The α-Effect and Mechanism of Reactions of Y-Substituted Phenyl Benzenesulfonates with Hydrogen Peroxide Ion

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Second-order rate constants (k_{HOO^-}) have been measured spectrophotometrically for nucleophilic substitution reactions of Y-substituted phenyl benzenesulfonates (**1a-g**) with HOO⁻ ion in H_2O at 25.0 ± 0.1 °C. The Brønsted-type plot is linear with $\beta_{lg} = -0.73$. The Hammett plot correlated with with σ⁻ constants results in much better linearity than σ° constants, indicating that expulsion of the leaving group occurs in the rate-determining step (RDS) either in a stepwise mechanism or in a concerted pathway. However, a stepwise mechanism in which departure of the leaving group occurs in the RDS has been excluded since HOO⁻ ion is more basic and a poorer leaving group than the leaving Y-substituted phenoxide ions. Thus, the reactions of **1a-g** with HOO⁻ ion have been concluded to proceed through a concerted mechanism. The α-nucleophile HOO⁻ ion is more reactive than its reference nucleophile OH⁻ ion although the former is *ca.* 4 pK_a units less basic than the latter (i.e., the α-effect). TS stabilization through intramolecular H-bonding interaction has been suggested to be irresponsible for the α-effect shown by HOO⁻ ion, since the magnitude of the α-effect is independent of the electronic nature of substituent Y in the leaving group. GS destabilization through desolvation of HOO⁻ ion has been concluded to be responsible for the α-effect found in the this study.

Key Words: The α-Effect, Brønsted-type plot, Hammett plot, Intramolecular H-bonding, Solvent effect

Introduction

The term α-effect was given to the abnormally enhanced reactivity exhibited by nucleophiles possessing one or more nonbonding electron pairs at the atom α to the nucleophilic site (i.e., α-nucleophiles).[1] Since this definition is somewhat ambiguous, an alternative definition of the α-effect was proposed, i.e., a positive deviation exhibited by an α-nucleophile from a Brønsted-type nucleophilicity plot.[2] However, structurally nucleophiles have often been used as the α- and reference nucleophiles, e.g., HOO⁻ *vs.* OH⁻ and ᵗBuOO⁻ *vs.* ᵗBuO⁻.[3-5]

Numerous studies have been performed to investigate the cause of the α-effect. Some important theories to explain the cause of the α-effect include ground-state (GS) destabilization due to the repulsion between the nonbonding electron pairs, transition-state (TS) stabilization including intramolecular general acid/base catalysis, thermodynamic product stabilization, and solvent effects.[6-24] However, none of these theories can explain the cause of the α-effect. Particularly, theories of solvent effect on the α-effect are controversial.[13-16] DePuy *et al.* found that HOO⁻ does not exhibit any enhanced nucleophilic reactivity in gas-phase reactions of methyl formate.[13b] Thus, the α-effect shown by HOO⁻ in aqueous solutions was attributed to a solvent effect.[13] A contrary conclusion has been drawn from recent gas-phase studies including theoretical calculations.[14-16] Patterson and Fountain found that α-nucleophile HOO⁻ ion exhibits 3.6 kcal/mol lower activation barrier than the reference nucleophile EtO⁻ in gas-phase S$_N$2 reactions and concluded that solvent effect on the α-effect is not important.[14] A similar conclusion has been drawn by McAnoy *et al.* from gas-phase reactions of dimethyl methylphospho-

nate with CD$_3$O⁻ and HOO⁻ anions in an ion-trap mass spectrometer.[15] and by Yamataka *et al.* from theoretical calculations at the G2(+) level on gas-phase S$_N$2 reactions of alkyl halides with 11 anionic nucleophiles.[16]

We have found that solvent effect on the α-effect is significant in nucleophilic substitution reactions of various electrophilic center (e.g., aryl acetates, benzoates, and thionobenzoates) with butane-2,3-dione monoximate (Ox⁻, as an α-nucleophile) and 4-chlorophenoxie (4-ClPhO⁻, as a reference nucleophile) in DMSO-H$_2$O mixtures of varying compositions.[6,17-22] Our calorimetric study has revealed that Ox⁻ is less strongly solvated than its reference nucleophile, 4-ClPhO⁻ in DMSO-H$_2$O mixtures (e.g., *ca.* 4 kcal/mol in H$_2$O and over 7 kcal/mol in DMSO content above 40 mol %).[17b] It has also been found that the magnitude of the α-effect is highly dependent on the solvent compositions, i.e., the α-effect increases with increasing DMSO content in the medium up to *ca.* 50 mol% DMSO and decreases thereafter, resulting a bell-shaped α-effect profile.[6,17-22]

Our study has been extended to reactions of Y-substituted phenyl benzenesulfonates, **1a-g** with HOO⁻ ion (Scheme 1). The kinetic results were compared with those reported recently for the corresponding reactions with HO⁻ ion[25] to investigate the origin of the α-effect. We wish to report the
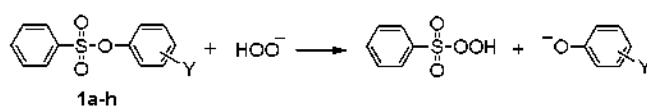
Y = 3,4-(NO$_2$)$_2$ (**1a**), 4-Cl-2-NO$_2$ (**1b**), 4-NO$_2$ (**1c**), 4-CHO (**1d**), 4-CN (**1e**), 4-COMe (**1f**), 3-COMe (**1g**).

Scheme 1

mechanism for the reactions of **1a-g** with HOO^- ion and the origin of the α-effect shown by HOO^- ion.

Results and Discussion

All reactions in this study were performed under pseudo-first-order conditions with the concentration of HOO^- in excess over the substrate concentration and obeyed first-order kinetics with quantitative liberation of Y-substituted phenoxide. 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. [HOO^-] were linear passing through the origin, indicating that contribution of H_2O to k_{obsd} is negligible in this study. Thus, the rate law is given by eq (1), and second-order rate constants (k_{HOO^-}) were determined from the slope of linear plots of k_{obsd} vs. [HOO^-]. It is estimated from replicate runs that the uncertainty in rate constants is less than $\pm$ 3%. The k_{HOO^-} values determined in this way are summarized in Table 1.

$$\text{rate} = k_{obsd}[\text{substrate}], \text{ where } k_{obsd} = k_{HOO^-}[HOO^-] \quad (1)$$

Effect of Leaving-Group Basicity on Reactivity: Brønsted-type Correlation. As shown in Table 1, the second-order rate constants (k_{HOO^-}) decreases as the leaving group basicity increases, e.g., k_{HOO^-} decreases from 49.5 $M^{-1} s^{-1}$ to 2.53 and 0.149 $M^{-1} s^{-1}$ as the pK_a of the conjugate acid of the leaving aryloxide increases from 5.42 to 7.14 and 9.19, in turn. A similar result is shown for the corresponding reactions with OH^- ion. However, HOO^- ion is more reactive than OH^- ion toward all the substrates studied, although the former is less basic than the latter by ca. 4 pK_a units.[26] The origin of the enhanced reactivity shown by HOO^- ion (i.e., the α-effect) will be discussed later.

The effect of leaving group basicity on reactivity for the reaction of **1a-g** with HOO^- is illustrated in Figure 1. The Brønsted-type plot is linear with $\beta_{lg} = -0.73$. Interestingly, **1b**, which possess a NO_2 group at the 2-position in the phenyl ring of the leaving aryloxide, does not exhibit negative deviation from the linearity. However, this is in contrast to the report that substrates possessing the substituent at the 2-position of the leaving aryloxide (e.g., 2-Cl or 2-NO_2) exhibit large

Table 1. Summary of Second-Order Rate Constants for Reactions of Y-Substituted Phenyl Benzenesulfonates (**1a-g**) with HOO^- and OH^- in H_2O at 25.0 $\pm$ 0.1 °C.[a]

| Y | pK_a^{Y-PhOH} | $k_N / M^{-1} s^{-1}$ | | α-effect |
		$k_{HOO^-}/ M^{-1}s^{-1}$	$10^2 k_{OH^-}/ M^{-1}s^{-1}$	k_{HOO^-}/k_{OH^-}
1a 3,4-($NO_2)_2$	5.42	49.5	129	38.4
1b 4-Cl-2-NO_2	6.46	25.4	62.2	40.8
1c 4-NO_2	7.14	2.53	4.91	51.5
1d 4-CHO	7.66	1.18	1.73	68.2
1e 4-CN	7.95	0.617	-	-
1f 4-$COCH_3$	8.05	0.596	1.94	30.7
1g 3-$COCH_3$	9.19	0.149	0.350	42.6

[a] Data for the reactions of **1a-g** with OH^- in 20 mol % DMSO were taken from ref. 25.
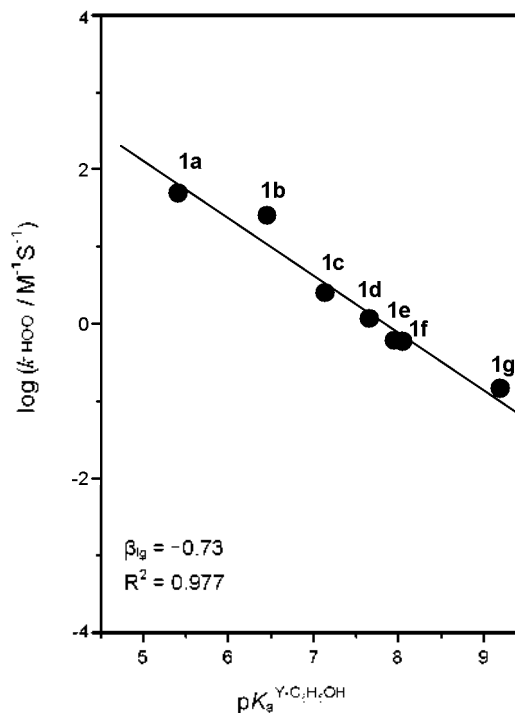
Figure 1. Brønsted-type plot for reactions of Y-substituted phenyl benzenesulfonates (**1a-g**) with HOO^- and OH^- in H_2O at 25.0 $\pm$ 0.1 °C. The identity of points is given in Table 1.

negative deviation from linear Brønsted-type plots (e.g., 2,4-dinitrophenyl phenyl carbonate,[27] 2,4-dinitrophenyl benzoate,[28a] 2-furoate,[28b] and thiophene-2-carboxylate[28c]). Thus, one can suggest that steric hindrance by the 2-nitro group in **1b** is absent. Absence of steric hindrance has also been reported for nucleophilic displacement reactions a P center, e.g., reactions of Y-substituted phenyl diphenylphosphinates with amines, hydroxide and ethoxide ions.[29]

Two factors can account for the absence of steric hindrance in the reaction of **1b**, i.e., the size and type of hybridization of the electrophilic center. The sulfonates **1a-g**, like the phosphinate esters, have a much larger electrophilic center than carboxylates (i.e., $O=S=O$ vs. $C=O$). Thus, the steric hindrance from the 2-NO_2 group would not be significant during nucleophilic attack by HOO^- at the large electrophilic center. One can suggest that the type of hybridization is also responsible for the absence of steric hindrance in the current reactions. The hybridization of the $C=O$ bond in carboxylate esters is sp^2 in the ground state (GS) but it becomes sp^3 in the transition state (TS). Consequently, the TS for the reactions of carboxylate esters becomes more crowded than the GS. In contrast, the hybridization of the sulfonate or phosphinate esters changes from tetrahedral in the GS to trigonal bipyramidal in the TS. Accordingly, the TS for the reactions of sulfonate **1a-g** becomes less crowded than the respective GS. This idea is consistent with the fact that **1b** does not exhibit negative deviation from the linearity in Figure 1.

The magnitude of $-\beta_{lg}$ values has been taken as a measure of reaction mechanism, e.g., for reactions proceeding through a stepwise mechanism with an intermediate. $-\beta_{lg}$ has been reported to be ca. 0.8 or larger when breakdown of the inter-

mediate is RDS, but *ca.* 0.4 or smaller when formation of the intermediate is RDS.[27,30-32] On the other hand, for reactions proceeding through a concerted pathway, $-\beta_{lg}$ has been reported to be 0.5 ± 0.1, e.g., reactions of Y-substituted phenyl diphenylphosphinates and phosphinothioates with piperidine, hydroxide and ethoxide.[29] The $-\beta_{lg}$ value of 0.73 found in the current reactions appears to be slightly larger than the $-\beta_{lg}$ value reported for a concerted mechanism, but is too large for reactions which proceed through a stepwise mechanism with formation of an intermediate being the RDS. Thus, the magnitude of the $-\beta_{lg}$ value alone cannot provide conclusive information on reaction mechanism.
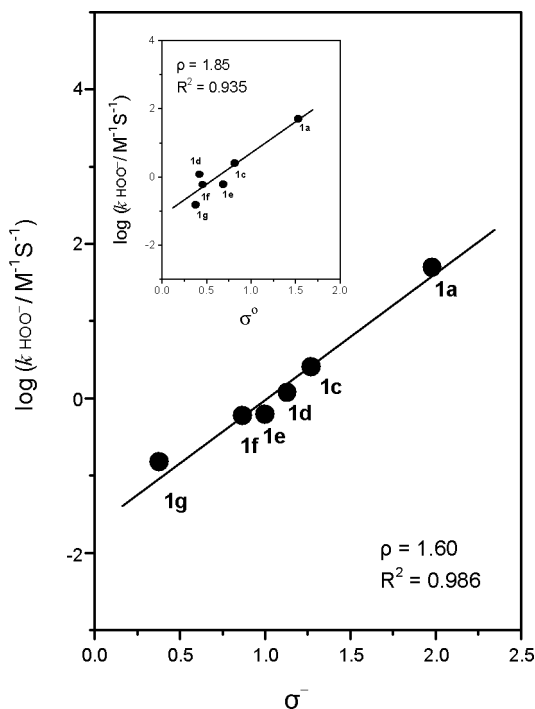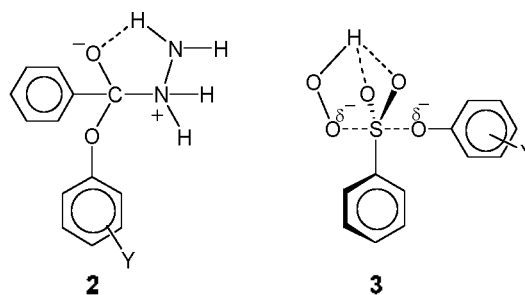
Deduction of Reaction Mechanism from Hammett Correlation. To get more conclusive information on the mechanism for the current reactions, Hammett plots have been constructed using σ° and σ⁻ constants. One might expect a better Hammett correlation with σ⁻ constants if expulsion of the leaving group occurs in the RDS whether the reaction proceeds in a concerted or a stepwise pathway. This is because a partial negative charge would develop on the oxygen atom of the leaving Y-substituted phenoxide, which can be delocalized on the substituent Y through resonance, when the leaving-group departure is advanced in the RDS. On the contrary, no negative charge would develop if expulsion of the leaving group occurs after the RDS. Then, σ° constants would result in better correlation than σ⁻ constants.

As shown in Figure 2, σ⁻ constants exhibits a better Hammett correlation than σ° constants, indicating that expulsion of the leaving group occurs at the RDS either in a concerted mechanism or in a stepwise pathway. However, one can exclude a stepwise mechanism in which departure of the leaving group

occurs in the RDS. since HOO⁻ ion is more basic and a poorer leaving group than all Y-substituted phenoxide ions studied. Thus, one can conclude the reaction of **1a-g** with HOO⁻ ion proceeds through a concerted mechanism. The reactions of **1a-g** with OH⁻ ion in 20 mol% DMSO has been reported to proceed also through a concerted mechanism on the basis of a linear Brønsted-type plot with $\beta_{lg} = -0.55$ and a linear Yukawa-Tsuno plot with $\rho_Y = 1.83$ and $r = 0.52$.[25]

Origin of the α-Effect. As discussed in the preceding section, HOO⁻ is more reactive than OH⁻ (i.e., the α-effect) although the former is *ca.* 4 pK_a units less basic than the latter. Since the reactions of **1a-g** with HOO⁻ and OH⁻ proceed through a common mechanism, the α-effect shown by HOO⁻ is not due to a difference in reaction mechanism.

Stabilization of the TS through 5-membered intramolecular H-bonding (e.g., **2**) has been suggested to be more important than destabilization of the GS for reactions of Y-substituted phenyl benzoates with hydrazine and glycylglycine, as an α-nucleophile and a reference nucleophile, respectively.[23] This is because such 5-membered structure **2** is not possible for the corresponding reactions with the reference nucleophile, glycylglycine.

2   **3**

The TS for reactions with HOO⁻ can be stabilized by forming intramolecular H-bonding structure **3**. Since such H-bonding structure is not possible for the corresponding reactions with OH⁻, one might suggest that TS stabilization through the H-bonding interaction is responsible for the α-effect found in the current reactions. However, if such TS stabilization is responsible for the α-effect, one might expect that the α-effect should be dependent on the electronic nature of the substituent Y. This is because the H-bonding interaction would be dependent on the electronic nature of the substituent Y. However, in fact, the magnitude of the α-effect (i.e., k_{HOO}/k_{OH}) ranges from 30 to 68 but is clearly independent of the electronic nature of the substituent Y, indicating that TS stabilization through the intramolecular H-bonding interaction is not responsible for the α-effect. Accordingly, one can suggest that GS destabilization is more important for the α-effect found in the current study. This idea is consistent with the report that HOO⁻ is 12 kcal/mol less strongly solvated than OH⁻ in H₂O.[33]

Conclusion

The current study has allowed us to conclude the following:
(1) Hammett plot correlated with σ⁻ constants results in much

Figure 2. Hammett correlations with σ⁻ and σ° constants (inset) for reactions of Y-substituted phenyl benzenesulfonates (**1a-g**) with HOO⁻ in H₂O at 25.0 ± 0.1 °C.

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better linearity than σ^o constants, indicating that expulsion of the leaving group occurs in the RDS. (2) A stepwise mechanism in which departure of the leaving group occurs in the RDS is excluded since HOO⁻ ion is more basic and a poorer leaving group than the leaving Y-substituted phenoxide ions. (3) The reactions of **1a-g** with HOO⁻ ion proceeds through a concerted mechanism. (4) The α-effect shown by HOO⁻ ion is not likely by TS stabilization through intramolecular H-bonding interaction since the magnitude of the α-effect is independent of the substituent Y. (5) GS destabilization through desolvation of HOO⁻ ion in H_2O is responsible for the current α-effect.

Experimental Section

Materials. Compounds **1a-g** were prepared readily from the reactions of benzenesulfonyl chloride with Y-substituted phenol in anhydrous ether in the presence of triethylamine as reported previously. Other chemicals including hydrogen peroxide used were of the highest quality available. Doubly glass distilled water was further boiled and cooled under nitrogen 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 ± 0.1 °C. The reaction was followed by monitoring the appearance of the leaving Y-substituted phenoxide ion. All the reactions were carried out under pseudo-first-order conditions in which the HOO⁻ concentration was at least 30 times greater than the substrate concentration. The H_2O_2 stock solution of *ca.* 0.2 M was prepared in a 25.0 mL vol. flask. Since H_2O_2 is not stable in a basic solution, HOO⁻ was directly generated in the UV cell by adding 0.2 equiv. of NaOH solution to 1.2 equiv. of H_2O_2 solution to maintain a constant [HOO⁻] concentration by keeping the buffer ratio $[H_2O_2]$/[HOO⁻] at 5/1 just before starting the reaction. All solutions were transferred by gas-tight syringes.

Product Analysis. Y-Substituted phenoxide 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.

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