The Kinetics of the Reactions of Picryl Chloride with Some Substituted Anilines. Part 6.[1] 4-Substituted and 3,4-Disubstituted Anilines

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Arrhenius parameters have been measured for the reactions of picryl chloride with the following substituted anilines in acetonitrile: 4-X- (X = F, Cl, Br, I, Me, or OMe); 3,4-X_2- (X = Cl, Br, Me, or OMe); 4-X-3-nitro- (X = F, Cl, or Me); 3-X-4-methoxy- (X = F, Cl, Br, or I); 3-fluoro-4-nitro-; and 3,4,5-trimethoxy-aniline. In the 3,4-disubstituted series the effect of two methyl groups on the free energy of activation is strictly additive, but for the rest the measured rate constants are greater than those calculated on the assumption of additivity. The results are rationalized in terms of the positions of the transition states on the reaction co-ordinate.

In previous parts of this series[1] we have investigated the reactions of 3-substituted and 3,5-disubstituted anilines with picryl chloride in acetonitrile. In this paper we discuss the reactions of some 4-substituted and 3,4-disubstituted anilines. Although there are several reports of the reactions of 4-substituted-anilines in aromatic nucleophilic substitution reactions, mostly in hydroxylic solvents, to the best of our knowledge there is no single report dealing with all four 4-halogenoanilines and the only reactions reported in acetonitrile are due to Kavalek, Haasova, and Sterba[2] who investigated the reactions of aniline and 4-methoxyaniline with 1-chloro-2,4-dinitrobenzene and a series of 3- and 4-substituted-anilines with 1-fluoro-2,4-dinitrobenzene. Only the reactions of the latter substrate were base-catalysed, indicating that the decomposition of the intermediate formed in these reactions is rate determining for the fluoro- but not for the chloro-substrate.

We have investigated the reactions of 4-X- (X = F, Cl, Br, I, Me, or OMe); 3,4-X_2- (X = Cl, Br, Me, or OMe); 4-X-3-nitro- (X = F, Cl, or Me); 3-X-4-methoxy- (X = F, Cl, Br, or I); 3-fluoro-4-nitro-; and 3,4,5-trimethoxy-aniline with picryl chloride in acetonitrile and the results are given in the Table. As we have shown previously[3] that the reaction of aniline with picryl chloride in acetonitrile is not base-catalysed, the second-order rate constants are those for the formation of the intermediate. The reactions were followed by the spectrophotometric determination of products with the amines in large enough excess to ensure first-order kinetics. The measured absorbances at the completion of the reaction agreed with the calculated ones.

The Monosubstituted Series.—For the 4-halogeno-anilines, the rate constant sequence F > Cl > Br > I is the same as that obtained by Crocker and Jones[4] for the reaction of substituted *NN*-dimethylanilines with allyl bromide in aqueous acetone, and does not vary between 0 and 100 °C, although the span encompassed by the constants decreases from 8.6 fold at 0 °C to 4.1 fold at 100 °C. In this respect they differ from the 3-halogenoanilines where variable rate constant sequences were observed[5] between 0 and 100 °C and the maximum spread of reactivity was only 2.8 fold. All four halogens are mildly deactivating, but the de-

Arrhenius parameters for the reactions of picryl chloride with some substituted anilines in acetonitrile and a comparison of the 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	$10^6 k_m$	$10^6 k_{calc.}$ [b]
4-F	7.77 ± 0.09	4.87	$1.49 \pm 0.01 \times 10^5$	
4-Cl	9.75 ± 0.1	5.63	$3.01 \pm 0.04 \times 10^4$	
4-Br	9.25 ± 0.09	5.12	$2.25 \pm 0.03 \times 10^4$	
4-I	9.39 ± 0.15	5.17	$1.89 \pm 0.05 \times 10^4$	
4-Me	7.84 ± 0.09	5.63	$7.66 \pm 0.02 \times 10^5$	
4-OMe	5.91 ± 0.15	4.74	$2.60 \pm 0.06 \times 10^6$	
4-NO_2 [c]	13.3 ± 0.1	5.22	29.3 ± 5.0	
H [c]	7.9 ± 0.27	5.06	$2.04 \pm 0.01 \times 10^5$	
3,4-$(Cl)_2$	11.1 ± 0.04	5.26	$1.43 \pm 0.07 \times 10^3$	$9.35 \pm 0.15 \times 10^2$
3,4-$(Br)_2$	10.3 ± 0.02	4.67	$1.31 \pm 0.05 \times 10^3$	$7.0 \pm 0.11 \times 10^2$
3,4-$(OMe)_2$	6.77 ± 0.04	5.21	$1.77 \pm 0.02 \times 10^6$	$1.13 \pm 0.03 \times 10^6$
3,4-$(Me)_2$	8.11 ± 0.04	5.98	$1.08 \pm 0.01 \times 10^6$	$1.08 \pm 0.01 \times 10^6$
3-NO_2-4-Me	10.4 ± 0.01	5.03	$2.49 \pm 0.06 \times 10^3$	$2.14 \pm 0.02 \times 10^3$
3-$NO_2$4-F	10.8 ± 0.07	4.69	$6.22 \pm 0.03 \times 10^2$	$4.16 \pm 0.05 \times 10^2$
3-NO_2-4-Cl	10.8 ± 0.2	4.06	$1.40 \pm 0.47 \times 10^2$ [d]	$8.40 \pm 0.13 \times 10$
3-F-4-NO_2	15.0 ± 0.19	5.27	1.83 ± 0.59 [d]	1.07 ± 0.18
3-F-4-OMe	8.66 ± 0.15	5.55	$1.59 \pm 0.02 \times 10^5$	$9.53 \pm 0.2 \times 10^4$
3-Cl-4-OMe	8.85 ± 0.05	5.62	$1.36 \pm 0.02 \times 10^5$	$8.08 \pm 0.2 \times 10^4$
3-Br-4-OMe	8.66 ± 0.10	5.57	$1.51 \pm 0.03 \times 10^5$	$8.48 \pm 0.2 \times 10^4$
3-I-4-OMe	8.31 ± 0.08	5.49	$2.49 \pm 0.02 \times 10^5$	$1.71 \pm 0.04 \times 10^5$
3,4,5-$(OMe)_3$	9.04 ± 0.07	6.03	$2.51 \pm 0.01 \times 10^5$	$4.94 \pm 0.14 \times 10^5$

[a] The errors quoted are standard errors of the mean. [b] For values of the rate constants for 3-substituted anilines used in these calculations see refs. 1, 5, and 7. [c] Values from ref. 3. [d] Values calculated from the Arrhenius parameters.

activation is less from the 4- than the 3-position; at 25 °C the rate constant ratios (k_4/k_3) are F, 19.1; Cl, 4.63; Br, 3.14; I, 1.38. These observations are consistent with the conjugative effect of the halogens relative to their inductive effect being greater at the 4- than the 3-position, and in accordance with the sequence I > Br > Cl > F found by Miller[6] for the rate constants of the reactions of 1-chloro-4-halogeno-2-nitrobenzenes with methoxide ions in methanol at 50 °C.

Both 3- and 4-methyl groups are mildly activating, the k_4/k_3 ratio at 25 °C being 2.66, whereas a methoxy-group in the 4-position is activating in contrast to its effect at the 3-position where it is mildly-deactivating,[7] the k_4/k_3 ratio being 28.7.

The 3,4-*Disubstituted Series*.—The introduction of 3-halogeno- and 3-methoxy-groups into 4-methoxyaniline does not appear to disturb the conjugation of the 4-methoxy-group with the benzene ring. The sequence of the rate constants I > F > Br > Cl measured at 25 °C is the same as the sequences observed for the 3-halogeno-[5] and 3-halogeno-5-methoxy-aniline[7] series and the $k_{3\text{-X-4-OMe}}/k_{3\text{-X}}$ ratios of I, 18.2; F, 20.4; Br, 21.6; Cl, 20.9 do not give any indication of steric inhibition of resonance of the methoxy-group due to increasing size of the halogen atom. For the methoxy-group the $k_{3,4\text{-(OMe)}_2}/k_{3\text{-OMe}}$ ratio is 19.9 compared with a $k_{4\text{-OMe}}/k_\text{H}$ ratio of 12.7, and as discussed later the value of the measured rate constant is greater than that calculated on the assumption of the additivity of substituent effects on the free energy of activation. The introduction at the 5-position of a third methoxy-group does reduce the conjugation of the 4-methoxy-group with the benzene ring. The measured rate constant for 3,4,5-trimethoxyaniline is less than that calculated on the assumption of additivity of substituent effects and the $k_{3,4,5\text{-(OMe)}_3}/k_{3,5\text{-(OMe)}_2}$ ratio is only 4.96. Construction of models shows that for 3,4-dimethoxyaniline conformations are available in which the 4-methoxy-group is in the plane of the benzene ring, but this is not possible in the 3,4,5-trisubstituted compound.

For two substituents the assumption of additivity of substituent effects on the free energy of activation gives $k_{xy} = k_x k_y / k_\text{H}$ where k_H is the rate constant for the unsubstituted compound and k_x, k_y, and k_{xy} are those for the mono- and di-substituted compounds. As discussed earlier,[1] because of the wide range of reactivities involved, we have calculated the rate constant for the disubstituted compound and its statistical error assuming the additivity of the free energies of activation and compared this with the value of the rate constant and its statistical error either obtained by direct measurement at the comparison temperature or calculated from the Arrhenius parameters (Table). If the results agree within three standard deviations the effects are taken to be additive. According to this criterion the substituent effects in 3,4-dimethyl-, 4-chloro-3-nitro-, and 3-fluoro-4-nitro-anilines are additive, but there are substantial standard errors associated with the values of the measured rate constants of the latter two compounds and it is possible that if more precise results were obtained they would be found to be non-additive. The effect of 3,4-dimethyl substituents on the free energy of reaction has previously been found to be additive for the dissociation of pyridinium ions in water at 25 °C by Fisher, Galloway, and Vaughan[8] and in the dissociation of phenols by Bolton, Ellis, and Hall.[9] Their additive effect on the free energy of activation has been shown by Fisher, Galloway, and Vaughan[10] in the reaction of substituted pyridines with ethyl iodine in nitrobenzene at 60 °C, by Rogne[11] for the reactions of 3,4-dimethylaniline with a series of substituted benzenesulphonyl chlorides in methanol at 25 °C, and by Crocker and Jones.[4]

With the exception of 3,4-dimethylaniline, the measured rate constants of all the disubstituted anilines are greater than those calculated on the assumption of the additivity of substituent effects. A similar observation was made by Crocker and Jones[4] in their study of the cumulative effects of substituents on the reactions of substituted *NN*-dimethylanilines with allyl bromide in aqueous acetone. We explain these results in the same way as for the 3,5-disubstituted series.[1] With the exception of 3,4-dimethylaniline, all the disubstituted nucleophiles contain at least one group whose overall electronic effect is deactivating in this reaction and at least one group which has a mechanism for electron release. The introduction of a deactivating group into a nucleophile containing an electron-releasing group leads to a later transition state, *i.e.*, one with an increase in the amount of positive charge on the amino nitrogen atom, which because of the polarizability of the electron-releasing group induces additional electron donation from this group leading to positive deviation from additivity.

EXPERIMENTAL

Materials.—A commercial sample of 4-fluoroaniline was fractionally distilled and the fraction boiling at 85 °C and 19 mmHg was collected. Commercial samples of 4-chloro-, 4-bromo-, 4-iodo-, 4-methyl-, 4-methoxy-, 3,4-dichloro-, 3,4-dibromo-, 3,4-dimethoxy-, 3,4-dimethyl-, 3-nitro-4-fluoro-, 3-nitro-4-chloro-, 3-nitro-4-methyl-, and 3,4,5-trimethoxy-aniline were recrystallized from appropriate solvents to constant m.p. In every case, their physical constants agreed with established literature values. Picryl chloride (B.D.H.) was recrystallized from carbon tetrachloride, m.p. 83.8 °C (lit.,[12] 84 °C).

3-*Fluoro*-4-*methoxyaniline*.—Nitration of 2-fluoroanisole by the method of Elderfield *et al.*[13] yielded 3-fluoro-4-methoxy-1-nitrobenzene, m.p. 103—104 °C (lit.,[13] 105 °C), which on reduction with tin(II) chloride gave 3-fluoro-4-methoxyaniline, m.p. 82 °C (lit.,[14] 82 °C).

3-*Chloro*-4-*methoxyaniline*.—Treatment of the diazonium salt obtained from 2-methoxy-5-nitroaniline with copper(I) chloride gave 1-chloro-2-methoxy-5-nitrobenzene, m.p. 97—98 °C (from methanol) (lit.,[15] 98 °C). Reduction with tin(II) chloride gave 3-chloro-4-methoxyaniline, m.p. 63 °C (lit.,[16] 62 °C).

3-*Bromo*-4-*methoxyaniline*.—1-Bromo-2-methoxy-5-nitrobenzene, m.p. 106 °C (lit.,[17] 106 °C), obtained from 2-methoxy-5-nitroaniline by the Sandmeyer reaction, on reduction with tin(II) chloride and hydrochloric acid gave 3-bromo-4-methoxyaniline, m.p. 63—64 °C (lit.,[18] 64 °C).

3-*Iodo*-4-*methoxyaniline*.—The iodination of 1-methoxy-4-nitrobenzene by stirring overnight with a suspension of iodine in concentrated nitric acid at 15 °C gave 3-iodo-4-methoxy-1-nitrobenzene, m.p. 97 °C (lit.,[19] 98 °C), which on reduction with tin(II) chloride produced 3-iodo-4-methoxyaniline, m.p. 72—74 °C (lit.,[20] 74—75 °C).

3-*Fluoro*-4-*nitroaniline*.—3-Fluoroaniline was nitrated by the method of Hodgson and Nicholson [21] to give 3-fluoro-4-nitroaniline, m.p. 155 °C (lit.,[21] 153 °C).

Kinetic Measurements.—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.[3] For the fast reactions of 4-methoxy-, 4-methyl-, and 4-fluoro-aniline the initial concentrations of picryl chloride and amines were reduced to 1.00×10^{-4} and 1.00×10^{-3}M. The rate constants at various temperatures are listed in Supplementary Publication No. SUP 22555 (3 pp.).*

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