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Kinetic Studies on the Addition of Phenol to S-Phenyl-S-vinyl-N-*p*-tosylsulfilimine Derivatives[1]

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Abstract—The rate constants of nucleophilic addition of phenyl to vinylsulfilimine(VSI) and its derivatives were determined by an ultraviolet spectrophotometer at 25°C, and the rate equations which can be applied over a wide pH range were obtained. On the basis of the pH-rate profile, product analysis, general base catalysis, and the substituent effect, a plausible mechanism of this addition reaction was proposed: Below pH 3.0, the reaction proceeded via the addition of a neutral molecule to the carbon–carbon double bond after protonation at the nitrogen atom of the sulfilimine. Above pH 10.0, the addition of a phenoxide ion to the carbon–carbon double bond was rate controlling. However, in the pH range of 3.0 to 10.0, these two reactions occurred competitively.

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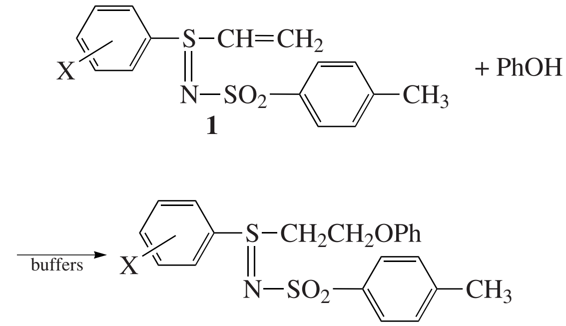
INTRODUCTION

The nucleophilic addition of activated carbon–carbon double bonds and carbon–nitrogen double bonds has been the subject of extensive mechanistic and synthetic studies [1–4]. Extensive studies of nucleophilic addition to the double bond of activated olefins and imine have led to a quantitative understanding of the relationship between the structure-reactivity and changes in reactant structure or reaction conditions. In contrast, much less is known about the sulfilimines, having a sulfur–nitrogen double bond (RR'S=NR"). Nicolet and Willard [5] reported the first synthesis of sulfilimines by reactions of sulfide with a positive halogen donor. Mann et al. [6] also prepared sulfilimines from the reactions of chloramine T(sodium-N-chloro-*p*-toluenesulfonamide) with sulfide. Earlier, Kim et al. [7] also synthesized a series of adducts from the reaction of vinylsulfilimine derivatives with various nucleophilies. These compounds are interesting because much information has appeared in the literature concerning the diuretic [8], weedkiller [9], and antimelancholia [10], as well as antitumor activities [11]. Particularly, the adducts exhibit potential utility as biochemical and pharmaceutical products.

In the previous report, we reported the hydrolysis mechanism of vinylsulfilimines over a wide pH range [12]. The hydrolysis mechanisms were sensitive to the change of pH. On the other hand, although synthetic studies for vinylsulfilimine and its nucleophilic addition reaction have been extensively conducted, only a few kinetic investigations of related nucleophilic addition reactions have been reported [13].

To further expand our understanding of the nucleophilic addition on the vinylsulfilimine, we have conducted kinetic studies of the mechanisms on the addition of phenol to S-phenyl-S-vinyl-N-*p*-tosylsulfilimine (VSI) (Eq. (1)).



(I)

X = H (**a**), *p*-CH_3 (**b**), *p*-Cl (**c**), *p*-Br (**d**).

EXPERIMENTAL

Materials. Vinylsulfilimines (**1a**–**1d**) were prepared by three-step reactions which started from the reaction of dibromoethane with thiophenol derivatives by known methods [14].

All buffer solutions were prepared from reagent grade chemicals. In all cases, the ionic strength was maintained to be 0.1 with NaCl except when pH 1.0.

Product studies. The substrate **1a** (0.3 g, 1 mmol) and sodium phenoxide (0.11 g, 1 mmol) were dissolved in 10 mL of a buffer solution (pH 9.0) of boric acid and

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[1] The text was submitted by the authors in English.

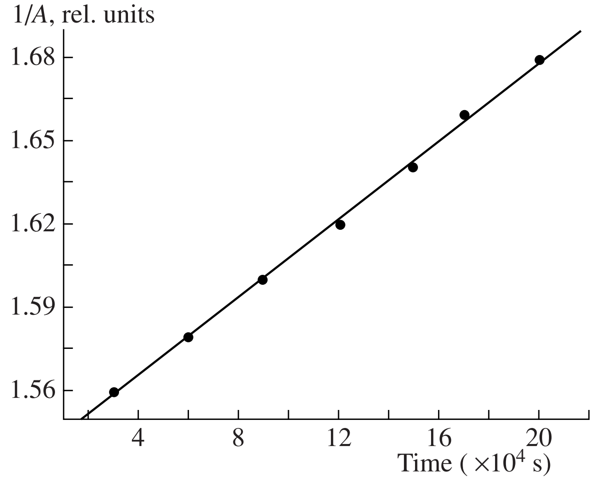


Fig. 1. Plot of 1/absorbance of vinylsulfilimine vs. time at pH 7.0 and 25°C.

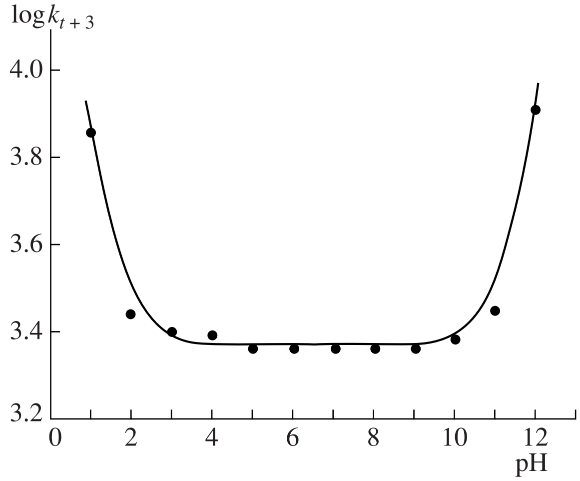


Fig. 2. pH-rate profile for the addition reaction of phenol to vinylsulfilimine at various pH and 25°C. The closed circles are experimental data, and the solid line shows the computer fitted curved by using Eq. (3).

sodium hydroxide containing 20% MeCN. The resultant solution was stirred for 6 h at room temperature, and the solvent was evaporated under reduced pressure. The residue was dissolved in dichloromethane, and pH was adjusted until 3 with 1 M HC1. The organic layer was then washed with water, dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. After recrystallization from ethyl acetate (white), the pure product melted at 128°C. IR(KBr): 1100, 1290 cm^{-1}; ^{1}H NMR($CDCl_3$): δ 2.30 (s, 3H, CH_3), 3.3–4.2 (m, 4H, CH_2CH_2), 6.5–7.9 (m, 14H, Ar–H); anal. calcd. for $C_{21}H_{21}NO_3S_2$: C, 63.16; H, 5.26; N, 3.50. Found: C, 63.20; 5.26; N, 3.52.

In acidic media, product analysis was carried out by the same method as in basic media except using a buffer solution (pH 3.0).

Kinetic studies. Reactions of **1** with phenol in buffer solutions were monitored as the decrease in the absorbance of the vinylsulfilimines (**1a**–**1d**) at 228–230 nm with a UV-vis spectrophotometer as described in [15].

RESULTS AND DISCUSSION

Determination of rate constants. The observed rates of reaction with excess phenol concentration were always pseudo–first order. Plots of the pseudo–first order rate constants against various phenol concentrations were also in all cases linear, showing the reactions are first order to vinylsulfilimine (**1a**) and phenol, respectively (plots not shown). Thus, the second-order rate constants could be calculated from the slope of the plot of 1/*A* against time for the reaction between equal initial concentrations (2.0×10^{-5} M) of vinylsulfilimine (**1a**) and phenol (Fig. 1). The second-order rate constants (k_t) determined at various pHs are given in the table and Fig. 2. The second-order rate constants of the VSI derivatives (**1b**–**1d**) were also determined in the same way (data not shown).

General base catalysis. To determine whether this reaction may be catalyzed by a general base, the rate constants were determined at various acetate ion concentrations at pH 4.78. As shown in Fig. 3, the rate constants are nearly identical regardless of the acetate ion concentration.

Substituent effect. The influence of S-aryl substituents upon the rates of addition of phenol to vinylsulfil-

Rate constants for the addition reaction of phenol[a] to vinylsulfilimine[b] at various pH and 25°C

pH	Buffer solution[c]	k_t (M^{-1}, s^{-1}) × 10^2	
		k_{obs}[d,e]	k_{calc}
1.0	HCl	7.32	7.54
2.0	″	2.75	2.86
3.0	″	2.50	2.39
4.0	HOAc + NaOAc	2.45	2.35
5.0	″	2.29	2.34
6.0	″	2.28	2.34
7.0	KH_2PO_4 + K_2HPO_4	2.30	2.34
8.0	H_3BO_3 + NaOH	2.30	2.34
9.0	″	2.30	2.34
10.0	″	2.42	2.40
11.0	NaOH	2.85	2.92
12.0	NaOH	8.28	8.32

Note: [a] [phenol] = 2.0×10^{-5} M.
[b] [VSI] = 2.0×10^{-5} M.
[c] The ionic strength was maintained at 0.1 with NaCl except for pH 1.0.
[d] Average of three or more kinetic runs.
[e] Estimated uncertainty, 3%.

imine derivatives gave excellent correlations with ρ values (Fig. 4). Hammett ρ values were 0.44, 0.43, and 0.82 for pH 2.0, 7.0, and 12.0, respectively. This result indicates that the rate of addition is accelerated by electron withdrawing groups at all pH ranges. The ρ value is larger for the basic media than for acidic conditions.

Rate equation and mechanism. As shown in Fig. 2, the rate of addition of phenol to vinylsulfilimines is given by an expression of the following Eq. (1).

$$\begin{aligned}\text{Rate} &= k_t[\mathrm{S}][\mathrm{PhOH}]_\mathrm{T}\\ &= \{k_0 + k_\mathrm{H}[\mathrm{H_3O^+}] + k_\mathrm{OH}[\mathrm{OH^-}]\}[\mathrm{S}][\mathrm{PhOH}]_\mathrm{T}\\ &= k_0[\mathrm{S}][\mathrm{PhOH}]_\mathrm{T} + k_\mathrm{H}[\mathrm{H_3O^+}][\mathrm{S}][\mathrm{PhOH}]_\mathrm{T} \qquad (1)\\ &\quad + k_\mathrm{OH}[\mathrm{OH^-}]\left\{\frac{1 + \mathrm{H_3O^+}}{\mathrm{K_a}}\right\}[\mathrm{PhO^-}][\mathrm{S}]\},\end{aligned}$$

where $[\mathrm{PhOH}]_\mathrm{T}$ is the total concentration of $[\mathrm{PhO^-}]$ and [PhOH] at equilibria; k_0 is the pH independent part, it is the constant due to catalysis of H_2O; and k_H and k_OH are the hydronium and hydroxide ion dependent rate constants, respectively. $\mathrm{K_a}$ is the acid ionization constant of phenol.

Then k_t is given as follows:

$$= k_0 + k_\mathrm{H}[\mathrm{H_3O^+}] + k_\mathrm{OH}[\mathrm{OH^-}]\left\{1 + \frac{[\mathrm{H_3O^+}]}{\mathrm{K_a}}\right\}. \qquad (2)$$

Substituting $\mathrm{K_a} = 1.28 \times 10^{-10}$ [16] and the obtained values of k_0, k_H, and k_OH from experimental data into Eq. (2),

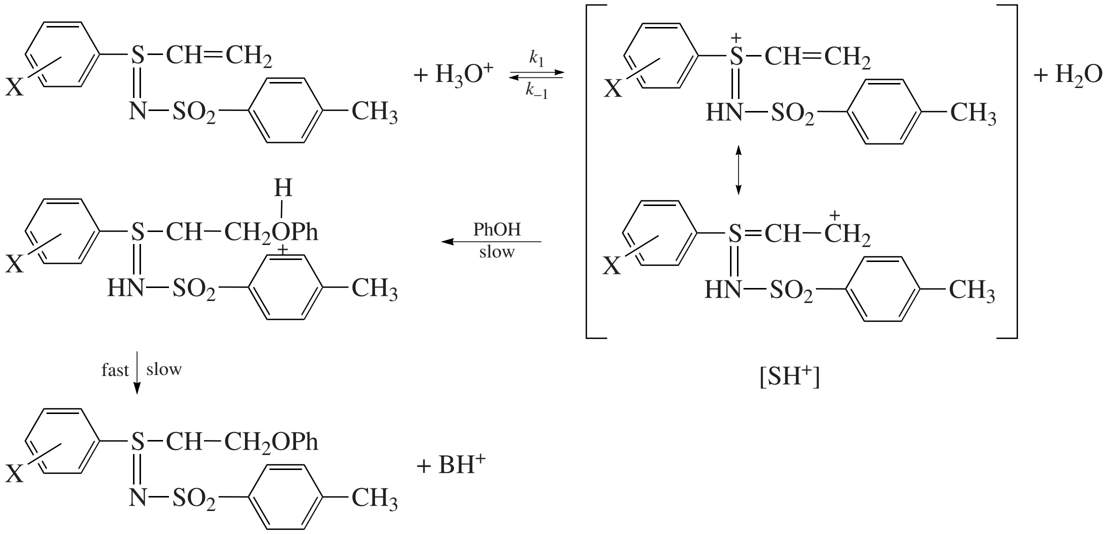
$$k_t = 2.34 \times 10^{-1} + 5.20 \times 10^{-1}[\mathrm{H_3O^+}] + 6.04[\mathrm{OH}]. \qquad (3)$$

The table and Fig. 2 show the overall rate constant (k_t) calculated by Eq. (3) was in good agreement with the observed values.

Similarly, the rate equation was obtained for the addition of phenol to vinylsulfilimine derivatives (**1b**–**1d**):

$$p\text{-}\mathrm{CH_3}\colon k_t = 1.29 \times 10^{-2}$$
$$+ 3.49 \times 10^{-1}[\mathrm{H_3O^+}] + 4.40[\mathrm{OH}],$$
$$p\text{-}\mathrm{Cl}\colon k_t = 2.48 \times 10^{-1}$$
$$+ 6.30 \times 10^{-1}[\mathrm{H_3O^+}] + 7.24[\mathrm{OH}],$$
$$p\text{-}\mathrm{Br}\colon k_t = 2.43 \times 10^{-1}$$
$$+ 7.0 \times 10^{-1}[\mathrm{H_3O^+}] + 7.85[\mathrm{OH}].$$

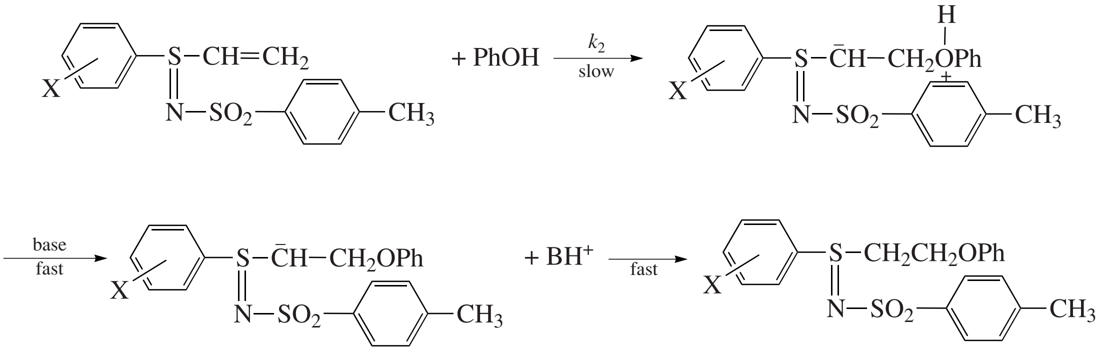
At low pH, S-phenyl-S-2-(phenoxyethyl)-N-*p*-tosylsulfilimine was isolated as a product. The rate of addition of phenol to vinylsulfilimine is not subject to general base catalysis (Fig. 3) and is proportional to the hydronium ion concentration (Fig. 2). Therefore, it can be proposed that the reaction proceeds by an attack of phenol on the carbon–carbon double bond after protonation at nitrogen of the sulfilimine group.



Scheme 1.

The rate-determining step of the reaction may be decided by the general base- and substituent effects. In the acidic solution, the third step is not rate limiting because this reaction does not exhibit a general base effect. The concentration of $\mathrm{SH^+}$ is expected to increase by the electron donating group, whereas k_2 should be enhanced by the electron-withdrawing substituents. Therefore, the observed ρ = 0.44 at pH 2.0 indicates that the second step must be rate limiting under this condition.

In the range of pH 3.0–10.0, the reaction is almost independent of pH change. Therefore, the following addition reaction mechanism was proposed.

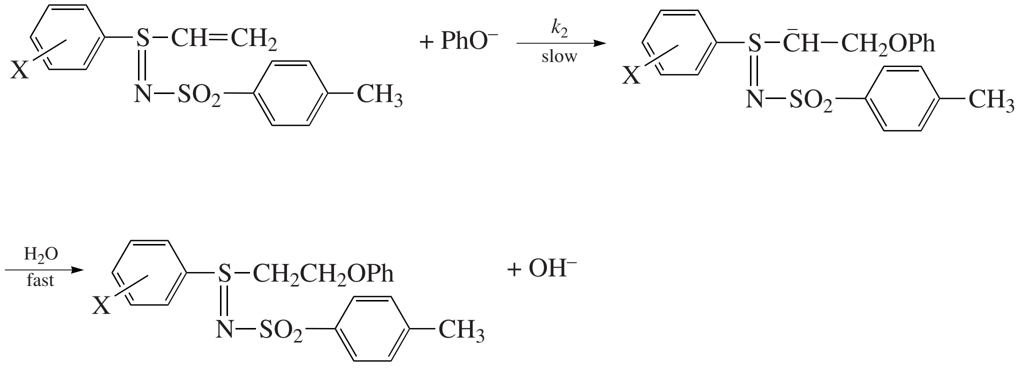


Scheme 2.

The observed $\rho = 0.43$ at pH 7.0 indicates that the first step must be rate limiting.

At high pH, it is expected that the phenoxide and hydroxide anions could be added to VSI. However, the spectral and analytical data indicated that the product obtained under the basic condition (pH 9.0) was the phenol adduct. Moreover, the kinetic results indicated that the rate for the phenoxide anion addition was approximately 10^5 times faster than that of hydroxide of VSI at all pH ranges [12]. Therefore, the most plausible mechanism under basic media is shown in Scheme 3.

$$\mathrm{PhOH + OH^- \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} PhO^- + H_2O}$$



Scheme 3.

Since the rate of the addition reaction is accelerated by the electron withdrawing group with $\rho = 0.82$ at pH 12.0, the attack of the phenoxide ion is the rate determining step in alkaline pHs. Noteworthy is the larger Hammett ρ values determined for the basic media rather than the acidic condition. In the acidic condition, the smaller ρ value was attributed to the cancellation of the opposing factor ($\rho = 0.44$, pH 2.0). The concentration of SH^+ is expected to increase by the electron donating group, whereas the k_2 should be enhanced by the electron-withdrawing substituents (Scheme 1). In contrast, the attack of the phenoxide ion is only the rate limiting step in the basic condition.

CONCLUSIONS

In conclusion, the rate equations which can be applied over a wide pH range for the nucleophilic addi-

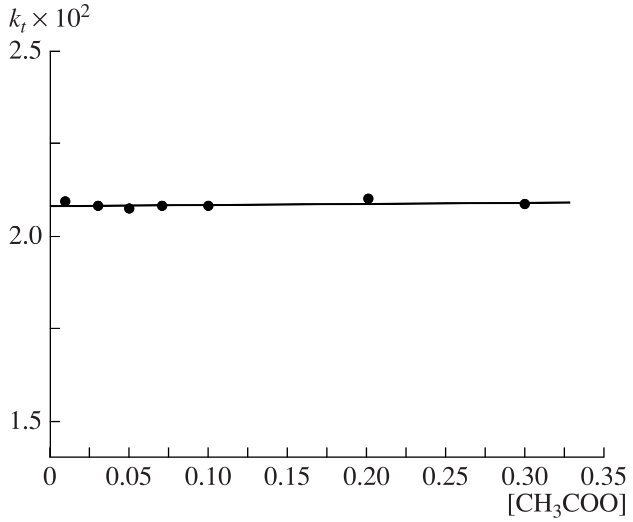


Fig. 3. Plot of rate constant k_t vs. concentration of acetate ion at pH 4.78 and 25.0°C.

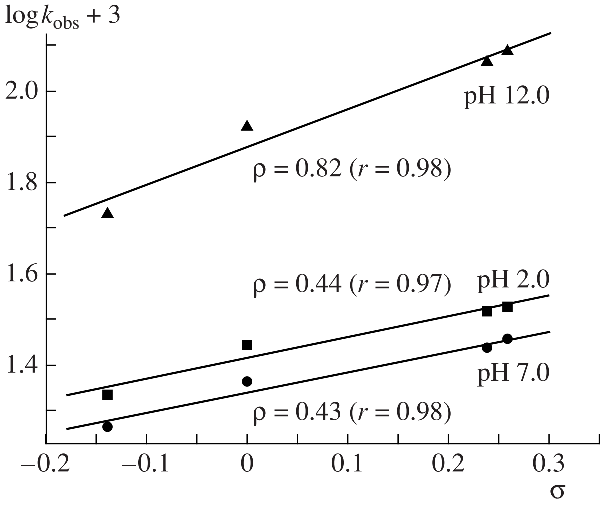


Fig. 4. Hammett plots for the addition reaction of phenol to vinylsulfilimine derivatives at various pH.

tion of activated carbon–carbon double bonds were obtained. On the basis of various kinetic results, the reaction mechanism was proposed.

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