The S_N Mechanism in Aromatic Compounds. Part 42.[1] *para*-Substituent Effects of Some Groups with a C=N Function joined to the Ring. A Possible Inverse α-Effect

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Kinetic measurements of reactions of N_3^-, OH^-, or OMe^- with a series of 4-chloro-3-nitro-X-benzenes were used to obtain values of Hammett substituent constants (σ^-) for *p*-CH=NPh, 0. 65 and 0. 70; *p*-$CH{=}NC_6H_4NO_2$-*p*, 0. 79; *p*-CH=NOH, 0.55; *p*-$CH{=}\overset{+}{N}(O^-)Ph$, 0.95. These values, plus those for *p*-N=NPh, 0.66; *p*-$N{=}\overset{+}{N}(O^-)Ph$, 0.62; *p*-CH=O, 0. 93; *p*-C≡N, 1.00; *p*-NO_2, 1.27, are analysed and discussed. The possible existence of an inverse α-effect is indicated.

WHILE addition reactions forming C=NX groups are well known, the substituent effects of these functions in *e.g.* S_NAr reactions are not. In contrast the substituent effects of related carbonyl (various), nitrile, azophenyl, and α- and β-azoxyphenyl groups are known.[2a—e] This paper constitutes a preliminary study of the *p* substituent effects of some neutral CH=NX groups linked to the benzene ring in 4-chloro-3-nitro-iminomethylbenzenes. The most appropriate comparisons are with formyl, cyano, azophenyl, and azoxyphenyl groups, plus nitro as reference group.

We were aware that the normally very convenient reagent, methoxide ion in methanol, is unsuitable with the formyl and cyano-groups because of reversible nucleophilic addition to the methine carbon atom (hemiacetal and iminoester formation). While this has only a small effect on the rates of the S_NAr reactions, there is a large effect on the derived Arrhenius parameters,[3-5] with both $\Delta E^\ddagger$ and $\log_{10}B$ considerably increased. This side reaction is of minor importance with azide ion and apparently absent with thiocyanate ion.[6] Since azide ion is considerably more reactive at aromatic carbon [2e] it was our first choice as reagent with the iminomethyl derivatives. Nevertheless we encountered some complications with this and with hydroxide and methoxide ions also used. Problems included low solubility of reagent or substrate in a particular solvent or solvent mixture, demethylation of a methoxy-product, and the above-mentioned reversible Ad_N reactions. Nevertheless these are interesting in themselves and our results serve well as an exploratory study.

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[3] J. Miller, *J. Amer. Chem. Soc.*, 1954, **76**, 448.

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EXPERIMENTAL

Materials.—1-Chloro-2,4-dinitrobenzene was a commercial product recrystallized from EtOH, m.p. 50—51° (lit.[7a] 49.5; 50; 50.2; 51; 51.5—52; 53.4°). 4-Chloro-3-nitrobenzaldehyde was prepared by nitration of *p*-chlorobenzaldehyde. Precipitated from $CHCl_3$ by light petroleum (b.p. 60—80°) it had m.p. 63—64° (lit.[7b] 62; 64.5; 65°). 4-Chloro-3-nitrobenzaldoxime was prepared from the aldehyde by reaction with hydroxylamine. After recrystallization from MeOH it had m.p. 143—144° (lit.[7b] 141.5—142.5; 146°). .The three following compounds have not previously been described. Structures were confirmed by elemental analysis and physical methods. 4-*Chloro*-3-*nitrobenzylideneaniline* was prepared from the aldehyde by reaction with aniline. After recrystallization from EtOH it had m.p. 69.5—70° (Found: C, 60.2; H, 3.6; N, 10.1. $C_{13}H_9ClN_2O_2$ requires C, 59.9; H, 3.5; N, 10.75%). N-(4-*Chloro*-3-*nitrobenzylidene*)-4-*nitroaniline* was prepared from the aldehyde by reaction with *p*-nitroaniline. After recrystallization from C_6H_6 it had m.p. 159—160° (Found: C, 50.5; H, 2.6; N, 12.9. $C_{13}H_8ClN_4O_4$ requires C, 51.0; H, 3.0; N, 13.0%). 4-*Chloro*-3-*nitrophenylbenzylideneaniline* N-*oxide* was prepared from the aldehyde by reaction with freshly prepared β-phenylhydroxylamine. After recrystallization from EtOH it had m.p. 170—172° (Found: C, 56.85; H, 3.7; N, 9.5. $C_{13}H_9ClN_2O_3$ requires C, 56.45; H, 3.3; N, 10.1%).

TABLE 1

Rate constants of S_NAr reactions of some 4-chloro-3-nitro-X-benzenes

X	Reagent/solvent	k_2/l mol^{-1} s^{-1} (t/°C)
CH=NPh	N_3^-/MeOH	2.63, 2.69 × 10^{-4} (89.2), 7.67, 8.13 × 10^{-4} (102.8), 2.82, 2.92 × 10^{-3} (122.1)
CH=NPh	OMe^-/MeOH	8.43 × 10^{-4} (50.0), 1.04 × 10^{-3} (51.8), 3.83 × 10^{-3} (65.3), 8.90 × 10^{-3}, 1.00 × 10^{-2} (75.5), 2.85, 2.95 × 10^{-2} (87.5)
$CH{=}NC_6H_4NO_2$-*p*	N_3^-/MeOH–C_6H_6 (60 : 40 v.v)	4.48, 4.73 × 10^{-4} (91.2), 1.29 × 10^{-3} (102.5), 1.43 × 10^{-3} (102.7), 5.91, 6.12 × 10^{-3} (120.0)
CH=NOH	N_3^-/MeOH	9.21 × 10^{-5} (103.5), 2.35 × 10^{-4} (120.5), 2.70 × 10^{-4} (122.9), 5.26 × 10^{-4} (133.5), 5.96 × 10^{-4} (134.7)
$CH{=}\overset{+}{N}(O^-)Ph$	OH^-/dioxan–MeOH (75 : 25 v/v)	3.48 × 10^{-3} (19.5), 3.75 × 10^{-3} (19.8), 5.56 × 10^{-3} (24.0), 2.20 × 10^{-2} (39.0), 2.42 × 10^{-2} (42.0)
CH=O	N_3^-/MeOH	1.21, 1.27 × 10^{-4} (50.6), 6.41 × 10^{-4} (66.1), 1.23, 1.26 × 10^{-3} (73.5), 2.57 × 10^{-3} (81.0), 2.57 × 10^{-3} (81.3)
CH=O	N_3^-/MeOH–C_6H_6 (60 : 40 v/v)	1.18, 1.24 × 10^{-4} (60.9), 5.83, 5.86 × 10^{-4} (76.8), 9.19 × 10^{-4} (81.5), 1.55 × 10^{-3} (90.8)
NO_2	N_3^-/MeOH	2.36 × 10^{-4} (17.1_5), 2.42 × 10^{-4} (17.3_5), 8.75, 8.79 × 10^{-4} (29.9_5), 4.35 × 10^{-3} (47.8_5), 4.60 × 10^{-3} (48.0_5)
NO_2	N_3^-/MeOH–C_6H_6 (60 : 40 v/v)	1.42, 1.53 × 10^{-3} (34.8), 6.90, 7.14 × 10^{-3} (51.5), 2.27, 2.29 × 10^{-2} (64.0)
NO_2	OH^-/dioxan–MeOH (75 : 25 v/v)	6.54 × 10^{-3} (-5.2_5), 1.07 × 10^{-2} (0.7), 1.91 × 10^{-2} (4.4_5), 1.93 × 10^{-2} (4.6), 3.49 × 10^{-2} (10.5), 4.82 × 10^{-2} (14.5)

TABLE 2

Derived kinetic data for S_NAr reactions of some 4-chloro-3-nitro-X-benzenes (50°) *

X	Reagent/solvent	k_2/l mol^{-1} s^{-1}	$\Delta E^‡$/kJ mol^{-1}	$\log_{10}$ (B/ l mol^{-1} s^{-1})	$\Delta S^‡$/J mol^{-1} K^{-1}	$\Delta G^‡$/kJ mol^{-1}	σ^-	ρ
CH=NPh	N_3^-/MeOH	8.55 × 10^{-6}	85.9	8.8_5	−84.8	110.6	0.70	4.88
CH=NOH		1.60 × 10^{-6}	75.7	6.4_5	−130.4	115.1	0.55	
CH=O		1.17 × 10^{-4}	94.5	11.3	−36.2	102.8	0.93	
NO_2		5.36 × 10^{-3}	74.0	9.7	−68.2	93.4	1.27	
$CH{=}NC_6H_4NO_2$-*p*	N_3^-/MeOH–C_6H_6 (60 : 40 v/v)	5.30 × 10^{-6}	106.2	11.9	−26.1	111.9	0.79	6.40
CH=O		4.26 × 10^{-5}	89.7	10.1_5	−59.8	106.3	0.93	
NO_2		6.39 × 10^{-3}	80.5	10.8_5	−46.6	92.9	1.27	
$CH{=}\overset{+}{N}(O^-)Ph$	OH^-/dioxan–MeOH (75 : 25 v/v)	5.20 × 10^{-2}	69.5	9.9_5	−63.2	87.3	0.95	4.05
NO_2		1.01	65.7	10.6_5	−49.3	79.3	1.27	
H	OMe^-/MeOH	2.52 × 10^{-6}	98.9	10.4	−54.8	113.9	0	3.90
CH=NPh		8.39 × 10^{-4}	90.7	11.6	−31.9	98.3	0.65	
N=NPh		1.04_5 × 10^{-3}	85.0	10.8	−47.7	97.7	0.64	
CH=O		5.64 × 10^{-3}	105.4	14.8	+29.4	93.2	0.93	
C≡N		7.06 × 10^{-3}	107.0	15.1_5	+36.2	92.6	1.00	
NO_2		2.88 × 10^{-1}	73.0	11.2_5	−38.2	82.6	1.27	

* Includes earlier work (see text). Derivation of ρ values indicated in the Discussion section.

Kinetics.—Reactions were carried out with temperature control better than ±0.1°, sealed ampoules were used for runs at elevated temperatures. All the reactions produce chloride ion, and runs were followed by potentiometric titration of chloride ion in portions withdrawn at appropriate intervals. Rates and derived Arrhenius parameters were obtained by least squares analysis of appropriate functions, using a PDP 10 computer. Solvents were purified by the usual methods. Table 1 sets out the new rate measurements. Table 2 sets out derived kinetic data including those of the comparison compounds. As an example of the precision of the results the reaction of azide ion in methanol with 4-chloro-3-nitrobenzylideaniline gave $\Delta E^‡$ 85.84 kJ mol^{-1} with an error of ±1.67% and correlation coefficient 0.999 4. The value of $\Delta S^‡$ was −84.61 J mol^{-1}

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[7] F. K. Beilstein, 'Handbuch der Organischen Chemie,' Springer-Verlag, Berlin (*a*) vol. V, 1922 (revised 1930, 1943, and 1964), p. 262; (*b*) vol. VII, 1923 (revised 1931, 1948, and 1968), p. 262.

K^{-1}. Complications encountered are discussed in the following section.

DISCUSSION

We comment first on reactions of methoxide ion with the CH=NPh compound which could involve some degree of competitive reversible addition to the methine carbon. However, the Arrhenius parameters are only slightly higher than those expected from the rates, in comparison with values for hydrogen, azo-, azoxy-, and nitro-groups *para* to chlorine. They are much lower than the grossly affected values for the CHO and CN compounds.[3] Thus we regard the value of σ^- of 0.65 as being hardly affected by competitive reaction. The value of the Hammett reaction constant (ρ) used, 3.90 at 50°, was obtained in earlier work.[8] Support for the above σ^- value came from the reaction of the CH=NPh compound with azide ion since even the CHO and CN compounds are reasonably well behaved with it. The value of σ^- for *p*-CH=NPh obtained is 0.70, concordant with the other value. These may be compared with σ^- values: *p*-N=NPh, 0.66 [2a,9]; *p*-CH=O, 0.93;[6] *p*-C≡N, 1.00;[6] and *p*-NO_2, 1.27.[2a,8]

It seems clear from the approximate equality of σ^- of *p*-CH=NPh and *p*-N=NPh that the iminomethyl function is considerably more effective in conjugative electron withdrawal since its inductive effect must be the smaller. Comparing *p*-CH=NPh and *p*-CH=O we suggest that the latter is superior in both inductive and conjugative electron withdrawal. Relating *p*-CH=NPh and *p*-C≡N, we ascribe the difference mainly to a greater inductive effect of the CN group though we have discussed earlier [9] the way in which a triple bond may be able to exert a greater conjugative effect than the corresponding double bond

With azide ion as reagent, we estimated a ρ value of 4.88 at 50° from values for the CHO and CN compounds. This was used to obtain the σ^- value for *p*-CH=NPh (see above), and for *p*-CH=NOH of 0.55.

It should be noted that hydroxyiminate ion is a much stronger base than azide ion, so that only an insignificant proportion of the oxime is in the conjugate base form. There are several factors to be considered in evaluating the substituent effects of the CH=NOH group. The inductive effect of oxygen should lead to *p*-CH=NOH having a larger value of σ^- than *p*-CH=NPh. Conjugative electron-release ($\mathrm{H\ddot{O}{-}N{=}C}$) is possible, but unlikely to be very significant since its direction is contrary to that involved in the permanent, and augmented during reaction, conjugation ($-M$ and $-E$ effects) of the C=N bond with the ring to which the carbon is attached. If this is so, some other explanation is required for the lower value of σ^- for *p*-CH=NOH.

We speculate as follows. Conjugative electron withdrawal by the C=N function of the oxime corresponds to a contribution of the canonical (part)-structure $=\mathrm{CH}{-}\overset{-}{\underset{..}{\mathrm{N}}}{-}\underset{..}{\mathrm{O}}\mathrm{H}$. In this there is negative charge on nitrogen, while both it and the neighbouring (α) oxygen atom have each two pairs of unshared electrons. The repulsions thus resulting are destabilising. It is the reverse situation to that in which a nucleophile with such initial state destabilization, relieves it in forming the transition state. Such alleviation is widely accepted as a contributing factor to what has been called the α-effect.[10] We stress that our suggestion of an inverse α-effect is highly speculative and requires verification or refutation in further studies.

Owing to the low solubility of the *N*-benzylidene-4-nitroaniline in methanol we studied its reactivity in methanol–benzene (60 : 40 v/v) in which we were able to dissolve sufficient sodium azide. For necessary comparisons, including the estimate of a ρ value, we also measured the rates of reaction of formyl and nitro-compounds with this reagent combination. We have previously commented [11] on similar benzene–methanol mixtures as solvents in S_NAr reactions. It was noted there that rates were not much affected, though changes in the Arrhenius parameters were more significant.

The value of ρ of 6.40 at 50° is significantly higher than in MeOH (4.88). The value of σ^- for *p*-CH=$NC_6H_4NO_2$-*p* is 0.79, only a small increase on *p*-CH=NPh but in the expected direction. The smallness of the increase is also as expected, since it is generally accepted (*e.g.* ref. 12) that there is little through conjugation in benzylidene anils but rather quasiseparate conjugation $\mathrm{Ar{-}C{=}N}$ and $\mathrm{\ddot{N}{-}Ar'}$. There are probably special features of solvation of the *N*-benzylidene-*p*-nitroaniline, with its two rings in benzene–methanol, compared with the formyl and nitro-compounds. We thus do not regard the σ^- value of 0.79 as definitive. More significant is that the σ^- value is greater than that obtained with the parent compound.

The nitrone [*p*-CH=$\overset{+}{\mathrm{N}}(\mathrm{O})^{-}$Ph] also caused some difficulties. Its solubility is inconveniently low in both methanol and methanol–benzene. It dissolved readily in dioxan–methanol (75 : 25 v/v), but we could not then dissolve the sodium azide. With methoxide as reagent the concentration of chloride increased at first then decreased. This suggested subsequent demethylation of the methoxy-product, a common type of reaction where a methoxy-group is attached to sufficiently electron-deficient centres. We have encountered this in earlier work.[1,13] We decided therefore to use OH^- in this solvent and comment that whereas in pure methanol (protic solvent) hydroxide is a weaker nucleophile than methoxide, it is more nucleophilic in the solvent with high dioxan content. Thus our reaction is with OH^- for which two equivalents were necessary (ArCl +

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[13] M. E. C. Biffin, J. Miller, and R. Roper, *Austral. J. Chem.*, 1969, **22**, 2555.

$2OH^- \longrightarrow ArO^- + Cl^- + H_2O$). Kinetic results showed the reaction to be fairly well behaved; there was just a slight curvature in the normally linear rate plot. We ascribe this to a small degree of competition by OMe^- with subsequent demethylation. The Arrhenius parameters were normal suggesting no significant competition by a reversible Ad_N reaction to methine carbon. Compared with the oxime internal conjugation has the more powerful donor O^- instead of OH. Thus despite its unfavourable direction, internal conjugation may sufficiently reduce the electrophilic character of the methine carbon, sufficiently to make the Ad_N reaction uncompetitive. Nevertheless the normal conjugation, assisting the S_N reaction, must be at a high level because the σ^- value is 0.95, essentially equating the group with CH=O and C≡N in activating power. This is a most interesting and potentially very useful result. In deriving the σ^- value we used the same ρ value as for OH^- in dioxan–water (75 : 25 v/v). In this solvent the σ^- value of the α-azoxyphenyl group [$-N{=}\overset{+}{N}(O^-)Ph$] has been measured and is only 0.62, much lower than the value for the nitrone. We interpret this as due to the lower conjugative effect of the azoxy-group and the much greater importance of internal conjugation, which also reduces its inductive effect. In fact the α-azoxyphenyl group has a smaller σ^- value than either azophenyl or β-azoxyphenyl groups (0.66 and 0.77 respectively).

As a final comment, it is worth pointing out the close parallelism of activating power of COX groups in S_N reactions and their carbonyl reactivity (Ad_N reactions).[3] The relatively high σ^- values now demonstrated for some neutral C=N functions suggests that more attention should be paid to Ad_N reactions of C=NX compounds and we have initiated studies in this direction.

[7/574 *Received, 1st April,* 1977]