

benzenesulfonate and 1.35 g. (10% excess) of potassium acetate in 25 ml. of acetic acid was heated under reflux for 48 hours. The products were isolated as in the acetolysis of *endo*-norbornyl-2,3-C₂¹⁴ *p*-bromobenzenesulfonate.³ The yield of the mixture of nortricyclyl and *exo*-dehydronorbornyl acetate was 1.2 g. (63%). The corresponding alcohol mixture (0.76 g.) obtained after lithium aluminum hydride reduction absorbed 17% of a molar equivalent of hydrogen. The hydrogenation product (0.64 g.) was mixed with 0.70 g. of inactive norborneol and the whole was oxidized with potassium permanganate, giving 0.69 g. (60% based on the norborneol present) of *cis*-cyclopentane-1,3-dicarboxylic acid. Results of radioactivity analyses of the degradation products are given in Table I.

Solvolysis of *exo*-Dehydronorbornyl-2,3-C₂¹⁴ *p*-Bromobenzenesulfonate in Formic Acid.—A mixture of 7.0 g. (0.021 mole) of mixed *p*-bromobenzenesulfonates prepared from the isomerized *exo*- and *endo*-dehydronorborneol-2,3-C₂¹⁴, 1.45 g. (0.021 mole) of sodium formate and 40 ml. of anhydrous formic acid was heated at 45° for 1 hour. The products were isolated as for the acetolysis experiment. The recovered *endo*-dehydronorbornyl-2,3-C₂¹⁴ *p*-bromobenzenesulfonate weighed 2.5 g. (36%). The yield of nortricyclyl and *exo*-dehydronorbornyl formate mixture, b.p.

60° (8 mm.), was 1.0 g. (34%). The mixture of formates was converted to the corresponding alcohols which absorbed 4% of a molar equivalent of hydrogen. The hydrogenation product and 0.40 g. of norborneol carrier was oxidized to give 0.40 g. of *cis*-cyclopentane-1,3-dicarboxylic acid. Degradation and radioactivity assays were carried out the usual way.

***endo*-Dehydronorbornyl-3-C¹⁴-amine with Nitrous Acid.**—The experiment using acetic acid as solvent was carried out as with *endo*-norbornyl-3-C¹⁴-amine.³ The crude ester from 2.5 g. of *endo*-dehydronorbornyl-3-C¹⁴-amine and sodium nitrite in acetic acid was cleaved with lithium aluminum hydride and yielded 0.56 g. of mixed alcohols, m.p. 85–95°. The product absorbed 17% of one molar equivalent of hydrogen. The hydrogenated material was diluted with carrier *exo*-norborneol and degraded as before.

The aqueous fluoboric acid deamination employed the previously described procedure³ and 2.5 g. of amine afforded 0.60 g. of crude alcohol mixture, m.p. 95–103°. On quantitative hydrogenation, 7% of one molar equivalent of hydrogen was absorbed. The reduction product was degraded in the usual way.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF PURDUE UNIVERSITY]

A Quantitative Treatment of Isomer Distribution in Aromatic Electrophilic Substitution^{1,2}

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An extension of the Hammett relationship to electrophilic substitution reactions is proposed. It has been demonstrated that the usual side-chain σ_p substituent constants are not suitable for such electrophilic reactions. New σ_p^+ values are developed which permit the quantitative treatment of directive effects in aromatic substitutions. Good agreement is obtained for *para/meta* ratios calculated in this way with ratios observed experimentally. *Ortho* and *meta* reactivities in electrophilic substitutions generally follow a relationship similar to that previously proposed for *para* and *meta* substitution. Only in the case of mercuration, chloromethylation and isopropylation are serious deviations observed. It is proposed therefore that the present quantitative treatment can be extended to include *ortho* substituents in many electrophilic aromatic substitutions where the steric factor is either moderate or negligible. The treatment has been extended mathematically to polysubstituted benzene derivatives. It is shown to be identical with the relationship demonstrated previously on an empirical basis for the chlorination and mercuration of the methylbenzenes.

In the development of the theory of aromatic substitution, attention has been directed primarily toward the aromatic component. Thus, orientation and relative rates have been interpreted qualitatively in terms of various electrical and steric effects in the substituent already present.⁵ In general, the effect of the activity of the substituting agent upon isomer distribution has been largely ignored. In a few cases where steric and polar explanations fail, such as in diazonium coupling,^{6a} such activity has been invoked occasionally to account for *ortho/para* ratios.^{6b}

A detailed discussion of the importance of the activity of the attacking species in controlling the

para/meta isomer distribution has been presented recently.^{7,8} Thus, it has been shown that in numerous reactions of aromatic nuclei, including chlorination, chloromethylation, base strength, nitration, mercuration and isopropylation of toluene, the orientation can be correlated with the "activity" or "selectivity" of the attacking species.

It has been demonstrated^{7,8} that these reactions obey the relationship

$$\log p_t = c \log (p_t/m_t) \quad (1)$$

where p_t and m_t are the partial rate factors for substitution in the *para* and *meta* positions of toluene and, presumably, of other monosubstituted benzenes. This expression was developed and tested as an empirical relationship. However, the validity of this relationship argues for the existence of a linear free energy expression for aromatic substitution of the same type as that developed by Hammett for side-chain aromatic derivatives

$$\log (k/k_0) = \rho \sigma^9 \quad (2)$$

The relationship between the empirical expres-

(1) Directive Effects in Aromatic Substitution. VII. Previous publications in this series: THIS JOURNAL, **77**, 2300 (1955); **77**, 2306 (1955); **77**, 2310 (1955).

(2) Based upon a thesis submitted by C. W. McGary, Jr., in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(3) Purdue Research Foundation Fellow, 1952–1953; American Cyanamid Corp. Fellow, 1953–1954. Research assistant on a grant from the National Science Foundation, 1954.

(4) Research assistant on a grant from the Petroleum Research Fund, 1954–1955.

(5) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, Chapt. VI.

(6) (a) A. Lapworth and R. Robinson, *Mem. Proc. Manchester Lit. and Phil. Soc.*, **72**, 243 (1928). See p. 284, ref. 4. (b) P. B. D. de la Mare, *J. Chem. Soc.*, 2871 (1949).

(7) H. C. Brown and K. L. Nelson, THIS JOURNAL, **75**, 6292 (1953).

(8) H. C. Brown and C. W. McGary, Jr., *ibid.*, **77**, 2300, 2306, 2310 (1955).

(9) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, Chapt. VII.

sion and linear free energy expressions of the Hammett type may be demonstrated simply. Writing the Hammett equation to apply to the partial rate factors for *para* and *meta* substitution, we have

$$\log p_t = \rho \sigma_p \quad (3)$$

$$\log m_t = \rho \sigma_m \quad (4)$$

Subtracting (4) from (3), we obtain

$$\log (p_t/m_t) = \rho(\sigma_p - \sigma_m) \quad (5)$$

Dividing (3) by (5) we have

$$\log p_t = \left(\frac{\sigma_p}{\sigma_p - \sigma_m} \right) \log \left(\frac{p_t}{m_t} \right) \quad (6)$$

This equation is identical with (1) with $c = \sigma_p / (\sigma_p - \sigma_m)$.

It appears reasonable, therefore, that a quantitative treatment of aromatic substitution should be possible. Indeed, Hammett has pointed out previously that the relative reactivities in the nitration of monosubstituted benzene derivatives may be qualitatively correlated with the side-chain σ -values.⁹ However, our attempts to develop a quantitative treatment based on these σ -values failed.

It has been observed that the rates of rearrangement of a series of *para* substituted acetophenone oximes do not follow the σ -values quantitatively and a separate set of values have been proposed for this electrophilic reaction.¹⁰ Furthermore, Condon has suggested that the σ -values for electrophilic substitutions may differ from those in side-chain reactions, since *para* and *meta* reactivities in the halogenation and hydrogen fluoride-boron trifluoride reactions are inconsistent with the Hammett σ -values.¹¹

More recently Roberts and his co-workers have looked into the possibility of a quantitative relationship between partial rate factors for nitration and the side-chain σ -constants.¹² However, large deviations were observed in the case of *para* substituents. They attributed these deviations to resonance interactions which occur in electrophilic *para* substitutions, but do not occur to the same extent in the side-chain reactions.

The nature of the problem may be clarified by reference to Table I where the data for thirteen reactions with toluene result in a ratio of $\log p_t / \log m_t$ of 4.24 ± 0.20 . The ratio calculated from the side-chain σ -values for *para* and *meta* methyl groups is 2.46.

From the foregoing discussion, then, the conclusion follows that in order to correlate reactivity data for electrophilic substitution reactions, substituent constants must be taken independently from those for side-chain reactions. This conclusion is supported also by the theoretical consideration of resonance factors operating in electrophilic substitution reactions.¹³ Consequently, we undertook to develop a treatment for electrophilic substitution reactions which was independent of side-chain σ -values.

Determination of Reaction and Substituent Constants.—It is assumed that aromatic substitu-

(10) D. E. Pearson, J. F. Baxter and J. C. Martin, *J. Org. Chem.*, **17**, 1511 (1952).

(11) F. E. Condon, *THIS JOURNAL*, **74**, 2528 (1952).

(12) J. D. Roberts, J. K. Sanford, F. L. J. Sixma, H. Cerfontain and R. Zagt, *ibid.*, **76**, 4525 (1954).

(13) F. L. J. Sixma, *Rec. trav. chim.*, **73**, 243 (1954).

TABLE I
PARTIAL RATE FACTORS IN TOLUENE SUBSTITUTION

Reaction	Partial rate factors of p_t			$\frac{\log p_t}{\log m_t}$	lit. ref.
Chlorination	600	5.0	870	4.21	21
Chloromethylation	117	4.37	430	4.11	7
Basicity					
A, HF	145	3.6	414	4.69	^a
B, HF-BF ₃	103	3.1	145	4.39	^b
Nitration					
A, 18°	43	3.0	55	3.65 ^c	^c
B, 45°	42	2.5	58	4.43	^d
Mercuration					
A, HClO ₄ catalyzed					
25°	4.98	2.25	32.9	4.31	8
B, Same, 50°	4.20	2.41	28.8	3.82	8
C, Same, 75°	3.24	2.23	24.5	3.99	8
D, uncatalyzed, 50°	4.60	1.98	16.8	4.13	8
E, Same, 70°	4.03	1.83	13.5	4.31	8
F, Same, 90°	3.51	1.70	11.2	4.55	8
Detrimethylsilylation	17.5	2.0	16.5	4.04	^e
Sulfonylation	5.44	1.67	7.99	4.05	^f
Isopropylation	2.37	1.80	4.27	2.47 ^g	^h
	Average				4.24 ± 0.20

^a Partial equilibrium factors calculated from the data of M. Kilpatrick and F. E. Luborsky, *THIS JOURNAL*, **75**, 577 (1953). ^b D. A. McCaulay and A. P. Lien, *ibid.*, **73**, 2013 (1951). ^c C. K. Ingold, A. Lapworth, E. Rothstein and D. Ward, *J. Chem. Soc.*, 1959 (1931). ^d H. Cohn, E. D. Hughes, M. H. Jones and M. A. Peeling, *Nature*, **169**, 291 (1952). ^e Private communication from Professor R. A. Benkeser, Dr. H. R. Krysiak and Mr. O. H. Thomas. ^f W. E. Truce and C. W. Vriesen, *THIS JOURNAL*, **75**, 5032 (1953). ^g S. C. J. Olivier, *Rec. trav. chim.*, **33**, 1963 (1914). ^h F. E. Condon, *THIS JOURNAL*, **70**, 2265 (1948); **71**, 3544 (1949). ⁱ Data for nitration at 18° and isopropylation are not included.

tion will obey a linear free energy expression of the Hammett type

$$\log k_t = \rho \sigma^+ \quad (7)$$

where k_t is the partial rate factor, ρ is the reaction constant and σ^+ is a substituent constant applicable to electrophilic aromatic substitution.¹⁰ The data in Table I show that for such reactions, the following relationship exists between the σ^+ -values for *para* and *meta* methyl.

$$\frac{\sigma^+_{p-Me}}{\sigma^+_{m-Me}} = \frac{\log p_t}{\log m_t} = 4.24 \quad (8)$$

The methyl group is of low polarity and of relatively low susceptibility to resonance interactions, particularly in the *meta* position. Let us assume that the value of σ^+_{m-Me} will not differ significantly from σ_{m-Me} (-0.069).¹⁴ We can immediately calculate a value for σ^+_{p-Me} (-0.293) and values of ρ for the various reactions for which data are available (Table I). These ρ -values are summarized in Table II.

It should be emphasized that sufficient data are now available to permit the determination of ρ only from substitution data for *para* and *meta* to methyl. However, it may be seen from the low mean deviations in Table II that the agreement is excellent with but two exceptions, isopropylation and the *meta* value for nitration at 18°. These data are the numerical expression of the empirical relationship previously observed (equation 1).^{7,8}

(14) H. H. Jaffe, *Chem. Revs.*, **53**, 191 (1953).

TABLE II
 REACTION CONSTANTS FOR ELECTROPHILIC SUBSTITUTION IN SUBSTITUTED BENZENE DERIVATIVES

Reaction	Conditions	Reaction constants		
		ρ_m	ρ_p	ρ
Chlorination	Cl ₂ in HOAc at 24°	-10.13	-10.05	-10.09 ± 0.04
Chloromethylation	CH ₂ O in HOAc at 60° with HCl and ZnCl ₂	-9.28	-9.00	-9.14 ± .14
Basicity	A, HF	-8.06	-8.94	-8.50 ± .49
	B, HF-BF ₃	-7.12	-7.39	-7.26 ± .14
Nitration	A, AcONO ₂ in Ac ₂ O at 18°	-6.91	-5.95	-6.43 ± .48
	B, HNO ₃ in 90% HOAc at 45°	-5.77	-6.03	-5.90 ± .13
Mercuration	A, Hg(OAc) ₂ in HOAc at 25° with HClO ₄	-5.10	-5.19	-5.15 ± .0
	B, 50°	-5.54	-4.99	-5.27 ± .28
	C, 75°	-5.04	-4.75	-4.90 ± .15
	D, Hg(OAc) ₂ in HOAc at 50°	-4.30	-4.19	-4.25 ± .06
	E, 70°	-3.80	-3.86	-3.83 ± .03
	F, 90°	-3.33	-3.59	-3.46 ± .13
Detrimethylsilylation	ArSi(CH ₃) ₃ + H ₃ O ⁺ in HOAc at 25°	-4.36	-4.16	-4.26 ± .10
Isopropylation	C ₃ H ₈ at 40° with AlCl ₃	-3.65	-2.15	-2.90 ± .75

The ρ_p -value for nitration with acetyl nitrate in acetic anhydride at 18°¹⁵ agrees closely with the ρ_m - and ρ_p -values for nitration with nitric acid in 90% acetic acid at 45° (Table II). We therefore may conclude that the ρ -values for these two reactions will not differ greatly and adopt the average value of -5.92 ± 0.10 for these nitration reactions.

It is now possible to calculate σ^+ - and σ^+ -values for substituents other than methyl by utilizing the available partial rate data for nitration of monosubstituted benzene derivatives. The σ^+ -values obtained in this way are listed in Table III together with the corresponding σ -values.¹⁴

TABLE III

COMPARISON OF SUBSTITUENT CONSTANTS FOR ELECTROPHILIC AND SIDE-CHAIN REACTIONS

Substituent	σ^+	σ^a	$\sigma^+ - \sigma$	Lit. ref.
<i>m</i> -C(CH ₃) ₃	-0.102	-0.120	0.018	<i>b</i>
<i>m</i> -CH ₃	-.0672	-.0690	.002	<i>b</i>
<i>m</i> -CH ₂ CO ₂ C ₂ H ₅	-.0109			<i>c</i>
<i>m</i> -CH ₂ Cl	.144			<i>c</i>
<i>m</i> -I	.325	.352	-.027	12, ^{<i>e</i>}
<i>m</i> -CO ₂ C ₂ H ₅	.355	.398	-.043	<i>f</i>
<i>m</i> -Br	.507	.391	.116	12 ^{<i>d</i>} , ^{<i>e</i>}
<i>m</i> -Cl	.520	.373	.147	12 ^{<i>d</i>} , ^{<i>e</i>}
<i>p</i> -C(CH ₃) ₃	-.317	-.197	-.120	<i>b</i>
<i>p</i> -CH ₃	-.297	-.170	-.128	<i>b</i>
<i>p</i> -CH ₂ CO ₂ C ₂ H ₅	-.172			<i>c</i>
<i>p</i> -CH ₂ Cl	.00372	.184	-.180	<i>c</i>
<i>p</i> -I	.0175	.276	-.258	12 ^{<i>e</i>}
<i>p</i> -Cl	.149	.227	-.078	12 ^{<i>d</i>} , ^{<i>e</i>}
<i>p</i> -Br	.167	.232	-.065	12 ^{<i>d</i>} , ^{<i>e</i>}
<i>p</i> -CO ₂ C ₂ H ₅	.514	.522	-.008	<i>f</i>
		.678(σ^*) ^{<i>g</i>}	-.164	

^a The σ -values are from ref. 14. ^b Table I, ref. *d*. ^c C. K. Ingold and F. R. Shaw, *J. Chem. Soc.*, 575 (1949). ^d M. L. Bird and C. K. Ingold, *ibid.*, 918 (1938). ^e Data obtained with acetyl nitrate in nitromethane. It is assumed that $\rho = -5.92$, as for acetyl nitrate in acetic anhydride. ^f C. K. Ingold and M. S. Smith, *ibid.*, 905 (1938). ^g It has proven necessary to assign two different values of σ for substituents in the *para* position which are capable of resonance interactions (ref. 14).

Roberts and his co-workers¹² have pointed out recently that electrophilic reactivities in the *meta* position parallel the *meta* σ -values quite closely.

(15) We consider the discrepancy in the σ_m -value in this reaction to experimental difficulties in analyzing for small quantities of the *meta* isomer. For example, the formation of 3.5% of *m*-nitrotoluene instead of 4.1% reported would eliminate the discrepancy.

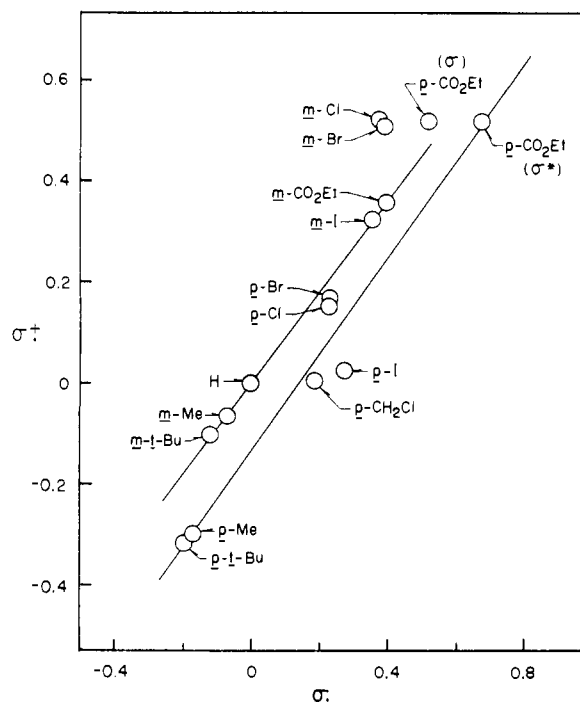
In Fig. 1 there are plotted the σ^+ -values versus the σ -values. The values for the *meta* constants follow the relationship

$$\sigma^+_m = 0.902\sigma_m$$

In view of the large uncertainty in the experimental data from which the σ^+_m constants were derived, it appears reasonable to assume that the σ^+_m -values are identical with the corresponding Hammett σ_m -values.

$$\sigma^+_m = \sigma_m \quad (9)$$

On the other hand, there is a significant difference between the σ^+_p and the corresponding σ_p -values (Table III, Fig. 1).

Fig. 1.—Comparison of σ^+ - and σ -constants.

An Empirical Approach to σ^+ -Values.—It would be highly desirable to have good quantitative data to permit the accurate determination of σ^+ -values and their utility in the proposed quantitative

treatment of aromatic substitution.¹⁶ However, such data are not now available. In the absence of such data, it has appeared necessary to develop an empirical procedure for the estimation of the σ^- -values.

It was pointed out by Roberts and his co-workers¹² that electrophilic reactivities in the *para* position are far greater than one would predict on the basis of the σ_p -values. These deviations were interpreted in terms of resonance interactions which occur in electrophilic substitutions but do not occur to the same degree in side-chain reactions.

In the case of the *p*-carbomethoxy group, however, the point was observed to fall on the *meta* line. It therefore was concluded that little or no resonance differences were apparently involved between the two reaction types for this and similar substituents.

There would appear to be serious difficulties with this interpretation. The σ -values for *meta* and *para* carboxyl groups are 0.355 and 0.265, respectively. On the basis of no resonance differences, one would predict from these values that benzoic acid would be *para*- rather than *meta*-directing, as it actually is. This argument may be extended to the cyano, nitro and formyl groups. Therefore, it appears highly improbable that such σ_p -values may be used to estimate σ^+ -values from the line defined by the *meta* values.

It is now well established that many *para* substituents possess two σ -values,^{9,14} each of which depends upon the particular reaction under consideration. The values referred to in the above discussion were the lower values (σ) which in general apply to reactions with no important resonance interaction between substituents. By utilizing the higher of the two values (σ^*) for the carboxyl, cyano, nitro and formyl groups, qualitative agreement may be obtained between the σ -values and the experimentally observed orientation. For example, σ_p^* is 0.728 for the carboxyl group. With the value of σ_m of 0.355, it would be predicted that *meta* orientation will predominate.

By utilizing the σ^* -value for the carbomethoxy group, the available σ^+ -values yield a reasonably good linear relationship (Fig. 1)

$$\sigma_p^+ = 0.956\sigma_p^* - 0.134 \quad (10)$$

In view of the large uncertainty in the available data, we are probably justified in assuming that the slope may be unity so that the relationship may be taken as

$$\sigma_p^+ = \sigma_p^* - 0.134^{17} \quad (11)$$

With the aid of equations 9 and 11, values of σ^+ may be calculated for a number of substituents. Values of σ^+ obtained in this manner are summarized in Table IV.

Application to *Para/Meta* Ratios in Monosubstituted Benzenes.—*Para/meta* ratios may be

(16) We have developed a method of determining such σ^+ -values and are actively applying it to obtain accurate values of these constants. Work in progress with Y. Okamoto.

(17) From the values of $\sigma_p^+ - \sigma_p^*$ in Table III, the relationship should be $\sigma_p^+ = \sigma_p^* - 0.142 \pm 0.051$. The σ^+ -value for *p*-iodo differs considerably from this relationship. Moreover, the rate of reaction of iodobenzene relative to benzene (ref. 12) is not consistent with similar data reported by Bird and Ingold (Table III, ref. d) for chloro- and bromobenzene in acetic anhydride and in nitromethane. If this value of σ_p^+ is omitted from the average, the relationship becomes $\sigma_p^+ = \sigma_p^* - 0.124 \pm 0.036$.

TABLE IV
CALCULATED VALUES OF σ^+ ^a

Substituent	Substituent constants ^a			
	σ_m	σ_p	σ_p^*	σ_p^+
N(CH ₃) ₃ ⁺	0.904	0.859	...	0.725
NO ₂	.710		1.270	1.136
CN	.678		1.000	0.866
SO ₂ CH ₃	.647		1.049	.915
CF ₃	.415	0.551417
CHO	.381		1.126	.992
CO ₂ C ₂ H ₅	.398		0.678	.544
CO ₂ CH ₃	.315		.636	.502
CO ₂ H	.355		.728	.594
CONH ₂	.280		.627	.493
F	.337	.062		-.072
Cl	.373	.227		.093
Br	.391	.232		.098
I	.352	.276		.142
NHCOC ₆ H ₅	.217	.078		-.054
CH ₃	-.069	-.170		-.304
C ₂ H ₅	-.043	-.151		-.285
C(CH ₃) ₃	-.120	-.197		-.331
C(CH ₃) ₂ COOH	-.027	-.066		-.300
Si(CH ₃) ₃	-.121	-.072		-.206
OH	-.002	-.357		-.491
NH ₂	-.161	-.660		-.794

^a Values of σ and σ^* from ref. 14.

calculated from these values of the substituent constants and the previously calculated values of the reaction constants (Table II) with the aid of equation 12.

$$\log \frac{\text{para}}{\text{meta}} = \rho(\sigma_p^+ - \sigma_m) - \log 2 \quad (12)$$

Unfortunately, reasonably good data for *para/meta* isomer distributions are now available only for the nitration reaction. Accordingly, we have restricted the present treatment to comparison of the calculated and experimental values for the *para/meta* ratios obtained in the nitration reaction.

The results are summarized in Table V.

It should be emphasized that these nitration data were obtained under a wide variety of experimental conditions. We have demonstrated recently that the activity and selectivity of a substitution reaction may be modified greatly by changes in the experimental conditions.⁸ Consequently, the use of the single reaction constant, -5.92 , for the different nitration conditions introduces a further error of uncertain magnitude.

Considering the uncertainty in the empirically derived σ^+ -values, the probable error in the experimental isomer distributions and the widely differing experimental reaction conditions (which should result in variations in ρ), it would appear that the agreement between the calculated and experimental ratios is quite good for most of the compounds. Only in the case of benzaldehyde, aniline, trimethylsilylbenzene, benzotrifluoride and phenyltrimethylammonium ion do the experimental ratios differ very seriously from the calculated values.

In the case of benzaldehyde, the disagreement may be due to the σ^* -value listed for the CHO group.¹⁴ This value is based on a single observation and is unusually high (σ_p^* 1.126) as compared to the accepted σ -value for this group (σ_p 0.216).

TABLE V
 COMPARISON OF CALCULATED *Para/Meta* NITRATION RATIOS WITH EXPERIMENTAL VALUES

Substituent	Isomer distribution			Ref.	<i>Para/meta</i> ratio	
	<i>o</i>	<i>m</i>	<i>p</i>		Expt.	Calcd.
NO ₂	46.4	93.2	<0.25	^a (1)	<0.0027	0.0015
	4.8	93.5	1.7	^a (2)	.018	
CN	17	81	<2	^b	<.025	.036
SO ₂ CH ₃	...	98.5	...	^c	<.015	.013
CHO	~19	72	~9	^d	~.13	.00012
CO ₂ C ₂ H ₅	24.1	72.0	4.0	^e	.056	.069
	28.3	68.4	3.3	^f (1)	.048	
	27.7	66.4	5.9	^f (2)	.089	
CO ₂ CH ₃	25.7	69.8	4.5	^f (3)	.064	.040
COOH	18.5	80.2	1.3	^f (4)	.016	.019
	22.3	76.5	1.2	^f (5)	.015	
CONH ₂	~27	70	~3	^g	~.043	.027
NHCOC ₆ H ₅	...	2.6	97.4	^h (1)	37.5	20.0
NH ₂	1.4	47	51.3	^h (2)	1.09	2800
F	12.4	0.2	87.4	ⁱ	440	110
Cl	29.6	0.9	69.5	^j	77	23
	30.2	0	69.8	^k (1)	Large	
	29.8	0.3	69.9	ⁱ	233	
Br	36.5	1.2	62.3	^j	52	27
	42.0	0	58.0	^k (2)	Large	
	37.6	0.3	62.1	ⁱ	207	
I	41.8	1.5	56.7	^j	33	8.7
	34.2	...	65.8	ⁱ	Large	
C(CH ₂) ₂ COOH	27	8	65	^l	8.1	5.3
CH ₃	58.4	4.4	37.2	^m (1)	8.45	12.0
	58.5	4.4	37.1	^m (2)	8.43	
	58.54	4.40	37.15	ⁿ	8.44	
C ₂ H ₅	45	6.5	48.5	^o	7.45	13.0
	55	...	45	^p	Large	
CH(CH ₃) ₂	30.0	7.7	62.3	^q	8.1	...
	14	...	86	^r	Large	
C(CH ₃) ₃	12.0	8.5	79.5	^r	9.3	8.9
	15.8	11.5	72.7	^s	6.3	
OH	40	...	60	^t	Large	390
Si(CH ₃) ₃	30	40	30	^u	0.750	0.16
	26.6	41.7	31.6	^v (1)	.760	
	32.5	34.7	32.7	^v (2)	.940	
CF ₃	89	^w	<.12	0.49
N(CH ₂) ₃ ⁺	100	^x	Small	5.9

^a A. F. Holleman and B. R. de Bruyn, *Rec. trav. chim.*, 19, 79 (1900): (1) with nitric acid at 0°; (2) with nitric and sulfuric acid at 0°. ^b J. W. Baker, K. E. Cooper and C. K. Ingold, *J. Chem. Soc.*, 426 (1928); with nitric acid at 0°. ^c W. A. Baldwin and R. Robinson, *ibid.*, 1445 (1932): with nitric acid at 18°. ^d D. L. Brady and S. Harris, *ibid.*, 123, 484 (1923); J. W. Baker and W. G. Moffitt, *ibid.*, 314 (1931): with nitric acid at 5°. ^e C. K. Ingold and M. S. Smith, *ibid.*, 905 (1938): with nitric acid in acetic anhydride at 18°. ^f A. F. Holleman, *Rec. trav. chim.*, 18, 267 (1899): with nitric acid (heterogeneous) (1) at 0°, (2) 30°, (3) 30°, (4) 0°, (5) 30°. ^g K. E. Cooper and C. K. Ingold, *J. Chem. Soc.*, 836 (1927): with nitric acid at -15°. ^h A. F. Holleman, *Chem. Revs.*, 1, 187 (1925): (1) with sulfuric acid and nitric acid; (2) with 96% nitric acid at -20°. ⁱ A. F. Holleman, *Rec. trav. chim.*, 24, 140 (1905): with nitric acid at 0°. ^j Ref. 12: with acetyl nitrate in nitromethane at 25°. ^k M. L. Bird and C. K. Ingold, *J. Chem. Soc.*, 918 (1938): with acetyl nitrate at 25° (1) in nitromethane, (2) in acetyl anhydride. ^l J. W. Baker, K. E. Cooper and C. K. Ingold, *ibid.*, 426 (1928): with nitric acid at -30°. ^m C. K. Ingold, A. Lapworth, E. Rothstein and D. Ward, *ibid.*, 1959 (1931): (1) with acetyl nitrate at 30°, (2) with nitric acid at 30°. ⁿ W. W. Jones and M. Russell, *ibid.*, 921 (1947): with nitric acid and sulfuric acid at 30°. ^o H. C. Brown and W. H. Bonner, *THIS JOURNAL*, 76, 605 (1954): with nitric acid and sulfuric acid at 25-40°. ^p E. L. Cline and E. E. Reid, *ibid.*, 49, 3150 (1927). ^q G. Vavon and A. Collier, *Bull. soc. chim.*, 49, 3150 (1927). ^r H. Cohn, E. D. Hughes, M. H. Jones and M. A. Peeling, *Nature*, 169, 291 (1952): with nitric acid in 90% aq. acetic acid at 45°. ^s K. L. Nelson and H. C. Brown, *THIS JOURNAL*, 73, 5605 (1951): with nitric acid and sulfuric acid at 25-40°. ^t Values for isomer distribution taken from ref. *h*; W. Körner, *Gazz. chim. ital.*, 4, 305, 446 (1874), ref. *j*. ^u R. H. Benkeser and P. E. Brumfield, *THIS JOURNAL*, 73, 4770 (1951): with cupric nitrate in acetic anhydride at 30-40°. ^v J. L. Speier, *ibid.*, 75, 2930 (1953): with fuming nitric acid (1) at 0-10°, (2) at 25-70°. ^w G. C. Finger, N. H. Nachtrieb and F. H. Reed, *Trans. Ill. State Acad. Sci.*, 31, 132 (1938); *C. A.*, 33, 6271 (1939): with concd. nitric acid and sulfuric acid. ^x D. Vorländer and E. Siebert, *Ber.*, 52, 283 (1919).

In the case of aniline, the discrepancy presumably arises from the fact that the molecular species undergoing nitration is not aniline, but is anilinium ion.

In the remaining three compounds the discrepancy may indicate a breakdown in the empirical

method for obtaining σ^+ -values, and the discrepancy may disappear with the availability of experimental σ^+ -values. We are currently engaged in determining experimental σ^+ -values for these groups.¹⁶

In view of the large measure of agreement despite

the various uncertainties, the present approach must be considered quite promising for the development of a truly quantitative theory of directive effects in aromatic substitution.

Application to *Ortho* Substitution.—The question of *ortho* substitution is in general a complex one. For side-chain reactions, no linear relationship is observed between either two reaction series or two substituent series and quantitative treatments are consequently limited.¹⁸ However, it may be seen in Fig. 2 that a linear relationship is followed for toluene substitution data, except for chloromethylation, mercuration and isopropylation. Apparently then, these reactions have steric requirements in excess of those of other reactions, such as chlorination, nitration and methylation, which show no *ortho* deviation.¹⁹

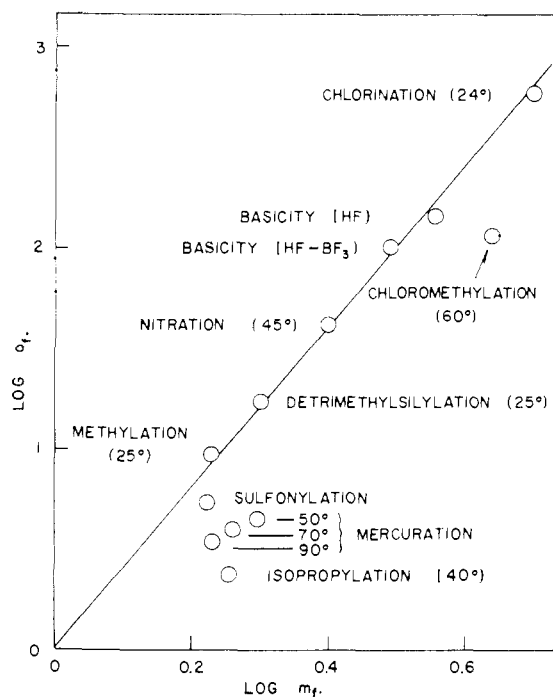


Fig. 2.—Comparison of *ortho* and *meta* partial rate factors.

Two treatments appear possible for *ortho* reactions. For reactions such as chlorination and nitration which exhibit no significant *ortho* effects, the ρ -values will be identical with those for the *meta* and *para* substituents, provided the substituent is one with only moderate steric requirements. Such reactions could be used to establish the σ^+ -values. However, in the case of mercuration, chloromethylation and isopropylation and other reactions with large steric factors, ρ_0 would differ from ρ (equation 13).

$$\log \sigma_f = \rho_0 \sigma^+, \quad (13)$$

Alternatively, Taft's equation 14 could be applied in a similar manner, the two systems being related by equation 15.

(18) R. W. Taft, Jr., THIS JOURNAL, **75**, 4231 (1953); **74**, 2729 (1952); **74**, 3126 (1952).

(19) It may be noted that the isopropylation data are not satisfactory even for the treatment involving only *para* and *meta* methyl substituents (Table I). The methylation data are from unpublished work with C. R. Smoot.

$$\log \sigma_f = \rho \sigma^+ + E_s \quad (14)$$

$$E_s = \rho_0 \sigma^+ - \rho \sigma^+ \quad (15)$$

In this paper, the first treatment has been adopted. In this way calculation of the σ^+ -value for methyl leads to the values of -0.275 , -0.274 and -0.277 for the chlorination, nitration (45°) and basicity ($\text{HF}-\text{BF}_3$) reactions, respectively. The results are summarized in Table VI.

TABLE VI

SUBSTITUENT AND REACTION CONSTANTS FOR *Ortho* SUBSTITUTION REACTIONS

Reaction	ρ	Substituent	σ^+
Chlorination	-10.09	CH_3	-0.276
Chloromethylation	-7.49	$\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$.112
Basicity		CH_2Cl	.0908
A, HF	-8.50	I	.101
B, $\text{HF}-\text{BF}_3$	-7.26	Br	.258
Nitration	-5.92	Cl	.263
Detrimethylsilylation	-4.51	$\text{CO}_2\text{C}_2\text{H}_5$.437
Mercuration			
A, HClO_4 catalyzed, 25°	-2.52		
B, Uncatalyzed, 50°	-2.40		

These reaction and substituent constants should permit calculation of complete isomer distributions for reactions and substituents of low or moderate steric requirements.²⁰ However, in the absence of satisfactory data for reactions other than nitration, it does not appear desirable to explore this approach further at this time.

It is interesting to consider the effect of the *ortho* factor on linear relationships of the type here considered. If one plots the logarithms of the relative rates for two reactions which have no significant *ortho* effect, a single straight line will be obtained. On the other hand, if a similar plot is made for two reactions which have unequal *ortho* effects, three parallel straight lines are obtained, one for positions having no *ortho* groups, a second for those having one *ortho* group and a third for those having two *ortho* groups.

The situation is illustrated in Fig. 3 where the values compared have been calculated from data in Table I for the two reactions: perchloric acid-catalyzed mercuration at 25° and the hydrogen fluoride-boron trifluoride basicity reaction.

Theoretical justification for this observation may be noted in the derivation

$$\log k_i = \rho \Sigma \sigma^+_{o,p} + \rho_0 \Sigma \sigma^+_o \quad (16)$$

$$\text{But since } \log k_i^0 = \Sigma \sigma^+_{m,p} + \Sigma \sigma^+_o$$

$$\log k_i = \rho \log k_i^0 + (\rho_o - \rho) \Sigma \sigma^+_o \quad (17)$$

Thus the three parallel straight lines of slope ρ have the intercepts zero, $(\rho_o - \rho) \sigma^+_o$ and $2(\rho_o - \rho) \sigma^+_o$ (Fig. 3).

It can be shown in a similar manner that if no correlation exists among the *para*, *meta* and *ortho* factors, six straight lines may be drawn each of which connects points corresponding to positions

(20) In many cases it is observed that much greater amounts of the *ortho* than *para* isomers are formed (Table V). This phenomenon is due presumably to coordination of the electrophilic reagent with the substituent followed by an enhanced rate of attack of the *ortho* position. This phenomenon will introduce an additional factor to be considered in the development of a complete theoretical treatment of *ortho* substitution.

which vary only in one particular partial rate factor. The criterion as to whether one, three or six straight lines will be obtained is determined by whether two, one or none, respectively, of the following relationships hold.

$$\frac{\log p_i}{\log p_i^0} = \frac{\log m_i}{\log m_i^0} = \frac{\log o_i}{\log o_i^0} \quad (18)$$

Application to Polysubstituted Benzenes.—An extension of the Hammett equation to polysubstituted benzene derivatives has been made for side-chain reactions.¹⁴ In the case of electrophilic substitution, assuming additivity in the substituent constants, the equation may be written

$$\log k_j = \rho^+ \sum_i \sigma_i^+ \quad (19)$$

where $\sum_i \sigma_i^+$ is the summation of substituent constants of the various substituents located on the ring and k_j is the rate of substitution in a given position relative to one position in benzene. By recalling the relationships between the partial rate factors and their respective σ_i^+ values and by solving for k_j and adding the rates of all available positions, we obtain

$$\begin{aligned} k_t &= \sum k_j = \sum_i e^{+\rho} \sum_i \sigma_i^+ \\ &= \sum_i \prod_i e^{+\rho \sigma_i^+} \\ k_t &= \sum_i \prod_i k_i \end{aligned} \quad (20)$$

where k_t is the over-all rate of substitution in the substituted aromatic relative to one position in benzene and k_i is the partial rate or equilibrium factor. In the case of *m*-xylene, for example, k_t is $o_i^2 + 2o_i p_i + m_i^2$. Consequently, from a knowledge of the partial rate factors, it is possible to calculate the relative rates of any polysubstituted benzene derivative.

Using equations of the above type, Condon²¹ has calculated the relative rates in the chlorination of the methylbenzenes. He also has utilized the reverse procedure in calculating the partial basicity factors from the data on the reaction of hydrogen fluoride-boron trifluoride with the methylbenzenes.¹¹

In the preceding paper of this series we have demonstrated that the relative rates of mercuration of all of the isomeric methylbenzenes can be calculated with considerable precision from partial rate factors.²² It also has been observed empirically that the logarithms of the relative rates of halogenation and the relative basicities (hydrogen fluoride-boron trifluoride) of the methylbenzenes are linearly related.^{14,23}

It is important that these empirical relationships can be shown to follow from the present treatment.

Thus, since $\sum_i \sigma_i^+$ will be the same for individual comparisons, the following relationship exists

$$\log k_j = (\rho/\rho') \log k_j' \quad (21)$$

where k_j is the relative rate of reaction at one site, k_j' is the same for the comparison reaction, and ρ and ρ' are the reaction constants for the two reac-

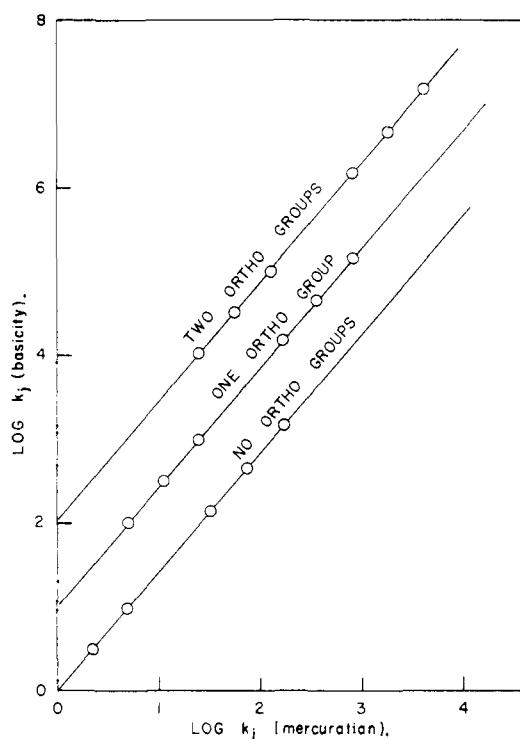


Fig. 3.—Relationship between the partial relative rates in the basicity and mercuration of methylbenzenes.

tions. For all available positions, however, the equation becomes

$$k_t = \sum k_j = \sum (k_j') \rho/\rho' \quad (22)$$

$$\log \sum k_j = \log \sum k_j' \rho/\rho' \quad (23)$$

To be consistent with the empirical linear relationship, equation 23 should be in the form

$$\log \sum k_j = (\rho/\rho') \log \sum k_j' \quad (24)$$

The condition for such a relationship to hold is that ρ/ρ' should be nearly unity or that one term in the summation should be large. Apparently one or both of these conditions must be responsible for the excellent quantitative relationship observed in the chlorination and basicity reactions ($\rho = -10.09$ and -7.26 , respectively). However, this derivation suggests that the empirical linear relationship may not be completely general.

Conclusions.—The Hammett equation, with the modifications here introduced, appears capable of correlating the available data on electrophilic aromatic substitutions. The treatment offers promise of providing a truly quantitative approach to isomer distribution in aromatic substitution.

A great deal of quantitative data on aromatic substitution will be required to test the approach presented in this paper. We wish at this time to encourage other workers to undertake research in this area in order that a rigorous test of the utility of the treatment may soon be possible.

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