Rates and Isomer Distributions for the Bromination and Mercuration of the Monoalkylbenzenes in Trifluoroacetic Acid[1-3]

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Contribution from the Richard B. Wetherill Laboratory of Purdue University, Lafayette, Indiana. *Received November 27, 1965*

Abstract: Second-order rate constants were determined for the reaction of bromine with the monoalkylbenzenes in trifluoroacetic acid at 25°, establishing the rates relative to benzene to be: toluene, 2580; ethylbenzene, 3740; isopropylbenzene, 4530; and *t*-butylbenzene, 3220. The isomer distribution reveals essentially no *meta* substitution, with decreasing *ortho* substitution with increasing size of the alkyl substituent: methyl-, 17.6%; ethyl-, 13.0%; isopropyl-, 8.1%; and *t*-butylbenzene, 0%. In the mercuration reaction, the more customary reactivity order is observed: toluene, 9.89; ethylbenzene, 8.58; isopropylbenzene, 7.41; and *t*-butylbenzene, 6.03. Here, also, the amount of *ortho* substitution decreases with the size of the alkyl group: (toluene) 12.2% *o*-, 8.6% *m*-, 79.2% *p*-; (ethylbenzene) 7.6% *o*-, 9.2% *m*-, 83.2% *p*-; (isopropylbenzene) 2.4% *o*-, 9.8% *m*-, and 87.8% *p*-; (*t*-butylbenzene) 0% *o*-, 10.9% *m*-, and 89.1% *p*-. The partial rate factors indicate that the mercuration data agree with the Selectivity Relationship, but that the bromination data for the higher alkyl groups exhibit significant deviations. Possible causes for the unusual behavior of the higher monoalkyl derivatives in the bromination reaction are discussed.

The relative rates for bromination of the monoalkylbenzenes (RC_6H_4, with R = Me, Et, *i*-Pr, *t*-Bu) reveal a regular decrease from toluene to *t*-butylbenzene,[6-12] commonly attributed to the loss in hyperconjugative stabilization of the transition state accompanying the successive replacement of α-hydrogen atoms by methyl groups.

A similar trend is observed in the mercuration of these monoalkylbenzenes in acetic acid.[13] However, the reactivity differences are considerably smaller, presumably because the reaction is less selective, so that the reaction is less sensitive to the electronic contributions of the substituents.

In view of the apparent advantages of trifluoroacetic acid as a reaction medium for bromination and mercuration,[14] it appeared desirable to apply these reactions to the monoalkylbenzenes. The results for toluene were reported earlier.[14] In the present paper are reported the rates of reaction and the isomer distributions for the mercuration and bromination of ethyl-, isopropyl-, and *t*-butylbenzene at 25° in trifluoroacetic acid.

Results

Bromination. The reaction of bromine with the aromatics was determined by following the decrease in bromine concentration titrimetrically with standard thiosulfate solution. Special care was taken to ensure immediate titration of the iodine solutions in order to obtain accurate and reproducible results. Blanks accompanying the reaction mixtures indicated that loss of bromine, either by reaction with the solvent or by voltalization, was negligible. Light was excluded to avoid side-chain halogenation.

Excellent second-order plots were obtained for reactions carried to 80% completion. The second-order rate constants and the derived relative rates are presented in Table I. Unexpectedly, the observed order did not follow the usual Baker–Nathan sequence.

Table I. Rate Constants and Relative Rates for the Bromination of the Monoalkylbenzenes in Trifluoroacetic Acid at 25.0°

Compound	Rate constant, k_2 (l. mole^{-1} sec^{-1})	—Relative rate[b]— k_R/k_B	k_R/k_T
Benzene[a]	7.62×10^{-7}	1.00	
Toluene[a]	1.97×10^{-3}	2,580	1.00
Ethylbenzene	2.85×10^{-3}	3,780	1.45
Isopropylbenzene	3.45×10^{-3}	4,530	1.75
t-Butylbenzene	2.45×10^{-3}	3,220	1.25
p-Xylene[a]	6.91×10^{-3}	9,080	
o-Xylene	38.4×10^{-3}	50,800	

[a] From ref 14. [b] k_R, k_T, and k_B are the rate constants for the alkylbenzene, toluene, and benzene, respectively.

In view of these unusual results, it appeared desirable to undertake an independent determination of the relative rates. Consequently, mixtures of each of the alkylbenzenes with toluene were brominated under conditions identical with those employed in the kinetic determinations, and the products were determined by gas chromatography. The data yielded relative rate values, k_R/k_T, 1.45 for ethyl-, 1.75 for isopropyl-, and 1.25 for *t*-butylbenzene, in good agreement with the values derived from the rate constants (Table I). Consequently, the unusual relative rates must be real.

o-Xylene yielded a rate constant of 3.84×10^{-2}, or a relative rate of 50,800. On the basis of the previously established partial rate factors,[14] o_f^{Me} 1360, m_f^{Me}10, and p_f^{Me} 12,700, the relative rate, *o*-xylene to

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(1) Directive Effects in Aromatic Substitution. LVII.

(2) Based upon a thesis submitted by Robert A. Wirkkala in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

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(4) National Science Foundation Summer Fellow at Purdue University, 1959.

(5) Ethyl Corporation Fellow at Purdue University, 1960–1961.

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(7) P. W. Robertson, P. B. D. de la Mare, and B. E. Swedlund, *ibid.*, 783 (1953).

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(12) L. M. Stock and H. C. Brown, *ibid.*, **81**, 5615 (1959).

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

(14) H. C. Brown and R. A. Wirkkala, *ibid.*, **88**, 1447 (1966).

Table II. Relative Rates, Isomer Distribution, and Partial Rate Factors for the Bromination of the Monoalkylbenzenes in Trifluoroacetic Acid at 25.0°

Compound	Relative rates, k_R/k_T	Isomer distribution, %: *ortho*	*meta*	*para*	Partial rate factors: o_f	m_f	p_f
Toluene	2580	17.6	0	82.4	1360	10	12,700
Ethylbenzene	3740	13.0	0	87.0	1460		19,500
Isopropylbenzene	4530	8.1	0	91.9	1090		25,000
t-Butylbenzene	3220	0	0	100			19,300

Table III. Rate Constants, Isomer Distributions, and Partial Rate Factors for the Reaction of the Monoalkylbenzenes with Mercuric Trifluoroacetate in Trifluoroacetic Acid at 25.0°

Compound	Rate constant, $k_2 \times 10^2$ l. mole^{-1} sec^{-1}	Relative rate	Isomer distribution, %: *ortho*	*meta*	*para*	Partial rate factors: o_f	m_f	p_f
Benzene	2.85	1.00						
Toluene	28.2	9.89	12.2	8.6	79.2	3.62	2.55	46.9
Ethylbenzene	24.4	8.58	7.6	9.2	83.2	1.97	2.37	42.8
Isopropylbenzene	21.1	7.41	2.4	9.8	87.8	0.533	2.18	39.0
t-Butylbenzene	17.2	6.03	0	10.9	89.1	0	1.97	32.2

benzene, is 45,900, in reasonable agreement with the observed value. Thus, the additivity of the partial rate factors, previously established for chlorination[15] and bromination[11] of the methylbenzenes in acetic acid, apparently holds in the present system, in spite of the anomalous behavior of the higher alkyl groups.

The isomer distributions for the bromination of the alkylbenzenes was established under conditions identical with those utilized for the kinetic determination. Since it had been established previously that the isomer distribution in toluene is independent of the bromine concentration, no attempt was made to vary this component. No *meta* isomer was found. However, the amount anticipated was in the neighborhood of only 0.1%, and the gas chromatographic procedure would not have provided an analysis for such a minute component. The isomer distributions and the derived partial rate factors are summarized in Table II.

Mercuration. The rates of mercuration were determined by the procedure previously described,[14] following the decrease in mercuric ion titrimetrically with standard thiocyanate solution. Excellent second-order plots were obtained in all cases, the kinetic runs generally being carried to 70–80% completion.

The isomer distributions in these mercurations were established under conditions identical with those utilized for the kinetic determinations. The isomeric arylmercuric bromides were recovered from the reaction mixtures and converted into the corresponding bromoaromatics, and the latter were analyzed by gas chromatography. The results are summarized in Table III.

Discussion

Both reactions, mercuration and bromination, exhibit a marked decrease in the amount of substitution in the *ortho* position with increasing branching of the alkyl substituent. Thus, in bromination, the *ortho* isomer changes from 17.6% for toluene to 13.0% for ethyl-, to 8.1% for isopropyl-, to 0% for *t*-butylbenzene. Similarly, in mercuration, the change is from 12.2% for toluene to 7.6% for ethyl-, to 2.4% for isopropyl-, to 0% for *t*-butylbenzene.

Presumably these changes are the result of the increasing steric requirements of the substituent. However, it is of interest that the steric factor appears to be more important in trifluoroacetic acid than in acetic acid for both reactions. Thus, the per cent *ortho* observed for bromination in acetic acid for the four monoalkylbenzenes decreases in the order: 32.9, 33.8, 23, 1.2.[16] Similarly, mercuration of toluene in acetic acid gives 29.7% *ortho*, as compared to the 12.2% realized in trifluoroacetic acid. Originally, we proposed to attribute this effect to the larger steric requirements of the solvent molecules which are associated with the attacking species in the transition state. However, it has been noted that the chlorination of toluene and *t*-butylbenzene in trifluoroacetic acid *increases* the per cent substitution in the *ortho* position over that observed in acetic acid.[17] It is apparent that we are still far from an understanding of the effects of solvent in these reactions.

This point is emphasized further by an examination of the effect of the alkyl group on the rate of substitution in the *para* position relative to one of the six positions in benzene, the *para* partial rate factor, p_f. For convenience pertinent data are summarized in Table IV.

Of these 15 reactions, 11 exhibit the Baker–Nathan trend, with the partial rate factor decreasing from p_f^{Me} to $p_f^{t\text{-Bu}}$. In two cases, nitration by acetyl nitrate in acetic anhydride[18] and mercuridesilylation,[19] the opposite order is exhibited: $p_f^{\mathrm{Me}} < p_f^{\mathrm{Et}} < p_f^{i\text{-Pr}} < p_f^{t\text{-Bu}}$. In the bromination reaction in trifluoroacetic acid, it is highly significant that the results establish a reversal

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[15] H. C. Brown and L. M. Stock, *J. Am. Chem. Soc.*, 79, 5195 (1957).

[16] For a summary of the pertinent data with literature references, see L. M. Stock and H. C. Brown, "Advances in Physical Organic Chemistry," Vol. I, V. Gold, Ed., Academic Press Inc., New York, N. Y., 1963, pp 35–154.

[17] Unpublished results of L. M. Stock and A. Himoe, quoted in ref 16.

[18] J. R. Knowles, R. O. C. Norman, and G. K. Radda, *J. Chem. Soc.*, 4885 (1960).

[19] R. A. Benkeser, T. B. Liston, and G. Stanton, *Tetrahedron Letters*, No. 15, 1 (1960).

Table IV. *para* Partial Rate Factors for the Monoalkylbenzenes

Reaction[a]	Partial rate factors			
	p_f^{Me}	p_f^{Et}	$p_f^{i\text{-}Pr}$	$p_f^{t\text{-}Bu}$
Bromination, Br_2, $HOAc\text{-}H_2O$, 25°	2,420	1,800	1,200	806
Bromination, Br_2, CF_3CO_2H, 25°	12,700	19,500	25,000	19,300
Chlorination, Cl_2, HOAc, 25°	820	840	650	401
Chlorination, Cl_2, CF_3CO_2H, 25°	928			1,375
Chlorination, Cl_2, MeCN, 25°	6,250			3,140
Benzoylation, PhCOCl, $AlCl_3$, $PhNO_2$, 25°	831	755	715	615
Benzoylation, PhCOCl, $AlCl_3$, $C_2H_4Cl_2$, 25°	626	563	519	398
Acetylation, MeCOCl, $AlCl_3$, $C_2H_4Cl_2$, 25°	749	753	745	658
Nitration, $AcONO_2$, Ac_2O, 0°	60	69	72	76
Mercuration, $Hg(OAc)_2$, HOAc, 25°	23			17
Mercuration, $Hg(O_2CCF_3)_2$, CF_3CO_2H, 25°	47	43	39	32
Desilylation, $ArSiMe_3$, Br_2, HOAc, 25°	49	45	33	29
Desilylation, $ArSiMe_3$, $HClO_4$, MeOH, 51°	21	20	18	16
Desilylation, $ArSiMe_3$, $Hg(OAc)_2$, HOAc, 25°	11.5	11.5	12	14
Degermylation, $ArGeEt_3$, $HClO_4$, MeOH, 50°	14	13	12	11.5

[a] Data from Tables 2, 10, 11, and 12 of ref 16, and present study.

at an intervening stage: $p_f^{Me} < p_f^{Et} < p_f^{i\text{-}Pr} > p_f^{t\text{-}Bu}$.

These results suggest the simultaneous operation of two factors, one which decreases regularly from methyl to *t*-butyl, the other of which increases regularly in that order. Varying magnitudes of the contribution of the two factors could result either in a regular increase in the rate, a regular decrease, or a point of inversion, examples for all of which are now available.

The π-complexing ability of the monoalkylbenzenes, as measured by the interaction of hydrogen chloride with the aromatics, presumably arising from the ininductive effect of the alkyl substituent, increases regularly from methyl to *t*-butyl.[20] On the other hand, the ability of the alkyl group to stabilize an electron-deficient center, as in the solvolysis of the *t*-cumyl chlorides, presumably a reflection of the hyperconjugative contributions of the alkyl substituent, decreases regularly from methyl to *t*-butyl.[21] The transition state for aromatic substitutions is doubtless a blend of π and σ contributions.[22] Evidently, in the case of alkyl groups whose electronic contributions are relatively small, variations in the solvent can result in variations in the blend, so that the observed trend in the effects of alkyl substituent varies from the Baker–Nathan order as one extreme to the reverse order as the opposite extreme, or to an intermediate order with an inversion.

This discussion of the variations which are observed in the effects of the alkyl substituents with changes in the reaction or the medium should not distract attention from the fact that these variations are minor, representing changes by a factor of 2 or 3 in reactions where the effect of the alkyl group is a factor of 1000. Possibly, we should always expect to find such minor discrepancies in correlations involving reactions in the liquid phase, where specific interactions of the solvent with the reactants and the substituents must be ignored in the present state of our knowledge.

In the mercuration reaction, the more usual Baker–Nathan order is observed, and the correlation with the Selectivity Relationship is excellent (Figure 1).

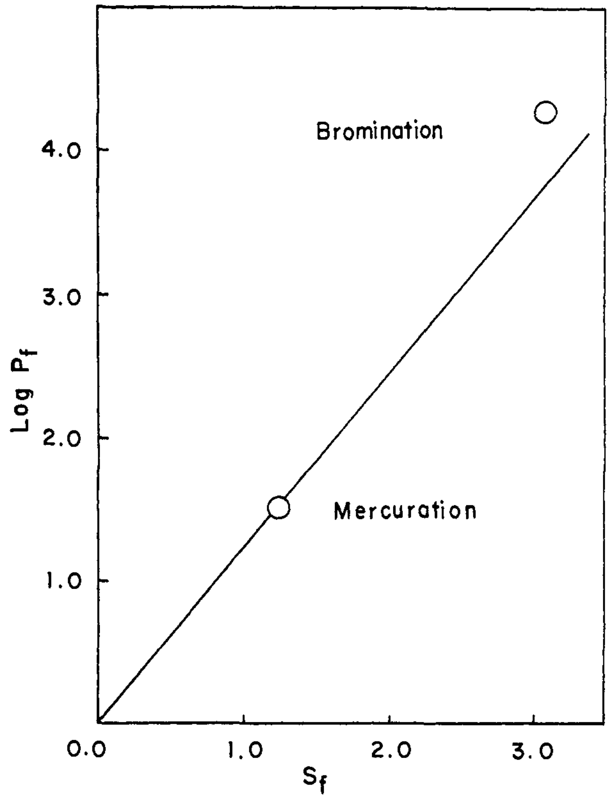

Figure 1. The bromination and mercuration reactions of *t*-butylbenzene in trifluoroacetic acid compared to the Selectivity Relationship as defined for 15 electrophilic substitution reactions.

Experimental Section

Materials. The benzene derivatives were highly purified samples with purities (from cooling curves) of better than 99.4 mole %. The following physical properties were noted: *o*-bromoethylbenzene, bp 205° (735 mm), $n^{20}D$ 1.5510; *m*-bromoethylbenzene, 202° (740 mm), $n^{20}D$ 1.5457; *p*-bromoethylbenzene, 188° (742 mm), $n^{20}D$ 1.5598; *o*-bromoisopropylbenzene, 205° (745 mm), $n^{20}D$ 1.5410; *m*-bromoisopropylbenzene, 207° (740 mm), $n^{20}D$ 1.5369; *p*-bromoisopropylbenzene, 100° (7 mm), $n^{20}D$ 1.5569; *o*-bromo-*t*-butylbenzene, 105° (6 mm), $n^{20}D$ 1.5441; *m*-bromo-*t*-butylbenzene, 100° (7 mm), $n^{20}D$ 1.5338; *p*-bromo-*t*-butylbenzene, 95° (6 mm), $n^{20}D$ 1.5331.

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(20) H. C. Brown and J. D. Brady, *J. Am. Chem. Soc.*, **74**, 3570 (1952).

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

(22) K. L. Nelson and H. C. Brown, "The Chemistry of Petroleum Hydrocarbons," B. T. Brooks, *et al.*, Ed., Reinhold Publishing Corp., New York, N. Y., 1955, Chapter 56.

The other solvents and reagents were purified in the manner described previously.[14]

Procedures. The kinetic procedures and the technique used to determine the isomer distributions were identical with those previously described for toluene.[14] A 150-ft capillary column packed with tricresyl phosphate was used for the analysis of the isomeric bromoalkylbenzenes: 125° for the bromoethyl-, 135° for the bromoisopropyl-, and 145° for the bromo-*t*-butylbenzenes. In all cases the isomers were eluted in the order *ortho*, *meta*, *para*.

Rates and Isomer Distributions for the Mercuration of the Monohalobenzenes in Trifluoroacetic Acid. Partial Rate Factors for the Mercuration Reaction[1-3]

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Abstract: The rate constants and isomer distributions for the mercuration of fluorobenzene, chlorobenzene, and bromobenzene in trifluoroacetic acid at 25° were determined. Simple, second-order kinetic data were realized in all cases. The product distribution in fluorobenzene is 11.4% *ortho*, 0.8% *meta*, and 87.8% *para*. Utilizing the relative rate value, 0.287, the partial rate factors become o_f^{F} 0.0983, m_f^{F} 0.00687, and p_f^{F} 1.51. The chlorobenzene/benzene reactivity ratio is 0.0470. The isomer distribution for the mercuration of chlorobenzene under these conditions is 11.9% *ortho*, 5.8% *meta*, and 82.3% *para*. These data provide the partial rate factors o_f^{Cl} 0.0168, m_f^{Cl} 0.00820, and p_f^{Cl} 0.232. Finally, in the case of bromobenzene, the relative rate, 0.0397, and the isomer distributions, 10.6% *ortho*, 8.0% *meta*, and 81.4% *para*, lead to the partial rate factors, o_f^{Br} 0.0126, m_f^{Br} 0.00954, and p_f^{Br} 0.194. The results reveal that the order of reactivity of the *ortho* and *para* positions is $F > Cl > Br$. In the *meta* position, the inductive order is obtained, $F < Cl < Br$. The available data for the mercuration of monosubstituted benzenes in trifluoroacetic acid are assembled and examined. An excellent linear free energy correlation is realized for the substitution data *vs.* the electrophilic substituent constants, σ^+, based on the solvolysis of the *t*-cumyl chlorides. The reaction constant ρ was established as -5.68.

The reaction of mercuric acetate in acetic acid with the monohalobenzenes was examined previously.[6] Unfortunately, a major difficulty was encountered. The reactions are quite slow and reaction of the mercuric acetate with the solvent competes seriously with the reaction with the aromatic constituent. For example, in the case of fluorobenzene, this side reaction represents 40% of the total mercuric acetate consumed, while for chlorobenzene it represents 80% of the total reaction. Consequently, it was necessary to utilize the less accurate competitive procedure for determining the relative rates of reaction of chlorobenzene and bromobenzene.

Application of this procedure to less active aromatics would mean that the reaction with the aromatic would involve a smaller and smaller fraction of the total reaction, greatly magnifying the experimental difficulties and uncertainties. To circumvent this problem, we examined the reaction of mercuric trifluoroacetate in trifluoroacetic acid with benzene and toluene[7] and with the higher monoalkylbenzenes.[8]

The reaction proved to involve simple kinetics, being clearly second order, and far faster by a factor of 10^5 than the related reaction in acetic acid. The enhanced speed is obviously a great advantage in studying the rates of reaction of aromatics containing deactivating substituents. Even more important, no evidence was encountered for any side reaction of the mercurating agent with the solvent. It appeared desirable, therefore, to apply this reaction to the monohalobenzenes. Accordingly, a study of the reaction rates and isomer distributions for the halobenzenes at 25° was undertaken.

Results

The rates of mercuration of the halobenzenes with mercuric trifluoroacetate were determined by following the decrease in mercuric ion concentration titrimetrically with standard thiocyanate solution employing ferric alum as indicator.[7] Second-order plots were made and the rate constants were obtained from a least-squares analysis of the slopes. Excellent second-order plots were obtained in experiments carried to 70–80% completion. The results are summarized in Table I.

The isomer distributions were determined for reaction conditions similar in all respects to those utilized for the kinetic measurements. The reaction mixtures were quenched at appropriate time intervals in aqueous sodium bromide. The precipitated arylmercuric bromides were converted into the isomeric bromohaloaromatics by treatment with bromine in carbon disulfide. The isomeric compositions were established by means of gas chromatography.

The observed rates and the isomer distributions were employed to calculate the partial rate factors. The

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[1] Directive Effects in Aromatic Substitution. LVIII.

[2] Based upon a thesis submitted by Robert A. Wirkkala in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

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[4] National Science Foundation Summer Fellow at Purdue University, 1959.

[5] Ethyl Corporation Fellow at Purdue University, 1960–1961.

[6] H. C. Brown and G. Goldman, *J. Am. Chem. Soc.*, **84**, 1650 (1962).

[7] H. C. Brown and R. A. Wirkkala, *ibid.*, **88**, 1447 (1966).

[8] H. C. Brown and R. A. Wirkkala, *ibid.*, **88**, 1453 (1966).