Structure–reactivity correlations in nucleophilic substitution reactions of Y-substituted phenyl X-substituted benzoates with anionic and neutral nucleophiles†

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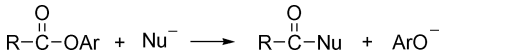
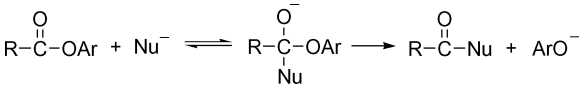
A kinetic study is reported for the reactions of 4-nitrophenyl X-substituted benzoates (**1a–l**) and Y-substituted phenyl benzoates (**2a–l**) with two anionic nucleophiles (OH^- and CN^-) and three amines (piperidine, hydrazine, and glycylglycine) in 80 mol% H_2O–20 mol% dimethyl sulfoxide (DMSO) at 25.0 ± 0.1 °C. Each Hammett plot exhibits two intersecting straight lines for the reactions of **1a–l** with the anionic nucleophiles and piperidine, while the Yukawa–Tsuno plots for the same reactions are linear. The Hammett plots for the reactions of **2a–l** with hydrazine and glycylglycine demonstrate much better linear correlations with σ^- constants than with σ° or σ constants, indicating that the leaving group departure occurs at the rate determining step (RDS). On the contrary, σ^- constants result in poorer Hammett correlation than σ° constants for the corresponding reactions with OH^- and CN^-, indicating that the leaving group departure occurs after the RDS for the reactions with the anionic nucleophiles. The large ρ_X value (1.7 ± 0.1) obtained for the reactions of **1a–l** with the anionic nucleophiles supports the proposal that the reactions proceed through an addition intermediate with its formation being the RDS.

Introduction

Due to their importance in biological processes as well as synthetic applications, acyl group transfer reactions of esters have been the subject of extensive experimental and theoretical studies.[1–15] One intriguing aspect is whether nucleophilic attack at the carbonyl carbon occurs concertedly with leaving group departure [eqn (1)], or whether reaction occurs through a discrete tetrahedral intermediate [eqn (2)].



(1)



(2)

Aminolysis of esters is now definitely understood to proceed through a stepwise mechanism.[1–5] Curved Brønsted-type plots, which have often been observed for aminolyses of carboxylic esters with a good leaving group, support a stepwise mechanism with a change in the rate-determining step (RDS).[1–5] The RDS has been suggested to change from breakdown of a zwitterionic tetrahedral intermediate ($T^\pm$) to its formation as the attacking amine becomes more basic than the leaving group by 4 to 5 pK_a units.[1–5] Recent computational studies also favor a stepwise mechanism over a concerted pathway, although some computational studies failed to identify the transition state and $T^\pm$ for aminolysis of various carboxylic esters.[6–9]

However, the mechanism for reactions with anionic nucleophiles is not completely understood.[10–15] In a series of important studies by Williams and coworkers, it has been concluded that acyl group transfer to aryloxide anions occurs through a concerted pathway.[10] The evidence provided was a Brønsted-type plot with absence of a break (or curvature) when the pK_a of the aryloxide nucleophile corresponded to that of the aryloxide leaving group.[10] The concerted mechanism has been supported through structure–reactivity correlations reported by Jencks,[11a] Rossi,[11b,c] and Castro,[11d–f] as well as kinetic isotope effect studies of Hengge,[12] Marcus analysis by Guthrie,[13a] and recent theoretical calculations by Xie *et al.*[13b] On the contrary, Buncel *et al.* have argued against a concerted mechanism for acyl group transfer to aryloxides, on the basis of Hammett plots exhibiting rather poor correlation with σ^- but significantly better correlation with σ° constants.[14] Thus, it has been concluded that the departure of the leaving group from a tetrahedral intermediate is little advanced, if at all, in the rate-determining transition state.[14] In fact, we have recently shown spectroscopic evidence, along with kinetic evidence, for an addition intermediate in the reaction of a cyclic sulfinate ester with sodium ethoxide in anhydrous ethanol.[15a]

One of the main reasons for the controversy about the reaction mechanism is considered to be the lack of systematic studies. The previous studies were limited mostly to investigation of the effect of substituents in the attacking nucleophile[10] or in the leaving group.[14] Thus, we have prepared two series of substrates, 4-nitrophenyl X-substituted benzoates (**1a–l**) and Y-substituted phenyl benzoates (**2a–l**) and performed a systematic study of nucleophilic substitution reactions with two representative anionic nucleophiles (OH^- and CN^-) and three different amines (piperidine, hydrazine, and

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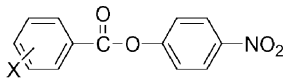
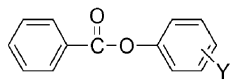
glycylglycine) to obtain more conclusive information about the reaction mechanism. Detailed reaction mechanisms are presented herein.



1

X = 3,5-$(NO_2)_2$(**1a**), 4-Cl-3-NO_2(**1b**), 4-NO_2(**1c**), 4-CN(**1d**), 3-Cl(**1e**), 4-Cl(**1f**), H(**1g**), 3-Me(**1h**), 4-Me(**1i**), 4-MeO(**1j**), 4-NMe_2(**1k**), 4-OH(**1l**)



2

Y = 3,4-$(NO_2)_2$(**2a**), 4-NO_2(**2b**), 4-CN(**2c**), 4-CHO(**2d**), 4-COMe(**2e**), 4-CO_2Et(**2f**), 3-NO_2(**2g**), 3-COMe(**2h**), 4-Cl(**2i**), H(**2j**), 4-Me(**2k**), 4-MeO(**2l**)

Results and discussion

Reactions of **1a–l** and **2a–l** with the anionic and neutral nucleophiles proceeded with quantitative liberation of 4-nitrophenoxide or the corresponding aryloxide. All reactions in this study obeyed pseudo-first-order kinetics under conditions of excess nucleophile. Pseudo-first-order rate constants (k_{obsd}) were determined from the equation $\ln(A_\infty - A_t) = -k_{obsd}t + c$. Correlation coefficients of the linear regressions were usually higher than 0.9995. The plots of k_{obsd} *vs.* nucleophile concentrations were linear and passed through the origin. Five different nucleophile concentrations were used to determine the second-order rate constant (k_N) from the slope of the linear plots. It is estimated from replicate runs that the uncertainty in rate constants is less than ±3%. The k_N values determined in this way are summarized in Tables 1 and 2.

Effect of nonleaving group substituent on reactivity and mechanism

As shown in Table 1, the second-order rate constant (k_N) for the reactions of **1a–l** with OH^- decreases as the substituent X in the nonleaving group changes from an electron withdrawing group to an electron donating group, *i.e.*, k_N decreases from 5010 $M^{-1}s^{-1}$ to 13.4 and 0.0101 $M^{-1}s^{-1}$ as the substituent X changes from 3,5-$(NO_2)_2$ to H and 4-OH, respectively. A similar result has been obtained for the corresponding reactions with CN^- and piperidine. It is noted that **1l** is much less reactive than **1k** regardless of the type of nucleophiles. This is an unexpected result since 4-OH is a weaker electron donating substituent than 4-NMe_2 on the basis of their σ (*e.g.*, $\sigma = -0.37$ and -0.77 for 4-OH and 4-NMe_2, respectively) or σ^+ values (*e.g.*, $\sigma^+ = -0.98$ and -1.73 for 4-OH and 4-NMe_2, respectively).

Table 1 Summary of second-order rate constants ($k_N/M^{-1}s^{-1}$) for nucleophilic substitution reactions of 4-nitrophenyl X-substituted benzoates (**1a–l**) with OH^-, CN^-, and piperidine in 80 mol% H_2O–20 mol% DMSO at 25.0 ± 0.1 °C

	$k_N/M^{-1}s^{-1}$			
No.	X	OH^-	CN^-	Piperidine
1a	3,5-$(NO_2)_2$	5010[a]	42.5	47.5
1b	4-Cl-3-NO_2	715[a]	8.17	23.1
1c	4-NO_2	531[a]	6.25	21.0[b]
1d	4-CN	354[a]	4.47	18.7[b]
1e	3-Cl	73.8[a]	1.33	12.8[b]
1f	4-Cl	39.6[a]	0.628	8.14[b]
1g	H	13.4[a]	0.228	5.94[b]
1h	3-Me	8.90[a]	0.189	4.56[b]
1i	4-Me	5.65[a]	0.117	3.68[b]
1j	4-MeO	2.64[a]	0.0460	1.95[b]
1k	4-NMe_2	0.144	0.00265	0.259
1l	4-OH	0.0101	3.57×10^{-4}	0.0659

[a] Data taken from reference 18. [b] Data taken from reference 5*c*.

Table 2 Summary of second-order rate constants ($k_N/M^{-1}s^{-1}$) for nucleophilic substitution reactions of Y-substituted phenyl benzoates (**2a–l**) with OH^-, CN^-, hydrazine and glycylglycine in 80 mol% H_2O–20 mol% DMSO at 25.0 ± 0.1 °C

	$k_N/M^{-1}s^{-1}$				
No.	Y	OH^-	CN^-	Hydrazine	Glycylglycine
2a	3,4-$(NO_2)_2$	98.9[a]	1.92	33.1	1.48
2b	4-NO_2	13.4[a]	0.231	2.39[b]	0.0240[b]
2c	4-CN	—	—	0.538[b]	0.00446[b]
2d	4-CHO	4.72[a]	0.103	—	0.0140[b]
2e	4-COMe	3.27[a]	0.0768	0.201[b]	0.00161[b]
2f	4-COOEt	—	—	0.0836[b]	6.00×10^{-4}[b]
2g	3-NO_2	5.97[a]	0.141	—	—
2h	3-COMe	1.80[a]	0.0359	—	—
2i	4-Cl	—	—	0.00520[b]	—
2j	H	0.449[a]	0.0102	—	—
2k	4-Me	0.316[a]	0.00783	—	—
2l	4-MeO	0.389[a]	0.00843	—	—

[a] Data taken from reference 14*d*. [b] Data taken from reference 5*f*.

The fact that **1l** is less reactive than **1k** might imply that the phenolic moiety of substrate **1l** exists as a phenoxide form under the reaction condition. This argument is reasonable since the phenolic moiety of **1l** is considered to be highly acidic. Although the pK_a of the phenolic moiety of **1l** has not been reported, it is expected to be lower than that of ethyl 4-hydroxybenzoate whose pK_a has been reported to be 8.50.[16] This is because the ethyl group of ethyl 4-hydroxybenzoate is a stronger electron donating group than the 4-nitrophenyl group of **1l**. Thus, it is plausible that the substituent 4-OH in substrate **1l** is present as its deprotonated form, *i.e.*, 4-O^- under the kinetic condition.

The effect of substituent X on reactivity is illustrated in Fig. 1. The Hammett plots for the reactions of **1a–l** with OH^- and CN^- ions consist of two intersecting straight lines (except for the negative deviation shown by the reactions of **1l**). Traditionally, such a nonlinear Hammett plot has been interpreted as a change in the RDS.[17–19] However, as shown in Fig. 2, the Yukawa–Tsuno plots for the same reactions are linear with an r value of *ca.* 0.5, indicating that the nonlinear Hammett plots are definitely not due to a change in the RDS. Besides, the Hammett plot for the reactions of **1a–l** with piperidine (Fig. 3) also exhibits two intersecting straight lines with a negative deviation for the reaction of **1l**, while the corresponding Yukawa–Tsuno plot (inset of Fig. 3) is linear with $r = 1.18$.

The Yukawa–Tsuno equation [eqn (3)] has been applied to numerous reactions in which a partial positive charge develops in the transition state of the RDS.[20]

$$\log (k_X/k_H) = \rho[\sigma^\circ + r(\sigma^+ - \sigma^\circ)] \quad (3)$$

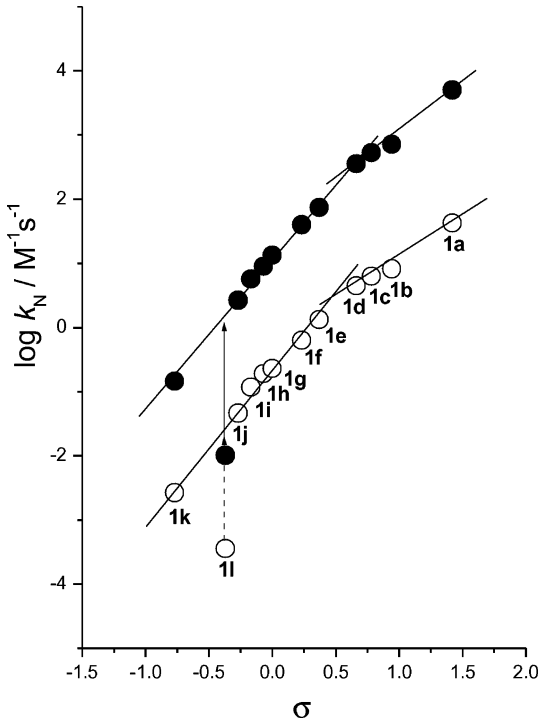


Fig. 1 Hammett plots for the reactions of 4-nitrophenyl X-substituted benzoates (**1a–l**) with OH^- (●) and CN^- (○) in 80 mol% H_2O–20 mol% DMSO at 25.0 ± 0.1 °C. The identity of points is given in Table 1.

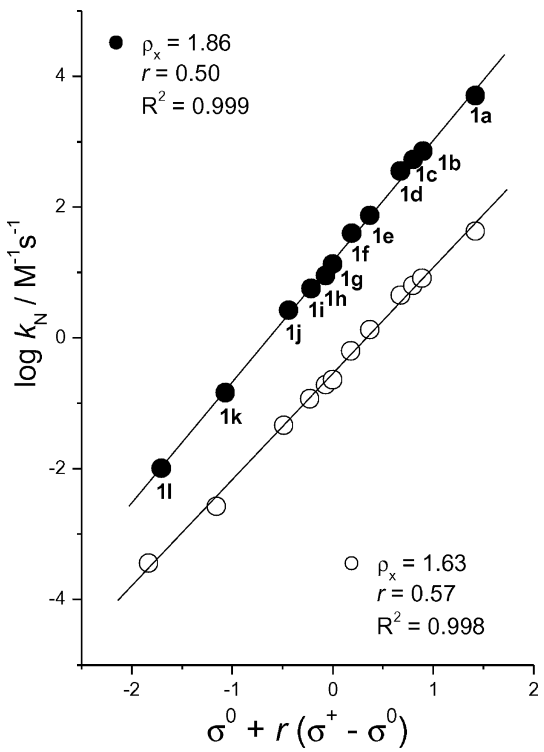


Fig. 2 Yukawa–Tsuno plots for the reactions of 4-nitrophenyl X-substituted benzoates (**1a–l**) with OH^- (●) and CN^- (○) in 80 mol% H_2O–20 mol% DMSO at 25.0 ± 0.1 °C. The identity of points is given in Table 1.

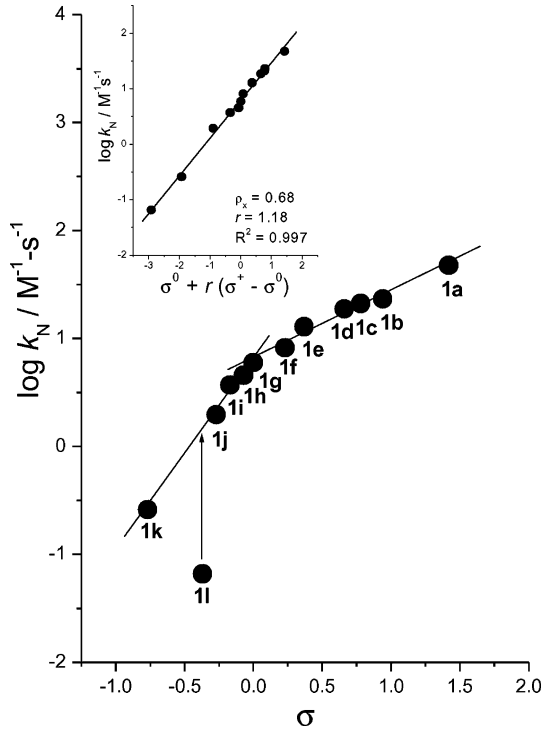
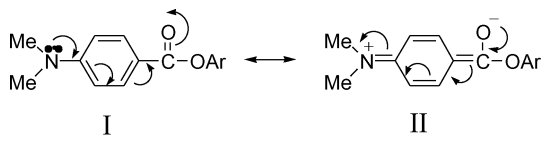


Fig. 3 Hammett and Yukawa–Tsuno plot (inset) for the reactions of 4-nitrophenyl X-substituted benzoates (**1a–l**) with piperidine in 80 mol% H_2O–20 mol% DMSO at 25.0 ± 0.1 °C. The identity of points is given in Table 1.

The magnitude of the *r* value represents the resonance demand of the reaction center or the extent of resonance contribution.[20] Eqn (3) becomes the Hammett equation when $r = 0$ or the Brown–Okamoto equation when $r = 1$. Since the *r* value is neither 0 nor 1 in this study, the Yukawa–Tsuno equation results in better correlation than the Hammett or Brown–Okamoto equations, in which σ or σ^+ constants alone are used. Thus, one can suggest that stabilization of the ground state through the resonance interaction as illustrated in resonance structures I ↔ II and III ↔ IV is responsible for the nonlinear Hammett plots, and the RDS for the reactions of **1a–l** does not vary on changing the electronic nature of the substituent X in the nonleaving group.



It is noted that **1l** is on the linear Yukawa–Tsuno plot regardless of the type of nucleophile when the σ^+ value of −2.6 for 4-O^- is used. This result is consistent with the preceding argument that 4-OH in **1l** becomes 4-O^- under the kinetic condition. The σ^+ value for 4-O^- has been calculated by Wepster *et al.*[21] using the acid dissociation constants of 4-hydroxyphenylacetic acid and 4-nitrophenol in aqueous ethanol, but never been determined

directly from kinetic studies. The reported σ^+ value for 4-O^- is −2.3,[21] which is slightly smaller than that determined in this study (−2.6) but much larger than the σ^+ value of −1.73 for 4-NMe_2. This is why **1l** is much less reactive than **1k** and exhibits a significant negative deviation from the Hammett plots in Fig. 1 and 3.

Effect of leaving group substituent on reactivity and mechanism

To get more information about the reaction mechanism, the effect of the leaving group substituent on reactivity has been investigated. As shown in Table 2, the k_N for the reactions of Y-substituted phenyl benzoates (**2a–l**) with OH^- ion decreases as the substituent Y in the leaving group becomes a weaker electron withdrawing (or a stronger electron donating) group, *i.e.*, k_N decreases from 98.9 $M^{-1}s^{-1}$ to 3.27 and 0.389 $M^{-1}s^{-1}$ as the substituent Y changes from 3,4-$(NO_2)_2$ to 4-COMe and 4-MeO, respectively. A similar result has been obtained for the corresponding reactions with CN^- ion and with the two amine nucleophiles.

Alkaline hydrolysis of aryl benzoates in aqueous MeCN has been proposed to proceed through a stepwise mechanism, in which formation of a tetrahedral intermediate is the RDS.[22] On the contrary, Williams *et al.* have concluded that the reactions of 4-nitrophenyl X-substituted benzoates with OH^- and phenoxide ions in aqueous MeCN proceed through a concerted mechanism.[10d] The evidence provided for a concerted mechanism is linear Hammett plots correlated with σ constants.[10d] Williams *et al.* have insisted that the Hammett plots should have exhibited sharp breaks on changing the electronic nature of the substituent X in the nonleaving benzoyl moiety, if the reaction proceeded through an intermediate. The absence of a break in the Hammett plots has been taken as evidence for a concerted mechanism.[10d] However, we have clearly shown that a sharp break in Hammett plots (*e.g.*, Fig. 1 and 3) is not necessarily due to a change in the RDS in the preceding section.

If the leaving group departure is involved in the RDS either in a concerted or stepwise mechanism, a partial negative charge would develop on the oxygen atom of the leaving aryloxides at the transition state of the RDS. Since such a negative charge can be delocalized on the substituent Y in the leaving group through resonance, σ^- constants should exhibit a better Hammett correlation than σ or σ° constants.

The above argument can be proved by the result obtained from the reactions of **2a–l** with hydrazine and glycylglycine. As shown in Fig. 4, the Hammett plots exhibit much better linear correlations with σ^- constants than with σ° or σ constants for the reactions with the two amines. This result clearly indicates that the leaving group departure occurs at the RDS for the reactions of **2a–l** with these amines, and the negative charge developed on the oxygen atom of the leaving aryloxide can be delocalized on the substituent Y through resonance.

The Hammett plots for the reactions of **2a–l** with the anionic nucleophiles are illustrated in Fig. 5. It is shown that σ^- constants exhibit many scattered points on the Hammett plots. This result contrasts with that obtained for the corresponding reactions with the amines. However, σ° constants exhibit only slightly better correlations than σ^- constants. Thus, the present result alone cannot be confidently taken as decisive evidence for one mechanism over another for the reactions of **1a–l** with the anionic nucleophiles. To obtain additional information about the reaction

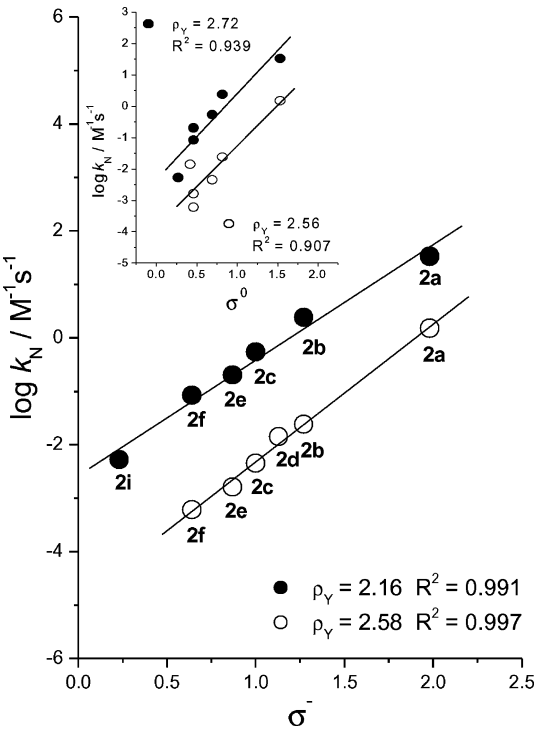


Fig. 4 Hammett correlations with σ^- and σ° constants (inset) for the reactions of Y-substituted phenyl benzoates (**2a–l**) with hydrazine (●) and glycylglycine (○) in 80 mol% H_2O–20 mol% DMSO at 25.0 ± 0.1 °C. The identity of the points is given in Table 2.

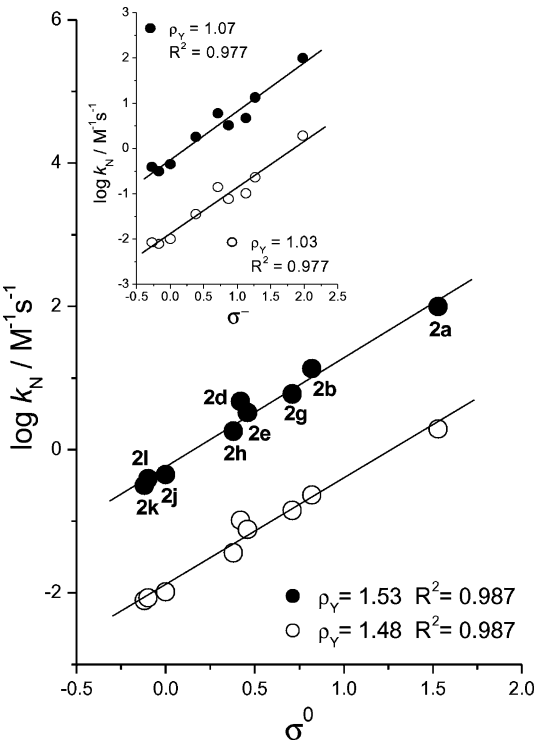


Fig. 5 Hammett correlations with σ° and σ^- constants (inset) for the reactions of Y-substituted phenyl benzoates (**2a–l**) with OH^- (●) and CN^- (○) in 80 mol% H_2O–20 mol% DMSO at 25.0 ± 0.1 °C. The identity of points is given in Table 2.

mechanism, the magnitude of the ρ_X and ρ_Y values has been analyzed in the following section since it can be an indirect probe for determination of reaction mechanism.

Factors influencing magnitude of ρ_X and ρ_Y

The ρ_X value has been determined to be *ca.* 1.7 for the reactions of **1a–l** with the anionic nucleophiles OH^- and CN^- (Fig. 2), while the ρ_Y is *ca.* 1.0 or 1.5 depending on the substituent constants used (*e.g.*, σ^- or σ°) for the corresponding reactions of **2a–l** (Fig. 5). A similar result has been reported for alkaline hydrolysis of Y-substituted phenyl X-substituted benzoates in 67% H_2O–33% MeCN (v/v).[22a] Kirsch *et al.* have found that the substituent in the benzoyl moiety (X) exerts a greater sensitivity than that in the aryl moiety (Y), *i.e.*, $\rho_X = 2.04$ and $\rho_Y = 1.24$.[22a] The greater sensitivity shown by the substituent X in the nonleaving group has been explained in terms of a distance effect under the assumption that the attack of OH^- ion to the carbonyl carbon is the RDS, since the reaction site is one atom closer to the benzoyl substituent X than to the aryl substituent Y.[22a] Thus, one might suggest that the distance effect is responsible for the fact that the ρ_X is larger than the ρ_Y value for the reactions of **1a–l** and **2a–l** with the anionic nucleophiles.

However, an opposite result has been obtained for the reactions with amines. The value of ρ_X has been determined to be much smaller than ρ_Y for the reactions with amine nucleophiles, *i.e.*, ρ_X and ρ_Y are 0.68 (Fig. 3) and 2.16–2.58 (Fig. 5), respectively. Although the substituent Y is one atom further away than the substituent X from the reaction site, the former exhibits a greater sensitivity than the latter. Therefore, the distance effect suggested by Kirsch *et al.* cannot be solely responsible for the result that ρ_X is larger than ρ_Y for the reactions with OH^- and CN^- ions.

One can suggest that the type of nucleophile might be an important factor in determining the ρ_X and ρ_Y values, since the transmission of electronic effects would be more significant for the reactions with anionic nucleophiles than for those with neutral amines. In fact, the reactions with the anionic nucleophiles result in much larger ρ_X values than those with the neutral amine, *i.e.*, the ρ_X value determined is 1.86 and 1.63 for the reactions of **1a–l** with OH^- and CN^-, respectively but only 0.68 for the corresponding reactions with piperidine. Thus, the magnitude of ρ_X appears to be highly dependent on the nature of the nucleophile (*e.g.*, anionic *vs.* neutral).

On the other hand, the magnitude of ρ_Y obtained for the reactions of **2a–l** contrasts with that of ρ_X determined for the reactions of **1a–l**. The ρ_Y values are 2.16–2.58 and *ca.* 1.0 (or 1.5) for the reactions of **2a–l** with the neutral amines (Fig. 4) and with the anionic nucleophiles (Fig. 5), respectively. Clearly, ρ_Y is much larger for the reactions with the amines than with the anionic nucleophiles. Thus, the type of nucleophile cannot be fully responsible for the fact that ρ_X is larger for the reactions with the OH^- and CN^- ions than for those with piperidine.

A small ρ_X value has often been reported for S_N2 reactions[17a,23] since the electronic effect of substituents in the nonleaving group can be compensated due to the opposing substituent effect, *i.e.*, an electron withdrawing substituent would accelerate the attack of nucleophiles but retard the departure of the negatively charged leaving group, while an electron donating substituent would prevent nucleophilic attack but enhance leaving group departure. In fact, ρ_X values have been reported to be 0.3 and up to −6.47 for the reaction of X-substituted benzyl chlorides with OH^- ion[17a,23a] and for solvolysis of α-methyl X-substituted benzyl chlorides,[20a] a typical S_N2 and S_N1 reaction, respectively. Jencks has shown that the nature of the RDS also influences the magnitude of ρ_X for the reactions of X-substituted benzaldehydes with semicarbazide in a weakly acidic solution (*e.g.*, pH = 3.9).[24] ρ_X has been found to decrease from a large positive value to near zero as the substituent changes from electron donating groups to electron withdrawing ones.[24] Jencks has attributed the decrease in the ρ_X value to a change in the RDS from formation of the addition intermediate to its breakdown as the substituent changes from electron donating groups to electron withdrawing ones.[24]

As mentioned in the preceding section, the leaving group departure has been suggested to occur at the RDS for the current aminolysis reactions. Accordingly, the rate of the leaving group departure would be strongly dependent on the electronic nature of the substituent Y in the leaving group, which is responsible for the large ρ_Y value (2.16–2.58). However, the substituent X in the nonleaving group would not exhibit a high sensitivity to the rate of reactions due to the opposing substituent effect when the leaving group departure occurs at the RDS. This argument can account for the fact that ρ_X has been determined to be much smaller (*i.e.*, 0.68) than the ρ_Y value for the aminolysis in the current study. In this regard, the ρ_X value of 1.7 ± 0.1 obtained for the reactions of **1a–l** with OH^- and CN^- appears to be too large for reactions which proceed through an S_N2-like mechanism. Such a large ρ_X value can be taken as indirect evidence that the reactions proceed through an addition intermediate with its formation being the RDS. This is in accord with the fact that σ° constants result in better Hammett correlation than σ^- constants for the reactions of **1a–l** with OH^- and CN^- although the difference in the correlation coefficient is not significant.

Conclusions

The present study has allowed us to conclude the following: (1) The nonlinear Hammett plots obtained for the reactions of **1a–l** with OH^-, CN^-, and piperidine are not due to a change in the RDS. (2) The linear Yukawa–Tsuno plots suggest that stabilization of the ground state through resonance interaction between the π-electron donor substituent X and the carbonyl functionality is responsible for the nonlinear Hammett plots. (3) Departure of the leaving group occurs at the RDS for the aminolysis of **1a–l** and **2a–l** since the Hammett plots exhibit good linear correlations with σ^- constants with a small ρ_X value. (4) The large ρ_X values and better Hammett correlations with σ° constants for the corresponding reactions with OH^- and CN^- ions suggest that the reactions proceed through an intermediate with its formation being the RDS. (5) The nature of reaction mechanism (or RDS) has been shown to be most important among the factors influencing the magnitude of ρ_X and ρ_Y values.

Experimental

Materials

Aryl benzoates ($X–C_6H_4CO_2C_6H_4–Y$) except **1k** and **1l** were prepared from the reaction of X-substituted benzoyl chloride

with Y-substituted phenol in the presence of triethylamine in anhydrous ether as reported in the literature.[22,25] Substrates **1k** and **1l** were prepared from the reactions of 4-nitrophenol and 4-hydroxybenzoic acid (or 4-dimethylaminobenzoic acid) in the presence of dicyclohexyl carbodiimide in ethyl acetate.[25d] Their purity was checked by means of melting point and spectral data such as IR and ^{1}H NMR characteristics. Doubly glass distilled water was further boiled and cooled under nitrogen just before use. Other chemicals used were of the highest quality available.

Kinetics

The kinetic studies were performed with a UV–vis spectrophotometer for slow reactions ($t_{1/2} \geq 10$ s) or with a stopped-flow spectrophotometer for fast reactions ($t_{1/2} < 10$ s) equipped with a constant temperature circulating bath to keep the temperature of the reaction mixture at 25.0 ± 0.1 °C. All the reactions were performed in 80 mol% H_2O–20 mol% DMSO to eliminate a solubility problem. The reactions were followed by monitoring the appearance of the leaving aryloxide at a fixed wavelength corresponding to the maximum absorption (λ_{max}) of Y–$C_6H_4O^-$. All reactions were carried out under pseudo-first-order conditions in which the concentration of nucleophiles was at least 20 times greater than that of the substrate. Nucleophile stock solution of *ca.* 0.2 M was prepared in a 25.0 mL volumetric flask just before use and transferred by gastight syringes. The amine stock solution of *ca.* 0.2 M was prepared by dissolving 2 equiv. of free amine (or amine hydrochloride) and 1 equiv. of standardized HCl (or NaOH) solution to make a self-buffered solution.

Typically, the reaction was initiated by adding 5 μL of a 0.01 M solution of the substrate in acetonitrile by a syringe to a 10 mm quartz UV cell containing 2.50 mL of the thermostated reaction mixture made up of solvent and an aliquot of the nucleophile stock solution. Generally, the nucleophile concentration was varied over the range (1–100) × 10^{-3} M, while the substrate concentration was 2 × 10^{-5} M. Usually, five different nucleophile concentrations were employed, and replicate k_{obsd} values were determined to calculate the second-order rate constants (k_N) from the slope of linear plots of k_{obsd} *vs.* nucleophile concentrations.

Products analysis

Y-Substituted phenoxide was liberated quantitatively and identified as one of the reaction products by comparison of the UV–vis spectra after completion of the reaction with those of the authentic sample under the same reaction conditions.

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