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Equilibrium and Kinetic Studies of Reactions of 2-Methyl-2-propanesulfenic Acid

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ABSTRACT

2-Methyl-2-propanesulfenic acid readily undergoes self-condensation to give S-t-butyl 2-methyl-2-propanethiosufinate. Rates of the reaction were measured in aqueous acetonitrile solution by use of NMR and UV spectroscopy. The reaction is second order in the substrate. The half-life in a neutral aqueous solution is about 150 hours at 35°C when the initial substrate concentration is 0.003 M. The rate is proportional to acid concentration in the range 0.004–0.2 M. In alkaline solution, the main reaction is self-condensation but some side reactions also seem to occur. The disappearance of the substrate does not follow satisfactory second-order kinetics, but the second-order rate constants obtained by the time-lag method show a maximum around pH 10–11. The pK_a (10.47) of the sulfenic acid was obtained at 14°C from a sigmoid curve of the initial absorbances (240 nm) determined by extrapolation of the time-dependent curve.

Sulfenic acids play important roles as transient intermediates in redox and rearrangement reactions of sulfur compounds that are of importance both in organic and biochemical processes [1–3]. Most simple sulfenic acids are, however, too unstable to be isolated, and direct studies of their chemistry are limited [1–3]. Kice and co-workers [4] have recently studied kinetically reactions of a stable sulfenic acid, 1-anthraquinonesulfenic acid. Less stable sulfenic acids can be generated by flash vacuum pyrolysis (FVP) and deposited on a cold finger [5–7]. The chemistry of these unstable acids was explored by analysis of the final products obtained on warming the acids in the presence or absence of an appropriate trapping agent [5–8].

In the present article, a simple, moderately stable sulfenic acid, 2-methyl-2-propanesulfenic acid (**1**), is chosen as the substrate for more precise and direct investigations of the chemistry of the sulfenic acid in aqueous solution at ambient temperatures.

RESULTS

The sulfenic acid **1** was generated by FVP of di-*t*-butyl sulfoxide, with deposition of the product on a cold finger cooled with liquid nitrogen [5], and it was stored as a solution at −196°C. The ^{1}H NMR spectra of stock solutions of **1** in various (deuterium) organic solvents were recorded at appropriate time intervals at the probe temperature of 35°C. Typically, in chloroform-d$_1$, a singlet at δ 1.21 attributable to **1** gradually disappeared with formation of two singlets at δ 1.30 and 1.48 attributable to the condensation product, *S-t*-butyl 2-methyl-2-propanethiosulfinate **2** [8] (Eq. 1). The total peak area of these signals was found to be constant within experimental error during the reaction, and no other signals were detectable. That is, the self-condensation is the sole reaction in a solution of **1** and no side reaction occurs.

$$\underset{\mathbf{1}}{2\mathrm{Me_3CSOH}} \rightarrow \underset{\mathbf{2}}{\mathrm{Me_3CS(O)SCMe_3}} + \mathrm{H_2O} \qquad (1)$$

Dedicated to Prof. Yao-Zeng Huang on the occasion of his eightieth birthday.

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The lifetime of **1** is very much dependent on the solvent as well as on the concentration of **1**. The reaction is second order with respect to **1**. Approximate half-lives of **1** in various solvents were evaluated by NMR spectroscopy at 35°C and with an initial concentration of **1** of 0.05 M: CCl_4, 30 seconds; $CDCl_3$, 3.6 minutes; C_6D_6, 17 minutes; CD_3CN, 2 hours; CD_3OD, 7 hours; D_2O containing 10 vol % CD_3CN, 10 hours (150 hours at 0.003 M). A similar trend of solvent effects on the sulfenic acid stability had previously been pointed out from observations taken during the thermal decomposition of *t*-butyl sulfoxide [8]. The retardation of self-condensation of the sulfenic acid in protic polar solvents is ascribed to the lack of hydrogen-bonding association (see subsequent text).

Although the self-condensation of **1** in a neutral aqueous solution is quite slow, it is accelerated both by acid and base. The rates in acidic D_2O containing about 20 vol % of CD_3CN and $DClO_4$ (0.004–0.23 M) were measured by NMR spectroscopy at the probe temperature of 35°C. The singlet at δ 1.13 due to **1** disappears with simultaneous formation of two singlets at δ 1.23 and 1.41 due to **2** (Figure 1). The total peak area is constant within experimental error during the reaction as seen in Figure 2. The reaction was followed by the decrease in peak area of the NMR signal of **1** which was quantified as the fraction of the total area or the relative area to that of the internal standard (CHD_2CN). The second-order plots were satisfactorily linear when reciprocals of the areas (or concentration of **1**) were plotted against reaction time (Figure 3). The observed second-order rate constants k_2 are summarized in Table 1.

The reaction was also monitored by UV spectroscopy. The absorbance at 240 nm increases with time of reaction, and the absorbance change follows the second-order kinetic law. The observed rate constants (given in Table 1) agree well with those obtained by the NMR method. The rate constants k_2 increase linearly with acid concentration (Figure 4), and the third-order rate constants k_3 calculated are practically constant ($k_3^D = 2.26\ M^{-2}s^{-1}$). The complete rate equation is presented by Equation 2.

$$\text{rate} = k_2[\mathbf{1}]^2 = k_3[\text{acid}][\mathbf{1}]^2 \qquad (2)$$

Kinetic measurements were also carried out in normal aqueous acid ($CH_3CN–H_2O$) by the UV method, and the second-order rate constants obtained are given in Table 2. The acid-catalytic constants k_3 are also calculated ($k_3^H = 1.74\ M^{-2}s^{-1}$). The solvent deuterium isotope effect is inverse: $k_D/k_H = 1.3$. The reaction in dilute HCl (0.08 M) is also second order in **1** but k_2 is about three times greater than that in $HClO_4$. Chloride ion is operating as a nucleophilic catalyst as is in the corresponding reaction of the sulfenate ester [9].

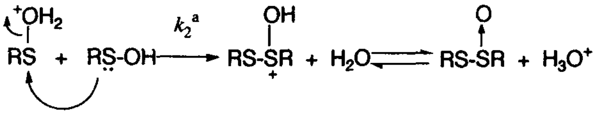
Reaction in alkaline solution is rapid and cannot be followed by NMR spectroscopy. The NMR spectra of the products in deuterium media show formation of considerable amounts of side products (δ 0.84, 1.06, and 1.16). The reaction was followed at 235 nm by UV spectroscopy. The absorbance decreases with reaction time above pH 11, while it increases at lower pH. Kinetic analysis by the second-order (or first-order) kinetic law encountered some difficulties that arise from unreliable infinity absorbance due to the side reactions. The second-order rate constants were evaluated by the time-lag method proposed by Espenson [10]. The k_{obsd} values obtained in this way were plotted against pH as shown in Figure 5. The rate shows a sharp maximum in the pH range 10–11.

The UV spectra of alkaline aqueous solutions of **1** just after dilution seem to be significantly different from those observed in acid or neutral solutions. The initial absorbances A_0 at 240 nm of alkaline buffer solutions of **1** were obtained by extrapolation of the time-dependent absorbance curves to time zero at 14°C. The absorbances A_0 adhere to a sigmoidal curve when plotted against pH, as shown in Figure 6. This is considered to be due to the acid dissociation of **1** and the pK_a is evaluated to be 10.47 ± 0.14.

$$\underset{\mathbf{1}}{Me_3CSOH} + H_2O \overset{K_a}{\rightleftharpoons} Me_3CSO^- + H_3O^+ \qquad (3)$$

DISCUSSION

The sulfenic acid **1** has a considerably long lifetime in a dilute, neutral aqueous solution, the second-order rate constant for the self-condensation being $5 \times 10^{-4}\ M^{-1}\ s^{-1}$ at 35°C. However, the self-condensation is accelerated by the presence of acid. The reaction must occur between a protonated molecule of **1** and a neutral molecule (Equation 4).



(4)

In this reaction, the rate can be given by Equation 5, which is comparable to Equation 2 with $k_3 = k_2^a/K_A$.

$$\begin{aligned}\text{rate} &= k_2^a[\text{RSOH}][\text{RSOH}_2^+] \\ &= (k_2^a/K_A)[H^+][\mathbf{1}]^2 \qquad (5)\end{aligned}$$

where K_A is the acid dissociation constant of the protonated sulfenic acid ($RSOH_2^+$). Since $[H^+] \ll K_A$ in the acidity range employed, $[RSOH_2^+] = [H^+][RSOH]/K_A$ and $[RSOH] = [\mathbf{1}]$.

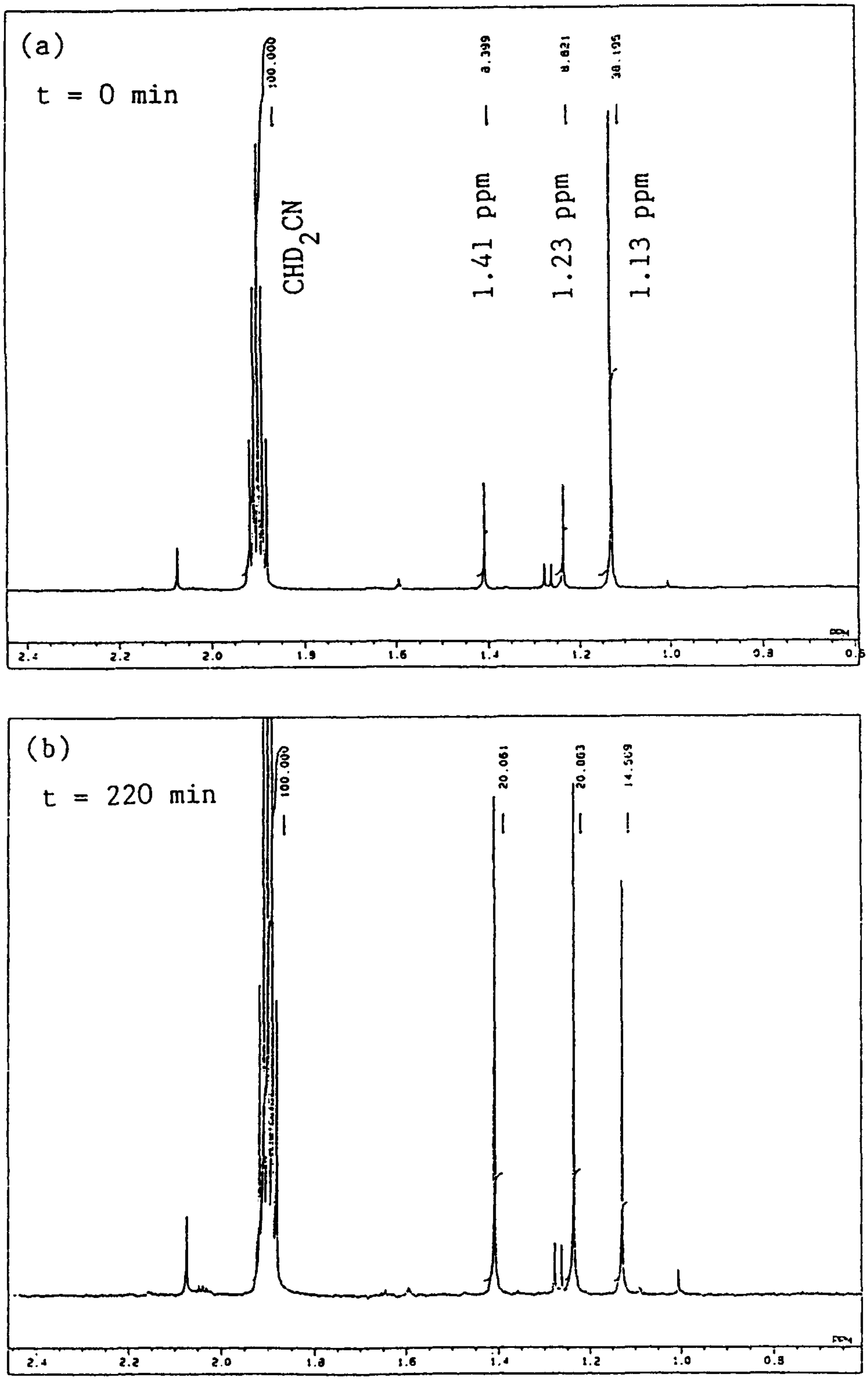


FIGURE 1 ^{1}H NMR spectra of 1 in 20% CD_3CN-80% D_2O at (a) reaction time zero and (b) 220 minutes. $[DClO_4] = 3.85 \times 10^{-2}$ M.

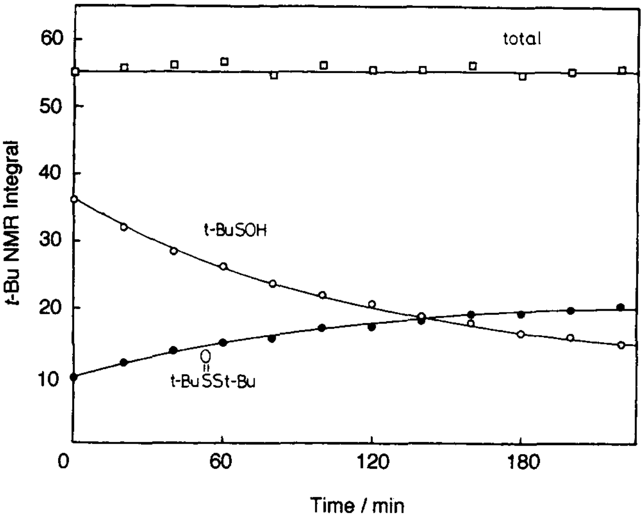


FIGURE 2 Time-dependent change in the integral intensities of the methyl signals of **1** and **2**. $[DClO_4] = 4.03 \times 10^{-3}$ M.

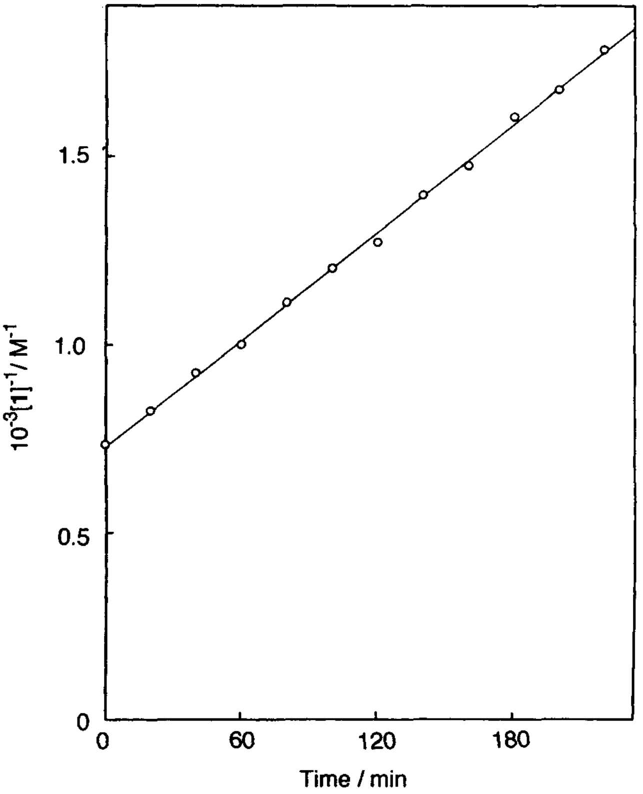
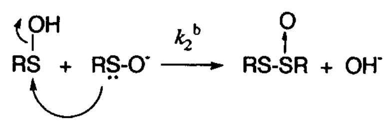


FIGURE 3 The second-order plot for the reaction of **1**. $[DClO_4] = 4.03 \times 10^{-3}$ M.

In alkaline solution, the rate shows a maximum at about pH 10.5, essentially the pK_a of the sulfenic acid (RSOH), which indicates that the reaction takes place between the neutral acid and the conjugate base (Equation 6).



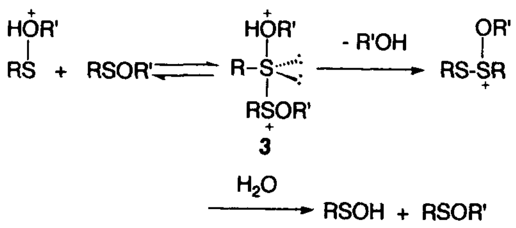
(6)

The rate of the self-condensation in alkaline solution can be expressed by Equation 7. The solid curve in Figure 5 is a theoretical one calculated with $pK_a = 10.5$ and $k_2^b = 220\ M^{-1}s^{-1}$.

$$\begin{aligned} \text{rate} &= k_2^b[RSO^-][RSOH] \\ &= k_2^bK_a[H^+][\mathbf{1}]^2/(K_a + [H^+])^2 \qquad (7) \end{aligned}$$

where $[\mathbf{1}]$ = total concentration of **1**; $[\mathbf{1}] = [RSOH] + [RSO^-]$. A proposed reaction between two molecules of the sulfenate anion with general acidic assistance by a water molecule [11] should be excluded.

The condensation reactions depicted by Equations 4 and 6 are nucleophilic substitution reactions at the sulfenyl sulfur by the other sulfenyl nucleophile. A similar reaction is involved in the nucleophilic self-catalysis of acid hydrolysis of sulfenate esters [9,12]. The latter reaction is considered to take place through a hypervalent intermediate, such as **3** (Equation 8).



(8)

A similar reaction mode can reasonably be considered for the present condensation reaction of the two molecules of sulfenic acid. A favorable hypervalent bonding interaction between the protonated sulfenic acid and free sulfenic acid with the OH_2 and the nucleophilic sulfur in the apical positions is, in fact, reproduced by theoretical ab initio MO calculations [13]. A general belief that the instability of sulfenic acids is due to their hydrogen-bonding association and a facile condensation through a five-membered cyclic transition state (Equation 9) [14] may only be partly true, since the cyclic transition state is forced to have the OH and the nucleophilic sulfur in the equatorial and apical positions, which may not be favorable for

TABLE 1 Rate Constants for the Condensation of **1** in Deuterium Acidic Solution[a]

	NMR			UV	
$[DClO_4]/M$	$k_{obsd}/M^{-1}\ s^{-1}$	$k_3/M^{-2}\ s^{-1}$	$[DClO_4]/M$	$k_{obsd}/M^{-1}\ s^{-1}$	$k_3/M^{-2}\ s^{-1}$
0.00403	7.86×10^{-3}	1.95	0.00795	1.89×10^{-2}	2.38
0.0101	2.37×10^{-2}	2.35	0.0385	7.80×10^{-2}	2.03
0.0385	7.97×10^{-2}	2.07	0.116	0.268	2.31
0.231	0.605	2.62	0.231	0.541	2.34
			0.925	3.28	(3.55)

[a] Measured by the NMR or UV spectral method in D_2O containing 19.5–22.1 vol % of acetonitrile at 35°C.

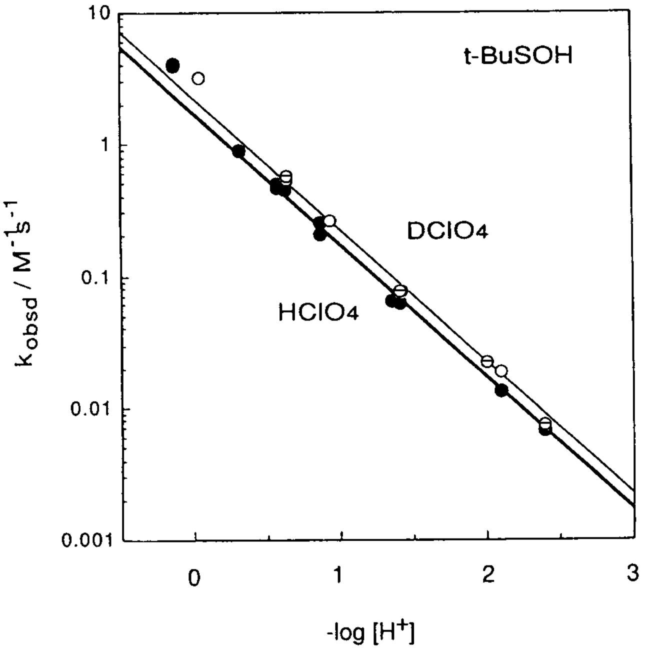


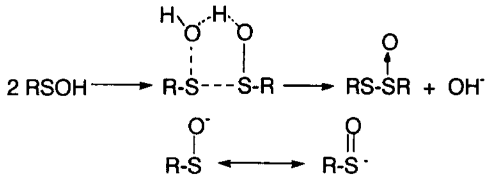
FIGURE 4 Logarithmic plots of the observed rate constants against acid concentration. Rates measured by NMR (⊖) and UV (○) in deuterium media and by UV in CH_3CN-H_2O (●).

TABLE 2 Rate Constants for the Condensation of **1** in Acidic Aqueous Solution[a]

$[HClO_4]/M$	$k_{obsd}/M^{-1}\ s^{-1}$	$k_3/M^{-2}\ s^{-1}$
0.00404	0.00695	1.72
0.00807	0.0134	1.67
0.0387	0.0624	1.61
0.135	0.235	1.74
0.242	0.456	1.88
0.270	0.484	1.79
0.484	0.920	(1.90)
1.35	3.96	(2.93)

[a] Measured in aqueous solution containing 22.1 vol % of acetonitrile at 35°C. In hydrochloric acid (20 vol % CH_3CN), k_{obsd} was 0.421 $M^{-1}\ s^{-1}$ at [HCl] = 0.0806 M.

the substitution. The hydrogen-bonding association may favor the bimolecular reaction only through concentration effects.



(9)

Acid dissociation constants for simple sulfenic acids have never been determined, and comparisons of the pK_a of **1** with those of some related compounds may be worthwhile. Table 3 lists such available data. The pK_a of anthraquinone-1-sulfenic acid (7.51) was found to be quite low [4] in spite of suggested intramolecular hydrogen bonding. The two carbonyl groups enhance acidity. Another stable sulfenic acid, 1,3,6-trimethyllumazine-7-sulfenic acid, has a pK_a of 4.84 as compared with pK_a = 2.29 of the corresponding thiol [15]. From this single example, the pK_a of the sulfenic acid was assumed to be somewhat higher than that of the corresponding thiol [16]. However, this is probably wrong for simple sulfenic acids. The sulfenic acid **1** is almost as acidic as or slightly more acidic than 2-methyl-2-propanethiol [17].

The sulfenic acid can be taken as an analog of a hydroperoxide. The peroxide is much more acidic than the alcohol [18–20]. Insertion of an oxygen atom between the alkyl and hydroxyl group of the alcohol enhances its acidity by 4–6 pK_a units. Such an effect of the sulfur insertion seems to be still greater: **1**, by more than 8 pK_a units, is a stronger acid than *t*-butyl alcohol. This may arise from the stability of the sulfenate anion, where the negative charge is delocalized to the sulfur atom. This delocalization of electrons gives rise to the ambident nucleophilicity of the sulfenate ion [21].

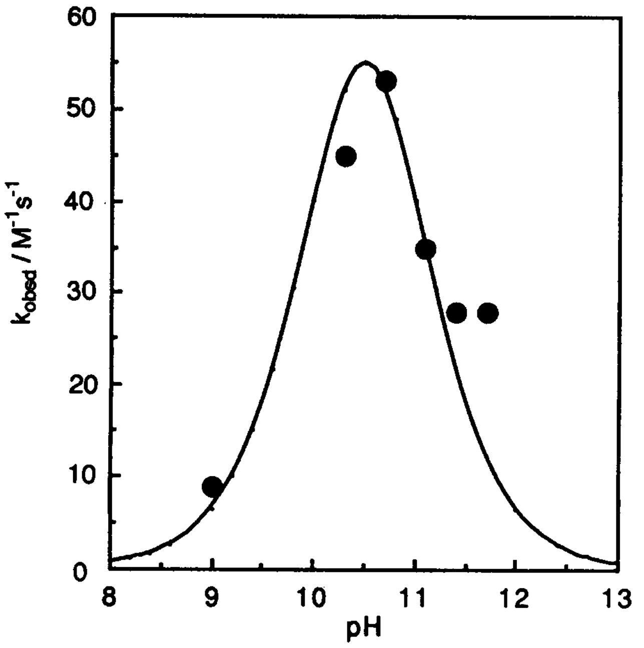
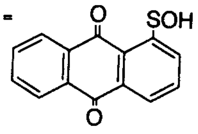


FIGURE 5 Rate constants for the reaction of **1** in alkaline solution. The solid curve is a theoretical one calculated by Equation 7.

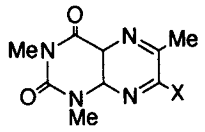
TABLE 3 Acid Dissociation Constants

Acid	*pK_a*	*Remarks*	*Reference*
Me_3COH	19.2	estimated	18
Me_3COOH	12.8	20°C	19
Me_3CSOH (**1**)	10.47	20% CH_3CN–H_2O, 14°C	present work
Me_3CSH	11.22	25°C	17
$MeCH_2OH$	15.9	estimated	18
$MeCH_2OOH$	11.8	20°C	19
$MeCH_2SH$	10.61	25°C	17
AQ-SOH[a]	7.51	15% CH_3CN–H_2O, 25°C	4
TML-SOH[b]	4.84		15
TML-SH[b]	2.29		15

[a] AQ-SOH =



[b] TML-X =



EXPERIMENTAL

The NMR and UV spectra were recorded on JNM GSX 270 and Shimadzu UV 200 or UV 265FS spectrometers, respectively.

Materials

Deuterium oxide (99.75%) was supplied by [Merck (Darmstadt, Germany).] Other deuterium solvents and $DClO_4$ in D_2O were obtained from [Sigma-Aldrich (Milwaukee, Wisconsin).] Acetonitrile was distilled from calcium hydride. Inorganic salts were of the best grade commercially available.

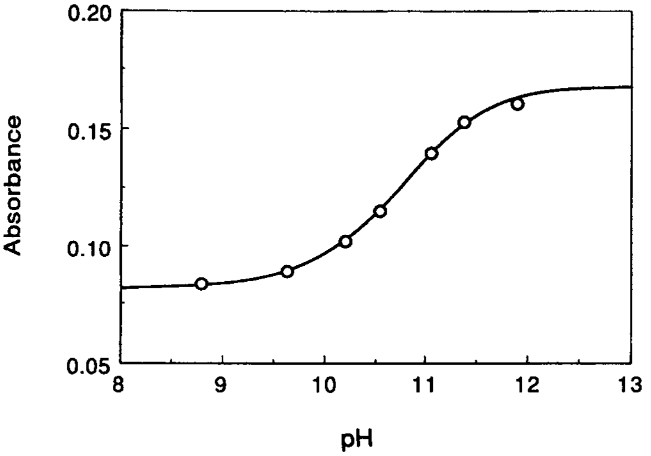


FIGURE 6 The initial absorbance of **1** in alkaline solution measured at 240 nm and 14°C.

2-Methyl-2-propanesulfenic acid (**1**) was synthesized by FVP of di-*t*-butyl sulfoxide, which was prepared by oxidation of di-*t*-butyl sulfide with *m*-chloroperbenzoic acid. The sulfoxide (0.2 g) was placed in the sample flask heated at ca. 80°C and pyrolyzed at 0.15 Torr by passing it through a 30 cm quartz tube heated at 340°C. The pyrolysate was condensed on a cold finger cooled with liquid nitrogen (−196°C). After all the sample had been pyrolyzed, an appropriate solvent was also condensed on the same cold finger and the condensates were collected in a sample tube by melting (typically at −70°C with a dry ice bath) to make a stock solution for kinetic determinations. The solution was stored at −196°C.

Determination of the Concentration of **1**. The concentration of **1** of a stock solution in acetonitrile-d_3 was determined by comparing intensities of the ^1H NMR signal of the methyl group of **1** and that of the contaminated CHD_2CN as the internal standard. The concentration of the CHD_2CN was determined in advance by dissolving a known amount of diphenylmethane and comparing the signals of the methylene group and the CHD_2CN. The concentration of the stock solution was usually adjusted at 0.04–0.05 M.

Kinetic Measurements by NMR Spectroscopy. Twenty to forty microliters of the stock solution of **1** in CD_3CN was added to an NMR sample tube containing 0.6 mL of acidic 5:1 (v/v) D_2O-CD_3CN and equilibrated at 35°C, and ^1H NMR spectra were recorded at appropriate time intervals. The substrate concentration was usually about

1.5×10^{-3} M. The relative intensities of the signals were determined from the integration curve.

Kinetic Measurements by UV Spectroscopy. An appropriate amount of the stock solution of **1** was added to an aqueous reaction solution (1 or 3 mL), thermally equilibrated at 35 ± 0.1°C in a quartz cuvette placed in the cell compartment of the spectrophotometer, and the absorption at 240 nm was followed, $[\mathbf{1}]_0$ usually being 4.5×10^{-4} M. The reactions in alkaline media were carried out in wholly aqueous solution and monitored at 235 nm. The recorded absorbances were used for calculation of the second-order rate constants.

pK_a Determination. Aqueous buffer solutions containing 20 vol % of acetonitrile were adjusted at 0.10 of the ionic strength with $NaClO_4$, and pH was measured with a Hitachi-Horiba F7 pH meter. Buffers used were borate, carbonate, and phosphate. Thirty microliters of the stock solution of **1** in acetonitrile was added from a microsyringe to 3.0 mL of the buffer solution equilibrated at 14 ± 0.2°C in a cuvette. The absorbance at 240 nm was recorded and extrapolated to the time of mixing to obtain the initial absorbance A_0. The absorbances in a neutral solution and in 0.1 M NaOH were used for those of the conjugate acid and base, respectively. The pK_a value was determined as an average of those calculated by the equation $pK_a = pH + \log([HA]/[A^-])$.

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