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Kinetics and mechanisms of the acid-catalyzed hydrolyses of *N*-(4-Substitued-arylsulfinyl)phthalimides

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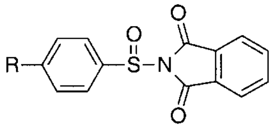
ABSTRACT: The acid-catalyzed hydrolyses of *N*-(4-substituted-arylsulfinyl)phthalimides were studied in aqueous solutions of perchloric and sulfuric acids at 50.0 ± 0.1 and of hydrochloric acid at 40.0 ± 0.1 °C. Analysis of the data by the Cox–Yates excess acidity method and substituent, temperature and solvent isotope effects indicate hydrolysis by an *A*2 mechanism at low acidity. At higher acidities a changeover to an *A*1 mechanism is observed. Copyright © 2001 John Wiley & Sons, Ltd.

KEYWORDS: *N*-(4-substituted-arylsulfinyl)phthalimides; excess acidity; hydrolysis; acid catalysis; mechanism

INTRODUCTION

In the literature the first reported sulfenimide was *N*-(trichloromethylthio)phthalimide, which was prepared by Kittleson[1] by the reaction of trichloromethanesulfenyl chloride with sodium phthalimide. Alkyl- and arylthioimides act as efficient sulfur transfer agents.[2] Harpp and Back[3] attempted to synthesize *N*-(alkyl- and arylsulfinyl)phthalimides for possible use as sulfinyl-transfer reagents and reported that thiophthalimides conveniently oxidized to the corresponding sulfinyl analogues in high yield by treatment with 1 equiv. of *m*-chloroperbenzoic acid.



1 **a**; R = CH_3
b; R = H
c; R = Cl

A study of the kinetics and mechanism of alkaline hydrolysis of *N*-substituted phthalimides[4,5] and *N*-hydroxyphthalimide[6,7] were studied. The kinetics of acid, neutral and hydroxide ion-catalyzed cleavage of phthalimide and *o*-carboxyphthalimide were carried out by Zerner and Bender[8] in various pH ranges. The acid-catalyzed hydrolysis of the arenesulfinamides with up to 2.0 M aqueous mineral acids was studied by Asefi and Tillett[9] by using a stopped-flow spectrophotometer and they suggested an *A*2 mechanism in this range. There has been no systematic study of the acid-catalyzed hydrolysis of sulfinylphthalimides in highly acidic solutions. We now report a complementary study of the acid-catalyzed hydrolysis of a series of *N*-(4-substitued-arylsulfinyl)phthalimides (**1a–c**) in concentrated aqueous mineral acids.

EXPERIMENTAL

Materials. *N*-(4-substitued-arylsulfinyl)phthalimides **1a–c** were prepared from the corresponding *N*-(4-substitued-arylthio)phthalimides with *m*-chloroperbenzoic acid in chloroform as described by Harpp and Back.[10] This involved the reaction of sulfenyl chloride with phthalimide in the presence of triethylamine in dimethylformamide to give the *N*-(4-substitued-arylthio) phthalimides.[11] Sulfinyl phthalimide **1a** had m.p. 191–192 °C (lit.[10] 191–194 °C); ^1H NMR ($CDCl_3$), δ 2.4 (s, 3H), 7.3–8.0 (m, 8H); found C, 62.99; H, 4.11; N, 4.98; calc. for $C_{15}H_{11}NSO_3$ C, 63.14; H, 3.89; N, 4.91%; **1b** had m.p. 150–153.5 °C (lit.[10] 150–153 °C); ^1H NMR ($CDCl_3$), δ 7.5–8.1 (m, 9H); found C, 61.71; H, 3.37; N, 4.83; calc. for $C_{14}H_9NSO_3$ C, 61.98; H, 3.34; N, 5.16%; **1c** had m.p. 212–213 °C; ^1H NMR ($CDCl_3$), δ 7.4–7.9 (m, 8H); found C, 55.31; H, 2.60; N, 4.78; calc. for $C_{14}H_8NSO_3Cl$ C, 55.00; H, 2.64; N, 4.58%.

Kinetic procedure. The rates of hydrolysis of *N*-(4-substitued-arylsulfinyl)phthalimides were followed spectrophotometrically at 225–230 nm using a Cintra Model 20 UV–VIS spectrometer with a thermostatted cell compartment (±0.05 °C). Good first-order behavior was observed with clean isosbestic points. Values of k_1 were

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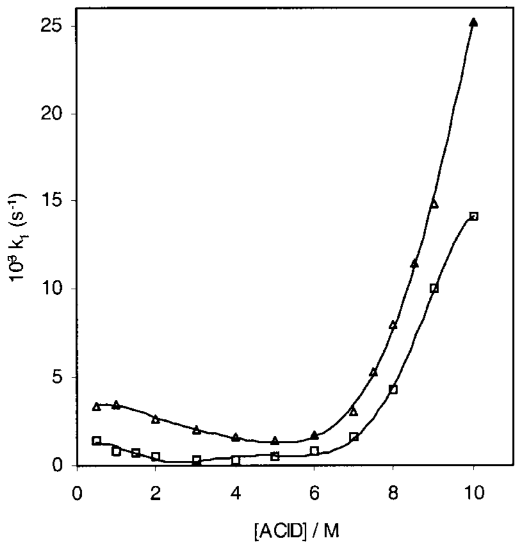


Figure 1. Plots of k_1 for acid-catalyzed hydrolysis of **1b** in aqueous acidic solutions at 50.0 °C. △, H_2SO_4; □ $HClO_4$

calculated from the standard equation using a least-squares procedure. All kinetic measurements were duplicated and the average deviation from the mean was <5%.

Product analysis. The UV spectra of the products of hydrolysis were shown to be identical with that of an equivalent mixture of phthalimide and the corresponding benzenesulfinic acids.

RESULTS AND DISCUSSION

The first-order rate coefficients, k_1, for the hydrolysis of *N*-(benzenesulfinyl)phthalimide **1b** in aqueous solutions of mineral acids are shown in Fig. 1. It can be seen that with increasing concentration of perchloric and sulfuric acids, the rate of hydrolysis decreases up to 5 M, but above ≈6 M acid the rates increase more rapidly and there is no indication of a rate maximum even at fairly high acidity. In all cases the rates of hydrolysis increase continuously with increasing concentration in hydrochloric acid solutions (Table 1). The behavior is very similar to that for **1a–c** in sulfuric acid solutions. Values of k_1 for the sulfuric acid-catalyzed hydrolyses of **1a–c** are shown in Fig. 2. The order of catalytic effectiveness of acids observed for the hydrolysis of **1b** was HCl > H_2SO_4 > $HClO_4$. Bunton *et al.* suggested that such an order is characteristic of a bimolecular mechanism, transition states of positive character being preferentially stabilized by anions of high charge density such as Cl^-, whereas the converse is usually the case for *A*1 reactions.[12] The kinetic data in Table 1 were also analyzed by the excess acidity treatment of Cox and Yates.[13] A simplified version of their relationship for mainly unprotonated substrates was used:

$$\begin{aligned}\log k_1 - \log C_{\mathrm{H+}} - \log c_{\mathrm{s}}/(c_{\mathrm{s}} + c_{\mathrm{SH+}}) \\ = m^* m^{\neq} X + \log a_{\mathrm{Nu}} + \log(k_0 k_{\mathrm{SH+}})\end{aligned} \qquad (1)$$

Values of *X* for aqueous solutions of acid were used.[14] Owing the extremely low basicity of the sulfinylphthalimides studied, the protonation correction term can be neglected.

A plot of $\log k_1 - \log C_{\mathrm{H+}}$ versus *X* is shown in Fig. 3 for hydrolyses of **1a–c** in sulfuric acid. Such graphs for the sulfinylphthalimides initially, in the low-acidity region all exhibit a downward curvature typical of *A*2 reactions involving water.[15] This changes with increasing acidity to an upward linear region characteristic of an *A*1 process. Similar behavior has been observed for the

Table 1. Values of 10^3 k_1 (s^{-1}) for the hydrolyses of *N*-(*p*-substitued-arylsulfinyl)phthalimides at 50.0 °C

[H^+](M)	**1b** (H_2SO_4)	**1b** ($HClO_4$)	**1b** (HCl)[a]	**1a** (H_2SO_4)	**1a** ($HClO_4$)	**1c** (H_2SO_4	**1c** ($HClO_4$)
1.00	3.50	0.80	16.7	3.70		7.70	
1.50	—	0.70	22.8	—		—	
2.00	2.70	0.40	29.6	3.30	0.30	6.10	0.60
2.50	—	—	36.5	—		—	
3.00	2.00	0.30	42.1	3.10		4.40	
3.50	—	—	47.5	—		—	
4.00	1.60	0.30	54.7	4.10		2.60	
5.00	1.40	0.39	70.4	4.20		2.10	
6.00	1.70	0.80	98.4	7.10		2.00	
7.00	3.10	1.60	—	16.1		2.70	
7.50	5.30	—	—	—		—	
8.00	8.00	4.30	—	42.9		4.90	
8.50	11.5	—	—	—		—	
9.00	14.8	10.0	—	102	21.2	9.00	4.90
10.00	25.2	14.1	—	—		19.3	

[a] At 40.0 °C.

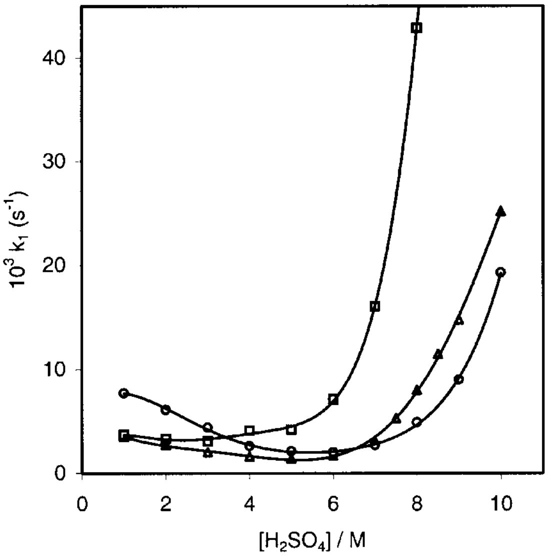


Figure 2. Plots of k_1 for sulfuric acid-catalyzed hydrolysis of **1a–c** at 50.0 °C. □ *p*-CH$_3$; △, *p*-H; ○, *p*-Cl

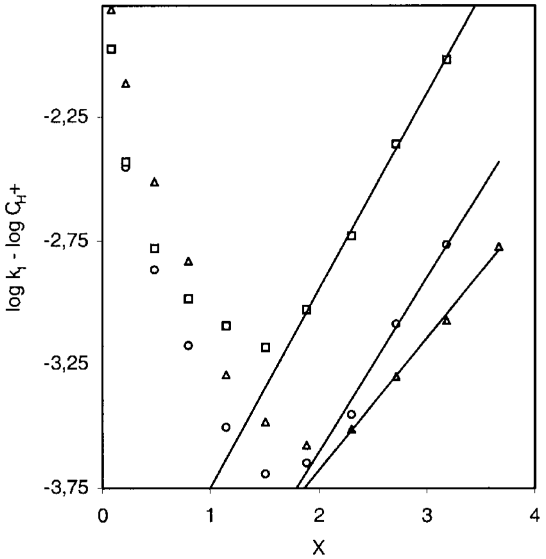


Figure 3. Plots of logk_1−logC_{H^+} vs excess acidity for the sulfuric acid-catalyzed hydrolysis of **1a–c** at 50.0 °C. □; *p*-CH$_3$; ○, *p*-H; △, *p*-Cl

Table 2. Arrhenius parameters for hydrolysis of *N*-(*p*-substitued-arylsulfinyl)phthalimides

Compound	Acid	$[H^+]$ (M)	$\Delta H^{\neq}$ (kJ mol^{-1})	$\Delta S^{\neq}$ (J mol^{-1} K^{-1})	Temperature range (°C)[a]	r^2
1b	H_2SO_4	1.00	54.8	−120.7	35–55	0.9940
		5.00	77.1	−60.8	35–55	0.9933
		8.00	73.8	−57.7	35–55	0.9989
		12.00	71.1	−45.8	30–45	0.9966
		14.00	71.2	−34.6	20–35	0.9980
	$HClO_4$	1.00	58.9	−121.9	45–60	0.9949
		4.00	82.2	−58.1	45–60	0.9970
		8.00	81.2	−38.0	45–60	0.9978
		10.50	82.0	−13.7	20–35	0.9985
1a	H_2SO_4	3.00	75.3	−60.5	35–50	0.9986
		9.00	72.6	−43.6	35–50	0.9997
	$HClO_4$	2.00	85.8	−43.3	45–60	0.9999
		10.50	90.5	+3.3	45–60	0.9999
1c	H_2SO_4	1.00	61.6	−95.8	30–50	0.9921
		12.00	72.4	−44.9	30–45	0.9927
		14.00	84.4	+3.9	25–35	0.9962

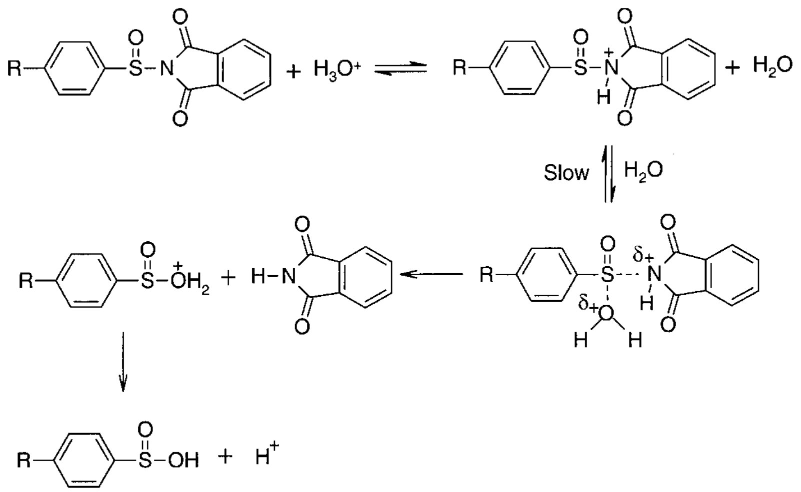
[a] The measurements were made at 5 °C intervals.

hydrolyses of a number esters[16] and benzohydroxamic acids.[17] This suggests that a gradual changeover in mechanism from *A*2 to *A*1 occurs with increasing concentration of acid.

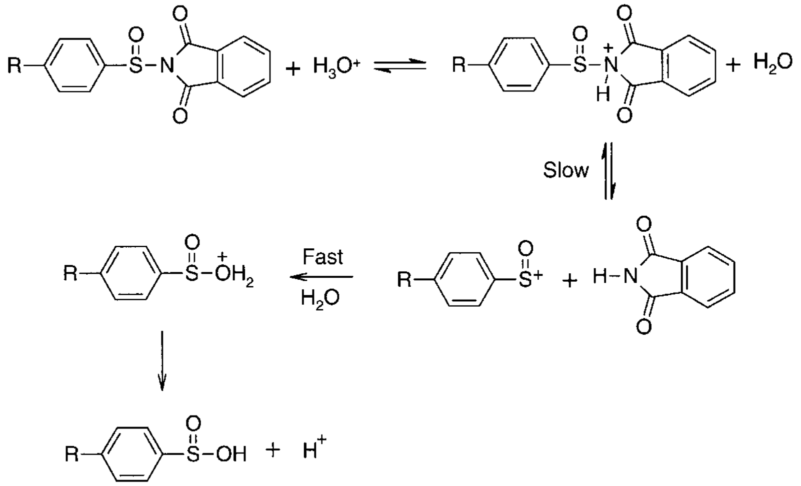
The temperature dependence of the rate constants of the hydrolysis reaction was analyzed by a least-squares procedure using a computer program (Eyring equation). The values at different acidities are shown in Table 2. Acid-catalyzed hydrolyses of esters and amides[18] proceeding by an *A*1 mechanism have $\Delta S^{\neq} \approx 0$ to -41.8 J K^{-1} mol^{-1}, while those proceeding by an *A*2 mechanism have $\Delta S^{\neq} \approx -62.8$ to -125.5 J K^{-1} mol^{-1}. Over the range 1.0–10.5 M perchloric acid, the values of $\Delta S^{\neq}$ change from -121.9 to -13.7 J K^{-1} mol^{-1} for the hydrolysis of **1b**. Values in sulfuric acid vary in a similar way as expected.

Table 3. Deuterium solvent isotope effect for hydrolysis of **1b** in sulfuric acid solutions

T(°C)	Acid (mol dm^{-3})	$10^3 k_1$/s^{-1}	k_{D_2O}/k_{H_2O}
49.8	H_2SO_4 (1.00)	3.49	1.02
	D_2SO_4 (1.00)	3.57	
40.0	H_2SO_4 (10.00)	8.85	1.92
	D_2SO_4 (10.00)	16.98	



Scheme 1



Scheme 2

The kinetic solvent isotope effect (k_D/k_H) observed for the hydrolysis of **1b** is shown in Table 3. The increasing values with acidity of the kinetic solvent isotope effect [e.g. for **1b**, $k_{1_{D_2O}}/k_{1_{H_2O}} = 1.02$ (1.00 M H_2SO_4) and 1.92 (10.00 M H_2SO_4)] are also consistent with a change from *A*2 to *A*1.[19] At acidities higher than 5.0 M [H^+], electron-donating substituents produce the highest rate of hydrolysis (i.e. **1a** > **1c**) and the substituent effects are well correlated by a satisfactory Hammett $\sigma\rho$ plot [at 9.00 M $HClO_4$, $\rho = -1.58$ (corr. 0.990)]. Clearly at these acidities electron-donating substituents both facilitate protonation of the substrate and stabilize the sulfur cation in the *A*1 mechanism. At lower acidities, however [e.g. 2.00 M $HClO_4$, $\rho = 0.75$ (corr. 0.999)], **1c** hydrolyses more rapidly than **1a**, consistent with a predominantly *A*2 mechanism in which substituent effects on the protonation and slow step operate in opposite directions. There is no direct evidence concerning the site of protonation of sulfinylphthalimides, however, protonation of sulfinamides[9,20] and sultams[21] occur preferentially at the nitrogen atom.

In the light of the overall evidence, we propose that the acid-catalyzed hydrolysis of *N*-(4-substitued-arylsulfinyl)phthalimides occur with an *A*2 mechanism at lower acidities and an *A*1 mechanism at higher acidities, as shown in Schemes **1** and **2**, respectively.

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