Analysis of substituent effects in the reactions of some 2-L-3-nitro-5-X-thiophenes with aniline in benzene. A new interpretation of the 'element effect'

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Dedicated to Professor Domenico Spinelli on his 70th birthday

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Abstract

The kinetic constants for the title reactions have been measured in benzene, at 25 ºC, at various aniline concentrations. In spite of the low k_B/k_0 ratios, the reactions are inferred to be genuinely base-catalyzed. The susceptibility constants estimated for the various steps of the reaction mechanism(s) have allowed to make clear the limits of the so-called "element effect" criterion.

Keywords: S_NAr reactions, thiophenes, base catalysis, element effect

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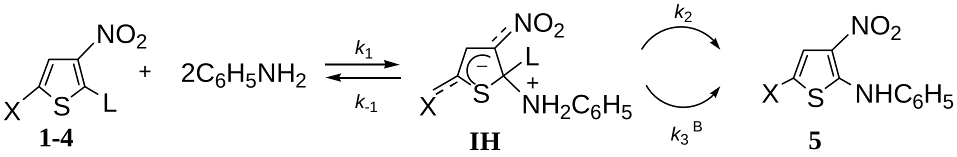
Introduction

The S_NAr reactions of nitro-activated thiophenes with primary and secondary amines can be catalyzed by the nucleophile.[1]

By applying the 'steady-state' approximation in the intermediate in the addition–elimination mechanism[2] shown in the Scheme, one obtains eq. (1)



1: L = Br, **2**: L = Cl, **3**: L = OC_6H_5, **4**: L = $OC_6H_4NO_2$-*p*

X = H, Br, $CONH_2$, CO_2Me, COMe, SO_2Me, CN, NO_2

Scheme 1

$$k_A = (k_1k_2 + k_1k_3^B[B])/(k_{-1} + k_2 + k_3^B[B]) \qquad \textbf{eq. (1)}$$

where k_A represents the apparent second-order kinetic constant.

According to eq. (1), when $(k_2 + k_3^B[B]) \gg k_{-1}$ or $k_{-1} > k_2$ and $k_2 \gg k_3^B[B]$, no base catalysis is observed.

Apart from some rare exceptions where the coefficient k_3^B is very small, for example because of steric hindrance, the insensitivity to base concentration generally indicates that the overall rate is controlled by the addition step, *i.e.*, $k_A = k_1$.

When $(k_2 + k_3^B[B]) \ll k_{-1}$ the kinetic constant increases linearly with increasing base concentration, following eq. (2)

$$k_A = \frac{k_1k_2}{k_{-1}} + \frac{k_1k_3^B[B]}{k_{-1}} \qquad \textbf{eq. (2)}$$

When $k_2 \ll k_{-1}$ and $k_{-1} \cong k_3^B[B]$, k_A varies in a curvilinear fashion as a function of [B], obeying to eq. (1).

The catalysis law observed depends on the nature of the aromatic substrate, the amine, the nucleofugal group, the base, and the solvent used.[1]

Results and Discussion

The apparent second-order kinetic constants, k_A, for reactions of compounds (**1–4**) with aniline in benzene, at various nucleophile concentrations, are listed in Tables 1-4.

Examination of the kinetic data shows that for each substrate k_A increases linearly with increasing nucleophile concentration.

A least-squares treatment of data according to eq. (3)

$$k_A = k_0 + k_B\,[B] \qquad \textbf{eq. (3)}$$

gave the results reported in Tables 5–8.

With reference to the Scheme and eq. (1), the fact that the apparent second-order kinetic constants are described correctly by eq. (3) would imply the condition $k_{-1} \gg (k_2 + k_3^B[B])$ where B represents the amine nucleophile. In fact, in this hypothesis, eq. (3) is equivalent to eq. (2)

Thus the k_B/k_0 shown in Tables 5–8 would represent the k_3^B/k_2 ratios.

Since the calculated k_B/k_0 values range between 2.4 and 6.9, according to Bunnett and Garst[3] they have to be analyzed very cautiously.

If the acceleration observed, expressed quantitatively by eq. (3) were not due to base catalysis but to some effects of unclear origin, the k_0 parameter should correspond to k_1.

According to this identification, this specific rate constant increases with increasing electron-withdrawing power of the substituent present in the thiophene ring, with the leaving group being equal (Tables 5–8), as expected on the grounds of the electronic substituent effects on the activation energy for the formation of the reaction intermediate.

In fact, the k_B parameter also increases *in the same way* and, moreover, there is an excellent linear correlation between log k_B and the corresponding log k_0 values (Table 9).

Since it is difficult to give an appealing interpretation of this rigorously quantitative dependence on the substituent effects of the phenomenon “measured” by k_B and, “effects due to the medium polarity”,[4] we must conclude that in this case a genuine base catalysis is involved.

The relatively low k_3^B/k_2 ratios certainly depend on the poor basicity of aniline and then on its poor catalytic efficiency.

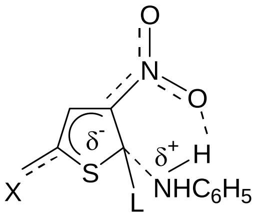
Plots of log k_B or log k_0 values versus σ^- substituent constants[5] show excellent linear correlations (Table 10).

Since

$$k_B = \frac{k_1k_3[B]}{k_{-1}}, \quad k_0 = \frac{k_1k_2}{k_{-1}} \quad \text{and} \quad \log k = \rho\sigma^- + c$$

the slopes of the straight lines obtained correspond, for each leaving group, respectively, to $\rho_1+\rho_3^B\rho_{-1}$ and $\rho_1+\rho_2-\rho_{-1}$.

In the k_{-1} step—that is, in the decomposition of reaction intermediate into starting compounds—one observes both the breaking of the intramolecular hydrogen bonding between the “anilinium” proton and the 3-nitro group and the breaking of the bond between nucleophilic nitrogen and aromatic carbon atom as exemplified in **6**.



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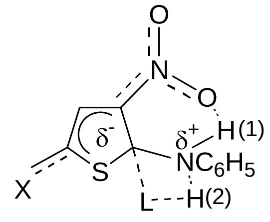
An electron-withdrawing substituent present in the thiophene ring favors, with respect to hydrogen, breaking of the first bond and hinders that of the second one. Of course, the more important effect is that on the carbon–nitrogen bond, in that it is the degree of formation or of breaking of this bond that controls predominantly the energy of the first transition state of the addition–elimination; thus ρ_{-1} should be negative.

In the k_2 step, where a spontaneous decomposition of the intermediate in the reaction products occurs, an “anilinium” proton transfer to the leaving group is concerted with the detachment of this group from the aromatic carbon atom, as shown in **7**.



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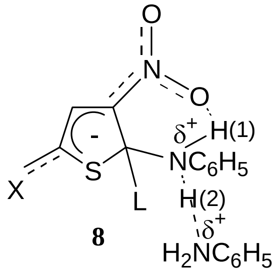
With increase in the electron-withdrawing power of X, the basicity of the oxygen atoms of the nitro group is reduced, and the acidity of the H(1) and H(2) hydrogen atoms increases.

As a matter of fact, the lower acidity of H(1) caused by the elimination of H(2) is partly counterbalanced by the increase in the acidity of H(1) caused by the change occurring from a mono-aryl-substituted amine (aniline) to a bi-aryl-substituted amine (N-thienyl-aniline); thus, there is nearly no effect on the hydrogen bond involving the nitro group and the H(1) hydrogen atom. On the grounds of the effect (not counterbalanced) on the acidity of H(2), ρ_2 should be positive.

The intramolecular acid catalysis occurring through the hydrogen bonding between L and H(2) is influenced in a direct way by the nucleofugality of the leaving group involved, as controlled by the electronic effect of the X substituent; thus ρ_2 should be negative.

It is evident that the more important effect is that on the carbon–leaving- group bond, in that it is the degree of formation or of breaking of this bond that controls, predominantly, the energy of the second transition state of the addition–elimination mechanism; thus, as a whole, ρ_2 should be negative.

As far as the k_3^B step is concerned, it is worthwhile to consider the possible catalysis mechanisms. The removal of the acidic anilinium proton in the reaction intermediate could happen in different ways.[6] In the first mechanism the rate-determining step involves the formation of the transition state **8**.



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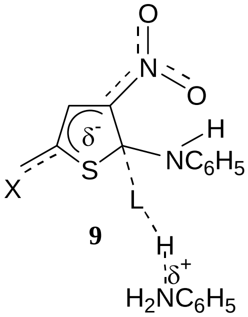
With increasing electron-withdrawing power of X, the basicity of the oxygen atoms of the 3-nitro group decreases, and the acidity of H(1) and H(2) hydrogen atoms increases. As a consequence of the detachment of H(2) the acidity of H(1) decreases, with the net effect of reducing the stabilization of the transition state owing to the intramolecular hydrogen bonding between the nitro group and H(1). Thus, there is a balancing between the favorable effect of the X- substituent variation and the unfavorable effect on the intramolecular hydrogen bonding.

As a whole, in this catalysis mechanism one should observe $\rho_3^B \sim 0$. In the SB–GA mechanism[1] a rapid pre-equilibrium occurs with a transition state like **8** where a proton is transferred from **1-H** to the amine.

In this case, at variance with what happens in the k_2 step (see above), the acidifying effect of the X substituent is complete. If this were the only factor operating it should give $\rho_3^B > 0$.

The subsequent step, that is, the acid catalysis for the leaving group's elimination by the conjugate acid of the amine [transition state **9**] is hampered by the electron-withdrawing X substituents and $\rho_3^B < 0$ should be observed. The effect of X on the C_{Ar}-L bond breaking should be similar to that seen above for the k_2 step.



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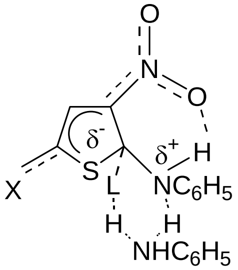
The mechanism for the intermediate's decomposition by bifunctional catalysis involves a breaking of the hydrogen bond between the "anilinium" proton and the nitrogen, which is concerted with the breaking of the bond between the leaving group and the aromatic carbon atom, as exemplified in **10**.



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Also in this case the effect of X on the acidity of the H(2) hydrogen is only partial, whereas that on the breaking of the C_{Ar}-L bond should be similar to that seen above for the SB–GA mechanism.

Let us now consider the values of ρ_0 (= $\rho_1 + \rho_2 - \rho_{-1}$) and of ρ_B (= $\rho_1 + \rho_3^B - \rho_{-1}$) for the various series of substrates (Table 11).

Since the ρ_1 values for the reactions of 2-L-3-nitro-5-X-thiophenes with aniline are known[5,7,8] (Table 11), by assuming $(\rho_1)_{\text{benzene}} = (\rho_1)_{\text{methanol}}$ it is possible to estimate the differences ρ_2-ρ_1 and ρ_3^B-ρ_{-1} for each leaving group concerned. The estimated values, as well as the observed ρ_3^B-ρ_2 values are shown in Table 11.

Both the ρ_2-ρ_{-1} and ρ_3^B-ρ_{-1} differences are rather small and suggest ρ_2 and ρ_3^B values, respectively, similar to the ρ_{-1} value.

On the reasonable hypothesis that $\rho_1 \cong |\rho_{-1}|$, the ρ_3^B-ρ_{-1} differences estimated allow us to exclude the idea that the studied reactions are catalyzed through the mechanism where the rate-determining step is the proton transfer [transition state **8**].

The transition states for the k_3^B step of the SB–GA mechanism [**9**] and that for bifunctional catalysis [**10**] involve, as in the case for the k_2 step [transition state **7**], the breaking of the bond between carbon atom and leaving group, but only in the SB–GA mechanism does the X substituent exert a complete acidifying effect on the H(2) hydrogen.

Since this effect opposes that on the breaking of the C_{Ar}-L bond, the observation of ρ_3^B-$\rho_2 > 0$, with the implication that $|\rho_3^B| < |\rho_2|$, represents a strong indication in favor of the SB–GA mechanism for the k_3^B step. On the hypothesis that the reactions studied are catalyzed by this mechanism, the leaving group variation should not greatly affect the pre-equilibrium where a proton is transferred from **1-H** to the amine. In the subsequent step [transition state **9**], the general- acid catalysis involves a transfer of the proton of the conjugate acid of nucleophile to the leaving group, concerted with its elimination from the aromatic carbon atom. Since the more basic is the leaving group, the more difficult is the breaking of the C_{Ar}–L bond, and thermodynamically more favorable is the pK difference between the leaving group and acid catalyst, it is likely that the influence of L on the position of the transition state [**9**] along the reaction coordinate is rather small.

Similar reasoning can be given for the k_2 step and the relevant transition state [**7**]. However, in this case, the situation could be complicated by the fact that the bulkier leaving group (for example, bromine as compared to chlorine) should have a more favorable geometry for the formation of the intramolecular hydrogen bonding.

In conclusion, the differences ρ_3^B–ρ_{-1} and ρ_2–ρ_{-1}, as a function of L, should be mainly determined by the effect of variation of the leaving group on the ρ_{-1} reaction constant. It turns out that the parameter k_{-1} is influenced by the electrophilicity of the carbon atom to which it is bonded in the reaction intermediate and that this electrophilicity is controlled by the inductive effect of the leaving group. The greater “efficient electronegativity” of phenoxy- and *p*-nitrophenoxy- groups causes, with respect to the two halogens, and with X being equal, greater k_1 values and lower k_{-1} values.

Thus, the ranges of transition states for these leaving groups are closer to the reactants, with respect to the corresponding ranges for halogen leaving groups, and consequently imply higher ρ_{-1} values.

By assuming $\rho_{-1} < 0$, $\rho_2 < 0$, and $\rho_3^B < 0$ (see above), on going from L = Cl or Br to L = OC_6H_5 or $OC_6H_4NO_2$-*p*, it is reasonable that the absolute value ρ_{-1} increases, and the same holds for the ρ_3^B–ρ_{-1} difference. For the reasons given above, the ρ_2–ρ_{-1} differences are more difficult to interpret.

The results obtained in the present work contribute to make clear the limits of the criterion called the, “absence of element effect”.[9]

From a comparison of the apparent relative nucleofugacities of the various leaving groups one observes that, whereas the mobility order is always $OC_6H_4NO_2$-*p* > OC_6H_5 > Cl > Br, the reactivity range for k_B (k_0) varies from 26 (18) for X = NO_2 to 91 (13) for X = Br.

These data would point out a remarkable element effect if they referred to the breaking of the C_{Ar}–L bond in the rate-determining step. From what we have said above, they refer, in contrast, to composite constants ($k_1k_3^B/k_{-1}$, k_1k_2/k_{-1}) and probably the effect of the leaving group variation on these parameters reflects mostly on the k_{-1} parameter which, indeed, pertains to the step where there is no breaking of the C_{Ar}-L bond!

Table 1. Apparent kinetic constants[a] for the reactions of 2-bromo-3-nitro-5-X-thiophenes with aniline in benzene at 25 °C

X = H									
[aniline]/ *M*	0.300	0.360	0.420	0.500					
10^9k_A/dm^3 mol^{-1} s^{-1}	1.55	1.70	1.86	2.06					
X = Br									
[aniline]/ *M*	0.202	0.253	0.303	0.354	0.404	0.455	0.505		
10^8k_A/dm^3 mol^{-1} s^{-1}	3.00	3.36	3.76	4.10	4.43	4.77	517		
X = $CONH_2$									
[aniline]/ *M*	0.160	0.220	0.280	0.340	0.400	0.460	0.520		
10^7k_A/dm^3 mol^{-1} s^{-1}	1.21	1.41	1.59	1.79	1.97	2.14	2.35		
X = CO_2Me									
[aniline]/ *M*	0.0980	0.156	0.221	0.294	0.353	0.431	0.490		
10^7k_A/dm^3 mol^{-1} s^{-1}	3.20	3.83	4.57	5.44	6.01	6.84	7.59		
X = COMe									
[aniline]/ *M*	0.103	0.165	0.227	0.288	0.350	0.433	0.494		
10^6k_A/dm^3 mol^{-1} s^{-1}	1.57	1.93	2.25	2.64	2.94	3.39	3.77		
X = SO_2Me									
[aniline]/ *M*	0.0900	0.145	0.185	0.255	0.352	0.420	0.500		
10^6k_A/dm^3 mol^{-1} s^{-1}	2.15	2.55	2.89	3.44	4.26	4.79	5.46		
X = CN									
[aniline]/ *M*	0.102	0.163	0.245	0.306	0.367	0.449	0.510		
10^6k_A/dm^3 mol^{-1} s^{-1}	2.86	3.59	4.49	5.16	5.91	6.70	7.49		
X = NO_2									
[aniline]/ *M*	0.0550	0.105	0.158	0.210	0.255	0.315	0.368	0.430	0.547
10^5k_A/dm^3 mol^{-1} s^{-1}	5.16	6.23	7.59	8.90	9.96	11.3	12.8	14.3	17.2

[a] The kinetic constants were reproducible to within ± 3 %.

Table 2. Apparent kinetic constants[a] for the reactions of 2-chloro-3-nitro-5-X-thiophenes with aniline in benzene at 25 °C

X = H								
[aniline]/ *M*	0.210	0.280	0.360	0.440	0.510			
$10^{9}k_{\mathrm{A}}$/dm^{3} mol^{-1} s^{-1}	3.56	4.11	4.75	5.41	5.94			
X = CONH$_2$								
[aniline]/ *M*	0.180	0.240	0.300	0.360	0.420	0.500		
$10^{7}k_{\mathrm{A}}$/dm^{3} mol^{-1} s^{-1}	2.55	2.97	3.40	3.83	4.26	4.80		
X = CO$_2$Me								
[aniline]/ *M*	0.120	0.180	0.240	0.300	0.360	0.420	0.510	
$10^{7}k_{\mathrm{A}}$/dm^{3} mol^{-1} s^{-1}	4.78	5.78	6.75	7.67	8.58	9.62	10.9	
X = COMe								
[aniline]/ *M*	0.122	0.184	0.245	0.306	0.388	0.439	0.510	
$10^{6}k_{\mathrm{A}}$/dm^{3} mol^{-1} s^{-1}	2.57	3.13	3.67	4.25	4.92	5.40	6.02	
X = SO$_2$Me								
[aniline]/ *M*	0.122	0.185	0.245	0.306	0.360	0.428	0.490	
$10^{6}k_{\mathrm{A}}$/dm^{3} mol^{-1} s^{-1}	3.20	3.82	4.45	4.97	5.56	6.26	6.78	
X = CN								
[aniline]/ *M*	0.118	0.176	0.235	0.284	0.353	0.407	0.490	
$10^{6}k_{\mathrm{A}}$/dm^{3} mol^{-1} s^{-1}	2.85	3.51	4.11	4.65	5.30	5.85	6.71	
X = NO$_2$								
[aniline]/ *M*	0.101	0.152	0.195	0.250	0.302	0.354	0.410	0.520
$10^{4}k_{\mathrm{A}}$/dm^{3} mol^{-1} s^{-1}	0.835	1.00	1.16	1.32	1.53	1.69	1.88	2.25

[a] The kinetic constants were reproducible to within ± 3 %.

Table 3. Apparent kinetic constants[a] for the reactions of 2-phenoxy-3-nitro-5-X-thiophenes with aniline in benzene at 25 °C

X = H							
[aniline]/ *M*	0.143	0.204	0.286	0.357	0.449	0.510	
$10^{8}k_{\mathrm{A}}$/dm^{3} mol^{-1} s^{-1}	1.41	1.59	1.83	2.03	2.29	2.45	
X = CONH$_2$							
[aniline]/ *M*	0.143	0.204	0.286	0.357	0.439	0.510	
$10^{6}k_{\mathrm{A}}$/dm^{3} mol^{-1} s^{-1}	0.832	0.945	1.11	1.25	1.41	1.57	
X = CO$_2$Me							
[aniline]/ *M*	0.120	0.180	0.240	0.300	0.360	0.440	0.500
$10^{6}k_{\mathrm{A}}$/dm^{3} mol^{-1} s^{-1}	2.09	2.42	2.74	3.07	3.38	3.82	4.16
X = COMe							
[aniline]/ *M*	0.121	0.182	0.242	0.303	0.364	0.444	0.505

Table 3. Continued

$10^{5}k_{\mathrm{A}}/\mathrm{dm}^{3}\,\mathrm{mol}^{-1}\,\mathrm{s}^{-1}$	0.718	0.846	0.971	1.10	1.23	1.40	1.54		
				X = SO_2Me					
[aniline]/ *M*	0.143	0.204	0.265	0.326	0.377	0.449	0.510		
$10^{5}k_{\mathrm{A}}/\mathrm{dm}^{3}\,\mathrm{mol}^{-1}\,\mathrm{s}^{-1}$	1.18	1.40	1.62	1.83	2.02	2.28	2.48		
				X = CN					
[aniline]/ *M*	0.140	0.200	0.260	0.320	0.380	0.440	0.500		
$10^{5}k_{\mathrm{A}}/\mathrm{dm}^{3}\,\mathrm{mol}^{-1}\,\mathrm{s}^{-1}$	1.41	1.69	1.96	2.23	2.48	2.75	3.02		
				X = NO_2					
[aniline]/ *M*	0.0520	0.104	0.156	0.208	0.250	0.333	0.374	0.458	0.497
$10^{4}k_{\mathrm{A}}/\mathrm{dm}^{3}\,\mathrm{mol}^{-1}\,\mathrm{s}^{-1}$	1.67	1.93	2.35	2.65	2.96	3.48	3.69	4.28	4.53

[a] The kinetic constants were reproducible to within ± 3 %.

Table 4. Apparent kinetic constants[a] for the reactions of 2-*p*-nitrophenoxy-3-nitro-5-X-thiophenes with aniline in benzene at 25 °C

				X = H				
[aniline]/ *M*	0.100	0.195	0.274	0.340	0.400	0.460	0.500	
$10^{7}k_{\mathrm{A}}/\mathrm{dm}^{3}\,\mathrm{mol}^{-1}\,\mathrm{s}^{-1}$	2.02	2.37	2.68	2.94	3.20	3.41	3.56	
				X = Br				
[aniline]/ *M*	0.117	0.195	0.216	0.280	0.338	0.400	0.455	0.515
$10^{7}k_{\mathrm{A}}/\mathrm{dm}^{3}\,\mathrm{mol}^{-1}\,\mathrm{s}^{-1}$	2.77	3.10	3.50	3.96	4.41	4.83	5.27	5.71
				X = $CONH_2$				
[aniline]/ *M*	0.105	0.175	0.240	0.310	0.365	0.430	0.490	
$10^{5}k_{\mathrm{A}}/\mathrm{dm}^{3}\,\mathrm{mol}^{-1}\,\mathrm{s}^{-1}$	0.750	0.903	1.03	1.20	1.32	1.47	1.62	
				X = CO_2Me				
[aniline]/ *M*	0.0850	0.137	0.195	0.248	0.317	0.370	0.415	0.480
$10^{5}k_{\mathrm{A}}/\mathrm{dm}^{3}\,\mathrm{mol}^{-1}\,\mathrm{s}^{-1}$	2.05	2.36	2.79	3.15	3.63	3.97	4.31	4.75
				X = COMe				
[aniline]/ *M*	0.0800	0.137	0.200	0.255	0.300	0.365	0.420	0.470
$10^{4}k_{\mathrm{A}}/\mathrm{dm}^{3}\,\mathrm{mol}^{-1}\,\mathrm{s}^{-1}$	0.623	0.737	0.870	1.00	1.08	1.22	1.33	1.43
				X = SO_2Me				
[aniline]/ *M*	0.0820	0.134	0.190	0.245	0.294	0.375	0.432	0.495
$10^{4}k_{\mathrm{A}}/\mathrm{dm}^{3}\,\mathrm{mol}^{-1}\,\mathrm{s}^{-1}$	1.01	1.20	1.42	1.65	1.84	2.20	2.41	2.69
				X = CN				
[aniline]/ *M*	0.0820	0.137	0.190	0.245	0.307	0.370	0.420	0.475
$10^{4}k_{\mathrm{A}}/\mathrm{dm}^{3}\,\mathrm{mol}^{-1}\,\mathrm{s}^{-1}$	1.14	1.36	1.56	1.80	2.06	2.34	2.52	2.76
				X = NO_2				
[aniline]/ *M*	0.0520	0.104	0.156	0.208	0.250	0.312	0.364	0.416

Table 4. Continued

10^3k_A/dm^3 mol^{-1} s^{-1}	1.4	1.70	1.97	2.29	2.63	3.00	3.32	3.68

[a] The kinetic constants were reproducible to within ± 3 %.

Table 5. Linear regression analysis[a] of apparent- second- order kinetic constants, k_A, for the reactions of 2-bromo-3-nitro-5-X-thiophenes with aniline in benzene, at 25 °C, according to the equation $k_A = k_0 + k_B[B]$

X	$10^7(k_0 \pm s_0)$	$10^7(k_B \pm s_B)$	k_B/k_0[b]	*r*	*n*
H	0.00782±0.00009	0.0256±0.0002	3.3	0.9996	4
Br	0.158±0.003	0.707±0.009	4.5	0.9999	7
$CONH_2$	0.715±0.011	3.13±0.03	4.4	0.9998	7
CO_2Me	2.11±0.04	11.1±0.1	5.3	0.9997	7
COMe	10.0±0.2	55.7±0.6	5.6	0.9997	7
SO_2Me	13.9±0.2	81.1±0.5	5.8	0.9999	7
CN	17.4±0.4	112±1	6.4	0.9997	7
NO_2	371±5	2460±17	6.6	0.9998	9

[a] s_0 and s_B are the standard deviations of the regression parameters k_0 and k_B, respectively; *r* is the correlation coefficient; *n* is the number of experimental points. [b] The maximum error of k_B/k_0 ratio is estimated to be 3.9 %.

Table 6. Linear regression analysis[a] of apparent- second- order kinetic constants, k_A, for the reactions of 2-chloro-3-nitro-5-X-thiophenes with aniline in benzene, at 25 °C, according to the equation $k_A = k_0 + k_B[B]$

X	$10^7(k_0 \pm s_0)$	$10^7(k_B \pm s_B)$	k_B/k_0[b]	*r*	*n*
H	0.0188±0.0002	0.0798±0.0005	4.2	0.9999	5
$CONH_2$	1.28±0.01	7.06±0.04	5.5	0.9999	6
CO_2Me	2.94±0.05	15.7±0.2	5.3	0.9998	7
COMe	15.0±0.2	88.8±0.6	5.9	0.9999	7
SO_2Me	20.1±0.4	98.1±1.2	4.9	0.9996	7
CN	16.8±0.3	103±1	6.1	0.9998	7
NO_2	491±9	3390±29	6.9	0.9998	8

[a] s_0 and s_B are the standard deviations of the regression parameters k_0 and k_B, respectively; *r* is the correlation coefficient; *n* is the number of experimental points. [b] The maximum error of k_B/k_0 ratio is estimated to 3.8 %.

Table 7. Linear regression analysis[a] of apparent- second-order kinetic constants, k_A, for the reactions of 2-phenoxy-3-nitro-5-X-thiophenes with aniline in benzene, at 25 °C, according to the equation $k_A = k_0 + k_B[B]$

X	$10^6(k_0 \pm s_0)$	$10^6(k_B \pm s_B)$	k_B/k_0 [b]	r	n
H	0.0101±0.0001	0.0284±0.0002	2.8	0.9999	6
$CONH_2$	0.539±0.008	2.00±0.02	3.7	0.9997	6
CO_2Me	1.44±0.01	5.42±0.02	3.8	0.9999	7
COMe	4.57±0.04	21.3±0.1	4.7	0.9999	7
SO_2Me	6.74±0.07	35.6±0.2	5.3	0.9999	7
CN	7.97±0.08	44.5±0.2	5.6	0.9999	7
NO_2	131±2	646±7	4.9	0.9996	9

[a] s_0 and s_B are the standard deviations of the regression parameters k_0 and k_B, respectively; r is the correlation coefficient; n is the number of experimental points. [b] The maximum error of k_B/k_0 ratio is estimated to 3.3 %.

Table 8. Linear regression analysis[a] of apparent second order kinetic constants, k_A, for the reactions of 2-*p*-nitrophenoxy-3-nitro-5-X-thiophenes with aniline in benzene, at 25 °C, according to the equation $k_A = k_0 + k_B[B]$

X	$10^5(k_0 \pm s_0)$	$10^5(k_B \pm s_B)$	k_B/k_0 [b]	r	n
H	0.0162±0.0001	0.0389±0.0004	2.4	0.9998	7
Br	0.189±0.001	0.740±0.004	3.9	0.9999	8
$CONH_2$	0.504±0.010	2.25±0.03	4.5	0.9995	7
CO_2Me	1.44±0.01	6.88±0.05	4.8	0.9999	8
COMe	4.57±0.05	20.8±0.2	4.6	0.9998	8
SO_2Me	6.55±0.12	40.8±0.4	6.2	0.9997	8
CN	7.90±0.10	41.4±0.3	5.2	0.9998	8
NO_2	100±2	640±8	6.4	0.9995	8

[a] s_0 and s_B are the standard deviations of the regression parameters k_0 and k_B, respectively; r is the correlation coefficient; n is the number of experimental points. [b] The maximum error of k_B/k_0 ratio is estimated to 4.2 %.

Table 9. Correlations[a] by the equation $\log(k_B)_X = a \log(k_0)_X + b$

L	$a \pm s_a$	$b \pm s_b$	n	r
Br	1.07±0.01	1.16±0.05	8	0.9998
Cl	1.04±0.01	1.01±0.07	7	0.9997
OC_6H_5	1.07±0.02	1.04±0.10	7	0.9993
OC_6H_4-NO_2-*p*	1.11±0.02	1.18±0.99	8	0.9992

[a] s_a and s_b, standard deviations of a and b; r, correlation coefficient; n, number of data points.

Table 10. Susceptibility constants and other statistical data[a] for the reactions of 2-L-3-nitro-5-X-thiophenes with aniline in benzene

L	$\rho \pm s_\rho$	$i \pm s_i$	r	$\rho_B \pm s_{\rho_B}$	$i_B \pm s_{i_B}$	r	n
Br	3.44±0.04	-0.02±0.04	0.9995	3.67±0.06	0.00±0.05	0.9991	8
Cl	3.20±0.07	-0.03±0.06	0.9989	3.33±0.07	-0.02±0.06	0.9988	7
OC_6H_5	2.99±0.01	0.00±0.01	0.9999	3.20±0.06	0.01±0.05	0.9990	7
OC_6H_4-NO_2-*p*	2.78±0.04	-0.04±0.03	0.9994	3.08±0.05	0.02±0.04	0.9993	8

[a] ρ, reaction constant; *i*, intercept of the regression line with the ordinate (σ= 0); *r*, correlation coefficient; *n*, number of data points.

Table 11. Susceptibility constants for the reactions of 2-L-3-nitro-5-X-thiophenes with aniline in benzene

L	ρ	ρ_B	$\rho_3 - \rho_2$	ρ_1 (methanol)	$\rho_2 - \rho_1$	$\rho_3 - \rho_1$
Br	3.44	3.67	0.23	3.65	-0.21	0.02
Cl	3.20	3.33	0.13	3.46	-0.26	-0.13
OC_6H_5	2.99	3.20	0.21	2.84	0.15	0.36
OC_6H_4-NO_2-*p*	2.78	3.08	0.30	2.99	-0.21	0.09

Experimental Section

Synthesis and Purification of Compounds. Benzene,[10] aniline,[11] 2-L-3-nitro-5-X-thiophenes,[12] and N-(3-nitro-5-X-2-thienyl)anilines[11] were prepared and/or purified as previously reported.

Kinetic Measurements. The kinetics were followed spectrophotometrically as previously described.[13] The concentrations used were 2.4 x 10^{-4} mol dm^{-3} for **1-4** and those indicated in Tables 1-4 for aniline. The wavelength and log ε values for UV spectral measurements are reported in Table 12.

Table 12. Spectroscopic data for 2-anilino-3-nitro-5-X-thiophenes **1-4**.

X	λ_{max} (benzene)/nm	log ε
H	406	4.046
Br	406	4.045
$CONH_2$	395	4.000
CO_2Me	395	4.009
COMe	390	4.026
SO_2Me	385	3.989
CN	382	4.036
NO_2	392	4.275

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