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Relative Rates and Isomer Distributions in the Gallium Bromide-Catalyzed Ethylation of the Halobenzenes in Ethylene Dichloride. Partial Rate Factors for the Ethylation Reaction[1]

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The gallium bromide-catalyzed reactions of ethyl bromide with the halobenzenes have been examined in ethylene dichloride solution at 25°. Using a competitive method, the rate of ethylation of fluorobenzene relative to benzene has been determined as 0.282. Under these conditions the isomeric fluoroethylbenzenes are formed in the proportion: 42.9% *o*-, 13.7% *m*- and 43.4% *p*-fluoroethylbenzene. These data provide the partial rate factors o_f^F 0.364, m_f^F 0.116 and p_f^F 0.738. In the ethylation of chlorobenzene, the rate ratio is 0.214, and the isomer distribution is 42.2% *o*-, 15.9% *m*- and 41.9% *p*-chloroethylbenzene. These results yield the partial rate factors for the ethylation of chlorobenzene o_f^{Cl} 0.271, m_f^{Cl} 0.102 and p_f^{Cl} 0.538. In the case of bromobenzene, the relative rate was determined to be 0.133 and the product ratio evaluated as 24.0% *o*-, 21.8% *m*- and 54.2% *p*-bromoethylbenzene. These observatons provide the partial rate factors o_f^{Br} 0.096, m_f^{Br} 0.087 and p_f^{Br} 0.433. Under conditions suitable for the ethylation of the other halobenzenes, iodobenzene–benzene reaction mixtures failed to yield ethylation products. The partial rate factors for ethylation reveal the halobenzenes are deactivated in all nuclear positions, least in the *para* position. The observation that p_f^F is less than unity contrasts with the results for *t*-cumyl chloride solvolysis and for the mercuration reaction. The available data for the gallium bromide-catalyzed ethylation of monosubstituted benzene are assembled and examined. With the exception of the partial rate factor for *p*-fluoro, these rate data are correlated by the electrophilic substituent constants, σ^+, based upon *t*-cumyl chloride solvolyses.

Introduction

At the time the Selectivity Relationship was originally proposed as a method for the correlation of electrophilic substitution reactions,[3,4] few quantitative experimental observations were available to provide a test of its utility. Accordingly, the necessary data were obtained for a number of representative monosubstituted benzenes, employing several suitable reactions. It was obviously desirable to utilize reactions covering a wide range on the Selectivity scale. For this purpose mercuration (S_f 1.014), nitration (S_f 1.366), acylation (S_f 2.192), chlorination (S_f 2.219) and bromination (S_f 2.644) were selected for investigation.

For biphenyl, it became desirable to obtain data defining the behavior of the Selectivity plot in the region nearer the origin than was possible with the mercuration reaction. The less selective gallium bromide-catalyzed ethylation reaction[5] (S_f 0.587) was adopted for this purpose.[6] In extending our examination of the applicability of the Selectivity Relationship to the halobenzenes, a study of the ethylation of these derivatives again seemed appropriate. The results of this investigation are reported in the present paper.

Results

The Halobenzene to Benzene Relative Rates.—The rate of ethylation of the halobenzenes relative to benzene was determined by a competitive procedure. Mixtures of a given halobenzene (X) and benzene (B) in ethylene dichloride were allowed to react with ethyl bromide in the presence of catalytic amounts of anhydrous gallium tribromide. The reaction mixtures were analyzed by gas chromatography employing tricresyl phosphate as the liquid phase. Rather than examine the complex product mixture, it proved far more convenient to determine the concentration of the starting materials before and after reaction. In this way, the relative rate of reaction of the two components could be obtained utilizing the well-known first order equation (1)

$$\frac{k_X}{k_B} = \frac{\log C_X^0 - \log C_X}{\log C_B^0 - \log C_B} \qquad (1)$$

This procedure worked satisfactorily for fluorobenzene, chlorobenzene and bromobenzene. In each case, the reaction proceeded smoothly. Only a relatively short reaction period, from 2 to 10 hours, was required for the desired conversion of the aromatics.

An attempt was made to extend the study to include iodobenzene. However, ethylation failed to occur under conditions similar to those employed for the other halobenzenes. Neither ethylbenzene nor ethyliodobenzene were observed among the products of the reaction even after a reaction interval of more than 24 hours. Titration of the reaction mixture with sodium thiosulfate revealed that considerable quantities of halogen were produced under the experimental conditions. Presumably, a side-reaction between iodobenzene and gallium bromide occurs rendering the catalyst ineffective. In view of this peculiar behavior of iodobenzene, further attempts to examine the ethylation of this halobenzene were abandoned.

The experimental results are summarized in Table I.

Isomer Distribution, Chlorobenzene.—The ethylation of chlorobenzene in ethylene dichloride solution led to the formation of significant amounts of diethylchlorobenzenes. Since the formation of these higher alkylated products might involve the selective alkylation of a particular monoethylchlorobenzene isomer, it appeared important to avoid this side reaction. The adoption of chlorobenzene as a solvent for the reaction prevented polyalkylation. Previously, the isomer distribution observed in the ethylation of toluene was found to be the same for ethylation either in the pure hydrocarbon or in ethylene dichloride solution.[6] Consequently, it appeared safe to adopt the product ratio ob-

(1) Directive Effects in Aromatic Substitution. LI.

(2) Post-doctorate research associate, 1959–1960, on project no. AT(11-1)-170 supported by the Atomic Energy Commission.

(3) H. C. Brown and K. L. Nelson, *J. Am. Chem. Soc.*, **75**, 6292 (1953).

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

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

(6) H. C. Brown and A. H. Neyens, *ibid.*, **84**, 1233 (1962).

TABLE I

HALOBENZENE TO BENZENE REACTIVITY RATIO FOR THE GALLIUM BROMIDE-CATALYZED ETHYLATION IN ETHYLENE DICHLORIDE AT 25.0°

Halobenzene	Concentrations, M — Initial [C_6H_5X]	Initial [C_6H_6]	Final [C_6H_5X]	Final [C_6H_6]	Relative rate $k_{C_6H_5X}/k_{C_6H_6}$
Fluoro	0.890	0.560	0.781	0.351	0.278
	0.920	0.390	0.811	0.253	0.286
				Mean value	0.282
Chloro	0.820	0.450	0.746	0.286	0.210
	.920	.450	.848	.310	.219
	.820	.350	.577	.240	.212
				Mean value	0.214
Bromo	0.785	0.560	0.725	0.299	0.127
	0.874	0.390	0.799	0.207	0.140
				Mean value	0.133

tained for alkylation in chlorobenzene as similar, if not identical, to the products of reaction in ethylene dichloride.

The gas chromatographic analysis (tricresyl phosphate liquid phase) indicated the presence of but three compounds. The chromatogram consisted of a single peak separated from two other partially resolved peaks. The identification of these peaks was achieved in the following manner. An authentic sample of *o*-chloroethylbenzene was prepared from pure *o*-ethylaniline. The fully resolved peak proved to be the *ortho* isomer. The unavailability of *p*-ethylaniline led us to adopt the following simple procedure for the analysis of the more complex partially resolved peaks. Ethylbenzene was chlorinated in 99.9% acetic acid to yield 51.5% *o*- and 48.5% of a second compound assigned the *para* structure. On the basis of retention time observed for the *para* compound, the partially resolved peaks were identified as *m*- and *p*-chloroethylbenzene. The analysis of the peak areas yielded the isomer distribution as 42.3% *o*-, 16.4% *m*- and 41.3% *p*-chloroethylbenzene.

The failure to achieve a complete resolution of the *meta* and *para* peaks raised a question as to the accuracy of the analysis. Fortunately, a complete resolution of the three peaks was achieved by analysis with a capillary column (polypropylene glycol). The results were in excellent agreement with the previous analysis: 42.2% *o*-, 15.9% *m*- and 41.9% *p*-chloroethylbenzene.

Isomer Distribution, Bromobenzene.—The ethylation of bromobenzene was carried out satisfactorily in ethylene dichloride solution. Gas chromatographic analysis on a tricresyl phosphate column indicated the formation of three compounds. As in the case of chlorobenzene, the chromatogram showed a single peak, presumably the *ortho* isomer, followed by an incompletely resolved double peak consisting of the *meta* and *para* isomers.

The *meta* isomer was identified by comparison with an authentic sample. The bromination of ethylbenzene in 99.9% acetic acid yielded two components in a ratio of 0.51, equivalent to an isomer distribution of 33.8 and 66.2%, respectively. In view of the isomer distribution realized in the bromination of toluene under similar conditions, 32.9% *o*-, 0.3% *m*- and 66.8% *p*-bromotoluene,[7] the assignment of smaller peak to *o*-bromoethylbenzene and the larger peak to the *p*-bromo isomer appears sound. The identification of the peaks in this manner provides the isomer distribution for the ethylation of bromobenzene as 24.0% *o*-, 21.8% *m*- and 54.2% *p*-bromoethylbenzene.

Isomer Distribution, Fluorobenzene.—For the more reactive fluorobenzene it also proved necessary to carry out the alkylation in the halobenzene as solvent. Gas chromatographic analysis on a 4-m. tricresyl phosphate column indicated the presence of three components. The resolution was very poor. The separation was improved, but still analytically unsatisfactory, on a 2-m. 7,8-benzoquinoline column. Fortunately, conditions were established whereby a capillary polypropylene column with flame ionization detector gave a complete separation of the three isomeric fluoroethylbenzenes.

In numerous cases we have observed that the capillary polypropylene column elutes the haloalkylbenzenes in the order: *ortho*, *meta* and *para*. Consequently, the structures are assigned on this basis leading to the analysis: 42.9% *o*-, 13.7% *m*- and 43.4% *p*-fluoroethylbenzene.[8]

The experimental data on the isomer distributions are summarized in Table II.

TABLE II

ISOMER DISTRIBUTIONS IN THE GALLIUM BROMIDE-CATALYZED ETHYLATION OF THE HALOBENZENES AT 25°

Halobenzene	Column	Ethylhalobenzene, % — *o*-	*m*-	*p*-
Chloro-	[a]	42.2	18.0	39.8
	[a]	41.7	16.7	41.6
	[a]	42.3	15.7	41.9
	[a]	42.6	15.4	41.1
	Mean value	42.2	16.5	41.3
	[b]	42.3	15.9	41.8
	[b]	42.1	15.9	42.0
	Mean value	42.2	15.9	41.9
Bromo-	[a]	23.2	21.2	55.6
	[a]	26.4	20.8	52.8
	[a]	22.7	23.0	54.3
	Mean value	24.0	21.8	54.2
Fluoro-	[b]	42.9	12.3	44.8
	[b]	42.8	12.4	44.2
	[b]	42.9	13.8	43.3
	Mean value	42.9	13.7	43.4

[a] 4-m. tricresyl phosphate on Celite column. [b] 50-m. polypropylene glycol capillary column.

Discussion

The observed relative rates and the isomer distributions provide the partial rate factors for the ethylation reaction. These data are summarized together with the partial rate factors for the solvolysis of the halosubstituted *t*-cumyl chlorides[9] in Table III.

(7) H. C. Brown and L. M. Stock, *J. Am. Chem. Soc.*, **79**, 1421 (1957).

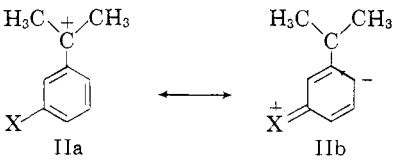
(8) It is unfortunate that the time available to Dr. Neyens did not permit the synthesis of the pure reference compounds. However, there can be little doubt that the minor component is the *meta* isomer. Since the other two isomers are formed in essentially equal amounts, no serious error can be involved in this assignment.

(9) H. C. Brown, Y. Okamoto and G. Ham, *J. Am. Chem. Soc.*, **79**, 1906 (1957).

TABLE III

PARTIAL RATE FACTORS FOR THE HALOGEN SUBSTITUENTS IN THE ETHYLATION REACTION AND THE *t*-CUMYL SOLVOLYSIS AT 25°

	Partial rate factors					
	Ethylation			*t*-Cumyl solvolysis		
Halogen	o_f	m_f	p_f	o_f	m_f	p_f
Fluoro	0.364	0.116	0.738	0.0502	0.0251	2.14
Chloro	.271	.102	.538	.00786	.0156	0.305
Bromo	.096	.087	.434	.00607	.0144	.208
Iodo				.0110	.0233	.244



IIa IIb

fluoro substituent in the *para* position has an activating effect (p_f^F 2.14). However, in the ethylation reaction, a *p*-fluoro group deactivates the ring (p_f^F 0.738). It has been noted previously that the fluoro substituent deactivates the *para* position in nitration and activates it in chlorination.[11] It is apparent that such variable behavior provides a serious obstacle to the realization of a simple quantitative treatment of aromatic substitution. A discussion of this problem will be deferred to the final paper of this group to enable a consideration of all available data.[12]

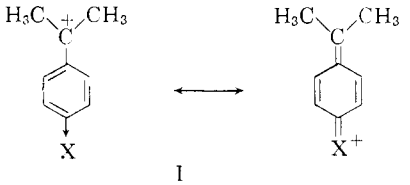
TABLE IV

PARTIAL RATE DATA FOR THE GALLIUM BROMIDE-CATALYZED ETHYLATION OF SUBSTITUTED BENZENES IN ETHYLENE DICHLORIDE AT 25.0°

Substituent	Rel. rate, k_R/k_B	Isomer distribution, %			Partial rate factors			Ref.
		ortho	*meta*	*para*	o_f	m_f	p_f	
Methyl	2.34	38.4	21.0	40.6	2.69	1.47	5.70	[a]
Phenyl	1.81	33.3	25.6	41.1	0.905	0.695	2.23	[b]
Hydrogen	1.00[c]				1.00[d]	1.00[d]	1.00[d]	
Fluoro	0.282	42.9	13.7	43.4	0.364	0.116	0.738	[e]
Chloro	.213	42.2	15.9	41.9	.271	.102	.538	[e]
Bromo	.133	24.0	21.8	54.2	.096	.087	.433	[e]

[a] Ref. 5. [b] Ref. 6. [c] For benzene. [d] For one position in benzene. [e] This study.

The partial rate factors for ethylation indicate the halogen substituents deactivate all ring positions. The deactivation is least in the *para* position. Presumably this result is a consequence of the ability of the halogen substituents to attenuate their electron-withdrawing properties by conjugation in the electron-deficient transition state. For ethylation and in the *t*-cumyl chloride solvolysis reaction, the order in the *para* position is F > Cl > Br. The observation is generally attributed to decreased conjugative electron-release with the increasing size of the atom (I).[10]



I

The deactivation of the *meta* position is substantially greater than in the *para* site. The decreased possibilities for conjugation in that position provide a rationale for the greater importance of the inductive influence of the halogens. However, both in the ethylation and in the solvolysis reactions, the observed order is not that anticipated from the electronegativities of the halogens, F < Cl < Br. Rather the order, F > Cl > Br, corresponding to the conjugative capacities[10] of these groups is obtained. As suggested earlier,[9] the halogens appear capable of transmitting electron density to the reaction center through a conjugative process even from the *meta* position. An increase in electron density at the *ortho* position through resonance interactions and inductive relay to the neighboring reaction center as illustrated in IIb provides a satisfactory mechanism.[9]

In the mercuration reaction, the *p*-fluoro partial rate factor is greater than unity (p_f^F 2.98). Similarly in the solvolysis of the *t*-cumyl chloride, a

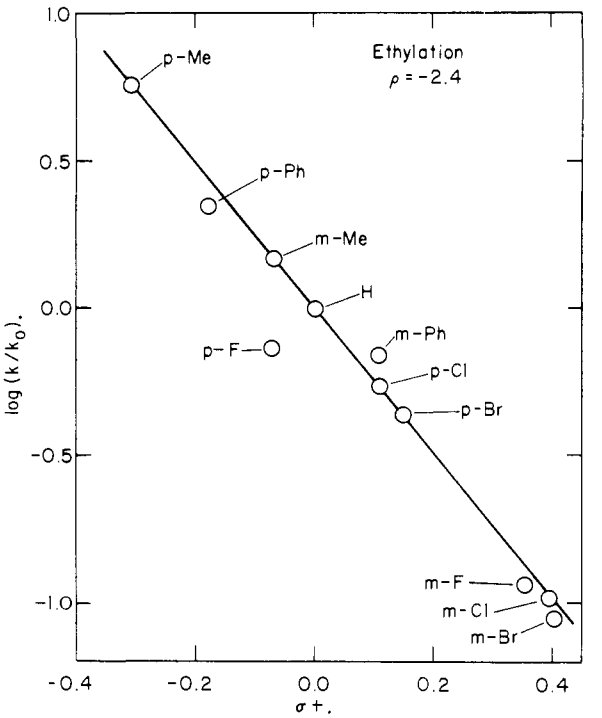


Fig. 1.—Relationship between $\log(k/k_0)$ for ethylation and the σ^+-constants.

Correlation of the Ethylation Data.—Quantitative data have now been obtained for the ethylation

(10) A. E. Remick, "Electronic Interpretation of Organic Chemistry," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1949.

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

(12) L. M. Stock and H. C. Brown, *J. Am. Chem. Soc.*, **84**, 1668 (1962).

of several aromatics. These observations are summarized in Table IV.

The logarithms of the partial rate factors are plotted against the standard electrophilic substituent constants,[13] σ^+, in Fig. 1. With but one exception, *p*-fluoro, the data are correlated with excellent precision. Omission of the *p*-fluoro point yields the reaction constant for the ethylation reaction as −2.44.

Experimental Part

Materials.—Gallium bromide,[5] ethyl bromide[5] and ethylene dichloride[14] were prepared and purified following procedures previously described. The halobenzenes were samples purified by Goldman.[15] Authentic *o*-chloroethylbenzene was prepared by the Sandmeyer reaction from *o*-ethylaniline. *m*-Bromoethylbenzene was available from an earlier study.[16] The chlorination and bromination of ethylbenzene providing the *ortho* and *para* isomers were carried out by procedures previously utilized to establish the isomer distribution in toluene.[7,17]

Relative Rates.—A solution of gallium tribromide in ethyl bromide was prepared with careful exclusion of moisture. An appropriate small quantity of this standard solution, usually about 1 ml., was taken up in a hypodermic syringe and introduced into 50 ml. of a solution of the halobenzene and benzene in ethylene dichloride at 25°. After an appropriate reaction period, 2 to 10 hours in different experiments, the reaction mixture was quenched in ice-water. The ethylene dichloride layer was separated, washed, and dried.

The solution was analyzed on a Perkin–Elmer Fractometer (model 154C) equipped with an integrator utilizing a 2-m. column with tricresyl phosphate as the liquid phase on Celite. The concentration of each aromatic was evaluated; *i.e.*, benzene in the ethylated mixture was determined relative to benzene in the original solution and each halobenzene similarly determined. In view of excellent reproducibility in sampling techniques, 1%, an internal standard was not employed. The temperatures utilized for the analyses were: benzene, 58°; fluorobenzene, 58°; chlorobenzene, 104°; bromobenzene, 130°. The results are summarized in Table I.

Isomer Distribution.—In a typical experiment an ethylene dichloride solution of bromobenzene, 0.7 *M*, was treated with gallium tribromide, 0.04 *M*, and ethyl bromide, 0.5 *M*. After 8 hours, the reaction mixture was quenched and analyzed on a 4-m. column of tricresyl phosphate on Celite.

For fluorobenzene and chlorobenzene, ethylene dichloride was eliminated and excess aromatic was employed as the solvent. Thus fluorobenzene was treated with ethyl bromide, 0.5 *M*, and gallium bromide, 0.04 *M*. After 2 hours, the reaction mixture was quenched, dried, and analyzed on a Perkin–Elmer Fractometer (model No. 154D) equipped with a 50-m. polypropylene glycol column and a flame ionization detector.

The isomer distributions obtained are summarized in Table II.

(13) H. C. Brown and Y. Okamoto, *J. Am. Chem. Soc.*, **80**, 4929 (1958).

(14) F. R. Jensen, G. Marino and H. C. Brown, *ibid.*, **81**, 3303 (1959).

(15) H. C. Brown and G. Goldman, *ibid.*, **84**, 1650 (1962).

(16) H. C. Brown, J. D. Brady, M. Grayson and W. H. Bonner, *ibid.*, **79**, 1897 (1957).

(17) H. C. Brown and L. M. Stock, *ibid.*, **79**, 5175 (1957).

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Relative Rates and Isomer Distributions in the Aluminum Chloride-Catalyzed Acetylation of the Halobenzenes in Ethylene Dichloride. Partial Rate Factors for the Acetylation Reaction[1]

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The rate of aluminum chloride-catalyzed acetylation of chlorobenzene relative to benzene in ethylene dichloride at 25° is 0.0209. Under these conditions the reaction yields 0.5% *m*- and 99.5% *p*-chloroacetophenone. These results lead to the partial rate factors m_f^{Cl} 0.0003 and p_f^{Cl} 0.125. Comparison of the rate of acetylation of fluorobenzene and bromobenzene relative to chlorobenzene leads to the relative rates, $k_{FC_6H_5}/k_{C_6H_6}$ 0.252 and $k_{BrC_6H_5}/k_{C_6H_6}$ 0.0140. In both cases essentially 100% substitution in the *para* position is observed. These results provide the partial rate factors, p_f^F 1.51 and p_f^{Br} 0.084. The negligible substitution in the *ortho* position is in accord with the very large steric requirements of the acetylation reaction, noted previously in the acetylation of toluene The order $p_f^F > p_f^{Cl} > p_f^{Br}$ agrees with the relative conjugative abilities of these halogens and with their relative effectiveness in facilitating reaction in mercuration, ethylation and *t*-cumyl solvolysis. The observation that p_f^F is greater than unity is in agreement with the results for mercuration and *t*-cumyl chloride solvolysis, but not with the behavior of *p*-fluoro in the ethylation reaction. The available data on the acetylation of monosubstituted benzenes provide an excellent linear free energy correlation with the electrophilic substituent constants, σ^+, derived from the solvolysis of the *t*-cumyl chlorides.

Introduction

The acetylation reaction has previously proved to be a convenient tool for the investigation of directive effects in toluene,[3] *t*-butylbenzene,[4] anisole,[5] biphenyl[6] and fluorene.[6] In previous papers of this group, electrophilic substitution data for the halobenzenes in the mercuration[7a] and ethylation[7b] reactions have been reported. These reactions exhibit a relatively low selectivity, with S_f 1.014 and 0.587, respectively. In the present paper, data for the acetylation reaction, one of higher selectivity, S_f 2.192, are presented. In the following paper the more selective halogenation reactions are examined[7c] and in the final paper[7d] the applicability of the Selectivity Relationship[8,9] for the correlation of the available data on the electrophilic substitution of the halobenzenes is considered.

Several studies of the acetylation of the halobenzenes have been reported. Thus, the acetylation of chlorobenzene, either in carbon disulfide[10–12] or

(1) Directive Effects in Aromatic Substitution. LII.

(2) Post-doctorate research associate, 1957–1959, on project no. AT(11-1)-170 supported by the Atomic Energy Commission.

(3) H. C. Brown, G. Marino and L. M. Stock, *J. Am. Chem. Soc.*, **81**, 3310 (1959).

(4) H. C. Brown and G. Marino, *ibid.*, **81**, 5611 (1959).

(5) H. C. Brown and G. Marino, unpublished research.

(6) H. C. Brown and G. Marino, *J. Am. Chem. Soc.*, **84**, 1236 (1962).

(7) (a) H. C. Brown and G. Goldman, *ibid.*, **84**, 1650 (1962); (b) H. C. Brown and A. H. Neyens, *ibid.*, **84**, 1655 (1962); (c) L. M. Stock and F. W. Baker, *ibid.*, **84**, 1661 (1962); (d) L. M. Stock and H. C. Brown, *ibid.*, **84**, 1668 (1962).

(8) H. C. Brown and K. L. Nelson, *ibid.*, **75**, 6292 (1953).

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