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Rates of Bromination of Anisole and Certain Derivatives. Partial Rate Factors for the Bromination Reaction. The Application of the Selectivity Relationship to the Substitution Reactions of Anisole[1,2]

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The non-catalytic bromination of anisole in acetic acid at 25° provides 1.6% *o*- and 98.4% *p*-bromoanisole. Under these conditions the relative rate, anisole to benzene, has been estimated as $1.79 \times 10^9/1.00$. The results provide the partial rate factors o_f 8.6×10^7 and p_f 1.10×10^{10}. The rate measurements for a series of disubstituted anisoles indicate that m_f is slightly greater than one. The available data for six substitution reactions of anisole have been examined for adherence to a linear relationship. The average percentage error in ρ is 3.32%. The only serious deviation from the relationship is the bromination reaction. The deviations are random and the statistical, graphical and percentage error in ρ analyses suggest the applicability of a linear relationship. A tentative value for σ^+_{p-OMe} is -0.74 ± 0.02. This result is in good agreement with the value derived from the *t*-cumyl solvolysis results, -0.764.

The suggestion that the electrophilic substitution reactions of monosubstituted benzenes obey a simple linear free energy relationship[5,6] prompted an examination of the available data for the methyl and *t*-butyl substituents.[7,8] The partial rate factors for each alkylbenzene provided an excellent fit to the Selectivity Relationship[9] and derived equations. The successful application of this relationship to these alkylbenzenes made it desirable to investigate the further extension of the relationship to other activating substituents.

The principal basis for criticism of the proposed general nature of the Selectivity Relationship[5,6] has been the view that resonance contributions to an electron-deficient transition state would not remain constant.[10-13] Moreover, the electrical influences of the alkyl groups, although clearly defined experimentally, have been a matter of considerable controversy. In this situation, it appeared necessary to examine the reactions of a monosubstituted benzene which was strongly activated through resonance. Since anisole clearly fulfills this requirement, it was selected for further study. Accordingly, the mercuration reaction was examined as an example of a reaction of low selectivity.[14,15] In addition, it was desirable to have available the results for the highly selective non-catalytic bromination reaction.

The bromination of anisole and certain of its derivatives has received some attention. Previously, the rate relative to benzene had been reported as 2.07×10^9 in 99% acetic acid.[16,17] A cryoscopic determination of the *para* isomer indicated that it represented 95.3% of the product.[17] A value for the *meta* partial rate factor was derived from the relative rates of bromination of *o*- and *p*-dimethoxybenzene and *p*-methylanisole. These rate data indicated that m_f^{OMe} was small, but greater than one. Illuminati has recently found m_f^{OMe} for the bromination reaction to be 0.2 through the determination of the rates of bromination of 2-methoxymesitylene and mesitylene.[18]

In view of these conflicting observations, we have re-examined the non-catalytic bromination reaction. In the course of this investigation much of the original work[16,17] has been repeated and the study has been expanded to include certain features which had been omitted in the earlier investigations.

Results

The rapid reaction of bromine with the anisoles was studied in dry acetic acid at 25°. The relative rates were established by the determination of the tenth and fifth-lives in order to avoid the kinetic difficulties associated with the bromination reaction.[16,19] The observed reaction times are summarized in Table I.

TABLE I

OBSERVED 10 AND 20% REACTION TIMES FOR THE BROMINATION OF ANISOLE AND *para*-SUBSTITUTED ANISOLES IN ACETIC ACID AT 25°

Compound	Concentration, M		Reaction interval examined[a]			
			Observed		Corrected[b]	
	[ArH]	[Br_2]	$t_{10\%}$	$t_{20\%}$	$t_{10\%}$	$t_{20\%}$
Anisole	0.0205	0.00763	0.46	1.19	0.36	0.94
	.0207	.00769	0.48	1.24	0.38	1.00
p-Methylanisole	.0204	.00925	9.10	21.0	8.58	19.8
	.0196	.00920	8.38	19.3	7.59	17.5
	.0196	.00851	9.65	19.2	8.21	16.6
p-*t*-Butylanisole	.0199	.00969	7.20	16.3	6.90	15.7
	.0198	.00957	6.50	16.6	6.13	15.7
p-Phenylanisole	.0201	.01021	142		145	
	.0201	.01026	135	331	139	341
	.0201	.01022	143	328	146	336
p-Dimethoxybenzene	.0200	.00880	5.01	13.2	4.41	11.6
	.0183	.01179	4.21	10.4	4.52	11.0

[a] Minutes. [b] Corrected to aromatic 0.0200 M and bromine 0.0100 M by third-order rate expression.

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[1] Directive Effects in Aromatic Substitution. XLIII.

[2] Based upon a thesis submitted by Leon M. Stock in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

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[4] Department of Chemistry, The University of Chicago.

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

(6) C. W. McGary, Y. Okamoto and H. C. Brown, *ibid.*, **77**, 3037 (1955).

(7) The data for *m*- and *p*-methyl are summarized; L. M. Stock and H. C. Brown, *ibid.*, **81**, 3323 (1959).

(8) The data for *m*- and *p*-*t*-butyl are summarized; L. M. Stock and H. C. Brown, *ibid.*, **81**, 5621 (1959).

(9) H. C. Brown and C. R. Smoot, *ibid.*, **78**, 6255 (1956).

(10) P. B. D. de la Mare, *J. Chem. Soc.*, 4450 (1954).

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(13) R. W. Taft, N. C. Deno and P. S. Skell, *Ann. Revs. Phys. Chem.*, **9**, 287 (1958).

(14) H. C. Brown and M. Dubeck, THIS JOURNAL, **82**, 1939 (1960).

(15) The acetylation reaction is under study: work in progress with Dr. G. Marino.

(16) P. W. Robertson, P. B. D. de la Mare and W. T. G. Johnston. *J. Chem. Soc.*, 276 (1943).

(17) P. B. D. de la Mare and C. A. Vernon, *ibid.*, 1764 (1951).

(18) G. Illuminati, THIS JOURNAL, **80**, 4945 (1958).

(19) H. C. Brown and L. M. Stock, *ibid.*, **79**, 1421 (1957).

These rate data were compared with the reaction intervals required for the bromination of pentamethylbenzene.[19] The relative rates were derived from the mean values for each $t_{10\%}$ and $t_{20\%}$ measurement. The results are compared with the other available data in Table II.

TABLE II

RELATIVE RATES OF BROMINATION OF ANISOLE AND *para*-SUBSTITUTED DERIVATIVES IN ACETIC ACID AT 25°

Compound	Relative rate	
	This study	Lit.,[a] ref.[16,17]
Benzene[b]	1.00	1.00
Pentamethylbenzene[b]	0.81×10^9	0.89×10^9
Anisole	1.79×10^9	2.07×10^9
p-Methylanisole	9.30×10^7	9.70×10^7
p-*t*-Butylanisole	1.10×10^8	
p-Phenylanisole	5.06×10^6	
p-Dimethoxybenzene	1.52×10^8	1.61×10^8

[a] The values presented by the authors, ref. 16, 17, have been corrected employing the now known rate of bromination of benzene to toluene 1.00/605, ref. 19. [b] Ref. 19.

The isomer distribution was determined for reactions carried out under conditions similar to those adopted for the kinetic experiments. In order to avoid disubstitution, a large excess of anisole was present in all experiments. Preliminary attempts to utilize infrared spectroscopy for the analysis of bromoanisole samples containing small quantities of residual anisole were unsuccessful. Anisole possesses a strong absorption at the only wave length suitable for the analysis of the *ortho* isomer in low concentrations. These experiments did indicate that the concentration of *o*-bromoanisole in the product was quite small. In subsequent experiments, reaction products were treated in an attempt to remove completely all traces of residual anisole. The results of infrared analysis indicated that the *ortho* isomer represented 2.3 ± 0.5% of the bromoanisole fraction. The product distribution was further examined through the application of vapor phase chromatography. The results of the latter analysis, 1.6 ± 0.2, are believed to be considerably more reliable than the spectroscopic value. The isomer distributions determined experimentally are presented in Table III.

TABLE III

ISOMER DISTRIBUTION IN THE BROMINATION OF ANISOLE IN ACETIC ACID AT 25°

Experiment	Bromoanisole, mole %	
	ortho	*para*
Detmn. A[a]	2.3 ± 0.5	97.7
Detmn. B[b]	1.55 ± .20	98.4
	1.78 ± .08	98.2
Detmn. C[b]	1.38 ± .04	98.6
	1.36 ± .05	98.6
Adopted value	1.6 ± .2	98.4

[a] Based on infrared analysis. [b] Based on vapor phase chromatographic analysis, each entry is a separate determination.

Discussion

The Partial Rate Factors.—In the determination of the relative rate of reaction for compounds which differ in reactivity to the degree observed for benzene and anisole, it is not practical to attempt to study them under identical conditions. The difficulty was circumvented by the comparison of anisole with pentamethylbenzene. In our earlier study, pentamethylbenzene had been compared to *m*-xylene, *m*-xylene to *p*-xylene, *p*-xylene to toluene and toluene to benzene.[19] As a consequence of these measurements there is a rather large uncertainty in the relative rate, anisole to benzene. However, de la Mare and Vernon have reported an almost identical value based on a different series of rate measurements.[17]

The isomer distribution obtained in this investigation is 1.6% *o*- and 98.4% *p*-bromoanisole. The earlier report of 95.3% *p*-isomer is not in serious disagreement with the latter result. However, the implication that the remainder of the product was *o*-bromoanisole is in quite serious disagreement with our observations.

The partial rate factors based on the isomer distribution and relative rate obtained in this study are o_f^{OMe} 8.6×10^7 and p_f^{OMe} 1.10×10^{10}. In order to further evaluate o_f^{OMe}, it is possible to utilize the relative rate data. The rate of bromination of *p*-methylanisole relative to benzene may be approximated (1)

$$\frac{k_{p\text{-methylanisole}}}{k_{\mathrm{B}}} = \frac{2\ o_f^{\mathrm{OMe}} m_f^{\mathrm{Me}}}{6} = 9.3 \times 10^7 \quad (1)$$

On the basis of m_f^{Me}, 5.5, established in our earlier study,[19] o_f^{OMe} is evaluated as 5.0×10^7 and % *ortho* isomer as 0.93. The same result is obtained from the earlier work.[16,17] A second approach is possible through a comparison of *o*- and *p*-dimethoxybenzene (2).

$$\frac{k_{o\text{-dimethoxybenzene}}}{k_{p\text{-dimethoxybenzene}}} = \frac{2m_f^{\mathrm{OMe}}(o_f^{\mathrm{OMe}} + p_f^{\mathrm{OMe}})}{4o_f^{\mathrm{OMe}} m_f^{\mathrm{OMe}}} = 44.2 \quad (2)$$

The adoption of p_f^{OMe} as 1.10×10^{10} provides o_f^{OMe} 1.26×10^8 and predicts 2.35% *o*-bromoanisole. In view of the experimental uncertanties in the relative rates for these fast reactions, the predicted values are probably not significantly different from that determined experimentally. Thus these results substantiate the isomer distribution obtained by direct analysis.

From a theoretical standpoint, the value of m_f^{OMe} is of considerable interest. From indirect data de la Mare and Vernon have estimated m_f^{OMe} to be in the range 1.7 to 4.1. This surprising result is confirmed in the present study.[20] Utilization of o_f^{OMe}, 8.6×10^7, and the relative rate for *p*-dimethoxybenzene provides m_f^{OMe} 1.7. Another procedure employing the relative rate of bromination of *p*-dimethoxybenzene and *p*-methylanisole indicates m_f^{OMe} to be 4.7. The treatment applied to *o*-dimethoxybenzene and anisole yields m_f^{OMe} 1.9. It is clear that the *rate* data for the bromination of the disubstituted anisoles indicate an enhanced reactivity for the *m*-methoxy group compared to hydrogen.

The conclusion that such an activation exists should be treated with considerable reservation. Employing the polymethylbenzene approach Illuminati has demonstrated that the group is deactivating in the bromination reaction.[18] Indeed, none of the results which are based on a direct

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(20) Since the procedures for the calculation of m_f^{OMe} have been outlined, ref. 17, the details are not presented here.

TABLE IV

SUMMARY OF PARTIAL RATE FACTORS AND ASSOCIATED QUANTITIES FOR TOLUENE AND ANISOLE

		Toluene[a]					Anisole				
	Reaction, conditions[b]	o_f	m_f	p_f	S_f	$-\rho$	o_f	m_f	p_f	$\frac{\log p_f^{OMe}}{\log p_f^{Me}}$	Ref.
1	Bromination, Br_2, $HOAc-H_2O$, 25°	600	5.5	2420	2.644	11.40	8.7×10^7	$(1.9)^c$	1.10×10^{10}	2.98	This study
2	Bromination, Br_2, HOAc, 30°[d]		4.7	534	2.053	9.66		0.2	1.64×10^5	1.91	18
3	Chlorination, Cl_2, HOAc, 25°	617	4.95	820	2.219	10.32	6.2×10^6		4.6×10^7	2.63	27–29
4	Deboronation, $ArB(OH)_2$, Br_2, $HOAc-H_2O$, 25°[d]		3.3	78.5	1.373	7.17			1.5×10^6	3.25	32, 33
5	Deboronation, $ArB(OH)_2$, $H_2SO_4-H_2O$, 60°			27.6		5.15			4.17×10^3	2.51	30
6	Deuterium exchange, ArD, $H_2SO_4-H_2O$, 25°	83	1.9	83	1.640	5.45	2.3×10^4	0.25	5.5×10^4	2.47	25
7	Desilylation, $ArSiMe_3$, $HClO_4$, 50% MeOH, 51°		2.3	21.2	0.964	5.00	3.35×10^2	0.25	1.51×10^3	2.40	24, 31
8	Mercuration, $Hg(OAc)_2$, HOAc, 25°	5.71	2.23	23.0	1.014	5.00	1.86×10^2	$(1.2)^c$	2.31×10^3	2.47	14
9	Solvolysis, $ArCMe_2Cl$, 90% H_2O–acetone, 25°[d]	3.63	2.00	26.0	1.114	4.54	1.05×10^2	0.61	3.36×10^3	2.49	23

[a] These results have been examined in detail, ref. 7. [b] The electrophilic reagent is present first, followed by the catalyst, solvent and temperature. [c] Evaluation was indirect, see Discussion. [d] Not treated in statistical analysis, see Discussion.

measurement of the reactivity of the position *meta* to the methoxy group indicate the position to be more active than benzene. In the solvolysis reactions of *m*-methoxybenzyl tosylate,[21] -benzyl chloride[22] and -phenyldimethylcarbinyl chloride,[23] the substituent reduces the rate compared to the parent compound. Similarly, the substituent reduces the rate of detrimethylsilylation[24] and deuterium exchange.[25]

It is apparent that the data for those substitution reactions where a direct experimental method is available, *e.g.*, deuterium exchange,[24] detrimethylsilylation[23] and the bromination of the polymethylbenzenes,[18] the methoxy group exhibits a consistent deactivating effect. There must be some factor in the poly-substituted anisoles which renders the indirect calculation unsatisfactory. The difficulty possibly arises from neglect of the stabilities of the π-complexes of anisole and the substituted anisoles and their contributions to the over-all rates.[26]

Applicability of a Linear Free Energy Relationship.—The available data for the substitution reactions of anisole are summarized in Table IV.[27–31] The relative rates of solvolysis of the substituted phenyldimethylcarbinyl chlorides, from which the σ^+-constants have been obtained, are included for comparison. This latter reaction has not been included in the statistical analysis or other computations.

In view of the limited amount of data available, we have carefully examined the experimental validity of each observation. The difficulties in the evaluation of the relative rate of bromination of anisole and benzene have been discussed. The same problem is encountered in other cases. The directive influence of the *p*-methoxy substituent in the bromination reaction has also been investigated by Illuminati.[18] He has discussed the limitations of the polymethylbenzene approach with respect to the intrusion of steric inhibition of resonance by the *o*-methyl substituents in some detail. Because of this major complication, this reaction has been discarded from further examination. The chlorination results are also uncertain. The second-order rate constants for the reaction of anisole and chlorine are only approximate.[27–28] Moreover, the isomer distribution is based upon a competitive kinetic technique.[29]

The deboronation reaction has been examined for replacement by bromine[32] and hydrogen.[30] In the bromination reaction, the second-order rate constant for *p*-methoxyphenylboronic acid has been reported as $> 7 \times 10^3$ l. mole^{-1} sec.$^{-1}$. This value can only be regarded as a rough estimate.[33] Consequently, this result has not been included in the following discussion. The protodeboronation reaction[30] has been studied as a function of H_0[34] for the *p*-methyl and *p*-methoxy derivatives. Although the slopes of the H_0 plots are not identically one, the relative rates are not significantly dependent upon the value of the acidity function.

The partial rate factors for the deuterium exchange reaction[25] have also been obtained from an evaluation of the H_0 dependence. The difficulties encountered in the correlation of the data for this reaction for *m*- and *p*-methyl have been discussed.[7,25] The detrimethylsilylation[31] and mercuration[14] reactions are less susceptible to the in-

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(21) J. Kochi and G. S. Hammond, THIS JOURNAL, **75**, 3445 (1953).

(22) M. Simonetta and G. Favini, *J. Chem. Soc.*, 1840 (1954).

(23) Y. Okamoto and H. C. Brown, THIS JOURNAL, **79**, 1909 (1957).

(24) R. A. Benkeser and D. I. Hoke, unpublished results.

(25) D. P. N. Satchell, *J. Chem. Soc.*, 3911 (1956).

(26) The influence of π-complexes in the relative rates of substitution reactions has been discussed previously, ref. 7.

(27) A. E. Bradfield, W. O. Jones and F. Spenser, *J. Chem. Soc.*, 2907 (1931).

(28) B. Jones, *ibid.*, 430 (1943).

(29) B. Jones and E. N. Richardson, *ibid.*, 3939 (1956).

(30) H. Kuivila, private communication.

(31) C. Eaborn, *J. Chem. Soc.*, 4858 (1956). Note added Sept. 22, 1959: In a recent paper, F. D. Dean and C. Eaborn, *J. Chem. Soc.*, 2299 (1959), the protodesilylation reaction has been examined in aqueous acetic acid containing added sulfuric acid at 50°. Through a series of comparisons the partial rate factors, p_f^{OMe} 1010, p_f^{Me} 1.255 and m_f^{OMe} 0.38, were obtained. The ratio, $\log p_f^{OMe}/\log p_f^{Me}$, is 2.39 in agreement with that found earlier for this reaction, Table I. Similarly, the m_f^{OMe} value is in accord with the discussion presented above.

(32) H. C. Kuivila and A. R. Hendricks, THIS JOURNAL, **74**, 5068 (1952).

(33) Professor Kuivila has generously provided us with his experimental results for this reaction. He also suggests that the rate constant may be smaller than that reported by a factor of 10. We believe this is an accurate statement of the situation. If it were different by a factor of ten it would be in virtual agreement with the relationship as eventually established.

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

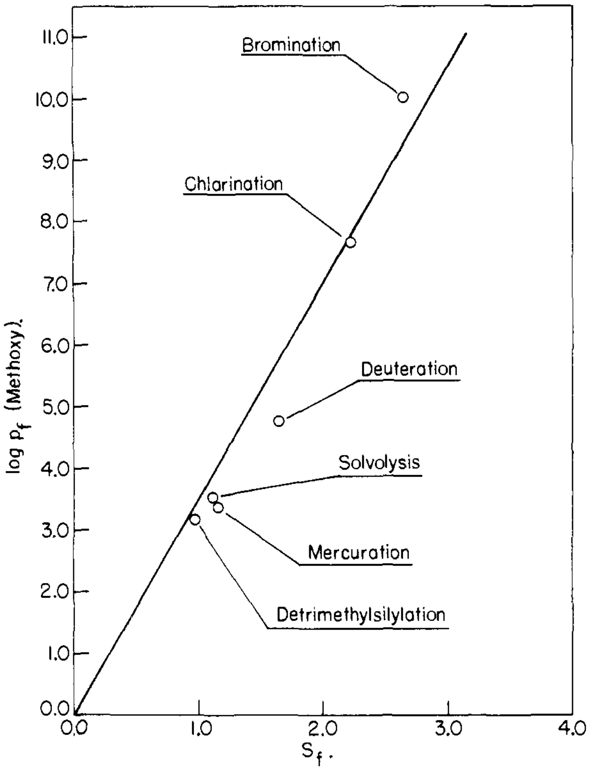

Fig. 1.—Linear relationship between log p_f^{OMe} and the Selectivity Factor (log $p_f^{\mathrm{Me}}/m_f^{\mathrm{Me}}$).

fluence of substituents. Accordingly, the kinetic measurements in these reactions are much less difficult.

On the basis of this discussion, six reactions of the *p*-methoxy substituent are available for further examination. For the *m*-methoxy group, only three electrophilic substitution reactions have been studied through reliable procedures. Applying the Selectivity Relationship in the form

$$\log p_f^{\mathrm{OMe}} = b^{\mathrm{OMe}} \log (p_f^{\mathrm{OMe}}/m_f^{\mathrm{OMe}}) \qquad (3)$$

to these three reactions (2, 7, 8) yields an average value of b^{OMe} of 0.89 ± 0.03. Evidently these three reactions obey the Selectivity Relationship with satisfactory precision.

Another approach to the problem, previously adopted for the examination of *p*-methyl and *p*-*t*-butyl, permits an examination of a greater portion of the available data. This approach utilizes the relationships 4 and 5.

$$\log p_f^{\mathrm{OMe}} = \frac{\sigma^+_{p\text{-OMe}}}{\sigma^+_{p\text{-Me}}} \log p_f^{\mathrm{Me}} \qquad (4)$$

$$\log p_f^{\mathrm{OMe}} = \frac{\sigma^+_{p\text{-OMe}}}{\sigma^+_{p\text{-Me}} - \sigma^+_{m\text{-Me}}} \log [p_f^{\mathrm{Me}}/m_f^{\mathrm{Me}}] = \frac{\sigma^+_{p\text{-OMe}}}{\sigma^+_{p\text{-Me}} - \sigma^+_{m\text{-Me}}} S_f \qquad (5)$$

These equations predict the ratios, log p_f^{OMe}/log p_f^{Me} and log p_f^{OMe}/S_f to be constant. The values for log p_f^{OMe}/log p_f^{Me} are given for each reaction in Table IV. The average value is 2.58 ± 0.15 for the six substitution reactions under consideration, entries 1,3,5,6,7,8. The average value for log p_f^{OMe}/S_f is also satisfactorily constant, 3.35 ± 0.22. The constancy of these ratios suggests that the substitution reactions in the *para* position of toluene and anisole are governed by a common relationship.

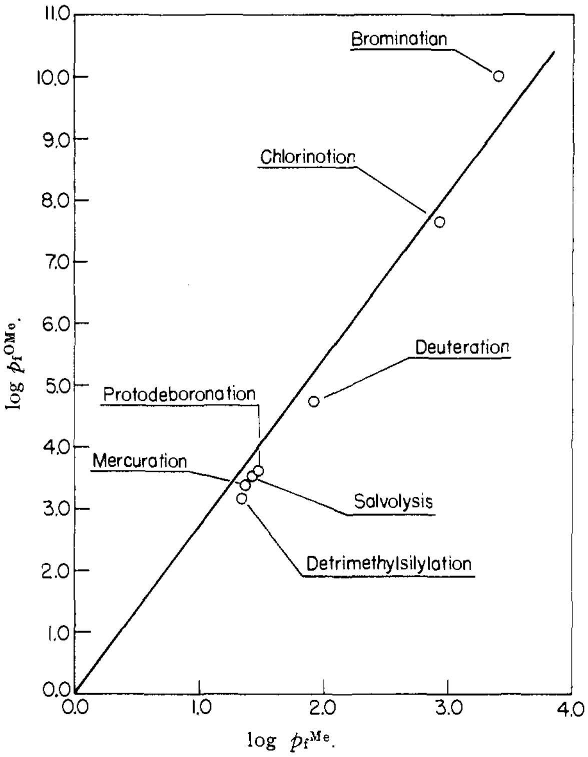

Fig. 2.—Linear relationship between log p_f^{OMe} and log p_f^{Me} in electrophilic substitution.

The validity of this observation was further tested through an inspection of graphical representations of the data, Figs. 1 and 2. It is evident that the data could be correlated by a line with a very slight upward curvature. Alternatively, the data appear to be correlated quite well by a straight line, with only one moderate deviation apparent, bromination.

To examine more fully the ability of a linear expression to correlate the data, the results were subjected to a least squares analysis. The parameters developed through this procedure are presented in Table V.

TABLE V

STATISTICAL PARAMETERS FOR ADHERENCE OF THE SUBSTITUTION DATA TO THE CORRELATION EQUATIONS

Equation	Dependent variable	Independent variable	Parameters b^a	r^b	s^c	n^d
4	log p_f^{OMe}	log p_f^{Me}	2.71	0.996	0.558	6[e]
5	log p_f^{OMe}	S_f	3.49	0.995	0.753	5[f]

[a] Least squares slope. [b] Correlation coefficient. [c] Standard deviation. [d] Number of reactions examined. [e] Entries 1, 3, 5, 6, 7, 8, Table IV. [f] Entries 1, 3, 6, 7, 8, Table IV.

The correlation coefficients reveal a high probability of linear dependence. However, the standard deviation, dependent on the magnitude of the data,[35] is quite large. To further investigate the quantitative merits of the correlation, the percentage error in the reaction constant has been evaluated.[7,8] The ρ-values were calculated from

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[35] H. H. Jaffé, *Chem. Revs.*, **53**, 191 (1953).

the Hammett equations (6, 7)

$$\rho_{p\text{-OMe}} = \log p_f^{\text{OMe}}/\sigma^+_{p\text{-OMe}} \qquad (6)$$

$$\rho_{p\text{-Me}} = \log p_f^{\text{Me}}/\sigma^+_{p\text{-Me}} \qquad (7)$$

For this evaluation, the value $\sigma_{p\text{-Me}}^+$ −0.280, based upon 47 substitution reactions of toluene,[4] has been adopted. Four different values for $\sigma^+_{p\text{-OMe}}$ have been employed. The latter procedure provides additional information concerning the utility of the least squares correlation equations (4, 5) for the prediction of σ^+ constants. The results of this analysis are summarized in Table VI.

TABLE VI

AVERAGE PERCENTAGE ERROR IN ρ FOR *para*-SUBSTITUTION OF TOLUENE AND ANISOLE

σ-Constants		Av. error in ρ,[a] %
$\sigma^+_{p\text{-Me}}$	$\sigma^+_{p\text{-OMe}}$	
−0.280	−0.764	4.37
.280	.740	3.32
.280	.720	2.79
.280	.700	3.29
[b]	.740	5.33

[a] Evaluated for entries, 1, 3, 5, 6, 7, 8; Table IV. [b] Based on ρ as determined for *m*- and *p*-methyl, Table IV.

When contrasted with observed percentage errors for toluene,[7] 7.4, and *t*-butylbenzene,[8] 8.6, the deviations in this series are quite small. Consequently, it appears that the data for the methoxy group obey the proposed quantitative treatment at least as well as those for the alkyl groups previously examined.

These results are quite encouraging. It should be recognized that the data are still sparse and a rigorous test of full applicability of the treatment to highly activating substituents will require considerable additional data. It is hoped that such data will be forthcoming.

The σ^+-Constant for the *p*-Methoxy Group.—It is of interest to compare the σ^+-values derived from the data presently available. The ratio log p_f^{OMe}/log p_f^{Me} provides the constant −0.722 ± 0.043 based on $\sigma^+_{p\text{-Me}}$ −0.280. Another constant −0.707 ± 0.046, is obtained from log p_f^{OMe}/S_f. The least squares slopes, Table V, yield −0.759 and −0.736 for equations 4 and 5, respectively. The examination of the percentage error in ρ suggests that the data are best correlated by $\sigma^+_{p\text{-OMe}}$ −0.74 ± 0.02. Although the available results do not provide a method for a final choice of this constant, the value −0.740 ± 0.020 appears to be most satisfactory for the treatment of the data. This parameter is within the limits of uncertainty for $\sigma^+_{p\text{-OMe}}$ evaluated for solvolysis of the *t*-cumyl chlorides, −0.764.[36]

In summary, a reasonably good linear relationship appears to exist for six substitution reactions of anisole encompassing a range of reactivity of 10^{10}. Only one significant discrepancy exists. The bromination reaction is experimentally four times more rapid than anticipated on the basis of the relationship. All the other reactions provide data which fall within 30% of the predicted values. The random nature of the deviations suggests that they may be the consequence of experimental extrapolations and are not necessarily real. The statistical and other analyses applied to these data provide −0.74 ± 0.02 as a preliminary value for $\sigma^+_{p\text{-OMe}}$ for electrophilic substitution.

Utilization of *p*-Substituted Anisoles for the Estimation of *meta* Partial Rate Factors.—In concurrent investigations, it was desirable to obtain independent confirmation for certain *meta* partial rate factors. In other instances, the minute amount of *meta* product resulting from direct substitution was so small as to preclude spectroscopic or chromatographic analyses. The substitution reactions of *p*-substituted anisoles are apparently free of side reactions. Moreover, the large directive effect of the *o*-methoxy group ensures that a single substitution product is obtained. Accordingly, this procedure provides a convenient method for the comparison of *meta* reactivity. In the course of this research program, we have had occasion to apply this technique. The rates and relative rates for several *p*-substituted anisoles are summarized in Tables I and II. The m_f-values for the bromination reaction obtained by this procedure are presented in Table VII. It is evident that $m_f^{t\text{-Bu}}$ is predicted with satisfactory precision, but that m_f^{OMe} appears to be high when compared with values estimated from direct measurements.

TABLE VII

meta PARTIAL RATE FACTORS FOR BROMINATION FROM *p*-SUBSTITUTED ANISOLES

p-Substituent	Relative rate[a]	*meta* partial rate factor
Methyl	1.00	5.5[b]
t-Butyl	1.18	6.5[c]
Methoxy	1.64	4.7

[a] From data presented in Table II. [b] Because of the relatively large uncertainty in o_f^{OMe}, *p*-methylanisole is taken as 1.00 together with the directly measured value of m_f^{Me} 5.5 to calculate the other partial rate factors. [c] Value from direct determination, 6.1; L. M. Stock and H. C. Brown, THIS JOURNAL, **81**, 5615 (1959).

Experimental Part

Materials.—All the aromatic compounds examined in this study were subjected to fractionation or crystallization prior to utilization for rate measurements. All possessed mole % purities greater than 99.5 as determined by analysis of the cooling curves.[37] The materials utilized exhibited the following physical properties, m.p., b.p., f.p., $n^{20}\text{D}$ mole % purity: anisole, 155° at 750 mm., $n^{20}\text{D}$ 1.5168, 99.5; *p*-methylanisole, 175.3° at 742 mm., −32.11°, 1.5121, 99.6; *p*-bromoanisole, 108.8° at 21 mm., +13.54°, 1.5639, 99.9; *o*-bromoanisole, 115° at 23 mm., 3.27°, 1.5737, 99.2; *p*-dimethoxybenzene, 59°; *p*-phenyl- and *p*-*t*-butylanisole were available from a concurrent study.[14]

Kinetic Measurements.—The methods employed in the kinetic investigations have been described previously.[19]

Isomer Distribution.—Determination A: The experiment was carried out essentially as described for B. The techniques employed and the spectroscopic analyses are available in detail.[38] The spectroscopic analysis indicated a yield of 95%. Determination B: In a 1-l. flask equipped with a dropping funnel were placed 50.0 g. (0.463 mole) of anisole and 250 ml. of glacial acetic acid. A solution of 15.6 g. (0.091 mole) of bromine in 200 ml. of acetic acid was added rapidly. The reaction was allowed to proceed to completion. The solution was quenched in water and the organic materials were carefully extracted into carbon tetrachloride. The extracts were combined, washed with carbonate and dried over calcium sulfate. The solvent was removed by careful fractionation. The residual materials were examined by gas chroma-

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(36) H. C. Brown and Y. Okamoto, THIS JOURNAL, **80**, 4979 (1958).

(37) K. Nelson, *Anal. Chem.*, **29**, 517 (1957).

(38) L. M. Stock, Ph.D. Thesis, Purdue University, 1959, p. 158.

tography for the isomer distribution. Determination C: In this experiment the same quantities were employed, the bromine was added dropwise to the solution. The analytical sample was obtained as described.

Gas Chromatographic Analysis.—Several attempts were made to achieve a resolution of the *o*- and *p*- isomers. It was found that liquid phases of tricresyl phosphate and Ucon polar showed considerable promise; Apiezon and various silicone fluids were unsatisfactory. For convenience, Ucon polar was selected for further work. The conditions adopted for analysis were a 7-m. column packed with Ucon polar (30%) on 30–60 mesh firebrick operated at 160° with a flow of 100 ml. of He min.$^{-1}$ measured at the outlet. Under these conditions the retention times were *p*-bromoanisole 128 min., *o*-bromoanisole 137 min. Resolution was not complete, but the degree of separation was more than satisfactory for this analysis. The integrated areas were employed to calculate the percentage area. A small correction factor, 0.84, was necessary to convert the observed % area to mole % *ortho*. The results are summarized in Table III.

LAFAYETTE, INDIANA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF DELAWARE]

The Acid-catalyzed Ring Opening of Epichlorohydrin

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The A-1 solvolysis mechanism for ring opening of epichlorohydrin, suggested by Long and Pritchard[2] on the basis of the observed h_0 dependence of the rate, has been re-examined here by means of other kinetic criteria.[7] The results obtained here, as well as other considerations, would appear to indicate that the earlier mechanism requires some modification.

The acid-catalyzed ring opening reactions of epoxides and trimethylene oxides have been extensively investigated by Long and Pritchard and their co-workers.[2] These authors have presented various lines of evidence that appear to permit a clear choice between the A-1 and A-2 modes among the possibilities for ring opening mechanisms discussed by Ingold.[3] Thus, by the use of the isotopic oxygen tracer, isobutylene and propylene oxide have been shown[2a] to observe predominantly the A-1 (carbonium ion) mechanism. The same conclusion was reached with regard to the mechanism of acid-catalyzed ring opening of ethylene and trimethylene oxides on the basis of similarity in the activation parameters to the case of isobutylene oxide[2c] and the observation of a linear, approximately unit slope, h_0 correlation when applying the Zucker–Hammett hypothesis.[4] Other criteria such as the magnitude of the k_D/k_H ratio also gave results which appear to agree with these conclusions.[2d,e]

These workers also reached the decision[2b] that epihalohydrins and glycidols underwent acid-catalyzed ring opening by a clear A-1 mechanism when they demonstrated a linear plot of log k_1^+ *vs.* $-H_0$ with a slope of 0.87. This suggestion by Long and Pritchard has been accepted as a basis for interpreting the acid-catalyzed ring opening of oxides with other polar substituents; *e.g.*, glycidic esters.[5] Some doubt, however, arises as to the validity of this mechanistic deduction based solely on the application of the familiar Zucker–Hammett hypothesis,[4] in view of several demonstrations[6] of contradictions therein.

In these laboratories we have recently illustrated how a more reliable criterion[7] of the carbonium ion mechanism may be established by an examination of the rate dependence on both solvent composition and acidity. We are reporting here the application of this criterion to review the mechanism of epichlorohydrin solvolysis in a range of acidic water–ethanol solutions.

Experimental

All reagents used were Eastman Kodak Co. white label grade. **Epichlorohydrin** was distilled through a helix-packed column at atmospheric pressure prior to use; only the fraction boiling between 116–117° was utilized in the rate studies. ***p*-Nitroaniline** was recrystallized from absolute ethanol just before use in the colorimetric measurements and the **nitrobenzene** was used only immediately after distillation under vacuum through a 10″ Vigreux column.

The rate measurements were carried out by means of a dilatometric technique and the rates computed from Guggenheim plots in exactly the fashion described by Pritchard and Long.[2b] However, though the dilatometer we actually used was of somewhat different construction, the results so obtained could be roughly checked aginst the data previously reported[2b,8] on the reaction in pure water. All measurements were taken at 30.02 ± 0.01°. The acidic aqueous ethanol solutions were composed by weighing into a 200-ml. volumetric flask the required amount of absolute ethanol which had previously been purified and dried over magnesium in the manner described by Vogel.[9] The calculated amount of sulfuric acid was then added carefully and the flask made up to the mark with distilled water. The acidic aqueous ethanol solutions prepared in this manner were brought to the reaction temperature in one compartment of the dilatometer while a second compartment containing the calculated amount of epichlorohydrin reagent was being thermostated. Means were available in the design of the dilatometer for rapidly uniting the contents of the two compartments and then rapidly filling the capillary section

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(1) Part of the work being reported here has been taken from the honors paper submitted by A. L. Goodman in partial fulfillment of the requirements for the degree of Bachelor of Science with Distinction in Chemistry at the University of Delaware, June, 1959.

(2) (a) F. A. Long and J. G. Pritchard, THIS JOURNAL, **78**, 2663 (1956); (b) J. G. Pritchard and F. A. Long, *ibid.*, **78**, 2667 (1956); (c) F. A. Long, J. G. Pritchard and F. E. Stafford, *ibid.*, **79**, 2362 (1957); (d) J. G. Pritchard and F. A. Long, *ibid.*, **78**, 6008 (1956); (e) **80**, 4162 (1958).

(3) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 341 ff.

(4) L. Zucker and L. P. Hammett, THIS JOURNAL, **61**, 2791 (1939).

(5) J. A. Durden, Jr., H. Am. Stansbury, Jr., and W. H. Catlette, *ibid.*, **81**, 1943 (1959).

(6) "Annual Review of Physical Chemistry," Section by N. Deno, H. Eyring, Editor, Palo Alto, Calif., 1958, p. 303 ff. However, see M. Paul and F. A. Long, *Chem. Revs.*, **57**, 935 (1957), and F. A. Long, *Proc. Chem. Soc.*, 220 (1957), for further discussion of these points.

(7) H. Kwart and L. B. Weisfield, THIS JOURNAL, **80**, 4670 (1958).

(8) A full description of the design and the range of application of this instrument will be discussed in a forthcoming publication from these laboratories.

(9) A. I. Vogel, "Practical Organic Chemistry," Longmans, Green and Co., New York, N. Y., 1956, p. 166.