Kinetics of the Reactions of 2-Bromo-3,5-dinitrothiophen with *ortho*-Substituted Anilines in Methanol. An Application of the Fujita–Nishioka Equation

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The rates of anilino-debromination of 2-bromo-3,5-dinitrothiophen (I) by some *ortho*-substituted anilines (II; X = OMe, Me, Et, Cl, Br, and F) have been measured in methanol. The kinetic results have been treated according to the multiparameter analysis of *ortho*-effects proposed by Fujita and Nishioka. This treatment of data has also been applied to acid–base equilibria of anilinium ions. The susceptibility constants obtained in the two series of reactions (respectively ρ −2.96 and −2.90, δ 1.31 and 0.56, f −1.83 and −1.70) have been explained by taking into account the structure of the transition states involved.

RECENTLY[1] we examined the reaction of 2-bromo-3,5-dinitrothiophen (I) with 14 *meta*- or *para*-substituted anilines in methanol and showed that the kinetic data obeyed the Ingold–Yukawa–Tsuno relationship[2] (1) with ρ −3.00, r^+ 0.38, and r^- 0.99.

TABLE 1

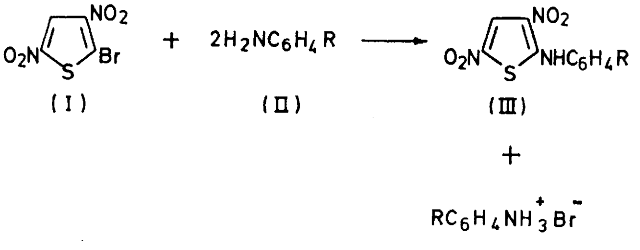
Physical and analytical data for *ortho*-substituted *N*-(3,5-dinitrothienyl)anilines (III)

Substituent	Crystallization solvent	M.p. (°C)	Found (%) C	Found (%) H	Found (%) N	Formula	Required (%) C	Required (%) H	Required (%) N	$\lambda_{max.}$/nm	log ε [a]
MeO	Ethanol–dioxan	196	45.0	3.1	14.1	$C_{11}H_9N_3O_5S$	44.7	3.1	14.2	402	4.30
Me [b]	Ethanol	168								404	4.20
Et	Ligroin–benzene	92	49.5	3.7	14.2	$C_{12}H_{11}N_3O_4S$	49.1	3.8	14.3	405	4.22
Cl	Ethanol–dioxan	184	40.3	2.0	13.8	$C_{10}H_6ClN_3O_4S$	40.1	2.0	14.0	394	4.25
Br	Ethanol–dioxan	174	35.1	1.7	12.0	$C_{10}H_6BrN_3O_4S$	34.9	1.8	12.2	394	4.24
F	Ethanol–dioxan	178	42.6	2.0	14.6	$C_{10}H_6FN_3O_4S$	42.4	2.1	14.8	394	4.24

[a] In methanol. [b] See ref. 3.

$$\log k/k_H = \rho(\sigma^n + r^+\Delta\sigma_R{}^+ + r^-\Delta\sigma_R{}^-) \qquad (1)$$

As a natural extension of this work we now report rate constants and activation parameters for the reaction



of (I) with some *ortho*-substituted anilines (II; R = MeO, Me, Et, Cl, Br, and F) in methanol. We will show that it is possible to embody ordinary and steric effects of substituents into a unique multiparameter free-energy relationship.

RESULTS

Products.—2-Bromo-3,5-dinitrothiophen (I) gave the expected anilino derivatives (III) on treatment with anilines (II) in very high yields, as shown by t.l.c. and u.v.–visible spectral analysis. The relevant physical and analytical data are shown in Table 1.

Kinetic Data.—Rate constants and activation parameters for anilino-debromination of (I) are reported in Table 2. All the reactions were first order both in (I) and (II). On changing from aniline to *ortho*-substituted anilines, irrespective of the nature of the electron-withdrawing or -repelling effect of the substituent, a decrease in the rate of substitution was observed, which indicated the occurrence of important steric effects.

TABLE 2

Rate constants and activation parameters for the reactions of 2-bromo-3,5-dinitrothiophen (I) with *ortho*-substituted anilines (II) in methanol

Substituent	10^3 *k*/l mol^{-1} s^{-1} [a] (*t*/°C)	$\Delta H^{\ddagger}$ [b]/kcal mol^{-1}	$-\Delta S^{\ddagger}$ [c]/cal mol^{-1} K^{-1}
Meo	15.3 (10.03), 28.0 (20.10), 46.1 (30.00)	8.8	35.5
Me [d]	3.49 (19.95), 6.36 (30.02), 11.0 (39.98)	9.9	35.9
Et	3.39 (20.05), 6.08 (30.02), 10.5 (40.08)	9.7	36.7
Cl	0.106 (20.10), 0.204 (29.98), 0.364 (40.02)	10.6	40.2
Br	0.0442 (20.10), 0.0872 (30.02), 0.166 (40.06)	11.5	39.2
F	0.694 (20.10), 1.27 (29.98), 2.21 (40.02)	10.0	38.8
H [d]	12.2 (0.02), 23.0 (10.02), 41.9 (20.05)	9.2	33.4

[a] The rate constants are accurate to within ±3%. [b] At 20°; the probable error is 0.5 kcal mol^{-1}. [c] At 20°. [d] See ref. 3.

DISCUSSION

Among the numerous attempts to understand the nature and composition of the '*ortho*-effect', those of Taft,[4] Charton,[5] Farthing and Nam,[6] and Chapman and Shorter[7] have met with varying degrees of success, but the approach proposed by Fujita and Nishioka[8] seems to us the most promising. According to these authors, the total effect of *ortho*-substituents is expressed in terms of (i) the ‘ordinary polar effect,’ defined as being equal to that of *para*-substituents; (ii) the ‘proximity polar effect,’ represented by the Swain–Lupton constant,[8,9] and (iii) the ‘primary steric effect,’ represented by the Taft E_s constant.[4,8,*]

TABLE 3

Linear free energy relationships[a] for the reaction of 2-bromo-3,5-dinitrothiophen with *ortho*-, *meta*-, and *para*-substituted anilines in methanol, at 20 °C (A) and for the dissociation of anilinium ions in water, at 25 °C (B)

System	Equation used	$\rho \pm s_\rho$	$\delta \pm s_\delta$	$f \pm s_f$	$i \pm s_i$	s	R	n	$r^2_{E_s.F}$	$r^2_{\sigma_{calc},F}$
A	(1)	-3.00 ± 0.05			0.00 ± 0.03	0.08	0.9983	14		
	(2)	$-2.75 + 0.05$	1.27 ± 0.08	-1.91 ± 0.21	-0.03 ± 0.09	0.09	0.9984	7	0.004	0.382
	(3)	-2.96 ± 0.05	1.31 ± 0.05	-1.83 ± 0.14	-0.01 ± 0.03	0.09	0.9980	20	0.229	
B	(1)	-2.93 ± 0.03			0.01 ± 0.02	0.05	0.9992	14		
	(2)	-2.65 ± 0.18	0.53 ± 0.05	-1.83 ± 0.16	-0.01 ± 0.06	0.06	0.9988	7	0.004	0.502
	(3)	-2.90 ± 0.04	0.56 ± 0.04	-1.70 ± 0.10	-0.01 ± 0.02	0.06	0.9989	20	0.229	

[a] s_ρ, s_δ, s_f, s_i represent standard errors, respectively, of ρ, δ, f, and i; i, intercept; s, standard error of estimate; R, correlation coefficient; n, number of data points; $r^2_{E_s.F}$ and $r^2_{\sigma_{calc},F}$ are the coefficients of determination for simple correlation, respectively, between E_s and F values and σ_{calc} and F values. The values of σ_{calc}, E_s, F, log k/k_H, and pK_a used in correlations are shown in Table 4.

The rate or equilibrium data of a series of *ortho*-substituted derivatives can be expressed by equation (2), where ρ, δ, and f are susceptibility constants, and c is a constant that corresponds to the log k_H value of the unsubstituted compound. If the separation of proximity

$$\log k_{ortho} = \rho\sigma_{ortho} + \delta E_s + fF + c \qquad (2)$$

polar and steric effects from the ordinary polar effect is complete in equation (2), a set of rate or equilibrium data for a series including *ortho*-, *meta*-, and *para*-substituted derivatives can be expressed by equation (3). When applied to the anilinodebromination of (I) (system A), equations (2) and (3) give the results set forth in Table 3.[†] For the sake of comparison, parallel calculations have been carried out on acid dissociation of anilinium ions (system B) and are also included in Table 3.[‡]

$$\log k_{o.m.p.} = \rho\sigma_{o.m.p.} + \delta E_s^{ortho} + fF_{ortho} + c \qquad (3)$$

The levels of significance of all correlations with equations (1)—(3) are better than 99.95% as examined by F tests.[14] One observes only a slight increase in the standard deviation, s, by including *ortho*-substituted derivatives; moreover all the terms in equations (2) and (3) are justified at better than 99.9% by t tests.[14]

The strict correspondence between the regression parameters obtained with equations (2) and (3) indicates that in both systems A and B the separation of proximity polar and steric effects from the ordinary polar effect is complete. We wish to emphasize that the set of combined *ortho*-, *meta*-, and *para*-substituted derivatives can be dealt with by means of a unique multiparameter free energy relationship, namely (4). Systems A and B show similar ρ and f values indicating much the same susceptibility to ordinary and proximity polar effects.

On the other hand, anilinodebromination has a δ value which is about two-fold higher than for the dissociation of anilinium ions. The different susceptibility to the

$$\log k/k_H = \rho(\sigma^n + r^+\Delta\sigma_R^+ + r^-\Delta\sigma_R^-) + \delta E_s + fF \qquad (4)$$

‘volume-filling’ factor originates from a different crowding of transition state in the two reactions and confirms indications from an examination of molecular models.

TABLE 4

Parameters used in statistical correlations

Substituent	log k/k_H[a]	σ_{calc}[b]	pK_a[c]	σ_{calc}[d]	E_s[e]	F[e]
p-OMe	1.086[f]	−0.36	5.36	−0.26		
p-Me	0.534[f]	−0.18	5.08	−0.15		
m-Me	0.188[f]	−0.069	4.71	−0.069		
H	0.000[f]	0.000	4.60	0.000		
p-Cl	−0.647[f]	0.22	3.98	0.24		
p-Br	−0.724[f]	0.24	3.89	0.26		
m-Cl	−1.109[f]	0.373	3.52	0.373		
m-F	−1.125[f]	0.337	3.59[h]	0.337		
m-Br	−1.130[f]	0.391	3.53	0.391		
p-CO_2Me	−2.063[f]	0.74	2.38[h]	0.74		
m-NO_2	−2.174[f]	0.710	2.46	0.710		
p-COMe	−2.290[f]	0.82	2.19[i]	0.82		
p-CN	−2.986[f]	0.99	1.74[h]	0.99		
p-NO_2	−3.785[f]	1.22	1.02	1.23		
o-OMe	−0.183[g]	−0.36	4.53	−0.26	−0.55	0.26
o-Me	−1.075[g]	−0.18	4.45	−0.15	−1.24	−0.04
o-Et	−1.090[g]	−0.19	4.37[j]	−0.17	−1.31	−0.05
o-Cl	−2.593[g]	0.22	2.66	0.24	−0.97	0.41
o-Br	−2.978[g]	0.24	2.53	0.26	−1.16	0.44
o-F	−1.779[g]	0.08	3.20[h]	0.12	−0.46	0.43

[a] From k values calculated at 20 °C by the activation parameters. [b] σ_{calc} for anilino-debromination, $\sigma_{calc} = \sigma^n + 0.38\,\Delta\sigma_R^+ + 0.99\Delta\sigma_R^-$, see ref. 1. [c] Values from ref. 10 unless noted otherwise. [d] σ_{calc} for the acid dissociation of anilinium ions, $\sigma_{calc} = \sigma^n + 0.24\,\Delta\sigma_R^+ + \Delta\sigma_R^-$, see ref. 1. [e] Values from ref. 8. [f] Values from ref. 1 [g] This work. [h] Values from ref. 11. [i] Values from ref. 12. [j] Value from ref. 13.

The activation parameters for anilino-debromination are consistent with this picture in that on going from aniline to *ortho*-substituted anilines $\Delta H^\ddagger$ increases and $\Delta S^\ddagger$ decreases, indicating some steric strain in the transition state.

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[*] According to Fujita and Nishioka[8] the reference substituent is changed to hydrogen.

[†] Taking for the ‘ordinary polar effect’ of *ortho*-substituent that of the *para*-substituent we have used $\sigma_{ortho} = \sigma^n + r^+\Delta\sigma_R^+ + r^-\Delta\sigma_R^-$ [see notes *b* and *d* of Table 4 and equation (4)].

[‡] The regression parameters obtained by us compare well with those obtained by Fujita and Nishioka[8] using a larger number of substituted anilinium ions.

EXPERIMENTAL

Synthesis and Purification of Compounds.—Methanol, (I), and (II) were prepared and/or purified as previously.[1] The anilino derivatives (III) were prepared according to the general method reported in ref. 15: physical and analytical data are shown in Table 1.

Kinetic Measurements.—The kinetics were followed spectrophotometrically as previously described.[16] The concentrations employed were $\simeq 10^{-3}$M for (I) and 6×10^{-3}—3×10^{-1}M for (II) as a function of the nucleophilicity.

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