Linear Free Energy Relationships in the Thiophen Series. Part I. Leaving Group Effect in Piperidino-substitution in Methanol of Some 2-L-3-Nitro-5-X-thiophens †

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The reaction rates at various temperatures for piperidino-substitution of some 2-L-3-nitro-5-X-thiophens (L = Cl, Br, I, $OC_6H_4NO_2$-*p*, or SO_2Ph; X = H, Br, $CONH_2$, CO_2Me, SO_2Me, Ac, CN, or NO_2) have been measured in methanol to give information on the influence of the leaving group and the substituent at C-5 on the position of the rate-determining transition state (r.d.t.s.) on the reaction co-ordinate. Taking into account the effects (electronic and steric) of the leaving group, the data obtained have been explained by a modified interpretation of the ρ values obtained. The ρ values give a measure of the sensitivity of the reaction to the changes in the position of the r.d.t.s. on the reaction coordinate as a function of the substituent at C-5. Dependence on the type of t.s. (early or late) is also shown.

THE data obtained from rate constant measurements for monosubstituted benzenes in various electrophilic aromatic substitutions have been correlated by using modified Hammett relationships (mono- or multilinear).[1] In the interpretation of data of this type there is a tendency[2] to equate a large (absolute) value of ρ for a substitution reaction with a rate-determining transition state (r.d.t.s.) far along the reaction co-ordinate, *e.g.*, in electrophilic aromatic substitution close resemblance between the r.d.t.s. and a Wheland intermediate (σ-complex) is assumed. On the other hand, some authors[3] have expressed doubt on the simultaneous application of the Hammett equation and the Hammond postulate[4] to these reactions.

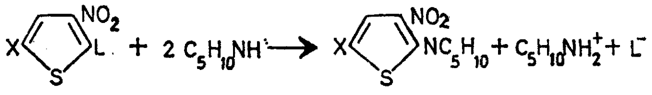
The current interpretation[2,3] and utilization of absolute ρ values, which starts from the hypothesis that transition states are the same for all compounds of the series considered, seems incorrect to us and we think more consideration of this point would be useful.

According to the Hammond postulate,[4] we think that a series of reactions (*e.g.* electrophilic aromatic substitution) wherein there are large changes in relative reactivity as a function of the substituent present *cannot* be described by the same r.d.t.s. A different r.d.t.s. corresponds to each compound and one can only speak about early or late ranges of r.d.t.s.s. The closer the r.d.t.s.s corresponding to the various substituted compounds, the less the ρ value.

Therefore a more suitable interpretation of Hammett relationship data should start from the observation that ' the absolute ρ value is an index of the sensitivity of the studied reaction to the changes of position of the r.d.t.s. on the reaction co-ordinate as a function of change of the substituent present.' The sensitivity is higher if the r.d.t.s.s lie in the range of late transition states than if they are early because of the different ' average ' extent of charge development in the two types of states. This fact can be related to differences in electronic effects exerted by the substituent in the ground and in the transition state, a factor which also affects the type [σ, $\sigma^{\pm}$, ($\sigma + r^{\pm}\Delta\sigma_R^{\pm}$) *etc.*] and the value of the substituent constant.

For nucleophilic aromatic substitution few data have been collected[5] with the aim of elucidating the relative position of the r.d.t.s., although other criteria have been used[6] to obtain information about the shape of the reaction co-ordinate.

To study this point for heteroaromatic nucleophilic substitution in the thiophen series we have in progress studies on the kinetics of the reaction of some 2-L-3-nitro-5-X-thiophens with different nucleophiles in various solvents (protic or aprotic, polar or non-polar). In this paper we report data for the reaction of compounds (I)—(V) with piperidine in methanol at 0—40°.



(I) L = Cl
(II) L = Br
(III) L = I
(IV) L = $OC_6H_4NO_2$-*p*
(V) L = SO_2Ph

(VI)

a; X = H
b; X = Br
c; X = $CONH_2$
d; X = CO_2Me
e; X = SO_2Me
f; X = Ac
g; X = CN
h; X = NO_2

RESULTS AND DISCUSSION

Kinetic Data.—Tables 1—5 report rate constants and activation parameters for piperidino-substitution of compounds (I)—(V).

The nucleophilic aromatic activated substitutions are bimolecular and proceed through a two-step mechanism with fast decomposition of the intermediate complex as shown by element effect data[6a,7] and the absence of

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† Presented at a meeting of the Società Chimica Italiana, Catania, 1973; D. Spinelli and G. Consiglio, *Chimica e Industria*, 1974, **56**, 655.

[1] (*a*) R. O. C. Norman and R. Taylor, ' Electrophilic Substitution in Benzenoid Compounds,' Elsevier, Amsterdam, 1965; (*b*) L. M. Stock and H. C. Brown, *Adv. Phys. Org. Chem.*, 1963, **1**, 35; (*c*) G. Marino, *Adv. Heterocyclic Chem.*, 1971, **13**, 235.

[2] Ref. 1*a*, p. 294.

[3] C. D. Johnson and K. Schofield, *J. Amer. Chem. Soc.*, 1973, **95**, 270; C. D. Johnson, *Chem. and Ind.*, 1973, 119.

[4] G. S. Hammond, *J. Amer. Chem. Soc.*, 1955, **77**, 334.

[5] C. F. Bernasconi, ' MTP International Review of Science; Organic Chemistry, Series 1,' Butterworths, London, 1973, vol. 3, p. 33 and references therein.

[6] (*a*) J. F. Bunnett, E. W. Garbisch, jun., and K. M. Pruitt, *J. Amer. Chem. Soc.*, 1957, **79**, 385; (*b*) J. Miller, 'Aromatic Nucleophilic Substitution,' Elsevier, Amsterdam, 1968.

[7] D. Spinelli, C. Dell'Erba, and A. Salvemini, *Ann. Chim.* (*Italy*), 1962, **52**, 1156.

TABLE 1

Kinetic data and activation parameters for the piperidino-substitution in methanol of 2-chloro-3-nitro-5-X-thiophens (Ia, c—h)

Compound	10^3k/l mol^{-1} s^{-1} (T/°C) [a]			$\Delta H^{\ddagger}$ [b]/ kcal mol^{-1}	$-\Delta S^{\ddagger}$ [c]/ kcal mol^{-1} K^{-1}
(Ia)	0·171 (20·03)	0·412 (30·05)	0·937 (40·05)	14·9	24·8
(Ic)	13·8 (20·00)	28·9(30·06)	52·9 (40·10)	11·6	27·4
(Id)	24·9 (9·98)	49·4 (19·97)	96·8 (30·02)	11·0	27·0
(Ie)	67·3 (9·98)	137 (20·00)	252 (29·95)	10·7	25·9
(If)	32·5 (0·00)	66·4 (10·10)	168 (20·03)	12·4	19·8
(Ig)	64·4 (0·05)	128 (10·00)	250 (20·02)	10·2	26·4
(Ih) [d]	866 (0·03)	1880 (9·99)	3740 (20·03)	11·0	18·1

[a] Rate constants are accurate to within ±3%. [b] At 20°, probable error is 0·5 kcal mol^{-1}. [c] At 20°. [d] See ref. 14.

TABLE 2

Kinetic data and activation parameters for the piperidino-substitution in methanol of 2-bromo-3-nitro-5-X-thiophens (IIa—h)

Compound	10^3k/l mol^{-1} s^{-1} (T/°C) [a]			$\Delta H^{\ddagger}$ [b]/ kcal mol^{-1}	$-\Delta S^{\ddagger}$ [c]/ kcal mol^{-1} K^{-1}
(IIa) [d]	0·114 (20·00)	0·268 (30·00)	0·958 (46·33)	14·4	27·2
(IIb) [d]	1·80 (20·00)	3·95 (30·00)	8·34 (40·50)	13·0	26·5
(IIc) [d]	3·61 (9·80)	7·82 (20·00)	16·7 (29·90)	12·4	25·8
(IId) [d]	13·6 (9·80)	27·8 (20·00)	54·8 (29·90)	11·2	27·3
(IIe) [d]	16·6 (0·16)	33·6 (9·85)	74·4 (20·00)	11·4	24·6
(IIf)	32·0 (9·98)	75·1 (20·04)	135 (30·02)	11·7	23·9
(IIg) [d]	29·7 (0·15)	64·8 (9·90)	127 (20·00)	11·0	24·8
(IIh) [d]	1060 (10·82)	1980 (20·00)	3780 (30·02)	10·7	20·5

[a–c] As in Table 1. [d] See ref. 10*b*.

TABLE 3

Kinetic data and activation parameters for the piperidino-substitution in methanol of 2-iodo-3-nitro-5-X-thiophens (IIIa, c—h)

Compound	10^3k/l mol^{-1} s^{-1} (T/°C) [a]			$\Delta H^{\ddagger}$ [b]/ kcal mol^{-1}	$-\Delta S^{\ddagger}$ [c]/ kcal mol^{-1} K^{-1}
(IIIa)	0·0115 (20·05)	0·0321(30·00)	0·0735 (40·10)	16·3	25·3
(IIIc)	0·710 (20·00)	1·59 (30·03)	3·42 (39·95)	13·8	25·9
(IIId)	2·26 (20·00)	4·94 (30·02)	9·94 (39·83)	13·0	26·2
(IIIe)	6·29 (20·03)	13·0 (30·01)	25·3 (39·95)	12·1	27·1
(IIIf)	7·72 (20·12)	15·4 (30·03)	31·7 (39·98)	12·4	25·9
(IIIg)	8·57 (20·03)	19·4 (30·01)	37·8 (39·95)	13·0	23·5
(IIIh) [d]	176 (20·00)	348 (30·03)	621 (39·95)	10·9	24·5

[a–d] As in Table 1.

TABLE 4

Kinetic data and activation parameters for the piperidino-substitution in methanol of 2-*p*-nitrophenoxy-3-nitro-5-X-thiophens (IVa, c—h)

Compound	10^3k/l mol^{-1} s^{-1} (T/°C) [a]			$\Delta H^{\ddagger}$ [b]/ kcal mol^{-1}	$-\Delta S^{\ddagger}$ [c]/ kcal mol^{-1} K^{-1}
(IVa)	6·98 (20·05)	14·0 (30·02)	26·8 (40·10)	11·7	28·5
(IVc)	58·7 (0·03)	99·2 (10·05)	227 (20·05)	10·1	27·0
(IVd)	158 (0·06)	319 (10·04)	585 (20·03)	9·8	26·0
(IVe)	378 (0·01)	770 (9·85)	1570 (20·02)	10·7	20·9
(IVf)	251 (0·07)	482 (10·05)	1040 (20·05)	10·7	21·8
(IVg)	571 (0·02)	1110 (10·06)	2220 (20·03)	10·2	22·1
(IVh)	4700 (0·04)	8800 (9·90)	15500 (20·02)	8·9	22·6

[a–c] As in Table 1.

TABLE 5

Kinetic data and activation parameters for the piperidino-substitution in methanol of 2-phenylsulphonyl-3-nitro-5-X-thiophens (Va—h)

Compound	10^3k/l mol^{-1} s^{-1} (T/°C) [a]			$\Delta H^{\ddagger}$ [b]/ kcal mol^{-1}	$-\Delta S^{\ddagger}$ [c]/ kcal mol^{-1} K^{-1}
(Va)	0·0592 (20·05)	0·148 (30·10)	0·288 (40·10)	13·8	30·5
(Vb)	1·32 (20·05)	2·81 (30·05)	5·60 (40·12)	12·5	28·9
(Vc)	9·64 (20·05)	18·3 (30·02)	33·4 (39·95)	10·8	30·8
(Vd)	19·5 (10·06)	38·0 (20·03)	67·8 (30·02)	10·0	30·7
(Ve)	48·2 (—0·15)	96·3 (10·07)	179 (20·05)	9·8	28·6
(Vf)	38·4 (0·03)	71·5 (10·06)	127 (20·03)	8·9	32·1
(Vg)	103 (0·02)	191 (10·01)	359 (20·00)	9·3	28·7
(Vh) [d]	2430 (0·02)	4140 (10·02)	6800 (20·03)	7·6	28·8

[a–d] As in Table 1.

piperidine catalysis; a large increase of reactivity is observed upon introduction of electron-withdrawing groups.

TABLE 6

Substituent constants *

X	H	Br	$CONH_2$	CO_2Me	SO_2Me	Ac	CN	NO_2
σ_p^-	0·00	0·30	0·62	0·74	1·05	0·82	0·99	1·23
σ_p^-	0·00	0·35	0·55	0·71	0·85	0·85	0·92	1·27

* Line 1, σ values from ref. 8; line 2, σ values recalculated by the method of ref. 9.

TABLE 7

Reaction constants and other statistical data [a] for the piperidino-substitution of 2-L-3-nitro-5-X-thiophens in methanol at 20°

L	$\rho \pm s_\rho$	r	n [b]	i [c]	$\rho \pm s_\rho$	r	n [d]	i [c]
Cl	3·47 ± 0·20	0·9937	6	−0·07	3·42 ± 0·03	0·9998	7	0·02
Br	3·27 ± 0·19	0·9921	7	0·02	3·31 ± 0·03	0·9998	8	0·01
I	3·30 ± 0·25	0·9887	6	−0·09	3·26 ± 0·07	0·9990	7	−0·02
$OC_6H_4NO_2$-*p*	2·68 ± 0·11	0·9969	6	−0·06	2·65 ± 0·07	0·9983	7	0·02
SO_2Ph	3·97 ± 0·18	0·9949	7	−0·03	4·02 ± 0·06	0·9993	8	−0·02

[a] ρ, Reaction constant; s_ρ, standard deviation of ρ; r, correlation coefficient. The t test for statistical significance indicates that the correlations by σ values of both lines 1 and 2 of Table 6 are significant at the 1% level. [b] Data for (Ie)—(Ve) have been excluded from the ρ calculation: see ref. 20. [c] $i = \log (k/k_H)$, intercept of the regression line with ordinate ($\sigma = 0$). [d] Data for (Ie)—(Ve) have been included in the ρ recalculation (see text) using $\sigma_p^- = 0{\cdot}85$ (Table 6, line 2).

TABLE 8

Correlations [a] by the equation $\log (k/k_H)_{L_1} = a \log (k/k_H)_{L_2} + b$

L_1	L_2	a	b	r [b]	s_a [c]	n [d]	ρ_{L_1}/ρ_{L_2}
SO_2Ph	Cl	1·17	−0·02	0·999	0·02	7	1·18
SO_2Ph	Br	1·21	−0·04	0·999	0·02	8	1·21
SO_2Ph	I	1·22	0·03	0·997	0·04	7	1·23
SO_2Ph	$OC_6H_4NO_2$-*p*	1·51	−0·03	0·999	0·03	7	1·52
Cl	Br	1·03	0·02	1·000	0·01	7	1·03
Cl	I	1·05	0·05	0·999	0·02	7	1·05
I	Br	0·98	−0·02	0·999	0·02	7	0·98
$OC_6H_4NO_2$-*p*	Cl	0·77	0·01	0·997	0·03	7	0·77
$OC_6H_4NO_2$-*p*	Br	0·80	0·02	0·998	0·02	7	0·80
$OC_6H_4NO_2$-*p*	I	0·81	0·04	0·995	0·04	7	0·81

[a] See text. [b] Correlation coefficient. [c] Standard deviation of a. [d] Number of points.

The kinetic data obtained have been correlated using a monolinear relationship of the Hammett type with σ_p^- constants [8,*] (Table 6, line 1). The ρ values at 20° [data for (Ie)—(Ve) have been excluded, see below] are reported with standard deviations, correlation coefficients, and number of points (Table 7, columns 2—4). To improve the correlation and to obtain a set of homogeneous σ constants for the heteroaromatic system considered, we have utilized the method of Brown [9] to calculate better σ_p^- values (Table 6, line 2). Using these new σ_p^- values † we have recalculated ρ_L, s_L, and r_L (Table 7, columns 6—8).‡

A significant test of correlation can also be obtained by plotting the log k/k_H for a leaving group against the same ratio for another leaving group: thus, the effectiveness of the leaving group in affecting the action of the substituent is more evident. The data obtained are collected in Table 8. In every case the values of b (the intercept of the straight line) is near zero (theoretically the straight line should pass through the origin). The values of a are practically coincident with the corresponding ratios between the ρ values (Table 8, columns 3 and 8).

In spite of variations of absolute reactivity with changing halogen leaving group [(I)—(III)] and 5 substituent we observe similar reactivity ratios and ρ values (Table 7, column 6).

In this case the selectivity–reactivity relationship [12] cannot be applied; § in fact the lowest reactivity with iodine as leaving group is not linked to the highest selectivity.

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* This imples the crude assumption that $r^- = 1$ in the equation $\log k/k_H = \rho(\sigma + r_R\Delta\sigma^-)$.[8] We shall return to this point in a forthcoming paper.

† The differences between the original σ_p^- data [8] and the new calculated values are small ($|\Delta\sigma_p^-| < 0{\cdot}07$) except in the case of X = SO_2Me ($|\Delta\sigma_p^-| = 0{\cdot}20$) for which (as we have already pointed out [10]) the benzene σ_p^- cannot be used.

‡ The results obtained point against the previous claim [11] that the ρ-values in nucleophilic aromatic nitroactivated substitutions are, other things being equal, only scarcely affected by the nature of the leaving group.

§ We think that the selectivity–reactivity relationship can only be used to compare very similar systems. The change in the leaving group seems to introduce factors which eliminate this possible use.

[8] A. J. Hoefnagel and B. M. Wepster, *J. Amer. Chem. Soc.*, 1973, **95**, 5357.

[9] H. C. Brown and L. M. Stock, *J. Amer. Chem. Soc.*, 1962, **84**, 3298.

[10] (*a*) C. Dell'Erba and D. Spinelli, *Tetrahedron*, 1965, **21**, 1061; (*b*) D. Spinelli, G. Consiglio, and A. Corrao, *J.C.S. Perkin II*, 1972, 1866.

[11] S. M. Shein and L. A. Kozorez, *Sposobnost. Org. Soedinenii Tartusk. fos. Univ. Reaktsionnaya*, 1966, **3**, 45.

[12] J E. Leffler and E. Grunwald, 'Rates and Equilibria of Organic Reactions,' Wiley, New York, 1963, 162.

According to our interpretation of ρ values in the case of the three halogens the variation of the 5-substituent present causes a similar change in the position of the r.d.t.s. on the reaction co-ordinate. The differences in the reactivity between the three series (I)—(III) are linked to the effectiveness of the halogen atom in controlling the formation of the r.d.t.s., *i.e.*, to its 'effective' electronegativity (a balancing of its electronic effects) and its size. The combination of these two factors (see also below) determines the ρ values.

When the leaving group is *p*-nitrophenoxy or phenylsulphonyl the ρ values are smaller (ρ +2·65) and greater (ρ +4·02) respectively than those for the halogens (ρ +3·33 ± 0·10), the first indicating a lower and the second a higher sensitivity to the change of position of the r.d.t.s. on the reaction co-ordinate as a function of the substituent relative to the halogen case.

This crude observation requires some attempt at interpretation. The leaving group, particularly in the starting compounds but also in the r.d.t.s. interacts with the ring and its substituents. So the *p*-nitrophenoxy-group acting as an electron donor [13] increases the electron density in the thiophen ring, thus exerting a levelling effect on the electronic effects of the substituent present. On the other hand, the phenylsulphonyl, an electron attracting group, affects the electronic density on C(2) and the ρ value in the opposite direction.

Moreover we think that the ease of formation of the r.d.t.s. is also a function of the size of the head-atoms of the leaving group. A small atom (*e.g.* oxygen in $OC_6H_4NO_2$-*p*) makes electronic interaction possible between nucleophile and reaction centre when the old bond [C(2)-L] is not much distorted and the new bond [C(2)-Nu] is but little formed: in this case the 5-substituent scarcely affects the energy of the r.d.t.s. which is presumably early on the reaction co-ordinate. On the other hand, a bulky leaving group * (*e.g.* SO_2Ph) makes interactions between nucleophile and reaction centre possible only when L is much out of the plane of the ring, the old bond deformed, and the new bond to a large extent formed: † in this case the 5-substituent present has more effect on the energy of r.d.t.s. which should be late.

As a consequence, the first situation (L = $OC_6H_4NO_2$-*p*) results, as observed, in a small effect by the substituent and the second in a large one: these two cases correspond to a small and a large ρ value.

EXPERIMENTAL

Synthesis and Purification of Compounds.—Compounds (Ia),[15] (Id),[15] (Ie),[16] (If),[15] (Ih),[15] (IIf),[10a] (IIIa),[17] (IIId),[17] (IIIh),[17] (IVa),[18] (IVh),[7] (Va),[18] (Vh),[7] and (VIa—h),[10b] were prepared and/or purified according to the methods reported. The other compounds were prepared as below and gave the anticipated n.m.r. spectra.

5-*Chloro*-4-*nitrothiophen*-2-*carboxamide* (Ic).—Potassium nitrate (1·03 g, 1·02 × 10^{-2} mol) was slowly added with stirring to a solution of 5-chlorothiophen-2-carboxamide [19] (1·62 g, 10^{-2} mol) in concentrated H_2SO_4 (10 ml) at 10°. The mixture was set aside at 10° for 30 min and then poured over crushed ice and the solid was filtered off and washed with water. The *amide* was crystallized from methanol, m.p. 209° (Found: Cl, 17·4; N, 13·8; S, 15·6. $C_5H_3ClN_2O_3S$ requires Cl, 17·2; N, 13·6; S, 15·5%).

5-*Chloro*-4-*nitrothiophen*-2-*carbonitrile* (Ig).—Fuming HNO_3 (5 ml) was slowly added with stirring to a solution of 5-chlorothiophen-2-carbonitrile [19] (7·8 g) in Ac_2O (10 ml) at 10—15°. The mixture was set aside for 3 h and then treated as before. The *nitrile* was crystallized from ethanol, m.p. 117° (Found: Cl, 18·7; N, 14·9; S, 17·0. $C_5H_4ClN_2O_2S$ requires Cl, 18·8; N, 14·8; S, 17·0%).

5-*Iodo*-4-*nitrothiophen*-2-*carboxamide* (IIIc).—Compound (IIIc) was obtained from 5-iodothiophen-2-carboxamide [20] as before. The *amide* obtained was crystallized from methanol, m.p. 237° (Found: N, 9·4; S, 10·9. $C_5H_3IN_2O_3S$ requires N, 9·4; S, 10·8%).

2-*Iodo*-5-*methylsulphonyl*-3-*nitrothiophen* (IIIe).—2-Iodo-5-methylsulphonylthiophen [21] (4·8 g) was slowly added to a cooled (0°), stirred solution of concentrated H_2SO_4 (11 ml) and fuming HNO_3 (13 ml) and stirring was continued for 30 min and then the mixture was treated as before. The *iodo-compound* (IIIe) was crystallized from methanol, m.p. 156° (Found: C, 18·1; H, 1·3; N, 4·2. $C_5H_4IO_4NS_2$ requires C, 18·0; H, 1·2; N, 4·2%).

5-*Acetyl*-2-*iodo*-3-*nitrothiophen* (IIIf).—Compound (IIIf) was obtained from 5-acetyl-2-iodothiophen [22] by nitration as before. The *iodo-compound* (IIIf) was crystallized from light petroleum, m.p. 127° (Found: N, 4·6; S, 10·9. $C_6H_4INO_3S$ requires N, 4·7; S, 10·8%).

5-*Iodo*-4-*nitrothiophen*-2-*carbonitrile* (IIIg).—Compound (IIIg) was obtained from 5-iodothiophen-2-carbonitrile [20] by nitration at 30° as before. The *nitrile* obtained was crystallized from ethanol, m.p. 173° (Found: N, 10·2; S, 11·3. $C_5HIN_2O_2S$ requires N, 10·0; S, 11·4%).

Ethers (IVc—g).—Potassium *p*-nitrophenoxide (0·16 g, 0·01 mol) was added to a solution of the corresponding 2-bromo-3-nitro-5-X-thiophen [10] (0·01 mol) in ethanol and the mixture kept at room temperature (30 min) or refluxed for 5 min—3 h depending on the nature of the 5-substituent. The mixture was evaporated at reduced pressure. The residue was washed with water and crystallized. The m.p.s, crystallization solvents, and analytical data of compounds (IVc—g) are reported in Table 9.

3-*Nitro*-2-*phenylsulphonyl*-5-X-*thiophens* (Vb—g).—Compounds (Vb—g) were prepared from the corresponding

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* The steric interactions between the 2-phenylsulphonyl and 3-nitro-group [14] can enhance the selectivity.

† According to this viewpoint the series with L = $SO_2C_6H_5$ presents the highest average value of activation entropies because of the highest charge development in the t.s. and highest steric requirements at reaction centre.

[13] O. Exner, 'Advances in Linear Free Energy Relationships,' eds. N. B. Chapman and J. Shorter, London, 1972, ch. 1.

[14] D. Spinelli, G. Consiglio, R. Noto, and A. Corrao, *J.C.S. Perkin II*, 1974, 1632.

[15] C. D. Hurd and K. L. Kreuz, *J. Amer. Chem. Soc.*, 1952, **74**, 2965.

[16] U.S.P. 2,825,726 (*Chem. Abs.*, 1958, **52**, 9613g).

[17] I. J. Rinkes, *Rec. Trav. chim.*, 1934, **53**, 643.

[18] C. Dell'Erba, G. Guanti, and P. Macera, *J. Heterocyclic Chem.*, 1971, **8**, 537.

[19] P. Fournari and J. P. Chané, *Bull. Soc. chim. France*, 1963, 479.

[20] R. Guilard, P. Fournari, and M. Person, *Bull. Soc. chim. France*, 1967, 4121.

[21] J. Cymerman-Craig and J. W. Loder, *J. Chem. Soc.*, 1954, 237.

[22] W. Steinkopf and W. Bauermeister, *Annalen*, 1914, **403**, 57.

TABLE 9

Physical and analytical data for ethers (IVc—g)

Compound	Crystallization solvent	M.p. (°C)	Found (%)		Formula	Required (%)	
			N	S		N	S
(IVc)	Methanol	194	13·8	10·4	$C_{11}H_7N_3O_6S$	13·6	10·4
(IVd)	Ethanol	116	8·4	10·0	$C_{12}H_8N_2O_7S$	8·6	9·9
(IVe)	Ethanol–dioxan	162	8·1	18·8	$C_{11}H_8N_2O_7S_2$	8·1	18·6
(IVf)	Methanol	133	8·9	10·3	$C_{12}H_8N_2O_6S$	9·1	10·4
(IVg)	Ethanol	144	14·4	11·0	$C_{22}H_5N_3O_5S$	14·4	11·0

TABLE 10

Physical and analytical data for 3-nitro-2-phenylsulphonyl-5-X-thiophens (Vb—g)

Compound	Crystallization solvent	M.p. (°C)	Found (%)		Formula	Required (%)	
			N	S		N	S
(Vb)	Ethanol–dioxan	180	4·0	18·2	$C_{10}H_6BrNO_4S_2$	4·0	18·4
(Vc)	Ethanol–dioxan	224	9·0	20·4	$C_{11}H_8N_2O_5S_2$	9·0	20·5
(Vd)	Ethanol	123	4·3	19·8	$C_{12}H_9NO_6S_2$	4·3	19·6
(Ve)	Ethanol–dioxan	206	4·0	27·5	$C_{11}H_9NO_6S_3$	4·0	27·7
(Vf)	Ethanol–dioxan	160	4·6	20·4	$C_{12}H_9NO_5S_2$	4·5	20·6
(Vg)	Ethanol–dioxan	183	9·4	21·7	$C_{11}H_6N_2O_4S_2$	9·5	21·8

2-bromo-3-nitro-5-X-thiophens[10] (0·01 mol) and sodium benzenesulphinate (0·012 mol) as described above for the synthesis of compounds (IVc—g). The m.p.s, crystallization solvents, and analytical data of compounds (Vb—g) are reported in Table 10.

Kinetic Measurements.—The kinetics were carried out in the presence of piperidine hydrochloride to avoid competitive methoxy-substitution[23] and followed spectrophotometrically as previously described[10b] at the wavelengths reported for compounds (IIa—e, g, h).[10b] In the case of (IIf) the corresponding piperidino-derivative (VIf) has $\lambda_{max.}$ 344 nm (log ε 4·22). The concentrations employed were 10^{-3}M for the substrates, 6×10^{-3}M for piperidine, and 3×10^{-2}M for piperidine hydrochloride. For the reactions of 2-L-3,5-dinitrothiophens (Ih) and (IIIh)—(Vh) the concentrations were respectively 10^{-4}M, 5×10^{-4}M, and 2×10^{-2}M.

The infinity optical densities in the range 200—450 nm indicate that the formation of the piperidino-derivatives (VI) is the only reaction occurring to any extent. T.l.c. of reaction mixtures confirms the photometric data.

We thank the Italian Research Council (C.N.R.) for financial support.

[4/1756 *Received*, 30*th August*, 1974]

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[23] D. Spinelli, G. Guanti, and C. Dell'Erba, *J. Heterocyclic Chem.*, 1968, **5**, 323 and references therein.