PERKIN 2

Nucleophilic substitutions at the pyridine ring. Conformational preference of the products and kinetics of the reactions of 2-chloro-3-nitro- and 2-chloro-5-nitro-pyridines with arenethiolates †

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The reactions of 2-chloro-3-nitropyridine 1 and 2-chloro-5-nitropyridine 2 with arenethiolates 3a–i result in arylthio-dechlorination to give 2-arylthio-3-nitropyridines 4a–i and 2-arylthio-5-nitropyridines 5a–i. A ^{1}H NMR study and AM1 calculations of 5a–i have shown that these compounds assume a skew conformation except the 2-(4-nitrophenylthio) derivative 5f which has a twist one. An addition–elimination mechanism is suggested based on second order kinetics and the dependence of rates on the nature of the nucleophile. It is found that 2 (*para*-like) reacts faster than 1 (*ortho*-like). Good correlations are obtained from plots of log k_2 against Hammett σ constants, pK_a and log K (thermodynamic affinity of arenethiolates towards carbon).

Introduction

Different reviews on nucleophilic substitution reactions of aromatic and heterocyclic compounds have been published.[1–3] The generally accepted mechanism of these reactions in polar hydroxylic solvents involves rate-limiting *ipso* addition to give a Meisenheimer complex which rapidly forms the substitution product.

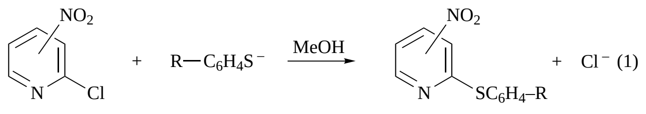
The quantitative aspects of the reactivity of heteroaromatic compounds are of interest.[4–6] In studies on nucleophilic heteroaromatic substitution, the physical organic aspects of aza activation have been contrasted with those of nitro activation.[7,8] In several instances the effect of the aza group on reactivity is similar to that of the nitro group, but significant differences exist, such as the lower steric requirements of the aza group and its H-bonding interactions with the medium.[8]

The aim of this work is to study the kinetics of the reactions between 2-chloro-3-nitropyridine **1** and 2-chloro-5-nitropyridine **2** with arenethiolates **3a**–**i**. Such reactions can give information on the heteroaromatic reactivity and also on the transmission of the electronic effects of the substituents through the arylthio ring. Furthermore, the conformation of the thioether products will be discussed.

Structural determination and conformational analysis of the products

The action of sodium arenethiolates **3a**–**i** on 2-chloro-3-nitropyridine **1** and 2-chloro-5-nitropyridine **2** gave the corresponding 2-arylthio derivatives, [reaction (1)]. Elemental analyses, UV, IR (Tables 1 and 2) and ^{1}H NMR (Tables 3 and 4) spectra indicated an arylthio-dechlorination process and the formation of 2-arylthio-3-nitropyridines **4a**–**i** and 2-arylthio-5-nitropyridines **5a**–**i**.

Table 3 shows that the chemical shifts of pyridyl protons are only affected by the 4′-substituent, indicating that either the sulfur atom decreases its electronic effect or the presence of both the nitro group at C-3 and pyridyl nitrogen atom represent a barrier against the inductive effect of the substituent on the pyridyl protons.



1, 2 **3a–i** **4a–i, 5a–i**

1, 4a–i : 3-NO_2; **2, 5a–i** : 5-NO_2

a R = H
b R = 4-CH_3
c R = 4-OCH_3
d R = 4-Br
e R = 4-Cl
f R = 4-NO_2
g R = 3-OCH_3
h R = 3-Br
i R = 3-Cl

The independence of the H-4 and H-6 chemical shifts from the substituent of the arylthio moiety in 2-arylthio-5-nitropyridines **5a**–**i**, Table 4, can be attributed mainly to two resonance effects (Scheme 1). The first involves conjugation of the sulfur atom with the 5-nitro group and the nitrogen atom of the pyridyl ring. This develops resonance interactions **I** and **II**, respectively, resulting in a partial bond between the π-electrons localized on the bridged head carbon atom and the unshared electron pairs of the sulfur atom.[9–12] The second one, is the resonance of sulfur atom with the 4′-substituent of the arylthio moiety,[13] **III** and **IV**.

It was noted earlier[14] that in diaryl sulfides, in the absence of steric factors, the ring bearing the relatively more electron withdrawing substituents is oriented nearly parallel to the C–S–C plane, with the other ring, which might bear electron donating substituents, oriented nearly perpendicular to this plane. This conformation would favour the interaction of the filled 3p_z orbital of the sulfur with the π system of the parallel ring which has, relative to the other ring, electron withdrawing substituents. Furthermore, the empty 3d_{xy} orbital of sulfur could interact with the π system of the other ring oriented perpendicular to the C–S–C plane and described as skew. Whereas, when the two phenyl rings are oriented approximately the same angle to C–S–C plane, the conformation is denoted as twist.[14]

^{1}H NMR data have helped to elucidate the conformation of the diaryl sulfides,[9–12,15,16] diarylmethanes[17] and diaryl ethers.[18] The fact that shielding due to ring current,[19] of the adjacent nucleus on the *ortho* protons is a function of molecular conformation confirmed that diaryl sulfides exist exclusively in the skew conformation.[9,12,15,16] Moreover, close examination of that data revealed that the 2,4-dinitrophenyl ethers preferentially adopt a twist conformation rather than a skew one because of

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Table 1 Properties and analysis of 2-arylthio-3-nitropyridines **4a**–**i**

Compound	R	Mp/°C	Yield (%)	λ^a/nm (ε/dm^3 mol^{-1} cm^{-3})	ν^b(NO$_2$)/cm^{-1}	Molecular formula	Calc. (%) (Found)			
							C	H	N	S
4a	H	92	94	216 (13 980)	1500, 1335, 685	$C_{11}H_8N_2SO_2$	56.89	3.44	12.06	13.79
				275 (7 420)			(57.03	3.32	12.25	13.74)
				361 (4 393)						
4b	4-CH$_3$	104	84	205 (14 820)	1511, 1336, 645	$C_{12}H_{10}N_2SO_2$	58.53	4.06	11.38	13.00
				275 (9 000)			(58.48	3.91	11.57	12.96)
				358 (3 656)						
4c	4-OCH$_3$	135	85	205 (28 000)	1507, 1328, 650	$C_{12}H_{10}N_2SO_3$	54.96	3.81	10.68	12.21
				275 (19 000)			(55.01	3.65	10.91	12.32)
				365 (4 520)						
4d	4-Br	80	86	220 (32 800)	1511, 1333, 631	$C_{11}H_7BrN_2SO_2$	42.44	2.25	9.00	10.28
				275 (15 000)			(42.64	2.05	9.13	10.46)
				364 (5 493)						
4e	4-Cl	112	86	225 (30 280)	1511, 1334, 646	$C_{11}H_7ClN_2SO_2$	49.53	2.62	10.50	12.00
				257 (14 500)			(49.02	2.37	10.18	11.50)
				357 (5 000)						
4f	4-NO$_2$	153	90	210 (33 500)	1511, 1336, 682	$C_{11}H_7N_3SO_4$	47.65	2.52	15.16	11.55
				256 (2 700)			(47.60	2.26	15.19	11.19)
				350 (17 000)						
4g	3-OCH$_3$	78	84	236 (10 580)	1505, 1331, 687	$C_{12}H_{10}N_2SO_3$	54.96	3.81	10.68	12.21
				277 (8 790)			(54.82	3.69	10.35	11.98)
				362 (3 720)						
4h	3-Br	120	85	235 (1 210)	1503, 1333, 673	$C_{11}H_7BrN_2SO_2$	42.44	2.25	9.00	10.28
				273 (8 740)			(42.42	2.21	8.84	10.08)
				357 (4 430)						
4i	3-Cl	101	88	234 (10 090)	1507, 1335, 673	$C_{11}H_7ClN_2SO_2$	49.53	2.62	10.50	12.00
				275 (7 220)			(49.33	2.68	10.43	11.84)
				357 (3 340)						

[a] In methanol. [b] C–S stretch.

Table 2 Properties and analysis of 2-arylthio-5-nitropyridines **5a**–**i**

Compound	R	Mp/°C	Yield (%)	λ^a/nm (ε/dm^3 mol^{-1} cm^{-1})	ν^b(NO$_2$)/cm^{-1}	Molecular formula	Calc. (%) (Found)			
							C	H	N	S
5a	H	104	89	210 (22 000)	1510, 1348, 691	$C_{11}H_8N_2SO_2$	56.89	3.44	12.06	13.79
				329 (1 478)			(57.08	3.37	11.70	14.33)
5b	4-CH$_3$	139	95	213 (18 000)	1510, 1346, 626	$C_{12}H_{10}N_2SO_2$	58.53	4.06	11.38	13.00
				331 (16 450)			(58.63	3.99	11.42	13.94)
5c	4-OCH$_3$	107	95	205 (25 500)	1509, 1346, 646	$C_{12}H_{10}N_2SO_3$	54.96	3.81	10.68	12.21
				231 (22 820)			(54.90	3.64	11.09	12.70)
				332 (16 140)						
5d	4-Br	108	79	205 (18 500)	1508, 1347, 630	$C_{11}H_7BrN_2SO_2$	42.44	2.25	9.00	10.28
				225 (17 320)			(42.68	2.16	8.70	10.04)
				326 (1 638)						
5e	4-Cl	120	98	205 (21 500)	1509, 1345, 632	$C_{11}H_7ClN_2SO_2$	49.53	2.62	10.50	12.00
				224 (24 000)			(49.78	2.51	10.17	12.04)
				325 (1 679)						
5f	4-NO$_2$	130	96	207 (31 000)	1503, 1341, 625	$C_{11}H_7N_3SO_4$	47.65	2.52	15.16	11.55
				320 (30 320)			(47.46	2.42	15.13	12.70)
5g	4-OCH$_3$	78	94	233 (3 460)	1507, 1346, 685	$C_{12}H_{10}N_2SO_3$	54.96	3.81	10.68	12.21
				330 (7 240)			(54.80	3.78	10.88	12.01)
5h	3-Br	85	90	231 (9 520)	1506, 1344, 679	$C_{11}H_7BrN_2SO_2$	42.44	2.25	9.00	10.28
				325 (14 720)			(42.18	2.07	8.94	10.09)
5i	3-Cl	83	94	213 (11 500)	1506, 1347, 682	$C_{11}H_7ClN_2SO_2$	49.53	2.62	10.50	12.00
				325 (12 760)			(49.32	2.77	10.13	11.81)

[a] In methanol. [b] C–S stretch.

its higher energy,[18] whereas tri-*ortho*-substituted diphenylmethanes exist predominantly in conformers other than the twist and skew ones.[17] In addition, benzyl aryl sulfides were found to exist as skew conformation.[20]

Examining the ^{1}H NMR spectra of the sulfides **5a**–**i** shows that H-3 resonates at somewhat higher field with respect to the corresponding protons in 2-ethylthio-5-nitropyridine **6**, Table 4. The difference between the chemical shifts of H-3 in **5a**–**i** and that of **6** indicates that the proton concerned experiences diamagnetic shielding by the adjacent aromatic ring.[12] Here in particular, because of the concerted effect of the strongly electron attracting nitro group and the pyridyl nitrogen atom, a partial double bond, as shown in Scheme 1, is formed. The percentage of this double bond character induced in the C_{py}–S bond is possibly high enough to cause the pyridyl ring to lie in the C_{py}–S–Ar plane. As a result, the molecule assumes skew conformation **V**, similar to that adopted by diaryl sulfides.[9,11,12,21]

Attempts were made to correlate the chemical shifts of an *ortho* proton in 2,4-dinitrophenyl aryl sulfides and ethers[9,18] with Hammett constants of substituents. These correlations gave linear relationships and showed that the *ortho* proton experiences shielding from ring current phenomenon of the adjacent aromatic ring.

A plot of the chemical shifts of H-3 in sulfides **5a**–**i** against Hammett constants gave a linear correlation (slope = 0.4,

Table 3 ^{1}H NMR chemical shifts[a] (δ/ppm) of 2-arylthio-3-nitropyridine **4a–i**

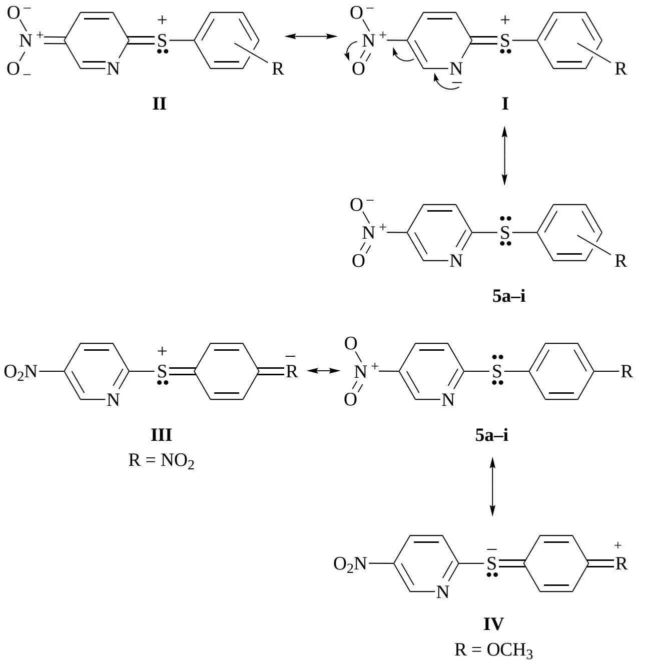
		Aromatic protons		Pyridine protons	
Compound	R	H-2′,6′	H-3′,5′	H-5	H-4,6
4a	H	7.37–7.00 (m, 5 H, H-4)		6.97–6.80 (m)	8.27–8.08 (m)
4b	4-CH_3[b]	7.20–7.00 (m)		7.00–6.83 (m)	8.30–8.10 (m)
4c	4-OCH_3[c]	7.33 (d)	6.80 (d)	6.77–6.90 (m)	8.33–8.27 (m)
4d	4-Br	7.17 (d)	7.43 (d)	7.13–6.97 (m)	8.20–8.13 (m)
4e	4-Cl	7.43–7.17 (m)		7.10–6.97 (m)	8.37–8.27 (m)
4f	4-NO_2	7.63 (d)	8.07 (d)	7.37–7.20 (m)	8.50–8.27 (m)
		H-2′,4′,5′,6′			
4g	3-OCH_3[d]	7.30–6.80 (m)			8.43–8.23 (m, H-5)
4h	3-Br	7.57–7.27 (m)		7.17–7.00 (m)	8.35 (dd)
4i	3-Cl	7.36–7.20 (m)		6.97–7.10 (m)	8.33 (dd)

[a] The chemical shifts are given relative to internal TMS in $CDCl_3$. [b] 4-CH_3 protons appear at δ 2.33 (s, 3H). [c] 4-OCH_3 protons appear at δ 3.77 (s, 3H). [d] 3-OCH_3 protons appear at δ 3.75 (s, H).

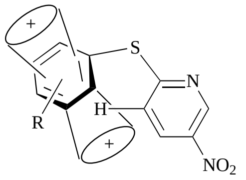
Table 4 ^{1}H NMR chemical shifts[a] (δ/ppm) of 2-arylthio-5-nitropyridine **5a–i** and 2-ethylthio-5-nitropyridine **6**

		Aromatic protons[b]		Pyridine protons[c]		
Compound	R	H-2′,6′ (d, 2H)	H-3′,5′ (d, 2H)	H-3 (d, 1H)	H-4 (dd, 1H)	H-6 (d, 1H)
5a	H	7.57–7.20 (m, H-4′)		6.83	8.03	9.00
5b	4-CH_3[d]	7.33	7.10	6.77	8.00	9.00
5c	4-OCH_3[e]	7.33	6.96	6.73	8.00	8.97
5d	4-Br	7.33	7.50	6.93	8.01	9.03
5e	4-Cl	7.53–7.23 (m)		6.93	8.07	9.00
5f	4-NO_2	7.70	8.27–8.13	7.30	8.35	9.20
		H-2′,4′,5′,6′				
5g	3-OCH_3[f]	7.40–6.90 (m)		6.87	8.03	9.05
5h	3-Br	7.60–7.10 (m)		6.93	8.10	9.05
5i	3-Cl	7.60–7.30 (m)		6.93	8.15	9.08
6[g]				7.17	8.03	9.10

[a] The chemical shifts are given relative to internal TMS in $CDCl_3$. [b] Coupling constants $J_{3',5'} = J_{2',6'} = 2.5$ Hz. [c] Coupling constants $J_{4,3} = 9$ Hz; $J_{4,6} = 2.5$ Hz. [d] 4-CH_3 Protons appear at δ 2.43 (s, 3H). [e] 4-OCH_3 Protons appear at δ 3.80 (s, 3H). [f] 3-OCH_3 Protons appear at δ 3.76 (s, H). [g] -CH_2 Protons appear at δ 3.17 (q, 2H); CH_3 protons appear at δ 1.33 (t, 3H).



Scheme 1



V

$r = 0.99 \pm 0.04$), except for **5f** (R = NO_2), Fig. 1. Consequently, we suggest that the substituents affect the ring current of the arylthio ring. The effect of this on the H-3 of the pyridyl ring provides evidence for the existence of compounds **5a–e**,**g–i** in the skew conformation, **V**.

To explain the deviation of compound **5f** (R = NO_2) from the Hammett plot let us assume that the two rings are not close enough to cause the pyridyl ring to lie in the C_{py}–S–C_{Ar} plane. This leads to a minimum ring current of the ring bearing the NO_2-substituent and implies that **5f** does not exist in a skew conformation. Furthermore, this deviation could be due to the competing conjugation on both sides of the C–S bond and hence develops resonance structures **II** and **III** (R = 4-NO_2).

In terms of simple valence bond theory and from the results of AMI semi-empirical calculations, Table 5, one can describe the electron distribution in **5a** as involving conjugation between the lone pair of the sulfur atom and the oxygen pair of the nitro group. The S–C_β bond attains partial double bond character, forcing the ring to orient parallel or nearly parallel to the C–S–C plane.[14] This then forces the other ring to a nearly perpendicular orientation. The dihedral angles for selective nitrophenyl phenyl sulfides[14] together with nitropyridyl phenyl sulfides **4a**, **5a** and **5f** are plotted in Fig. 2. It can be seen that the unsymmetrically substituted sulfides fall into the skew con-

Table 5 Conformation and structural parameters using AM1 program[a]

Compound	Dihedral angle/°		C–S bond lengths/Å		C–S–C bond angle	
	α	β	S–Cβ	S–Cα	θ/°	Conformation
4-Nitrophenyl phenyl sulfide[b]	84	−2	1.778	1.780	103	Skew
2,4-Dinitrophenyl phenyl sulfide[b]	86	12	1.751	1.784	103	Skew
Bis(2-nitrophenyl) sulfide[b]	20	65	1.768	1.777	101	Skew/twist
4-Aminophenyl 4-nitrophenyl sulfide[b]	90	0	1.771	1.780	104	Skew
2-Phenylthio-3-nitropyridine **4a**	83	21	1.799	1.810	110	Skew
2-Phenylthio-5-nitropyridine **5a**	79	23	1.807	1.872	111	Skew
2-(4-Nitrophenylthio)-5-nitropyridine **5f**	33	36	1.730	1.805	107	Twist

[a] AM1 (QCPE 137) program is available from the Quantum Chemistry Program Exchange, University of Indiana, Bloomington, IN 47405. [b] Ref. 14.

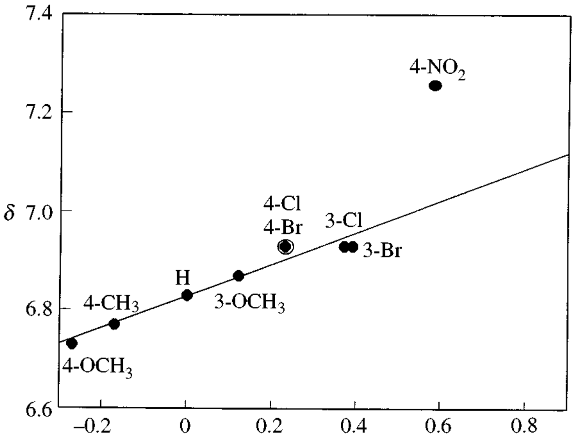


Fig. 1 Plot of the chemical shifts of H-3 in sulfides **5a–i** against Hammett σ constants

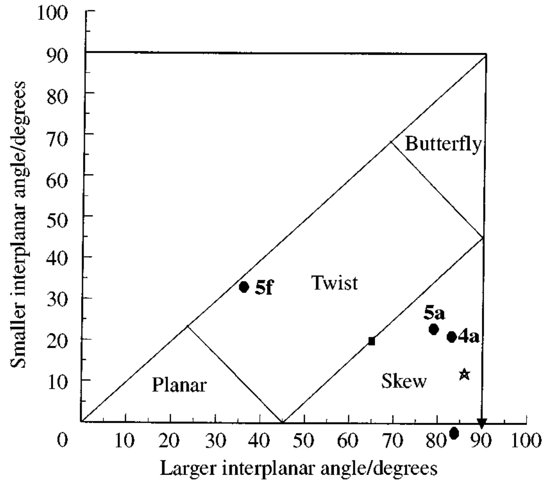


Fig. 2 Plot of the dihedral angles listed in Table 5. (■) Bis(2-nitrophenyl) sulfide, (★) 2,4-dinitrophenyl phenyl sulfide, (▲) 4-aminophenyl 4-nitrophenyl sulfide, (●) 4-nitrophenyl phenyl sulfide.

formation, while for symmetrically substituted ones the trend is fairly close to the twist/skew boundary and only **5f** is twisted.[14] Steric factors, rather than conjugation, are possibly responsible for the conformation adopted by the symmetrically *ortho* substituted nitrophenyl sulfide and **4a**. The twist conformation that model **5f** is pictured as involving alternates conjugation of both S–C$_\alpha$ and S–C$_\beta$ bonds.

Inspecting the S–C bond lengths one finds that the bond to the ring with the more electron-withdrawing substituent is shorter than that to the other ring, which supports the relevance of the conjugative effect postulated above. It is therefore electronic rather than steric factors which influence the orientation of the rings in para-nitroaryl sulfides and 5-nitropyridyl aryl sulfides **5a** and **5f**.

Kinetics and mechanism of the reaction

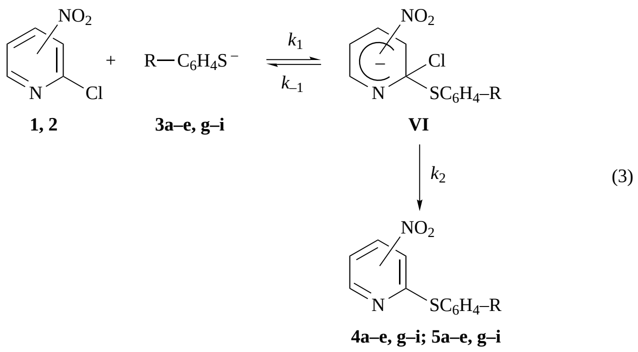
The kinetics of the reactions of **1** and **2** with sodium arenethiolate ions **3a–e**,**g–i** in methanol were studied spectrophotometrically at five different temperatures (20, 25, 30, 35 and 40 °C). These reactions were measured under pseudo first-order conditions using a 1 : 10 ratio of **1** or **2** to thiolate ions **3a–e**,**g–i**.

In order to check the effect of the concentration of the nucleophile, the rate constants (k_{obs}) were measured for a series of solutions where the concentrations of the substrate **1** and **2** remained constant while that of benzenethiolate (in the range 5×10^{-3}–2.5×10^{-2} M for reaction with **1** and 5×10^{-4}–2.5×10^{-3} M for reaction with **2**) were varied. Plots of k_{obs} values *versus* benzenethiolate ion concentrations at 40 °C gave a straight line passing through the origin indicating a second-order reaction, first-order in nucleophile and first-order in substrate **1** or **2**. Thus the second-order rate constants are calculated by eqn. (2).

$$k_2 = k_{obs}/[\text{nucleophile}] \qquad (2)$$

For practical reasons arenethiolate ion concentrations of 5×10^{-3} and 5×10^{-4} M, for the reaction with **1** and **2** respectively, were chosen for all comparative experiments.

An addition–elimination mechanism is suggested similar to the commonly accepted aromatic bimolecular two stage process in which the formation of the intermediate is the rate determining step with rapid decomposition of this intermediate into product[1,2] ($k_2 \gg k_1,k_{-1}$), reaction (3).



1, 2 **3a–e, g–i** **VI** **4a–e, g–i; 5a–e, g–i** (3)

This assumption is made on the basis of clean second-order kinetics, first-order in both substrate and thiolate ion, and dependence of the rates on the nature and position of substituent in the nucleophile.

Examination of the data in Tables 6 and 7 reveal that 2-chloro-5-nitropyridine **2** (*para*-like) reacts with arenethiolates **3a–e**,**g–i**, under the aforementioned conditions, *ca.* 10 to 31 times as fast as 2-chloro-3-nitropyridine **1** (*ortho*-like). This ratio is almost similar to that found for the reactions of *p*-chloro- and *p*-bromo-nitrobenzenes and their *ortho* analogues with benzenethiolate.[22] This is consistent with the fact that for

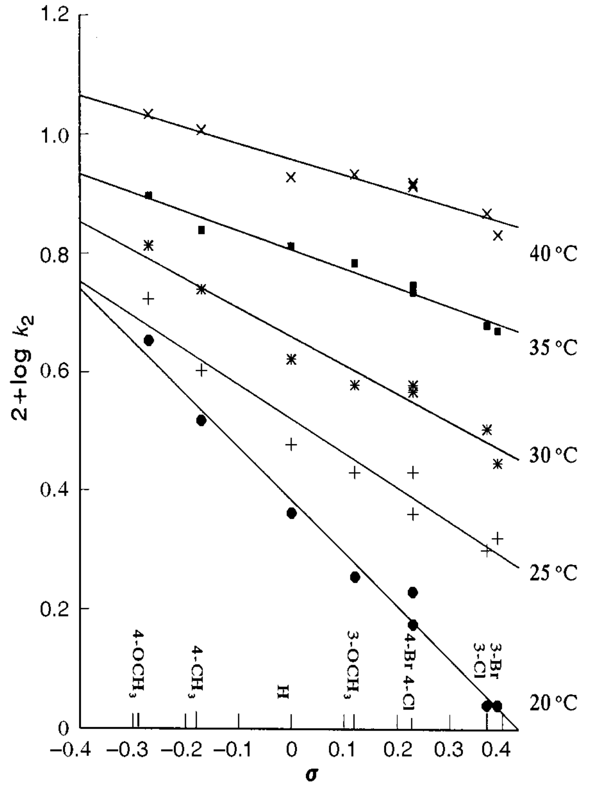


Fig. 3 Plot of log k_2 against the Hammett σ constants for the reaction of **1** with arenethiolate ions at different temperatures

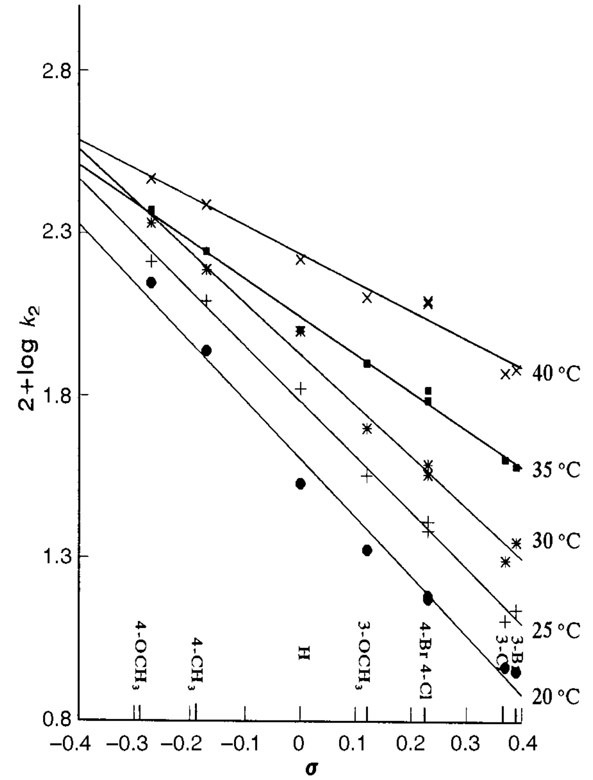


Fig. 4 Plot of log k_2 against the Hammett σ constants for the reaction of **2** with arenethiolate ions at different temperatures

any σ-adduct forming reaction a *p*-nitro group is more stabilising, by *ca.* 6 kJ mol^{-1}, than an *o*-nitro group.[1a]

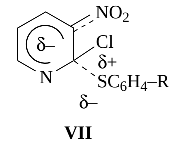
The reactivity of compounds **1** and **2** towards benzenethiolate indicates that they react more rapidly than that of the *o*- and *p*-halo-nitrobenzene, respectively.[23] This increase in reactivity is possibly due to the presence of the aza group in the former compounds, which stabilizes the negative charge developed in the intermediate.[24]

To evaluate the aza and $=C-NO_2$ activation we used the comparison of kinetic data for phenylthio-dechlorination of 1-chloro-2,4-dinitrobenzene[25] with that of 2-chloro-5-nitropyridine **2** towards benzenethiolate.[25] This gave a high reactivity ratio, by one or two orders of magnitude, *i.e.* the $=C-NO_2$ group is more stabilizing than the aza one. This may be due to the more efficient delocalization of the negative charge with a nitro group than with an aza group in the transition state.[24,26]

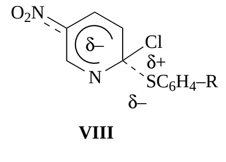
The entropy of activation values in both series under investigation are negative, as expected for bimolecular reactions. In each reaction series the entropy of activation $\Delta S^{\ddagger}$ is substituent dependent. Since all the substituents are in the *para* and *meta* position, direct steric interaction is unlikely, and the only reasonable explanation appears to lie in changes in solvation between the reactants and transition state. Within the same series, electron donating substituents in benzenethiolate ion, through their resonance and/or inductive effect, localize the formal charge on the sulfur atom. This favours the formation of a more ordered transition state, reflecting a higher negative entropy value of activation. On the other hand, benzenethiolate ions containing electron withdrawing substituents differ in their nature so that the formal charge on sulfur is delocalized over a great part of this ion leading to a lower negative entropy value of activation.

Since the reactions under investigation are nucleophilic, electron donating substituents in the arenethiolate should increase the rate, while electron withdrawing ones decrease it. These conditions are verified in our case, as in passing from 4-methoxybenzenethiolate, the most highly reactive nucleophile, to 3-chloro- or 3-bromo-benzenethiolate, the least reactive nucleophiles, an increase of ≈4- to 15-fold is found. Consequently, the variation of the rate depends on the type and position of the substituent in the thiol. The order of decreasing reactivity of arenethiolate ions towards **1** and **2** is found to be as follows: $4\text{-OCH}_3 > 4\text{-CH}_3 > 4\text{-H} > 3\text{-OCH}_3 > 4\text{-Cl} \approx 4\text{-Br} > 3\text{-Cl} \approx 3\text{-Br}$.

It is customary to correlate the effect of *meta* and *para*-substituents in the benzene ring by the simple Hammett relationship. Multiparameter treatments of the data[27,28] are not justified in our case, owing to the small number of substituents considered. Plots of log k_2 values *versus* the Hammett σ constants for the different substituents in benzenethiol give good straight lines for compounds **1** and **2** at different temperatures, Figs. 3 and 4, respectively. The p values for the reactions of arenethiolates with compound **1** varied between −0.89 and −0.28, whereas those for the same reactions with compound **2** ranged between −1.80 and −0.87, Tables 6 and 7. This implies that when the substituents are on the nucleophile negative ρ values are expected. In turn the approach of thiolate ion to C-2 leads to a case where the pyridyl ring and the nitro group attain a negative charge, while C-2 exhibits positive charge as shown in **VII** and **VIII**, respectively.



VII



VIII

Good correlations are obtained from plots of log k_2 for the reactions of arenethiolates with **1** and **2**, and the pK_a of the corresponding thiols[29] at 20 °C with slopes of 0.29 ($r = 0.92$) and 0.59 ($r = 0.92$) respectively. This indicates a similar sensitivity of the two reactions to the change in the nucleophilicity (polarisability) of the sulfur atom as a function of the substituent present in the nucleophile.[29] Meanwhile, linear plots of log k_2 values at 20 °C are obtained for the reactions of arenethiolates with compounds **1** and **2** *versus* log K (carbon basicity) with slopes 0.24 ($r = 0.92$) and 0.49 ($r = 0.97$), respectively. Similar slopes were found in other reactions, such as 1-chloro-

Table 6 Second-order rate constants,[a] activation parameters, ρ and basicity coefficients for the reaction of 2-chloro-3-nitropyridine **1** with arenethiolates **3a–e**,**g–i** in methanol

		$k_2/10^{-1}$ dm^3 mol^{-1} s^{-1} at T/°C						
Compound	R	20	25	30	35	40	$\Delta H^‡$/kJ mol^{-1}	$-\Delta S^‡$/J mol^{-1} deg^{-1} [b]
3b	4-OCH$_3$	0.45	0.53	0.65	0.79	1.08	30.3 ± 3	167.9
3c	4-CH$_3$	0.33	0.40	0.55	0.69	1.02	40.2 ± 3	136.5
3a	H	0.23	0.30	0.42	0.65	0.85	49.2 ± 3	109.1
3g	3-OCH$_3$	0.18	0.27	0.38	0.61	0.86	57.7 ± 2	81.8
3d	4-Cl	0.15	0.23	0.38	0.56	0.83	63.4 ± 1	63.1
3e	4-Br	0.17	0.27	0.37	0.58	0.82	57.3 ± 2	83.5
3h	3-Cl	0.11	0.20	0.32	0.48	0.74	69.2 ± 3	45.4
3i	3-Br	0.11	0.21	0.28	0.47	0.68	65.4 ± 4	58.6
ρ		−0.89	−0.58	−0.47	−0.31	−0.26		
β_H		0.29						
β_C		0.24						

[a] $k_2 = k_{obs}$/[**1a–e**,**g–i**]. Rate constants were calculated by the least-squares method and the correlation coefficient was 0.99 in most cases. [b] $\Delta S^‡ = (19.11 \log k/T) + E_a/(T - 205.89)$.

Table 7 Second-order rate constants,[a] activation parameters, ρ and basicity coefficients for the reaction of 2-chloro-5-nitropyridine **2** with arenethiolates **3a–e**,**g–i** in methanol

		$k_2/10^{-1}$ dm^3 mol^{-1} s^{-1} at T/°C						
Compound	R	20	25	30	35	40	$\Delta H^‡$/kJ mol^{-1}	$-\Delta S^‡$/J mol^{-1} deg^{-1} [b]
3b	4-OCH$_3$	14.07	16.40	21.49	23.49	29.40	25.5 ± 2	154.5
3c	4-CH$_3$	8.70	12.40	15.50	14.60	24.50	31.6 ± 7	137.1
3a	H	3.39	6.63	9.21	10.13	16.69	52.8 ± 7	71.6
3g	3-OCH$_3$	2.11	3.58	5.02	7.99	12.79	64.8 ± 2	37.0
3d	4-Cl	1.60	2.40	3.80	6.60	12.40	75.3 ± 5	4.5
3e	4-Br	1.50	2.59	3.61	6.14	12.30	73.1 ± 6	6.8
3h	3-Cl	1.00	1.21	2.00	4.00	7.40	76.7 ± 9	5.2
3i	3-Br	0.90	1.40	2.20	3.80	7.60	77.7 ± 5	1.9
ρ		−1.80	−1.70	−1.56	−1.01	−0.87		
β_H		0.59						
β_C		0.49						

[a] $k_2 = k_{obs}$/[**2a–e**,**g–i**]. Rate constants were calculated by the least-squares method and the correlation coefficient was 0.99 in most cases. [b] $\Delta S^‡ = (19.11 \log k/T) + E_a/(T - 205.89)$.

2,4-dinitrobenzene[25] (0.51), 1-chloro-4-nitrobenzene[30] (0.48) and 2-chloro-3,5-dinitropyridine[31] (0.34) with arenethiolates. This similarity in behaviour between the reactions of thiolates towards the above compounds and towards compounds **1** and **2** reflects the fact that these reactions involve the formation of a sulfur–carbon bond in the rate-determining step.[29,31] On the other hand, the nearly half value of slope for **1** (0.24) compared to **2** (0.49) indicates that in its transition state roughly half the negative charge has been transferred from arenethiolate ion to **1** with respect to **2**. This presumably is consistent with the ρ values for both reactions at 20 °C where **1** gives nearly half ρ value (−0.89) of that obtained for **2** (−1.80), Tables 6 and 7.

Experimental

Melting points are uncorrected. The UV spectra were recorded on a Shimadzu 160-A. Infrared spectra were recorded on a Perkin-Elmer 1430 ratio recording infrared spectrophotometer using potassium bromide pellets. The ^{1}H NMR spectra were measured in CDCl$_3$ and recorded on a Variant EM 390,90 MHz spectrometer. Elemental analyses of the reaction products were carried out on Perkin-Elmer Series 2400 carbon, hydrogen, nitrogen and sulfur, Faculty of Science, Central Laboratory Unit, Alexandria University, Egypt.

Starting Materials

2-Chloro-3-nitropyridine 1. Commercially available (Aldrich) material was purified by crystallization twice from methanol and twice from light petroleum as yellow needles, mp 102 °C.

2-Chloro-5-nitropyridine 2. Commercially available (Aldrich) material was purified by crystallization from methanol as yellow crystals, mp 107–8 °C.

We found compounds **1** and **2** quite unaffected by boiling methanol from their mp and UV spectra.

Arenethiols 3a–i. Arenethiols were commercially available (Aldrich). Arenethiols used are: benzenethiol, 4-methylbenzenethiol, 4-methoxybenzenethiol, 4-chlorobenzenethiol, 4-bromobenzenethiol, 4-nitrobenzenethiol, 3-methoxybenzenethiol, 3-chlorobenzenethiol and 3-bromobenzenethiol.

Preparation of 2-arylthio-3-nitropyridines 4a–i and 2-arylthio-5-nitropyridines 5a–i

General Procedure. The appropriate material (1 g, 6.3 mmol) was dissolved in absolute methanol (10 ml) and a methanolic solution of sodium arenethiolate (6.4 mmol) (prepared by dissolving 0.69–1.2 g, of arene thiol in 10 ml methanol containing 6.3 mmol sodium metal) was added to it at room temperature. The reaction mixture was left for 10–30 min and then poured into cold 5% aqueous NaOH. The precipitate was filtered, washed with cold water and then crystallized from methanol and the purity was checked by TLC (1:9 ethyl acetate–*n*–hexane). The compounds were dried under vacuum over P$_2$O$_5$ for more than 4 h. ^{1}H NMR data, properties and analyses are given in Tables 1–4.

2-Ethylthio-5-nitropyridine 6. 2-Chloro-5-nitropyridine (1 g, 6.3 mmol) dissolved in 20 ml ethanol was treated with sodium thioethoxide (6.3 mmol) in 10 ml ethanol and stirred for 15 min at room temperature. The reaction mixture was poured on cold water and the formed precipitate was filtered, dried and recrystallized from dilute methanol as yellow needles (0.85 g,

Table 8 Positions of λ for the reaction of **1** and **2** with substituted arenethiolates

Benzenethiolate substituent	λ/nm	
	1	**2**
H	361	329
4-CH_3	358	331
4-OCH_3	365	332
4-Br	364	326
4-Cl	357	325
3-OCH_3	362	330
3-Br	357	325
3-Cl	357	325

73%), mp 45–6 °C. ν_{max}(KBr)/cm^{-1} 1505, 1336 (NO_2, unsym. and sym. respectively) and 621 (C–S); λ_{max}(MeOH)/nm 336.5 (ε/dm^3 mol^{-1} cm^{-1} 15580), 221.5 (7640) (Calc. for $C_7H_8N_2SO_2$: C, 45.65; H, 4.34; N, 15.21; S, 17.39. Found: C, 45.22; H, 4.35; N, 15.44; S, 17.16%). ^{1}H NMR data are given in Table 4.

Kinetic procedure

The reactions of 2-chloro-3-nitropyridine **1** and 2-chloro-5-nitropyridine **2** with different arenethiolates **3a–e,g–i** in absolute methanol were followed spectrophotometrically. In all reactions studied, the recorded spectra at the end of the reaction are identical to the spectra of the corresponding authentic sample of the substitution product in the same solvent.

A stock solution of 2-chloro-3-nitropyridine **1** or 2-chloro-5-nitro-pyridine **2** in absolute methanol was prepared (1.0 × 10^{-3} M) and diluted before use (1.0 × 10^{-4}–5.0 × 10^{-5} M). Solutions of various sodium arenethiolates (1.0 × 10^{-3} M) were prepared just before use by dissolving a weighed amount of the required thiol in a known volume of methanol and the required quantity (equal molarity) of standardized sodium methoxide in methanol. A sufficient excess of thiol over base was used to ensure virtually complete conversion of methoxide ion into arylthiolate.

Solutions of 2-chloro-3-nitropyridine **1** or 2-chloro-5-nitropyridine **2** and sodium arenethiolate were allowed separately to attain the desired temperature ±0.5 °C in a thermostat bath before being mixed. The resultant change with time of the absorbance emergent from the measuring cell was recorded by kinetic mode or time scan mode on UV–VIS Shimadzu 160-A spectrophotometer at the indicated wavelengths given in Table 8.

Owing to interference from absorption by some arenethiolate ions (in the case of 4-OCH_3, 4-Br and 4-Cl) measurements were generally made by using the same concentration of thiolate ion in the reference cell.

The first-order rate constants are calculated by the following eqn. (4), where A_0, A_t and A_∞ are the values of the absorbance at

$$\log(A_\infty - A_t) = \frac{-k_{obs}}{2.303}t + \log(A_\infty - A_0) \qquad (4)$$

zero time, time t and infinite time, respectively. The values of A_∞ for each kinetic run were taken as the experimentally determined value. For each system studied the values of k_{obs} measured with different arenethiolates were determined and the second-order rate constants $k_2 = k_{obs}$/[thiolate] were calculated.

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