from a large capacity g.l.c. column; n^{20}D 1.3978. It was identified by its infrared and mass spectra, the latter indicating a molecular weight of 132. *Anal.* Calcd. for $C_7H_{16}O_2$: C, 63.6; H, 12.2. Found: C, 64.8; H, 12.3. The principal impurity was an unidentified carbonyl as shown by infrared analysis.

RELATIVE AREAS ($\sim$% W.) AS DETERMINED BY G.L.C. (UNCALIBRATED)-ANALYSIS ON DIISODECYL PHTHALATE PACKING

Product	Weight, %
Methanol	0.8
Acetone	76.6 (prob. includes some ethanol $\leq$3%)
Methyl ethyl ketone	$\sim$0.8
t-Amyl alcohol	3.2
Ethyl *t*-amyl peroxide	16.1
2-Methyl-2-hexanol	2.4

2,5-Dimethyl-2,5-dihydroperoxyhexane (in the Presence of Cupric Chloride).—Cupric chloride (1.0 mole in 100 ml. of H_2O + 150 ml. of CH_3OH) was mixed with the methanolic solution of the peroxide (0.2 mole/250 ml. of methanol), and ferrous sulfate (0.48 mole/250 ml. of water) was added to maintain a temperature of 25–40°. Gas production was nil. The crude reaction mixture was distilled (I) through a 20-cm. heli-grid column until $\sim$438 g. of distillate were collected. This distillate was refractionated (after removal of a 20-g. aliquot for analyses) in a 100-cm. helice-packed column (distillation II). Fractions 1 to 4 (95.2 g., b.p. 55.5–64.5°, n^{20}D 1.3345 to 1.3290) were analyzed by mass spectrometry: 1.6% mole 1,2-dichloroethane, 6.8% mole acetone and 92% mole methanol; g.l.c. analyses were qualitatively consistent with this analysis. On the basis of a chlorine analysis (0.52 %), the amount of 1,2-dichloroethane was calculated to be 0.0074 mole. Methanol is known to azeotrope with the 1,2-dichloroethane (b.p. 60.95°).[19]

The concentrate remaining from distillation II was saturated with potassium carbonate and extracted with ether. The ether extract was combined with the extract obtained by continuous extraction of the original aqueous inorganic salt phase.[20] The ether was distilled and the residual liquid was fractionated (distillation III) to give four volatile fractions (3 to 6) containing chlorine and hydroxyl groups.

An authentic sample of 4-chloro-2-methyl-2-butanol (β-chloro-*t*-amyl alcohol; b.p. 53–54° (6 to 7 mm.), n^{20}D 1.4446; lit. value[21] b.p. 62–63° (14 mm.)) was prepared from ethyl β-chloroacetate and methylmagnesium iodide, and its infrared spectrum recorded. *Anal.* Calcd. for $C_5H_{11}OCl$: C, 49.0; H, 9.05; Cl, 28.92. Found: C, 49.3; H, 9.1; Cl, 28.6.

Direct comparison of the authentic spectrum of β-chloro-*t*-amyl alcohol with fractions 3 to 6 and g.l.c. analyses established the presence of that alcohol as a principal constituent of each fraction. Chlorine analyses (21.6%) of a sample simulating the composition of fractions 4 to 6 placed on upper limit of 74.5% (0.05 mole) as the content of β-chloro-*t*-amyl alcohol. Likewise, fraction 3 (19.5%Cl) was found to contain $\sim$67% w. (0.014 mole) of the same alcohol. Further analytical detail is shown below.

Fraction 3 (b.p. 60–108° (115 mm.), n^{20}D 1.4290, 2.6 g.) was analyzed for water (5.5% w.) and total carbonyl (0.10 equiv./100 g.). One carbonyl was isolated as a reddish-orange 2,4-DNP (dinitrophenylhydrazone), m.p. 175–176°. *Anal.* Calcd. for $C_{11}H_{12}N_4O_4$: C, 50.0; H, 4.7; N, 21.2. Found: C, 50.3; H, 4.8; N, 21.4. Analyses and m.p. are thus in good agreement with the 2,4-DNP of 3-methyl-2-butenal (m.p. 179°).[22] Another minor impurity was 2,2,-5,5-tetramethyltetrahydrofuran—established by g.l.c. correlation with the known compound.

Fraction 4 (b.p. 109–110° (115 mm.), n^{20}D 1.4427, 5.2 g.) was analyzed for hydroxyl (calcd. for $C_5H_{11}OCl$: 0.82 equiv./100 g.; found: 0.86 equiv./100 g.) and chlorine (24.5%). These data and the infrared analyses indicated a distribution of roughly 17% 2-methyl-2-buten-1-ol and 83% β-chloro-*t*-amyl alcohol. Analysis of combined fractions 4 to 6 (by bromine number) showed the presence of 0.15 mole of double bond/100 g.

Fraction 5 (b.p. 72.5° (11 mm.), n^{20}D 1.4440, 2.3 g.) gave an infrared spectrum essentially identical with fracton 4. Fraction 6 (b.p. 45° (1 to 2 mm.), n^{20}D 1.4480, 0.7 g.) was found by infrared analysis to contain some β-chloro-*t*-amyl alcohol (Found: C, 59.9; H, 10.3; Cl, 12.9), but the principal component was not identified conclusively.

Analytical Methods.—The functional groups were determined by conventional methods; gases were analyzed by mass spectrometry.

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(19) L. H. Horsley, *et al.*, "Azeotropic Data," American Chemical Society Publication, Washington, D. C., 1952, p. 28.

(20) Wet carbon analysis was carried out on the extracted inorganic salt phase (after removal of the ether); total of 278 g. at 0.16% w. carbon. Thus, the loss of organic material to this phase is very low.

(21) E. H. Huntress, "Organic Chlorine Compounds," John Wiley and Sons, Inc., New York, N. Y., 1948, p. 1148.

(22) E. A. Braude and E. R. H. Jones, *J. Chem. Soc.*, 500 (1945).

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[CONTRIBUTION FROM THE RICHARD B. WETHERILL LABORATORY OF PURDUE UNIVERSITY]

Rate Data and Isomer Distribution in the Reaction of Anisole with Mercuric Acetate in Acetic Acid Solution. Partial Rate Factors for the Mercuration Reaction[1-3]

BY HERBERT C. BROWN AND M. DUBECK[4]

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The rate constant for the mercuration of anisole with mercuric acetate in glacial acetic acid is 1.85×10^{-5} l. mole^{-1} sec.$^{-1}$ at 25.0°. Under these conditions substitution occurs 14.0% in the *ortho* and 86% in the *para* position, with no detectable reaction in the *meta* position. These data lead to the partial rate factors: o_f 188 and p_f 2310. The value m_f 1.2 is estimated from the rate constant for *p*-methoxyanisole, 0.634×10^{-5} l. mole^{-1} sec.$^{-1}$. The observed rate constants for *p*-methyl- and *p*-*t*-butylanisole, 0.93 and 1.06×10^{-5} l. mole^{-1} sec.$^{-1}$, are in reasonable agreement with the values calculated from the partial rate factors, 0.58 and 0.88×10^{-5} l. mole^{-1} sec.$^{-1}$, respectively. The rate constants for mercuration of diphenyl ether and acetanilide are 2.67×10^{-6} and 1.91×10^{-6} l. mole^{-1} sec.$^{-1}$, respectively. The available data for the mercuration reaction are correlated with reasonable precision by the electrophilic substituent constants, σ^+.

Previous studies have demonstrated that the available data on electrophilic substitution reactions of toluene[5] and of *t*-butylbenzene[6] are cor-

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(1) Directive Effects in Aromatic Substitution. XLII.

(2) This research supported in part by a grant from the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgment is hereby made to the donors of the Petroleum Research Fund.

(3) Based upon a thesis submitted by M. Dubeck in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(4) Monsanto Chemical Co. Fellow, 1956–1957.

(5) F. R. Jensen, G. Marino and H. C. Brown, THIS JOURNAL, **81**, 3303 (1959); H. C. Brown and G. Marino, *ibid.*, **81**, 3308 (1959); H. C. Brown, G. Marino and L. M. Stock, *ibid.*, **81**, 3310 (1959); S. U. Choi and H. C. Brown, *ibid.*, **81**, 3315 (1959); H. C. Brown and B. A. Bolto, *ibid.*, **81**, 3320 (1959); L. M. Stock and H. C. Brown, *ibid.*, **81**, 3323 (1959).

(6) (a) H. C. Brown and M. Dubeck, *ibid.*, **81**, 5608 (1959); (b) H. C. Brown and G. Marino, *ibid.*, **81**, 5611 (1959); (c) L. M. Stock and H. C. Brown, *ibid.*, **81**, 5613, 5621 (1959).

related with satisfactory precision by the Selectivity Relationship.[7,8]

$$\log p_f^{\mathrm{Me}} = b^{\mathrm{Me}} \log (p_f^{\mathrm{Me}} / m_f^{\mathrm{Me}}) = b^{\mathrm{Me}} S_f$$

$$\log p_f^{t\text{-}\mathrm{Bu}} = b^{t\text{-}\mathrm{Bu}} S_f$$

The activating effects of the methyl and *t*-butyl substituents on electrophilic substitution in the benzene nucleus are appreciable and therefore point to a resonance contribution by these groups to the transition state of some significance. Consequently, it was gratifying to achieve a satisfactory correlation extending over the full range of available electrophilic substitution reactions.

It is obvious that a substituent capable of greater resonance interactions with the ring would provide a more rigorous test of the utility of the proposed treatment. The methoxy group is a substituent whose large resonance contributions have been demonstrated in many reactions. Accordingly, we undertook to obtain rate and isomer substitution data for anisole in order to test the applicability of the Selectivity Relationship

$$\log p_f^{\mathrm{OMe}} = b_f^{\mathrm{OMe}} S_f$$

as well as the applicability of the electrophilic substituent constants, σ^+.[9] In the present paper we report the results of our study of the mercuration of anisole, *p*-methoxy-, *p*-methyl-, *p*-*t*-butylanisole, acetanilide and diphenyl ether.

Results

The mercuration of the various compounds was accomplished by reaction with mercuric acetate in glacial acetic acid at 25.0°. The rates of the reaction were followed by determining the rate of loss of mercuric acetate by titration of aliquots of the reaction mixture with standard potassium thiocyanate solution. The aromatic was present in large excess (1.00 *M*) over the mercuric acetate (0.100 *M*) in order to minimize polysubstitution. Excellent second-order rate behavior was observed throughout the reaction course. The rate constants in successive runs agree to within ±3%.

The rate constants are summarized in Table I.

Table I

Rate Constants for the Reactions of Aromatics Containing Activating Substituents with Mercuric Acetate in Glacial Acetic Acid at 25.0°

Aromatic	Second-order rate constant, k_2 (l. mole^{-1} sec.$^{-1}$) × 10^5
Anisole	1.85
p-Methoxyanisole	0.634
p-Methylanisole	0.931
p-*t*-Butylanisole	1.06
Diphenyl ether	0.267
Acetanilide	0.191

The isomer distribution in the mercuration of anisole was established by the following procedure. A reaction mixture, identical with those used for the kinetic measurements, was allowed to react at 25.0° for an appropriate interval of time and then quenched with water. The excess anisole was removed and the isomeric methoxyphenylmercuric acetates were converted into the bromides by treatment with excess potassium bromide. The product, slurried in carbon disulfide, was converted into the corresponding bromoanisoles by treatment with bromine. The proportions of the isomeric bromoanisoles were determined through infrared analysis of their solutions in carbon disulfide.

The yields of the methoxyphenylmercuric bromides were quantitative, and their conversion into the isomeric bromoanisoles (in carbon disulfide solution) was achieved in yields of 92 to 94%.

The analysis indicated the formation of 14% of the *ortho* and 86% of the *para* isomer. *Meta* substitution could not be detected. Calculations employing the known substituent constants for the methoxy group indicate that *meta* substitution probably occurs to less than 0.1%, beyond the limits of detection of our methods. Consequently, no further attempt was made to fix precisely the minute amounts of *meta* substitution which presumably occurs.

Discussion

Utilizing the rate of mercuration of anisole and of benzene[10] at 25.0°, the partial rate factors for mercuration *ortho* and *para* to the methoxy group can be calculated to be 188 and 2310, respectively.

If we could assume that the rate of substitution of the substituted anisoles is a simple function of the individual partial rate factors, we should be in a position to calculate the partial rate factor for substitution *meta* to the methoxy group from the rate constant for *p*-methoxyanisole and the relationship

$$\frac{4\, o_f^{\mathrm{OMe}} m_f^{\mathrm{OMe}}}{6} = \frac{k_{p\text{-}\mathrm{MeOC_6H_4OMe}}}{k_{\mathrm{B}}}$$

In this way, m_f is estimated to be 1.2. These results are summarized in Table II.

Table II

Partial Rate Factors for the Mercuration of Anisole by Mercuric Acetate in Glacial Acetic Acid at 25.0°

Relative rate,[a] anisole/ benzene	Isomer distribution, %			Partial rate factors		
	o-	*m*-	*p*-	o_f	m_f	p_f
448	14.0	0	86.0	188	1.2	2310

[a] Rate of mercuration of benzene at 25.0°: 4.13 × 10^{-8} l. mole^{-1} sec.$^{-1}$.

That the above assumption is roughly satisfactory is indicated by a comparison of the calculated and observed rates for the mercuration of *p*-methyl- and *p*-*t*-butylanisole (Table III). In this calculation it is assumed that substitution occurs *ortho* to the methoxy group exclusively. Calculation of the relative rates of substitution *ortho* to the methoxy group and *ortho* to the alkyl group indicate that only traces of the latter product would be formed.

We did not determine the isomer distribution in the mercuration of diphenyl ether or acetanilide. However, the mercuration reaction has large steric requirements. Thus mercuration of anisole yields but 14% *ortho* substitution. Considering the relative steric requirements of the methoxy group with those of the phenoxy and acetamide groups, it would be expected that the amount of *ortho*

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(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 (1955).

(9) H. Brown and Y. Okamoto, *ibid.*, **80**, 4979 (1958).

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

TABLE III

RATE CONSTANTS FOR THE MERCURATION OF *p*-SUBSTITUTED ANISOLES AT 25.0°

Compound	Rate constant, $k_2 \times 10^5$ l. mole^{-1} sec.$^{-1}$ Obsd.	Calcd.[a]
p-Methylanisole	0.93	0.58
p-*t*-Butylanisole	1.06	0.88

[a] Based on the partial rate factors: o_f^{OMe} 188; m_f^{OMe} 2.23 (ref. 10); $m_f^{t\text{-Bu}}$ 3.41 (ref. 6a).

substitution in both diphenyl ether and acetanilide would be quite small. On this basis, no great error should be involved in utilizing the observed rate constants for estimating the partial rate factors in the *para* position for these substituents.

The available data on the partial rate factors for the mercuration reaction are summarized in Table IV.

TABLE IV

SUMMARY OF PARTIAL RATE FACTORS FOR MERCURATION OF SUBSTITUTED BENZENES WITH MERCURIC ACETATE IN GLACIAL ACETIC ACID AT 25°

Substituent	Partial rate factors o_f	m_f	p_f
Methoxy	188	1.2[a]	2310
Acetamido			277[b]
Phenoxy			194[b,c]
Methyl[d]	5.71	2.26	23.2
t-Butyl[e]	0	3.41	17.2
Phenyl[f]	0.08	0.77	6.42

[a] Estimated from the rate for *p*-methoxyanisole and o_f^{OMe}. [b] Assuming essentially 100% *para*. [c] Corrected for statistical factor of 2. [d] Ref. 10. [e] Ref. 6a [f] M. Dubeck, Ph.D. thesis, Purdue Libraries.

It is of interest that these partial rate factors are correlated with quite satisfactory precision by the electrophilic substituent constants, σ^+, derived from the solvolysis of the substituted *t*-cumyl chlorides[9] (Fig. 1). Least squares treatment of the data gives $\rho = -4.10$ for the mercuration reaction.

The degree of fit of the data for anisole to the Selectivity Relationship will be considered in the following paper.[11]

Experimental Part

Materials.—Baker and Adamson reagent grade acetic acid that was approximately 0.1 *M* in water, as determined by a Karl Fisher analysis, was employed as the reaction medium. It had been established previously that minor variations in water content at these levels does not affect the rate of reaction. The mercuric acetate was Mallinckrodt analytical reagent material. The aromatic compounds were purified by careful fractionation or recrystallization. They possessed the following properties: anisole, n^{20}D 1.5168; *o*-bromoanisole, b.p. 115° at 22 mm., n^{20}D 1.5737; *m*-bromoanisole, b.p. 104° at 22 mm., n^{20}D 1.5639; *p*-bromoanisole, 110° at 27 mm., n^{20}D 1.5641; *p*-methylanisole, b.p. 175.2° at 742 mm., n^{20}D 1.5121; *p*-dimethoxybenzene, m.p. 59°; *p*-*t*-butylanisole, b.p. 114° at 25 mm., n^{20}D 1.5032; acetanilide, m.p. 113.5°; diphenyl ether, m.p. 26°. The liquid samples possessed purities greater than 99.5 mole per cent., as determined from cooling curve analysis.

Rate Measurements.—The measurements were generally carried out by mixing 50.00 ml. of a 0.1500 *M* mercuric acetate solution with 25.00 ml. of a 3.000 *M* solution of the aromatic compound in glacial acetic acid. The resulting reaction mixture, which was 1.00 *M* in aromatic and 0.100 *M* in mercuric acetate, was kept at 25.0° in a constant temperature bath, and the decrease of mercuric acetate concentration was followed titrimetrically with standard potassium thiocyanate solution.[10]

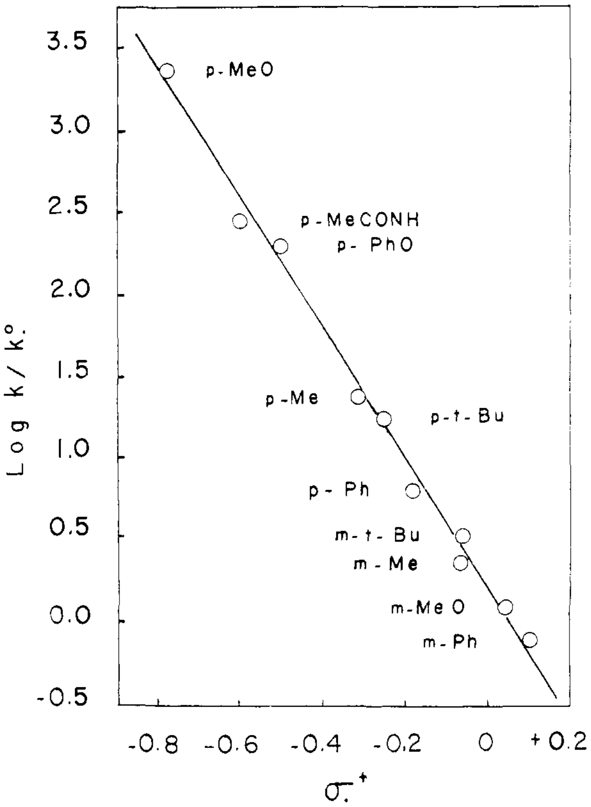

Fig. 1.—Correlation of the partial rate factors for mercuration by mercuric acetate in glacial acetic acid at 25.0°

Isomer Distribution Measurements.—The isomer distribution measurements for the mercuration of anisole were carried out on a reaction mixture that was identical in all respects to those employed in the kinetic measurements. Reaction was allowed to proceed to approximately 50% completion and was then quenched in an equal volume of water. The unreacted anisole was removed by aspiration under vacuum at room temperature, and the isomeric methoxyphenylmercuric acetates were converted to the bromide derivatives by the addition of a two- to threefold excess of potassium bromide. The isomeric arylmercuric bromides were then filtered and thoroughly dried under vacuum over phosphorus pentoxide. Yields of the mercuric bromide derivatives were quantitative. Conversion of the isomeric methoxyphenylmercuric bromides into the bromoanisoles was accomplished by treating a 0.5-g. slurry of the bromide in carbon disulfide with a 50 weight % solution of bromine in carbon disulfide until a faint red color persisted, indicating the presence of a slight excess of bromine. The solution was allowed to stand for about one-half hour with occasional shaking, and then the supernatant liquid was filtered. Traces of excess bromine were removed by washing with sodium bisulfite and water. After thorough drying with calcium hydride, the carbon disulfide solution of the isomeric bromoanisoles was analyzed by means of infrared spectrophotometry. Yields of 92 to 94% of monobromoanisoles were realized. The proportions of the isomers were determined by utilizing the 12.20 μ absorption band for the *para* and the 13.40 μ band for the *ortho* isomer. *m*-Bromoanisole could not be detected by means of differential analysis with the aid of a double beam infrared spectrophotometer. The possibility that bromination of the aromatic nucleus might occur during the conversion of the methoxyphenylmercuric bromides into the bromoanisoles was tested by treating a known mixture of the isomeric bromoanisoles with bromine in a manner similar to that utilized in the unknown samples. Analysis of the proportions of the isomers by means of infrared showed an excellent recovery with no change in composition. This supports the conclusion that extraneous bromination of the aromatic nucleus is not a significant factor.

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(11) L. M. Stock and H. C. Brown, THIS JOURNAL, **82**, 1942 (1960).