

# Nucleophilic Substitution Reactions of Y-Substituted-Phenyl Benzoates with Potassium Ethoxide in Anhydrous Ethanol: Reaction Mechanism and Role of K<sup>+</sup> Ion

Song-I Kim, Hyo-Jin Cho,<sup>†</sup> and Ik-Hwan Um<sup>\*</sup>

Department of Chemistry and Nano Science, Ewha Womans University, Seoul 120-750, Korea. \*E-mail: ihum@ewha.ac.kr

<sup>†</sup>Department of Chemistry, Duksung Women's University, Seoul 132-714, Korea

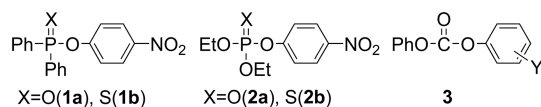
Received September 16, 2013, Accepted October 21, 2013

Pseudo-first-order rate constants ( $k_{\text{obsd}}$ ) have been measured spectrophotometrically for the reactions of Y-substituted-phenyl benzoates (**5a-j**) with potassium ethoxide (EtOK) in anhydrous ethanol at  $25.0 \pm 0.1$  °C. The plots of  $k_{\text{obsd}}$  vs. [EtOK] curve upward regardless of the electronic nature of the substituent Y in the leaving group. Dissection of  $k_{\text{obsd}}$  into the second-order rate constants for the reactions with the dissociated EtO<sup>-</sup> and ion-paired EtOK (*i.e.*,  $k_{\text{EtO}^-}$  and  $k_{\text{EtOK}}$ , respectively) has revealed that the ion-paired EtOK is more reactive than the dissociated EtO<sup>-</sup>. The Brønsted-type plots for the reactions with the dissociated EtO<sup>-</sup> and ion-paired EtOK exhibit highly scattered points with  $\beta_{\text{lg}} = -0.5 \pm 0.1$ . The Hammett plots correlated with  $\sigma^{\circ}$  constants result in excellent linear correlations, indicating that no negative charge develops on the O atom of the leaving Y-substituted-phenoxide ion in transition state. Thus, it has been concluded that the reactions with the dissociated EtO<sup>-</sup> and ion-paired EtOK proceed through a stepwise mechanism, in which departure of the leaving group occurs after the RDS, and that K<sup>+</sup> ion catalyzes the reactions by increasing the electrophilicity of the reaction center through a four-membered cyclic TS structure.

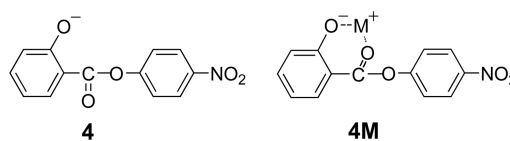
**Key Words** : K<sup>+</sup> ion catalysis, Concerted mechanism, Stepwise mechanism, Electrophilicity, Nucleofugality

## Introduction

Metal ions have often been reported to behave as a Lewis acid catalyst in nucleophilic substitution reactions of esters.<sup>1-11</sup> Since Lewis acidity increases as the charge density increases, most studies have focused on reactions involving multi-valent metal ions (*e.g.*, Mg<sup>2+</sup>, Co<sup>2+</sup>, Zn<sup>2+</sup>, La<sup>3+</sup>, Eu<sup>3+</sup>, *etc.*).<sup>2-4</sup> Effects of alkali-metal ions on nucleophilic substitution reactions have been investigated much less intensively.<sup>5-11</sup> Buncl and his coworkers have initiated the first systematic study on alkaline ethanolysis of 4-nitrophenyl diphenylphosphinate (**1a**) in anhydrous ethanol to investigate alkali-metal ion effect.<sup>5a</sup> They have found that alkali-metal ions catalyze the reaction in the order K<sup>+</sup> < Na<sup>+</sup> < Li<sup>+</sup> and that the catalytic effect disappears in the presence of complexing agents (*e.g.*, crown ethers or cryptands).<sup>5a</sup> In contrast, we have shown that Li<sup>+</sup> ion inhibits the corresponding reaction of 4-nitrophenyl diphenylphosphinothioate (**1b**) while K<sup>+</sup> and 18C6-complexed K<sup>+</sup> ions catalyze the reaction.<sup>8</sup> A similar result has been reported for the reactions of 4-nitrophenyl diethyl phosphate (**2a**, paraoxon) and 4-nitrophenyl diethyl phosphorothioate (**2b**, parathion) with EtOM (M = Li, Na, K), *e.g.*, M<sup>+</sup> ions catalyze the reactions of **2a** in the order K<sup>+</sup> < Na<sup>+</sup> < Li<sup>+</sup> while the reaction of **2b** is strongly inhibited by Li<sup>+</sup> ion but is catalyzed by K<sup>+</sup> and 18C6-complexed K<sup>+</sup> ions.<sup>9</sup> These demonstrate convincingly that the effect of M<sup>+</sup> ions is dependent on the nature of the electrophilic centers (*e.g.*, P=O vs. P=S).

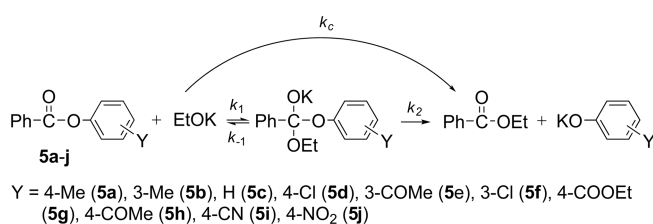


Effects of alkali-metal ions have also been investigated for the reactions of Y-substituted-phenyl phenyl carbonates (**3**) with EtOM.<sup>10c</sup> The reactions of **3** with the dissociated EtO<sup>-</sup> and ion-paired EtOK have been concluded to proceed through a concerted mechanism on the basis of excellent linear Yukawa-Tsuno plots with  $\rho_{\text{Y}} = 2.11$  and  $r = 0.21$  for the reaction with EtO<sup>-</sup> and  $\rho_{\text{Y}} = 1.62$  and  $r = 0.26$  for the reaction with EtOK. We have also shown that M<sup>+</sup> ions catalyze the reaction in the order Li<sup>+</sup> < Na<sup>+</sup> < K<sup>+</sup>.<sup>10c</sup>



On the contrary, we have reported that M<sup>+</sup> ions strongly inhibit the reaction of 4-nitrophenyl salicylate (**4**) with EtOM in anhydrous ethanol, *e.g.*, the  $k_{\text{obsd}}$  value decreases as the concentration of M<sup>+</sup> ions increases up to a certain concentration and then levels off thereafter. The inhibitory effect of M<sup>+</sup> ions has been found to be in the order K<sup>+</sup> < Na<sup>+</sup> < Li<sup>+</sup>.<sup>11a</sup> Formation of a stable 6-membered cyclic complex (**4M**) has been suggested to be responsible for the inhibitory effect since **4M** would prevent the subsequent reaction (*i.e.*, formation of  $\alpha$ -oxoketene through an E1cb mechanism).<sup>11a</sup>

Our study has been extended to reactions of Y-substituted-phenyl benzoates (**5a-j**) with EtOK in anhydrous ethanol to investigate the role of K<sup>+</sup> ion as well as the reaction mechanism (Scheme 1). We wish to report that the reactions proceed through a stepwise mechanism, in which departure of the leaving group occurs after the rate-determining step (RDS), and that K<sup>+</sup> ion catalyzes the reaction by increasing



Scheme 1

the electrophilicity of the reaction center rather than by increasing the nucleofugality of the leaving group.

## Results and Discussion

The kinetic study was performed spectrophotometrically under pseudo-first-order conditions in which the concentration of EtOK was in large excess over that of **5a-j**. All the reactions in this study obeyed pseudo-first-order kinetics and proceeded with quantitative liberation of Y-substituted phenoxide ion. Pseudo-first-order rate constants ( $k_{\text{obsd}}$ ) were calculated from the slope of linear plots of  $\ln(A_{\infty} - A_t)$  vs. time. It is estimated from replicate runs that the uncertainty in the  $k_{\text{obsd}}$  values is less than  $\pm 3\%$ . The second-order rate constants for the reactions of **5a-j** with the dissociated EtO<sup>-</sup> and ion-paired EtOK (*i.e.*,  $k_{\text{EtO}^-}$  and  $k_{\text{EtOK}}$ , respectively) were calculated from the ion-pairing treatment of the kinetic data as shown in the following section and are summarized in Table 1.

**Dissection of  $k_{\text{obsd}}$  into  $k_{\text{EtO}^-}$  and  $k_{\text{EtOK}}$ .** As shown in Figure 1, the plot of  $k_{\text{obsd}}$  vs. [EtOK] for the reaction of 4-methylphenyl benzoate (**5a**) curves upward. A similar result is obtained for the corresponding reactions of the other aryl benzoates **5b-j** (Figures not shown). Such upward curvature has often been reported for alkaline ethanolysis of esters in which alkali-metal ions behave as a Lewis acid catalysis.<sup>5-11</sup> Thus, one can suggest that K<sup>+</sup> ion catalyzes the current reactions.

Alkali-metal ethoxides (EtOM, M = Li, Na, K) have been reported to exist as the dissociated EtO<sup>-</sup> and ion-paired EtOM when [EtOM] < 0.1 M.<sup>12</sup> Since the concentration of EtOK used in the present study was lower than 0.1 M, one can suggest that substrates **5a-j** would react with the dissociated EtO<sup>-</sup> and ion-paired EtOK as shown in Scheme 2.

A rate equation can be derived as Eq. (1) on the basis of the reactions proposed in Scheme 2. Under pseudo-first-order kinetic conditions (*e.g.*, [EtOK]  $\gg$  [**5a-j**]),  $k_{\text{obsd}}$  can be expressed as Eq. (2). Since the dissociation constant  $K_d = [\text{EtO}^-]_{\text{eq}}[\text{K}^+]_{\text{eq}}/[\text{EtOK}]_{\text{eq}}$ , and  $[\text{EtO}^-]_{\text{eq}} = [\text{K}^+]_{\text{eq}}$  at equilibrium, Eq. (2) becomes Eq. (3). The concentrations of  $[\text{EtO}^-]_{\text{eq}}$  and  $[\text{EtOK}]_{\text{eq}}$  can be calculated from the reported  $K_d$  value of  $1.11 \times 10^{-2}$  M for EtOK<sup>13</sup> and the initial concentration [EtOK] using Eqs. (4) and (5).

$$\text{Rate} = k_{\text{EtO}^-}[\text{EtO}^-]_{\text{eq}}[\mathbf{5a-j}] + k_{\text{EtOK}}[\text{EtOK}]_{\text{eq}}[\mathbf{5a-j}] \quad (1)$$

$$k_{\text{obsd}} = k_{\text{EtO}^-}[\text{EtO}^-]_{\text{eq}} + k_{\text{EtOK}}[\text{EtOK}]_{\text{eq}} \quad (2)$$

$$k_{\text{obsd}}/[\text{EtO}^-]_{\text{eq}} = k_{\text{EtO}^-} + k_{\text{EtOK}}[\text{EtO}^-]_{\text{eq}}/K_d \quad (3)$$

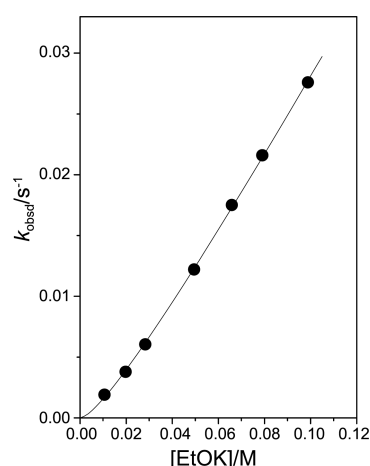
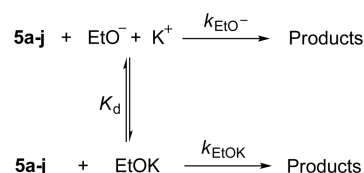


Figure 1. Plots of  $k_{\text{obsd}}$  vs. [EtOK] for the reactions of 4-methylphenyl benzoate (**5a**) with EtOK in anhydrous EtOH at  $25.0 \pm 0.1$  °C.



Scheme 2. Reactions of **5a-j** with the dissociated EtO<sup>-</sup> and ion-paired EtOK.

$$[\text{EtOK}] = [\text{EtO}^-]_{\text{eq}} + [\text{EtOK}]_{\text{eq}} \quad (4)$$

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

Thus, the plot of  $k_{\text{obsd}}/[\text{EtO}^-]_{\text{eq}}$  vs.  $[\text{EtO}^-]_{\text{eq}}$  would be linear with a positive intercept, if the reaction proceed as proposed in Scheme 2 and the derived equations are correct. In fact, the plot shown in Figure 2 is linear with a positive intercept for the reaction of **5a** with EtOK. A similar result was obtained for the corresponding reactions of the other aryl benzoates (*i.e.*, **5b-j**). Accordingly, the  $k_{\text{EtO}^-}$  and  $k_{\text{EtOK}}/K_d$  values have been calculated from the intercept and the slope

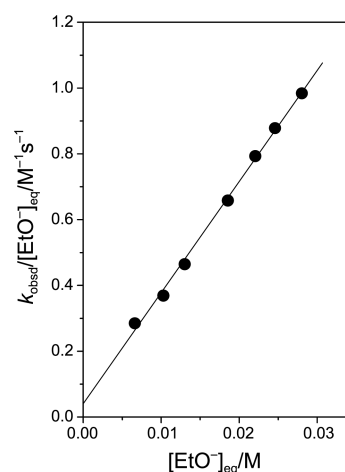


Figure 2. Plot illustrating dissection of  $k_{\text{obsd}}$  into second-order rate constants  $k_{\text{EtO}^-}$  and  $k_{\text{EtOK}}$  for the reaction of 4-methylphenyl benzoate (**5a**) with EtOK in anhydrous EtOH at  $25.0 \pm 0.1$  °C.

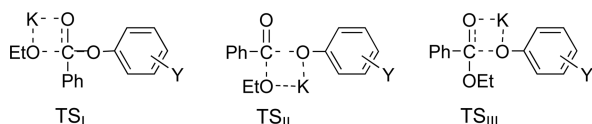
**Table 1.** Summary of Second-Order Rate Constants from Ion-Pairing Treatment of the Kinetic Data for Reactions of Y-Substituted-Phenyl Benzoates (**5a-j**) with EtOK in Anhydrous EtOH at 25.0 ± 0.1 °C

Entry	Y	pK <sub>a</sub> <sup>a</sup>	k <sub>EtOK</sub> /M <sup>-1</sup> s <sup>-1</sup>	k <sub>EtO<sup>-</sup></sub> /M <sup>-1</sup> s <sup>-1</sup>	k <sub>EtOK</sub> /k <sub>EtO<sup>-</sup></sub>
<b>5a</b>	4-Me	15.99	0.380	0.028	13.6
<b>5b</b>	3-Me	15.83	0.430	0.030	14.3
<b>5c</b>	H	15.76	0.557	0.0421	13.2
<b>5d</b>	4-Cl	14.90	1.80	0.337	5.34
<b>5e</b>	3-COMe	14.64	2.59	0.587	4.41
<b>5f</b>	3-Cl	14.47	2.59	0.553	4.68
<b>5g</b>	4-COOEt	13.78	3.40	1.10	3.09
<b>5h</b>	4-COMe	13.26	4.19	1.10	3.81
<b>5i</b>	4-CN	13.04	12.6	4.90	2.51
<b>5j</b>	4-NO <sub>2</sub>	11.98	19.8	8.86	2.23

<sup>a</sup>The pK<sub>a</sub> data for Y-substituted-phenols in anhydrous EtOH were taken from ref 14.

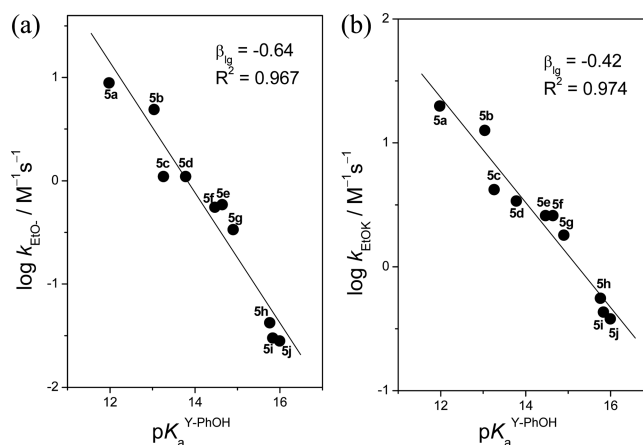
of the linear plots, respectively. The k<sub>EtOK</sub> values have been calculated from the above k<sub>EtOK</sub>/K<sub>d</sub> values and the reported K<sub>d</sub> value for EtOK. The calculated k<sub>EtO<sup>-</sup></sub> and k<sub>EtOK</sub> values in this way are summarized in Table 1 together with the pK<sub>a</sub> values of Y-substituted phenols in EtOH and the k<sub>EtOK</sub>/k<sub>EtO<sup>-</sup></sub> ratios.

**Deduction of Reaction Mechanism.** As shown in Table 1, the second-order rate constant for the reaction with the ion-paired EtOK (*i.e.*, k<sub>EtOK</sub>) is larger than that for the reaction with the dissociated EtO<sup>-</sup> (*i.e.*, k<sub>EtO<sup>-</sup></sub>) in all cases. This implies that the ion-paired EtOK is more reactive than the dissociated EtO<sup>-</sup> and is consistent with the idea that K<sup>+</sup> ion catalyzes the current reactions.



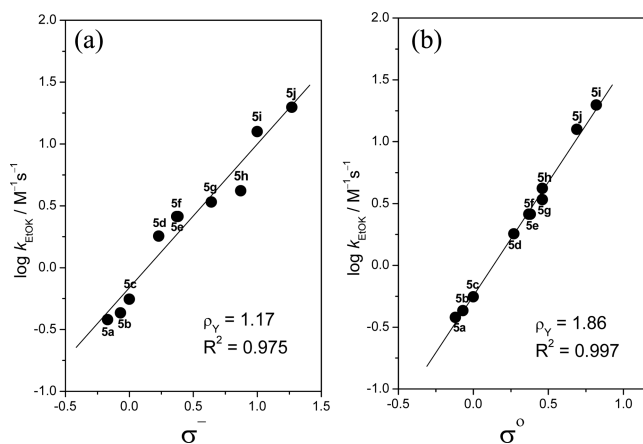
K<sup>+</sup> ion could catalyze the current reactions either by increasing the electrophilicity of the electrophilic center through TS<sub>I</sub> or by enhancing the nucleofugality of the leaving group *via* TS<sub>II</sub>. One might exclude TS<sub>III</sub>, which would increase both the electrophilicity of the reaction center and the nucleofugality of the leaving group. This is because the EtO<sup>-</sup> and K<sup>+</sup> ions in TS<sub>III</sub> are not ion-paired species. It is apparent that the enhanced nucleofugality through TS<sub>II</sub> is effective only for reactions in which departure of the leaving group occurs in the rate-determining step (RDS) but is ineffective for reactions in which the leaving group departs after the RDS. Thus, information on the reaction mechanism including the RDS is necessary to investigate the role of K<sup>+</sup> ion in the current reactions.

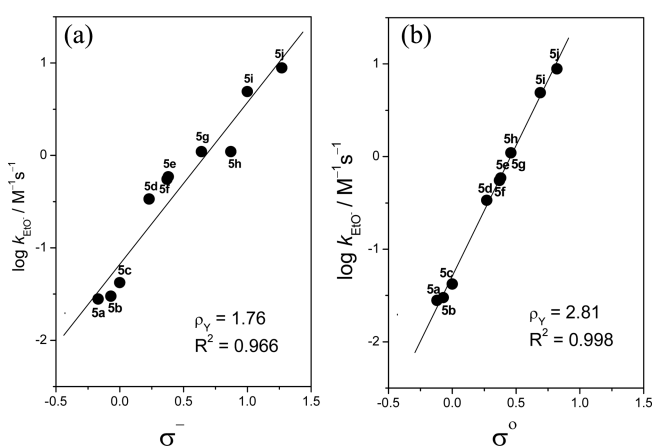
Nucleophilic substitution reactions of esters have been reported to proceed through a concerted mechanism or *via* a stepwise pathway in which the rate-determining step (RDS) is dependent on the basicity of the incoming nucleophile and the leaving group (Scheme 1).<sup>15-20</sup> To investigate the reaction mechanism, Brønsted-type plots have been constructed for the reactions of **5a-j** with the dissociated EtO<sup>-</sup> and ion-paired

**Figure 3.** Brønsted-type plots for the reactions of **5a-j** with dissociated EtO<sup>-</sup> (a) and ion-paired EtOK (b) in anhydrous EtOH at 25.0 ± 0.1 °C. The identity of points is given in Table 1.

EtOK. As shown in Figure 3, the Brønsted-type plots are linear but exhibit highly scattered points with a β<sub>lg</sub> value of -0.64 or -0.42. A β<sub>lg</sub> value of -0.5 ± 0.1 is typical for reactions reported previously to proceed through a concerted mechanism.<sup>15-20</sup> However, one cannot conclude whether the reactions in this study proceed through a concerted mechanism or *via* a stepwise pathway from the poorly correlated Brønsted-type plots. More conclusive information is required to deduce the reaction mechanism.

One might expect that a partial negative charge develops on the O atom of the leaving aryloxy, if departure of the leaving group occurs in the RDS. Since such negative charge could be delocalized to the substituent Y in the leaving group through the resonance interaction, σ<sup>-</sup> constants should result in a much better Hammett correlation than σ<sup>o</sup> constants. In contrast, if the reaction proceeds through a stepwise mechanism, departure of the leaving group would occur after the RDS, because EtO<sup>-</sup> is more basic and a poorer nucleofuge than Y-substituted-phenoxide. Accordingly, if the current reaction proceeds through a stepwise mechanism, no negative charge would develop on the O atom of the

**Figure 4.** Hammett correlations with σ<sup>-</sup> (a) and σ<sup>o</sup> (b) constants for the reactions of **5a-j** with the ion-paired EtOK in anhydrous EtOH at 25.0 ± 0.1 °C. The identity of points is given in Table 1.



**Figure 5.** Hammett correlations with  $\sigma^-$  (a) and  $\sigma^o$  (b) constants for the reactions of **5a-j** with the dissociated  $\text{EtO}^-$  in anhydrous  $\text{EtOH}$  at  $25.0 \pm 0.1$  °C. The identity of points is given in Table 1.

leaving group in the rate-determining TS. In this case,  $\sigma^o$  constants should result in a much better Hammett correlation than  $\sigma^-$  constants.

To deduce the reaction mechanism, Hammett plots have been constructed using  $\sigma^-$  and  $\sigma^o$  constants for the reactions with the ion-paired  $\text{EtOK}$ . As shown in Figure 4, the Hammett plot correlated with  $\sigma^-$  constants (a) exhibits highly scattered points ( $R^2 = 0.975$ ). In contrast, the corresponding plot correlated with  $\sigma^o$  constants (b) results in an excellent linear correlation ( $R^2 = 0.997$ ) with  $\rho_Y = 1.86$ . This is only possible for a stepwise mechanism in which departure of the leaving group occurs after RDS.

A similar result is demonstrated in Figure 5, although the slope of the Hammett plot is larger for the reactions with the dissociated  $\text{EtO}^-$  ( $\rho_Y = 2.81$ ) than for those with the ion-paired  $\text{EtOK}$  ( $\rho_Y = 1.86$ ). Thus, one can conclude that the reactions of **5a-j** with the dissociated  $\text{EtO}^-$  and ion-paired  $\text{EtOK}$  proceed through a stepwise mechanism with formation of an intermediate being the RDS.

**Role of  $\text{K}^+$  Ion.** As mentioned in the preceding section,  $\text{K}^+$  ion could catalyze the reaction by increasing either the electrophilicity of the reaction center through  $\text{TS}_I$  or the nucleofugality of the leaving group *via*  $\text{TS}_{II}$ . However,  $\text{TS}_{II}$  is not effective for reactions in which departure of the leaving group occurs after the RDS. It is noted that the current reactions proceed through a stepwise mechanism in which departure of the leaving group occurs after RDS. Thus, one can conclude that the current reactions are catalyzed by increasing the electrophilicity through  $\text{TS}_I$  rather than by enhancing the nucleofugality of the leaving group *via*  $\text{TS}_{II}$ .

The above argument can be further supported by the  $k_{\text{EtOK}}/k_{\text{EtO}^-}$  ratio (Table 1), which represents the magnitude of the catalytic effect shown by  $\text{K}^+$  ion. One might expect that the  $k_{\text{EtOK}}/k_{\text{EtO}^-}$  ratio would be strongly dependent on the electronic nature of the substituent Y in the leaving group, if the reactions are catalyzed through  $\text{TS}_{II}$ . This is because the substituent Y is close to the O atom of the leaving group (proximal). On the contrary, the  $k_{\text{EtOK}}/k_{\text{EtO}^-}$  ratio would be independent of the electronic nature of the substituent Y, if

the reactions are catalyzed through  $\text{TS}_I$ . This is because the substituent Y is located too far from the O atom of the C=O bond to influence the electron density of the O atom (distal). In fact, Table 1 shows that the  $k_{\text{EtOK}}/k_{\text{EtO}^-}$  ratio is almost independent of the electronic nature of the substituent Y. This supports the preceding idea that the current reactions are catalyzed by increasing the electrophilicity of the reaction center through  $\text{TS}_I$ .

## Conclusions

The current study has allowed us to conclude the following: (1) The ion-paired  $\text{EtOK}$  is more reactive than the dissociated  $\text{EtO}^-$  toward the substrates **5a-j**. (2) The Brønsted-type plots for the reactions with the dissociated  $\text{EtO}^-$  and ion-paired  $\text{EtOK}$  exhibit highly scattered points with  $\beta_{\text{lg}} = -0.5 \pm 0.1$ . (3) The Hammett plots correlated with  $\sigma^o$  constants result in excellent linear correlations, indicating that no negative charge develops on the O atom of the leaving aryloxides. (4) The reactions with the dissociated  $\text{EtO}^-$  and ion-paired  $\text{EtOK}$  proceed through a stepwise mechanism in which departure of the leaving group occurs after the RDS. (5)  $\text{K}^+$  ion catalyzes the reactions by increasing the electrophilicity of the reaction center through  $\text{TS}_I$ .

## Experimental Section

**Materials.** Y-Substituted-phenyl benzoates (**5a-j**) were prepared by modification of literature procedures by adding the respective phenol to the solution of benzoyl chloride in methylene chloride as reported previously.<sup>21</sup> The crude product was purified by column chromatography (silica gel, methylene chloride/*n*-hexane 50/50). The purity was checked by their melting points and  $^1\text{H}$  NMR spectra. 18-Crown-6-ether was recrystallized from MeCN and dried under vacuum. The anhydrous ethanol used was further dried over magnesium and distilled under  $\text{N}_2$  just before use.

**Kinetics.** The kinetic study was performed with a UV-vis spectrophotometer equipped with a constant temperature circulating bath to maintain the temperature in the reaction cell at  $25.0 \pm 0.1$  °C. The reaction was followed by monitoring the appearance of the leaving Y-substituted phenoxide ion. All reactions were carried out under pseudo-first-order conditions in which  $\text{EtOK}$  concentrations were at least 20 times greater than the substrate concentration. The  $\text{EtOK}$  stock solution was prepared by dissolving potassium metal in anhydrous ethanol under nitrogen and stored in the refrigerator. The concentration of  $\text{EtOK}$  was determined by titration with mono potassium phthalate.

All solutions were prepared freshly just before use under nitrogen and transferred by gas-tight syringes. Typically, the reaction was initiated by adding 5  $\mu\text{L}$  of a 0.02 M solution of the substrate in  $\text{CH}_3\text{CN}$  by a 10  $\mu\text{L}$  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  $\text{EtOK}$  solution.

**Product Analysis.** Y-Substituted phenoxide 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.

**Acknowledgments.** This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (2012-R1A1B-3001637).

## References

- (a) Anslyn, E. V.; Dougherty, D. E. *Modern Physical Organic Chemistry*; University Science Books: Sausalito, U.S.A., 2006; pp 500-502. (b) Carroll, F. A. *Perspectives on Structure and Mechanism in Organic Chemistry*; Brooks/Cole: New York, U.S.A., 1998; p 445. (c) Page, M. I.; Williams, A. *Organic & Bioorganic Mechanisms*; Longman: Singapore, 1997; pp 179-183.
- (a) Mohamed, M. F.; Sanchez-Lombardo, I.; Neverov, A. A.; Brown, R. S. *Org. Biomol. Chem.* **2012**, *10*, 631-639. (b) Barrera, I. F.; Maxwell, C. I.; Neverov, A. A.; Brown, R. S. *J. Org. Chem.* **2012**, *77*, 4156-4160. (c) Raycroft, M. A. R.; Liu, C. T.; Brown, R. S. *Inorg. Chem.* **2012**, *51*, 3846-3854. (d) Brown, R. S. *Prog. Inorg. Chem.* **2012**, *57*, 55-117. (e) Dhar, B. B.; Edwards, D. R.; Brown, R. S. *Inorg. Chem.* **2011**, *50*, 3071-3077. (f) Edwards, D. R.; Neverov, A. A.; Brown, R. S. *Inorg. Chem.* **2011**, *50*, 1786-1797. (g) Brown, R. S.; Lu, Z. L.; Liu, C. T.; Tsang, W. Y.; Edwards, D. R.; Neverov, A. A. *J. Phys. Org. Chem.* **2010**, *23*, 1-15.
- (a) Feng, G.; Tanifum, E. A.; Adams, H.; Hengge, A. C. *J. Am. Chem. Soc.* **2009**, *131*, 12771-12779. (b) 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. (c) 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. (d) Davies, A. G. *J. Chem. Res.* **2008**, 361-375. (e) Davies, A. G. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1997-2010. (f) Fife, T. H.; Chaffee, L. *Bioorg. Chem.* **2000**, *28*, 357-373.
- (a) Chei, W. S.; Ju, H.; Suh, J. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 1533-1537. (b) Chei, W. S.; Ju, H.; Suh, J. *J. Biol. Inorg. Chem.* **2011**, *16*, 511-519. (c) Kim, H. M.; Jang, B.; Cheon, Y. E.; Suh, M. P.; Suh, J. *J. Biol. Inorg. Chem.* **2009**, *14*, 151-157. (d) Chei, W. S.; Suh, J. *Prog. Inorg. Chem.* **2007**, *55*, 79-142. (e) Jeung, C. S.; Song, J. B.; Kim, Y. H.; Suh, J. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 3061-3064. (f) Suh, J.; Son, S. J.; Suh, M. P. *Inorg. Chem.* **1998**, *37*, 4872-4877. (g) Suh, J. *Acc. Chem. Res.* **1992**, *25*, 273-279. (h) Lee, J. H.; Park, J.; Lah, M. S.; Chin, J.; Hong, J. I. *Org. Lett.* **2007**, *9*, 3729-3731. (i) Livieri, M.; Manicin, F.; Saielli, G.; Chin, J.; Tonellato, U. *Chem. Eur. J.* **2007**, *13*, 2246-2256.
- (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.
- (a) Koo, I. S.; Ali, D.; Yang, K.; Park, Y.; Esbata, A.; van Loon, G. W.; Buncel, E. *Can. J. Chem.* **2009**, *87*, 433-439. (b) Buncel, E.; Albright, K. G.; Onyido, I. *Org. Biomol. Chem.* **2005**, *3*, 1468-1475. (c) Buncel, E.; Albright, K. G.; Onyido, I. *Org. Biomol. Chem.* **2004**, *2*, 601-610. (d) Nagelkerke, R.; Thatcher, G. R. J.; Buncel, E. *Org. Biomol. Chem.* **2003**, *1*, 163-167. (e) Buncel, E.; Nagelkerke, R.; Thatcher, G. R. J. *Can. J. Chem.* **2003**, *81*, 53-63.
- (a) Cacciapaglia, R.; Mandolini, L. *Chem. Soc. Rev.* **1993**, *22*, 221-231. (b) Cacciapaglia, R.; Mandolini, L.; Tomei, A. *J. Chem. Soc., Perkin Trans. 2* **1994**, 367372. (c) Cacciapaglia, R.; Van Doorn, A. R.; Mandolini, L.; Reinhoudt, D. N.; Verboom, W. *J. Am. Chem. Soc.* **1992**, *114*, 2611-2617. (d) Cacciapaglia, R.; Mandolini, L.; Reinhoudt, D. N.; Verboom, W. *J. Phys. Org. Chem.* **1992**, *5*, 663-669.
- Um, I. H.; Shin, Y. H.; Park, J. E.; Kang, J. S.; Buncel, E. *Chem. Eur. J.* **2012**, *18*, 961-968.
- (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.
- (a) Um, I. H.; Kang, J. S.; Shin, Y. H.; Buncel, E. *J. Org. Chem.* **2013**, *78*, 490-497. (b) Um, I. H.; Kang, J. S.; Shin, M. A. *Bull. Chem. Soc. Jpn.* **2013**, *86*, 736-741. (c) Um, I. H.; Seo, J. Y.; Kang, J. S.; An, J. S. *Bull. Chem. Soc. Jpn.* **2012**, *85*, 1007-1013.
- (a) Um, I. H.; Seo, J. A.; Mishima, M. *Chem. Eur. J.* **2011**, *17*, 3021-3027. (b) Um, I. H.; Kim, C. W.; Kang, J. S.; Lee, J. I. *Bull. Korean Chem. Soc.* **2012**, *33*, 519-523.
- Pechanec, V.; Kocian, O.; Zavada, J. *Collect. Czech. Chem. Commun.* **1982**, *47*, 3405-3411.
- Barthel, J.; Justice, J.-C.; Wachter, R. Z. *Phys. Chem.* **1973**, *84*, 100-113.
- Um, I. H.; Hong, Y. J.; Kwon, D. S. *Tetrahedron* **1997**, *53*, 5073-5082.
- (a) Um, I. H.; Bea, A. R. *J. Org. Chem.* **2012**, *77*, 5781-5787. (b) Um, I. H.; Bea, A. R. *J. Org. Chem.* **2011**, *76*, 7510-7515. (c) Um, I. H.; Im, L. R.; Kim, E. H.; Shin, J. H. *Org. Biomol. Chem.* **2010**, *8*, 3801-3806. (d) Um, I. H.; Park, Y. M.; Fujio, M.; Mishima, M.; Tsuno, Y. *J. Org. Chem.* **2007**, *72*, 4816-4821.
- (a) Um, I. H.; Kim, E. H.; Lee, J. Y. *J. Org. Chem.* **2009**, *74*, 1212-1217. (b) Um, I. H.; Yoon, S. R.; Park, H. R.; Han, H. J. *Org. Biomol. Chem.* **2008**, *6*, 1618-1624. (c) Um, I. H.; Hwang, S. J.; Yoon, S. R.; Jeon, S. E.; Bae, S. K. *J. Org. Chem.* **2008**, *73*, 7671-7677.
- (a) Um, I. H.; Han, J. Y.; Shin, Y. H. *J. Org. Chem.* **2009**, *74*, 3073-3078. (b) Um, I. H.; Han, J. Y.; Hwang, S. J. *Chem. Eur. J.* **2008**, *14*, 7324-7330. (c) Um, I. H.; Akhtar, K.; Shin, Y. H.; Han, J. Y. *J. Org. Chem.* **2007**, *72*, 3823-3829.
- (a) Page, M. I.; Williams, A. *Organic and Bio-organic Mechanisms*; Longman: Singapore, 1997; Chapt. 7. (b) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 3rd ed.; Harper Collins Publishers: New York, 1987; Chapt. 8. (c) Jencks, W. P. *Catalysis in Chemistry and Enzymology*; McGraw Hill: New York, 1969; Chapt. 10.
- (a) Oh, H. K.; Ku, M. H.; Lee, H. W.; Lee, I. *J. Org. Chem.* **2002**, *67*, 8995-8998. (b) Oh, H. K.; Ku, M. H.; Lee, H. W.; Lee, I. *J. Org. Chem.* **2002**, *67*, 3874-3877. (c) Oh, H. K.; Kim, S. K.; Lee, H. W.; Lee, I. *New J. Chem.* **2001**, *25*, 313-317.
- (a) Castro, E. A.; Aliaga, M.; Campodonico, P. R.; Cepeda, M.; Contreras, R.; Santos, J. G. *J. Org. Chem.* **2009**, *74*, 9173-9179. (b) Castro, E. A.; Ramos, M.; Santos, J. G. *J. Org. Chem.* **2009**, *74*, 6374-6377. (c) Castro, E. A.; Ugarte, D.; Rojas, M. F.; Pavez, P.; Santos, J. G. *Int. J. Chem. Kinet.* **2011**, *43*, 708-714. (d) Castro, E. A.; Aliaga, M.; Santos, J. G. *J. Org. Chem.* **2005**, *70*, 2679-2685.
- Kim, S. I.; Kim, E. H.; Um, I. H. *Bull. Korean Chem. Soc.* **2010**, *31*, 689-693.