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Study of the Mechanism for the Hydrolysis of Alkoxy(aryl)(phenyl)-λ⁶-sulfanenitriles,# ArPhS(OR)(≡N)

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The hydrolysis of alkoxy(aryl)(phenyl)-λ^6-sulfanenitriles in several buffer solutions was found to follow a good pseudo-first-order kinetic equation, giving the corresponding sulfoximides and alcohols (for the case of the hydrolysis of neopentyloxy-λ^6-sulfanenitrile, giving a rearranged product, 2-methyl-2-butanol). The dependence of the rate of hydrolysis on the structure of the alkyl group showed the opposite trend to the usual S_N2 character, i.e. Me < Pr < Bu ≈ Et < *i*-Pr, except for neopentyl. The pH-rate profiles indicated that the rate of hydrolysis is also first order in $[H^+]$ at pH more than 6.08, and trends to saturate at low pH. According to these kinetic results, a two-step reaction mechanism was proposed which involves a pre-equilibrium protonation on the nitrogen atom of the alkoxy-λ^6-sulfanenitriles, followed by a rate-determining C–O bond cleavage via an S_N2 or S_N1 mechanism on the alkyl carbon atom depending on the structure of the alkyl group. From a double-reciprocal plot of $1/k_{obs}$ vs. $1/[H^+]$, the pK_a value and the rate constant of the second reaction of neopentyloxy(diphenyl)-λ^6-sulfanenitrile were estimated to be 5.02 and 7.02×10^{-3} s^{-1}, respectively. The substituent effects on the phenyl group of neopentyloxy(diphenyl)-λ^6-sulfanenitrile afforded a large negative ρ-value (−1.88) for pK_a and positive one (+1.66) for the second reaction at 25.2 °C. The small negative ρ-values observed at pH 6.27 for diphenyl(propoxy)-λ^6-sulfanenitrile (−0.42) and neopentyloxy(diphenyl)-λ^6-sulfanenitrile (−0.26) were found to be the results of a cancellation of those for the opposite trend of the reactions of the pre-equilibrium and the second step. The activation parameters for both the pre-equilibrium and the subsequent reactions were also estimated based on the parameters for the hydrolysis of neopentyloxy(diphenyl)-λ^6-sulfanenitrile at pH 6.22 and 2.99. The buffer effect is due to a nucleophilic attack of the buffer base to the alkyl carbon atom of the protonated alkoxy-λ^6-sulfanenitriles. The sulfoximide moiety in the protonated λ^6-sulfanenitrile is revealed to be a very good leaving group.

λ^6-Sulfanenitriles are unusual compounds bearing a kind of sulfur-nitrogen triple bond. Only a few inorganic λ^6-sulfanenitriles, such as F_3SN, have been known, and their chemistry has been developed by Glemser et al.[1] in the field of inorganic or fluorine chemistry. Meanwhile, examples of organic λ^6-sulfanenitriles[2] had been very few before our first report concerning the formation of a methoxy(diphenyl)-λ^6-sulfanenitrile in the alkaline hydrolysis of *N*-bromo-*S*,*S*-diphenylsulfilimide in aqueous methanol.[3]

In recent years, we have prepared a series of organic λ^6-sulfanenitriles,[3,4] and have reported on the X-ray structural analysis of some of these λ^6-sulfanenitriles.[4c,4d,4e] Our main interest for organic λ^6-sulfanenitriles is how the SN triple bond activates other sulfur bonds. In our previous paper,[4c] it was reported that alkoxy-λ^6-sulfanenitriles **1** exceptionally undergo a facile Ei reaction, although λ^6-sulfanenitriles are tetracoordinated hexavalent sulfur compounds like sulfones and sulfoximides. Furthermore, during the synthesis and the assignment of the structure of these alkoxy-λ^6-sulfanenitriles **1**, they were found to be readily hydrolyzed, especially even under a very week acidic condition, to yield the corresponding sulfoximide **2**. For example, methoxy(diphenyl)-λ^6-sulfanenitrile (**1a**) was almost completely hydrolyzed to give the corresponding sulfoximide by bubbling CO_2 into a CD_3OD/D_2O solution for 1 min or stirring with silica gel in methanol for 23 h.[4c] Therefore, it is very interesting to elucidate the mechanism for such a very facile hydrolysis. In order to study the reactivities of alkoxy-λ^6-sulfanenitriles on the hydrolysis, several alkoxy(aryl)(phenyl)-λ^6-sulfanenitriles **1a**—**f** were prepared,[3,4c] and kinetic investigations on their hydrolysis were carried out in phosphate, borate, and three Good's buffer solutions.[5]

Results and Discussion

Hydrolysis Products: In order to study the hydrolysis products, the hydrolysis of alkoxy(diphenyl)-λ^6-sulfanenitriles **1a**—**f** was carried out in a phosphate buffer or a borate buffer solution in an NMR tube at room temperature. The reactions were found to afford the corresponding alcohols and *S*,*S*-diphenylsulfoximide (**2**) almost quantitatively, ex-

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This type of compound was first named as "thiazyne" by Clifford et al.[2] previously, and we have also used this name. But because of confusing with heterocyclic didehydrothiazine etc., the name, "λ^6-sulfanenitrile", is used in this paper based on IUPAC recommendation.

cept **1f** and **1a**. The neopentyloxy-λ^6-sulfanenitrile **1f** gave a rearranged alcohol, 2-methyl-2-butanol. The hydrolysis of methoxy-λ^6-sulfanenitrile **1a** in phosphate buffer gave an unexpected alkylation by-product of phosphate anion, that is, monomethyl phosphate. The results are summarized in Table 1.

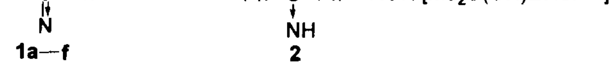
The possible route for the formation of alcohols can be explained by substitution on the sulfur atom or on the alkyl carbon atom with water, although in the case of the neopentyloxy derivative the only formation of the rearranged alcohol suggests a mechanism involving alkyl–O bond fission. In order to clarify which route is the case, an ^{18}O-tracer experiment was carried out. The isopropoxy-λ^6-sulfanenitrile **1d** was treated with $H_2{}^{18}O$ (97.1% ^{18}O-atom content) in dried CD_3CN to give the *S,S*-dipenylsulfoximide in which no ^{18}O was incorporated. The result reveals that the reaction proceeds via substitution on the alkyl carbon atom. The formation of monomethyl phosphate for the hydrolysis of **1a** in phosphate buffer also suggests the involvement of C–O bond fission.

Kinetics: Effect of Alkyl Group. The hydrolysis of alkoxy-λ^6-sulfanenitriles **1a**—**c**, **1e**, and **1f** was carried out in phosphate buffer in pH range of 2.83—6.56. The hydrolysis of the isopropoxy-λ^6-sulfanenitrile **1d** was too fast to determine its rate in the above pH range, so that in this case the borate buffer solution in pH range of 8.31—9.35 was used. As the hydrolysis proceeds, the UV spectrum of each reaction mixture of these alkoxy-λ^6-sulfanenitriles **1** changed gradually with two isosbestic points. The rate of hydrolysis was measured by following the UV absorption change at a proper wavelength, λ. The hydrolysis reactions were found to follow a good pseudo-first-order kinetic equation in all buffer solutions. The observed first-order rate constants, k_{obs}, for **1a**—**c**, **1e**, and **1f** at pH 6.27 and for **1d** at pH 8.72 in the ionic strength of 0.01 are given in Table 2 together with the isosbestic points and λ values at which the rate was followed.

As can be seen in Table 2, the rates of hydrolysis of alkoxy-λ^6-sulfanenitriles **1** increase in such an order as **1f** < **1a** < **1c** < **1b** ≈ **1e** ≪ **1d**. This sequence is apparently related to the structure of the alkyl group. The hydrolysis of isopropoxy-λ^6-sulfanenitrile **1d** showed a much higher reactivity. The hydrolysis of neopentyloxy-λ^6-sulfanenitrile **1f** bearing a bulky group could unexpectedly occur rather facilely at a rate of 0.17 times that of **1b**. The change in the reactivity with the alkyl groups of the λ^6-sulfanenitriles is in opposite order to that for the usual S_N2 reaction[6] on the alkyl carbon atom, except for **1f**. In the case of the reaction of **1f**, the formation of the rearranged product apparently reveals that the mechanism is S_N1.

The relative rate sequences similar to that of the alkoxy-λ^6-sulfanenitriles **1** (0.53 : 1 : 0.85 : 1.0 : 580 : 0.17 for Me : Et : Pr : Bu : *i*-Pr : neopentyl in Table 2) have been reported for the solvolysis of alkyl *p*-toluenesulfonates in some good ionizing solvents, i.e., 1.11 : 1 : 51 : 0.11 for Me : Et : *i*-Pr : neopentyl in acetic acid, and 0.56 : 1 : 202 : 1.0 in formic acid.[7] Bently et al. also reported that the sequence was 1 : 1 : 3 for the hydrolysis of methyl, ethyl, and isopropyl tosylates under neutral conditions, and became 0.34 : 1 : 260 in 70% w/w aqueous sulfuric acid.[8] The more rapid increase in the rate for secondary alkyl tosylates in aqueous sulfuric acid was thought to be due to a shift of the transition state to the more cationic side by protonation of these sulfonates. The nitrogen atoms of the alkoxy-λ^6-sulfanenitriles **1** should have a basicity similar to those of diphenyl(piperidino)-λ^6-sulfanenitrile (pK_a = 7.47, the protonation site is the unsaturated λ^6-sulfanenitrile nitrogen as discussed previously)[4b] and triphenyl-λ^6-sulfanenitrile (pK_a = 7.44).[4c] ^{1}H NMR spectra were taken during the hydrolysis in phosphate buffer in D_2O at pD ca. 3. An observation of a lager down-field shift from 3.69 to 4.15 of decreasing methylene signals of neopentyloxy(phenyl)(*p*-tolyl)-λ^6-sulfanenitrile (**1f-m**) also suggests the involvement of the protonated intermediate in the hydrolysis of alkoxy-λ^6-sulfanenitriles. The easy protonation of the alkoxy-λ^6-sulfanenitriles **1** makes a good leaving group even in a high pH range, and leads to the facile hydrol-

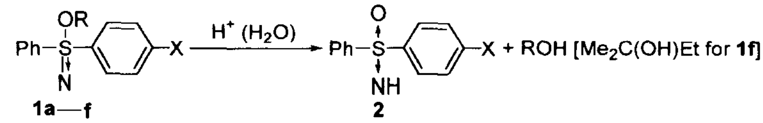
Table 1. Hydrolysis Products of Alkoxy-λ^6-sulfanenitriles **1**[a)]



[1]	R	Conditions[b)]	Products (yield/%)[c)]
a	Me	Solvent A, r.t., 1 h	**2** (99), MeOD (71), $CH_3OPO(OH)_2$ (24)
b	Et	Solvent A, r.t., 45 min	**2** (99), EtOD (86)
c	Pr	Solvent A, r.t., 1 h	**2** (99), PrOD (98)
d	*i*-Pr	Solvent C, r.t., 20 min	**2** (99), *i*-PrOD (97)
e	Bu	Solvent B, r.t., 45 min	**2** (99), BuOD (98)
f	Neopentyl	Solvent A, r.t., 1 h 45 min	**2** (99), $Me_2C(OD)CH_2CH_3$ (99)

a) Substrate: ca. 0.035 mol dm^{-3}. b) Solvent A: phosphate buffer of D_2O/CD_3CN (8 : 1) at pD ca. 6.1, ionic strength 0.09, total buffer concentration $[B]_t$ 0.065 mol dm^{-3}, fraction of buffer acid 0.84. Solvent B: phosphate buffer of D_2O/CD_3CN (5 : 1) at pD ca. 6.1, ionic strength 0.19, total buffer concentration $[B]_t$ 0.144 mmol dm^{-3}, fraction of buffer acid 0.85. Solvent C: borate buffer of D_2O/CD_3CN (8 : 1) at pD ca. 8.7, ionic strength 0.10. c) Yields were determined by ^{1}H NMR analysis.

Table 2. Rates of the Hydrolysis of Alkoxy-λ^6-sulfanenitriles **1**[a)]



[1]	R	X	Isosbestic points nm	λ nm	$k_{obs} \times 10^3$ s^{-1}	ρ-value	Relative rate[b)]
a	Me	H	232, 246	220	1.17±0.01		0.53
b	Et	H	231, 246	220	2.20±0.02		1
c	Pr	H	231, 246	220	1.87±0.01	−0.42	0.85
c-m	Pr	Me	237, 252	225	2.17±0.01		
c-c	Pr	Cl	239, 257	225	1.56±0.01		
c-n	Pr	NO_2	258, 293	240	0.861±0.001		
d	*i*-Pr	H	229, 247	220	4.82±0.01[c)]		
d	*i*-Pr	H			1280[d)]		580[d)]
e	Bu	H	230, 246	220	2.20±0.01		1
f	Neopentyl	H	230, 245	221	0.374±0.001	−0.26	0.17
f-m	Neopentyl	Me	235, 253	224	0.432±0.001		
f-c	Neopentyl	Cl	238, 258	225	0.357±0.001		
f-n	Neopentyl	NO_2	258, 293	240	0.241±0.001		

a) In phosphate buffer at pH 6.27 and ionic strength 0.01, 25.2 °C. b) Rates relative to **1b**, and relative rate of **1b** = 1, at pH 6.27 and ionic strength 0.01, 25.2 °C. c) In borate buffer at pH 8.72 and ionic strength 0.01, 25.2 °C. d) The rate constant was estimated by extrapolation of the rate constant of **1d** in borate buffer at pH 8.72 and ionic strength 0.01, 25.2 °C to the pH 6.27.

ysis in a cation-like mechanism, which results in the opposite order of the alkyl-group reactivity to the usual S_N2 reactions.[6] In this case, the nucleophilic reaction on the primary alkyl carbon atom of protonated λ^6-sulfanenitriles may involve an open transition state with a small degree of bond formation and a large extent of bond cleavage proposed by Knier and Jencks in the reactions of *N*-(methoxymethyl)-*N*,*N*-dimethylanilinium ion with nucleophilic reagents in water.[9] The transition states for the nucleophilic reactions of isopropoxy-λ^6-sulfanenitrile **1d** may be S_N1 in view of the almost limiting S_N1 mechanism in the solvolysis of isopropyl tosylate in 70% w/w sulfuric acid.[8] The formation of a rearranged alcohol, 2-methyl-2-butanol, for the hydrolysis of **1f** supports a mechanism involving a carbocation. Since the substitution reaction proceeding via the more cation-like transition state gives the larger relative rate of the neopentyl derivative to the simple primary alkyl one, as shown in the above examples, the relative rate (0.17) should be attributed to acceleration for the other simple alkoxy-λ^6-sulfanenitriles by a nucleophilic assistance of solvents with the S_N2 character.

pH-Dependence of Rate. The effect of the pH on the rate of hydrolysis was examined. The pH-rate profiles of these reactions are shown in Fig. 1. In all cases, linear correlations of $\log k_{obs}$ vs. pH with almost the same slope (−0.92——0.97) were observed for **1a**—**c**, **1e**, and **1f** in the pH range of 6.08—6.56, and for **1d** in the pH range of 8.31—9.35. The relatively slow hydrolysis of **1f** made it possible to determine its rate in a much lower pH region, resulting in the observation of a saturation of the rate of hydrolysis at lower pH. A re-examination of the rate of hydrolysis of **1c** in the pH range 5.12—6.08 exhibited a tendency to curve. These results suggest that all cases have the first-order dependence of the rate on [H⁺] in the higher pH region and saturation in the lower pH region; also, the reaction proceeds via a two-step mechanism involving an initial protonation followed by a rate-determining substitution on the alkoxy carbon atom.

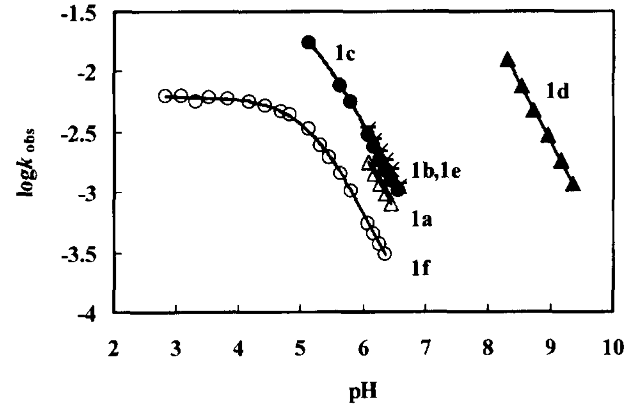


Fig. 1. pH-rate profiles for the hydrolysis of **1a**—**c**, **1e**, and **1f** in phosphate buffer and **1d** in borate buffer at ionic strength 0.01, 25.2 °C.

Since the present data have not yet been considered buffer effects, a possible participation of some buffer effect should be examined.

The hydrolysis of **1a**, **1c**, and **1f** was carried out in various diluted buffers with aqueous $LiClO_4$ maintaining the ionic strength at 0.01. The buffer effect was obviously negligibly small. Therefore, the data shown in Fig. 1 and Table 2 are considered to be free from any buffer effect on the rate of hydrolysis; for this reason, all of the kinetic data, Hammett-substituent effects and activation parameters were examined under these conditions as mentioned later in Fig. 2 and Ta-

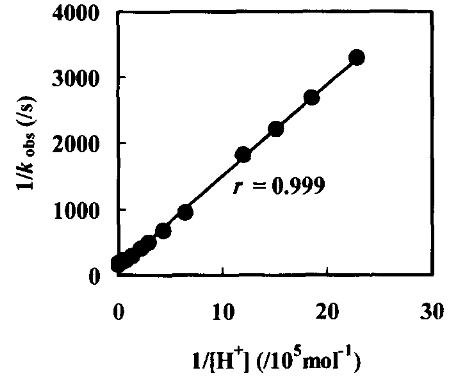


Fig. 2. Double-reciprocal plot of $1/k_{obs}$ vs. $1/[H^+]$ for the hydrolysis of **1f** in phosphate buffer at ionic strength 0.01, 25.2 °C.

bles 3 and 4.

Determination of pK_{aSN} Values of Neopentyloxy-λ^6-sulfanenitriles. The behavior of the saturation for the hydrolysis of **1f** made it possible to determine its pK_a value. The kinetic analysis for the above reaction mechanism affords the following Eq. 1, and therefore a rearrangement yields:

$$k_{obs} = \frac{k'_2[H^+]}{K_{aSN} + [H^+]}, \tag{1}$$

$$\frac{1}{k_{obs}} = \frac{K_{aSN}}{k'_2}\frac{1}{[H^+]} + \frac{1}{k'_2}, \tag{2}$$

where k'_2 is the pseudo first-order rate constant for the nucleophilic substitution with a water molecule. K_{aSN} is the dissociation constant of the conjugate acid of λ^6-sulfanenitrile. Equation 2 shows that $1/k_{obs}$ should be linearly correlated to $1/[H^+]$ with a slope of K_{aSN}/k'_2 and an intercept of $1/k'_2$. A typical double-reciprocal plot of $1/k_{obs}$ vs. $1/[H^+]$ for the hydrolysis of neopentyloxy-λ^6-sulfanenitrile **1f** is presented in Fig. 2. In this manner, the pK_{aSN} and k'_2 for several neopentyloxy(phenyl)(*p*-substituted phenyl)-λ^6-sulfanenitriles were calculated as shown in Table 3. The pK_{aSN} values of these neopentyloxy-λ^6-sulfanenitriles were found to be lower than that of diphenyl(piperidino)-λ^6-sulfanenitrile (7.47)[4b] and triphenyl-λ^6-sulfanenitrile (7.44),[4c] as expected by considering the electronegative oxygen atom in the alkoxy group.

Substituent Effect and Activation Parameters. The *p*-

Table 3. pK_{aSN} Values of the Conjugate Acids of Neopentyloxy(phenyl)(*p*-substituted phenyl)-λ^6-sulfanenitriles and Their Rate Constants k'_2 of the Subsequent Reaction[a)]

[1]	X	$K_{aSN} \times 10^6$	$k'_2 \times 10^3$	pK_{aSN}
		mol dm^{-3}	s^{-1}	
f	H	9.60	7.02	5.02
f-m	Me	4.33	3.91	5.36
f-c	Cl	20.2	13.8	4.69
f-n	NO_2	275	128	3.56
ρ			+1.60	−1.88
r			0.998	0.998

a) In phosphate buffer at ionic strength 0.01, 25.2 °C.

Table 4. Activation Parameters of the Hydrolysis of Alkoxy-λ^6-sulfanenitriles **1** at 25 °C[a)]

[1]	R	X	pH	$k_{obs}/[H^+] \times 10^{-3}$/s^{-1} mol^{-1} dm^3				$k_{obs} \times 10^3$/s^{-1}			$\Delta H^{\ddagger}$ [b)]	$\Delta S^{\ddagger}$ [b)]	$\Delta H_2^{\ddagger}$ [c)]	$\Delta S_2^{\ddagger}$ [c)]
				15.6 °C	25.2 °C	34.6 °C	43.9 °C	10.9 °C	20.4 °C	30.0 °C	kJ mol^{-1}	J K^{-1} mol^{-1}	kJ mol^{-1}	J K^{-1} mol^{-1}
a	Me	H	6.27	0.892	2.18	4.67					62±1	26±5	78	−17
b	Et	H	6.27	1.56	4.10	8.90					65±3	43±9	81	0
c	Pr	H	6.27	1.38	3.48	7.76					65±1	40±4	81	−3
c-m	Pr	Me	6.27	1.52	4.04	8.36					64±4	38±13		
c-c	Pr	Cl	6.27	1.12	2.90	6.16					64±3	35±9		
c-n	Pr	NO_2	6.27	0.624	1.60	3.44					64±2	31±8		
d	*i*-Pr	H	8.72	1100	2530	5980					63±2	90±7	79	47
e	Bu	H	6.27	1.77	4.36	9.38					62±1	34±5	78	−9
f	Neopentyl	H	6.22		0.679	1.94	4.86				80±1	79±5	96	36
f	Neopentyl	H	2.99					8.91	34.0	124			96±1	36±2

a) The hydrolysis of **1a**—**c**, **1e**, and **1f** in phosphate buffer at ionic strength 0.01, and **1d** in borate buffer at ionic strength 0.01. b) $\Delta H^{\ddagger} = \Delta H_1 + \Delta H_2^{\ddagger}$, $\Delta S^{\ddagger} = \Delta S_1 + \Delta S_2^{\ddagger}$. The footnote 1 and 2 denote the first protonation and the second step nucleophilic reaction in Scheme 1 respectively. c) Estimated according to $\Delta H_1 = -16$ kJ mol^{-1} and $\Delta S_1 = 43$ J K^{-1} mol^{-1} of the first protonation of **1f**.

substituent effect on the one phenyl group of alkoxy(diphenyl)-λ^6-sulfanenitriles was studied for the hydrolysis of **1c** and **1f** in phosphate buffer with the same ionic strength of 0.01. The obtained Hammett ρ-value for **1c** and **1f** were −0.42 and −0.26 at pH 6.27, respectively (see Table 2). Meanwhile, Hammett plots for both pK_{aSN} and k_2' for the reaction of **1f** afforded ρ-values of −1.88 and 1.60, respectively. Under the condition $[H^+] \ll K_{aSN}$, an approximation of the Eq. 1 gives $k_{obs} = k_2'[H^+]/K_{aSN}$. In this case, the Hammett ρ-value for the k_{obs} is considered to be the sum of that for the second reaction and the pre-equilibrium protonation. Because the ρ-value for the pre-equilibrium protonation is identical to that for pK_{aSN}, the ρ-value for **1f** is estimated to be −0.28 (−1.88+1.60), which shows good agreement with that of the observed value (−0.26) at pH 6.27. The slight difference is probably due to the approximation. The small negative Hammett ρ-value of −0.42 for **1c** at pH 6.27 is also the result of a similar cancellation. Since the ρ-values for pK_a of both **1c** and **1f** are not considered to be very different, the ρ-value for the second reaction of **1c** is smaller than that (+1.60) of **1f**, suggesting that the C–O bond fission of **1c** is less progressed than that of **1f** in the transition state, in agreement with that in the range of the S_N2 mechanism. A slightly larger negative ρ-value for the pK_{aSN} of neopentyloxy(diphenyl)-λ^6-sulfanenitrile than that for diphenyl(piperidino)-λ^6-sulfanenitrile ($\rho = -1.67$)[4b] may be the result of development of more positive charge on the sulfur atom, reflected by the smaller contribution of the oxygen lone pair to neutralization of the positive charge on the sulfur atom than that of the nitrogen lone pair.

The activation parameters were calculated from Arrehenius plots for the second-order rate constants obtained by dividing the k_{obs} values by $[H^+]$ for the hydrolysis of **1a**—**c** and **1e** at pH 6.27, **1f** at pH 6.22, and **1d** at 8.72 with the ionic strength 0.01, respectively, and summarized in Table 4. The activation enthalpies and entropies at a pH over 6.27 at 25 °C for **1a**—**e** are in the ranges 62—65 $kJ\,mol^{-1}$ and 26—90 $J\,K^{-1}\,mol^{-1}$, respectively. These values are considered to be the results of the sum of those for both the pre-equilibrium protonation and the subsequent substitution reaction ($\Delta H^\ddagger = \Delta H_1 + \Delta H_2^\ddagger$, $\Delta S^\ddagger = \Delta S_1 + \Delta S_2^\ddagger$). Meanwhile, the activation parameters for **1f** at pH 2.99 were calculated using the observed first-order rate constants, k_{obs}. A large activation enthalpy ($\Delta H_2^\ddagger = 96\ kJ\,mol^{-1}$) and a large positive activation entropy ($\Delta S_2^\ddagger = +36\ J\,K^{-1}\,mol^{-1}$) are consistent with the S_N1 mechanism for the second reaction of **1f**, since most of the λ^6-sulfanenitrile molecules are considered to be protonated at pH 2.99 and the activation parameters reflect only the second reaction. Therefore, the enthalpy (ΔH_1) and entropy (ΔS_1) for the pre-equilibrium protonation are estimated as $-16\ kJ\,mol^{-1}$ and $43\ J\,K^{-1}\,mol^{-1}$, respectively. Assuming that these parameters are nearly equal to those for the other λ^6-sulfanenitriles **1a**—**e**, the activation entropies for the second reaction of **1a**—**e** are estimated to be almost zero, or small negative values (0—−17 $J\,K^{-1}\,mol^{-1}$), as shown in Table 4. These values are larger than those of the usual S_N2 reactions, and may suggest a loose transition state.

Buffer Effect. In order to clarify the stepwise mechanism of the acid-catalyzed hydrolysis, it is important to examine the buffer effect in a more concentrated buffer system. Further, in order to estimate the influence of pK_a of the buffer reagents on the buffer effect, three Good's buffers with the different pK_a values, MES (2-morpholinoethanesulfonate, $pK_a = 6.15$, 20 °C), MOPSO (2-hydroxy-3-morpholinopropanesulfonate, $pK_a = 6.90$) and MOPS (3-morpholinopropanesulfonate, $pK_a = 7.20$, 20 °C) buffers, were also used besides the phosphate buffer. Typical buffer dependences of the hydrolysis of **1a**—**c** are shown for the MES buffer at pH 6.12 with an ionic strength of 0.1 in Fig. 3. In almost all cases, the observed rate constants, k_{obs}, are linearly dependent on the total buffer concentration ($[B]_t$): $k_{obs} = k_0 + k_B[B]_t$, where k_0 is the rate constant extrapolated to zero buffer concentration, and k_B is the buffer-dependent second-order rate constant. The k_0 and k_B values for the hydrolysis of **1** in different buffer solutions are summarized in Table 5. The k_B values for **1d** and **1f** are actually zero within the experimental error, which is consistent with the S_N1 mechanism free from the attack of buffer nucleophiles in the transition state. The k_0 and k_B values for the phosphate buffer in Table 5 were obtained from the corrected k_{obs} by adjusting the data to the same pH using the results of the pH-rate profile obtained in the phosphate buffer at an ionic strength of 0.01, because in the case of phosphate buffer it is difficult to maintain a constant pH in the usual dilution method to change the buffer concentration using an aqueous solution of salt while maintaining the constant ionic strength.

As shown in Table 5, the k_0 values for **1a**—**f** in both phosphate and MES buffer show similar relative rates (the values in parentheses) to those in buffer solutions with an ionic strength of 0.01, shown earlier in Table 2.

On the other hand, the k_B rate sequences for **1a**, **1b**, and **1c** in MES buffer (6.35 : 1 : 0.45) and for **1a**, **1b**, **1c**, and **1e** in phosphate buffer (1.35 : 1 : 0.67 : 0.73) are roughly consistent with the order of the usual S_N2 reactivity[6] on the alkyl carbon atom. These changes in the relative rates are smaller than that for the usual S_N2 reactivity, suggesting the looseness of the

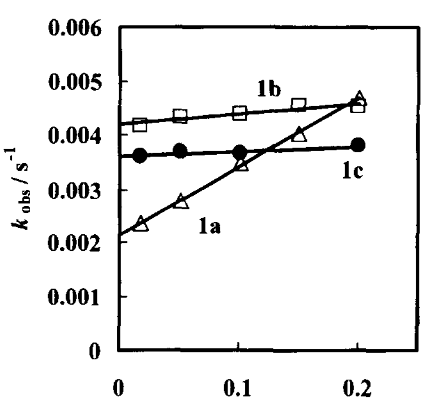


Fig. 3. Buffer effect on the hydrolysis of **1a**—**c** in MES buffer at pH 6.12 and ionic strength 0.1 maintained with $LiClO_4$ at 25.2 °C.

Table 5. Buffer Effect for the Hydrolysis of Alkoxy-λ^6-sulfanenitriles **1**[a]

[**1**]	R	Buffer[b]	Fraction of buffer acid[c]	pH	$k_0 \times 10^3$ [d] $\mathrm{s^{-1}}$	$k_B \times 10^2$ [d] $\mathrm{s^{-1}\,mol^{-1}\,dm^3}$
a	Me	Phosphate[e]	0.80	6.14	1.9 (0.51)[f]	0.85 (1.35)[f]
a	Me	Phosphate	0.67	6.56	0.8	0.53
a	Me	Phosphate	0.50	6.87	0.4	0.33
a	Me	MES	0.80	5.51	7.5	1.63
a	Me	MES	0.60	5.94	3.1	1.53
a	Me	MES	0.50	6.12	2.2 (0.52)[g]	1.27 (6.35)[g]
a	Me	MES	0.33	6.45	1.2	0.81
a	Me	MOPSO	0.50	6.93	0.4	0.33
a	Me	MOPS	0.80	6.59	0.9	0.43
a	Me	MOPS	0.67	6.90	0.5	0.38
a	Me	MOPS	0.50	7.20	0.2	0.23
b	Et	Phosphate[e]	0.80	6.14	3.7 (1)[f]	0.63 (1)[f]
b	Et	MES	0.50	6.12	4.2 (1)[g]	0.20 (1)[g]
c	Pr	Phosphate[e]	0.90	5.79	6.0	0.76
c	Pr	Phosphate[e]	0.80	6.14	3.1 (0.84)[f]	0.42 (0.67)[f]
c	Pr	Phosphate[e]	0.68	6.38	1.8	0.14
c	Pr	Phosphate	0.50	6.87	0.8[h]	—
c	Pr	MES	0.50	6.12	3.6 (0.86)[g]	0.09 (0.45)[g]
c	Pr	MOPS	0.50	7.20	0.4[h]	—
d	*i*-Pr	Borate	0.50	9.24	2.6[h]	0
e	Bu	Phosphate[e]	0.80	6.14	3.6 (0.97)[f]	0.46 (0.73)[f]
f	Neopentyl	Phosphate[e]	0.80	6.14	0.7[h] (0.19)[f]	0
f	Neopentyl	MES	0.50	6.12	0.8[h] (0.19)[g]	0

a) Determined at 25.2 °C and the ionic strength 0.10 ($LiClO_4$). Rates of the hydrolysis in MES, MOPS, and MOPSO buffer solutions were determined by following the decrease in absorption at 260 nm. b) MES: 2-morpholinoethanesulfonate (pK_a 6.15, 20 °C), MOPSO: 2-hydroxy-3-morpholinopropanesulfonate (pK_a 6.90), MOPS: 3-morpholinopropanesulfonate (pK_a 7.20, 20 °C). c) [buffer acid]/total buffer concentration, and in the case of phosphate buffer [$H_2PO_4^-$]/total buffer concentration d) The data for phosphate buffer are the corrected values, and the values in parentheses are rates relative to **1b**, and relative rate of **1b** = 1. e) Ionic strength 0.20 ($LiClO_4$). f) Rates relative to **1b** in phosphate buffer. g) Rates relative to **1b** in MES buffer. h) Average value for the rate constants in five different concentrations of buffer.

transition state. The larger change in the MES buffer than that in the phosphate buffer may be attributable to the different looseness of the transition state or the bulkier nucleophile tertiary amine buffer than the phosphate buffer, or both.

The k_B values in Table 5 were found to decrease with an increase of the pK_a value of the buffer reagent in the order of MES, MOPSO, phosphate, and MOPS at the same fraction of buffer acid, and to increase with the decrease of pH for the same buffer reagent. Typical plots of k_B vs. fraction of buffer acid for **1a** in several buffer solutions are shown in Fig. 4. There are three possibilities for this buffer behavior. One is a general acid catalysis,[10,11] which should involve a rate-determining protonation step, most likely on the nitrogen atom. The almost absence of buffer effects for **1d** and **1f** in Table 5 and other kinetic behavior suggesting two step mechanism account for that general acid catalysis is unlikely. The other one, which refers to the same kinetic equation, involves a specific acid-general base catalysis,[10,11] in which the buffer effect arises from the general base catalysis of a buffer base abstracting a proton from the attacking water molecule. Also, the third is that the buffer base attacks as a nucleophile on the alkyl carbon of the protonated λ^6-sulfanenitriles. Although these mechanisms are indistinguishable only from the kinetic behavior, the formation of monomethyl phosphate in the product analysis, shown in Table 1, suggests that the third mechanism is the most plausible. The observation of the S_N2 character in the buffer effect toward the k_B values is also consistent with the third mechanism, although the product analysis of methylated MES was difficult. The protonated alkoxy-λ^6-sulfanenitriles may be strong alkylating agents like 1-methyl-3-methoxysulfonylpyridium cation,[12] in view of the very facile attack of even poor nucleophiles such as water and phosphate anions ($H_2PO_4^-$).

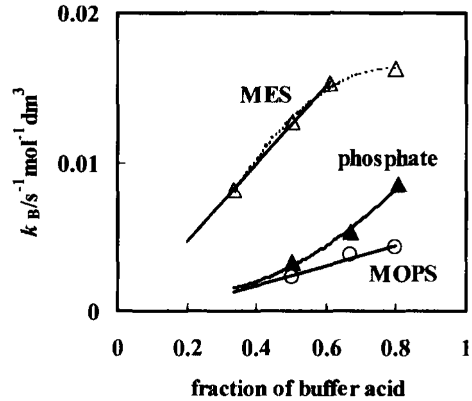


Fig. 4. Plots of k_B for the hydrolysis of **1a** vs. fraction of buffer acid in buffer at ionic strength 0.1 maintained with $LiClO_4$ at 25.2 °C.

Mechanism for the Hydrolysis: According to the above experimental results, a two-step reaction mechanism, as shown in Scheme 1, is reasonably considered, which involves a pre-equilibrium protonation on the nitrogen atom of the alkoxy-λ^6-sulfanenitriles **1** followed by a rate-determining C–O bond cleavage via an S_N2 or S_N1 reaction, depending on the structure of the alkyl group. The protonated alkoxy-λ^6-sulfanenitriles are subject to a nucleophilic attack of both water and buffer base in concentrated buffer solutions.

Kinetic Analysis. A kinetic analysis of the reaction mechanism provides a rate-law:

$$k_{\mathrm{obs}} = \frac{k_2'[\mathrm{H^+}]}{K_{\mathrm{aSN}} + [\mathrm{H^+}]} + \frac{k_2'' K_{\mathrm{aHA}}[\mathrm{HA}]}{K_{\mathrm{aSN}} + [\mathrm{H^+}]}, \tag{3}$$

where k_2'' is a second-order rate constant for the nucleophilic substitution with a buffer base. K_{aHA} is the dissociation constant of the buffer reagent. [HA] represents the concentration of the buffer acid.

When the buffer effect is negligibly small in the case of the hydrolysis in a very dilute buffer with ionic strength of 0.01, the observed rate constant, k_{obs}, is only related to the first term in Eq. 3, and is linearly dependent on $[\mathrm{H^+}]$ in the higher pH region than the $\mathrm{p}K_{\mathrm{aSN}}$ value, while in the lower pH region it becomes saturated to k_2', consistent with the pH-rate profiles in Fig. 1.

Kinetic Analysis for Buffer Effect. It is clear that buffer-dependent second-order rate constant, k_{B}, can be described by Eq. 4 from the second term of Eq. 3,

$$k_{\mathrm{B}} = \frac{k_2'' K_{\mathrm{aHA}}}{K_{\mathrm{aSN}} + [\mathrm{H^+}]} \frac{[\mathrm{HA}]}{[\mathrm{B}]_{\mathrm{t}}}, \tag{4}$$

where $[\mathrm{B}]_{\mathrm{t}}$ is the total buffer concentration. Equation 4 shows a nearly linear dependence of k_{B} on the fraction of buffer acid ($[\mathrm{HA}]/[\mathrm{B}]_{\mathrm{t}}$) in a higher pH region than the $\mathrm{p}K_{\mathrm{aSN}}$ value of the conjugate acid of λ^6-sulfanenitrile. The plots of k_{B} vs. fraction of buffer acid for **1a** in the MES and MOPS buffers in Fig. 4 are in accord with the relationship described by Eq. 4. The downward curvature (the dotted line in Fig. 4) in the higher fraction of buffer acid for the MES buffer may be due to the close pH value to the $\mathrm{p}K_{\mathrm{aSN}}$ value of **1a**. The upward curvature for the phosphate buffer may be interpreted on the basis of an acceleration by the additional nucleophilic function of the increasing acid fraction of $\mathrm{H_2PO_4^-}$, although the possible experimental error due to the data by correction to maintain constant pH value could not be completely neglected. When the buffer system mainly consists of a solution of $\mathrm{H_2PO_4^-/HPO_4^{2-}}$, the k_{B} is described by Eq. 5 considering both of these two anions as nucleophiles:

$$k_{\mathrm{B}} = \frac{k_{21}''[\mathrm{H^+}]}{K_{\mathrm{aSN}} + [\mathrm{H^+}]} \frac{[\mathrm{H_2PO_4^-}]}{[\mathrm{B}]_{\mathrm{t}}} + \frac{k_{22}''[\mathrm{H^+}]}{K_{\mathrm{aSN}} + [\mathrm{H^+}]} \frac{[\mathrm{HPO_4^{2-}}]}{[\mathrm{B}]_{\mathrm{t}}}$$
$$= \frac{(k_{21}''[\mathrm{H^+}] + k_{22}'' K_{\mathrm{aHA2}})}{K_{\mathrm{aSN}} + [\mathrm{H^+}]} \frac{[\mathrm{H_2PO_4^-}]}{[\mathrm{B}]_{\mathrm{t}}}, \tag{5}$$

where k_{21}'' and k_{22}'' are the second-order rate constants of nucleophilic substitution by $\mathrm{H_2PO_4^-}$ and $\mathrm{HPO_4^{2-}}$, respectively. K_{aHA2} is the second dissociation constant of phosphoric acid. The curve for the phosphate buffer in Fig. 4 is apparently composed of a linear dependence of the second term on the fraction of $\mathrm{H_2PO_4^-}$ in the low acid fraction region in which the nucleophilic reaction of $\mathrm{HPO_4^{2-}}$ is involved and an acceleration factor of the first term in the more acidic region contributed by the nucleophilic reaction of $\mathrm{H_2PO_4^-}$ as described in Eq. 5. The balance of these two factors changes depending on the acid fraction, resulting in the nonlinear relationship between k_{B} and fraction of buffer acid.

Although k_2'' and K_{aHA} have complementary character for a buffer, the increment of k_2'' by changing the buffer is smaller than the decrement of K_{aHA}, because the Brønsted β-value is generally smaller than unity, and thus the larger is the K_{aHA} value the larger is the product $k_2'' K_{\mathrm{aHA}}$. Accordingly, there appears an order of buffer effect, MES > MOPSO ≈ phosphate (K_{aHA2}) > MOPS (Table 5) similar to that in a general acid catalysis. A rearrangement of Eq. 4 at the fraction of buffer acid of 0.5 gives

$$k_2'' = 2(K_{\mathrm{aSN}} + [\mathrm{H^+}]) \frac{k_{\mathrm{B}}}{K_{\mathrm{aHA}}}. \tag{6}$$

Thus, the β-value of Brønsted-type correlation for the second-step nucleophilic substitution is roughly estimated to be 0.28 from a plot of $\log k_2'' - \log 2(K_{\mathrm{aSN}} + [\mathrm{H^+}])$ against $\mathrm{p}K_{\mathrm{aHA}}$ in Fig. 5 when $\log 2(K_{\mathrm{aSN}} + [\mathrm{H^+}])$ is nearly constant. Here, the data for the phosphate buffer were not used, considering its

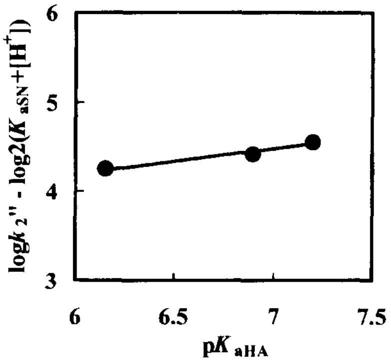
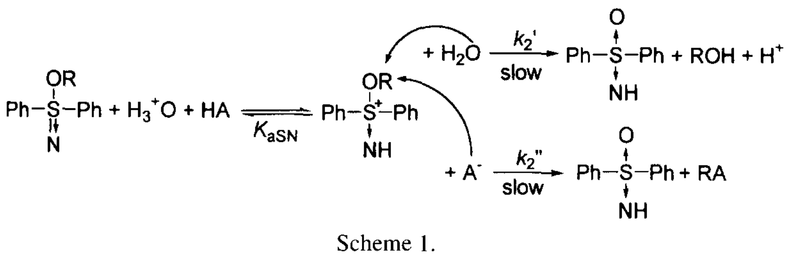


Fig. 5. Brønsted-type correlation.



Scheme 1.

complex effect of more than one basic species. This β-value is in the range of those values, 0.15—0.39, for the aminolysis of methyl 4-nitrobenzenesulfonate in an aqueous solution.[13] The loose transition state for the nucleophilic substitution by the nitrogen buffer nucleophiles makes us expect to the more loose transition state for the phosphate or water nucleophile resulting in the opposite reaction order of alkyl structures.

Conclusion

The hydrolysis of alkoxy-λ^6-sulfanenitriles was found to proceed via an initial protonation of the nitrogen atom followed by a rate-determining C–O bond cleavage via S_N2 or S_N1 mechanism on the alkyl carbon atom. In the case of neopentyloxy(phenyl)(*p*-substituted phenyl)-λ^6-sulfanenitriles, the pK_a values of their conjugate acids and their rate constants for the subsequent reaction were estimated from the curvature of pH-rate profiles. The sulfoximide moiety of the protonated alkoxy-λ^6-sulfanenitriles was found to be a very good leaving group to make it possible to proceed via an S_N1 or a very loose cation-like S_N2 mechanism, even under mild conditions. The buffer effect is due to a nucleophilic attack of the buffer base toward the alkyl carbon atom of the protonated alkoxy-λ^6-sulfanenitriles.

Experimental

Reagents and Instruments: All reagents and solvents were obtained commercially, and were further purified by general methods when necessary.

Buffer solutions were prepared according to the reference.[5] The pH value of the buffer solution was measured by a Horiba F-13 pH meter.

IR spectra were taken on a Horiba FT-710 spectrometer, and the ^{1}H NMR and ^{13}C NMR spectra were obtained on a JEOL-JNM 400 NMR spectrometer in $CDCl_3$ with TMS or D_2O/CD_3CN with DSS as an internal standard. Elemental analyses were performed on a Yanaco MT-5 CHN CORDER. Mass spectra were obtained on a JEOL-JMS-D 300 spectrometer. UV spectra were measured by a Hitachi U-3000 spectrophotometer.

Alkoxy-λ^6-sulfanenitriles: The alkoxy(aryl)(phenyl)-λ^6-sulfanenitriles **1a-f** were prepared according to the methods reported in our previous papers.[3,4e] Three neopentyloxy(phenyl)(*p*-substituted phenyl)-λ^6-sulfanenitriles, **1f-m**, **1f-c**, and **1f-n**, were prepared by using the method of preparation of **1f**.[4e]

Neopentyloxy(phenyl)(*p*-tolyl)-λ^6-sulfanenitrile (1f-m). Yield 16%; mp 111—113 °C (decomp); IR (KBr) 1334 cm^{-1} (ν_{SN}); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.00 (s, 9H), 2.39 (s, 3H), 3.67, 3.69 (ABq, J = 8.8 Hz, 2H), 7.26—7.28 (m, 2H), 7.43—7.51(m, 3H), 7.80—7.83 (m, 2H), 7.90—7.93 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 21.4, 26.6, 31.7, 70.5, 127.0, 127.3, 128.9, 129.5, 131.8, 142.0; 142.7, 145.5. Found: C, 71.89; H, 7.56; N, 4.76%. Calcd for $C_{18}H_{23}NOS$: C, 71.72; H, 7.69, N, 4.65%.

***p*-Chlorophenyl(neopentyloxy)(phenyl)-λ^6-sulfanenitrile (1f-c).** Yield 40%; mp 114—115 °C (decomp); IR (KBr) 1337 cm^{-1} (ν_{SN}); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.00 (s, 9H), 3.69, 3.71 (ABq, J = 9.2 Hz, 2H), 7.43—7.55 (m, 5H), 7.84—7.93 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 26.6, 31.7, 70.8, 127.1, 128.6, 129.1, 129.2, 132.2, 138.4, 143.6, 144.8. Found: C, 63.25; H, 6.33; N, 4.18%. Calcd for $C_{17}H_{20}ClNOS$: C, 63.48; H, 6.27; N, 4.35%.

Neopentyloxy(*p*-nitrophenyl)(phenyl)-λ^6-sulfanenitrile (1f-n). Yield 11%; mp 119—122 °C (decomp); IR (KBr) 1348 cm^{-1} (ν_{SN}); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.02 (s, 9H), 3.74, 3.77 (ABq, J = 9.2 Hz, 2H), 7.51—7.60 (m, 3H), 7.93—7.95 (m, 2H), 8.07—8.10 (m, 2H), 8.30—8.33 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 26.6, 30.9, 31.8, 71.2, 124.3, 127.4, 128.1, 129.4, 132.8, 143.7, 149.5, 150.8. Found: C, 61.25; H, 6.25; N, 8.29%. Calcd for $C_{17}H_{20}N_2O_3S$: C, 61.42; H, 6.06; N, 8.43%.

Hydrolysis Product Analysis: To a solution of alkoxy-λ^6-sulfanenitriles **1** (5.5 mg) in CD_3CN (0.06—0.1 ml) in an NMR tube was added buffer solution (0.52 ml, prepared by mixing the calculated amounts of salt solutions in D_2O to give a pD value close to the desired value shown in Table 1) containing an internal standard, DSS (5.0 mg) and ^{1}H NMR spectrum was taken immediately. Then its ^{1}H NMR spectrum was measured at an appropriate time interval until the reaction completion. These ^{1}H NMR spectra showed a gradual disappearance of four *o*-hydrogen signals of the λ^6-sulfanenitrile and those of the alkoxy group, instead of an increase of new signals of the sulfoximide and the corresponding alcohols. For **1a**, after the reaction started, a doublet signal at δ = 3.53 (J_{PH} = 10.4 Hz) for monomethyl phosphate was simultaneously observed to increase with time. The yields were calculated on the basis of the conversion of four *o*-hydrogen atoms of λ^6-sulfanenitrile. The yields of alcohol and other products were obtained based on the yield of sulfoximide.

Intermediate of Protonated λ^6-Sulfanenitrile: To a solution of neopentyloxy(phenyl)(*p*-tolyl)-λ^6-sulfanenitrile (**1f-m**) (5.5 mg) in CD_3CN (0.08 ml) in an NMR tube at 0 °C was added phosphate buffer solution (0.66 ml) of D_2O at pD ca. 3 containing an internal standard, DSS (5.0 mg) at the same temperature, and ^{1}H NMR spectrum was taken immediately. A comparative operation was carried out using D_2O instead of buffer solution.

^{1}H NMR (400 MHz, $D_2O:CD_3CN$) for hydrolysis of **1f-m** in D_2O : **1f-m**, δ = 0.99 (s, 9H), 2.37 (s, 3H), 3.69 (s, 2H), 7.39—7.41 (m, 2H), 7.57—7.68 (m, 3H), 7.76—7.79 (m, 2H), 7.87—7.89 (m, 2H); 2-methyl-2-butanol (hydrolysis product) δ = 0.87 (t, 3H), 1.17 (s, 6H), 1.48, 1.50, (ABq, J = 7.6 Hz, 2H); sulfoximide (hydrolysis product) δ = 2.38(s, 3H), 7.41—7.43 (m, 2H), 7.56—7.62 (m, 2H), 7.65—7.69 (m, 1H), 7.86—7.88 (m, 2H), 7.97—7.99 (m, 2H).

^{1}H NMR (400 MHz, $D_2O:CD_3CN$) for hydrolysis of **1f-m** in phosphate buffer at pD ca. 3, ionic strength 0.07: Intermediate of protonated **1f-m**, δ = 1.06 (s, 9H), 2.48 (s, 3H), 4.15 (s, 2H), 7.61—7.63 (m, 2H), 7.79—7.83 (m, 3H), 8.01—8.03 (m, 2H), 8.16—8.18 (m, 2H); 2-methyl-2-butanol δ = 0.88 (t, 3H), 1.19 (s, 6H), 1.50, 1.51, (ABq, J = 7.6 Hz, 2H); sulfoximide δ = 2.40 (s, 3H), 7.44—7.47 (m, 2H), 7.62—7.67 (m, 2H), 7.72—7.75 (m, 1H), 7.91—7.94 (m, 2H), 8.03—8.06 (m, 2H).

Reaction with $H_2{}^{18}O$: To a solution of λ^6-sulfanenitrile **1d** (20 mg) in dried CD_3CN (0.55 ml) in an NMR tube was added 0.2 ml of $H_2{}^{18}O$ (97.1% ^{18}O-content). The tube was immediately immersed in an oil bath thermostated at a constant temperature 50 °C (±1 °C). The reaction process was monitored by observing the disappearance of the signals of the four *o*-hydrogens and of the isopropoxy group in terms of the ^{1}H NMR spectra. After the reaction finished, the predominant product, *S*,*S*-diphenylsulfoximide, was shown not to incorporate with ^{18}O by GC-MS spectrometry.

Kinetic Measurement: The hydrolysis reaction was started by adding 2 μl sample of the acetonitrile solution of **1** (0.14 mol dm^{-3}) to 3.0 ml of a buffer solution in a 10 mm quartz cell equilibrated at 25.2±0.1 °C in a cell compartment of a Hitachi U-3000 spectrophotometer. The variation of the UV absorption of λ^6-sulfanenitrile at a proper wavelength (see also Table 2) was automatically recorded at 10-second intervals. The experimental infinity was decided to be 10-times of the half-life. The data were analyzed by a pseudo-first-order kinetic program on a personal computer.

The buffer effect was examined by measuring the rates of hydrolysis in five concentrations of buffer solutions with the same pH and the same ionic strength, which were prepared by diluting a stock concentrated buffer solution with a $LiClO_4$ solution.

To accurately attain the activation parameters, the pH values of the buffer solutions at other temperatures besides 25.2 °C were adjusted to be the same as that at 25.2 °C. The activation parameters were obtained from a least-squares treatment of $\ln k$ against T^{-1} at three temperatures with an interval 10 °C.

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References

1 a) O. Glemser and H. SchrOder, *Z. Anorg. Allg. Chem.*, **279**, 28 (1955). b) O. Glemser and H. Richert, *Z. Anorg. Allg. Chem.*, **307**, 313 (1961). c) H. Richert and O. Glemser, *Z. Anorg. Allg. Chem.*, **307**, 328 (1961). d) O. Glemser, H. Meyer, and A. Haas, *Chem. Ber.*, **97**, 1704 (1964). e) O. Glemser and R. Mews, *Angew. Chem., Int. Ed. Engl.*, **19**, 883 (1980).

2 A. F. Clifford, J. L. Howell, and D. L. Wooton, *J. Fluorine Chem.*, **11**, 433 (1978).

3 T. Yoshimura, E. Tsukurimichi, H. Kita, H. Fujii, and C. Shimasaki, *Tetrahedron Lett.*, **30**, 6339 (1989).

4 a) T. Yoshimura, H. Kita, K. Takeuchi, E. Takata, K. Hasegawa, C. Shimasaki, and E. Tsukurimichi, *Chem. Lett.*, **1992**, 1433. b) T. Yoshimura, E. Takata, T. Miyake, C. Shimasaki, K. Hasegawa, and E. Tsukurimichi, *Chem. Lett.*, **1992**, 2213. c) T. Yoshimura, K. Hamada, M. Imado, K. Hamata, K. Tomoda, T. Fujii, H. Morita, C. Shimasaki, S. Ono, E. Tsukurimichi, N. Furukawa, and T. Kimura, *J. Org. Chem.*, **62**, 3802 (1997). d) M. Ohkubo, T. Fujii, S. Ono, H. Morita, T. Yoshimura, E. Horn, and S. Sato, *Chem. Lett.*, **1997**, 153. e) T. Yoshimura, M. Ohkubo, T. Fujii, H. Kita, Y. Wakai, S. Ono, H. Morita, C. Shimasaki, and E. Horn, *Bull. Chem. Soc. Jpn.*, **71**, 1629 (1998).

5 D. D. Perrin and B. Dempsy, "Buffers for pH and Metal Ion Control," Chapman and Hall, New York (1974).

6 S. H. Pine, "Organic Chemistry," 5th ed, McGraw-Hill, New York (1987), p. 333.

7 S. Winstein, and H. Marshall, *J. Am. Chem. Soc.*, **74**, 1120 (1952)

8 T. W. Bentley, S. Jurczyk, and K. Roberts, *J. Chem. Soc. Perkin Trans. 2*, **1987**, 293.

9 B. L. Knier and W. P. Jencks, *J. Am. Chem. Soc.*, **102**, 6789 (1980); W. P. Jencks, *Acc. Chem. Res.*, **13**, 161 (1980).

10 a) W. P. Jenks, "Catalysis in Chemistry and Enzymology," McGraw-Hill, New York (1969). b) M. L. Bender, "Mechanism of Homogenous Catalysis from Protons to Proteins," Wiley & Sons, New York (1971). c) T. Okuyama, *Kagaku*, **40**, 154 (1985).

11 W. P. Jenks, *Prog. Phys. Org. Chem.*, **2**, 63 (1964).

12 A. B. Ash, P. Blumbergs, C. L. Stevens, H. O. Michel, B. E. Hackley, Jr., and J. Epstein, *J. Org. Chem.*, **34**, 4070 (1969).

13 a) M. S. Morgan and L. H. Cretcher, *J. Am. Chem. Soc.*, **70**, 375 (1948). b) R. E. Robertson, *Can. J. Chem.*, **31**, 589 (1953). c) I. Lee, Y. H. Choi, K. W. Rhyu, and C. S. Shim, *J. Chem. Soc., Perkin Trans. 2*, **1989**, 1881.