

Reaction Kinetics of 3-Thiophenesulfonyl Chloride with Anilines in Methanol

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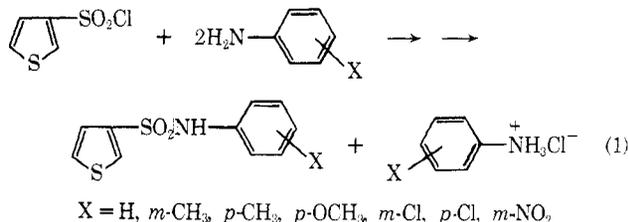
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The reaction rate constants and the activation parameters for the reaction of 3-thiophenesulfonyl chloride with some meta- and para-substituted anilines have been measured in methanol. The reaction is second order overall and pseudo first order with respect to each reactant. 3-Thiophenesulfonyl chloride is more reactive than 2-thiophenesulfonyl chloride but less than benzenesulfonyl chloride. The slopes of Hammett ($\rho = -2.25$) and Brønsted plots ($\beta = 0.54$) closely resemble those obtained for the analogous reactions of 2-thiophenesulfonyl chloride and benzenesulfonyl chloride, indicating a similar transition-state structure for all three substrates. An addition-elimination mechanism, in which the rate-determining step is the aniline nucleophilic attack to the substrate, is proposed.

Following work on the reaction kinetics of 2-thiophenesulfonyl chloride with anilines,^{1,2} in this paper we report the results of a kinetic study of the reaction between 3-thiophenesulfonyl chloride and meta- and para-substituted anilines in methanol solution and the comparison of the reactivity data with those obtained for 2-thiophenesulfonyl chloride¹ and benzenesulfonyl chloride.³

The reaction of 3-thiophenesulfonyl chloride with anilines takes place quantitatively according to eq 1.



The reaction is second order overall, first order with respect to each reactant, and was followed by continuous titration of the acid produced with 0.1 *N* sodium hydroxide (see Experimental Section).

The reactivity of 3-thiophenesulfonyl chloride is greater than that of 2-thiophenesulfonyl chloride,¹ but lower than that of the benzene derivative.³

The values of Hammett and Brønsted plot slopes for the reactions of 3-thiophenesulfonyl chloride are very similar to those obtained for the 2-thiophene isomer¹ and the benzene derivative;³ then the reaction mechanism ought to be the same for all three substrates.

Results and Discussion

The reaction kinetics of 3-thiophenesulfonyl chloride with a large excess of aniline in methanol is pseudo first order with respect to 3-thiophenesulfonyl chloride, to at least 70% completion.

The plot of pseudo-first-order rate constants (k_{ps}) against aniline concentration is linear; then the reaction is first order also with respect to the aniline.

The reaction, as expected from eq 1, follows the rate law eq 2.

$$\text{rate} = k_2[\text{C}_4\text{H}_3\text{SSO}_2\text{Cl}][\text{H}_2\text{NC}_6\text{H}_4\text{X}] \quad (2)$$

The second-order overall rate constants (k_2) at different temperatures, reported in Table I together with the pK_a values at 25° of protonated anilines in methanol,⁴ were calculated from the plot of k_{ps} against aniline concentrations, using eq 3.⁵

$$k_{ps} = k_{\text{solv}} + k_2[\text{aniline}] \quad (3)$$

The reaction products are sulfonamides, as the solvolysis rate constant (k_{solv}) is remarkably smaller than k_2 .

The rate-constant values are higher than those calculated for the analogous reaction of 2-thiophenesulfonyl chloride,¹ and lower than those measured for benzenesulfonyl chloride.³ In particular, for the reactions of the examined sulfonyl chlorides with aniline at 25°, the ratios 4 and 5 were obtained.

$$k_{\text{PhSO}_2\text{Cl}}/k_{3\text{-ThSO}_2\text{Cl}} = 3.3 \quad (4)$$

$$k_{3\text{-ThSO}_2\text{Cl}}/k_{2\text{-ThSO}_2\text{Cl}} = 3.7 \quad (5)$$

The thiophene ring deactivates the sulfonyl group more than the benzene ring does, probably owing to the greater mesomeric interaction between the heterocycle and the sulfonyl group.

The greater reactivity of 3-thiophenesulfonyl chloride with respect to the 2-substituted isomer could be ascribed to the lower contribution of the thiophene-sulfonyl resonance forms.^{6,7}

The activation parameters for the examined reactions are reported in Table II, together with the linear correlation coefficients and the standard deviations.

The E_A values, lower than those of the analogous reactions of 2-thiophenesulfonyl chloride, indicate that the transition state is energetically favored.

Figure 1, where the Hammett plot is reported, shows that the reaction rate depends on the electron density on the nitrogen atom of aniline; electron-donating substituents, in fact, increase the rate, while electron-withdrawing substituents decrease it.

The slope ($\rho = -2.25$) is very similar to that calculated for the benzenesulfonyl chloride reaction ($\rho = -2.15$)³ and the same as that found for 2-thiophenesulfonyl chloride ($\rho = -2.25$),¹ indicating the same rate sensitivity to substituents in the aniline.

The Brønsted plot, obtained using the pK_a of anilines calculated in methanol,⁴ reported in Figure 2, is linear; this verifies that the reaction rate depends on the basicity of the nucleophilic reagent.

The slope value ($\beta = 0.54$), related to the degree of S-N bond formation in the transition state,⁸ is equal, within experimental errors, to the values found for 2-thiophenesulfonyl chloride ($\beta = 0.53$)¹ and benzenesulfonyl chloride ($\beta = 0.52$), the latter calculated by us from Rogne data.³ This finding indicates that the transition-state structure ought to be the same in all three reactions.

The results of this work, in connection with the kinetic study on the halogen mobilities in the reaction of 2-thiophenesulfonyl halides⁹ and benzenesulfonyl halides¹⁰ with aniline, suggest that the reaction proceeds following an addition-elimination mechanism (Scheme I), where the

Table I
Second-Order Rate Constants for the Reaction of 3-Thiophenesulfonyl Chloride with Substituted Anilines

Registry no.	No.	Substituent	pK_a at 25° in methanol ^a	$k_2 \times 10^3$, l. mol ⁻¹ sec ⁻¹ ^b			
				15°	25°	25°	45°
62-53-3	1	H	-0.195	12.2 (0.3)	20.8 (0.7)	33.6 (1.1)	51.6 (1.5)
108-44-1	2	<i>m</i> -CH ₃	-0.0079	14.9 (1.1)	24.4 (1.8)	36.8 (0.4)	56.4 (3.5)
106-49-0	3	<i>p</i> -CH ₃	0.3426	33.9 (1.2)	53.6 (1.1)	88.7 (3.5)	146.7 (5.6)
104-94-9	4	<i>p</i> -OCH ₃		68.8 (3.5)	105 (7)	161 (6)	236 (11)
108-42-9	5	<i>m</i> -Cl	-1.727	1.34 (0.02)	2.68 (0.18)	4.83 (0.01)	8.42 (0.47)
106-47-8	6	<i>p</i> -Cl	-1.199	2.85 (0.17)	4.98 (0.15)	7.16 (0.70)	15.6 (1.6)
99-09-2	7	<i>m</i> -NO ₂	-3.1035	0.319 (0.022)	0.654 (0.027)	1.29 (0.01)	2.70 (0.11)

^a M. Kilpatrick and C. A. Arenberg, *J. Amer. Chem. Soc.*, **75**, 3812 (1953). ^b Maximum error in parentheses.

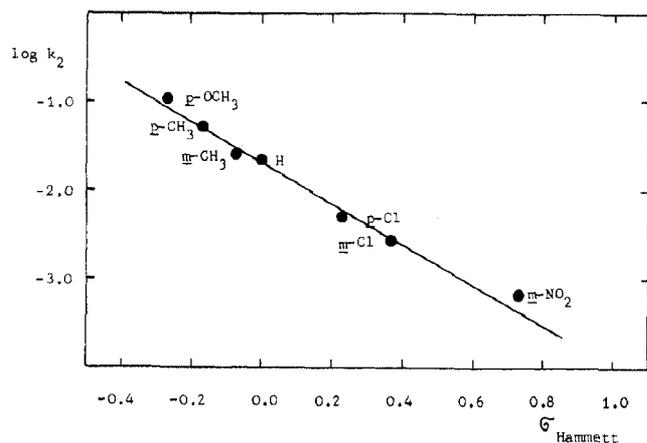


Figure 1. Hammett plot at 25°.

rate-determining step is the aniline nucleophilic attack to the substrate.

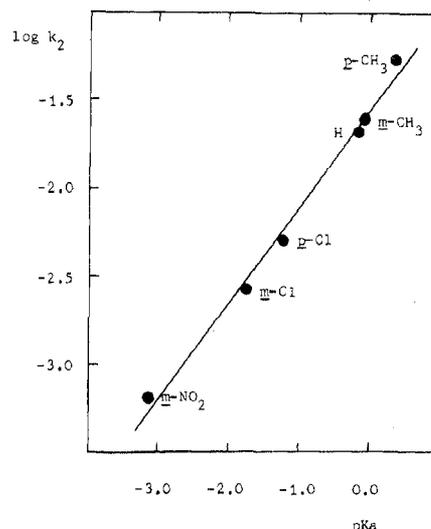
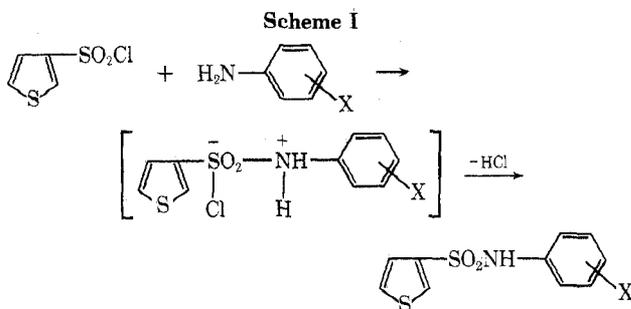


Figure 2. Brønsted plot at 25°.



Experimental Section

3-Thiophenesulfonic Acid. Sodium 2,5-dibromo-3-thiophenesulfonate (50 g) obtained by sulfonation of 2,5-dibromothiophene¹¹ was debrominated with 5% sodium amalgam in aqueous solution.¹² The solution was separated from mercury, neutralized with HCl, and evaporated to dryness. The solid was treated with boiling methanol to extract the organic product. The liquid was evaporated and sodium 3-thiophenesulfonate (igroscopic) was collected (50% yield).

3-Thiophenesulfonyl Chloride. Dry sodium 3-thiophenesulfonate (20 g) was treated with 50 ml of POCl₃ and refluxed for 2 hr.

The mixture was poured dropwise, with caution, into crushed ice, and, after stirring, a solid separated. The solid was filtered, mp 47°^{12,13} from petroleum ether (bp 30–50°), 61% yield.

The uv spectrum in 95% ethanol shows a maximum at 241 nm (log ϵ 3.79).

The ir absorption frequencies, characteristic of the sulfonyl asymmetric and symmetric stretching, measured in KBr disks, are located respectively at 1370 and 1160 cm⁻¹.

The nmr peaks (CCl₄) occur at δ 7.96 (1 H, triplet, H₂) and 7.25 ppm (2 H, doublet, H₄ and H₅).

3-Thiophenesulfonamides. 3-Thiophenesulfonamides were synthesized by adding 0.03 mol of 3-thiophenesulfonyl chloride in methanol (10 ml) to a methanol solution (50 ml) containing 0.065 mol of aniline, following the procedure previously described for 2-thiophenesulfonamides.¹

The products were characterized by C, H, N analysis and uv and ir spectroscopy. In Table III are reported the melting points, the analytical data, and the spectroscopic characteristics.

The anilines used were commercial products, purified by several crystallizations or distillations.

Methanol used for the kinetic runs was RS Carlo Erba.

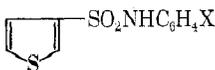
Kinetic Procedure. Rate measurements were done by a digital pH meter Amel Model 333 by continuous titration of the acid produced with 0.1 N sodium hydroxide.

Table II
Activation Parameters for the Reaction of 3-Thiophenesulfonyl Chloride with Substituted Anilines

No.	Substituent	r^a	E_A , kcal mol ⁻¹	Log A	ΔS^\ddagger , cal mol ⁻¹ °K ⁻¹
1	H	0.9998	8.8 ± 0.1 ^b	4.7 ± 0.1 ^b	-39 ± 0.5 ^b
2	<i>m</i> -CH ₃	0.9997	8.0 ± 0.1	4.3 ± 0.1	-41 ± 0.5
3	<i>p</i> -CH ₃	0.999	8.9 ± 0.3	5.3 ± 0.2	-36 ± 1
4	<i>p</i> -OCH ₃	0.9999	7.5 ± 0.1	4.5 ± 0.1	-40 ± 0.5
5	<i>m</i> -Cl	0.9997	11.1 ± 0.2	5.6 ± 0.2	-35 ± 1
6	<i>p</i> -Cl	0.987	9.9 ± 1.1	5.0 ± 0.8	-38 ± 4
7	<i>m</i> -NO ₂	0.999	12.9 ± 0.4	6.3 ± 0.3	-31.5 ± 1.5

^a Linear correlation coefficients. ^b Standard deviations.

Table III
Physical Constants and Absorption Spectra of Substituted 3-Thiophenesulfonanilides^{a,b}



Registry no.	No.	X	Mp, °C	Formula	Ultraviolet spectra, nm		Infrared spectra, cm ⁻¹		
					λ_{\max}	Log ϵ	NH stretch	SO ₂ stretch asym	SO ₂ stretch sym
51175-66-7	1	H	111-112	C ₁₀ H ₉ NO ₂ S ₂	227	4.08	3240	1335	1145
					240 ^c	3.94			
51175-67-8	2	<i>m</i> -CH ₃	71	C ₁₁ H ₁₁ NO ₂ S ₂	229	4.05	3235	1330	1145
51202-24-5	3	<i>p</i> -CH ₃	114-115	C ₁₁ H ₁₁ NO ₂ S ₂	229	4.12	3240	1330	1145
51175-68-9	4	<i>p</i> -OCH ₃	128	C ₁₁ H ₁₁ NO ₃ S ₂	232	4.19	3230	1335	1155
					280 ^c	3.24			
51175-69-0	5	<i>m</i> -Cl	83	C ₁₀ H ₈ ClNO ₂ S ₂	234	4.08	3240	1330	1150
51202-25-6	6	<i>p</i> -Cl	108	C ₁₀ H ₈ ClNO ₂ S ₂	235	4.20	3235	1320	1150
51175-70-3	7	<i>m</i> -NO ₂	166-167	C ₁₀ H ₈ N ₂ O ₄ S ₂	225 ^c	4.12	3240	1330	1145
					237	4.14			
					270 ^c	3.68			

^a All the compounds were crystallized from aqueous ethanol. ^b Satisfactory combustion analytical data for C, H, N ($\pm 0.35\%$) were reported for these compounds: Ed. ^c Inflection.

In a typical kinetic run a solution containing *ca.* 3×10^{-4} mol of 3-thiophenesulfonyl chloride in methanol (10 ml) was added to a methanol solution (90 ml) containing *ca.* 1×10^{-2} mol of aniline.

The pseudo-first-order rate constants were calculated from conventional plots of $\log(a-x)$ against time from the slope obtained using the least-squares method.

The second-order rate constant was calculated from the slope of the line obtained by plotting the pseudo-first-order rate constants against aniline concentrations. At least three kinetic runs, at different aniline concentrations, were carried out at the established temperature.

The activation energies and $\log A$ values were calculated from the Arrhenius equation, while the activation entropies were computed for 25° using the suitable equation.¹⁴

Spectroscopy. The uv spectra were recorded on a Hitachi Perkin-Elmer Model EPS 3T spectrometer in ethanol solutions (1×10^{-5} mol l.⁻¹). The ir spectra were recorded in KBr disks on a Perkin-Elmer Model 237 spectrometer. The nmr spectra were obtained with a Varian A-60 spectrometer in carbon tetrachloride, using TMS as internal standard.

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Registry No.—3-Thiophenesulfonyl chloride, 51175-71-4; sodium 3-thiophenesulfonate, 51175-72-5.

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Effect of a Neighboring Trimethylsilyl Group on the Photochemical and Mass Spectral Fragmentation Pathways of S-Alkyl Thioacetates

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The photolyses of 3-(trimethylsilyl)propyl thioacetate (I) and 2-(trimethylsilyl)ethyl thioacetate (II) have been studied. Products arising from both sulfur-acyl and sulfur-alkyl bond cleavage have been observed. Sulfur-alkyl bond cleavage is more important in II. The mass spectrum of II, on the other hand, is dominated by ions arising from interaction of the silyl center with the oxygen and sulfur atoms of the thioacetate group.

The photochemistry of S-alkyl thiocarboxylates has been shown to be dominated by products arising from cleavage of the sulfur-acyl bond to the exclusion of products arising from the Norrish type II process.^{1,2} This "normal behavior" dominates the photolysis of 3-(trimethylsilyl)propyl thioacetate (I) in dilute benzene solution. Thus the major products of photolysis of I were found to be acetaldehyde (22.7%), 3-(trimethylsilyl)propyl methyl sul-

fide (41.2%), and bis-3-(trimethylsilyl)propyl disulfide (3.9%). In addition, however, trimethylpropylsilane (6.3%) was isolated and shown to be a primary photolysis product since it was present in reactions carried to less than 5% conversion.^{3,4} Formation of trimethylpropylsilane may be economically explained as arising from initial sulfur-alkyl bond scission followed by abstraction of a hydrogen atom by the initially formed carbon radical. Sulfur-alkyl bond