Anal. Calcd. for $C_5H_7BrO_2S$: C, 28.45; H, 3.34; Br, 37.86; S, 15.19. Found: C, 27.72, 27.86; H, 3.45, 3.36; Br, 37.68; S, 14.41.

When a suspension of 0.68 g. of this product in 6 ml. of 5% aqueous sodium hydroxide was allowed to stand at room temperature for one hour with occasional agitation, the crystalline solid obtained on filtration (0.52 g., 76%) melted at 144–145° after recrystallization from water and failed to depress the m.p. of the compound previously described[1] as 4-bromo-$\Delta^{3(\text{or }2)}$-dihydrothiapyran 1,1-dioxide.

Ultraviolet Absorption Spectra.—The spectra were determined with a Beckman quartz spectrophotometer, model DU, using an approximately constant spectral band width of 1–2 mμ down to wave lengths in the neighborhood of 220 mμ. Readings at shorter wave lengths were obtained by using the 0.1 switch position and balancing the galvanometer for 100% transmission with the solvent in position before the phototube. Absolute ethanol was used as the solvent. Spectra of other thiapyran derivatives prepared in the present investigation will be described in a forthcoming communication on the ultraviolet absorption spectra of heterocyclic sulfur compounds.

SWARTHMORE, PA. RECEIVED SEPTEMBER 18, 1951

[CONTRIBUTION FROM THE MARION EDWARDS PARK LABORATORY OF BRYN MAWR COLLEGE]

Nucleophilic Displacement in the Benzene Series[1]

BY ERNST BERLINER AND LOUISE C. MONACK

The rate constants of the reaction of 4-substituted 2-nitrobromobenzenes with piperidine have been determined. The reaction follows a Hammett relationship with a rho value of 4.95. Differences in rates are mainly determined by differences in activation energies.

Most studies of nucleophilic displacement on aromatic halides have dealt with the effect of three factors: the displaced halogen,[2] the nucleophilic reagent,[3] and the substituent. Of these, the effect of substituents has been investigated least. The activating effect of the nitro group and other electron attracting substituents has been qualitatively observed for many years,[4] and relative activating powers of different groups have also been studied quantitatively.[5] Much less information is available on the effect of electron repelling or deactivating substituents,[6] and very little work is reported in which a series including both activating and deactivating groups has been investigated.[7,8] This is understandable; for reasons which have often been discussed[9] nucleophilic displacement on aryl halides, as on vinyl halides, is a very difficult reaction, which proceeds hardly at measurable rates at room temperature, whereas activated displacements, particularly nitro-activated, are fairly rapid, even at room temperature. Chlorobenzene reacts less than 1% with piperidine in 48 hours at 165°,[10] and aryl halides containing electron repelling groups react slower still. Differences of reactivity under the very drastic conditions necessary to affect any reaction at all become difficult to assess. De Crauw, who studied a series of chlorobenzenes containing both activating and deactivating groups, reports that the amino, hydroxy, methoxy and sulfhydryl compounds were completely inert to sodium methoxide at 180° and eight hours,[8] and almost no difference was found between chlorobenzene and *p*-chloroaniline toward piperidine in boiling benzene.[11] In addition, there is reason to believe that nucleophilic displacement with and without activating groups may proceed by different mechanisms, which in itself makes a comparison meaningless.[10,12]

To overcome these difficulties, and in order to evaluate the effect of both activating and deactivating groups on a nucleophilic displacement reaction under identical conditions, fourteen compounds of the type I were studied with piperidine as reactant and solvent. The ortho-nitro group was introduced in order to activate the bromine, and its effect on the rate constants was assumed to be a constant factor.[13] All differences in rate are then due

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[1] Taken from a dissertation submitted by Miss L. C. Monack to the Graduate School of Bryn Mawr College in partial fulfillment of the requirements for the Ph.D. degree.

[2] For instance: R. Löwenherz, *Z. physik. Chem.*, **29**, 401 (1899); H. Franzen and E. Bockhacker, *Ber.*, **53**, 1174 (1920); A. Rheinlander, *J. Chem. Soc.*, **123**, 3099 (1923); B. V. Tronov and E. A. Krueger, *J. Russ. Phys. Chem. Soc.*, **58**, 1270 (1926) [*C. A.*, **21**, 3887 (1927)]; F. W. Bergstrom, R. E. Wright, C. Chandler and W. A. Gilkey, *J. Org. Chem.*, **1**, 170 (1936).

[3] For instance: W. Borsche, *Ann.*, **386**, 351 (1912); *Ber.*, **56**, 1488 (1923); W. Borsche and D. Rantscheff, *Ann.*, **379**, 152 (1911); W. Borsche and H. Bahr, *ibid.*, **402**, 81 (1914); K. W. Rosenmund and E. Struck, *Ber.*, **52**, 1749 (1919); R. J. W. Le Fevre and E. E. Turner, *J. Chem. Soc.*, 1113 (1927); H. J. Van Opstall, *Rec. trav. chim.*, **52**, 901 (1933); A. Singh and D. H. Peacock, *J. Chem. Phys.*, **40**, 669 (1936); O. L. Brady and F. R. Cropper, *J. Chem. Soc.*, 507 (1950).

[4] Pisani, *Ann.*, **92**, 326 (1854); E. Lellmann, *Ber.*, **20**, 680 (1887); M. Schoepf, *ibid.*, **22**, 3281 (1889); **23**, 3440 (1890); **24**, 3771 (1891); P. Fischer, *ibid.*, **24**, 3785 (1891); W. Borsche and I. Exss, *ibid.*, **56**, 2353 (1923); J. Kenner, *J. Chem. Soc.*, **105**, 2717 (1914).

[5] A. F. Holleman and F. E. van Haeften, *Rec. trav. chim.*, **40**, 67 (1921), and many preceding papers of Holleman and his students; Th. J. F. Mattaar, *ibid.*, **41**, 103 (1922); H. Ph. Baudet, *ibid.*, **43**, 707 (1924); A. Brewin and E. E. Turner, *J. Chem. Soc.*, 332 (1928); W. Davies and E. S. Wood, *ibid.*, 1122 (1928); R. B. Sandin and M. Liskear, THIS JOURNAL, **57**, 1304 (1935); W. C. Spitzer and G. W. Wheland, *ibid.*, **62**, 2995 (1940); J. F. Bunnett and A. Levitt, *ibid.*, **70**, 2778 (1948).

[6] H. F. J. Lorang, *Rec. trav. chim.*, **46**, 891 (1927); H. Lindemann and A. Pabst, *Ann.*, **462**, 24 (1928); E. A. Krueger and M. S. Bednova, *J. Gen. Chem.* (*U. S. S. R.*), **3**, 67 (1923) [*C. A.*, **28**, 1593 (1934)]; N. Cambell, W. Anderson and J. Gilmore, *J. Chem. Soc.*, 446 (1940).

[7] G. M. Kraay, *Rec. trav. chim.*, **49**, 1082 (1930); L. M. F. van de Lande, *ibid.*, **51**, 98 (1932).

[8] Th. de Crauw, *ibid.*, **50**, 753 (1931).

[9] E. D. Hughes, *Trans. Faraday Soc.*, **37**, 627 (1941); J. W. Baker, *ibid.*, **37**, 635 (1941); E. D. Hughes and C. K. Ingold *J. chim. phys.*, **45**, 241 (1948); G. W. Wheland, "The Theory of Resonance and its Application to Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1944, p. 272.

[10] E. Berliner, M. J. Quinn and P. J. Edgerton, THIS JOURNAL, **72**, 5305 (1950).

[11] G. M. Badger, J. W. Cook and W. P. Vidal, *J. Chem. Soc.*, 1109 (1947).

[12] See also J. F. Bunnett, Abstracts of Papers, Meeting of the American Chemical Society, Chicago, Ill., September, 1950, p. 98N.

[13] A similar system, containing various activating groups, was recently studied by J. F. Bunnett, F. M. Draper, P. R. Ryason, P. Noble, R. Zahler and R. G. Tonkyn, abstracts of papers presented to the Meeting of the American Chemical Society, Boston, Mass., April, 1951, p. 47M.

TABLE I

THE REACTION BETWEEN 4-R-2-NITROBROMOBENZENES AND PIPERIDINE

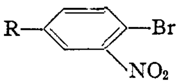
Substituent R	k_{25}, min.$^{-1}$	k_{35}, min.$^{-1}$	E, kcal.	log PZ, min.$^{-1}$	Deviation from sigma[a]
NO_2	Very fast				
Br	$2.27 \pm 0.05 \times 10^{-2}$	$4.21 \pm 0.11 \times 10^{-2}$	11.3 ± 0.9	6.64	0.025
Cl	$1.62 \pm .04 \times 10^{-2}$	$3.07 \pm .11 \times 10^{-2}$	11.7 ± 1.1	6.79	.001
I	$1.57 \pm .03 \times 10^{-2}$	$3.11 \pm .06 \times 10^{-2}$	12.5 ± 0.7	7.36	.051
COO^-	$7.30 \pm .23 \times 10^{-3}$	$14.39 \pm .23 \times 10^{-3}$	12.4 ± 0.9	6.95	....
H	$2.90 \pm .06 \times 10^{-3}$	$5.63 \pm .14 \times 10^{-3}$	12.1 ± 0.8	6.34	.075
F	$7.55 \pm .11 \times 10^{-4}$	$15.55 \pm .37 \times 10^{-4}$	13.2 ± 0.7	6.56	.109
$C(CH_3)_3$	$4.94 \pm .03 \times 10^{-4}$	$9.99 \pm .15 \times 10^{-4}$	12.9 ± 0.4	6.12	.112
CH_3	$4.23 \pm .05 \times 10^{-4}$	$8.74 \pm .15 \times 10^{-4}$	13.2 ± 0.6	6.30	.072
OCH_3	$5.22 \pm .14 \times 10^{-5}$	$11.60 \pm .25 \times 10^{-5}$	14.6 ± 0.9	6.42	.015
OC_2H_5	$4.38 \pm .16 \times 10^{-5}$	$9.43 \pm .21 \times 10^{-5}$	14.0 ± 1.1	5.90	.049
$N(CH_3)_2$	$3.52 \pm .48 \times 10^{-6}$	$7.18 \pm .27 \times 10^{-6}$	(13.0 ± 3.2)	(4.08)	...
OH	$1.69 \pm .08 \times 10^{-6}$	$4.42 \pm .25 \times 10^{-6}$	17.6 ± 1.9	7.13	...
NH_2	$3.60 \pm .20 \times 10^{-7}$	$8.33 \pm 1.27 \times 10^{-7}$	(15.3 ± 3.8)	(4.78)	.061

[a] At 25°.

to the effect of the group R, all reactions being of the "activated" type. Substituents meta to the bromine were avoided in order to eliminate as much as possible secondary effects, arising from resonance interaction of the nitro group with the substituent R. Under these conditions the measured variations in rate constants were 100,000-fold.

A further interest attaches itself to the validity of the Hammett equation[14] for this type of reaction. Of all the reactions listed by Hammett, none involves a direct attack on the benzene ring (although calculations are reported for aromatic nitration), all of them being side chain reactions. There is no *a priori* reason why the set of sigma constants, obtained from dissociation constants, should be applicable to a reaction where a direct interaction with the aromatic system is involved, although a reasonable qualitative agreement should be expected. As a corollary to the Hammett equation, it was also of interest to observe whether, as is the case in electrophilic substitution,[15] differences in rate are caused essentially by energy of activation terms. The presence of the ortho-nitro group should have no effect on the validity of Hammett's equation; the standard compound is simply *o*-nitrobromobenzene.[16]

In Table I are summarized the data for the reaction of 4-substituted 2-nitrobromobenzenes with piperidine at 25 and 35°, the compounds being listed in the order of decreasing reactivity. According to the sigma constants, the order of reactivity should be: $NO_2 > COOH > I > Br > Cl > F > H > CH_3 > C(CH_3)_3 > N(CH_3)_2 > OC_2H_5 > OCH_3 > NH_2$. The order found experimentally is: $NO_2 > Br > Cl > I > COOH > H > F > C(CH_3)_3 > CH_3 > OCH_3 > OC_2H_5 > N(CH_3)_2 > OH > NH_2$. In general, the order of reactivity follows clearly the order predicted from the electronic effects of the substituents, and therefore their sigma values. Some of the individual values and some of the deviations from the "sigma order" deserve brief comment.



(I)

Fig. 1.

The Sigma Constants. The Nitro Group.—2,4-Dinitrobromobenzene reacted too fast for measurement. On adding the compound to piperidine, a vigorous reaction took place accompanied by a rise in temperature and by the conversion of the material into a deeply colored orange-yellow substance, which appeared to be insoluble in piperidine. It probably is a quinoid salt of the type described often in the literature.[17] Assuming the *p*-nitro compound to fall on the line (Fig. 2), $k_{p\text{-}NO_2}$ would be about 2.44×10^3.[18] The introduction of a *p*-nitro group into *o*-chloronitrobenzene raises the reactivity of the compound toward sodium methoxide by a factor of 1.7×10^5 (at 25°).[19] If this is also true in the present system the rate constant for the dinitro compound should be 0.5×10^3, which is of the same order of magnitude as the value calculated from sigma and rho.[20]

The Halogens.—Following Branch and Calvin[21] the individual differences among the halogens are not considered significant, except for the *p*-fluoro compound, which stands out. The *p*-fluoro compound is in the right order relative to the other halogens. By resonance it has the strongest electron repelling effect, and is therefore the most deactivating of the halogen compounds, but in the present reaction it is electron releasing even relative to hydrogen, *i.e.*, the *p*-fluoro compound reacts slower than the unsubstituted one. Such a strong effect should not have been anticipated in a

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[14] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Company, Inc., New York and London, 1940, Chapter VII.

[15] F. E. C. Scheffer and W. F. Blanksma, *Rec. trav. chim.*, **45**, 522 (1926); A. E. Bradfield and B. Jones, *J. Chem. Soc.*, 1006, 3073 (1928).

[16] J. D. Roberts and J. A. Yancey, THIS JOURNAL, **73**, 1011 (1951).

[17] F. Reitzenstein, *J. prakt. Chem.*, **68**, 251 (1903); N. V. Sidgwick, T. W. J. Taylor and W. Baker, "The Organic Chemistry of Nitrogen," Oxford University Press, Oxford, 1942, p. 259 ff.; J. D. Farr, C. C. Bard and G. W. Wheland, THIS JOURNAL, **71**, 2013 (1949).

[18] The "phenolic" sigma constant was used.

[19] From A. F. Holleman, J. de Mooy and J. Ter Weel, *Rec. trav. chim.*, **35**, 1 (1915); Mattaar, ref. 5; also ref. 13.

[20] This apparent agreement may be fortuitous. In the interpretation of C. G. Swain and W. P. Langsdorf (THIS JOURNAL, **73**, 2813 (1951)) the *p*-nitro compound would be expected to be much more reactive and not to fall on the straight line.

[21] G. E. K. Branch and M. Calvin, "The Theory of Organic Chemistry," Prentice Hall, Inc., New York, N. Y., 1941, pp. 248, 416 ff.

reaction which is not assisted by the resonance effect of the fluorine atom. The fluorine atom acts as it does on the dissociation constants of phenols (*p*-fluorophenol weaker than phenol[22]) and in the halogenation of phenyl and naphthyl halides.[23] In fact, the *p*-halogen compounds, including their relative position with regard to hydrogen, are in exactly the reverse order from that displayed by them in the halogenation of the 1-halonaphthalenes (ArF > ArH > ArI > ArCl > ArBr).[23] They have therefore the same effect on the two reactions, in spite of the opposite nature of these reactions. In electrophilic halogenation a strong time-variable polarizability effect is supposed to assist the reaction in the transition state, whereas in the nucleophilic attack by piperidine the additional effects should not be evoked, and yet, in both reactions the four halogens display the same effect. While it is true that the relative magnitude of the effects of which the halogens appear to be capable differ from system to system,[24] in the present system the fluorine atom must be assigned a greater permanent electron release effect than hydrogen and the other halogens.

Alkyl Groups.—The *p*-methyl compound reacts slower than the *p*-*t*-butyl compound, indicating the operation of the hyperconjugation effect, even though the reaction is not electron demanding.[25,26] The order of the two substituents therefore does not correspond to their sigma values, which is not surprising, in view of the fact that the dissociation constants of the *p*-alkylbenzoic acids do not show a clear-cut order.[27]

Amino Groups.—Both the *p*-amino and the *p*-dimethylamino compounds react very slowly, the former less than 1% in one week at 25°, and the rate constants therefore are subject to considerable error, although they are of the right order of magnitude. The dimethylamino compound reacts ten times faster than the *p*-amino compound. Although this is in line with their respective sigma values, the two N-methyl groups would have been expected to exert an additional inhibiting effect on the reaction, which is not the case. The value for the dimethylamino compound is the farthest off the line; however, the sigma constant for this group has been questioned[28] and should be considerably more negative, certainly more negative than that of the alkoxyl groups. A recent compilation of experimental sigma values for this group suggests a value of −0.57 ± 0.04,[28] which agrees reasonably well with the value found in this investigation (−0.516). The difference in reactivity between the unsubstituted and the *p*-amino compound (a factor of 10,000) is in appreciable contrast to the reported behavior in a non-activated displacement, where chlorobenzene and *p*-aminochlorobenzene show almost the same reactivity toward piperidine in boiling benzene.[11]

Alkoxyl and Hydroxyl Groups.—These groups decrease the rate of reaction appreciably. The *p*-methoxy compound reacts slightly faster than the *p*-ethoxy compound, in a reversal of their sigma values. Since these values were originally announced, the dissociation constant of *p*-ethoxybenzoic acid has been determined and is somewhat less than that of *p*-anisic acid.[29] This would give the *p*-ethoxyl group a somewhat more negative sigma constant than the *p*-methoxyl group, *i.e.*, more electron repulsion, as found in this and a number of other reactions.[30] Both alkoxyl compounds react between 25 and 30 times faster than the *p*-hydroxyl compound indicating less electron release by these groups. By analogy with the dimethylamino compound an additional electron release by the alkyl groups might have been expected, but the hydroxyl group is probably partly ionized and the negatively charged oxygen should have a stronger deactivating power. A sigma value of −0.58 is found experimentally, while values of −0.34[31] and −0.53[32] have been reported from other reactions. Because of partial or complete ionization probably no fixed value can be assigned to this group, but if the value derived from the first dissociation constant of *p*-hydroxybenzoic acid is accepted for the undissociated hydroxyl group (−0.34)[33] partial conversion to the phenoxide ion must have occurred.

The Carboxyl Group.—The carboxyl group is probably completely ionized and its effect should be discussed in terms of the carboxylate ion, which is much less electron attracting than the carboxyl group. Its sigma value should therefore be less positive than that of the latter. The present value is +0.154, which agrees well with the constant of +0.16 obtained for the carboxylate ion from both the alkaline hydrolysis of the sodium salt of monoethyl terephthalate[34] and the alkaline hydrolysis of *p*-carboxyphenyl acetate.[35] A constant of +0.16 can therefore probably be accepted as the sigma constant for the carboxylate ion.[36]

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[22] H. B. Watson, "Modern Theories of Organic Chemistry," Oxford University Press, Oxford, sec. edit., 1941, p. 102.

[23] P. B. D. De La Mare and P. W. Robertson, *J. Chem. Soc.*, 100 (1948).

[24] For a recent discussion of the effects of halogens see ref. 23 and J. W. Baker and H. B. Hopkins, *ibid.*, 1089 (1949).

[25] J. W. Baker, W. S. Nathan and C. W. Shoppee, *ibid.*, 1847 (1935).

[26] The same relative order was observed with the two respective iodo compounds. Unpublished results with Miss M. J. Quinn, Senior Honors Thesis, 1947.

[27] J. W. Baker, J. F. J. Dippy and J. E. Page, *ibid.*, 1774 (1937).

[28] H. Gilman and G. E. Dunn, This Journal, **73**, 3404 (1951). Also ref. 21.

[29] B. Jones and J. C. Speakman, *J. Chem. Soc.*, 19 (1944); G. W. K. Cavill, N. A. Gibson and R. S. Nyholm, *ibid.*, 2466 (1949).

[30] R. Robinson and J. C. Smith, *ibid.*, 392 (1926); J. Allen, A. E. Oxford, R. Robinson and J. C. Smith, *ibid.*, 401 (1926); B. Jones, *Trans. Faraday Soc.*, **37**, 726 (1941).

[31] J. D. Roberts, E. A. McElhill and R. Armstrong, This Journal, **71**, 2923 (1949.

[32] E. Berliner and E. A. Blommers, *ibid.*, **73**, 2479 (1951).

[33] G. E. K. Branch and D. L. Yabroff, *ibid.*, **56**, 2568 (1934). See also D. Pressman and D. H. Brown, *ibid.*, **65**, 540 (1943). A value of −0.36 is obtained from the first dissociation constant of hydroquinone, corrected by a factor of two; R. Kuhn and A. Wassermann, *Helv. Chim. Acta*, 11, 3 (1928). An approximate constant of −0.9 is obtained for the *p*-O^- group from the second dissociation constant of hydroquinone (at 30°), corrected by a factor of two [C. T. Abichandani and S. K. K. Jatkar, *J. Indian Inst. Sci.*, **21A**, 417 (1938)] [*C. A.*, **33**, 3662 (1939)], and a constant of −1.07 from the alkaline hydrolysis of ethyl *p*-hydroxybenzoate [E. Tommila, *Suomen Kemistilehti*, **A17**, 6 (1944)]. This is the most negative of all sigma constants, as it should be.

[34] S. Tommila and E. Tommila, *Ann. Acad. Sci. Fennicae*, Ser. **A59**, No. 5, 3 (1942) [*C. A.*, **38**, 6173 (1944)].

[35] E. Tommila and C. N. Hinshelwood, *J. Chem. Soc.*, 1801 (1938).

[36] However, from the second dissociation constant of terephthalic acid, corrected by a factor of two, a constant of −0.33 is obtained, *i.e.*, the acid is weaker than benzoic acid and the carboxylate ion appears to be electron releasing [R. Kuhn and A. Wassermann, *Helv. Chim. Acta*, 11, 44 (1928)].

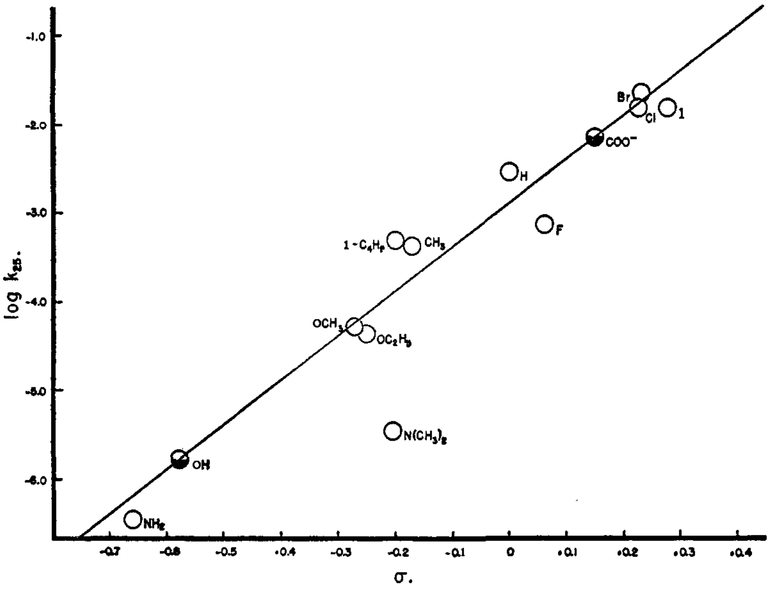

Fig. 2.—A plot of σ against log k_{25}. The values represented by the half-circles were obtained from the plot.

In Fig. 2 log k for the compounds studied is plotted against Hammett's sigma values. For the reasons given above the values for the carboxyl and dimethylamino group were omitted in calculating the least square line. The differences between the accepted sigma values and those found experimentally fall within the given errors (Table I), except for the p-hydrogen and the p-fluoro group, the latter having a negative value.

The Rho Value.—The slope of the line, rho, has the very high value of +4.95, which is higher than any of those reported originally for side chain reactions, except that for aromatic nitration, which has a rho constant of about −5.[37] The reaction is therefore very sensitive to electronic changes brought about by substituents, as much so as electrophilic nitration, the substituents having opposite effect. The powerful o-nitro group does not appear to dampen the effect of the other substituents. While there is no doubt that the points in Fig. 2 tend to fall on the line, thus substantiating what has been anticipated to be the effect of substituents on a nucleophilic displacement reaction,[38] it is also clear that the points show a relatively wide scatter. This is borne out by the median deviation from the straight line, which is 0.244.[39] Of the 52 original reactions there are seven for which the probable error is greater than 0.1 and one for which it is greater than 0.2, the mean value being 0.06. The large deviation is not thought to be without significance, nor is it thought to be wholly due to experimental errors. The sigma values are identified with dissociation constants and other side chain reactions. As pointed out by Hammett,[14] a different constant had to be assigned to the nitro group (and probably other groups) in phenol or aniline derivatives, because of the strong resonance interaction of the functional group and the substituent. Two sigma constants have since also been reported for other groups.[28,40] Reactions taking place on the benzene ring directly, such as the present one, where strong resonance interactions involving the substituent take place in the transition state, must require an adjusted set of sigma constants. The sigma values probably do not only depend on the substituent alone, but also on the type of reaction, the attacking reagent, the pH of the medium and the solvent.[41] In reactions like the present one, they have to take into account resonance interactions which are stronger than those interactions where side chains or other atoms are interposed between the aromatic ring and the seat of reaction. Clearly, the sigma constants are "not made" for this reaction. That the agreement is as good as it is, and that the adjustments probably need only be slight, shows how well in general the sigma values indicate the electronic effect of the substituents.

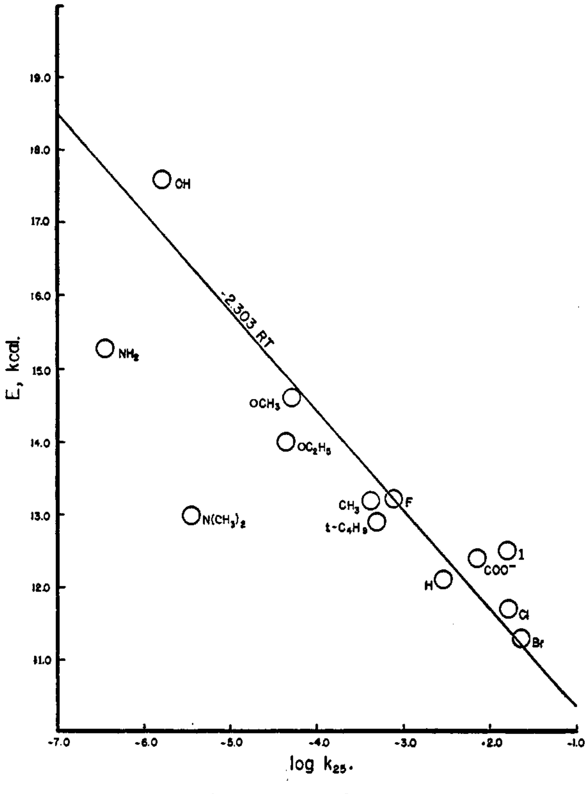

Fig. 3.—A plot of log k_{25} against E.

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[37] A rho value of −6.33 has been reported for the dissociation of substituted triphenyl methyl chlorides. P. D. Bartlett, Paper presented before the Twelfth National Organic Chemistry Symposium of the American Chemical Society, Denver, Colorado, June, 1951, p. 3.

[38] See, for instance, C. K. Ingold, *Rec. trav. chim.*, **48**, 797 (1929).

[39] T. W. Wright and J. F. Hayford, "The Adjustment of Observations," D. Van Nostrand Co., New York, N. Y., 1906, pp. 132–133.

[40] J. D. Roberts and E. A. McElhill, THIS JOURNAL, **72**, 628 (1950); J. D. Roberts, R. L. Webb and E. A. McElhill, *ibid.*, **72**, 411 (1950).

[41] See ref. 21, p. 418. Also A. E. Remick, "Record of Chemical Progress," Kresge-Hooker Scientific Library, Detroit, Michigan, Vol. 11, No. 1 (1950), p. 52.

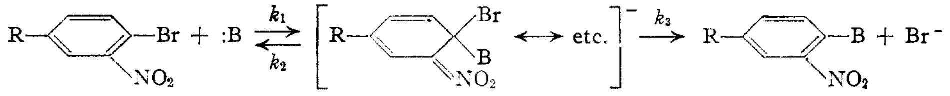

Fig. 4.

Activation Energies and *PZ* Terms.—Of the energies of activation listed in Table I the values for the amino compounds are certainly too low, most likely because of the experimental uncertainties, mentioned before. Some of the other values are very close to each other, and no attempt is made to differentiate between them. It is, however, evident that there is a tendency for the activation energies to increase with decreasing rate constants, while the *PZ* terms stay constant (log $PZ = 6.59 \pm 0.35$).[42] If the differences in rate constants are determined solely by energy terms, a plot of log k against E should be a straight line of the slope $-2.303\ RT$.[43] In Fig. 3 a line of this slope has been drawn, and it can be seen that the points approximate the slope. The differences in rates are therefore determined predominantly by E terms, as is the case in electrophilic substitution.[15] It has been stated that differences in rates in nucleophilic displacement are determined chiefly by *PZ* terms,[44] but this statement was based on an analysis of data of Holleman and his school on various polychloronitrobenzenes, where steric effects and steric inhibition of resonance obscure the situation.

Mechanism.—It has previously been suggested that nucleophilic displacement on activated halides is a two-step mechanism involving a quinoid intermediate (Fig. 4).[10,12,45] Whether the rate-determining step is the formation of the new bond, *i.e.*, the formation of the intermediate (k_1), or the breaking of the carbon–halogen bond (k_3), cannot yet be decisively answered. The effect of substituents on the rate of reaction is in agreement with both views. By virtue of their electronic effects the substituents will favor or impede the approach of the reagent and the formation and stability of the intermediate. Their effect on the loss of the halogen will not be decisive, because the halogen is lost from a nearly aliphatic (sp^3) carbon atom,[46] with which conjugation has been broken, and to which the effect of the substituent cannot be easily relayed. Ultimately, therefore, only the approach of the reagent and the formation and the stability of the intermediate are affected by the substituent, even if the second step is rate-determining. Unlike in electrophilic substitution, where the proton loss occurs after the rate-determining step,[47] the rates of nucleophilic displacement depend on the displaced halogens, and roughly parallel their electronegativities.[10,12] This is the reason why a rate-determining breaking of the carbon–halogen bond had to be considered. If the reaction is analogous to electrophilic substitution (k_1 rate-determining and $k_3 >> k_2$), the halogens affect the approach of the reagent either sterically or through their inductive effects, by which they create a positive pole on the carbon to which they are linked. In either case the order of reactivity of the displaced halogen would be that found experimentally.

Experimental

Materials.—Monsanto piperidine, containing about 1% of pyridine, was dried over potassium hydroxide and then fractionated, b.p. 106–106.2° (760 mm.). *o*-Bromonitrobenzene, m.p, 40.9–41.3°[48] (lit.[49] 41–42°) and 2,4-dinitrobromobenzene, m.p. 70.7–71.4° (lit.[50] 72°) were commercial samples, several times recrystallized. 2,5-Dibromonitrobenzene, m.p. 83.5–84.1° (lit.[51] 84°), 4-bromo-3-nitro-N,N-dimethylaniline,[52] m.p. 92.7–94° (lit. 93.5°) and 4-bromo-3-nitroaniline, m.p. 128.8–129.6° (lit.[53] 131°) were prepared by nitration of the appropriate para-substituted bromobenzene with mixed acid, and 4-bromo-3-nitrobenzoic acid,[54] m.p. 198–199° (lit. 199°) by nitration with fuming nitric acid.

A modification of the method of Henley and Turner[55] was used for the preparation of 4-bromo-3-nitrophenol, m.p. 146.6–147.6° (lit. 146.5–147.5°), from O,N-diacetyl-*p*-aminophenol.[56] 4-Chloro-2-nitrobromobenzene, m.p. 68.2–68.7° (lit.[57] 69–70°) was prepared from 4-chloro-2-nitroaniline and 4-fluoro-2-nitrobromobenzene, m.p. 39.5–40.0° (lit.[58] 40.3°) from 4-fluoro-2-nitroaniline[59,60] by the method of Hodgson and Walker.[61]

4-Iodo-2-nitrobromobenzene was prepared by the same method.[61] A solution of 15.6 g. (0.06 mole) of 4-iodo-2-nitroaniline[62] in 190 ml. of glacial acetic acid was diazotized below 20° with a solution of 4.8 g. of sodium nitrite in 34 ml. of concd. sulfuric acid. The diazonium salt solution was treated with a 20% excess of cuprous bromide in hydrobromic acid and, after completion of the reaction, the mixture was poured on ice. The product, 12.3 g. (62.4%), was recrystallized from ethanol and forms small, white crystals, m.p. 93.6–94.3°.

Anal. Calcd. for $C_6H_3O_2NBr$: C, 21.97; H, 0.92. Found: C, 21.75; H, 1.06.

4-Bromo-3-nitroanisole,[63] prepared from 2-nitro-4-meth-

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[42] The amino compounds are omitted.

[43] Ref. 22, p. 75–78.

[44] W. Hückel and H. Havekoss, *Ber.*, **62,** 2041 (1929); W. Hückel, "Theoretische Grundlagen der Organischen Chemie," Akademische Verlagsgesellschaft, Leipzig, 1948, 5th ed., pp. 505–507.

[45] The idea of an intermediate in this type of reaction has been expressed repeatedly and appears to have been first made by E. Bamberger and J. Müller [*Ber.*, **33,** 102 (1900)], who isolated an addition compound between picryl chloride and α-naphthylamine. See also J. Meisenheimer, *Ann.*, **323**, 205 (1902); J. J. Sudborough and N. Picton, *J. Chem. Soc.*, **89**, 583 (1906); W. Borsche, ref. 3; J. Kenner ref. 4; J. Kenner and M. Parkin, *J. Chem. Soc.*, **117**, **852** (1920); Th. de Crauw, ref. 8; A. Brewin and E. E. Turner, *J. Chem. Soc.*, **334** (1928); ref. 21, p. 481; ref. 17.

[46] G. W. Wheland, This Journal, **64**, 900 (1942); E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, 608 (1941); V. Gold, *ibid.*, 1430 (1951).

[47] L. Melander, *Acta Chem. Scand.*, **3**, 95 (1949); *Arkiv for Kemi*, **2**, 211 (1950); E. D. Hughes, C. K. Ingold and R. I. Reed, *J. Chem. Soc.*, 2400 (1950).

[48] All melting points are corrected unless otherwise stated.

[49] A. F. Holleman, *Rec. trav. chim.*, **19**, 367 (1900).

[50] A. Kekule, *Ann.*, **137**, 167 (1866).

[51] J. Booy and J. W. Dienske, *Rec. trav. chim.*, **45,** 449 (1926); also ref. 50.

[52] G. R. Clemo and J. M. Smith, *J. Chem. Soc.*, 2414 (1928).

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[57] L. M. F. van de Lande, ref. 7.

[58] T. van Hove, *Bull. Acad. Roy. Belg.*, [5] **12**, 801 (1926).

[59] H. L. Bradlow and C. A. VanderWerf, This Journal, **70**, 654 (1948).

[60] F. Swarts, *Rec. trav. chim.*, **35**, 131 (1915).

[61] H. H. Hodgson and J. Walker, *J. Chem. Soc.*, 1620 (1933).

[62] A. E. Bradfield, K. J. P. Orton and I. C. Roberts, *ibid.*, 782 (1928).

[63] H. H. Hodgson and R. J. H. Dyson, *ibid.*, 947 (1935); B. V. Samant, *Ber.*, **75**, 1008 (1942).

oxyaniline,[64] was distilled and then recrystallized from ethanol, m.p. 31–32° (uncor.) (lit. 32°).

4-Bromo-3-nitrophenetole.—A solution of 18 g. (0.1 mole) of 2-nitro-4-ethoxyaniline[65] in a mixture of 30 ml. of concd. sulfuric acid and 100 ml. of water was cooled to 5° and diazotized with a solution of 7 g. of sodium nitrite in 20 ml. of water. After one hour the filtered diazonium salt solution was added to a solution of cuprous bromide (10% excess) in hydrobromic acid. The reaction mixture was heated on the steam-bath, extracted with ether, and the ethereal solution was washed with sodium hydroxide and water and dried over calcium chloride. Distillation afforded 11.9 g. (48.4%) of the product, b.p. 153–156° (3 mm.) which on crystallization from ethanol forms small yellow needles, m.p. 59.3–60.6°.

Anal. Calcd. for $C_8H_8O_3NBr$: C, 39.05; H, 3.28. Found: C, 39.16; H, 3.54.

4-Bromo-3-nitrotoluene was synthesized from *m*-nitro-*p*-toluidine.[66] The product was purified by distillation *in vacuo* (b.p. 123–124°, 3–4 mm.), and recrystallized from methanol, m.p. 30.2–31.2° (lit.[67] 31–32°).

4-Bromo-3-nitro-*t*-butylbenzene.—*p*-*t*-Butylacetanilide was prepared essentially by the method reported in the patent literature.[68] 4-Acetamino-3-nitro-*t*-butylbenzene[69] was synthesized by adding 22.5 ml. of fuming nitric acid to a suspension of 11.1 g. (0.058 mole) of *p*-*t*-butylacetanilide in glacial acetic acid, the temperature being kept at 10°. The reaction mixture was heated to 60° for 10 minutes and then poured on ice. The nitro compound was recrystallized from ethanol, m.p. 104–106° (uncor.) (lit.[70] 104.5°). 4-Amino-3-nitro-*t*-butylbenzene was obtained from the acetamino compound by treatment with Claisen alkali, m.p. 103–104.5° (uncor.) (lit.[70] 106.5°). A solution of the above amine (10.7 g., 0.055 mole) in 130 ml. of glacial acetic acid was added slowly with stirring to 4.3 g. of sodium nitrite in 30 ml. of concd. sulfuric acid,[61] the temperature being kept below 20°. The diazonium salt solution was added to cuprous bromide (20% excess) in hydrobromic acid. After the evolution of nitrogen had ceased, the reaction mixture was diluted with water and the oily layer taken up in benzene. After drying the product was distilled *in vacuo* (8.86 g., 62.4%) and was obtained as a yellow oil, b.p. 124–126° (3 mm.).

Anal. Calcd. for $C_{10}H_{12}O_2NBr$: C, 46.53; H, 4.69. Found: C, 46.92; H, 4.91.

Method.—Approximately 0.0004 mole of the bromo compound was weighed accurately into a 5-ml. volumetric flask fitted with a ground-glass stopper. The flask was filled to volume with piperidine previously brought to temperature, thoroughly shaken and returned to the thermostat (25 ± 0.05°, 35 ± 0.1°). The initial time of the reaction was taken as that at which half the piperidine had been added; the whole content of the flask was used for one determination. After a suitable time interval the contents of the flask were transferred to a separatory funnel containing 20 ml. of water and the flask was rinsed with two 5-ml. portions of each benzene and water. An additional 20 ml. of benzene was added, the benzene extract was washed thoroughly with water and the bromide ion in the combined aqueous layers was determined by the Volhard method. For each compound the rate constants were usually determined in groups of four, and at least two such group-determinations were carried out. The results of two typical determinations are recorded in Table II. The errors in the rate constants (Table I) are average errors,[71] and those in the activation energies represent the maximum limits that can reasonably be expected,[71] estimated from the errors in the rate constants.

TABLE II

The Reaction between *o*-Bromonitrobenzene and Piperidine (5 ml.) at 25°

Time, min.	Concn. *o*-bromonitrobenzene × 10^4	Reaction, %	$k \times 10^3$, min.$^{-1}$
90	5.232	23.6	2.98
120	4.935	29.2	2.88
180	4.896	40.9	2.92
210	5.158	44.9	2.83
240	5.024	50.2	2.89
300	4.831	57.4	2.84
360	4.940	63.7	2.81
420	5.084	69.8	2.85

The reaction between 4-bromo-3-nitrotoluene and piperidine (5 ml.) at 25°

	Concn. 4-bromo-3-nitrotoluene × 10^4		$k \times 10^4$ min.$^{-1}$
780	4.772	27.4	4.11
960	4.666	33.5	4.25
1200	4.610	39.5	4.19
1680	4.490	51.0	4.25
1740	4.620	51.4	4.15
753	3.995	27.2	4.22
830	3.897	29.7	4.25
1056	3.990	35.9	4.22
1116	3.958	37.1	4.16

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