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Linear free energy *ortho*-correlations in the reactions of some 2-bromo-5-nitro-3-X-thiophenes with primary and secondary amines in benzene

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The kinetics of S_NAr reactions of some 2-bromo-3-X-5-nitrothiophenes (X = Me, H, Br, $CONH_2$, CO_2Me, COMe, SO_2Me, CN and NO_2) with some primary (*n*-butylamine and benzylamine) and secondary (pyrrolidine, piperidine, morpholine and *N*-benzylamine) amines have been measured in benzene as a function of nucleophile concentration. Most of the reactions studied show apparent kinetic constants little affected or not affected by an increase in amine concentration, indicating that the overall reaction rate is controlled by the formation of the reaction intermediate. The reactions of the substrates where X = Br and CN with the two primary amines proved to be base-catalysed. The k_3^B/k_{-1} values calculated for these substituents are inconsistent with the hypothesis of a base catalysis for the intermediate decomposition and strongly suggest a catalysis of the first step of the reaction pathway.

Introduction

In the preceding paper we reported on the overall effect of *ortho*-like substituents in S_NAr reactions of some thiophene substrates in methanol. These reactions are second order, *i.e.*, first order both in substrates and in nucleophile; thus the overall reaction rate is controlled by the rate of formation of the reaction intermediate.

Changing the solvent, from methanol to benzene, usually increases the probability of observing base catalysis for the reaction intermediate decomposition. For example, pyrrolidine substitution of 2-methoxy-3-nitrothiophene which is not catalysed in methanol, in contrast, needs catalysis in benzene.

In this paper we report on the results of a kinetic study of the reactions of some 2-bromo-3-X-5-nitrothiophenes **1** with some primary and secondary amines in benzene.

We will show that also in benzene it is possible to obtain linear free energy *ortho*-correlations and will bring evidence that for the substituents X = Br and X = CN, the kinetic data suggest a rather special kind of base catalysis.

Results and discussion

An analysis of kinetic data reported in Table 1 shows that for most of the reactions studied the apparent second order kinetic constant, k_A, does not change within the experimental uncertainty, or increases linearly according to eqn. (1), with increasing amine concentration.

$$k_A = k_0 + k_B[B] \qquad (1)$$

The k_B/k_0 ratios observed (Table 2) are relatively low. Thus, on the grounds of the classification of Bunnett and Garst,[2] one can conclude that even if the reactions studied have been carried out in benzene, that is, a solvent incapable of assisting in the decomposition of the intermediate, they do not need base catalysis on account of the high nucleofugality of the leaving group bromine[3] at C-2.

By applying the steady state approximation to the intermediate of Scheme 1, one obtains eqn. (2), which describes all the possible experimental situations.[4]

$$k_A = (k_1k_2 + k_1k_3^{B_i}[B_i])/(k_{-1} + k_2 + k_3^{B_i}[B_i]) \qquad (2)$$

With reference to Scheme 1 and eqn. (2), the absence of base catalysis implies the condition $k_{-1} \ll (k_2 + k_3^{B_i}[B_i])$, that is, $k_0 = k_1$, and therefore the apparent increase in reactivity has to be ascribed to a medium effect.[5] As a confirmation of this hypothesis, the k_B/k_0 ratios are not correlated, the substituent being equal, with the basic strength of the amine but they rather reflect a dependence on the concentration range used.

In the cases of the reactions of the substrates where X = Br and X = CN with the two primary amines, the apparent second order kinetic constant, k_A, increases with increasing nucleophile concentration, according to eqn. (3)

$$k_A = k_{III}[B] + k_{IV}[B]^2 \qquad (3)$$

which implies a third order (first order in substrate and second order in amine) term and a fourth order (first order in substrate and third order in amine) term. In consideration of the low value of the k_{IV}/k_{III} ratio, the $k_{IV}[B]^2$ term can be imputed, as above, to a medium effect but the third order term is representative of a genuine base catalysis![4]

If one compares the obtained apparent catalysis law with eqn. (2), the conditions $k_2 = 0$ and $k_{-1} \gg (k_2 + k_3^{B_i}[B_i])$, with $k_{III} = k_1k_3^{B_i}/k_{-1}$ should hold.

Such conditions would imply that the rate determining transition state is the dipolar intermediate decomposition, and that the second step of the mechanism shown in Scheme 1 is wholly catalysed by the nucleophile. Since it is not possible to isolate the factors k_1 and $k_3^{B_i}/k_{-1}$, information about the relative importance of the reaction pathway controlled by $k_3^{B_i}$ and k_{-1} is not obtainable, at least directly. However, in order to estimate the necessary k_1 values, an "indirect" procedure can be followed.

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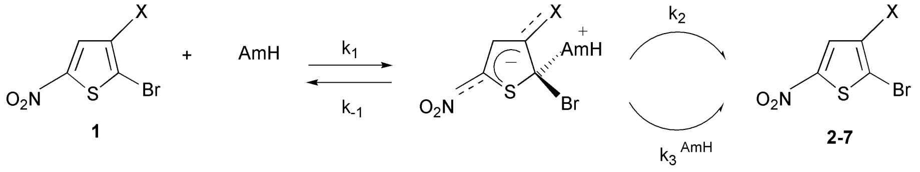
Table 1 Apparent kinetic constants for the reactions of 2-Br-3-X-5-nitrothiophenes with amines in benzene at 293 K

	X = Me									
[PYRH]/M	0.0808	0.101	0.152	0.202	0.303	0.404	0.505	0.606	0.707	0.808
10^7k_A/dm^3 mol^{-1} s^{-1}	2.97	3.21	4.19	5.26	7.26	9.47	11.5	14.2	16.6	19.0
[PIPH]/M	0.306	0.408	0.612	0.714	0.816	1.02				
10^8k_A/dm^3 mol^{-1} s^{-1}	5.65	6.65	8.68	9.75	11.1	12.9				
[MORH]/M	0.202	0.404	0.606	0.808	1.01					
10^8k_A/dm^3 mol^{-1} s^{-1}	0.500	0.946	1.34	1.73	2.14					
[BuAH]/M	0.490	0.588	0.784	0.882	0.980					
10^9k_A/dm^3 mol^{-1} s^{-1}	0.967	1.02	1.12	1.17	1.22					
[BzAH]/M	0.490	0.627	0.745	0.862	0.980					
$10^{10}k_A$/dm^3 mol^{-1} s^{-1}	1.28	1.50	1.69	1.88	2.07					
	X = H									
[PYRH]/M	0.202	0.303	0.404	0.505	0.758	1.01				
10^5k_A/dm^3 mol^{-1} s^{-1}	0.943	1.26	1.60	1.98	2.90	3.91				
[PIPH]/M	0.0200	0.102	0.255	0.510	0.765	1.02				
10^6k_A/dm^3 mol^{-1} s^{-1}	0.970	1.2	2.05	3.23	4.45	5.49				
[MORH]/M	0.101	0.202	0.404	0.505	0.606	0.808	1.01			
10^7k_A/dm^3 mol^{-1} s^{-1}	0.554	0.851	1.44	1.72	2.00	2.60	3.17			
[BMAH]/M	0.253	0.404	0.505	0.606	0.707	0.808	0.909	1.01		
10^8k_A/dm^3 mol^{-1} s^{-1}	3.60	5.05	6.14	7.15	7.95	9.08	10.1	11.1		
[BuAH]/M	0.283	0.404	0.505	0.606	0.707	0.808	0.909	1.01		
10^8k_A/dm^3 mol^{-1} s^{-1}	2.10	2.42	2.67	2.94	3.18	3.45	3.71	3.99		
[BzAH]/M	0.372	0.480	0.549	0.666	0.784	0.882	0.980			
10^9k_A/dm^3 mol^{-1} s^{-1}	4.87	5.92	6.52	7.51	8.66	9.46	10.5			
	X = Br									
[PYRH]/M	0.198	0.298	0.397	0.496						
10^4k_A/dm^3 mol^{-1} s^{-1}	1.51	2.01	2.47	2.96						
[PIPH]/M	0.255	0.510	1.02							
10^5k_A/dm^3 mol^{-1} s^{-1}	1.88	2.85	4.63							
[MORH]/M	0.202	0.303	0.404	0.505	0.606	0.707	0.808	0.909		
10^7k_A/dm^3 mol^{-1} s^{-1}	5.45	6.73	7.80	8.99	10.2	11.5	12.6	13.9		
[BMAH]/M	0.263	0.404	0.505	0.606	0.707	0.808	0.909	1.01		
10^7k_A/dm^3 mol^{-1} s^{-1}	2.85	3.64	4.12	4.72	5.25	5.83	6.41	6.94		
[BuAH]/M	0.162	0.283	0.404	0.525	0.646	0.768	0.879	1.01		
10^7k_A/dm^3 mol^{-1} s^{-1}	6.86	7.08	7.23	7.44	7.60	7.78	7.95	8.15		
[BzAH]/M	0.290	0.400	0.520	0.640	0.760	0.880	1.00			
10^7k_A/dm^3 mol^{-1} s^{-1}	1.49	1.64	1.79	1.98	2.15	2.30	2.48			
	X = $CONH_2$[a]									
[MORH]/M	0.0306	0.0612	0.102	0.143	0.184	0.224	0.265	0.306		
10^3k_A/dm^3 mol^{-1} s^{-1}	5.72	5.88	6.11	6.34	6.58	6.8	7.06	7.29		
[BMAH]/M	0.0505	0.101	0.202	0.303	0.404	0.505	0.606			
10^3k_A/dm^3 mol^{-1} s^{-1}	3.90	4.02	4.27	4.49	4.75	5.01	5.25			
	X = CO_2Me[a]									
[MORH]/M	0.0306	0.0612	0.102	0.143	0.184	0.224	0.265	0.306		
10^3k_A/dm^3 mol^{-1} s^{-1}	2.51	2.58	2.68	2.78	2.89	3.00	3.10	3.20		
[BMAH]/M	0.0600	0.120	0.170	0.240	0.300	0.360	0.460	0.600		
10^3k_A/dm^3 mol^{-1} s^{-1}	1.98	2.03	2.09	2.15	2.21	2.27	2.37	2.50		
	X = COMe									
10^3[PYRH]/M	0.498	0.747	0.996							
k_A/dm^3 mol^{-1} s^{-1}	0.147	0.149	0.147							
10^2[PIPH]/M	0.101	0.202	0.212	0.303						
k_A/dm^3 mol^{-1} s^{-1}	0.340	0.334	0.339	0.342						
[BuAH]/M	0.102	0.203	0.305	0.406	0.508					
10^3k_A/dm^3 mol^{-1} s^{-1}	1.85	2.17	2.53	2.97	3.40					
	X = SO_2Me									
10^3[PYRH]/M	0.199	0.398								
k_A/dm^3 mol^{-1} s^{-1}	3.20	3.26								
10^2[PIPH]/M	0.202	0.212								
k_A/dm^3 mol^{-1} s^{-1}	1.16	1.20								
10^2[MORH]/M	0.300	0.600	0.900	1.20	1.50	1.80	2.20	2.60		
10^2k_A/dm^3 mol^{-1} s^{-1}	8.43	8.33	8.39	8.25	8.20	8.33	8.32	8.31		
10^2[BMAH]/M	0.495	0.990	1.98	2.97	3.96	4.95	5.94			

Table 1 (*Contd.*)

	X = SO$_2$Me							
10^2k_A/dm^3 mol^{-1} s^{-1}	6.34	6.22	6.36	6.43	6.36	6.26	6.23	
10[BuAH]/M	0.102	0.235	0.459	0.571	0.734	0.908	1.02	
10^3k_A/dm^3 mol^{-1} s^{-1}	5.48	5.74	6.17	6.43	6.73	7.04	7.27	
[BzAH]/M	0.0588	0.118	0.176	0.235	0.294	0.353	0.431	0.490
10^3k_A/dm^3 mol^{-1} s^{-1}	1.05	1.24	1.43	1.61	1.80	1.98	2.22	2.41
	X = CN							
10^2[PYRH]/M	0.199	0.398	0.997					
k_A/dm^3 mol^{-1} s^{-1}	0.101	0.104	0.110					
10^2[PIPH]/M	0.808	1.01	1.21					
$10k_A$/dm^3 mol^{-1} s^{-1}	0.294	0.299	0.308					
[MORH]/M	0.0306	0.0612	0.102	0.143	0.184	0.224	0.265	0.306
10^3k_A/dm^3 mol^{-1} s^{-1}	0.954	1.16	1.44	1.73	2.05	2.35	2.65	2.93
[BMAH]/M	0.0800	0.160	0.230	0.320	0.400	0.480	0.560	0.640
10^3k_A/dm^3 mol^{-1} s^{-1}	0.674	0.838	1.03	1.26	1.44	1.63	1.82	2.03
[BuAH]/M	0.0808	0.172	0.323	0.485	0.606	0.727	0.889	1.01
10^3k_A/dm^3 mol^{-1} s^{-1}	1.47	1.53	1.64	1.74	1.82	1.91	2.00	2.09
[BzAH]/M	0.120	0.240	0.360	0.480	0.600	0.720	0.840	1.00
10^4k_A/dm^3 mol^{-1} s^{-1}	2.87	3.04	3.22	3.36	3.53	3.70	3.85	4.08
	X = NO$_2$							
10^3[PYRH]/M	0.998	1.50	2.00	2.99				
k_A/dm^3 mol^{-1} s^{-1}	47.6	46.0	47.6	48.8				
10^2[PIPH]/M	0.102	0.153	0.204					
$10k_A$/dm^3 mol^{-1} s^{-1}	14.3	14.5	14.5					
10^2[MORH]/M	0.109	0.198	0.277	0.356	0.436	0.515	0.594	
k_A/dm^3 mol^{-1} s^{-1}	0.755	0.753	0.758	0.750	0.748	0.757	0.766	
10^2[BMAH]/M	0.184	0.240	0.306	0.367	0.449	0.510		
k_A/dm^3 mol^{-1} s^{-1}	0.488	0.490	0.480	0.475	0.795	0.500		
10^2[BuAH]/M	0.505	1.01	1.41	2.12	2.52			
$10k_A$/dm^3 mol^{-1} s^{-1}	0.507	0.515	0.531	0.528	0.539			
10^2[BzAH]/M	0.990	1.98	2.97	3.96	4.95			
10^2k_A/dm^3 mol^{-1} s^{-1}	0.986	1.04	1.10	1.15	1.21			

[a] For kinetic constants for the reactions with PYRH, PIPH, BuAH and BzAH see ref. 1.



AmH = pyrrolidine (PYRH), piperidine (PIPH), morpholine (MORH), *N*-benzylmethylamine (BMAH), *n*-butylamine (BuAH), benzylamine (BzAH)

a: X = CH$_3$, **b**: X = H, **c**: X = Br, **d**: X = CONH$_2$, **e**: X = CO$_2$CH$_3$, **f**: X = COCH$_3$, **g**: X = SO$_2$CH$_3$, **h**: X = CN, **i**: X = NO$_2$

2: Am = PYR, **3**: Am = PIP, **4**: Am = MORF,**5**: Am = BMA, **6**: Am = BuA, **7**: Am = BzA

Scheme 1

The kinetic data ($k_0 = k_1$) obtained for the reactions (not catalysed) of 2-bromo-3-X-5-nitrothiophenes with the various amines constitute a matrix of 9 (substituents) *per* six (amines) where there are only a few empty entries.

Thus, for each amine it is possible to carry out a Hammett type correlation, by using the σ^- constants of Table 3 (line 1).

In the thiophene substrates used in the present work, the activating nitro group is located in a *para*-like position whereas the substituent, which is *ortho*-like with respect to the reaction centre, can display variable electronic effects and geometry.

It is evident that the 3-X group modulates the energy of the first transition state of the mechanism not only by means of its electronic effects but also by its proximity effects.

In benzene derivatives, due to the important substituent proximity effects, which alter the electronic effects of substituents, it is not possible, generally, to obtain linear free energy *ortho*-correlations.

In contrast, thanks to the more favourable geometry of the thiophene with respect to the benzene ring, for such S$_N$Ar reactions as those studied in this research work, satisfactory linear free energy *ortho*-correlations can be obtained (Table 4).

The correlation coefficients calculated are not as good as might be desired but the confidence level of each correlation is more than acceptable, bearing in mind that the k_0 values correlated have not been obtained directly but by extrapolation and that the sigma constants used could be rather inadequate to describe correctly the behaviour of *ortho*-like substituents.

However, the six ρ values now available allow us to apply the EST treatment to our data.[7]

Thus, by using the same procedure as that used to calculate the corresponding sigma values in methanol (see preceding paper), it is possible to obtain an optimised set of thiophene substituent constants for benzene solvent $(\sigma_{o,T})_B$.

The correlations of $\log[(k_X/k_H)]$ values with $(\sigma_{o,T})_B$ constants

Table 2 Linear regression analysis[a] of apparent second order kinetic constants, k_A, for the reaction of 2-Br-3-X-5-nitrothiophenes with amines in benzene, at 293 K, according to equations (2) or (3)

X	AmH	$k_0 \pm s_0$	$k_B \pm s_B$	n	r	k_B/k_0
Me	PYRH	$(0.823 \pm 0.169)10^{-7}$	$(22.1 \pm 0.4)10^{-7}$	10	0.9989	27
Me	PIPH	$(2.46 \pm 0.16)10^{-7}$	$(10.3 \pm 0.2)10^{-8}$	6	0.9990	4.2
Me	MORH	$(1.12 \pm 0.19)10^{-9}$	$(2.01 \pm 0.03)10^{-9}$	5	0.9997	17.9
Me	BuAH	$(7.16 \pm 0.02)10^{-10}$	$(5.15 \pm 0.03)10^{-10}$	5	0.9999	0.72
Me	BzAH	$(5.04 \pm 0.02)10^{-11}$	$(1.61 \pm 0.03)10^{-10}$	5	0.9996	3.2
H	PYRH	$(0.145 \pm 0.040)10^{-5}$	$(3.68 \pm 0.07)10^{-5}$	6	0.9994	25
H	PIPH	$(0.880 \pm 0.031)10^{-6}$	$(4.58 \pm 0.05)10^{-6}$	6	0.9997	5.2
H	MORH	$(2.68 \pm 0.01)10^{-8}$	$(2.88 \pm 0.01)10^{-7}$	7	0.9999	10.7
H	BMAH	$(1.09 \pm 0.07)10^{-8}$	$(9.89 \pm 0.10)10^{-8}$	8	0.9997	9.07
H	BuAH	$(1.37 \pm 0.01)10^{-8}$	$(2.58 \pm 0.01)10^{-8}$	8	0.9999	1.9
H	BzAH	$(1.49 \pm 0.08)10^{-9}$	$(9.12 \pm 0.11)10^{-9}$	7	0.9997	6.1
Br	PYRH	$(0.555 \pm 0.017)10^{-4}$	$(4.84 \pm 0.05)10^{-4}$	4	0.9999	8.7
Br	PIPH	$(0.990 \pm 0.052)10^{-5}$	$(3.58 \pm 0.08)10^{-5}$	3	0.9998	3.6
Br	MORH	$(3.05 \pm 0.06)10^{-7}$	$(1.19 \pm 0.01)10^{-6}$	8	0.9998	3.9
Br	BMAH	$(1.39 \pm 0.03)10^{-7}$	$(5.49 \pm 0.04)10^{-7}$	8	0.9998	3.95
$CONH_2$[b]	MORH	$(5.53 \pm 0.01)10^{-3}$	$(5.75 \pm 0.04)10^{-3}$	8	0.9999	1.05
$CONH_2$[b]	BMAH	$(3.77 \pm 0.01)10^{-3}$	$(2.43 \pm 0.02)10^{-3}$	7	0.9998	0.64
CO_2Me[b]	MORH	$(2.43 \pm 0.00)10^{-3}$	$(2.54 \pm 0.02)10^{-3}$	8	0.9998	1.05
CO_2Me[b]	BMAH	$(1.92 \pm 0.00)10^{-3}$	$(0.971 \pm 0.008)10^{-3}$	8	0.9998	0.51
COMe	PYRH	1.06 ± 0.01		2		
COMe	PIPH	0.339 ± 0.002		4		
COMe	BuAH	$(1.41 \pm 0.05)10^{-3}$	$(3.84 \pm 0.15)10^{-3}$	5	0.9978	2.7
SO_2Me	PYRH	3.23 ± 0.03		2		
SO_2Me	PIPH	1.18 ± 0.02		2		
SO_2Me	MORH	$(8.32 \pm 0.05)10^{-2}$		8		
SO_2Me	BMAH	$(6.31 \pm 0.07)10^{-2}$		7		
SO_2Me	BuAH	$(5.29 \pm 0.01)10^{-3}$	$(1.95 \pm 0.02)10^{-2}$	7	0.9997	3.7
SO_2Me	BzAH	$(8.74 \pm 0.04)10^{-4}$	$(3.14 \pm 0.01)10^{-3}$	8	0.9999	3.6
CN	PYRH	0.105 ± 0.003		3		
CN	PIPH	0.0300 ± 0.0005		3		
CN	MORH	$(7.14 \pm 0.11)10^{-4}$	$(7.26 \pm 0.06)10^{-3}$	8	0.9998	10.1
CN	BMAH	$(0.468 \pm 0.009)10^{-3}$	$(2.43 \pm 0.02)10^{-3}$	8	0.9998	5.19
NO_2	PYRH	47.5 ± 0.8		4		
NO_2	PIPH	14.4 ± 0.1		3		
NO_2	MORH	0.755 ± 0.004		7		
NO_2	BMAH	0.488 ± 0.007		6		
NO_2	BuAH	0.0524 ± 0.001		5		
NO_2	BzAH	$(9.30 \pm 0.03)10^{-3}$	$(5.64 \pm 0.08)10^{-2}$	5	0.9997	6.1
		$k_{III} \pm s_{III}$	$k_{IV} \pm s_{IV}$			
Br	BuAH	$(2.81 \pm 0.00)10^{-7}$	$(4.19 \pm 0.04)10^{-8}$	9	0.9997	
Br	BzAH	$(4.72 \pm 0.03)10^{-8}$	$(4.92 \pm 0.04)10^{-8}$	7	0.9998	
CN	BuAH	$(1.51 \pm 0.00)10^{-3}$	$(8.38 \pm 0.06)10^{-4}$	12	0.9998	
CN	BzAH	$(2.70 \pm 0.00)10^{-4}$	$(4.80 \pm 0.05)10^{-5}$	11	0.9999	

[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. The confidence levels for significance of regression are all better than 1%. [b] For kinetic constants for the reactions with PYRH, PIPH, BuAH and BzAH see ref. 1.

Table 3 Substituent constants

	Me	H	Br	$CONH_2$	CO_2Me	COMe	SO_2Me	CN	NO_2
σ_p^{-}[a]	−0.10	0.00	0.30	0.62	0.74	0.82	1.05	0.99	1.23
$(\sigma_{X,Br})_B$	−0.22	0.00	0.19	0.82	0.77	0.91	1.01	0.74	1.18
$(\sigma_{o,T})_{Br}$	−0.23	0.00	0.20	0.85	0.80	0.95	1.05	0.77	1.23

[a] Values from ref. 6.

Table 4 Susceptibility constants and other statistical data[a] for the reactions of 2-bromo-3-X-5-nitrothiophenes with amines in benzene

Amine	ρ[b]	i	r	n	ρ[c]	i	r	n
PYRH	6.28	−0.04	0.968	9	5.98	0.16	0.999	9
PIPH	6.23	−0.29	0.964	9	5.97	−0.10	0.999	9
MORH	6.36	−0.18	0.953	9	6.15	−0.03	0.999	9
BMAH	6.07	0.14	0.934	7	6.39	−0.06	0.998	7
BuAH	5.79	−0.12	0.984	7	5.33	0.05	0.999	7
BzAH	6.07	−0.14	0.977	7	5.62	−0.10	0.999	7

[a] ρ, reaction constant; r, correlation coefficient; i, intercept of the regression line with the ordinate ($\sigma = 0$); n, number of data points. [b] Values obtained by using σ_p^{-} constants (Table 3). [c] Values obtained by using $(\sigma_{o,T})_{Br}$ constants (Table 3).

Table 5 Ratios k_1k_3/k_{-1} and k_3/k_{-1} calculated

Amine	X	k_1k_3/k_{-1}	$(k_1)_{\text{calculated}}$	$(k_3/k_{-1})_{\text{calculated}}$
BuAH	Br	2.81×10^{-7}	1.59×10^{-7}	1.8
BuAH	CN	1.51×10^{-3}	1.74×10^{-3}	8.7
BzAH	Br	4.72×10^{-8}	1.98×10^{-8}	2.4
BzAH	CN	2.70×10^{-4}	3.17×10^{-5}	8.5

for each amine afford the new ρ values given in Table 4, column 6, and also in these cases the improvement in the quality of correlations is remarkable.

The excellent Hammett-type *ortho*-correlations grant to ρ values obtained a great predicting power. So, for each system

Table 6 Spectroscopic data[a] for compounds **2**–**7**

	2	**3**	**4**	**5**	**6**	**7**
X	λ_{max}/nm log ε	λ_{max}/nm log ε	λ_{max}/nm log ε	λ_{max}/nm log ε	λ_{max}/nm log ε	λ_{max}/ nm log ε
	449	416	404	439	421	444
Me	4.476	4.120	4.063	4.266	4.402	4.278
	438	432	422	437	443	432
H	4.499	4.409	4.344	4.440	3.446	4.391
	445	420	404	426	425	432
Br	4.403	4.120	3.068	4.204	4.346	4.317
	430	422	411	424	422	418
$CONH_2$	4.412	3.881	3.882	4.260	4.345	4.332
	420	414	401	417	409	403
CO_2Me	4.367	4.212	4.168	4.274	4.327	4.3327
	420	420	412	410	414	410
COMe	4.359	4.228	4.123	4.283	4.265	4.319
SO_2Me	420	400	386	400	396	396
	4.320	4.053	4.003	4.164	4.284	4.265
	420	420	406	414	400	408
CN	4.359	4.281	4.296	4.321	4.200	4.273
	415	386	380	398	405	400
NO_2	4.212	4.179	4.156	4.190	4.215	4.169

[a] In benzene.

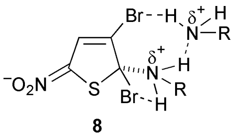
substrate–nucleophile following eqn. (3), it is possible to calculate the relevant k_1 value and from k_{III}, supposedly coincident with $k_1k_3^{B_i}/k_{-1}$, one can obtain the $k_3^{B_i}/k_{-1}$ ratios reported in Table 5. They are, without exception, greater than unity and contradict clearly the mechanistic hypothesis expressed above ($k_{-1} \gg k_3^{B_i}$[Bi]).

Of course, this obvious incongruity arises from the assumption, proved to be wrong, that for such systems as those studied in this work, which show third-order kinetics, the intermediate decomposition step is base-catalysed.

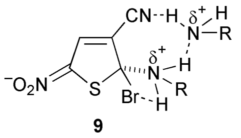
Thus, it is necessary to express an alternative mechanistic hypothesis: a base catalysis of the first step is involved!

At variance with the substrates that in an *ortho*-like position present substituents capable of forming the hydrogen bonding of the 'built-in solvation'[8] (X = $CONH_2$, CO_2CH_3, $COCH_3$, SO_2CH_3 and NO_2), in the case of the substrates with X = Br and X = CN, the unfavourable steric proximity effects, which hinder the approach of the nucleophile, are not counterbalanced by the favourable effect of this solvation, otherwise possible with all the other substituents (of course, except X = H and X = Me); thus, in the formation of the first transition state assistance by a second amine molecule becomes necessary.

A possible explanation of this behaviour can be based on the formation of the transition states **8** and **9** where a second molecule of primary amine determines some solvation through a hydrogen bonding with one of the two 'ammonium' protons. At the same time the other 'ammonium' proton is engaged in an intermolecular hydrogen bonding with the leaving group, in view of the expulsion of this latter to form the final product.



8



9

This peculiar kind of stabilization can be observed obviously only with the primary amines.

On the other hand for the substrates with X = H or X = Me, there is no significant steric hindrance to the formation of the first transition state, k_{-1} is relatively low with respect to k_2 and no catalysis is observed.

Experimental

Synthesis and purification of compounds

Compounds **1a**–**i** were prepared and purified by the methods reported in the preceding paper.

Kinetic data

Optical density measurements were carried out, after dilution with acidified benzene, by using a Zeiss PMQ II UV–Vis spectrophotometer. The wavelength and log ε values for UV spectral measurements are shown in Table 6. The concentrations used were 5.0×10^{-5} to 2.3×10^{-5} M for substrates and those reported in Table 1 for the amines.

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