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Nonlinear Hammett plots in pyridinolysis of 2,4-dinitrophenyl X-substituted benzoates: change in RDS *versus* resonance contribution†‡

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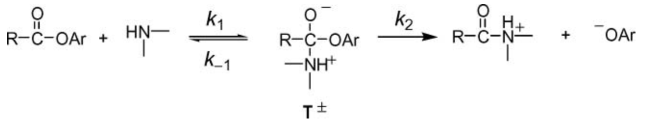
Second-order rate constants (k_{OH^-}) have been measured for nucleophilic substitution reactions of 2,4-dinitrophenyl X-substituted benzoates (**1a–j**) with *Z*-substituted pyridines in 80 mol% H_2O/20 mol% DMSO at 25.0 ± 0.1 °C. The Hammett plots for the reactions of **1a–j** with pyridines consist of two intersecting straight lines, *i.e.*, a large ρ value for the reactions of substrates (**1a–c**) possessing an electron-donating group (EDG) in the benzoyl moiety and a small one for substrates (**1e–j**) bearing an electron-withdrawing group (EWG). The nonlinear Hammett plots have been attributed to stabilization of the ground state of substrates **1a–c** through resonance interactions between the electron-donating substituent and the carbonyl functionality, since the corresponding Yukawa–Tsuno plots exhibit excellent linear correlations with large *r* values. It has been shown that substrates **1e–j** are not unusually more reactive than would be expected from the Hammett substituent constants, but rather, substrates **1a–c** exhibit lower reactivity than would be predicted. The Brønsted-type plots for pyridinolysis of **1a–j** are linear with β_{nuc} = 0.74–0.98, indicating that the reaction proceeds through a stepwise mechanism in which the second step is the RDS. It has been concluded that the electronic nature of the substituent X in the benzoyl moiety does not influence the RDS, but the degree of bond formation (or the effective charge on the nucleophilic site) in the transition state becomes more significant as the substituent X changes from a strong EDG to a strong EWG.

Introduction

Nucleophilic substitution reactions of esters with amines have intensively been investigated due to their importance in biological processes as well as synthetic applications.[1–12] Aminolysis of carboxylic esters has been reported to proceed through a stepwise mechanism as shown in Scheme 1 on the basis of curved Brønsted-type plots often observed for reactions of esters possessing a good leaving group (*e.g.*, 2,4-dinitrophenoxide).[1–12] It is now firmly understood that RDS is governed by the basicity of the incoming amine and the leaving group, *i.e.*, rate-determining step changes from breakdown of a zwitterionic tetrahedral intermediate $T^{\pm}$ (*i.e.*, the k_2 step) to its formation (*i.e.*, the k_1 step) as the amine becomes more basic than the leaving group by 4 to 5 pK_a units or the leaving group becomes less basic than the amine.



Scheme 1 Aminolysis of carboxylic esters.

However, the effect of substituents in the nonleaving group on mechanism remains controversial. In nucleophilic substitution reactions of diaryl carbonates with quinuclidines in H_2O, Gresser and Jencks have concluded that the departure of the amine from $T^{\pm}$ (the k_{-1} process) is favored over that of the leaving group (the k_2 process), as the substituent in the nonleaving group changes from an electron-donating group (EDG) to a strong electron-withdrawing group (EWG).[10] A similar conclusion has been drawn in pyridinolysis of 2,4-dinitrophenyl X-substituted benzoates,[11] aminolysis of *S*-2,4-dinitrophenyl X-substituted thiobenzoates,[12] pyridinolysis of aryl dithiobenzoates and related esters,[8f,g] and in theoretical calculations on phenolysis of aryl acetates.[8h] Accordingly, it has been concluded that the k_2/k_{-1} ratio decreases as the substituent X in the nonleaving group changes from an EDG to an EWG.[10–12] In contrast, we have proposed that the k_2/k_{-1} ratio is independent of the electronic nature of the substituent in the nonleaving-group. This is because expulsion of the nucleofuges (*i.e.*, the k_2 and k_{-1} processes) would be retarded by an EWG in the nonleaving group but accelerated by an EDG, since both nucleofuges depart with the electron pair originally bonded to the remainder of the zwitterionic tetrahedral intermediate $T^{\pm}$. In fact, we have shown that the k_2/k_{-1} ratio is little influenced by the nature of substituents X in the nonleaving group for nucleophilic substitution reactions of *O*-4-nitrophenyl X-substituted thionobenzoates with a series of pyridines.[6d]

Pyridinolysis of 2,4-dinitrophenyl benzoate has recently been reported to proceed through a stepwise mechanism with a change in rate-determining step on the basis of a curved Brønsted-type plot, *i.e.*, RDS changes from the k_2 step to the k_1 process as the incoming pyridine becomes more basic than the leaving

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† This paper is dedicated with respect and affection to the late Professor Chi Sun Hahn, an inspiring teacher and mentor.

‡ Electronic supplementary information (ESI) available: Brønsted-type plots for reactions of **1a–j** with pyridines (Figures S1–S10). Kinetic conditions and results for reactions of **1a–j** with pyridines (Table S1–S30). See DOI: 10.1039/c0ob00031k

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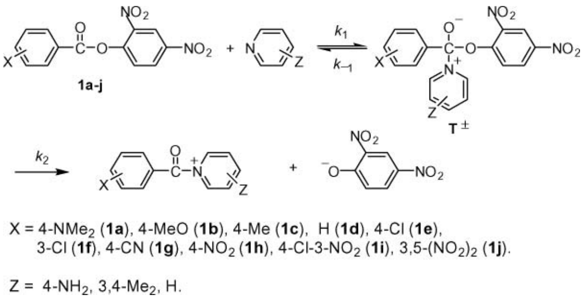
2,4-dinitrophenoxide ion by 5.4 pK_a units.[6f] The microscopic rate constants determined have also supported the proposed mechanism. Our study has been extended to reactions of 2,4-dinitrophenyl X-substituted benzoates (**1a–j**) with three *Z*-substituted pyridines (Scheme 2) to get further information on the mechanism and transition-state (TS) structures. We wish to report that the electronic nature of the substituent X does not influence RDS but the degree of bond formation between the nucleophile and electrophile (or the effective charge on the nucleophilic site) in the TS becomes more significant as the substituent X changes from a strong EDG to a strong EWG.



Scheme 2 Pyridinolysis of 2,4-dinitrophenyl X-substituted benzoates.

Results and discussion

All reactions in this study obeyed pseudo-first-order kinetics. Pseudo-first-order rate constants (k_{obsd}) were determined from the equation ln ($A_\infty - A_t$) = $-k_{obsd}t + C$. The plots of k_{obsd} *vs.* pyridine concentration were linear and passed through the origin, indicating that contribution of H_2O and/or OH^- ion from hydrolysis of pyridines to k_{obsd} is negligible. Thus, the rate law is given by eqn (1), in which [S] and [Pyr] represent the concentration of the substrate and pyridine, respectively. The second-order rate constants (k_{OH^-}) were determined from the slope of the linear plots of k_{obsd} *vs.* pyridine concentration, and are summarized in Table 1.

$$\text{Rate} = k_{obsd}[\text{S}], \text{ where } k_{obsd} = k_{OH^-}[\text{Pyr}] \quad (1)$$

Effect of substituent X on reactivity and RDS

As shown in Table 1, the second-order rate constant (k_{OH^-}) increases significantly as the substituent X changes from a strong EDG to a strong EWG, *e.g.*, the k_{OH^-} value for reactions of **1a–j** with 4-aminopyridine increases from 0.499 $M^{-1}s^{-1}$ to 32.0 and 2340 $M^{-1}s^{-1}$ as the substituent X in the benzoyl moiety changes from 4-NMe_2 to H and 3,5-$(NO_2)_2$, respectively. A similar result is shown for the corresponding reactions with 3,4-dimethylpyridine and unsubstituted pyridine, indicating that the reactivity of **1a–j** is highly dependent on the electronic nature of the substituent X in the benzoyl moiety.

The effect of substituent X on reactivity is illustrated in Fig. 1 for the reactions of **1a–j** with the three pyridines. One can see that each Hammett plot consists of two intersecting straight lines. The slope of the Hammett plot for substrates possessing EDGs is steeper than that for substrates bearing EWGs, *e.g.*, $\rho = 1.68$ when $\sigma_X \leq 0$, while $\rho = 0.91$ when $\sigma_X \geq 0$ for the reactions with unsubstituted pyridine.

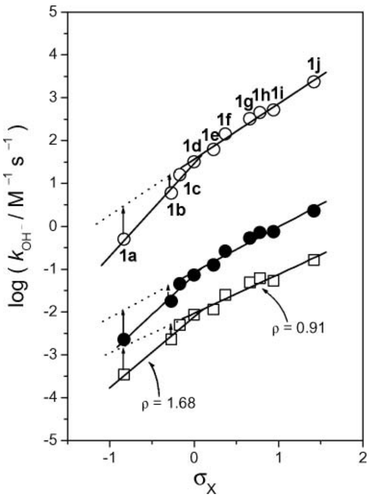


Fig. 1 Hammett plots for the reactions of 2,4-dinitrophenyl X-substituted benzoates (**1a–j**) with 4-aminopyridine (○), 3,4-dimethylpyridine (●), and pyridine (□) in 20 mol% DMSO at 25.0 ± 0.1 °C. The identity of points is given in Table 1.

Nonlinear Hammett plots have traditionally been interpreted as a change in reaction mechanism or RDS depending on the shape of curvature.[13,14] Upward curvature often found for nucleophilic substitution reactions of benzylic systems has been attributed to a change in mechanism from S_N1 to S_N2, *e.g.*, substrates possessing an EDG proceed through an S_N1 mechanism with a

Table 1 Summary of second-order rate constants (k_{OH^-}) for reactions of 2,4-dinitrophenyl X-substituted benzoates (**1a–j**) with 4-aminopyridine, 3,4-dimethylpyridine, and pyridine in 20 mol% DMSO at 25.0 ± 0.1 °C

		k_{OH^-}/$M^{-1}s^{-1}$		
	X	4-Aminopyridine	3,4-Dimethylpyridine	Pyridine
1a	4-NMe_2	$(4.99 \pm 0.08) \times 10^{-1}$	$(2.27 \pm 0.05) \times 10^{-3}$	$(3.47 \pm 0.02) \times 10^{-4}$
1b	4-MeO	5.97 ± 0.04	$(1.77 \pm 0.03) \times 10^{-2}$	$(2.31 \pm 0.10) \times 10^{-3}$
1c	4-Me	15.8 ± 0.1	$(4.53 \pm 0.07) \times 10^{-2}$	$(4.96 \pm 0.08) \times 10^{-3}$
1d	H	32.0 ± 1.6	$(7.25 \pm 0.09) \times 10^{-2}$	$(8.61 \pm 0.01) \times 10^{-3}$
1e	4-Cl	62.0 ± 1.4	$(1.24 \pm 0.02) \times 10^{-1}$	$(1.14 \pm 0.01) \times 10^{-2}$
1f	3-Cl	142 ± 4	$(2.61 \pm 0.05) \times 10^{-1}$	$(2.48 \pm 0.004) \times 10^{-2}$
1g	4-CN	321 ± 3	$(5.31 \pm 0.08) \times 10^{-1}$	$(4.85 \pm 0.07) \times 10^{-2}$
1h	4-NO_2	446 ± 3	$(7.13 \pm 0.08) \times 10^{-1}$	$(6.14 \pm 0.40) \times 10^{-2}$
1i	4-Cl-3-NO_2	520 ± 5	$(7.43 \pm 0.08) \times 10^{-1}$	$(5.34 \pm 0.07) \times 10^{-2}$
1j	3,5-$(NO_2)_2$	2340 ± 20	2.28 ± 0.03	$(1.64 \pm 0.06) \times 10^{-1}$

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negative ρ value, while those bearing an EWG proceed through an S_N2 pathway with a positive ρ value.[13,14] In contrast, downward curvature has been ascribed to a change in RDS upon changing substituents from EDGs to EWGs.[13,14] Such a downward Hammett plot has been reported for reactions of a series of X-substituted benzaldehydes with ammonia, *i.e.*, benzaldehydes possessing an EDG result in a positive ρ value while those with an EWG yield a negative ρ value.[13a] A similar downward curvature has been found for the corresponding reactions with semicarbazide in a weakly acidic medium (pH = 3.9), *i.e.*, the ρ for the Hammett plot changes from a large positive value to a small one as the substituent changes from EDGs to EWGs.[13b]

Therefore, one might attribute the nonlinear Hammett plots shown in Fig. 1 to a change in RDS, *i.e.*, from formation of $T^{\pm}$ to its breakdown to yield the products as the substituent in the benzoyl moiety changes from EDGs to EWGs. This idea appears to be reasonable, since one can expect that an EDG in the benzoyl moiety would retard nucleophilic attack (*i.e.*, a decrease in k_1) but would accelerate departure of the negatively charged leaving group (*i.e.*, an increase in k_2). In contrast, an EWG would increase k_1 but would decrease k_2. Accordingly, one can expect a large ρ value when the k_1 step is the RDS but a small one when the k_2 process is the RDS due to the opposite substituent effect. In fact, Fig. 1 shows that the ρ value decreases from 1.68 for the reactions of pyridine with substrates **1a–d** to 0.91 for those with **1d–j**. Thus, the nonlinear Hammett plots might be taken as evidence for a change in RDS upon changing the substituent X in the benzoyl moiety.

However, we propose that the nonlinear Hammett plots in Fig. 1 are not due to a change in RDS. This is because the RDS of a stepwise mechanism should be determined by the k_2/k_{-1} ratio (*i.e.*, RDS = k_1 when $k_2/k_{-1} > 1$ or RDS = k_2 when $k_2/k_{-1} < 1$) but not by the magnitude of k_1 and k_2. Furthermore, k_1 and k_2 values cannot be compared directly, since the former is a second-order rate constant while the latter is a first-order rate constant.

Origin of nonlinear Hammett plots

To examine the above argument that the nonlinear Hammett plots shown in Fig. 1 are not due to a change in RDS, Yukawa–Tsuno plots have been constructed. The Yukawa–Tsuno equation, eqn (2), has originally been derived to account for solvolysis of benzylic systems in which a positive charge develops in the TS.[15,16] We have recently shown that Yukawa–Tsuno plots are highly effective to elucidate ambiguities in the mechanism for nucleophilic substitution reactions of aryl diphenylphosphinates and related esters.[17]

$$\log (k_X/k_H) = \rho[\sigma_X^{\circ} + r(\sigma_X^{+} - \sigma_X^{\circ})] \qquad (2)$$

As shown in Fig. 2, the Yukawa–Tsuno plots exhibit excellent linear correlations with $\rho = 0.92$–1.31 and $r = 0.79$–0.92, indicating that the reactions proceed through a common mechanism without changing the RDS. The r value in eqn (2) represents the resonance demand of the reaction center or the extent of resonance contribution, while the term $(\sigma_X^{+} - \sigma_X^{\circ})$ is the resonance substituent constant that measures the capacity for π-delocalization of the π-electron donor substituent.[15,16] The r values of 0.79–0.92 found in the current study suggest that resonance interaction is relatively significant.

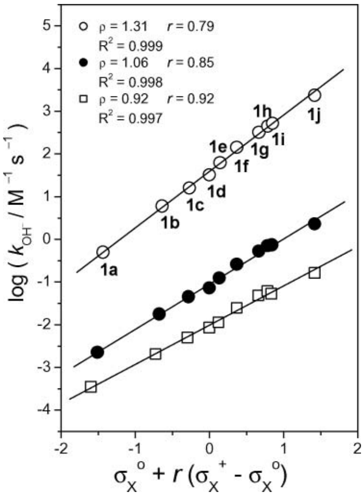
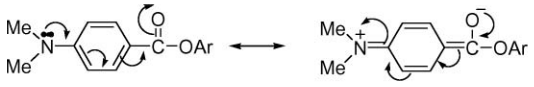


Fig. 2 Yukawa–Tsuno plots for reactions of 2,4-dinitrophenyl X-substituted benzoates (**1a–j**) with 4-aminopyridine (○), 3,4-dimethylpyridine (●), and pyridine (□) in 20 mol% DMSO at 25.0 ± 0.1 °C. The identity of points is given in Table 1.

Resonance structures as modeled by I and II are possible for substrates possessing an EDG in the benzoyl moiety (*e.g.*, **1a–c**). Accordingly, one can suggest that stabilization of the ground state (GS) through resonance interactions is responsible for the negative deviation exhibited by substrates **1a–c** from the Hammett plots shown in Fig. 1. This argument can be further supported by the fact that the substrate possessing a stronger EDG (*e.g.*, **1a**) deviates more significantly from the Hammett plot. Thus, one can conclude that the nonlinear Hammett plots shown in Fig. 1 are not due to a change in RDS and deduction of reaction mechanism based just on a nonlinear Hammett plot can be misleading.



I II

GS destabilization *vs.* GS stabilization

Table 1 shows that substrates possessing an EWG in the benzoyl moiety are more reactive than those bearing an EDG. Neuvonen *et al.* have investigated the origin of enhanced reactivities of esters possessing an EWG in the leaving group of aryl acetates or in the nonleaving group of alkyl benzoates.[18] They measured ^{13}C NMR shifts of the carbonyl carbon and frequencies of the C=O stretching vibration in various Y-substituted phenyl X-substituted benzoates and acetates, and found that an EWG in the leaving- or nonleaving-group causes upfield ^{13}C NMR shifts of the carbonyl carbon and higher frequencies of the C=O stretching vibration.[18] Their PM3 calculations have also shown that an EWG increases the electron density of the carbonyl carbon, implying that an EWG in the leaving- or nonleaving-group does not increase the electrophilicity of the carbonyl carbon.[18] Thus, the enhanced reactivity of esters possessing an EWG has been attributed to destabilization of the GS of substrates, since an EWG in the leaving group or in the nonleaving benzoyl moiety would inhibit the resonance interactions III ↔ IV ↔ V.[18]

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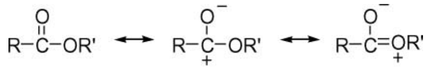
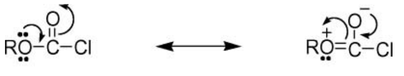


III IV V

However, we propose that the GS stabilization is more responsible than the GS destabilization suggested previously by Neuvonen *et al.* for the reactivity pattern found in the current reactions on the basis of the following reasons. If destabilization of the GS through decreased resonance interactions (*e.g.*, III, IV and V) were responsible for the high reactivity shown by substrates possessing an EWG, these substrates should have resulted in positive deviation from the Hammett plot. A careful examination of the Hammett plots in Fig. 1 reveals that substrates possessing an EWG (*i.e.*, **1e–j**) do not exhibit positive deviation from the Hammett plots. On the contrary, substrates bearing an EDG (*i.e.*, **1a–c**) result in negative deviation from the linear Hammett plot composed of substrates **1d–j**. This is consistent with the preceding argument that **1a–c** exhibit lower reactivity than would be expected from the Hammett substituent constant due to stabilization of the GS through the resonance interaction as modeled by I and II.

A similar conclusion has been drawn for solvolysis of methyl chloroformate and acetyl chloride in aqueous acetone. The former was reported to be 9 × 10^3 times less reactive than the latter.[19] Kevill *et al.* have concluded that stabilization of the GS through the resonance interaction VI ↔ VII, analogous to that suggested in the current system (*i.e.*, I ↔ II), is responsible for the decreased reactivity of methyl chloroformate, since such resonance interactions are not possible for acetyl chloride.[19]



VI VII

Effect of substituent X on TS structure

To investigate the effect of substituent X on the TS structure, Brønsted-type plots for the reactions of **1a–j** with three pyridines have been constructed. The plots shown in Figures S1–S10 in the ESI† exhibit excellent linear correlation with $\beta_{nuc} = 0.74–0.98$ (see also Table 2).[20] One can get useful information on reaction mechanisms from the magnitude of β_{nuc} values as well as the shape of Brønsted-type plots.[13] In fact, the biphasic Brønsted-type plot obtained from reactions of 2,4-dinitrophenyl benzoate (**1d**) with a series of pyridines has been taken as evidence for a stepwise mechanism.[6f] Besides, the RDS for the pyridinolysis of **1d** has been suggested to change from the k_2 step to the k_1 process as the pK_a of the conjugate acids of pyridines becomes larger than 9.5 on the basis of the magnitude of the β_{nuc} values, *i.e.*, $\beta_{nuc} = 0.90$ when p$K_a < 9.5$ and $\beta_{nuc} = 0.40$ when p$K_a > 9.5$.[6f]

Table 2 Summary of β_{nuc} values for the reactions of 2,4-dinitrophenyl X-substituted benzoates (**1a–j**) with pyridines in 80 mol% H_2O/20 mol% DMSO at 25.0 ± 0.1 °C

	X	β_{nuc}
1a	4-NMe_2	0.74 ± 0.05
1b	4-MeO	0.81 ± 0.01
1c	4-Me	0.83 ± 0.02
1d	H	0.85 ± 0.01
1e	4-Cl	0.88 ± 0.02
1f	3-Cl	0.89 ± 0.02
1g	4-CN	0.90 ± 0.02
1h	4-NO_2	0.91 ± 0.01
1i	4-Cl-3-NO_2	0.94 ± 0.04
1j	3,5-$(NO_2)_2$	0.98 ± 0.03

It is noted that the pK_a of the conjugate acids of the pyridines employed in this study is smaller than 9.5. Furthermore, β_{nuc} values of 0.74–0.98 obtained in this study are typical for reactions reported previously to proceed through a stepwise mechanism in which breakdown of $T^{\pm}$ is the RDS.[1–12] Therefore, one can suggest that the pyridinolysis of **1a–j** proceeds through a stepwise mechanism with breakdown of $T^{\pm}$ to the products being the RDS regardless of the nature of substituent X. This is consistent with the preceding argument that the RDS is not influenced by the nature of substituent X in the benzoyl moiety.

To investigate the effect of the substituent X on the TS structure, the β_{nuc} values are correlated with σ_X constants. As shown in Fig. 3, β_{nuc} increases linearly as the substituent X changes from a strong EDG to a strong EWG. It has generally been understood that the magnitude of β_{nuc} values represents a relative degree of bond formation between the nucleophile and electrophile (or an effective charge developed on the nucleophilic site) in the TS.[13] Thus, one can suggest that the degree of bond formation (or the effective charge) in the TS becomes more significant as the substituent X in the benzoyl moiety changes from a strong EDG to a strong EWG since β_{nuc} increases linearly with increasing electron withdrawing ability of the substituent X.

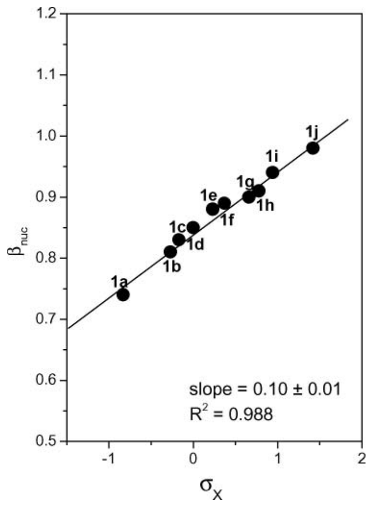


Fig. 3 Plot of β_{nuc} *versus* σ constants for the reactions of **1a–j** with pyridines in 80 mol% H_2O/20 mol% DMSO at 25.0 ± 0.1 °C. The identity of points is given in Table 2.

Conclusions

The current study has allowed us to conclude the following: (1) the Hammett plots obtained from reactions of **1a–j** with pyridines consist of two intersecting straight lines. (2) The nonlinear Hammett plots are not due to a change in RDS but are caused by stabilization of the GS of substrates possessing an EDG (*e.g.*, **1a–c**) through the resonance interactions I ↔ II, since the Yukawa–Tsuno plots exhibit excellent linear correlations with $\rho = 0.92–1.31$ and $r = 0.79–0.92$. (3) Substrates possessing an EWG (*e.g.*, **1e–j**)

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are not unusually more reactive than would be predicted from their Hammett substituent constants, but rather, substrates **1a–c** exhibit lower reactivity than would be expected due to stabilization of the GS through resonance interactions. (4) The pyridinolysis of **1a–j** proceeds through a stepwise mechanism with the k_2 step being the RDS. (5) The RDS is not influenced by the nature of the substituent X. However, the degree of bond formation (or the effective charge on the nucleophilic site) in the TS becomes more significant as the substituent X changes from a strong EDG to a stronger EWG.

Experimental

Materials

Compounds **1a–j** were readily prepared from the reaction of X-substituted benzoyl chloride with 2,4-dinitrophenol in the presence of triethylamine in anhydrous ether as reported previously.[2] Their purity was confirmed from melting point and spectral data such as ^{1}H NMR. Pyridines and other chemicals were of the highest quality available. Doubly glass distilled water was further boiled and cooled under nitrogen just before use. Due to low solubility of **1a–j** in pure H_2O, 80 mol% H_2O/20 mol% DMSO was used as the reaction medium.

Kinetics

The kinetic study was performed using a UV-vis spectrophotometer for slow reactions ($t_{1/2} \geq 10$ s) or a stopped-flow spectrophotometer for fast reactions ($t_{1/2} < 10$ s) equipped with a constant temperature circulating bath to keep the reaction temperature at 25.0 ± 0.1 °C. The reactions were followed by monitoring the leaving 2,4-dinitrophenoxide at 410 nm. All reactions were carried out under pseudo-first-order conditions in which the pyridine concentration was at least 20 times greater than the substrate concentration. The pyridine stock solution of *ca.* 0.2 M was prepared by dissolving 2 equiv. of pyridine and 1 equiv. of standardized HCl solution to keep the pH constant by making a self-buffered solution.

Product analysis

2,4-Dinitrophenoxide was liberated quantitatively and identified as one of the reaction products by comparison of the UV-vis spectra after completing the reactions with those of authentic samples under the same kinetic conditions.

Acknowledgements

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References

1 (*a*) W. P. Jencks, *Chem. Rev.*, 1985, **85**, 511–527; (*b*) E. A. Castro, *Chem. Rev.*, 1999, **99**, 3505–3524; (*c*) M. I. Page and A. Williams, *Organic and Bio-organic Mechanisms*, Longman, Singapore, 1997, Chapter 7.

2 (*a*) F. M. Menger and J. H. Smith, *J. Am. Chem. Soc.*, 1972, **94**, 3824–3829; (*b*) A. B. Maude and A. Williams, *J. Chem. Soc., Perkin Trans. 2*, 1997, 179–183.

3 (*a*) E. A. Castro, M. Aliaga and J. G. Santos, *J. Org. Chem.*, 2005, **70**, 2679–2685; (*b*) E. A. Castro, M. Gazitua and J. G. Santos, *J. Org. Chem.*, 2005, **70**, 8088–8092; (*c*) E. A. Castro, M. Aliaga and J. G. Santos, *J. Org. Chem.*, 2004, **69**, 6711–6714; (*d*) E. A. Castro, M. Cubillos and J. G. Santos, *J. Org. Chem.*, 2004, **69**, 4802–4807; (*e*) E. A. Castro, M. Cubillos, M. Aliaga, S. Evangelisti and J. G. Santos, *J. Org. Chem.*, 2004, **69**, 2411–2416; (*f*) E. A. Castro, M. Acuña, C. Soto, C. Trujillo, B. Vásquez and G. Santos, *J. Phys. Org. Chem.*, 2008, **21**, 816–822; (*g*) B. Galabov, S. Ilieva, B. Hadjieva, Y. Atanasov Schaefer III and H. F., *J. Phys. Chem. A*, 2008, **112**, 6700–6707.

4 (*a*) I. H. Um, Y. M. Park, M. Fujio, M. Mishima and Y. Tsuno, *J. Org. Chem.*, 2007, **72**, 4816–4821; (*b*) I. H. Um, J. Y. Lee, S. H. Ko and S. K. Bae, *J. Org. Chem.*, 2006, **71**, 5800–5803; (*c*) I. H. Um, S. E. Jeon and J. A. Seok, *Chem.–Eur. J.*, 2006, **12**, 1237–1243; (*d*) I. H. Um, J. Y. Lee, H. W. Lee, Y. Nagano, M. Fujio and Y. Ysuno, *J. Org. Chem.*, 2005, **70**, 4980–4987; (*e*) I. H. Um, K. H. Kim, H. R. Prak, M. Fujio and Y. Tsuno, *J. Org. Chem.*, 2004, **69**, 3937–3942.

5 (*a*) J. A. Ahn, Y. M. Park and I. H. Um, *Bull. Korean Chem. Soc.*, 2009, **30**, 214–218; (*b*) J. A. Seo, H. M. Lee and I. H. Um, *Bull. Korean Chem. Soc.*, 2008, **29**, 1915–1919.

6 (*a*) I. H. Um, E. H. Kim and J. Y. Lee, *J. Org. Chem.*, 2009, **74**, 1212–1217; (*b*) I. H. Um, S. J. Hwang, S. Yoon, S. E. Jeon and S. K. Bae, *J. Org. Chem.*, 2008, **73**, 7671–7677; (*c*) I. H. Um, S. Yoon, H. R. Park and H. J. Han, *Org. Biomol. Chem.*, 2008, **6**, 1618–1624; (*d*) I. H. Um, S. J. Hwang, M. H. Baek and E. J. Park, *J. Org. Chem.*, 2006, **71**, 9191–9197; (*e*) I. H. Um, E. Y. Kim, H. R. Park and S. E. Jeon, *J. Org. Chem.*, 2006, **71**, 2302–2306; (*f*) I. H. Um, H. J. Han, M. H. Baek and S. Y. Bae, *J. Org. Chem.*, 2004, **69**, 6365–6370.

7 (*a*) I. H. Um, J. Y. Hong and J. A. Seok, *J. Org. Chem.*, 2005, **70**, 1438–1444; (*b*) I. H. Um, S. M. Chun, O. M. Chae, M. Fujio and Y. Tsuno, *J. Org. Chem.*, 2004, **69**, 3166–3172; (*c*) I. H. Um, J. Y. Hong, J. J. Kim, O. M. Chae and S. K. Bae, *J. Org. Chem.*, 2003, **68**, 5180–5185; (*d*) I. H. Um, J. Y. Han and S. J. Hwang, *Chem.–Eur. J.*, 2008, **14**, 7324–7330; (*e*) I. H. Um, Y. H. Shin, J. Y. Han and M. Mishima, *J. Org. Chem.*, 2006, **71**, 7715–7720.

8 (*a*) H. K. Oh, J. Y. Oh, D. D. Sung and I. Lee, *J. Org. Chem.*, 2005, **70**, 5624–5629; (*b*) I. Lee and D. D. Sung, *Curr. Org. Chem.*, 2004, **8**, 557–567; (*c*) H. K. Oh, J. E. Park, D. D. Sung and I. Lee, *J. Org. Chem.*, 2004, **69**, 9285–9288; (*d*) H. K. Oh, J. S. Ha, D. D. Sung and I. Lee, *J. Org. Chem.*, 2004, **69**, 8219–8223; (*e*) H. K. Oh, J. E. Park, D. D. Sung and I. Lee, *J. Org. Chem.*, 2004, **69**, 3150–3153; (*f*) H. K. Oh, S. K. Kim, H. W. Lee and I. Lee, *New J. Chem.*, 2001, **25**, 313–317; (*g*) H. K. Oh, S. K. Kim, I. H. Cho, H. W. Lee and I. Lee, *J. Chem. Soc., Perkin Trans. 2*, 2000, 2306–2310; (*h*) W. M. Lim, W. K. Kim, H. J. Jung and I. Lee, *Bull. Korean Chem. Soc*, 1995, **16**, 252–256.

9 (*a*) B. J. Lumbiny and H. W. Lee, *Bull. Korean Chem. Soc.*, 2008, **29**, 2065–2068; (*b*) B. J. Lumbiny, K. K. Adhikar, B. S. Lee and H. W. Lee, *Bull. Korean Chem. Soc.*, 2008, **29**, 1769–1773; (*c*) K. K. Adhikary, B. J. Lumbiny, C. K. Kim and H. W. Lee, *Bull. Korean Chem. Soc.*, 2008, **29**, 851–855; (*d*) H. K. Oh, J. M. Lee, H. W. Lee and I. C. Lee, *Int. J. Chem. Kinet.*, 2004, **36**, 434–440; (*e*) H. K. Oh, I. K. Kim, H. W. Lee and I. C. Lee, *J. Org. Chem.*, 2004, **69**, 3806–3810.

10 M. J. Gresser and W. P. Jencks, *J. Am. Chem. Soc.*, 1977, **99**, 6970–6980.

11 (*a*) E. A. Castro and C. L. Santander, *J. Org. Chem.*, 1985, **50**, 3595–3600; (*b*) E. A. Castro and J. L. Valdivia, *J. Org. Chem.*, 1986, **51**, 1668–1672; (*c*) E. A. Castro and G. B. Steinfort, *J. Chem. Soc., Perkin Trans. 2*, 1983, 453–457.

12 (*a*) E. A. Castro, R. Aguayo, J. Bessolo and J. G. Santos, *J. Org. Chem.*, 2005, **70**, 7788–7791; (*b*) E. A. Castro, R. Aguayo, J. Bessolo and J. G. Santos, *J. Org. Chem.*, 2005, **70**, 3530–3536; (*c*) E. A. Castro, M. Vivanco, R. Aguayo and J. G. Santos, *J. Org. Chem.*, 2004, **69**, 5399–5404; (*d*) E. A. Castro, R. Aguayo and J. G. Santos, *J. Org. Chem.*, 2003, **68**, 8157–8161.

13 (*a*) F. A. Carroll, *Perspectives on Structure and Mechanism in Organic Chemistry*, Brooks/Cole, New York, 1998, pp. 371–386; (*b*) W. P. Jencks, *Catalysis in Chemistry and Enzymology*, McGraw-Hill, New York, 1969, pp. 480–483; (*c*) T. H. Lowry, K. S. Richardson, *Mechanism and Theory in Organic Chemistry*, 3rd edn, Harper Collins Publishers, New York, 1987, pp. 143–151.

14 (*a*) S. Swansburg, E. Buncel and R. P. Lemieux, *J. Am. Chem. Soc.*, 2000, **122**, 6594–6600; (*b*) A. Pross, *Theoretical & Physical Principles of Organic Reactivity*, Wiley & Sons, New York, 1995, pp. 165–169.

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Downloaded by Institute of Organic Chemistry of the SB RAS on 16 August 2010

15 (*a*) Y. Tsuno and M. Fujio, *Adv. Phys. Org. Chem.*, 1999, **32**, 267–385; (*b*) Y. Tsuno and M. Fujio, *Chem. Soc. Rev.*, 1996, **25**, 129–139; (*c*) Y. Yukawa and Y. Tsuno, *Bull. Chem. Soc. Jpn.*, 1959, **32**, 965–970.

16 (*a*) S. Than, H. Maeda, M. Irie, K. Kikukawa and M. Mishima, *Int. J. Mass Spectrom.*, 2007, **267**, 205–214; (*b*) H. Maeda, M. Irie, S. Than, K. Kikukawa and M. Mishima, *Bull. Chem. Soc. Jpn.*, 2007, **80**, 195–203; (*c*) M. Mishima, H. Maeda, S. Than, M. Irie and K. Kikukawa, *J. Phys. Org. Chem.*, 2006, **19**, 616–623; (*d*) M. Fujio, M. A. Alam, Y. Umezaki, K. Kikukawa, R. Fujiyama and Y. Tsuno, *Bull. Chem. Soc. Jpn.*, 2007, **80**, 2378–2383; (*e*) M. Fujio, Y. Umezaki, M. A. Alam, K. Kikukawa, R. Fujiyama and Y. Tsuno, *Bull. Chem. Soc. Jpn.*, 2006, **79**, 1091–1099.

17 (*a*) I. H. Um, J. Y. Han and Y. H. Shin, *J. Org. Chem.*, 2009, **74**, 3073–3078; (*b*) I. H. Um, J. Y. Han and S. J. Hwang, *Chem.–Eur. J.*, 2008, **14**, 7324–7330; (*c*) I. H. Um, Y. H. Shin, J. Y. Han and M. Mishima, *J. Org. Chem.*, 2006, **71**, 7715–7720.

18 (*a*) H. Neuvonen, K. Neuvonen, A. Koch and E. Kleinpeter, *J. Phys. Chem. A*, 2005, **109**, 6279–6289; (*b*) H. Neuvonen, K. Neuvonen and P. Pasanen, *J. Org. Chem.*, 2004, **69**, 3794–3800; (*c*) H. Neuvonen, K. Neuvonen, A. Koch, E. Kleinpeter and P. Pasanen, *J. Org. Chem.*, 2002, **67**, 6995–7003; (*d*) H. Neuvonen and K. Neuvonen, *J. Chem. Soc., Perkin Trans. 2*, 1999, 1497–1502.

19 (*a*) D. N. Kevill and M. J. D'Souza, *J. Org. Chem.*, 2004, **69**, 7044–7050; (*b*) D. N. Kevill, in *The Chemistry of the Functional Groups. The Chemistry of Acyl Halides*, ed. S. Patai, Wiley, New York, 1972, Chapter 12; (*c*) D. N. Kevill and J. B. Kyong, *J. Chem. Res. (S)*, 2007, **2007**, 210–215; (*d*) D. N. Kevill and H. J. Koh, *J. Phys. Org. Chem.*, 2007, **20**, 88–92; (*e*) D. N. Kevill, B. C. Park, K. H. Park, M. J. D'Souza, L. Yaakoubd, S. L. Mlynarski and J. B. Kyong, *Org. Biomol. Chem.*, 2006, **4**, 1580–1586.

20 Although only three different pyridines were employed to construct the Brønsted-type plots, the magnitudes of the β_{nuc} values are considered to be reliable since each plot exhibits excellent linear correlation.

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