Kinetics Studies on the Mechanism of Hydrolysis of
S-Phenyl-S-vinyl-N-p-tosylsulfilimine Derivatives

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Hydrolysis reactions of S-phenyl-S-vinyl-N-p-tosylsulfilimine (VSI) and its derivatives at various pH have been investigated kinetically. The hydrolysis reactions produced phenylvinylsulfoxide and p-toluene sulfonamide as the products. The reactions are first order and Hammett ρ values for pH 1.0, 6.0, and 11.0 are 0.82, 0.45, and 0.57, respectively. This reaction is not catalyzed by general base. The plot of k vs pH shows that there are three different regions of the rate constants (k_t) in the profile.; At pH < 2 and pH > 10, the rate constants are directly proportional to the concentrations of hydronium and hydroxide ion catalyzed reactions, respectively. The rate constant remains nearly the same at 2 < pH < 10. On the bases of these results, the plausible hydrolysis mechanism and a rate equation have been proposed: At pH < 2.0, the reaction proceeds *via* the addition of water molecule to sulfur after protonation at the nitrogen atom of the sulfilimine, whereas at pH > 10.0, the reaction proceeds by the addition of hydroxide ion to sulfur directly. In the range of pH 2.0-10.0, the addition of water to sulfur of sulfilimine appears to be the rate controlling step.

Key Words : Hydrolysis, General base catalysis, Hammett ρ

Introduction

The nucleophilic addition of activated carbon-carbon double bonds and carbon-nitrogen double bonds has been subjected to 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 sulfur-nitrogen double bond (RR' S=NR'). Nicolet and Willard[5] reported the first synthesis of sulfilimines by reactions of sulfide with positive halogen donor. Mann *et al.*[6] also prepared sulfilimines from the reactions of chloramine T(sodium-N-chloro-p-toluenesulfonamide) with sulfide. These compounds are interesting because much information has appeared in the literature concerning the diuretic,[7] weedkiller,[8] and antimelancholia,[9] as well as anti-tumour activities.[10] Kim and coworkers[11] have synthesized a series of adducts from the reaction of vinylsulfilimine derivatives with thiophenol, 1-methyl-5-mercap-1,2,3,4,-tetrazole, and phenol. Such adducts would exhibit potential utility as biochemical and pharmaceutical products. They also suggested a mechanism on the addition of mercaptan to vinylsulfilimines in a wide pH range.[12]

As shown in above references, some kinetic studies for the nucleophilic addition of nucleophilic such as thiol to vinyl-sulfilimines have been reported. However, the kinetic studies for the hydrolysis of vinylsulfilimine derivatives have not reported yet.

To understand the detailed mechanism of hydrolysis reaction on the vinylsulfilimine, we have investigated the mechanism of hydrolysis and the rate equation of S-phenyl-S-vinyl-N-p-tosylsulfilimine (VSI) over a wide pH range.

Experimental Section

General procedure. All chemicals were reagent grade unless otherwise specified. The ionic strength of the buffer solutions was kept constant to 0.1 M by adding sodium chloride except below pH 1.0. Kinetic runs and UV spectra were obtained from a Hatachi Recording Spectrophotometer 200-20. IR spectra were taken with a Perkin-Elmer Infrared 710B. NMR spectra were obtained with a Varian EM 360 (60 MHz) and Prerkin-Elmer R-32 (90 MHz) spectrometer in CDCl$_3$. Elemental analysis was performed by Perkin-Elmer 240 CHN Analyzer and melting points were measured with a Haake Büchler apparatus.

Synthesis of VSI. Vinylsulfilimine and its derivatives were prepared by three-step reactions which started from the reaction of dibromoethane with thiophenol derivatives by known methods.[13]

Product studies of hydrolysis from VSI. VSI (1.5 g, 5.0×10^{-3} mol) was dissolved in 30 mL of a buffer solution (pH = 9.0) of boric acid and sodium hydroxide containing 20% methanol. The solution was stirred for 24 hrs at 50 °C, extracted with diethylether (50 mL), washed with brine, dried over anhydrous MgSO$_4$, and then evaporated. The remaining residue was flash chromatographed on silica gel (Hexane/EtOAc. 2/1) to afford phenylvinyl sulfoxide and p-toluenesulfonamide. **phenylvinyl sulfoxide**: IR (liquid, cm^{-1}) 1050 (S=O); ^{1}H NMR (CDCl$_3$) δ 7.5-7.6 (m, 5H, phenyl), 6.7 (m, 1H, SOC_H_), 5.9-6.2 (dd, 2H CH=C_H$_2$). **p-toluene-sulfonamide**: mp 138-139 °C; IR (KBr, cm^{-1}) 3350, 3250
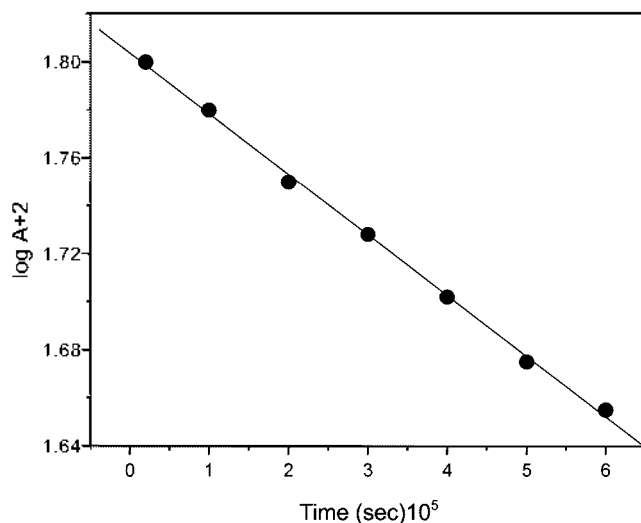
Figure 1. Plot of log absorbance *vs.* time for the hydrolysis of VSI at pH 1.0 and 50 °C.

(N-H), 1325, 1140 (O=S=O): ^{1}H NMR (CDCl$_3$) δ 7.5-7.8 (dd, 4H. phenyl), 7.2 (s, 2H, NH$_2$), 2.3 (s, 3H. CH$_3$).

In acidic media. product analysis was carried out by the same method as in the basic media except using buffer solution (pH = 2.0).

Kinetic studies. Kinetic runs were made in water at 50 °C. The vinylsulfilimine was introduced as 1 mL of 1.0×10^{-3} M methanolic solution in 100 mL of final aqueous solution and the flask was quickly shaken. Each aliquot (3 mL) of the solution was removed from the volumetric flask at time intervals and was placed in a quartz cuvette. The decrease of absorbance at the wavelength of maximum (*p*-OCH$_3$: λ_{max} = 227 nm, *p*-CH$_3$: λ_{max} = 230 nm. H: λ_{max} = 228 nm. *p*-Cl: λ_{max} = 230 nm, *p*-NO$_2$: λ_{max} = 229 nm) for the VSI and its derivatives with time was monitored.

Results and Discussion

Determination of rate constants. Figure 1 shows the typical plot of logarimathic absorbance versus time for the hydrolysis reaction of VSI. The observed rate constant (k_{obs}) was estimated from the slope of plot of log absorbance vs. time in Figure 1. Similar plots were obtained for the hydrolysis reactions of its derivatives at all pH ranges (plots not shown). As shown in Figure 1, the observed rates of VSI was always of the first-order. The first-order rate constants (k_{obs}) obtained from the slope at various pH are given in Table 1 and Figure 2 shows pH-log (rate) profile of this reaction. First-order rate constants of the VSI derivatives were also determined by the same method (Table 2).

Substituent effect. The influence of *S*-aryl substituent upon hydrolysis rates correlated statifactorily with the Hammett equation using σ values (Figure 3). Hammett ρ values were 0.82. 0.45. and 0.57 for pH 1.0. 6.0 and. 11.0, respectively. This result indicates that the rate of hydrolysis is accelerated by electron withdrawing groups at all pH ranges.

General base catalysis. To determine whether this reac-

Table 1. Rate constants for the hydrolysis of VSI[a] at various pH and 50 °C

pH	Buffer solution[b]	k_t (sec^{-1}) $\times$ 10$^-$	
		k_{obsd}[c,d]	k_{calcd}
0.0	HCl	9.82	9.92
1.0	HCl	4.50	4.35
2.0	HCl	1.90	1.81
2.5	HCl	1.70	1.66
3.0	HCl	1.69	1.61
3.5	HOAc + NaOAc	1.67	1.60
4.0	HOAc + NaOAc	1.57	1.60
5.0	HOAc + NaOAc	1.59	1.59
6.0	HOAc + NaOAc	1.54	1.59
7.0	KH$_2$PO$_4$ + K$_2$HPO$_4$	1.53	1.59
8.0	H$_3$BO$_3$ · NaOH	1.58	1.59
8.5	H$_3$BO$_3$ · NaOH	1.59	1.59
9.0	H$_3$BO$_3$ · NaOH	1.66	1.59
9.5	H$_3$BO$_3$ · NaOH	1.79	1.60
10.0	H$_3$BO$_3$ · NaOH	1.80	1.62
11.0	NaOH	2.30	2.21
12.0	NaOH	4.30	4.37

[a] |Substrate| = (1-2)$\times$ 10^{-5} M. [b] The ionic strength of the buffer solutions was kept constant to 0.1 M by adding sodium chloride except below pH 1.0. [c] Average rate constant for two or more kinetic runs. [d] Estimated uncertainty. 3%.
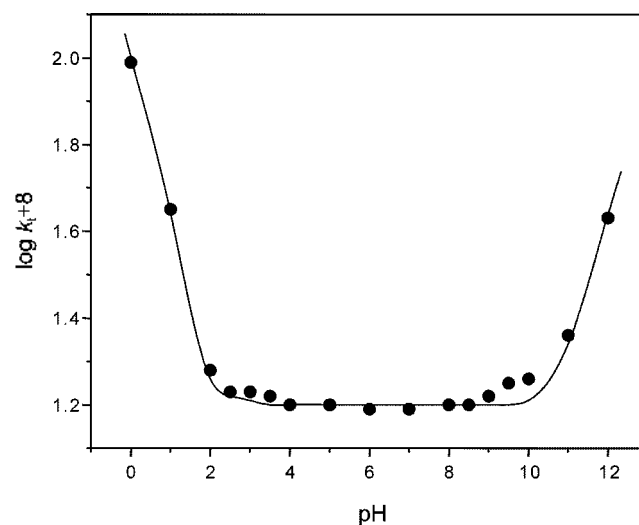
Figure 2. pH dependence of the first order rate constant for the hydrolysis of VSI at 50 °C. Circles are experimental points and the solid line is drawn according to (3).

tion may be catalyzed by general base. the rate constants were determined at various acetate ion concentrations at pH 4.78. Figure 4 shows this reaction is not catalyzed by general base.

Rate equation and mechanism. As shown in Figure 2. the hydrolysis rate of VSI can be expressed by the following equation (1).

$$\text{Rate} = k_t[\text{VSI}] = \{k_1^{H_2O} + k_1^H[\text{H}_3\text{O}^+] + k_1^{OH}[\text{OH}^-]\}[\text{VSI}]$$

(1)

Table 2. Rate constants for the hydrolysis of VSI[a] derivatives at various pH and 50 °C

pH	[b]k_{total} (sec^{-1}) × 10^7			
	p-OCH$_3$	p-CH$_3$	p-Cl	p-NO$_2$
0.0	4.62	5.52	16.1	53.8
1.0	2.92	3.48	7.01	20.5
2.0	1.83	2.45	5.42	7.46
2.5	1.40	1.79	4.08	4.37
3.0	1.25	1.49	3.03	3.31
3.5	1.24	1.35	2.36	3.05
4.0	1.20	1.32	2.32	2.87
5.0	1.22	1.32	2.10	2.76
6.0	1.21	1.32	2.05	2.76
7.0	1.27	1.35	2.15	2.77
8.0	1.23	1.32	2.19	2.83
8.5	1.25	1.36	2.34	2.89
9.0	1.24	1.40	2.24	2.97
9.5	1.35	1.44	2.53	3.66
10.0	1.42	1.58	2.93	4.71
11.0	1.66	2.01	3.63	6.67
12.0	1.93	2.52	4.48	–

[a][Substrate] = (1-2) × 10^{-5}. [b]Average rate constant for two or more kinetic runs. [c]Estimated uncertainty, ± 3%.

where k_1^{H2O} is the pH independent rate, *i.e.,* the constant due to the catalysis by H$_2$O, and k^H and k_1^{OH} are the hydronium and hydroxide ion dependent rate constant, respectively.

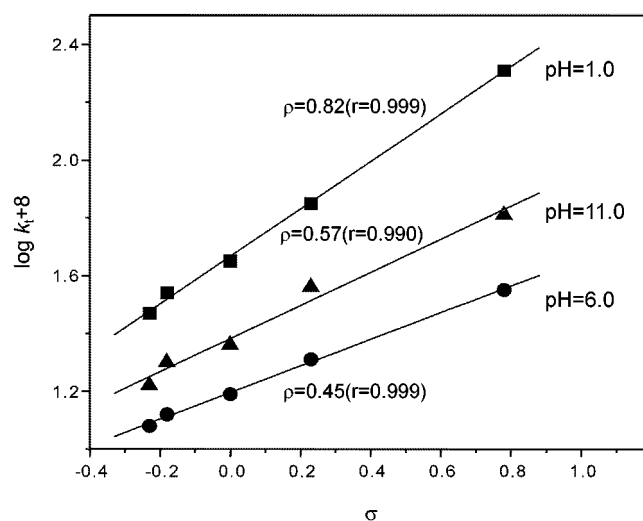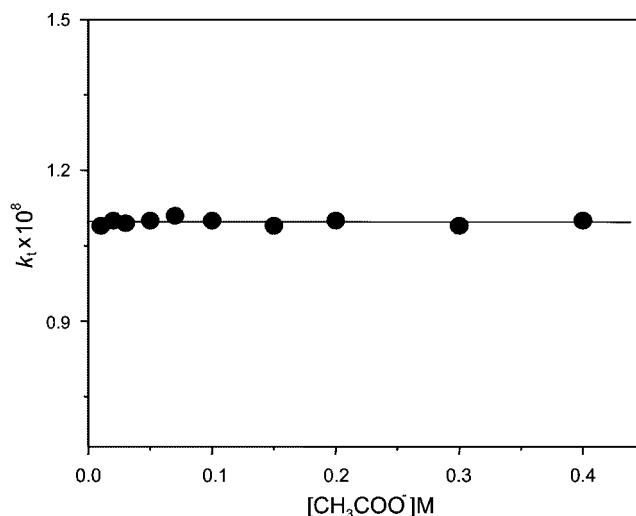As the result, over all rate equation becomes:

$$k_t = k_1^{H2O} + k^H[H_3O^+] + k_1^{OH}[OH^-] \tag{2}$$

Substituting the numerical values obtained from the fit of experimental data to equation (2), the k_t is given by equation (3)

$$k_t = 1.59 × 10^{-7} + 2.21 × 10^{-6}[H_3O^+] + 2.77 × 10^{-5}[OH^-] \tag{3}$$

Table 1 and Figure 2 show that the overall rate constant, k_t

Figure 3. Hammett plots for the hydrolysis of VSI.

Figure 4. Effect of general base concentration on the rate of hydrolysis of VSI at pH 2.85 and 50 °C.

calculated by equation (3) are in good agreement with the observed values.

Similarly, the rate equation obtained for the hydrolysis of VIP derivatives are as follows.

S-p-Methoxyphenyl-S-vinyl-N-p-tosylsulfilimine:
$$k_t = 1.22 × 10^{-7} + 1.21 × 10^{-6}[H_3O^+] + 2.66 × 10^{-5}[OH^-]$$
S-p-Methylphenyl-S-vinyl-N-p-tosylsulfilimine:
$$k_t = 1.45 × 10^{-7} + 2.28 × 10^{-6}[H_3O^+] + 8.33 × 10^{-5}[OH^-]$$
S-p-Chlorophenyl-S-vinyl-N-p-tosylsulfilimine:
$$k_t = 2.10 × 10^{-7} + 3.85 × 10^{-6}[H_3O^+] + 7.76 × 10^{-5}[OH^-]$$
S-p-Nitrophenyl-S-vinyl-N-p-tosylsulfilimine:
$$k_t = 2.76 × 10^{-7} + 1.45 × 10^{-5}[H_3O^+] + 1.96 × 10^{-4}[OH^-]$$

At low pH, hydrolysis of VSI is not subject to general base catalysis (Figure 4) and the rate of hydrolysis is proportional to the hydronium ion concentration (Figure 2). Thus pH dependence must be caused by very rapid equilibrium of VSI, S, with its conjugated acid, SH$^+$ which undergoes rate controlling through the attack of water. It follows that $k_{II} = k_2^{H2O}K = 2.21 × 10^{-6}sec^{-1}$. These results may be explained in term of the mechanism in following reaction scheme.

The rate-determining step of the reaction may be decided by the general base effect and Hammett ρ value. In the acidic solution, the third step is not rate liming because this reaction does not exhibit a general base effect. 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. The observed $\rho = 0.82$ at pH = 1.0, indicates that the second step must be the rate limiting under this condition.

The structure of the transition state for the rate limiting step may also be deduced by considering the Hammett ρ value. The ρ value indicates the extent of charge development at the reaction site in the transition state. In the acidic mechanism, the ρ value was given as 0.82, indicating that electron-withdrawing groups facilitate the reaction. A positive ρ value means that electron density on reaction site increases

Scheme 1

Scheme 2
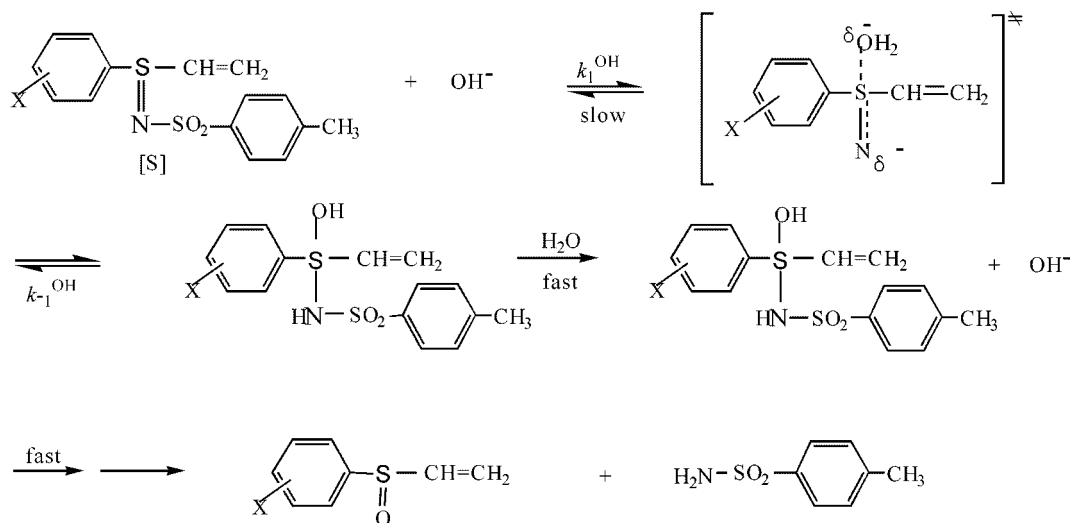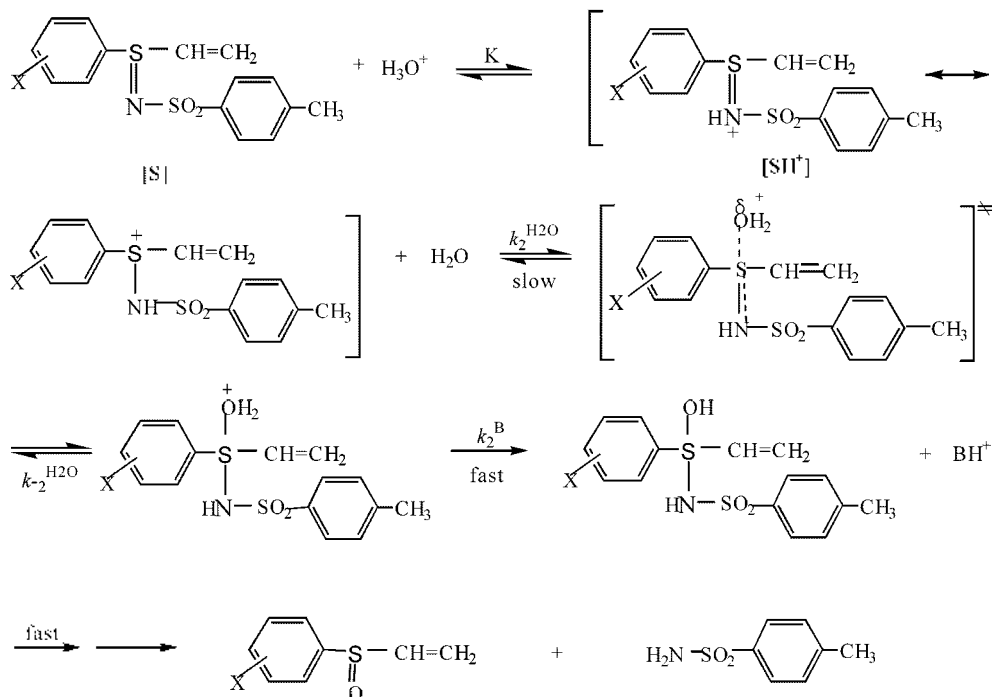
in going from reactant to transition state.

At high pH. since the rate constant is directly proportional to hydroxide ion concentration. the following reaction mechanism is proposed.

In alkaline pH's. since the rate of hydrolysis is accelerated by the electron-withdrawing group with $\rho = 0.57$ at pH = 11.0. the rate limiting step should be the direct attack of hydroxide ion at sulfur atom. As shown in acidic solution, electron-withdrawing groups can facilitate the addition of the OH⁻ by favorable interaction with the electron-rich sulfur atom that develops in the rate determining step.

In addition. the magnitude of ρ. whether positive or negative. also provides information about the rate-determin-

ing step of a reaction. A large ρ indicates high sensitivity to substituent groups and implies that there is a large redistribution of charge involved in forming the transition state.[14] The rate constant k_1^{OH} would be less sensitive to change in σ than k^H because the hydroxide ion should be more reactive than water in the addition step ($\rho = 0.82$ at pH = 1.0. $\rho = 0.57$ at pH = 11.0).

At $2 < $ pH $ < 10$. the hydrolysis rate of VSI is almost independent of pH change. therefore. it seems most reasonable to conclude that the addition of water to sulfur atom is the rate controlling step.

The structure of this transition state can also be rationalized using the ρ value similarly. Considering that water is less
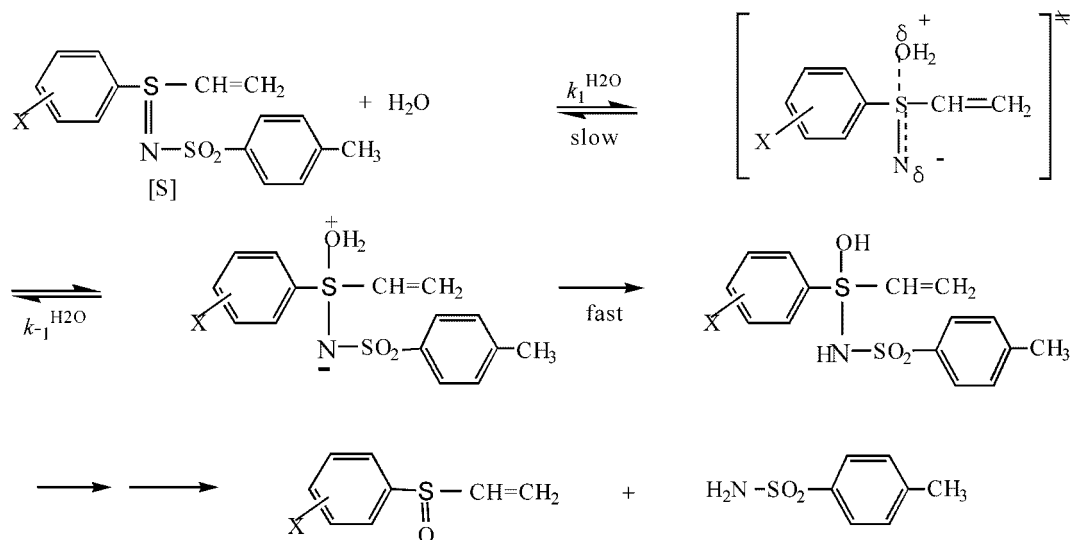
Scheme 3

reactive than hydroxide ion. the p value for this reaction is expected to be larger than that determined under basic condition. However, the observed $p = 0.45$ at pH 6.0 is smaller than $p = 0.51$ at pH = 11.0. At present the origin of this dichotomy is not clear.

As shown in above mechanism. if the intermediate is a reactive, unstable species. its concentration will never be very large. Therefore, when the steady-state approximation is applied with respect to the [intermediate], the k_{obsd} values (Table 1 & 2) shown in Figure 2 are given by eq. 2.

In conclusion, the rate equations which can be applied over a wide pH range were obtained. On the basis of various kinetic results. a reaction mechanism was proposed. However, to further expand our understanding of the transition state and intermediate on the this reaction mechanism. the detailed mechanism of the hydrolysis will be the subject of our future investigation.

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