**, in parenthesis) with EtOM in Anhydrous EtOH at 25.0 ± 0.1 °C

| EtOM	k_{EtOM}/M^{-1}s^{-1}	k_{EtO^-}/M^{-1}s^{-1}	k_{EtOM}/k_{EtO^-}
EtOLi	4700 (2.91)[a]	52.7 (1.64)[a]	89.2 (1.74)[a]
EtONa	7410 (6.06)[a]	52.7 (1.60)[a]	141 (3.63)[a]
EtOK	1760 (3.96)[a]	52.7 (1.74)[a]	33.4 (2.37)[a]
EtOK/18C6	–	52.7 (1.67)[a]	–

[a]The data in parenthesis for the reactions of **5** were taken from ref. 10b.

Effect of Modification of Nonleaving Group from Benzoyl to Picolinyl on Reactivity. Table 2 shows that the reactivity of the ion-paired EtOM is highly dependent on the nature of M$^+$ ions, *e.g.*, the k_{EtOM} value for the reaction of substrate **6** decreases in the order EtONa > EtOLi > EtOK. It is also shown that the ion-paired EtOM is significantly more reactive than the dissociated EtO$^-$ (*i.e.*, k_{EtOM}/k_{EtO-} = 33.4-141). This indicates that M$^+$ ions strongly catalyze the reaction of **6**. A similar result is shown for the corresponding reaction of 5-nitro-8-quinolyl benzoate (**5**), although the benzoate ester **5** is much less reactive than the picolinate ester **6**. Furthermore, the k_{EtOM}/k_{EtO-} ratio for the reaction of **5** is much smaller than that for the reaction of **6**.

We have previously shown that an acid-strengthening substituent (or an electron-withdrawing group) in the nonleaving group of esters increases the reactivity of esters by increasing electrophilicity of the reaction center (*e.g.*, 2,4-dinitrophenyl X-substituted benzoates and benzenesulfonates are more reactive as the substituent X becomes a stronger electron-withdrawing group).[13,14] Since benzoic acid (pK_a = 4.20) is a stronger acid than picolinic acid (pK_a = 5.40), one might expect that the benzoate ester **5** would be more reactive than the picolinate ester **6**. However, Table 2 shows that **5** is much less reactive than **6**, indicating that their reactivity is not solely affected by acidity of the acid moiety of esters.

It is apparent that reactivity of esters is influenced by electrophilicity of the reaction center as well as by nucleofugality of the leaving group. Since 5-nitro-8-quinolinolate ion is a common leaving group for the reactions of esters **5** and **6**, the difference in reactivity of **5** and **6** would be determined mainly by the difference in electrophilicity of their reaction centers. It is apparent that the presence of an electronegative N atom in the picolinyl moiety of **6** would increase the electrophilicity of the reaction center through an inductive effect by the N atom. In fact, pyridine is known to be a π-deficient aromatic compound and heterocyclic analogue of benzene ring that carries an EWG. Thus, one can suggest that the increased electrophilicity of the reaction center is responsible for the kinetic result that **6** is more reactive than the benzoate ester **5**.

Deduction of Transition-State Structure. Table 2 shows that the ion-paired EtOM is more reactive than the dissociated EtO$^-$. Thus, one can suggest that EtOM catalyzes the reaction of **6** by increasing either the nucleofugality of the leaving group through TS$_{IV}$ or the electrophilicity of the reaction center through TS$_V$. However, one can exclude TS$_{VI}$ because EtO$^-$ and M$^+$ ions in TS$_{VI}$ are not ion-paired species. It is noted that TS$_{IV}$ is similar to TS$_{III}$, which was previously reported as a plausible TS structure to explain the M$^+$ ion catalysis in the reaction of **5**.[10b] However, the enhanced nucleofugality through TS$_{IV}$ (or TS$_{III}$) would be ineffective for reactions in which departure of the leaving group occurs after RDS. It is evident that departure of the leaving group would occur after RDS if the reaction proceeds through a stepwise mechanism. This is because EtO$^-$ is much more basic and a poorer nucleofuge than the leaving 5-nitro-8-quinolinolate ion.

TS$_{IV}$ TS$_V$ TS$_{VI}$
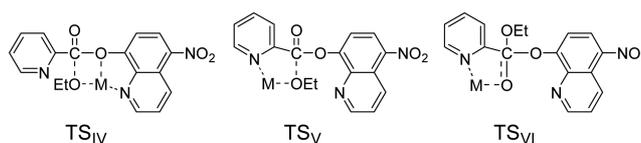
If the reactions of **5** and **6** proceed through TS$_{III}$ and TS$_{IV}$, respectively, one might expect a similar M$^+$ effect for the reactions of **5** and **6** due to the similarity of their TS structures. However, scrutiny of Table 2 reveals that M$^+$ ions catalyze the reaction of **6** more strongly than that of **5** (*e.g.*, k_{EtOM}/k_{EtO-} = 33.4-141 for the reaction of **6** while k_{EtOM}/k_{EtO-} = 1.74-3.63 for the reaction of **5**). Moreover, the order of the catalytic effect is not the same for the reactions of **5** and **6** (*e.g.*, Na$^+$ > K$^+$ > Li$^+$ for the reaction of **5** while Na$^+$ > Li$^+$ > K$^+$ for that of **6**). These results clearly exclude a possibility that M$^+$ ion catalyzes the reaction of **6** by increasing the nucleofugality of the leaving group through TS$_{IV}$. Thus, one can conclude that M$^+$ ions catalyze the reaction of **6** by increasing the electrophilicity of the reaction center through TS$_V$, which is structurally impossible for the reaction of **5**.

Conclusions

Based on the experimental results, we present the following conclusions: (1) The ion-paired EtOM is more reactive than the dissociated EtO$^-$. The reactivity decreases in the order EtONa > EtOLi > EtOK >> EtOK/18C6, indicating that M$^+$ ions catalyze the reaction in the order Na$^+$ > Li$^+$ > K$^+$. (2) Picolinate ester **6** is significantly more reactive than benzoate ester **5** toward both EtO$^-$ and EtOM. The N atom in the picolinyl moiety of **6** increases the electrophilicity of the reaction center through an inductive effect, which is responsible for the enhanced reactivity. (3) M$^+$ ions catalyze the reaction of **6** by increasing the electrophilicity of the reaction center through TS$_V$, which is structurally not possible for the corresponding reaction of **5**.

Experimental Section

Materials. 5-Nitro-8-quinolyl picolinate (**6**) was readily prepared by adding 5-nitro-8-quinolinol to the solution of picolinyl chloride in anhydrous diethyl ether as reported previously.[10] The crude product was purified by column chromatography (silica gel, methylene chloride/*n*-hexane 50/50). The purity was checked by the melting point and ^{1}H NMR spectrum.

Kinetics. The kinetic study was performed with a UV-vis spectrophotometer for slow reactions (*e.g.*, $t_{1/2}$ > 10 s) or with a stopped-flow spectrophotometer for fast reactions (*e.g.*, $t_{1/2}$ ≤ 10 s) equipped with a constant temperature circulating bath to maintain the temperature in the reaction cell at 25.0 ± 0.1 °C. The reaction was followed by monitoring the appearance of 5-nitro-8-quinolinolate ion at 450 nm. All reactions were carried out under pseudo-first-order conditions in which EtOM concentration was at least 20 times greater than the substrate concentration. The stock solution of EtOM was prepared by dissolving alkali metal in an-

hydrous ethanol under nitrogen and stored in the refrigerator. The concentration of EtOM was determined by titration with potassium hydrogen phthalate. The anhydrous ethanol was further dried over magnesium and was distilled under N_2 just before use.

All solutions were prepared freshly just before use under nitrogen and transferred by gas-tight syringes. Typically, the reaction was initiated by adding 5 μL of a 0.01 M solution of the substrate in CH_3CN by a 10 μL syringe to a 10 mm quartz UV cell containing 2.50 mL of the thermostatted reaction mixture made up of anhydrous ethanol and aliquot of the EtOM solution.

Product Analysis. 5-Nitro-8-quinolinolate ion was liberated quantitatively and identified as one of the products by comparison of the UV-vis spectrum at the end of reaction with the authentic sample under the experimental condition.

References

1. (a) Neverov, A. A.; Chen, L. D.; George, S.; Simon, D.; Maxwell, C. I.; Brown, R. S. *Can. J. Chem.* **2013**, *91*, 1139-1146. (b) Maxwell, C. I.; Mosey, N. J.; Brown, R. S. *J. Am. Chem. Soc.* **2013**, *135*, 17209-17222. (c) Mohamed, M. F.; Sanchez-Lombardo, I.; Neverov, A. A.; Brown, R. S. *Org. Biomol. Chem.* **2012**, *10*, 631-639. (d) Barrera, I. F.; Maxwell, C. I.; Neverov, A. A.; Brown, R. S. *J. Org. Chem.* **2012**, *77*, 4156-4160. (e) Raycroft, M. A. R.; Liu, C. T.; Brown, R. S. *Inorg. Chem.* **2012**, *51*, 3846-3854. (f) Brown, R. S. *Prog. Inorg. Chem.* **2012**, *57*, 55-117.
2. (a) Mitic, N.; Hadler, K. S.; Gahan, L. R.; Hengge, A. C.; Schenk, G. *J. Am. Chem. Soc.* **2010**, *132*, 7049-7054. (b) Feng, G.; Tanifum, E. A.; Adams, H.; Hengge, A. C. *J. Am. Chem. Soc.* **2009**, *131*, 12771-12779. (c) Humphry, T.; Iyer, S.; Iranzo, O.; Morrow, J. R.; Richard, J. P.; Paneth, P.; Hengge, A. C. *J. Am. Chem. Soc.* **2008**, *130*, 17858-17866. (d) Zalatan, J. G.; Catrina, I.; Mitchell, R.; Grzyska, P. K.; O'Brien, P. J.; Herschlag, D.; Hengge, A. C. *J. Am. Chem. Soc.* **2007**, *129*, 9789-9798. (e) Davies, A. G. *J. Chem. Res.* **2008**, 361-375. (f) Davies, A. G. *J. Chem Soc. Perkin 1* **2000**, 1997-2010.
3. (a) Lee, J. I. *Bull. Korean Chem. Soc.* **2010**, *31*, 749-752. (b) Lee, J. I. *Bull. Korean Chem. Soc.* **2007**, *28*, 863-866. (c) Kim, S.; Lee, J. I. *J. Org. Chem.* **1984**, *49*, 1712-1716. (d) Kim, S.; Lee, J. I.; Ko, Y. K. *Tetrahedron Lett.* **1984**, *25*, 4943-4946. (e) Kim, S.; Lee, J. I. *J. Org. Chem.* **1983**, *48*, 2608-1716.
4. (a) Lee, J. H.; Park, J.; Lah, M. S.; Chin, J.; Hong, J. I. *Org. Lett.* **2007**, *9*, 3729-3731. (b) Livieri, M.; Manicin, F.; Saielli, G.; Chin, J.; Tonellato, U. *Chem. Eur. J.* **2007**, *13*, 2246-2256. (c) Livieri, M.; Mancin, F.; Tonellato, U.; Chin, J. *Chem. Commun.* **2004**, 2862-2863. (d) Williams, N. H.; Takasaki, B.; Wall, M.; Chin, J.

5. (a) Fife, T. H.; Chauffe, L. *Bioorg. Chem.* **2000**, *28*, 357-373. (b) Fife, T. H.; Bembi, R. *J. Am. Chem. Soc.* **1993**, *115*, 11358-11363. (c) Fife, T. H.; Pujari, M. P. *J. Am. Chem. Soc.* **1990**, *112*, 5551-5557. (d) Chei, W. S.; Ju, H.; Suh, J. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 1533-1537. (e) Chei, W. S.; Ju, H.; Suh, J. *J. Biol. Inorg. Chem.* **2011**, *16*, 511-519. (f) Kim, H. M.; Jang, B.; Cheon, Y. E.; Suh, M. P.; Suh, J. *J. Biol. Inorg. Chem.* **2009**, *14*, 151-157. (g) Chei, W. S.; Suh, J. *Prog. Inorg. Chem.* **2007**, *55*, 79-142. (h) Jeung, C. S.; Song, J. B.; Kim, Y. H.; Suh, J. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 3061-3064. (i) Suh, J.; Son, S. J.; Suh, M. P. *Inorg. Chem.* **1998**, *37*, 4872-4877. (j) Suh, J.; Kim, N.; Cho, H. S. *Bioorg. Med. Chem. Lett.* **1994**, *4*, 1889-1892. (k) Suh, J. *Acc. Chem. Res.* **1992**, *25*, 273-279.
6. (a) Buncel, E.; Dunn, E. J.; Bannard, R. B.; Purdon, J. G. *J. Chem. Soc., Chem. Commun.* **1984**, 162-163. (b) Dunn, E. J.; Buncel, E. *Can. J. Chem.* **1989**, *67*, 1440-1448. (c) Pregel, M. J.; Dunn, E. J.; Nagelkerke, R.; Thatcher, G. R. J.; Buncel, E. *Chem. Soc. Rev.* **1995**, *24*, 449-455. (d) Buncel, E.; Nagelkerke, R.; Thatcher, G. R. J. *Can. J. Chem.* **2003**, *81*, 53-63. (e) Nagelkerke, R.; Thatcher, G. R. J.; Buncel, E. *Org. Biomol. Chem.* **2003**, *1*, 163-167. (f) Buncel, E.; Albright, K. G.; Onyido, I. *Org. Biomol. Chem.* **2004**, *2*, 601-610. (g) Buncel, E.; Albright, K. G.; Onyido, I. *Org. Biomol. Chem.* **2005**, *3*, 1468-1475. (h) Koo, I. S.; Ali, D.; Yang, K.; Park, Y.; Esbata, A.; van Loon, G. W.; Buncel, E. *Can. J. Chem.* **2009**, *87*, 433-439.
7. (a) Um, I. H.; Shin, Y. H.; Park, J. E.; Kang, J. S.; Buncel, E. *Chem. Eur. J.* **2012**, *18*, 961-968. (b) Um, I. H.; Kang, J. S.; Shin, Y. H.; Buncel, E. *J. Org. Chem.* **2013**, *78*, 490-497.
8. (a) Um, I. H.; Shin, Y. H.; Lee, S. E.; Yang K. Y.; Buncel, E. *J. Org. Chem.* **2008**, *73*, 923-930. (b) Um, I. H.; Jeon, S. E.; Baek, M. H.; Park, H. R. *Chem. Commun.* **2003**, 3016-3017.
9. Um, I. H.; Seo, J. A.; Mishima, M. *Chem. Eur. J.* **2011**, *17*, 3021-3027.
10. (a) Um, I. H.; Kang, J. S.; Kim, C. W.; Lee, J. I. *Bull. Korean Chem. Soc.* **2012**, *33*, 519-523. (b) Um, I. H.; Lee, S. E.; Hong, Y. J.; Park, J. E. *Bull. Korean Chem. Soc.* **2008**, *29*, 117-121. (c) Um, I. H.; Song, Y. J.; Kim, M. Y.; Lee, J. I. *Bull. Korean Chem. Soc.* **2013**, *34*, 1525-1529.
11. Pechanec, V.; Kocian, O.; Zavada, J. *Collect. Czech. Chem. Commun.* **1982**, *47*, 3405-3411.
12. Barthel, J.; Justice, J.-C.; Wachter, R. *Z. Phys. Chem.* **1973**, *84*, 100-113.
13. (a) Um, I. H.; Im, L. R.; Kim, E. H.; Shin, J. H. *Org. Biomol. Chem.* **2010**, *8*, 3801-3806. (b) Um, I. H.; Hwang, S. J.; Yoon, S. R.; Jeon, S. E.; Bae, S. K. *J. Org. Chem.* **2008**, *73*, 7671-7677. (c) Um, I. H.; Jeon, S. E.; Seok, J. A. *Chem. Eur. J.* **2006**, *12*, 1237-1243. (d) Um, I. H.; Lee, J. Y.; Ko, S. H.; Bae, S. K. *J. Org. Chem.* **2006**, *71*, 5800-5803. (e) Um, I. H.; Lee, J. Y.; Fujio, M.; Tsuno, Y. *Org. Biomol. Chem.* **2006**, *4*, 2979-2985. (f) Um, I. H.; Kim, K. H.; Park, H. R.; Fujio, M.; Tsuno, Y. *J. Org. Chem.* **2004**, *69*, 3937-3942.
14. (a) Um, I. H.; Hong, J. Y.; Seok, J. A. *J. Org. Chem.* **2005**, *70*, 1438-1444. (b) Um, I. H.; Chun, S. M.; Chae, O. M.; Fujio, M.; Tsuno, Y. *J. Org. Chem.* **2004**, *69*, 3166-3172. (c) Um, I. H.; Hong, J. Y.; Kim, J. J.; Chae, O. M.; Bae, S. K. *J. Org. Chem.* **2003**, *68*, 5180-5185.