http://dx.doi.org/10.5012/bkcs.2012.33.7.2269

Kinetics and Reaction Mechanism for Aminolysis of Benzyl 4-Pyridyl Carbonate in H_2O: Effect of Modification of Nucleofuge from 2-Pyridyloxide to 4-Pyridyloxide on Reactivity and Reaction Mechanism

Ji-Sun Kang and Ik-Hwan Um*

*Department of Chemistry and Nano Science, Ewha Womans University, Seoul 120-750, Korea. *E-mail: ihum@ewha.ac.kr*
Received February 19, 2012, Accepted April 8, 2012

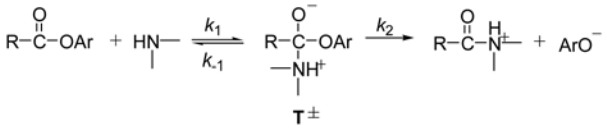
Pseudo-first-order rate constants k_{amine} have been measured spectrophotometrically for the reactions of benzyl 4-pyridyl carbonate **6** with a series of alicyclic secondary amines in H_2O at 25.0 °C. The plots of k_{amine} *vs.* [amine] curve upward, indicating that the reactions proceed through a stepwise mechanism with two intermediates, a zwitterionic tetrahedral intermediate $T^{\pm}$ and its deprotonated form T^{-}. This contrasts to the report that the corresponding reactions of benzyl 2-pyridyl carbonate **5** proceed through a forced concerted pathway. The k_{amine} values for the reactions of **6** have been dissected into the second-order rate constant Kk_2 and the third-order rate constant Kk_3. The Brønsted-type plots are linear with β_{nuc} = 0.94 and 1.18 for Kk_2 and Kk_3, respectively. The Kk_2 for the reaction of **6** is smaller than the second-order rate constant k_N for the corresponding reaction of **5**, although 4-pyridyloxide in **6** is less basic and a better nucleofuge than 2-pyridyloxide in **5**.

Key Words : Aminolysis, Brønsted-type plot, Nucleofuge, Concerted mechanism, Stepwise mechanism

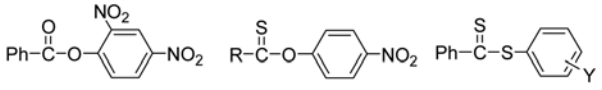
Introduction

Aminolyses of esters have been reported to proceed through a concerted mechanism or through a stepwise pathway with a zwitterionic tetrahedral intermediate $T^{\pm}$ as shown in Scheme 1.[1-9] A linear Brønsted-type plot with β_{nuc} = 0.5 ± 0.1 has been suggested as evidence for a concerted mechanism while a curved Brønsted-type plot often observed for aminolysis of esters possessing a good leaving group (*e.g.*, 2,4-dinitrophenoxide) has been interpreted as a change in the rate-determining step (RDS) of a stepwise reaction.[1-9]

In fact, reactions of 2,4-dinitrophenyl benzoate **1** with a series of alicyclic secondary amines in MeCN have been reported to proceed through a concerted mechanism on the basis of a linear Brønsted-type plot with β_{nuc} = 0.40.[6] In contrast, the corresponding reactions of **1** in H_2O have been suggested to proceed through a stepwise mechanism, since the Brønsted-type plot exhibits downward curvature (*e.g.*, β_{nuc} decreases from 0.74 to 0.34 as the basicity of the incoming amine increases),[7] indicating that the nature of solvents is an important factor to determine the reaction mechanism. On the other hand, aminolyses of thiono esters (*e.g.*, *O*-4-nitrophenyl thionobenzoate **2**, *O*-phenyl *O*-4-nitrophenyl thionocarbonate **3** and aryl dithiobenzoates **4**) have often been reported to proceed through two intermediates $T^{\pm}$ and its deprotonated form T^{-}, implying that the nature of electrophilic center also determines the reaction mechanism.[8,9]

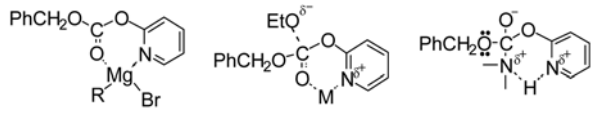


Scheme 1



1 R = Ph (**2**), PhO (**3**) **4**

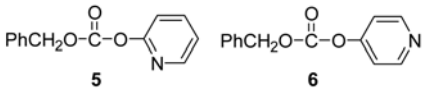
Esters possessing a 2-pyridyl moiety have been reported as an excellent acylating agent in reactions with Grignard reagents as well as in reactions with cupric bromide or lithium dialkylcuprate.[10,11] The reactions have been concluded to proceed through a 6-membered cyclic complex (*e.g.*, I), in which Mg^{2+} ion acts as a strong Lewis acid catalyst.[10,11] We have also shown that alkali metal ions catalyze the reactions of **5** with alkali metal ethoxides EtOM (M = Li, Na, K) through a transition state similar to II.[12]



I II III

Thus, aminolysis of benzyl 2-pyridyl carbonate **5** was expected to proceed through a stepwise mechanism with an intermediate as modeled by III, which is structurally similar to I or II.[13] However, we have reported that aminolysis of **5** in MeCN proceeds through a concerted mechanism on the basis of a linear Brønsted-type plot with β_{nuc} = 0.57.[13a] One might suggest that solvent effect is responsible for the concerted mechanism, since the ionic species $T^{\pm}$ would be highly unstable in the aprotic solvent. However, this argument appears to be little persuasive, since the reactions of **5** in H_2O were found to proceed also through a concerted mech-

anism.[13b]



5 **6**

Our study has now extended to the reactions of benzyl 4-pyridyl carbonate **6** with a series of alicyclic secondary amines in H_2O to get further information on the reaction mechanism. We wish to report that the effect of modification of the nucleofuge from 2-pyridyloxide to 4-pyridyloxide (*i.e.*, **5** → **6**) on reactivity and reaction mechanism is significant (*e.g.*, **6** is less reactive than **5** although the former possesses a less basic nucleofuge than the latter, and the aminolysis of **6** proceeds through a stepwise mechanism with two intermediates $T^{\pm}$ and T^{-} while that of **5** proceeds through a concerted pathway).

Results and Discussion

First-order kinetics were observed under the reaction conditions with the amine concentration in large excess. Pseudo-first-order rate constants (k_{obsd}) were calculated from the slopes of the linear plots of ln ($A_\infty - A_t$) *vs*. *t*. It is estimated from replicate runs that the uncertainty in the k_{obsd} values is less than ± 3%. The k_{obsd} values with the reaction conditions are summarized in Tables S1-S6 in the Supporting Information.

As shown in Figure 1, the plot of k_{obsd} *vs*. [amine] for the reactions of **6** with piperidine curves upward as a function of increasing amine concentration. It is noted that the $k_{obsd} >> 0$ at [amine] = 0.0 M. Similarly curved plots with a positive k_{obsd} value at [amine] = 0.0 M are obtained for the reactions with the other amines (see Figures S1a-S5a in the Supporting Information). However, the k_{obsd} at [amine] = 0.0 M becomes smaller as the amine becomes less basic. This indicates that the contribution of H_2O and/or OH^- generated from hydrolysis of amines to the k_{obsd} value is significant, particularly for the reactions with strongly basic amines (*e.g.*, piperidine and 3-methylpiperidine). From our preliminary experiment, we found that **6** is rapidly hydrolyzed even at a low OH^- concentration, *e.g.*, the second-order rate constant for the reaction of **6** with OH^- was measured to be 193 $M^{-1}s^{-1}$ in H_2O at 25.0 °C (see Figures S6 in the Supporting Information).

Reaction Mechanism. It is apparent that the k_{obsd} at [amine] = 0.0 M represents the contribution of the reaction of **6** with H_2O and/or OH^- ion, which was generated from hydrolysis of amines in the reaction condition. Thus, the k_{amine} (*i.e.*, the pseudo-first-order rate constant for the reactions of **6** with amines) has been calculated from the relationship $k_{amine} = k_{obsd} - 193\ M^{-1}s^{-1} \times [OH^-]$. The concentration of OH^- ion in the reaction mixture can be calculated from the Henderson-Hasselbalch equation, *i.e.*, pH = pK_a of the conjugate acid of amines – log [amine]/[conjugate acid of amine]. The k_{amine} values calculated in this way are graphically demonstrated in Figure 2 for the reaction of **6** with piperidine and in Figures S1b-S5b for those of **6** with other amines.

As shown in Figure 2, the plot of k_{amine} *vs*. [amine] curves upward passing through the origin. Such upward curvature is typical for aminolysis of esters reported previously to proceed through a rate-determining deprotonation process from $T^{\pm}$ to give T^-.[8,9] Thus, one can suggest that aminolysis of **6** proceeds through a stepwise mechanism with two intermediates $T^{\pm}$ and T^- as shown in Scheme 2. This contrasts to our recent report that the corresponding aminolysis of **5** proceeds through a concerted mechanism.[13b] It is evident that modification of the nucleofuge from 2-pyridyloxide to 4-pyridyloxide (*i.e.*, **5** → **6**) causes a change in the reaction mechanism.

Dissection of k_{amine} into Kk_2 and Kk_3. The k_{amine} values calculated above have been dissected into the second-order rate constants (Kk_2) and the third-order rate constants (Kk_3). One can express the pseudo-first-order rate constant (k_{amine}) for the reactions of **6** with amines as Eq. (1) on the basis of the kinetic results and the mechanism proposed in Scheme 2. Under the assumption, $k_{-1} >> k_2 + k_3$[amine], Eq. (1) can be simplified as Eq. (2). Thus, one might expect that the plot of k_{amine}/[amine] *vs*. [amine] is linear if the above assumption is valid.

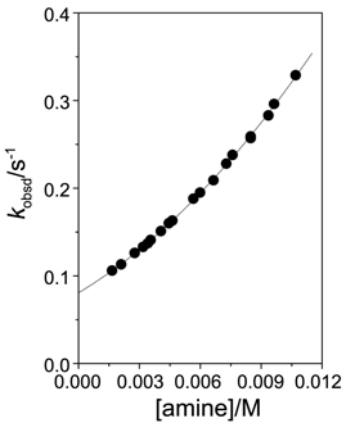


Figure 1. Plot of k_{obsd} *vs*. [amine] for the reaction of benzyl 4-pyridyl carbonate **6** with piperidine in H_2O at 25.0 ± 0.1 °C.

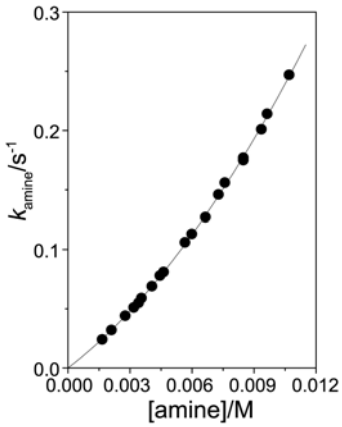
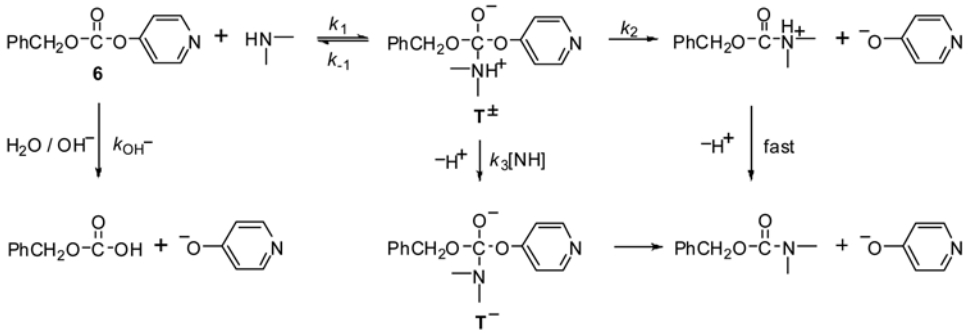


Figure 2. Plot of k_{amine} *vs*. [amine] for the reaction of benzyl 4-pyridyl carbonate **6** with piperidine in H_2O at 25.0 ± 0.1°C.



Scheme 2

$$k_{amine} = (k_1k_2[amine] + k_1k_3[amine]^2)/(k_{-1} + k_2 + k_3[amine]) \quad (1)$$

$$k_{amine}/[amine] = Kk_2 + Kk_3[amine], \text{ where } K = k_1/k_{-1} \quad (2)$$

In fact, the plot of k_{amine}/[amine] *vs*. [amine] is linear for the reaction with piperidine as shown in Figure 3. The corresponding plots for the reactions with the other amines are also linear (see Figures S1c-S5c in the Supporting Information), indicating that the current aminolysis of **6** proceeds through a stepwise mechanism with two intermediates $T^{\pm}$ and T^{-} and the assumption (*i.e*., $k_{-1} >> k_2 + k_3$[amine]) is valid. Accordingly, the Kk_2 and Kk_3 values were calculated from the intercept and the slope of the linear plots of k_{amine}/[amine] *vs*. [amine], respectively and are summarized in Table 1 together with the second-order rate constants k_N reported recently for the corresponding reactions of **5** for comparison.[13b]

Effect of Modification of Nucleofuge on Reactivity. As shown in Table 1, the Kk_2 and Kk_3 values for the reactions of **6** decrease rapidly as the amine basicity decreases, *e.g*., Kk_2 decreases from 13.4 $M^{-1}s^{-1}$ to 0.759 and 0.0104 $M^{-1}s^{-1}$, as the pK_a of the conjugate acid of amines decreases from 11.22 to 9.82 and 7.98, in turn. The k_N for the corresponding reactions of **5** also decreases as the amine basicity decreases but the dependence of k_N on pK_a is much less sensitive than that of Kk_2 (or Kk_3) for the reaction of **6**. Interestingly, the Kk_2 for the reactions of **6** is smaller than the k_N for the corresponding reaction of **5**, although 4-pyridyloxide in **6** is *ca*. 0.4 pK_a units less basic and a better nucleofuge than 2-pyridyloxide in **5**.[14] One might suggest that the difference in the reaction mechanisms (*i.e*., a concerted mechanism for the reactions of **5** *vs*. a stepwise mechanism with two intermediates $T^{\pm}$ and T^{-} for those of **6**) is responsible for the difference in reactivity.

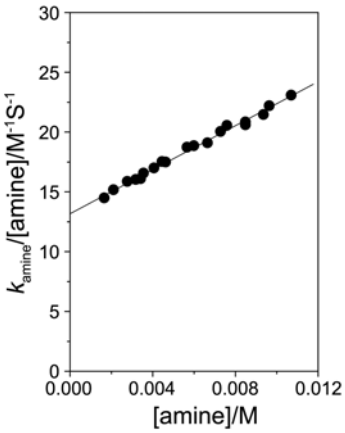


Figure 3. Plot of k_{amine}/[amine] *vs*. [amine] for the reaction of benzyl 4-pyridyl carbonate **6** with piperidine in H_2O at 25.0 ± 0.1 °C.

The effects of amine basicity on the second-order rate constants Kk_2 and on the third-order rate constants Kk_3 are illustrated in Figures 4(a) and (b), respectively. The Brønsted-type plots are linear with β_{nuc} = 0.94 and 1.18 for Kk_2 and Kk_3, respectively. These β_{nuc} values appear to be the upper limit of β_{nuc} for reactions reported previously to proceed through a stepwise mechanism. Such large β_{nuc} values are consistent with the results that the Kk_2 and Kk_3 exhibit high sensitivity to the amine basicity as mentioned in the preceding section (Table 1).

Factors Determining Presence/Absence of Deprotonation Process. It has been reported that reactions of *O*-phenyl *O*-

Table 1. Summary of kinetic data for the reactions of benzyl 2-pyridyl carbonate **5** and benzyl 4-pyridyl carbonate **6** with alicyclic secondary amines in H_2O at 25.0 ± 0.1 °C

	Amines	pK_a	**5**[a]	**6**	
			k_N/$M^{-1}s^{-1}$	Kk_2/$M^{-1}s^{-1}$	Kk_3/$M^{-2}s^{-1}$
1	piperidine	11.22	37.9	13.4 ± 0.2	899 ± 24
2	3-methylpiperidine	11.07	44.0	12.9 ± 0.1	894 ± 17
3	piperazine	9.82	19.1	0.759 ± 0.03	23.6 ± 0.4
4	1-(2-hydroxyethyl)piperazine	9.38	5.03	0.112 ± 0.007	3.05 ± 0.05
5	morpholine	8.36	3.07	0.0543 ± 0.001	0.811 ± 0.01
6	*N*-formylpiperazine	7.98	1.09	0.0104 ± 0.0004	0.139 ± 0.004

[a]The kinetic data for the reactions of **5** were taken from ref. 13b.

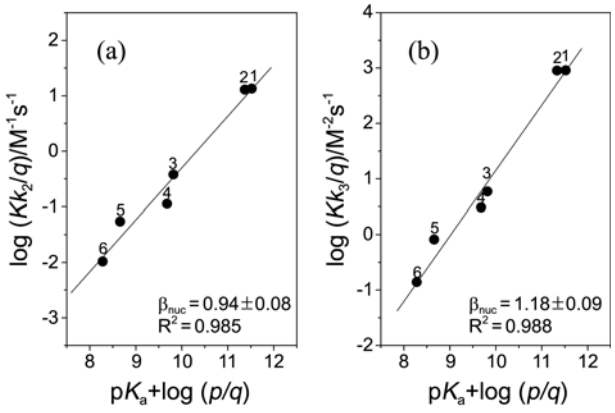


Figure 4. Brønsted-type plots for the reactions of benzyl 4-pyridyl carbonate **6** with alicyclic secondary amines in H_2O at 25.0 ± 0.1 °C: log Kk_2 *vs*. pK_a (**a**) and log Kk_3 *vs*. pK_a (**b**). The identity of points is given in Table 1.

4-nitrophenyl thionocarbonate **3** (and its derivatives) with weakly basic amines (*e.g.*, piperazinium ion and *N*-formylpiperazine) proceed through $T^{\pm}$ and T^{-} in an aqueous solution, while the corresponding reactions with strongly basic amines (*e.g.*, piperidine and piperazine) proceed without the deprotonation process from $T^{\pm}$.[9] Thus, Castro *et al*. have concluded that basicity of the attacking amine is a determinant that selects the mechanistic pathway.[9] On the other hand, we have shown that reactions of *O*-aryl thionobenzoates (**2** and its derivatives) with amines proceed through a stepwise mechanism with one or two intermediates depending on the basicity of the incoming amine and the nucleofuge (*i.e.*, the reaction proceeds through $T^{\pm}$ when the leaving aryloxide is less basic than the incoming amine but through $T^{\pm}$ and T^{-} when the leaving group is more basic than the nucleophile).[8]

It is evident that the reactions with a weakly basic amine would result in a large k_{-1} while those of substrates possessing a strongly basic nucleofuge would give a small k_2. Thus, one might suggest that the reactions of **2** and **3**, which were reported to proceed through a deprotonation process from $T^{\pm}$ to yield T^{-}, would exhibit a small k_2/k_{-1} ratio by decreasing k_2 or by increasing k_{-1}.

The above argument can also account for the difference in the reaction mechanisms for aminolyses of **5** and **6**. As mentioned above, aminolysis of **5** in H_2O was concluded to proceed through a concerted mechanism on the basis of a linear Brønsted-type plot with β_{nuc} = 0.49, although the reaction was predicted to proceed through a stepwise mechanism with an intermediate as modeled by III.[13b] Since the H-bonding interaction in III would accelerate the rate of leaving-group expulsion (*i.e.*, an increase in k_2) but would retard departure of the amine from III (*i.e.*, a decrease in k_{-1}), aminolysis of **5** would result in a large k_2/k_{-1} ratio. In contrast, such H-bonding interaction is structurally impossible for the reactions of **6**, indicating that the determinant of an increasing k_2 and a decreasing k_{-1} is absent. Accordingly, the reactions of **6** would result in a small k_2/k_{-1} ratio. This idea can be further supported by the fact that the k_N for the reactions of **5** is larger than the Kk_2 for the corresponding reaction of **6** (Table 1), although 2-pyridyloxide in **5** is *ca*. 0.4 pK_a units more basic and a poorer nucleofuge than 4-pyridyloxide in **6**.[14] Thus, it is proposed that aminolysis of **6** proceeds through $T^{\pm}$ and T^{-} as intermediates with a small k_2/k_{-1} ratio.

Conclusions

Our study has allowed us to conclude the following; (1) The effect of modification of the nucleofuge from 2-pyridyloxide to 4-pyridyloxide on reaction mechanism is significant. The aminolysis of **6** proceeds through a stepwise mechanism with $T^{\pm}$ and T^{-} as intermediates while the corresponding reaction of **5** was reported to proceed through a forced concerted mechanism. (2) The Kk_2 for the reaction of **6** is smaller than the k_N for the corresponding reaction of **5**, although 4-pyridyloxide in **6** is less basic and a better nucleofuge than 2-pyridyloxide in **5**. (3) The reaction of **6** would result in a smaller k_2 with a larger k_{-1} (*i.e.*, a small k_2/k_{-1} ratio) than that of **5** since the intramolecular H-bonding interaction, which was proposed for the reaction of **5**, is structurally impossible. The small k_2/k_{-1} ratio causes the reaction of **6** to proceed through $T^{\pm}$ and T^{-} and is responsible for the fact that **6** is less reactive than **5**.

Experimental Section

Materials. Substrate **6** was synthesized from the reaction of 4-hydroxypyridine with benzyl chloroformate in methylene chloride, which was generated from the reaction of phosgene and benzyl alcohol as described previously.[15] The crude product was purified by recrystallization and its purity was checked by its melting point and ^{1}H and ^{13}C NMR spectra. Amines and other chemicals were of the highest quality available. Doubly glass distilled water was further boiled and cooled under nitrogen to remove any dissolved CO_2 just before use.

Kinetics. Kinetic study was performed using a UV-Vis spectrophotometer equipped with a constant-temperature circulating bath. All the reactions were carried out under pseudo-first-order conditions in which the amine concentration was at least 20 times greater than the substrate concentration. Typically, the reaction was initiated by adding 5 μL of a 0.01 M of substrate stock solution in MeCN by a 10 μL syringe to a 10 mm UV cell containing 2.50 mL of the reaction medium and the amine nucleophile. The amine stock solution of *ca*. 0.2 M was prepared in a 25.0 mL volumetric flask by adding 2 equiv. of amine and 1 equiv. of HCl solution to make a self-buffered solution except for the solutions of piperidine and 3-methylpiperidine (the stock solutions of these amines were prepared by adding 5 equiv. amine and 4 equiv. of HCl solution to decrease the OH^{-} concentration in the self-buffered solution. The reactions were followed by monitoring disappearance of the substrate at 275 nm. Reactions were followed generally for 9-10 half-lives and k_{obsd} were calculated using the equation, ln (A_∞ –

A_t) *vs*. *t*.

Product Analysis. 4-Pyridyloxide was liberated and identified as one of the reaction products by comparison of the UV-Vis spectra after completion of the reactions with those of the authentic samples under the reaction conditions.

Acknowledgments. This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (2009-0075488). J. S. Kang is also grateful for the BK 21 Scholarship.

References

1. (a) Castro, E. A. *Pure Appl. Chem.* **2009**, *81*, 685-696. (b) Jencks, W. P. *Chem. Rev.* **1985**, *85*, 511-527. (c) Jencks, W. P. *Chem. Soc. Rev.* **1981**, *10*, 345-375. (d) Jencks, W. P. *Acc. Chem. Res*. **1980**, *13*, 161-169.
2. (a) Menger, F. M.; Smith, J. H. *J. Am. Chem. Soc.* **1972**, *94*, 3824-3829. (b) Maude, A. B.; Williams, A. *J. Chem. Soc., Perkin Trans. 2* **1997**, 179-183. (c) Maude, A. B.; Williams, A. *J. Chem. Soc., Perkin Trans. 2* **1995**, 691-696. (d) Menger, F. M.; Brian, J.; Azov, V. A. *Angew. Chem. Int. Ed.* **2002**, *41*, 2581-2584. (e) Perreux, L.; Loupy, A.; Delmotte, M. *Tetrahedron* **2003**, *59*, 2185-2189. (f) Fife, T. H.; Chauffe, L. *J. Org. Chem*. **2000**, *65*, 3579-3586. (g) Spillane, W. J.; Brack, C. *J. Chem. Soc., Perkin Trans. 2* **1998**, 2381-2384. (h) Llinas, A.; Page, M. I. *Org. Biomol. Chem.* **2004**, *2*, 651-654.
3. (a) Castro, E. A.; Gazitua, M.; Santos, J. G. *J. Phys. Org. Chem.* **2011**, *24*, 466-473. (b) Castro, E. A.; Aliaga, M. E.; Cepeda, M.; Santos, J. G. *Int. J. Chem. Kinet.* **2011**, *43*, 353-358. (c) Castro, E. A.; Aliaga, M.; Campodonico, P. R.; Cepeda, M.; Contreras, R.; Santos, J. G. *J. Org. Chem*. **2009**, *74*, 9173-9179. (d) Castro, E. A.; Ramos, M.; Santos, J. G. *J. Org. Chem*. **2009**, *74*, 6374-6377. (e) Castro, E. A.; Aliaga, M.; Santos, J. G. *J. Org. Chem.* **2005**, *70*, 2679-2685. (f) Castro, E. A.; Gazitua, M.; Santos, J. G. *J. Org. Chem.* **2005**, *70*, 8088-8092.
4. (a) Sung, D. D.; Jang, H. M.; Jung, D. I.; Lee, I. *J. Phys. Org. Chem.* **2008**, *21*, 1014-1019. (b) Sung, D. D.; Koo, I. S.; Yang, K.; Lee, I. *Chem. Phys. Lett*. **2006**, *432*, 426-430. (c) Sung, D. D.; Koo, I. S.; Yang, K.; Lee, I. *Chem. Phys. Lett*. **2006**, *426*, 280-284. (d) Oh, H. K.; Oh, J. Y.; Sung, D. D.; Lee, I. *J. Org. Chem.* **2005**, *70*, 5624-5629. (e) Oh, H. K.; Jin, Y. C.; Sung, D. D.; Lee, I. *Org. Biomol. Chem.* **2005**, *3*, 1240-1244.
5. (a) Oh, H. K. *Bull. Korean Chem. Soc*. **2011**, *32*, 4095-4098. (b) Oh, H. K. *Bull. Korean Chem. Soc*. **2011**, *32*, 1539-1542. (c) Oh, H. K. *Bull. Korean Chem. Soc*. **2011**, *32*, 137-140. (d) Oh, H. K.; Ku, M. H.; Lee, H. W.; Lee, I. *J. Org. Chem*. **2002**, *67*, 8995-8998. (e) Oh, H. K.; Ku, M. H.; Lee, H. W.; Lee, I. *J. Org. Chem*. **2002**, *67*, 3874-3877.
6. Um, I. H.; Jeon, S. E.; Seok, J. A. *Chem. Eur. J*. **2006**, *12*, 1237-1243.
7. (a) Um, I. H.; Lee, J. Y.; Ko, S. H.; Bae, S. K. *J. Org. Chem*. **2006**, *71*, 5800-5803. (b) Um, I. H.; Kim, K. H.; Park, H. R.; Fujio, M.; Tsuno, Y. *J. Org. Chem*. **2004**, *69*, 3937-3942. (c) Um, I. H.; Min, J. S.; Ahn, J. A.; Hahn, H. J. *J. Org. Chem*. **2000**, *65*, 5659-5663.
8. (a) Um, I. H.; Seok, J. A.; Kim, H. T.; Bae, S. K. *J. Org. Chem*. **2003**, *68*, 7742-7746. (b) Um, I. H.; Hwang, S. J.; Baek, M. H.; Park, E. J. *J. Org. Chem*. **2006**, *71*, 9191-9197.
9. (a) Castro, E. A. *Chem. Rev.* **1999**, *99*, 3505-3524. (b) Castro, E. A.; Ibanez, F.; Santos, J. G.; Ureta, C. *J. Org. Chem.* **1993**, *58*, 4908-4912. (c) Castro, E. A.; Galvez, A.; Leandro, L.; Santos, J. G. *J. Org. Chem.* **2002**, *67*, 4309-4315. (d) Castro, E. A.; Cubillos, M.; Santos, J. G. *J. Org. Chem.* **2001**, *66*, 6000-6003. (e) Castro, E. A.; Garcia, P.; Leandro, L.; Quesieh, N.; Rebolledo, A.; Santos, J. G. *J. Org. Chem.* **2000**, *65*, 9047-9053. (f) Castro, E. A.; Saavedra, C.; Santos, J. G.; Umana, M. I. *J. Org. Chem.* **1999**, *64*, 5401-5407.
10. (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) Lee, J. I.; Kim, S. *Bull. Korean Chem. Soc.* **1989**, *10*, 611-612. (d) Kim, S.; Lee, J. I. *J. Org. Chem.* **1984**, *49*, 1712-1716. (e) Kim, S.; Lee, J. I.; Ko, Y. K. *Tetrahedron Lett.* **1984**, *25*, 4943-4946. (f) Kim, S.; Lee, J. I. *J. Org. Chem.* **1983**, *48*, 2608-2610.
11. (a) Mukaiyama, T.; Araki, M.; Takei, H. *J. Am. Chem. Soc*. **1973**, *95*, 4763-4765. (b) Araki, M.; Sakata, S.; Takei, H.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 1777-1780.
12. (a) Um, I. H.; Kang, J. S.; Kim, C. W.; Lee, J. I. *Bull. Korean Chem. Soc*. **2012**, *33*, 519-523. (b) Lee, J. I.; Kang, J. S.; Kim, S. I.; Um, I. H. *Bull. Korean Chem. Soc*. **2010**, *31*, 2929-2933. (c) Lee, J. I.; Kang, J. S.; Im, L. R.; Um, I. H. *Bull. Korean Chem. Soc*. **2010**, *31*, 3543-3548.
13. (a) Bae, A. R.; Um, I. H. *Bull. Korean Chem. Soc*. **2012**, *33*, 1547-1550. (b) Kang, J. S.; Lee, J. I.; Um, I. H. *Bull. Korean Chem. Soc*. **2012**, *33*, 1551-1555.
14. Jencks, W. P.; Regenstein, J. *In Handbook of Biochemistry, Selected Data for Molecular Biology*; Sober, H. A., Ed.; The Chemical Rubber Co.: Cleveland, OH, 1968; p 216.
15. (a) Kim, S.; Lee, J. I. *Chem. Lett.* **1984**, 237-238. (b) Kim, S.; Lee, J. I.; Yi, K. Y. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 3570-3575.