Kinetics of Aromatic Nucleophilic Substitution by Toluene-p-thiolate in Dimethylformamide. Effect of Solvent on Hammett-type Correlations

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The kinetics of the reaction of some 4-substituted 2-nitrochlorobenzenes with toluene-p-thiolate in dimethylformamide have been measured at temperatures from $-39 \cdot 7$ to $71 \cdot 9$ °C. Correlation of rates by Hammett-type equations gives, using the best set of σ values, $\rho = +6 \cdot 65$ at 10 °C. The dependence of the ρ value on the solvent is discussed. A comparison of these reactions with those of $Ar_2C=CHCl$ and of $ArC\equiv CCl$ with the same nucleophile–solvent system shows that the substituent effects are markedly attenuated by the interposition of $C=C$ or $C\equiv C$ bonds.

POLAR effects of substituents on equilibria and on rates of reactions in solution, as expressed by Hammett ρ constants,[1] depend on the solvent used. While, for a given reaction and temperature, ρ values generally increase when the dielectric constant of the solvent decreases,[2] examples of contrary behaviour are known,[3] particularly for a transition from protic to dipolar, aprotic solvents, such as methanol and dimethylformamide.

In the past, experimental ρ values for nucleophilic substitution at the ethylenic and acetylenic carbon, obtained from kinetic studies in dimethylformamide, have been compared directly [4,5] with values reported for $S_N Ar$ reactions in protic solvents,[6,7] for lack of data on the latter reactions in dipolar aprotic media.[8] In order
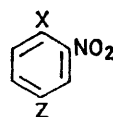
	(I) Z = OMe	
	(II) Z = Me	
X	(III) Z = H	a; X = Cl
	(IV) Z = Cl	
NO2	(V) Z = CO_2Me	b; X = p-MeC_6H_4S
	(VI) Z = COMe	
Z	(VII) Z = NO_2	

to clarify this point more, the reaction of compounds (Ia)—(VIIa) with sodium toluene-p-thiolate in dimethylformamide has been studied. The reaction of most of

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[2] K. B. Wiberg, 'Physical Organic Chemistry,' Wiley, New York, 1964, p. 289.

[3] A. Buckley, N. B. Chapman, M. R. J. Dack, J. Shorter, and H. M. Wall, J. Chem. Soc. (B), 1968, 631.

[4] (a) P. Beltrame, D. Pitea, and M. Simonetta, J. Chem. Soc. (B), 1967, 1108; (b) P. Beltrame, P. L. Beltrame, and L. Bellotti, ibid., 1969, 932; (c) P. Beltrame, P. L. Beltrame, M. L. Cereda, and G. Lazzerini, ibid., p. 1100.

[5] P. Beltrame, P. L. Beltrame, M. G. Cattania, and M. Simonetta, J.C.S. Perkin II, 1973, 63.

[6] J. F. Bunnett and R. F. Snipes, J. Amer. Chem. Soc., 1955, 77, 5422.

[7] A. M. Porto, L. Altieri, A. J. Castro, and J. A. Brieux, J. Chem. Soc. (B), 1966, 963.

[8] T. J. de Boer and I. P. Dirkx, 'The Chemistry of the Nitro and Nitroso Groups,' ed. H. Feuer, Interscience, New York, 1969, part 1, p. 534.

these compounds with benzenethiolate in methanol had been studied by Brieux et al.[7] The influence of the 2-nitro-group can be considered constant throughout the series.[7]

RESULTS AND DISCUSSION

The reactions of (Ia)—(VIIa) with toluene-p-thiolate gave the corresponding products (Ib)—(VIIb) in good yield. Only six chloro-derivatives could be studied kinetically, since the reaction of chlorodinitrobenzene (VIIa) was too fast.

Kinetics were measured spectrophotometrically by use of the rate of appearance of the product band at 370—405 nm. Rate coefficients are given in Table 1. Activa-

TABLE 1

Rate coefficients (k/l mol^{-1} s^{-1}) for the reaction of 4-substituted-2-nitrochlorobenzenes with p-MeC$_6$H$_4$S$^-$ in dimethylformamide at various temperatures t/°C

Z	k	t	k	t
OMe	0·0182	20·0	0·0769	39·6
Me	0·1524	40·9	0·275	50·0
H	0·00745	—9·5	0·1159	20·0
Cl	0·211	—31·1	0·500 ᵃ	—21·0
			0·531 ᵇ	—21·3
			0·486 ᶜ	—21·3
CO₂Me	50·8	—39·7	103·3	—29·4
			111·3	—29·4
COMe	84·5	—39·7	170	—29·4
	80·0	—39·7		
OMe	0·177	50·0	0·322	60·1
Me	0·534 ᵃ	60·5	1·061	71·9
	0·534 ᵇ	60·5		
	0·594 ᶜ	60·5		
H	0·586 ᵃ	40·2	1·293	50·3
	0·682 ᵇ	40·2		
	0·638 ᶜ	40·2		
Cl	1·418	—10·6	2·82	—0·2
CO₂Me	189	—21·0	343	—10·8
COMe	261	—20·9	536	—10·8

ᵃ Thiolate, ca. 1 × 10⁻²M. ᵇ Thiolate, ca. 2 × 10⁻²M.
ᶜ Thiolate, ca. 4 × 10⁻²M.

TABLE 2

Activation parameters and calculated rate ratios at 10 °C

Z	log A	$\Delta E^{\ddagger}$ kcal mol^{-1}	$\Delta S^{\ddagger}$ cal mol^{-1} K^{-1}	$\Delta H^{\ddagger}$ kcal mol^{-1}	$\frac{k_Z}{k_H}$
OMe	8·71	14·03	—20·75	13·41	0·1522
	±0·18	±0·26	±0·83	±0·26	
Me	8·65	13·60	—21·13	12·95	0·279
	±0·23	±0·35	±1·07	±0·35	
H	10·04	14·69	—14·52	14·12	1·00
	±0·11	±0·15	±0·48	±0·15	
Cl	9·50	11·28	—16·76	10·77	123·2
	±0·22	±0·25	±0·99	±0·25	
CO₂Me	9·25	8·06	—17·81	7·57	21,500
	±0·11	±0·13	±0·51	±0·13	
COMe	9·15	7·73	—18·28	7·24	30,300
	±0·18	±0·20	±0·80	±0·20	

tion parameters are shown in Table 2, together with relative rate coefficients calculated by the Arrhenius

equation for a temperature near the centre of the experimental range (10 °C).

Values of log k at 10 and 35 °C were correlated linearly with values of σ,[9] σ$^-$,[10a] linear combinations of σ^0 [10b] and σ$^-$ according to the Yukawa–Tsuno treatment,[10a] and with the substituent constants suggested by Brieux et al. (σ$_B$).[7] Results are shown in Table 3. Since a

TABLE 3

Correlation of rates by Hammett-type equations (r = correlation coefficient)

Substituent constants	No. of points	10 °C ρ	r	35 °C ρ	r
σ	6	7·39 ± 0·44	0·985	6·84 ± 0·37	0·987
	5 ᵃ	7·27 ± 0·62	0·977	6·75 ± 0·52	0·981
σ$^-$	6	5·19 ± 0·34	0·982	4·79 ± 0·31	0·982
	5 ᵃ	5·98 ± 0·34	0·990	5·54 ± 0·28	0·992
σ$_Y$ ᵇ	6	7·04 ± 0·21	0·996	6·65 ± 0·16	0·997
	5 ᵃ	7·21 ± 0·28	0·995	6·76 ± 0·22	0·996
σ$_B$ ᶜ	5 ᵃ	6·65 ± 0·23	0·996	6·15 ± 0·22	0·996

ᵃ Z = COMe is not included. ᵇ σ$_Y$ = σ^0 + r^-(σ$^-$ — σ^0); the best values of r^-, obtained by the six point correlation, were 0·45 and 0·40, at 10 and 35 °C, respectively, and were used also for the five point correlation. ᶜ Indicated as σ$_{PhS^-/MeOH}$ by ref. 7.

σ$_B$ value is not available for COMe, the relevant correlation was for five points only (Z, σ$_B$: OMe, —0·11; Me, —0·125; H, 0; Cl, 0·26; CO₂Me, 0·65). The temperature of 35 °C was chosen by Brieux et al.[7] for their reactivity comparisons. At this temperature, allowing a factor of 1·5 for the greater nucleophilicity of p-MeC$_6$-H$_4$S$^-$ than of PhS$^-$,[11] reactions of compounds (Ia)—(Va) are 4 × 10³—3 × 10⁴ times faster in dimethylformamide than in methanol. A high rate increase for the reactions of anionic nucleophiles due to this solvent change is common, and in the case of S_NAr reactions it can be attributed mainly to differing solvation of the nucleophile.[12] A comparison of the activation parameters for the reactions in dimethylformamide (Table 2) and in methanol[7] shows that the latter reactions are slower essentially because of higher values of the activation energy ($\Delta\Delta E^{\ddagger}$ 5—7 kcal mol^{-1}), in agreement with what is normally observed.[12]

The Hammett-type correlations (Table 3) show rather unsatisfactory correlation coefficients when σ or σ$^-$ values are used. The Yukawa–Tsuno correlation log (k/k_0) = ρ[σ^0 + r^-(σ$^-$ — σ^0)] is satisfactory; it corresponds to a value 0·40—0·45 for r^-, indicating a significant conjugative delocalisation of the negative charge in the transition state of the rate-determining step. Good correlation was obtained also with σ$_B$ constants, specifically calculated from the analogous reaction in methanol.[7] For direct comparison of the substituent effects in the two solvents, the ρ value obtained from the latter correlation is taken as the basis for discussion.

[9] D. H. McDaniel and H. C. Brown, J. Org. Chem., 1958, 23, 420.

[10] J. E. Leffler and E. Grunwald, 'Rates and Equilibria of Organic Reactions,' Wiley, New York, 1963 (a) p. 211; (b) p. 215.

[11] (a) G. S. Krishnamurthy and S. I. Miller, J. Amer. Chem. Soc., 1961, 83, 3961; (b) R. F. Hudson and G. Klopman, J. Chem. Soc., 1962, 1062; (c) D. J. McLennan, J. Chem. Soc. (B), 1966, 705; (d) p. 709; (e) G. Modena and P. E. Todesco, Gazzetta, 1959, 89, 866.

[12] A. J. Parker, Chem. Rev., 1969, 69, 1.

The reaction constant, $+6\cdot65$ at 10 and $+6\cdot15$ at 35 °C (Table 3), is evidence of a substituent effect significantly larger than for the reaction with benzenethiolate in methanol, which has ρ $+5\cdot15$ at 35 °C.[7] This result is not dependent on the particular choice of σ_B constants. Using other sets of σ values for correlating the experimental data of Brieux et al., one finds in any case a ρ value about one unit lower than the corresponding value in Table 3. The comparison is between reactions which differ in two points, namely the solvent (methanol for dimethylformamide) and the substituent on the arenethiolate (H for p-Me).

There are indications that the enhancement of reactivity by electron-withdrawing groups on the substrate is slightly greater when the thiolate is activated by electron-donating substituents, such as a $para$-methyl group, than when it is unsubstituted or deactivated.[11b] Therefore, part of the difference in ρ values can be justified by the different nucleophiles employed. However, this effect should be small, since toluene-p-thiolate has nucleophilic reactivity similar to that of benzenethiolate,[11] whichever the substrate. It seems reasonable to attribute a large fraction of the observed difference in ρ values to the change of solvent. Accordingly, this would appear to be a case where the reaction in dimethylformamide is not only faster, but also more sensitive to substituents, than the reaction in methanol, i.e., a case where higher reactivity is associated with higher selectivity. An analogous result has been reported by Bowden et al.[13] for the alkaline hydrolysis of 4-substituted 1-methoxy-2-nitrobenzenes in aqueous dimethyl sulphoxide with varying water content. Accepting the conclusion drawn in that case,[13,14] it is suggested that in the present case the transition state in methanol is stabilised through efficient charge dispersal by the 2-nitro-group solvated by the protic solvent using hydrogen bonding; the lack of this stabilisation of the transition state by solvation in dimethylformamide would increase the sensitivity of the reaction to substituents. A larger ρ value in dimethylformamide (dielectric constant D $36\cdot7$)[15] than in methanol ($D = 32\cdot6$)[16] represents another exception to the inverse dependence of ρ on the solvent polarity.

Having measured the substituent effect on the S_NAr reaction with toluene-p-thiolate in dimethylformamide, comparison is possible between the reactions of the substrates ArCl, $Ar_2C{=}CHCl$, and $ArC{\equiv}CCl$ with the same nucleophile–solvent system. Since the measured ρ values are $\rho_{Ar} = 6\cdot65$ (at 10 °C), $\rho_{ArC=C} = 4\cdot32$ (at 24 °C),[4b] and $\rho_{ArC\equiv C} = 3\cdot41$ (at -25 °C)[5] it is apparent that the three cases are similar,[5] but also that the transmission of substituent effects is attenuated in the last two cases. The ratio $\rho_{Ar} : \rho_{ArC=C}$ is $1 : 0\cdot68$ and the

ratio $\rho_{Ar} : \rho_{ArC\equiv C}$ is $1 : 0\cdot45$, when the ρ value for aromatic substitution is corrected to 24 and -25 °C, respectively. These ratios represent lower limits of the fall-off factors[17] for transmission through C=C and C≡C bonds, because in the ethylenic and acetylenic compounds only one substituent has been considered for each phenyl ring, while the present measurements involve chlorobenzene derivatives already activated by a 2-nitro-group: data for S_NAr reactions with alkoxide ions in alcohols[8] indicate ρ values of ca. 4 for 4-substituted 2-nitrohalogenobenzenes, and ca. 8 for 4-substituted halogenobenzenes.

Substituent effects on acid dissociation are attenuated by factors of ca. $1 : 0\cdot5$ when transmitted through either C=C or C≡C bonds.[1,18,19]

The spectroscopic properties of the products merit brief comment. N.m.r. spectra (Table 4) show that the

TABLE 4

N.m.r. spectra of sulphides [τ ($CDCl_3$)] (positions o, m, p are related to the nitro-group)

| Compound | Aromatic protons [b] | | | Methyl protons | |
	o	p	m	In p-MeC$_6$H$_4$S	In Z
(Ib) [a]	2·32	3·07	3·19	7·60	6·18
(IIb) [a]	2·00	2·87	3·24	7·60	7·66
(IIIb)	1·65—2·05(m)	c	c	7·58	
(IVb) [a]	1·81	2·76	3·20	7·57	
(Vb) [a]	1·18	2·06	3·08	7·56	6·08
(VIb) [a]	1·28	2·16	3·08	7·56	7·42
(VIIb) [a]	0·96	1·90	2·99	7·53	

[a] Protons o, m, p constitute an ABX system with J_{mp} 8—9·5 and J_{op} 2—2·5 Hz. [b] Signals from MeC$_6$H$_4$S gave a multiplet at τ 2·4—2·9. [c] τ 2·4—3·3(m) overlapping with the signals from MeC$_6$H$_4$S.

chemical shifts of the protons $ortho$ and $para$ to the nitro-group (which are $ortho$ with respect to Z) are markedly dependent on the electron-withdrawing capacity of the substituent Z, while the $meta$-protons have less variable chemical shifts.

U.v. spectra in dimethylformamide are limited to the

TABLE 5

U.v. absorption in dimethylformamide solutions

| | Reagents | | | Products | |
Compd.	$\lambda_{max.}$/nm	log ε	Compd.	$\lambda_{max.}$/nm	log ε
(Ia)	333	3·194	(Ib)	406	3·606
(IIa)	302	3·162	(IIb)	385	3·653
(IIIa)	294sh	3·129	(IIIb)	375	3·667
(IVa)	305	3·165	(IVb)	385	3·661
(Va)	294	3·099	(Vb)	287·5	4·191
				371·5	3·683
(VIa)	295sh	3·113	(VIb)	295·5	4·184
				370	3·710
(VIIa)	No features (280—400)		(VIIb)	342	4·045

longest wavelength band for most reagents and products. Both $\lambda_{max.}$ and ε of this band (Table 5) are higher for products than for reagents, assuring good conditions for

[13] K. Bowden and R. S. Cook, J. Chem. Soc., (B) 1971, 1765.
[14] See also C. D. Ritchie and W. F. Sager, Progr. Phys. Org. Chem., 1964, 2, 381.
[15] G. R. Leader and J. F. Gormley, J. Amer. Chem. Soc., 1951, 73, 5731.
[16] 'Landolt-Börnstein Zahlenwerte und Funktionen,' Band II, Teil 6, Springer Verlag, Berlin, 1959, p. 632.

[17] W. K. Kwok, R. A. More O'Ferrall, and S. I. Miller, Tetrahedron, 1964, 20, 1913.
[18] M. S. Newman and S. H. Merrill, J. Amer. Chem. Soc., 1955, 77, 5552.
[19] P. R. Wells, Chem. Rev., 1963, 63, 171.

analysis during kinetics. The spectra of diaryl sulphides (Ib)—(Vb) and (VIIb) in dimethylformamide can be compared with those of the corresponding 4-substituted 2-nitrodiphenyl sulphides, which differ only in the absence of the 4'-methyl group, in cyclohexane and in alcohols.[20,21]

A close analogy is observed. In all cases $\lambda_{max.}$ decreases, as a function of the substituent, in the order OMe > Cl $\simeq$ Me > H > CO$_2$Me > NO$_2$. The maxima listed in Table 5 appear at a longer wavelength than those of 4-substituted 2-nitrodiphenyl sulphides in methanol[21] (Z, $\Delta\lambda$: OMe, 6; Me, 10; H, 9; Cl, 8; CO$_2$Me, 11·5; NO$_2$, 13 nm). Since this bathochromic shift seems only slightly dependent on the nature of the substituent, it seems adequate to interpret it predominantly as a solvent effect. Similar bathochromic shifts have been observed for 4-substituted 2-nitrodiphenyl sulphides on changing the solvent from cyclohexane to methanol[21]

EXPERIMENTAL

U.v. and n.m.r. spectra were usually taken on Beckmann DK-2A (occasionally a Hitachi–Perkin-Elmer 124) and Varian A-60 instruments, respectively. Tetramethylsilane was used as standard and CDCl$_3$ as solvent for n.m.r. spectroscopy. Purity was checked by g.l.c. on SE-30 5—20% columns at 200—250 °C with a C. Erba Fractovap GT chromatograph (flame ionisation detector). Dimethylformamide for kinetic runs was a ' spectrograde ' C. Erba RS solvent. Sodium toluene-p-thiolate was prepared as described[5] from recrystallised toluene-p-thiol. Substituted chloronitrobenzenes, either purified commercial products or prepared by standard procedures, were $\geqslant$99·5% pure by g.l.c. and had correct elemental analyses; their m.p.s agreed with literature values within 1 °C.

4-*Substituted* 2-*Nitro*-p-*tolylthiobenzenes* (Ib)—(VIIb).— These were prepared from the reaction of the corresponding chlorobenzenes and toluene-p-thiolate, both *ca.* 1M ([thiolate]/[substrate] = 1·06), during 4 h at room temperature, in 85—98% yield. The solvent was dimethylformamide purified by distillation with water and benzene.[22] Products were >99% pure by g.l.c., and had correct analysis. U.v. spectra of (IIIb) and (VIIb) in ethanol agreed with those in the literature.[20]

4-*Methoxy*-2-*nitro*-p-*tolylthiobenzene* (Ib).—This was obtained as yellow *crystals*, m.p. 92—93 °C (from carbon tetrachloride) (Found: C, 61·8; H, 4·8; N, 5·4. C$_{14}$H$_{13}$-NO$_3$S requires C, 61·1; H, 4·8; N, 5·1%).

Methyl 3-*Nitro*-4-p-*tolylthiobenzoate* (Vb).—This was obtained as yellow *crystals*, m.p. 98—99 °C (from ethanol) (Found: C, 60·1; H, 4·3; N, 4·6. C$_{15}$H$_{13}$NO$_4$S requires C, 59·4; H, 4·3; N, 4·6%).

Kinetics.—(a) In one case [(Ia) at 20 °C] the reaction was carried out in a thermostatted ($\pm$0·1 °C) Pyrex vessel, with weighed amounts of reactants (*ca.* 10^{-2}M; [thiolate]/ [substrate] = 2). Samples were taken and analysed by spectrophotometry after quenching by dilution.

(b) In other cases [(Va) and (VIa)] reactions were carried out in a 10 mm quartz cell in the thermostatted ($\pm$0·1 °C) cell compartment of the spectrophotometer. *ca.* 10^{-2}M Solutions were prepared by weighing reactants separately; known amounts (30—40 μl) of the substrate and (later) of the thiolate solution were added to the thermostatted solvent by means of a syringe; *ca.* 10^{-4}M solutions were obtained ([thiolate]/[substrate] 1·2—1·5). Oxidation of the thiolate was negligible at the low temperature and during the short times of the runs.

(c) The remaining reactions were carried out by a procedure similar to (b). Known amounts of the substrate solution were added to the thermostatted ($\pm$0·1 °C) thiolate solution, in order to obtain concentrations of the order of 10^{-2}M for the thiolate and 10^{-4}M for the substrate.

Reactions were carried out under nitrogen. In cases (b) and (c) the gas, injected by syringe, had also the effect of thoroughly mixing the solutions.

Absorbance values were read at fixed wavelengths; experimental ' zero ' and ' infinity ' values were used throughout. Infinity values were close to the theoretical. In cases (a) and (b) second-order rate coefficients (k) were obtained; their probable errors were on the average 1·2% of each measured value. In cases (c), pseudo-first order coefficients (k') were calculated; probable errors were in this case 0·6% on the average. Second-order rate coefficients were obtained as $k = k'/$[thiolate].

Activation parameters were calculated by the Arrhenius (log A, $\Delta E^{\ddagger}$) and the Eyring ($\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$) equations. Least squares fitting by computer was used throughout. Uncertainties are given as probable errors.

[20] (a) A. Mangini and R. Passerini, *J. Chem. Soc.*, 1952, 1168; (b) G. Leandri, A. Mangini, and R. Passerini, *Gazzetta*, 1954, **84**, 3.

[21] A. M. Porto, L. Altieri, A. J. Castro, and J. A. Brieux, *J. Chem. Soc.* (B), 1971, 1360.
[22] W. Bunge, ' Houben-Weyl, Methoden der Organischen Chemie,' Thieme Verlag, Stuttgart, vol. I/2, 1959, p. 831.