The Kinetics of the Reactions of Picryl Chloride with Some Substituted Anilines. Part II.[1]

By **Sunday I. Ette** and **Jack Hirst,*** Department of Chemistry, University of Ibadan, Ibadan, Nigeria

Arrhenius parameters have been measured for the reactions of 3-X- and 3,5-di-X-substituted anilines (X = F, Cl, Br, or I) with picryl chloride in methanol. The reactions of the disubstituted anilines obey an isokinetic relationship and one may exist for the monosubstituted nucleophiles. The rate sequence for the disubstituted anilines between -30 and $75°$ is governed by the $-I$ effect of the halogens, but the rate sequences of the monosubstituted anilines are temperature dependent. The effect of the fluoro-, chloro-, and iodo-substituents on the free energy of activation is not additive.

THE effect of 3-halogeno-substituents in the nucleophile on the rates of aromatic nucleophilic substitution reactions has not been studied extensively. When substituted anilines are the nucleophiles, the effects of 3-chloro- and -bromo-substituents with 1-fluoro-2,4-dinitrobenzene as the substrate have been studied by Chapman and Parker,[2] and with 1-chloro-2,4-dinitrobenzene as the substrate by Singh and Peacock.[3] The rates of reaction of 3-fluoro- and -chloro-anilines with 2-chloro-3-cyano-5-nitropyridine have been measured

[1] Part I, J. Hirst and Khalil-Ur-Rahman, *J.C.S. Perkin II*, 1973, 2119.

[2] N. B. Chapman and R. E. Parker, *J. Chem. Soc.*, 1951, 3301.
[3] A. Singh and D. H. Peacock, *J. Chem. Soc.*, 1935, 1411.

by Chapman *et al.*[4] As far as we are aware, there has been no investigation of the effect of all four halogens from the 3-position of nucleophiles in aromatic nucleophilic substitution reactions.

The objects of the present work were to study the kinetics of the reactions of all eight 3-X- and 3,5-X$_2$-substituted anilines (X = F, Cl, Br, or I) with picryl chloride in methanol. The results for the mono-substituted series could then be compared with the effects of similar substitutions on the rates of methoxy-defluorination of 3-X-5-nitrofluorobenzenes[5] and the effect of 3-halogen substitution in the nucleophile and

measurements were made, the plot does not necessarily establish an isokinetic relationship.[6]

The rates of reaction calculated at various temperatures are given in Table 2. The effect of 3-halogen substitution is moderately deactivating, the rates being *ca.* 15 times less than for aniline itself. The rate span encompassed by the four halogens is extremely small, and within this span the rate sequences are temperature dependent, being F > I > Cl ~ Br at 0°; F > Cl ~ Br > I at 25°; and Br > Cl > F > I between 50 and 100°. This latter sequence is also that of the entropies of activation. Hirst and Rahman[1]

TABLE 1

Arrhenius parameters for the reaction of picryl chloride with some substituted anilines in methanol

Substituent	3-F	3-Cl	3-Br	3-I	3,5-F$_2$
E/kcal mol^{-1} [a]	9·7 ± 0·03	10·4 ± 0·03	10·8 ± 0·17	9·1 ± 0·08	15·2 ± 0·10
log(A/s^{-1})	5·75	6·24	6·53	5·24	7·98
Substituent	3,5-Cl$_2$	3,5-Br$_2$	3,5-I$_2$	3-NO$_2$	H
E/kcal mol^{-1} [a]	14·1 ± 0·03	12·5 ± 0·07	11·2 ± 0·10	10·6 ± 0·10 (10·7)[b] (10·9)[c]	7·9 ± 0·35[c]
log(A/s^{-1})	7·30	6·29	5·73	5·08 (5·20)[b] (5·34)[c]	5·59[c]

[a] Errors are standard deviations. [b] Values of ref. 1. [c] Values of C. W. L. Bevan and J. Hirst, *J. Chem. Soc.*, 1956, 254.

TABLE 2

Rate constants (1 mol^{-1} s^{-1}) calculated at various temperatures for the reactions of picryl chloride with 3-halogeno- and 3,5-dihalogeno-anilines in methanol

t/°C	−30	0	25	50	75	100
Substituent	$10^6 k_2$	$10^5 k_2$	$10^4 k_2$	$10^3 k_2$	$10^2 k_2$	$10^2 k_2$
3-F	1·12 × 10³	1·00 × 10³	4·49 × 10²	1·54 × 10²	45·7	117
3-Cl	7·80 × 10²	8·23 × 10²	4·12 × 10²	1·60 × 10²	50·9	140
3-Br	6·65 × 10²	7·97 × 10²	4·09 × 10²	1·68 × 10²	56·1	160
3-I	1·15 × 10³	9·10 × 10²	3·71 × 10²	1·22 × 10²	33·6	81·1
3,5-F$_2$	2·04	6·59	6·90	5·00	2·78	12·1
3,5-Cl$_2$	4·17	10·3	9·12	5·79	2·82	11·1
3,5-Br$_2$	11·2	19·6	13·4	6·89	2·79	9·33
3,5-I$_2$	45·7	58·2	33·0	14·2	4·99	14·7
H	3·35 × 10⁴ [a]		7·04 × 10³ [b]			

[a] Calculated from the results of C. W. L. Bevan, J. Hirst, and W. O. Uwamu, *Nigerian J. Sci.*, 1968, 2, 151. [b] Value measured at 25° reported in ref. 1.

substrate in aromatic nucleophilic substitution compared. From the results for the mono- and di-substituted series information would be obtained on the additivity of substituent effects from the 3-position on the free energies of activation of these reactions. The Arrhenius parameters for the reactions of 3-nitroaniline with picryl chloride were also measured to establish the validity of any comparison of the present results with those of previous workers. The results are presented in Table 1.

The Monosubstituted Series.—From Table 1 the log of the frequency factor increases with increase in the activation energy and a plot of ΔH^* against ΔS^* gives a straight line of slope 288. However as the variations in ΔH^* and ΔS^* are small, and the value of the slope is only 15° above the temperature at which some of the

have reported that for the same reaction system in acetonitrile, when the substituents are 3-CF$_3$, 3-SO$_2$Me, and 3-NO$_2$, the rate sequence is entirely entropy controlled. Because of the small rate span and the temperature dependence of the rate sequence, it is not legitimate to compare any particular sequence with the sequence I > Br > Cl obtained by Bolton and Hall[7] for the pK_a values of the dissociation of anilinium ions between 5 and 50° or the activation sequence Br > Cl > I > F obtained by Bevan *et al.*[5] for the methoxydefluorination of 3-halogeno-5-nitrofluorobenzenes, although the deactivation sequence Br > Cl > I ~ F obtained at −30°, a temperature where any possible compensation effects should be small, is very similar to the activating sequence in the methoxydefluorination.

[4] N. B. Chapman, D. K. Chaudhury, and J. Shorter, *J. Chem. Soc.*, 1962, 1975.

[5] C. W. L. Bevan, J. Hirst, and S. J. Una, *Nigerian J. Sci.*, 1966, 1, 27.

[6] J. F. Bunnett, ' Technique of Organic Chemistry,' Interscience, New York, 1961, vol. VIII, part I, p. 204.

[7] P. D. Bolton and F. M. Hall, *Austral. J. Chem.*, 1968, 21, 939.

None of the rate sequences quoted above, nor the sequence of activation energies are those expected from the operation of a pure inductive or mesomeric effect, and the substituent effect must be due to a combination of the two effects. The effect of 3-halogeno-substituents was discussed by Dippy and Lewis,[8] who showed that any halogen sequence from F > Cl > Br > I to the reverse F < Cl < Br < I, could be obtained by a judicious combination of the two effects. More recently, Brown and Okomato [9] have investigated the effect of 3-halogeno-substituents on the solvolysis of 1-methyl-1-phenylethyl chloride in aqueous acetone and the sequences of activation energies and log A factors they obtained are very similar to the ones reported here.

The Disubstituted Series.—In this series the activation energies increase from iodine, through chlorine and bromine, to fluorine, and the log A factors increase with increasing activation energies. A plot of ΔH^* against ΔS^* has a slope of 368 and a plot of log k_2^{25} against log k_2^{-30} is linear. As the variations in both ΔH^* and ΔS^* are much greater than in the monosubstituted series and the isokinetic temperature is 45° greater than the highest temperature at which the rate measurements were made, we take this as demonstrating a true iso-kinetic relationship.

The spread of reactivity is much greater in this series than in the monosubstituted one; at −30° there is an *ca.* 20-fold difference between the slowest and fastest members. In the temperature range −30 to 50°, temperatures well removed from the iso-kinetic one, the rate sequence is I > Br > Cl > F, and the sequence is determined by the energies of activation. This sequence shows that the −I effect dominates the total substituent effect of the halogens in this series. As the isokinetic temperature is approached the pattern changes showing the increased importance of the entropy of activation. The span of reactivities also decreases as would be expected, and at 100°, a temperature very close to the isokinetic one, there is only approximately a 1·5-fold difference between the slowest and fastest reactions.

In considering the additivity of substituent effects, it is usually stated that this is most likely to occur in the benzene series when the substituents are in positions 3 and 5 to the reaction centre.[10] The assumption of additivity of the free energies of activation leads to the expression $k_{xy} = k_x k_y / k_H$, where k_H, k_x, k_y, and k_{xy} are the rate constants for the unsubstituted, mono-, and di-substituted reactants. The rate constants, and their statistical deviations, at 25° for the reactions of the 3,5-dihalogenoanilines calculated in this manner * are assembled in Table 3, together with the rate constants (and their statistical deviations) obtained by calculation

* The value for aniline of $7·04 \pm 0·01 \times 10^{-1}$, determined directly at 25° by Hirst and Rahman,[1] was used in these calculations.

[8] J. F. J. Dippy and R. H. Lewis, *J. Chem. Soc.*, 1936, 644.
[9] H. C. Brown, Y. Okomato, and C. Ham, *J. Amer. Chem. Soc.*, 1957, **79**, 1906.

from the experimentally determined Arrhenius parameters. According to the criteria described previously,[1] only the effect of the bromo-substituent is additive.

TABLE 3

A comparison of the rate constants (l mol⁻¹ s⁻¹) at 25° for the reactions of 3,5-dihalogenoanilines with picryl chloride in methanol calculated (i) on the assumption of additivity of the free energies of activation ($k_{calc.}$) and (ii) from the measured Arrhenius parameters of the reaction (k_m)

Substituent	F	Cl	Br	I
$10^4 k_{calc.}$	28 ± 2	24 ± 2	23 ± 10	20 ± 4
$10^4 k_m$	$6·9 \pm 1$	$9·1 \pm 0·5$	$13·4 \pm 1·5$	33 ± 6

The concept of additivity of substituent effects from the 3- and 5-positions rests on the assumption that these substituents influence the reaction centre by their inductive effects, and all other effects are of very minor importance. In the reactions investigated, the rates are strongly influenced by conjugation of the nitrogen lone pair electrons with the benzene ring,
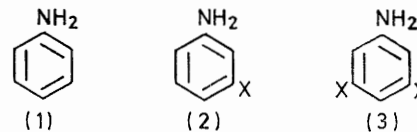
and the extent of this conjugation is dependent on the charges present on the carbon atoms *ortho* and *para* to the amino-group. In the series (1)—(3) where X is a substituent that can release electrons mesomerically, the effective distribution of charges at positions *ortho* and *para* to the amino-group is different in all three compounds. Hence the difference in the mesomeric interaction energy of the amino-group between aniline and the monosubstituted aniline is unlikely to be the same as the difference between the mono- and di-substituted anilines, and hence the changes in the free energies of activation when aniline and 3-substituted anilines are the nucleophiles are not expected to be the same as when the nucleophiles are 3- and 3,5-substituted anilines. Thus it is not surprising that at least when the substituents are fluorine and chlorine, the two halogens with the most powerful +M effects, additivity of substituent effects on the free energies of activation is not observed.

EXPERIMENTAL

Materials.—3-Fluoro-, b.p. 52° at 2 mmHg, 3-chloro-, b.p. 70° at 0·3 mmHg, 3-bromo-, b.p. 92° at 1·5 mmHg, and 3-iodo-, b.p. 80° at 0·2 mmHg, -anilines were commercial samples purified by fractionation. A commercial sample of 3,5-dichloroaniline was recrystallised from aqueous methanol, m.p. 50—51° (lit.,[11] 50°). Picryl chloride, m.p. 84—84·5° (lit.,[12] 84°), was prepared by the method of Boyer *et al.*[12]

[10] P. D. Bolton and F. M. Hall, *J. Chem. Soc.* (B), 1970, 1248.
[11] G. M. Dyson, H. J. George, and R. F. Hunter, *J. Chem. Soc.*, 1926, 3043.
[12] R. Boyer, E. Y. Spencer, and G. F. Wright, *Canad. J. Res.*, 1946, **24B**, 202.

3,5-*Di-iodoaniline.*—2,6-Di-iodo-4-nitroaniline, m.p. 244—246° (lit.,[13] 243—245°), prepared by Sandin's [13] procedure, was deaminated by the method of Hodgson and Turner,[14] using one-twelfth of the specified amount of cuprous oxide. Recrystallisation of the product from methanol gave 3,5-di-iodonitrobenzene, m.p. 104° (lit.,[15] 103°). Reduction of the nitro-compound with hydrazine and Raney nickel gave 3,5-di-iodoaniline, m.p. 106° (lit.,[15] 107°).

3,5-*Dibromoaniline.*—2,6-Dibromo-4-nitroaniline, m.p. 205—206° (lit.,[16] 206°), prepared by the method of Shepherd,[16] was deaminated and reduced by the methods described for the iodo-compound. The 3,5-dibromoaniline had m.p. 56·5—57° (lit.,[16] 56—57°).

were left for sufficient time to ensure completion of the reaction. For the reactions of the monosubstituted anilines, the reaction mixture was poured into ice–water, filtered, washed, dried, and weighed. The products of the reactions of the disubstituted anilines are insoluble in methanol, and were filtered off directly from the reaction mixture. All the products were recrystallised and the m.p.s determined. The following yields of products were obtained: 3-*fluoro*-2′,4′,6′-*trinitrodiphenylamine*, 98·8%, m.p. 135—136° (Found: C, 44·65; H, 2·25; N, 17·3. $C_{12}H_7FN_4O_6$ requires C, 44·75; H, 2·2; N, 17·4%); 3-chloro-2′,4′,6′-trinitrodiphenylamine, 98%, m.p. 141—142° (lit.,[19] 137—139°); 3-*bromo*-2′,4′,6′-*trinitrodiphenylamine*, 97·8%, m.p. 144—145° (Found: C, 37·7; H, 1·9;

TABLE 4

Rate constants for the reactions of 3-halogeno- and 3,5-dihalogeno-anilines with picryl chloride in methanol at various temperatures

Substituent	3-F		3-Cl		3-Br		3-I	
	$t/°C$	$\dfrac{10^3 k_2}{\text{l mol}^{-1}\,\text{s}^{-1}}$	$t/°C$	$\dfrac{10^4 k_2}{\text{l mol}^{-1}\,\text{s}^{-1}}$	$t/°C$	$\dfrac{10^4 k_2}{\text{l mol}^{-1}\,\text{s}^{-1}}$	$t/°C$	$\dfrac{10^3 k_2}{\text{l mol}^{-1}\,\text{s}^{-1}}$
	0·1	10·0	−0·5	82·3	−0·7	79·7	−0·8	8·75
	−10·3	4·95	−10·1	40·7	−9·4	38·2	−10·3	4·75
	−20·3	2·37	−20·3	18·4	−20·3	15·5	−19·5	2·51
	−30·3	1·07	−28·5	8·99	−28·3	7·61	−30·3	1·16

Substituent	3,5-F$_2$		3,5-Cl$_2$		3,5-Br$_2$		3,5-I$_2$	
	$t/°C$	$\dfrac{10^4 k_2}{\text{l mol}^{-1}\,\text{s}^{-1}}$	$t/°C$	$\dfrac{10^4 k_2}{\text{l mol}^{-1}\,\text{s}^{-1}}$	$t/°C$	$\dfrac{10^4 k_2}{\text{l mol}^{-1}\,\text{s}^{-1}}$	$t/°C$	$\dfrac{10^3 k_2}{\text{l mol}^{-1}\,\text{s}^{-1}}$
	41·1	24·5	49·9	54·4	39·9	36·0	40·4	8·13
	29·9	10·9	41·1	29·3	30·2	18·9	30·8	4·58
	19·7	4·65	29·9	12·7	21·9	10·5	9·4	1·13
	10·1	1·88	19·9	5·70	10·3	4·41		

3,5-*Difluoroaniline.*—3-Fluoro-5-nitroaniline, m.p. 112—115° (lit.,[4] 115°), was obtained by reduction of 3,5-dinitrofluorobenzene with methanolic sodium hydrogen sulphide. Fluorination of the amine by Steck and Fletcher's [17] modification of the Schiemann reaction gave 3,5-difluoronitrobenzene as a yellow oil which was purified by chromotography on an alumina column. Reduction of a methanolic solution of the nitro compound with Raney nickel and hydrazine gave 3,5-difluoroaniline, m.p. 37—39° (lit.,[18] 40°).

Kinetic Measurements.—Details of the method of purification of methanol and the procedure for following the rates of the reactions by potentiometric titration of liberated chloride ions have been given elsewhere.[1] In all kinetic runs the initial concentrations of amine and picryl chloride were *ca.* 1×10^{-1}M and *ca.* 3×10^{-2}M. The results at various temperatures are given in Table 4.

Product Analyses.—Known values of the reaction mixture

N, 14·6; Br, 20·8. $C_{12}H_7BrN_4O_6$ requires C, 37·6; H, 1·8; N, 14·6; Br, 20·9%); 3-iodo-2′,4′,6′-trinitrodiphenylamine, 98·2%, m.p. 151—152° (lit.,[20] 150—152°); 3,5-*difluoro*-2′,4′,6′-*trinitrodiphenylamine*, 99%, m.p. 190—194° (Found: C, 42·45; H, 1·6; N, 16·6. $C_{12}H_6F_2N_4O_6$ requires C, 42·4; H, 1·8; N, 16·5%); 3,5-*dichloro*-2′,4′,6′-*trinitrodiphenylamine*, 98·2%, m.p. 221·5—222° (Found: C, 38·6; H, 1·7; N, 15·2. $C_{12}H_6Cl_2N_4O_6$ requires C, 38·6; H, 1·6; N, 15·0%); 3,5-*dibromo*-2′,4′,6′-*trinitrodiphenylamine*, 99·4%, m.p. 240·5—241° (Found: C, 31·25; H, 1·35; N, 12·25. $C_{12}H_6Br_2N_4O_6$ requires C, 31·2; H, 1·3; N, 12·1%); 3,5-*di-iodo*-2′,4′,6′-*trinitrodiphenylamine*, 99·4%, m.p. 241—242° (Found: C, 25·8; H, 1·2; N, 10·25. $C_{12}H_6I_2N_4O_6$ requires C, 25·9; H, 1·1; N, 10·1%).

[13] R. B. Sandin, W. V. Drake, and F. Leger, *Organic Synth.*, Coll. Vol. II, 1943, p. 196.
[14] H. H. Hodgson and H. S. Turner, *J. Chem. Soc.*, 1942, 748.
[15] V. Brenans, *Comp. rend.*, 1903, **136**, 236.
[16] R. G. Shepherd, *J. Org. Chem.*, 1947, **12**, 275.
[17] E. A. Steck and L. T. Fletcher, *J. Amer. Chem. Soc.*, 1948, **70**, 439.
[18] G. C. Finger and R. H. Reed, *J. Amer. Chem. Soc.*, 1951, **73**, 153.
[19] E. Wedekind, *Ber.*, 1900, **33**, 432.
[20] B. Linke, *Ber.*, 1923, **56B**, 848.