The Kinetics of the Reactions of Picryl Chloride with Some Substituted Anilines. Part 7.[1] 2-Substituted and 2,5-Disubstituted Anilines

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Arrhenius parameters have been measured for the reactions of picryl chloride with the following substituted anilines in acetonitrile: 2-X (X = F, Cl, Br, I, Me, or OMe); 2,5-X_2 (X = Cl, Br, Me, or OMe); 2-X-5-NO_2 (X = F, Cl, Me, or OMe). Steric effects are shown to be present in the reactions of the 2-substituted series. In the disubstituted series the effect of 2,5-dimethyl and 2-methoxy-5-nitro-groups on the free energy of activation is strictly additive, but for the rest the measured rate constants are less than those calculated on the assumption of additivity. The results are consistent with a previously proposed explanation of deviation of substituent effects from additivity.

In Part 6[1] we investigated the reactions of some 4-substituted and 3,4-disubstituted anilines with picryl chloride in acetonitrile. We now discuss the reactions of some 2-substituted and 2,5-disubstituted anilines. There are only a few reports in the literature of the reactions of 2-substituted anilines in nucleophilic aromatic substitution. Van Opstall[2] measured the rate of reaction at some 2-substituted anilines with 1-chloro-2,4-dinitrobenzene and 1-chloro-2,4-dinitronaphthalene in ethanol and Singh and Peacock[3] obtained the Arrhenius parameters for the reactions of 2-methyl- and 2-methoxy-anilines with 1-chloro-2,4-dinitrobenzene in the same solvent. More recently Chapman *et al.*[4] studied the reactions of 2-methyl-, 2-fluoro-, and 2-chloro-anilines with 2-chloro-3-cyano-5-nitropyridine in methanol and Consiglio *et al.*[5] have shown that the rate constants for the reactions of six 2-substituted anilines with 2-bromo-3,5-dinitrothiophen in the same solvent obey the Fujita–Nishioka equation.[6] An attempt by Bevan *et al.*[7] to study the reaction of 2-nitroaniline with picryl chloride in methanol failed because the nucleophile was so unreactive that only solvolysis occurred.

Arrhenius parameters for the reactions of picryl chloride with some substituted anilines in acetonitrile and a comparison of rate constants (l mol^{-1} s^{-1}) measured directly at 25 °C (k_m) with those calculated on the assumption of additivity of the free energies of activation (k_{calc})

Substituent	E/kcal mol^{-1} [a]	log A	10^7k_m	10^7 k_{calc} [b]
2-F	9.5 ± 0.01	4.50	$3.32 \pm 0.05 \times 10^4$	
2-Cl	10.3 ± 0.06	3.56	$1.02 \pm 0.003 \times 10^3$	
2-Br	10.5 ± 0.09	3.28	$3.80 \pm 0.01 \times 10^2$	
2-I	13.7 ± 0.1	5.18	$1.44 \pm 0.05 \times 10^2$	
2-Me	9.15 ± 0.1	4.55	$6.90 \pm 0.02 \times 10^4$	
2-OMe	8.2 ± 0.06	5.35	$2.20 \pm 0.008 \times 10^6$	
2-5-$(Cl)_2$	13.4 ± 0.1	4.08	$1.68 \pm 0.14 \times 10$ [c]	$3.17 \pm 0.03 \times 10$
2,5Br_2	13.6 ± 0.07	3.94	9.15 ± 1.08 [c]	$1.26 \pm 0.01 \times 10$
2,5-Me_2	9.8 ± 0.1	5.18	$9.80 \pm 0.05 \times 10^4$	$9.74 \pm 0.9 \times 10^4$
2,5-$(OMe)_2$	9.3 ± 0.1	5.77	$8.45 \pm 0.07 \times 10^5$	$9.59 \pm 0.1 \times 10^5$
2-F-5-NO_2	12.3 ± 0.2	3.67	$4.48 \pm 1.21 \times 10$ [c]	$9.26 \pm 0.16 \times 10$
2-Cl-5-NO_2	13.1 ± 0.07	3.00	2.48 ± 0.3 [c]	2.85 ± 0.02
2-Me-5-NO_2	12.4 ± 0.1	4.21	$1.27 \pm 0.21 \times 10^2$ [c]	$1.92 \pm 0.02 \times 10^2$
2-OMe-5-NO_2	10.9 ± 0.1	4.81	$6.24 \pm 0.07 \times 10^3$	$6.14 \pm 0.06 \times 10^3$
H [d]	7.9 ± 0.27	5.06	$2.04 \pm 0.01 \times 10^6$	

[a] The errors quoted are standard errors of the mean. [b] For values of the rate constants for aniline and 5-substituted-anilines used in these calculations see refs. 10 and 14 and T. A. Emokpae, O. Equavuen, and J. Hirst, *J. Chem. Soc., Perkin Trans. 2,* 1980, 829. [c] Values calculated from the Arrhenius parameters. [d] Values from ref. 15.

We have studied the reactions of 2-X- (X = F, Cl, Br, I, Me, or OMe), 2,5-X_2- (X = Cl, Br, Me, or OMe), and 2-X-5-nitro- (X = F, Cl, Me, or OMe) anilines with picryl chloride in acetonitrile and the results are given in the Table. The reactions were monitored by the spectrophotometric determination of the products of reaction with the amines in large enough excess to ensure first-order kinetics. Good kinetics were obtained except initially for 2-iodoaniline. As this compound is not very reactive, initial measurements were made at 90° and upwards, but at these temperatures iodine was liberated. By using extended reaction times at the much lower temperature range 25—46° however a clean reaction was obtained. In all cases the absorbances measured at the completion of the reaction agreed with the calculated ones.

The effect of 2-halogen substituents is strongly deactivating, reducing the rate constants by factors of between 1.6×10^{-2} to 7×10^{-5} at 25°. The reactivity sequence F > Cl > Br > I observed at 0—25° changes to F > Cl > I > Br at 100 and in this respect differs from the 4-series[1] where the order F > Cl > Br > I is invariant at 0—100°. The span of reactivity is also much greater in the 2-series, due chiefly to the large difference in the rate constant between fluorine and the rest of the halogens. The halogens are much more deactivating from the 2- than from the 4-position; at 25° the k_2/k_4 values are F, 2.23×10^{-2}; Cl, 3.39×10^{-3};

Br, 1.69×10^{-3}; I, 7.62×10^{-4}. The introduction of a 2-methoxy-group has a very slight activating effect (k_2/k_H 1.08 at 25°) compared with its effect at the 4-position [1] where it increases the rate constant by a factor of 12.7. This result is in contrast to its deactivating effect in the reaction of aniline with 1-chloro-2,4-dinitrobenzene [3] and the anilinodebromination of 2-bromo-3,5-dinitrothiophen [5] where the introduction of a methoxy-group reduces the rate constant by factors of 3.2 and 1.5, respectively. It is also in contrast to the mild, 1.4-fold deactivation observed for this group by Vizgert *et al.*[8] for the reaction of substituted anilines with 2,4-dinitrophenyl benzenesulphonates although the factor of 11.8 obtained for the difference in the effect of the group on changing from the 2- to the 4-position is similar to that of 13.7 observed by these authors for the same change. A 2-methyl group has a pronounced deactivating effect, reducing the rate constant by a factor of *ca.* 30, which can be compared with an enhancement of 3.8 when it is substituted at the 4-position.[1] Deactivating effects of a 2-methyl group have previously been reported for the reactions of substituted anilines with 2-chloro-3-cyano-5-nitropyridine,[4] 2-bromo-3,5-dinitrothiophen,[5] 2,4-dinitrophenyl benzenesulphonate,[8] and by both Van Opstall [2] and Singh and Peacock [3] for reaction with 1-chloro-2,4-dinitrobenzene. The halogens and the methoxy-group are $-I + K$ substituents and the deactivating effect observed when they are moved from the 4- to the 2-position could be due to a relative increase in the inductive effect compared with the conjugative effect as they become closer to the reaction centre. This explanation cannot hold for the methyl group and its deactivating effect in the 2-position must be due to a steric or *ortho*-effect.

Apart from Consiglio *et al.*'s demonstration [5] that the anilinodebromination of 2-bromo-3,5-dinitrothiophen obeys the Fugita–Nishioka equation, the only discussion of which we are aware of *ortho*-effects in the nucleophile of nucleophilic aromatic substitution reactions is due to Chapman *et al.*[4] These authors analysed their results in terms of a primary steric effect tending to decrease log A and steric inhibition of solvation of the transition state tending to increase log A. Using these criteria, together with models of the transition state, they concluded that while for their system a 2-fluoro-substituent had no steric effect, with 2-chloro there was compensation between two opposing factors, a primary steric effect due to a slight restriction of the rotation of the aniline ring round the ring–N bond and steric inhibition of solvation of the transition state. As the log A factor for 2-methylaniline was *ca.* 1.5 units higher than for aniline they concluded that the effect of the methyl group was probably due to steric inhibition of solvation of the transition state.

As the steric requirement of a methyl group is slightly less than that of chlorine,[9] the observation of an *ortho*-effect for a 2-methyl group in the present work implies than this effect must also be present in the reactions of 2-chloro-, -bromo-, and -iodo-anilines. The log A factors for 2-methyl and all the 2-halogeno-substituted anilines with the exception of the iodo-compound are all less than that of aniline and values of $\Delta\log A$ ($= \log A_2 - \log A_4$) of Cl, -2 07; Br, -1.84; and Me, -1.08, would seem to indicate the operation of a primary steric effect. There is a dramatic increase of 3.2 kcal mol^{-1} in the activation energy of the 2-iodo-compound compared with that of the 2-bromo-derivative and its value of $\Delta E (= E_2 - E_4)$ of 4.3 compared with 1.3 kcal mol^{-1} for the bromoanilines. This together with the log A value of the 2-iodo, 1.9 units greater than that of the 2-bromo, and a $\Delta\log A$ value of $+0.01$ suggests that a large increase in steric hindrance to solvation of the transition state occurs between the 2-bromo- and 2-iodo-substituted anilines.

The methoxy-group is smaller than the methyl group and there is no unambiguous experimental evidence for the operation of an *ortho*-effect when it is in the 2-position, the value of log A being very close to that of 5.25 recorded for 3-methoxyaniline.[10] There is however indirect evidence that the presence of 2,6-dinitro-groups in the substrate leads to small steric retardations of rate in nucleophilic aromatic aminodehalogenation reactions. Thus Miller [11] has interpreted Parker and Read's observation [12] that 2,6-dinitrohalogenobenzenes are less reactive towards aniline than 2,4-dinitrohalogenobenzenes as due to greater steric interactions in the 2,6-isomer. Similarly Alexander *et al.*[13] have attributed the lower reactivity of picryl chloride compared with that of 1-chloro-2,4-dinitrobenzene towards piperidine * as due to steric effects. The much greater values of the enthalpy, entropy, and volume of activation for the picryl substrate suggest a large contribution from steric hindrance of solvation of the transition state. Hence on this basis even small groups in the 2-position of aniline would have some steric interaction with the substrate.

The present results allow a comparison of the deactivating effect of a 5-nitro-group in the 2-, 3-, and 4-substituted aniline series. In the 2-series, a 5-nitro-group reduces the rate constant by a factor of between 1.4×10^{-3} and 2.8×10^{-3}; in the 3-series the factor is 2—3.8×10^{-3} and in the 4-series 3.3—4.7×10^{-3}. Hence there is little difference in its effect on the three series; at the most there is a factor of two between its effect in the most (2-) and least (4-) sensitive series. This result would be expected if the effects of the groups in the three series were roughly additive. For precise additivity the factor is [14] 2.8×10^{-3}.

In earlier Parts we have tested for the additivity of substituent effects on the free energy of activation by

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* This result implies a great sensitivity of the steric effect to the nucleophile employed, as Parker and Read (*J. Chem. Soc.*, 1962, 9) have shown that in ethanol the rate constants for the reactions of picryl halides with aniline are 7 000—20 000 times greater than those of the corresponding 2,4-dinitrohalogenobenzenes due to decreases of 2—3 kcal mol^{-1} in the activation energies and increases of 2—3 units in log A. Eggimann *et al.* (*Helv. Chim. Acta*, 1975, **58**, 257) have reported a factor of 20 800 between the rate constants for the reactions of aniline with picryl chloride and 1-chloro-2,4-dinitrobenzene in acetonitrile.

comparing the experimental value of k_{XY} and its statistical error with the value, and its statistical error, calculated from $k_{XY} = k_X k_Y / k_H$ where k_{XY}, k_X, k_Y, and k_H are the rate constants for the disubstituted, monosubstituted, and unsubstituted anilines. If the results agreed within three standard deviations the effects were said to be additive. Deviations from additivity were explained by movement of the transition state on the reaction co-ordinate. The introduction of deactivating groups leads to later transition states and greater sensitivity to electronic effects; in particular if $+K$ groups are also present additional electron release occurs leading to positive deviations from additivity. These papers dealt with substituents in the 3-, 4-, and 5-positions in aniline, so as the transition state for the reactions is approximately tetrahedral and the direction of attack perpendicular to the plane of the aniline ring, steric effects due to these substituents were not involved. For 2-substituents, steric effects do occur as we have shown, and any shift towards later transition states will accentuate them, giving a progressive decrease in reaction rate. A consequence of this on additivity considerations is that the effect of small $+K$ groups such as methoxy in the 2-position will be ambiguous as there is the possibility of a small steric effect acting in opposition to its conjugative effect.

Applying the above criterion, the effects of 2,5-dimethyl, 2-methoxy-5-nitro-, 2-methyl-5-nitro-, and 2-chloro-5-nitro-substituents are additive. The classification of the last two combinations as additive is due to a rather wide range of error associated with the measured rate constants, and it is possible that if more precise results were obtained they would be found to be non-additive. In both cases the measured rate constants have a lower value than the calculated ones, and this is the case also for all the combinations which are not additive. As, with the exception of the methyl group all the 5-substituents are deactivating in this reaction, the results are consistent with their introduction into the 2-series leading to later transition states and hence increased steric hindrance.

EXPERIMENTAL

The compounds used were commercial samples purified by standard procedures until their physical constants agreed with the literature values. Details of the purification of acetonitrile and the procedure for following the rate of the reactions by spectrophotometric estimation of the products have been described elsewhere.[15] The rate constants at various temperatures are listed in Supplementary Publication No. SUP 22997 (4 pp.).*

[0/1639 *Received, 27th October*, 1980]

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* For details of Supplementary Publications see Notice to Authors No. 7 in *J. Chem. Soc., Perkin Trans. 2*, 1980, Index Issue.

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