m.p. 134.5–136° (Bertram[41] assigned this structure to the reduction compound from what he incorrectly considered to be VIIIe; his reduction product is reported to melt at 160°). The infrared spectrum showed maxima at 2.94 and 3.01μ. The ultraviolet spectrum showed $\lambda_{\max}$ 233 mμ, ϵ 14,700; $\lambda_{\max}$ 286 mμ, ϵ 4.510.

Anal. Calcd. for $C_{13}H_{14}N_2$: C, 78.75; H, 7.12; N, 14.13. Found: C, 78.79; H, 7.15; N, 13.91.

2,2'-Azoxydiphenylmethane (XVI).—The dinitrodiamine XIV was converted to the cyclic azoxy compound XV according to Duval[16]; m.p 247° (reported[16] m.p. 273°). This compound was treated with nitrous acid followed by hypophosphorous acid as described for the preparation of VIIIe, except the reaction with hypophosphorous acid was allowed to continue for 45 hours at 0°. The reaction product was isolated by continuous extraction with ligroin (b.p. 40–60°) as before. There was obtained 1.86 g. (14%) of yellow needles, m.p. 130–132°. An analytical sample, twice recrystallized from petroleum ether, had m.p. 134.5–135.5°.

Anal. Calcd. for $C_{13}H_{10}N_2O$: C, 74.26; H, 4.80; N, 13.33. Found: C, 74.24; H, 4.90; N, 13.40.

2,3,6,7-Dibenzo-4,5-diazacyclohepta-2,6-diene (IIe) Reduction of XVI with hydrazine (method I) gave IIe, pale yellow needles, m.p. 98–100°, yield 82%. The analytical sample was recrystallized from ether–hexane, m.p. 99–101°, m p. 105–105.5° (in vac.). The infrared spectrum showed bands at 3.0 and 3.1μ. The ultraviolet spectrum had $\lambda_{\max}$ 247, ϵ 6,550; $\lambda_{\max}$ 289, ϵ 1,810.

Anal. Calcd. for $C_{13}H_{12}N_2$: C, 79.56; H, 6.17; N, 14.28; mol. wt., 210. Found: C, 79.48; H, 6.40; N, 14.28; mol. wt., 187 (Rast).

The compound decomposed upon standing in air, but was stable when sealed under nitrogen. It was oxidized to the azo compound XIIe with mercuric oxide as described in 95% yield, and reduced to the diamine catalytically as described in 66% yield. These products were identified by lack of mixture melting point depression with authentic samples.

2,3,6,7-Dibenzo-4,5-diazacyclohepta-2,4,6-triene (XIIe).—Reduction of 0.66 g. of the azoxy compound XVI with sodium sulfide (method C) was carried out as described, but the reflux period was extended to 3 hours. Chromatography of the reaction product on alumina gave crude XIIe from the pentane–ether fractions, which was recrystallized from hexane and gave 0.10 g. (17%) as yellow needles, m.p. 111.5–112.5°. The mixture melting point with material from the lithium aluminum hydride reduction was undepressed.

From the ether fractions was also recovered a small amount of starting material, melting point and mixture melting point 135–136°.

Reduction of 0.70 g. of compound XVI was also carried out with lithium aluminum hydride (method D) except ether was used as the solvent and the mixture was heated under reflux for 3 days. Chromatography was carried out as described using benzene, ether and methanol in turn for the elution. From the methanol fractions was isolated 0.24 g. (36%) of 2,2'-diaminodiphenylmethane (IXe), m.p. and mixture m.p. 134.5–135.5°. From the benzene fractions after recrystallization from hexane was obtained 0.08 g. (12%) of XIIe as yellow needles, m.p. 111–112°. The analytical sample had m.p. 112.5–113.5°. The ultraviolet spectrum showed $\lambda_{\max}$ 242 mμ, ϵ 6,820; $\lambda_{\max}$ 314 mμ, ϵ 7,620; $\lambda_{\max}$ 423 mμ, ϵ 976.

Anal. Calcd. for $C_{13}H_{10}N_2$: C, 80.36; H, 5.19; N, 14.43. Found: C, 80.13; H, 5.14; N, 14.11.

N.m.r. Spectra.—All determinations were made in acetone solvent with a concentration of 5–10%. Compounds XVIII and XVII were run at 60 m.c. and referenced by external benzene. The protons on nitrogen appeared at −95 and −187 c.p.s. Compounds IIe and IIb were run at 60 mc. with internal tetramethylsilane as reference and showed absorption at −371 and −376 c.p.s. Compounds XIX and IId were run at 40 mc. with external methylene chloride reference, and showed resonance at −72 and −21 c.p.s. All values were corrected approximately to the τ scale by using[42] benzene = 3.60 τ, methylene chloride = 4.70 τ. No susceptibility corrections were made.

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[CONTRIBUTION FROM THE LABORATORIO DE QUIMICA ORGANICA, FACULTAD DE CIENCIAS EXACTAS Y NATURALES, UNIVERSIDAD NACIONAL DE BUENOS AIRES, BUENOS AIRES, ARGENTINA]

Polar Effects of Substituents on the Reaction Rates of 4-R- and 5-R-2-Nitrochlorobenzenes with Piperidine in Benzene

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The rate constants for the reaction of fourteen 4-R- and of twelve 5-R-2-nitrochlorobenzenes with piperidine in benzene have been determined. The reaction follows the Hammett relationship log $k_R/k_H = \sigma^*\rho$ with a ρ-value of +3.80. Differences in rates are mainly determined by differences in activation energies.

The extensive literature on aromatic nucleophilic substitution, has been recently reviewed by Bunnett and Zahler,[3] Bunnett[4] and Sauer and Huisgen.[5] Miller,[6,7] Hammond and Hawthorne[8] and Kalberer,[9] have published partial reviews.

The nucleophilic substitution of halogen in 4-R-2-nitrohalogenobenzenes has been studied quantitatively by Berliner and Monack[10] in the solvolysis of 4-R-2-nitrobromobenzenes in piperidine; by Miller and coworkers,[11] by Bunnett and coworkers[12] and by Eliel and Nelson[13] in the reactions of 4-R-2-nitrochlorobenzenes with sodium methoxide in methanol. Bunnett and Snipes[14] studied the

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[1] Based in part on the D.Chem. thesis of W. G. (1960) and R. A. B. (1959).

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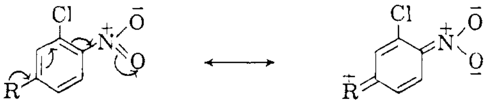
reaction of 4-R-2-nitrochlorobenzenes with sodium thiophenoxide in aqueous 60% dioxane, and Bevan[15] the reactions of 4-R-2-nitrofluorobenzenes with sodium ethoxide in ethanol.

In these reactions the rate of substitution of the halogen can be correlated with the polar effects of substituents *para* to the site of substitution, the activating effect of the *o*-nitro group being considered as constant.

Similar studies on 5-R-2-nitrohalogenobenzenes have not been made, although some papers of semiquantitative or preparative character have been published.[16-20]

In this series there is a possibility for a secondary effect by resonance between the substituent and the nitro group, *para* to each other. The constancy of the activating effect of the nitro group can eventually be affected by the contribution of structures of type I. In our opinion the difficulty of the evaluation of its relative importance has been the main reason for the lack of interest in quantitative studies of nucleophilic reactions of 5-R-2-nitrohalogenobenzenes.

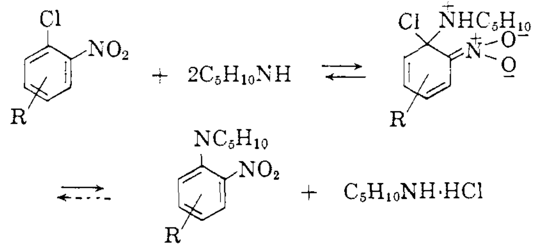


I

Most of the information on the polar effect of substituents, *meta* to the site of the reaction in aromatic nucleophilic substitutions comes from papers by Capon and Chapman[21] on the reaction of 5-chloro-2,4-dinitroalkylbenzenes with several reagents, and by Bevan[22] and Miller[23] and their coworkers on the replacement of an activated halogen atom in *m*-substituted compounds with sodium methoxide in methanol.

We have determined the rates of reaction at several temperatures for a series of 4-R- and 5-R-2-nitrochlorobenzenes with piperidine in benzene. A correlation has been found for the polar effects of a wide variety of substituents, *meta* and *para* to the site of substitution, in a reaction with a powerful nucleophile in a non-polar solvent, benzene, not generally used in this type of study.[24]

The experimental evidence reported mainly by Bunnett[4] supports the idea of an intermediate of type II, in which the formation of the carbon–nitrogen bond and the heterolysis of the carbon–halogen bond are not synchronous[25,26] and which in systems adequately activated has a certain degree of stability.



II

Experimental

Solvents and Reagents. Piperidine.—The Eastman Kodak Co. product (b.p. 98–108°) was dried over potassium hydroxide, and distilled over sodium in a column of 22–23 theoretical plates (Fenske); the fraction of b.p. 106.5° (760 mm.) was employed.

Benzene.—Reagent grade thiophene-free, dried and distilled over sodium, b.p. 80–81°, was used.

***o*-Nitrochlorobenzene.**—The Eastman Kodak Co. white label product was recrystallized from ethanol; m.p. 32°.

4-Chloro-3-nitrobiphenyl.—4-Amino-3-nitrobiphenyl (23.8 g.) obtained by the procedure of Campbell, Anderson and Gilmore,[27] gave by the Sandmeyer reaction on the diazonium salt (obtained by Hodgson and Walker's method[28]) 15.3 g. of 4-chloro-3-nitrobiphenyl, m.p. 42° (crystallized from petroleum ether, b.p. 60–70°), b.p. 163.5° (1 mm.).

Anal. Calcd. for $C_{12}H_8NO_2Cl$: C, 61.7; H, 3.45; N, 6.0; Cl, 15.2. Found: C, 61.87; H, 3.54; N, 6.18; Cl, 15.14.

3-Chloro-4-nitrobiphenyl.—Starting with 3-nitrobiphenyl, prepared by the method of France, Heilbron and Hey[29] with the modifications of Bachmann and Hoffman,[30] 3-amino-4-nitrobiphenyl was obtained following the procedure of Blackley and Scarbourgh[31]; 12 g. of this amine diazotized by the method of Hodgson and Walker gave by the Sandmeyer reaction 6 g. of 3-chloro-4-nitrobiphenyl, m.p. 64–65° (crystallized from petroleum ether, b.p. 60–70°), b.p. 170–172° (1 mm.).

Anal. Calcd. for $C_{12}H_8NO_2Cl$: C, 61.7; H, 3.45; N, 6.0; Cl, 15.2. Found: C, 62.37, H, 3.79; N, 5.91; Cl, 14.74.

4-Chloro-3-nitroanisole.—From 23 g. of 4-amino-3-nitroanisole, 18 g. of the product was obtained by the procedures of Van Erp[32] and Reverdin and Düring[33]; m.p. 43–45°.

4-Chloro-3-nitriphenetole.—With the same procedure, 25 g. of 4-amino-3-nitrophenetole gave 23 g. of 4-chloro-3-nitrophenetole, m.p. 48° (crystallized from ethanol).

3-Chloro-4-nitrophenetole.—From *m*-aminophenol, *m*-ethoxyacetanilide was obtained by the procedures of Reverdin and de Luc[34] and Reverdin and Lokietek.[35] 3-Amino-4-nitrophenetole was then obtained according to Verkade and Witjens[36] and Reverdin and Lokietek introducing the modifications of Hodgson and Clay[37] for the 3-amino-4-nitropropoxybenzene.

A solution of 10 g. of nitric acid (d. 1.50) in 50 ml. of acetic anhydride was added dropwise into a vigorously stirred suspension of 18 g. of *m*-ethoxyacetanilide in 100 ml.

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of acetic anhydride kept at −5°. After 2 hours the product was poured on ice. The dried product (13.5–14.5 g.) extracted with dry petroleum ether (b.p. 60–70°) gave after evaporation of the solvent 8.2 g. of 5-ethoxy-2-nitroacetanilide, m.p. 94–95°. The residue, dissolved in chloroform and treated with activated charcoal, gave by reprecipitation with petroleum ether 4 g. of 3-ethoxy-4-nitroacetanilide, m.p. 146–147°. Following the procedure of Verkade and Witjens, 15 g. of 5-ethoxy-2-nitroacetanilide was refluxed in 200 ml. of 0.02 *N* sodium ethoxide solution. After pouring into water, 11.7 g. of 5-ethoxy-2-nitroaniline, m.p. 105°, was obtained.

Diazotization by Hodgson and Walker's procedure and steam distillation of the product of the Sandmeyer reaction gave 11.3 g. of 3-chloro-4-nitrophenetole, m.p. 37–38° (crystallized from ethanol).

3-Chloro-4-nitroanisole was obtained from *m*-hydroxyacetanilide by a similar procedure; m.p. 58° (crystallized from ethanol).

4-Chloro-3-nitroaniline.—The procedure of Fourneau, Tréfouel, Tréfouel and Wancolle[38] was used; m.p. 102–103°.

3-Chloro-4-nitroaniline was obtained as indicated by Fourneau, Tréfouel, Tréfouel and Wancolle; m.p. 157°. The 3-chloro-6-nitroaniline obtained simultaneously was purified more conveniently following the methods of Hodgson and Kershaw[39]; m.p. 126°.

3-Chloro-4-nitrobenzonitrile was prepared as described by Bower, Stephens and Wibberley[40]; m.p. 85–86° (crystallized from ethanol).

3-Chloro-4-nitrobenzoic Acid.—The procedure employed was that of Claus and Kurz[41]; m.p. 183–184° (crystallized from cloroform).

4-Chloro-3-nitrobenzonitrile.—The method of Dunlop, Macrae and Tücker[42] was modified as follows: 10 g. of *p*-chlorobenzonitrile was dissolved in 50 ml. of nitric acid obtained by distillation of one volume of nitric acid, d. 1.42, with 1.5 volumes of concentrated sulfuric acid. After 24 hours at room temperature, the product was poured into water. Recrystallization from petroleum ether (b.p. 60–70°) and treatment with activated charcoal yielded 8.5 g. of 4-chloro-3-nitrobenzonitrile, m.p. 100–101°.

4-Chloro-3-nitrobenzoic Acid.—The modifications of Thompson and Turner[43] to the method of Hübner[44] were employed; m.p. 180° (crystallized from ethanol–water, 7:3 v./v.).

Ethyl 3-chloro-4-nitrobenzoate and ethyl 4-chloro-3-nitrobenzoate were prepared by the method of the silver salt as described by Vogel.[45] Ethyl 4-chloro-3-nitrobenzoate had m.p. 60–61° (ethanol). Ethyl-3-chloro-4-nitrobenzoate has not been previously reported, m.p. 50–51° (ethanol).

Anal. Calcd. for $C_9H_8O_4N$: C, 47.07; H, 3.51; N, 6.10, Cl, 15.44. Found: C, 47.35; H, 3.53, N, 5.95; Cl, 15.52.

2,5-Dichloronitrobenzene.—4-Chloro-3-nitroaniline (17.3 g.), diazotized by the procedure of Hodgson and Walker and poured into a cuprous chloride, solution yielded 13.5 g. of 2,5-dichloronitrobenzene, b.p. 96–98° (3 mm.), m.p. 52–53°.

2,4-Dichloronitrobenzene.—With a similar procedure 43.4 of 3-chloro-6-nitroaniline yielded 35.1 g. of 2,4-dichloronitrobenzene, b.p. 102–104° (3 mm.), m.p. 32–33°.

5-Bromo-2-chloronitrobenzene.—Diazotization of 4-chloro-3-nitroaniline by the method of Hodgson and Walker and subsequent pouring into cuprous bromide solution yielded the product with m.p. 71–72° (crystallized from ethanol).

4-Bromo-2-chloronitrobenzene.—A similar method was followed: m.p. 43–44° (crystallized from ethanol).

2-Chloro-5-iodonitrobenzene.—4-Chloro-3-nitroaniline, diazotized as above yielded after pouring into a solution of potassium iodide 2-chloro-5-iodonitrobenzene, m.p. 73–73.5° (crystallized from methanol).

2-Chloro-4-iodonitrobenzene.—In a similar way 3-chloro-4-nitroaniline yielded 2-chloro-4-iodonitrobenzene, m.p. 61–62° (crystallized from ethanol).

4-Chloro-3-nitro-*t*-butylbenzene.—2-Nitro-4-*t*-butylaniline prepared, as indicated by Carpenter, Easter and Wood[46] and diazotized by the method of Hodgson and Walker, gave the desired product by the Sandmeyer reaction; b.p. 118–122° (3 mm.).

3-Chloro-4-nitro-*t*-butylbenzene.—*m*-Nitro-*t*-butylbenzene, b.p. 97–99° (2.5 mm.), obtained as described by Carpenter, Easter and Wood[46] was reduced with hydrogen (40 p.s.i.) using as catalyst 5% by weight of platinum on alumina with 0.25% of platinum, *m-tert*-butylaniline was obtained in quantitative yield. This amine was nitrated and diazotized by the procedures described by Capon and Chapman,[21] b.p. 96–97° (0.2 mm.).

4-Chloro-3-nitrotoluene, prepared by the method of Gattermann and Kaiser,[47] had b.p. 95–96° (1 mm.), solidification point 7°.

3-Chloro-4-nitrotoluene was obtained according to Wepster and Verkade[48]; b.p. 99–101° (2 mm.), m.p. 22°.

4-Chloro-3-nitroazobenzene was made by the method of Borsche and Exss[49]; m.p. 87° (crystallized from ethanol).

4-Chloro-3-nitrobenzotrifluoride.—The Maumee Chemical Co. product was distilled, b.p. 85.5–86° (3 mm.).

Kinetic Measurements.—Several Pyrex sealed tubes each containing 10 ml. of a benzene solution of the reactants, roughly 0.1 *M* in the halogen compound and 1.0 *M* in piperidine, were placed in a thermostat regulated to ±0.1°. Tubes were removed and frozen, and after addition of 10 ml. of 20% nitric acid, chloride ion was determined by potentiometric titration.

Rate constants were calculated as in previous papers[50] by means of the equation

$$k_2 = \{2.303/[t(b - 2a)]\} \log \{a(b - 2x)/b(a - x)\}$$

where a and b are, respectively, the molar concentrations of halogen compound and piperidine and x is the concentration of chloride ion at time t. Data from two tubes removed simultaneously usually did not differ by more than 1%, and reproducibility of rate constants by independent experiments lay within ±2%. Data for a typical run are given in Table I.

TABLE I

REACTION OF 4-CHLORO-3-NITRO-*t*-BUTYLBENZENE WITH PIPERIDINE IN BENZENE AT 60°

$a = 0.0975M$, $b = 1.0022M$

Time, sec.	x, mole l.$^{-1}$	$k_2 \times 10^7$, l. mole^{-1} sec.$^{-1}$
61740	0.0105	18.22
78720	.0135	18.80
141960	.0226	18.57
257040	.0369	18.83
319740	.0425	18.37
415200	.0499	18.41
505800	.0570	18.18
	Average	18.48 ± 0.1

This technique could not be used for the very reactive compounds having the following substituents: 4-NO_2, 4-CN, 4-$CO_2C_2H_5$, 4-$C_6H_5N{=}N$, 4-F_3C and 5-CN. A spectrophotometric technique was used instead. The absorption due to the substituted N-phenylpiperidine produced in the reaction was measured at a convenient wave length, usually 390–420 mμ, with a Beckman DU spectrophotometer.

Initial concentrations ranged from 10^{-4} to 10^{-5} *M* for the halogenated compound, and piperidine was 10^2 to 10^3

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TABLE II

REACTION OF 4-CHLORO-3-NITROBENZOTRIFLUORIDE WITH PIPERIDINE IN BENZENE AT 35°

$a = 5.61 \times 10^{-4}$ *M*; $b = 1.77 \times 10^{-1}$ *M*; O.D.$_\infty$ = 1.111

Time, min.	O.D.$_t$	Time, min.	O.D.$_t$
8	0.128	41	0.451
15	.204	50	.520
20	.255	57	.568
30	.354	62	.601

$k_\psi = 2.02 \times 10^{-4}$ sec.$^{-1}$; $k_2 = 1.14 \times 10^{-3}$ l. mole^{-1} sec.$^{-1}$

times in excess. Samples were removed from the thermostat, cooled rapidly to room temperature and the absorbancy measured directly.

Table II shows the results of a typical run. Pseudomonomolecular rate constants were calculated graphically from the plot of log (O.D.$_{\infty\text{exp}}$ − O.D$_t$) *vs. t*; second-order rate constants were obtained from these by dividing by the concentration of piperidine.

Results

Results are summarized in Table III. Data for 2,4-dinitrochlorobenzene communicated by Mr. T. H. Suarez have been added. In general a good parallelism is observed between these results and those of other investigators in similar studies.[51,52] Nearly all are predictable from the polar effects of substituents from the *m*- and *p*-positions to the site of reaction.

The order of decreasing rates can be observed in Table III, which also shows a fairly good constancy of the entropy of activation, with only one or two exceptions, and corresponding dependence of reaction rates on the energy of activation. When our results are compared with those of other investigators, in which the leaving group, the nucleophile and the solvent are different, the qualitative order of influence of substituents from the *p*-position is nearly the same, and it becomes evident that in the nucleophilic substitutions of these compounds the polarity of the substituted carbon atom is mainly determined by the over-all polar effect of the substituent.

Discussion

The Hammett Equation.—Hammett[53] established the empirical relation $\log k_R - \log k_H = \sigma\rho$.

This equation has been extensively used for studies on aromatic nucleophilic substitution.[7,10,12a,b,13–15,24c,54–56]

The subject has been reviewed by Jaffé[57] and recently critically revaluated by Okamoto and Brown,[58] McDaniel and Brown,[59] Taft and coworkers[60,61] and Van Bekkum, Verkade and Wepster.[62]

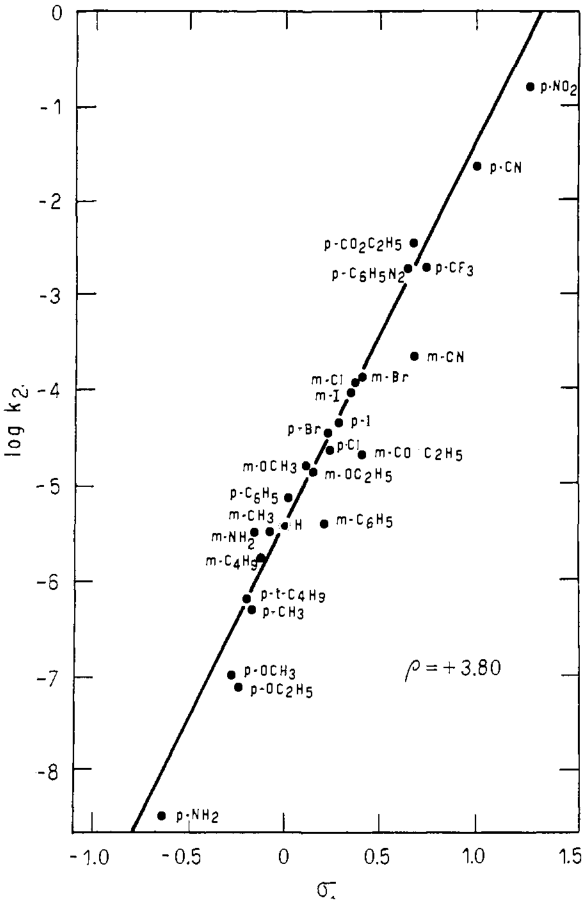

Fig. 1.

High positive values of ρ are characteristic of aromatic nucleophilic substitutions, in accordance with the sensitivity of these reactions to the polar effect of substituents in the aromatic nucleus.

The σ-constants correlate the polar influences of substituents. The original values given by Hammett[53] did not prove completely satisfactory in aromatic nucleophilic substitution. The more recent ones recorded by Jaffé[57] as σ^* are generally employed.

Using Jaffé's σ^*-values which are equivalent to Hammett's σ constants for all substituents studied with the exceptions of groups *p*-NO$_2$, *p*-CN, *m*-*t*-C$_4$H$_9$, *m*-CO$_2$C$_2$H$_5$ and *p*-CO$_2$C$_2$H$_5$ and employing for substituent *p*-CF$_3$ the constant recorded by Bunnett and co-workers,[12b] a ρ-value of +3.80 with a correlation coefficient $r = 0.934$ results.

For the 4-R-2-nitrochlorobenzenes alone a ρ constant of +4.08 with a correlation coefficient 0.992 is obtained. Kalberer[9] has found a value of $\rho = +4.82$ for the reaction of 4-R-bromobenzenes with piperidine in benzene comparable to ours and those obtained by other workers summarized by Jaffé. This clearly shows that the differences in rate are mainly due in these series to the polar influences of substituents from the *p*-position.

The interesting question arises: what is the in-

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TABLE III

REACTIONS OF 4-R- AND 5-R-2-NITROCHLOROBENZENES WITH PIPERIDINE IN BENZENE

Substituent	$k_2 \times 10^5$, l. mole^{-1} sec.$^{-1}$ 30°	35°	45°	60°	75°	100°	$(k_R/k_H)_{45°}$	E, kcal./mole	$-\Delta S^*_{45}$, e.u.
4-NO_2	7.83×10^{3a}	11.4×10^3	14.9×10^3				41100	6.5	42
4-CN		1.33×10^3	2.14×10^3	4.57×10^3			5890	10.0	35
4-$CO_2C_2H_5$		197	335	612			922	9.4	41
4-F_3C		114	191	452			527	11.3	36
4-$C_6H_5N_2$		119	184	335			508	8.6	44
5-CN	6.93^a		21.2	50.0	103		58.5	11.8	38
5-Br	5.38		12.5	27.9			34.5	11.0	42
5-Cl	4.93		11.7	26.5	52.2		32.3	11.5	40
5-I	3.37		9.07	20.2			24.9	11.8	40
4-CO_2H			5.20		21.9		14.3	10.4	46
4-I	1.69		4.41	10.6			12.1	12.0	41
4-Br	1.28		3.49	7.99			9.6	12.3	40
4-Cl	0.842		2.29	4.99	11.5		6.2	12.1	42
5-$CO_2C_2H_5$			1.91	4.22	9.91	31.7	5.3	11.9	43
5-OCH_3			1.52		8.12		4.2	12.4	42
5-OC_2H_5			1.34		7.15		3.7	13.0	40
4-C_6H_5			0.758		4.46	16.3	2.1	13.0	41
5-C_6H_5			.380		2.61		1.05	14.1	39
H			.363		2.48	9.10	1	13.9	40
5-NH_2			.311		2.33		0.86	13.7	41
5-CH_3			.312		2.00		.86	13.8	40
5-CO_2H			.196	0.621	1.84		.54	16.4	33
5-$C(CH_3)_3$			.167		1.16		.46	14.0	41
4-$C(CH_3)_3$			.061	0.183	0.414		.17	14.2	43
4-CH_3			.053		.359	1.52	.15	14.5	42
4-OCH_3			(.0091)		.0796	0.359	.025	15.5	42
4-OC_2H_5			(.0078)		.0680	.302	.022	15.6	42
4-NH_2			(.0003)		.0051	.034	.001	19.6	36

^{a} At 25°.

fluence of conjugative interactions between a 5-substituent R and the nitro group *para* to each other?

Miller and co-workers[23] have considered this point previously in the reactions of 5-R-2,4-dinitrochlorobenzenes and 4-R-2,6-dinitrochlorobenzenes with sodium methoxide in methanol.

The activating systems in these 2,4- and 2,6-dinitro series are not equivalent, since it is known that the activating influence of the *o*- and *p*-nitro groups differ in magnitude and also with the nucleophile. This makes any direct comparison of both series difficult.

In reactions of 4-R-2,6-dinitrochlorobenzenes the rates can be correlated with the polar effects of *p*-substituents R, but these influences cannot be compared with those of substituents 5-R in the reactions of 5-R-2,4-dinitrochlorobenzenes, where the over-all effect of R includes the polar influences from the *m*-position, the conjugative interactions with the nitro groups and the steric influence over the 4-nitro group, factors which are difficult to evaluate independently.

Miller and co-workers have correlated in a Hammett plot their log k_2 values against amended σ constants in order to give extra weight to the polar and steric influences of 5-R substituents with the nitro groups.

For the reaction of 5-R-2-nitrochlorobenzenes with piperidine in benzene a low value of $\rho = 2.63$ is obtained with $r = 0.893$.

The different values of ρ for the 4-R and 5-R series would show once more, and in accordance with the views of Hine[63] and Jaffé,[64] that ρ in spite of formal analogies is not a measure of the same magnitude for both series of compounds. In most cases differences are small and often lie within the experimental error, but in the reactions we have studied they are significant. As there is a qualitative agreement with the findings of Miller and co-workers, it was thought that the idea underlying the treatment of their results could be applied in a more direct way to ours, in order to estimate the mesomeric interactions 5-R-2-NO_2.

The values of log $k_{2\ 5\text{-R}}$ *vs.* $\sigma_{meta}{}^*$ were introduced into the Hammett's graphic plot of log $k_{2\ 4\text{-R}}$ *vs.* $\sigma_{4\text{-R}}{}^*$ with $\rho = +4.08$.

From this, the difference between $\sigma_{meta}{}^*$ values employed and the amended σ-values fitting the experimental data into equation

$$\log k_{2\ 5\text{-R}} = \log k_{2\ \text{H}} + 4.08 \times \sigma_{\text{amended}}$$

was evaluated for each *m*-substituent.

The differences for most substituents included in Fig. 1 are small, but for substituents *m*-cyano, *m*-carbethoxy and *m*-phenyl σ_{amended} values are smaller than the σ^*-constants by 0.24, 0.20 and 0.20 units, respectively, showing that the activating influence of the nitro group *ortho* to the site of substitution is roughly constant but smaller than its over-all effect in most of the compounds studied.

For the *m*-amino group the σ^*-constant should be increased by 0.15 unit in order to bring the log

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k_2 for 5-amino-2-nitrochlorobenzene into the Hammett plot with $\rho = +4.08$.

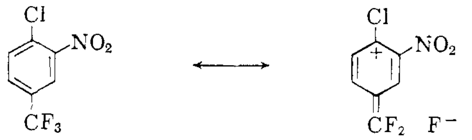
The Hammett plot log $k_{2\ 4\text{-R}}$ *vs.* σ^* shows certain differences between the accepted σ^*-values and those graphically determined for the reaction, but taking into account the correlation coefficient 0.992 of the experimental data for the *p*-series obtained, no great significance is attached to this.

Nevertheless it is interesting to point out that for the *p*-phenyl group the value $\sigma = +0.07$ indicated by Berliner and co-workers[65,66] fits the experimental data better for this compound than the smaller value recorded by Hammett and by Jaffé employed by us.

Polar Effects of Substituents.—4-Chloro-3-nitrobenzotrifluoride and 4-chloro-3-nitroazobenzene show an inversion of relative reactivity (an isokinetic temperature) between 35° and 45°, but the order found for the more reactive compounds at 45°, $k_{4\text{-NO}_2} > k_{4\text{-CN}} > k_{4\text{-CO}_2\text{C}_2\text{H}_5} > k_{4\text{-F}_3\text{C}} > k_{4\text{-C}_6\text{H}_5\text{N}_2} > k_{4\text{-CO}_2\text{H}} > k_{4\text{-halogen}}$ is essentially that expected from their total polar effects upon the site of substitution.

2,4-Dinitrochlorobenzene is by far the most reactive among the compounds studied, due to the powerful mesomeric effect of the nitro groups (relative rates: R.R. = 4×10^4). Groups 4-cyano, 4-carbethoxy and 4-phenylazo act through their combined inductive and mesomeric actions, of which the latter is apparently the more important.

Superimposed to the strong negative inductive effect of the 4-trifluoromethyl group, there is very likely a hyperconjugative effect of the type stated by Roberts, Webb and McElhill[67] and represented by the formulas of type III.



III

In agreement with the results of Walborsky and Schwarz,[68] in electrophilic addition to the ethyl γ,γ,γ-trifluorocrotonate the oberved order $k_{p\text{-CO}_2\text{C}_2\text{H}_5} > k_{p\text{-CF}_3}$ points to the greater capacity of the carbethoxy group to stabilize a negative charge on the neighboring carbon atom.

The mesomeric effects of cyano and carbethoxy groups from the *m*-position are only transmitted to the site of substitution by a secondary relay effect causing the corresponding substituted compounds to react faster than *o*-chloronitrobenzene but much slower than the isomers with these groups *para*.

The sequence $k_{4\text{-NO}_2} > k_{4\text{-CO}_2\text{H}} > k_{4\text{-halogen}}$ and the relative rate $k_{4\text{-CO}_2\text{H}}/k_\text{H} = 14.3$ found by us differ from those of Berliner and Monack,[10] $k_{4\text{-NO}_2} > k_{4\text{-halogen}} > k_{4\text{-CO}_2^-}$ and $k_{4\text{-CO}_2^-}/k_\text{H} = 2.5$.

Since these figures are directly comparable due to the similarity of ρ constants for both reactions, it can be concluded that in the conditions employed by Berliner and Monack the reacting species of 4-chloro-3-nitrobenzoic acid is the ionized form of the acid, while in our conditions, if there is an equilibrium between the carboxy and the carboxylate form, the most reactive species is very likely the un-ionized acid.

The order $\text{CO}_2\text{CH}_3 > \text{I} > \text{Br} > \text{Cl} > \text{CO}_2^- > \text{H}$ found by Miller[7] in the reaction of 4-R-2-nitrochlorobenzenes with sodium methoxide in methanol reinforces this point of view, because in the condition of his experiments there is no doubt about the total ionization of the carboxy groups.

The 3-chloro-4-nitrobenzoic acid reacts slower than the *p*-substituted isomer and *o*-chloronitrobenzene, ($k_{4\text{-CO}_2\text{H}}/k_{5\text{-CO}_2\text{H}} = 27$; R.R. 5-$\text{CO}_2\text{H}$ = 0.54).

These results indicate an electronic releasing effect of the substituent from the *m*-position more compatible with an ionic structure of the substituent.

The primary and secondary dissociation constants of phthalic acids as compiled by Brown and co-workers[69] show a similar inversion, determined by the appearance of a charged structure, in the accepting and releasing electronic effects of carboxy and carboxylate groups.

By the action of their mesomeric effect, the substituents 4-methoxy, 4-ethoxy and 4-amino are all strongly deactivating. The partial sequence $k_{4\text{-OCH}_3} > k_{4\text{-OC}_2\text{H}_5}$ reflects the secondary influence of alkyl groups through the oxygen atom, showing an inductive order. From the *m*-position the mesomeric effect of these groups can reach the site of substitution only through a secondary inductive effect from the *o*-carbon atoms. In the amino group this effect is almost compensated by the negative inductive effect of the substituent while in the alkoxyl groups induction predominates and these compounds react faster than *o*-chloronitrobenzene.

All the halogens studied produce a marked increase in the rate, specially from the *m*-position, due to their negative inductive effect. The mesomeric effect acts in these compounds in a sense opposite to the inductive effect, with enough intensity as to produce an "inverted inductive" order series for the *p*-halogen compounds: $k_{4\text{-I}} > k_{4\text{-Br}} > k_{4\text{-Cl}}$. This effect is substantially damped from the *m*-position. The *m*-halogen compounds are thus as a whole more reactive than *p*-halogen substituted isomers; besides no "inverted order" is observed.

Nevertheless there is an inversion between the substituents chlorine and bromine.

The introduction of a *m*-methyl group produces a slight decrease in rate; this is more pronounced if the group is in the *p*-position.

The *p*-*t*-butyl group acts much the same as *p*-methyl, as Berliner and Monack[10] have earlier found, but the influence is clearly different from the *m*-position. The ratio $k_{5\text{-}t\text{-C}_4\text{H}_9}/k_{4\text{-}t\text{-C}_4\text{H}_9} = 2.7$ is smaller than $k_{5\text{-CH}_3}/k_{4\text{-CH}_3} = 5.9$.

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Both inductive and hyperconjugative effects for these substituents are positive causing them to be deactivating with respect to hydrogen.

The inductive effect should not be very different when the substituent is in *m*- or *p*-position, but hyperconjugation determines the order $k_{5\text{-R}} > k_{4\text{-R}}$ because it can only act directly when the alkyl group is in the *p*-position.

The ratio k_m/k_p for *t*-butyl, significantly greater than unity, suggests that for this substituent as well as for methyl, hyperconjugation plays an important role. These results agree with those of Capon and Chapman.[21]

The effects of the phenyl group cannot be interpreted for both positions of the substituent on the same basis of negative inductive and positive mesomeric effects.

Ingold[70] pointed out the variable capacity of the phenyl group to act as an electron acceptor or donor, depending on the reaction requirements, and the general structure to which it is attached.

De la Mare and Ridd[71] have recently discussed the influence of several factors on electrophilic substitutions in diphenyls and structurally related compounds. Berliner and co-workers[66,72] have established that transmission of polar effects of substituents through the diphenyl moiety is less intense than through benzene itself. In the activation of the chlorine atom by the phenyl group in 4-chloro-3-nitrobiphenyl, the negative inductive effect of the substituent is more powerful than the opposing mesomeric effect; but in 3-chloro-4-nitrobiphenyl, where the phenyl group is *para* to the nitro group, mesomeric interaction by *para*-conjugation operates with its consequent electronic release balancing the electron-attracting effect of the phenyl group.

In the conditions of our experiments the phenyl group slightly enhances the reactivity from the *m*-position (R.R. = 1.05); a greater increment is observed from the *p*-position (R.R. = 2.1).

Berliner and co-workers have obtained a similar result in the reaction of 4-bromo-3-nitrobiphenyl with piperidine in which this compound reacts 2.2 times as fast as *o*-bromonitrobenzene.

Brown, Okamoto and Inukai[73] found that the phenyl substituent, in the solvolysis of phenyldimethylcarbinyl chlorides system in which no nitro group is present, increases the rate by six times from the *p*-position while it is deactivating from the *m*-position (R.R. = 0.32). These results can be compared with those of Berliner and Shieh[74] for the solvolysis of α-phenylethyl chlorides in which they find that forcing both rings of the biphenyl moiety to be coplanar, by introduction of an *ortho–ortho* methylenic bridge (fluorenyl derivative), increases the rate of reaction by a factor of seven hundred.

Finally we wish to record from experiments made in this Laboratory by Miss Hebe B. Belmonte that it has not been possible to obtain 3-chloro-4-nitroazobenzene by condensation of nitrosobenzene with 3-chloro-4-nitroaniline and hence to study the polar effects of the *m*-phenylazo substituent in the reaction.

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The *ortho:para* Ratio in the Activation of the Nucleophilic Aromatic Substitution by the Nitro Group

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The amount of substitution of the chlorine atoms of 2,4-dichloronitrobenzene-4-Cl^{36} by piperidine in benzene and methanol has been determined by a radiochemical method. The results have been compared with the reactions of *o*- and *p*-chloronitrobenzene with piperidine in the same solvents and in ethanol. It is concluded that while the change from benzene to methanol lowers the over-all rate of substitution, it enhances selectively the reactivity of the chlorine atom *para* to the nitro group. Reaction kinetics are tentatively explained and Arrhenius parameters presented.

Bunnett and Zahler[2] and more recently Bunnett and Morath[3] have reviewed the extensive literature on the activating effect of the nitro group in aromatic nucleophilic substitution.

It is well known that in the series of nitro-halogenobenzenes, the *para* isomers are the more reactive with reagents that have lone pairs of electrons on an atom of Group VI of the periodic table, such as alkoxides, phenoxides, thiophenoxides, etc.,

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