period of 100 min. After 1 additional hr, the temperature was raised to 160° and maintained there for 8 hr. There was evolved 104 mmoles of hydrogen. Addition of 1 ml of water liberated an additional 13 mmoles of hydrogen. (In the acetone trap was found a total of 3 mmoles of boric acid.) Oxidation was carried out as described above. The gas chromatographic analysis showed 118 mmoles of 2,4,4-trimethyl-1-pentanol and 70 mmoles of the -1,5-diol. Distillation yielded 9.47 g, 65 mmoles, of 2,4,4-trimethyl-1,5-pentanediol, bp 132–133° (8.5 mm), $n^{22}\text{D}$ 1.4565.

Equilibration–Cyclization for the Trialkylboranes from 1-Pentene and 1-Hexene. The procedure for the hydroboration and equilibration was as described above. However, hydrogen evolution was slow so cyclization was carried on for 24 hr. Because of the greater water solubility of the diols, borax was precipitated and removed. The remaining mixture then was distilled. From 1-pentene there was obtained 3.43 g, 33 mmoles, of pentanediols, bp 223–241° (743 mm), $n^{20}\text{D}$ 1.4435 and 1.4457.

Anal. Calcd for $C_5H_{12}O_2$: C, 57.66; H, 11.61. Found: C, 57.82; H, 11.49.

From 1-hexene there was obtained 3.75 g, 31.8 mmoles, of hexanediols, bp 226–242° (744 mm), $n^{22}\text{D}$ 1.4425.

Anal. Calcd for $C_6H_{12}O_2$: C, 60.97; H, 11.98. Found: C, 61.06; H, 12.22.

The results are summarized in Table II.

Equilibration–Cyclization under Neat Conditions. The olefin, 200 mmoles, was mixed with 50 ml of a 1.0 *M* solution of diborane in tetrahydrofuran at 0°. The solution then was maintained at 60° for 2 hr to achieve equilibration. The tetrahydrofuran was removed under vacuum and the clear liquid organoborane residue was heated at 200° for 2 hr (nitrogen atmosphere). The gas evolution was noted. Tetrahydrofuran (50 ml) was added to facilitate the oxidation. The work-up then was similar to the above. The results are summarized in Table II.

Cyclization of Monoalkylthexylborane. The apparatus consisted of a three-neck flask equipped with a thermometer, a rubber cap through which the olefin could be added to the solution of diborane in tetrahydrofuran and which could later be replaced by a glass stopper for the cyclization phase, and a short Vigreux column. The thexylborane was synthesized *in situ* by adding 8.4 g (100 mmoles) of 2,3-dimethyl-2-butene to 50 ml of 1.00 *M* solution of diborane in tetrahydrofuran, cooled to approximately 5°. After 0.5 hr, 100 mmoles of the olefin was added slowly to the solution of the thexylborane, the temperature of the solution being maintained at 5° until the addition of the olefin was over (approximately 10 min). After another hour, the solvent was taken off though the short Vigreux column, and the reaction mixture then was slowly taken up to 200°. (In the case of thexyl-*n*-pentylborane, the most volatile derivative used, it was desirable to provide additional cooling capacity by inserting a small reflux condenser on the top of the Vigreux.) At the end of the reaction, usually 10 hr, the receiver usually contained small quantities (5 to 10 mmoles) of 2,3-dimethyl-1-butene and -2-butene and about 3 mmoles of a borane. The contents of the flask was allowed to cool, 50 ml of tetrahydrofuran was added to facilitate the oxidation, and the product was treated with 30 ml of 3 *N* sodium hydroxide, followed by 36 ml of 30% hydrogen peroxide. The oxidation was carried out at 50 to 60° to ensure complete conversion of the less reactive heterocycle. The yields were determined by gas chomatography on a 6-ft column filled with 10% Carbowax 20M, A/W Chromosorb W-DMCS 70–80. The results are summarized in Table III.

Trifluoroacetic Acid as a Medium for Electrophilic Substitution Reactions. Rates and Isomer Distributions for the Bromination, Nitration, and Mercuration of Benzene and Toluene in Trifluoroacetic Acid[1-3]

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Contribution from the Richard B. Wetherill Laboratory of Purdue University, Lafayette, Indiana.
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Abstract: The applicability of trifluoroacetic acid as a reaction medium for electrophilic substitution reactions was investigated as a means of circumventing some of the difficulties encountered with acetic acid itself. In contrast to the complex kinetics observed in acetic acid, bromination in trifluoroacetic acid exhibits simple second-order kinetics. The rate constants at 0, 25, and 35° for the bromination of toluene yield $\Delta H^* = 11.3$ kcal mole^{-1} and $\Delta S^* = -33.2$ eu. The observed rate constants for benzene and toluene at 25°, 7.62×10^{-7} and 1.97×10^{-3} l. mole^{-1} sec^{-1}, respectively, and the isomer distribution in toluene, 17.6% *ortho* and 82.4% *para*, yield the partial rate factors o_f 1360 and p_f 12,700. Thus bromination in trifluoroacetic acid is the most selective of the known reactions. The relative rate, toluene to benzene, for nitration in trifluoroacetic acid at 25.0° is 28. Combined with the isomer distribution, 61.6% *o*-, 2.6% *m*-, and 35.8% *p*-nitrotoluene, the data yield values for the partial rate factors o_f 51.7, m_f 2.18, and p_f 60.1. The reaction of mercuric trifluoroacetate with benzene and toluene in trifluoroacetic acid yielded second-order rate constants at 25° of 2.85×10^{-2} and 2.82×10^{-1} l. mole^{-1} sec^{-1}, respectively, and an isomer distribution in toluene of 12.2% *o*-, 8.6% *m*-, and 79.2% *p*-tolylmercuric trifluoroacetate, resulting in partial rate factors o_f 3.62, m_f 2.55, and p_f 46.9. Mercuration in trifluoroacetic acid proceeds at a rate 690,000 times faster than mercuration by mercuric acetate in acetic acid. The results for the three reactions are correlated satisfactorily by the Selectivity Relationship. In contrast to acetic acid, the mercuration of relatively inert aromatics proceeds without interference by the solvent. Consequently, trifluoroacetic acid promises to be a useful medium for extending study of the Selectivity Relationship to the less reactive aromatic derivatives.

The utilization of acetic acid as a medium for electrophilic substitution reactions suffers from several serious disadvantages. Thus bromination in acetic acid exhibits complex kinetics, approximating third order[6,7] (second order in bromine), but complicated by

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(1) Directive Effects in Aromatic Substitutions. LVI.

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

(3) This research was supported in part by the Petroleum Research Fund administered by the American Chemical Society.

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

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

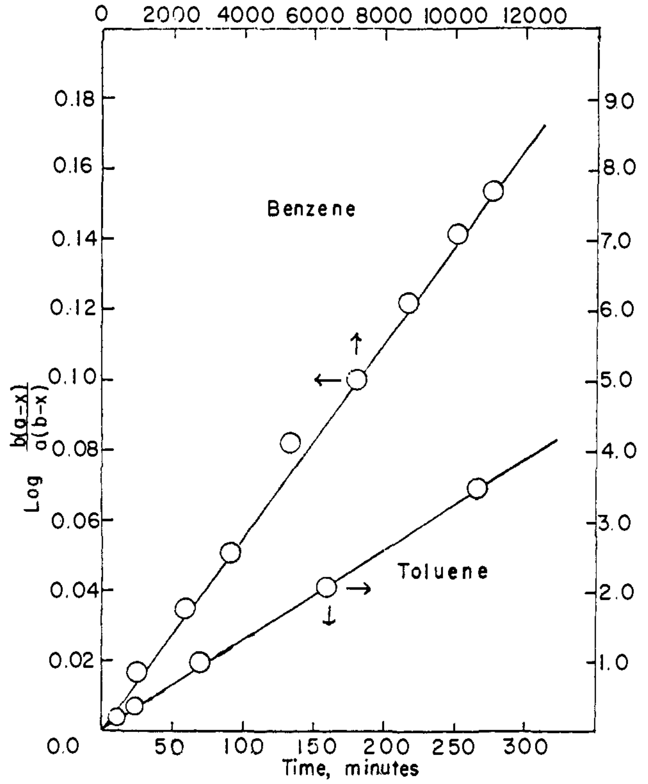

Figure 1. Second-order plots for the reaction of benzene and toluene with bromine in trifluoroacetic acid at 25.0°.

the presence of a second-order term[8] (first order in bromine[8]). In order to avoid these kinetic difficulties, relative rates are generally based upon the time required to achieve 10 and 20% reaction under a standardized set of reaction conditions.[6,9] Moreover, the isomer distribution in toluene has been observed to vary with the initial bromine concentration.[10] The slow rate of reaction and a concurrent reaction of bromine with the solvent prevent the application of the reaction to aromatic derivatives less active than benzene itself.[11]

Mercuration studies with mercuric acetate in acetic acid are similarly handicapped by slow reaction rates[12,13] and by a side reaction of mercuric acetate with the solvent.[12,14] Indeed, in applying the reaction to the halobenzenes, the side reaction constituted the major path for utilization of the mercuric acetate and it was necessary to have recourse to indirect methods to obtain the desired partial rate factors.[14] Application of the procedure to less active aromatics appears impractical.

Mercuration in acetic acid is strongly catalyzed by perchloric acid.[12] Consequently, we had originally hoped that this procedure would allow us to extend the mercuration reaction to aromatics containing deactivating substituents. However, a detailed kinetic study revealed that the reaction does not exhibit simple kinetics, reflecting the fact that the mechanism proceeds through more than one electrophilic species.[15] Moreover, under these conditions isomerization of the arylmercuric acetates occurs, complicating the determination of the kinetically controlled isomer distribution.[12]

These considerations influenced us to seek some other reaction medium that would circumvent these difficulties. Some results already in the literature suggested that trifluoroacetic acid might serve our needs. Thus, the chlorination of toluene in trifluoroacetic acid,[16] $k_2 = 7 \times 10^{-3}$, proceeds 4500 times faster than chlorination in acetic acid,[17] $k_2 = 1.54 \times 10^{-6}$ l. mole^{-1} sec^{-1}. Iodination[18] and solvolytic reactions[19] also proceed quite rapidly in trifluoroacetic acid without complications.

Accordingly, we undertook to study the general utility of trifluoroacetic acid as a reaction medium for electrophilic substitution reactions. Bromination, nitration, and mercuration were selected as reactions of high, moderate, and low selectivity.[20]

Results

Bromination. The reaction of bromine with the aromatics in trifluoroacetic acid was determined by following the rate of decrease of the bromine concentration titrimetrically with standard thiosulfate solution. It was necessary to take special care to titrate the iodine solutions immediately, since iodide ions are oxidized to iodine by oxygen in highly acidic media.[21] Light was excluded from the bromination reaction to avoid substitution in the side chain. Experiments indicated that such side-chain bromination was less than 1% and could be neglected.

Typical kinetic results are summarized in Table I. The second-order plots (Figure 1) reveal that the reaction is clearly second order, first order in each reactant, over the large concentration range utilized.

The rate constants for the bromination of toluene were also measured at 0°, $k_2 = 2.88 \times 10^{-4}$, and at 35°, $k_2 = 3.81 \times 10^{-3}$. These values yield $\Delta H^* = 11.3$ kcal mole^{-1} and $\Delta S^* = -33.2$ eu. The entropy of activation term is in close agreement with the value, -32 eu, noted for the chlorination of benzene in the same solvent.[22]

Benzene and toluene also were brominated in 87% aqueous trifluoroacetic acid in order to determine the effect of water on the reaction rates. The results (Table I) show that the water causes an 18.5-fold increase in the rate constants, but no change in the toluene to benzene rate ratio.

The isomer distribution for the bromination of toluene at 25° in the anhydrous solvent was determined to be 17.6% *o*- and 82.4% *p*-bromotoluene. The

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

(7) P. W. Robertson, *ibid.*, 1276 (1954).

(8) R. M. Keefer, A. Ottenberg, and L. J. Andrews, *J. Am. Chem. Soc.*, 78, 255 (1956).

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

(10) Unpublished results of Dr. A. H. Neyens, Purdue University.

(11) Even in the case of benzene it is necessary to apply a significant correction term for bromine utilized by the solvent.[9]

(12) H. C. Brown and C. W. McGary, Jr., *J. Am. Chem. Soc.*, 77, 2300, 2306, 2310 (1955).

(13) H. C. Brown and M. Dubeck, *ibid.*, **81**, 5608 (1959).

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

(15) A. J. Kresge, H. C. Brown, and M. Dubeck, *ibid.*, in press.

(16) R. M. Keefer and L. J. Andrews, *ibid.*, **79**, 5169 (1957).

(17) H. C. Brown and L. M. Stock, *ibid.*, **79**, 5195 (1957).

(18) L. J. Andrews and R. M. Keefer, *ibid.*, **79**, 1412 (1957).

(19) P. E. Peterson, *ibid.*, **82**, 5834 (1960).

(20) For a review of the selectivity relationship, with all pertinent data and literature references, see L. M. Stock and H. C. Brown in "Advances in Physical Organic Chemistry," Vol. I, V. Gold, Ed., Academic Press Inc., New York, N. Y., 1963, pp 35–154.

(21) I. M. Kolthoff and E. B. Sandell, "Textbook of Quantitative Inorganic Analysis," 3rd ed, The Macmillan Co., New York, N. Y. 1952, p 587.

(22) R. M. Keefer and L. J. Andrews, *J. Am. Chem. Soc.*, **81**, 1360 (1959).

Table I. Second-Order Rate Constants for the Reaction of Bromine with Benzene, Toluene, and *p*-Xylene in Trifluoroacetic Acid at 25.0°

Compound	Concentration, M [ArH]	[Br_2]	Rate constant, $k_2 \times 10^7$ l. mole^{-1} sec^{-1}	Relative rate, k_T/k_B
Benzene	0.400	0.200	7.54	
	0.400	0.199	7.81	
	0.800	0.198	7.57	
	0.800	0.195	7.17	
	0.800	0.0967	7.78	
	0.800	0.0945	7.26	1.00
		Mean value	7.62[a]	
Toluene	0.200	0.0270	19,900	
	0.200	0.0270	19,800	
	0.0400	0.00927	18,700	
	0.0400	0.00927	19,200	2580
		Mean value	19,700[a]	
p-Xylene	0.0401	0.0163	71,100	
	0.0401	0.0163	63,400	
		Mean value	69,100[a]	9080
Benzene[b]	0.100	0.0942	144	1.00
Toluene[b]	0.0406	0.0197	363,000	2500

[a] Mean values include additional determinations not listed in the table. [b] In 87% (by weight) aqueous trifluoroacetic acid.

aqueous solvent yielded almost the same distribution, 17.5% *ortho* and 82.5% *para*. The *meta* isomer is present in these reaction mixtures in such small amounts, estimated to be in the range of 0.1%, that meaningful analyses could not be realized. Accordingly, the *meta* partial rate factor was calculated from the relative rates of toluene and *p*-xylene and the *ortho* partial rate factor (o_f) calculated from the rate and isomer distribution values. This treatment leads to the partial rate factors, o_f 1360, m_f 10, p_f 12700.

In the case of toluene, we have observed that the isomer distribution in the bromination of toluene in acetic acid varies with the initial bromine concentrations.[10] Apparently, the third- and second-order components of the reaction are associated with different isomer distributions, and the relative contribution of each component to the total reaction varies with the concentration. However, in the present case, no variation was observed as the initial bromine concentration was varied from 0.0214 to 0.161 M.

Nitration. Nitration in trifluoroacetic acid proceeds at a reasonable rate at room temperature, even with quite dilute solutions, without addition of the usual mineral acids. For example, a reaction mixture which was 0.050 M in toluene and 0.050 M in nitric acid proceeded to 80% completion in 18 hr at 25°.

The toluene to benzene reactivity ratio was established by the competitive nitration of benzene and toluene, utilizing the usual relationship

$$\frac{k_T}{k_B} = \frac{\log C^0{}_T - \log C_T}{\log C^0{}_B - \log C_B}$$

where C^0 refers to the initial concentration of the aromatic and C refers to its concentration at the end of the reaction. The final concentrations were established by gas chromatographic analysis of the reaction mixtures.

Toluene is considerably more reactive than benzene in this reaction. Consequently, it was necessary to use benzene in large excess over toluene. Even so, only a small fraction of the benzene underwent nitration. Rather than rely on the direct analysis of the hydrocarbon in the product, which in most cases would provide a relatively small difference between relatively large numbers for use in the calculation, we analyzed for the nitroaromatics and subtracted this value from the initial concentration of the aromatic to obtain the value of the final concentration.

The data and results are summarized in Table II.

Table II. Competitive Nitration of Benzene and Toluene in Trifluoroacetic Acid at 25.0°

Concentrations, M: Initial [$C_6H_3C_6H_5$]	[C_6H_6]	Final [$CH_3C_6H_4NO_2$]	[$C_6H_5NO_2$]	Relative rate, k_T/k_B
0.0504[a]	0.251	0.0378	0.0103	32
0.0510[a]	0.502	0.0311	0.0177	27
0.102[b]	0.254	0.0453	0.0041	25
			Mean value	28

[a] 0.050 M nitric acid, 18 hr of reaction time. [b] 0.050 M nitric acid, 8 hr of reaction time.

The isomer distribution was established by the gas chromatographic analysis to be 61.6% *o*-, 2.6% *m*-, and 35.8% *p*-nitrotoluene. Combined with the relative rate of toluene to benzene of 28, we obtain for the partial rate factors o_f 51.7, m_f 2.18, p_f 60.1.

Mercuration. The rate of reaction of mercuric trifluoroacetate with aromatics in trifluoroacetic acid proved to be enormously faster than the corresponding value for mercuric acetate in acetic acid.[12] Consequently, it was not necessary to run the reactions at elevated temperatures in order to obtain rate constants which could be extrapolated down to 25°.[12] Moreover, solutions of mercuric trifluoroacetate in trifluoroacetic acid were found to be quite stable, with no loss of mercuric ion being detectable from standard solutions over several weeks of storage.

Table III. Second-Order Rate Constants for the Reaction of Mercuric Trifluoroacetate with Benzene and Toluene in Trifluoroacetic Acid at 25.0°

Compound	Concentration, M [ArH]	[$(CF_3CO_2)_2Hg$]	Rate constant, $k_2 \times 10^2$ l. mole^{-1} sec^{-1}	Relative rate, k_T/k_B
Benzene	0.0100	0.00947	2.87	
	0.0100	0.00947	2.90	
	0.0100	0.00460	2.82	
	0.0100	0.00454	2.85	
	0.00500	0.00454	2.78	
	0.00500	0.00454	2.89	
		Mean value	2.85	1.00
Toluene	0.0100	0.00947	28.1	
	0.0100	0.00947	28.2	
	0.0100	0.00947	28.4	
		Mean value	28.2	9.89

Table IV. Relative Rates, Isomer Distributions, and Partial Rate Factors for the Bromination, Nitration, and Mercuration of Benzene and Toluene

Reaction conditions	Relative rate, k_T/k_B	Isomer distribution, %			Partial rate factors			Selectivity factor, S_f
		ortho	*meta*	*para*	o_f	m_f	p_f	
A. Bromination								
85% CH_3CO_2H, 25°	605[a]	32.9	0.3	66.8	600	5.5	2420	2.64
CF_3CO_2H, 25°	2580[b]	17.6	0	82.4	1360	10.0	12700	3.10
B. Nitration								
90% CH_3CO_2H, 45°	24[c]	56.5	3.5	40.0	52	2.5	58	1.37
CH_3NO_2, 30°	21[d]	58.5	4.4	37.1	36.6	2.33	46.1	1.30
$(CH_3CO)_2O$, 30°	23[d]	58.4	4.4	37.2	40.4	3.04	51.2	1.23
$(CH_3CO)_2O$, 0°	27[d]	58.1	3.7	38.2	47.2	3.56	60.3	1.33
CF_3CO_2H, 25°	28[b]	61.6	2.6	35.8	51.7	2.18	60.1	1.44
C. Mercuration								
CH_3CO_2H, 25°	6.41[e]	29.7	11.9	59.7	5.71	2.23	23.0	1.01
CH_3CO_2H, 0.29 *M* $HClO_4$, 25°	7.9[e]	21.0	9.5	69.5	4.98	2.25	32.9	1.17
CH_3CO_2H, 0.50 *M* $HClO_4$, 25°	9.1[f]	19.4	8.3	72.6	5.27	2.26	39.3	
CF_3CO_2H, 25°	9.89[b]	12.2	8.6	79.2	3.62	2.55	46.9	1.26

[a] Reference 9. [b] Present study. [c] H. Cohen, E. D. Hughes, M. H. Jones, and M. A. Peeling, *Nature*, **169**, 291 (1951). [d] C. K. Ingold, A. Lapworth, E. Rothstein, and D. Ward, *J. Chem. Soc.*, 1959 (1931). [e] Reference 12. [f] Reference 15.

The rate of mercuration of benzene and toluene was determined by following the rate of disappearance of mercuric ion titrimetrically with standard thiocyanate solution. Typical rate data are presented in Table III. The data clearly follow simple second-order kinetics, as indicated by Figure 2. Consequently, the relative rates were established by a direct comparison of the experimental rate constants.

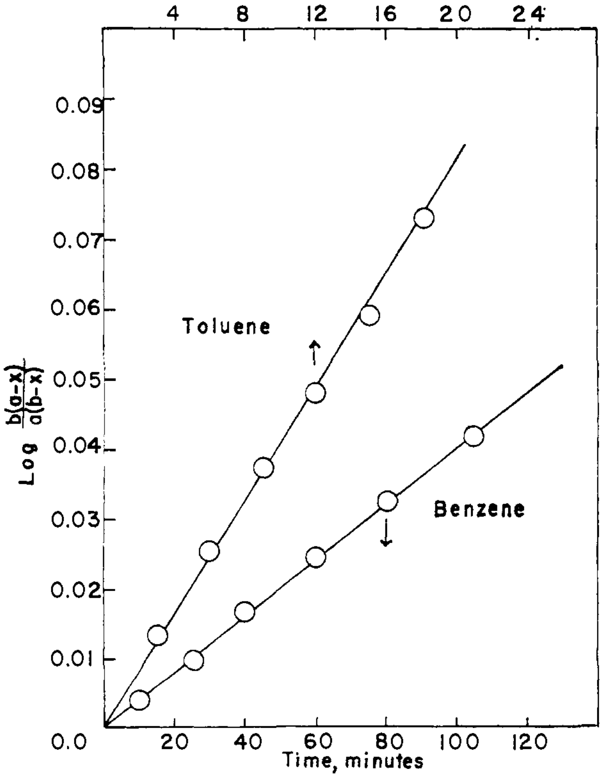

Figure 2. Second-order plots for the reaction of benzene and toluene with mercuric trifluoroacetate in trifluoroacetic acid at 25.0°.

To determine the isomer distributions, the reaction mixtures were quenched at appropriate time intervals in aqueous sodium bromide. The insoluble tolylmercuric bromides were converted into the isomeric bromotoluenes by treatment with bromine. The isomeric composition then was established by gas chromatographic examination.

As was pointed out earlier, mercuration in acetic acid, catalyzed by perchloric acid, results in significant isomerization of the initially formed derivatives.[12] However, in the present case no change in the isomer distribution was observed for 20, 40, 60, and 80% reaction. Moreover, the constancy in the isomer distribution even in reaction mixtures containing the aromatic in the precise stoichiometric amount argues for the essential absence of dimercuration, a complication in the acetic acid reaction.[15] Consequently, mercuration in trifluoroacetic acid appears to be free of the complications present in the uncatalyzed reaction in acetic acid,[12] or in the perchloric acid catalyzed reaction.[15]

Utilizing the relative rate, $k_T/k_B = 9.89$, and the isomer distribution *ortho* 12.2%, *meta* 8.6%, *para* 79.2%, all at 25°, yields the partial rate factors, o_f 3.62, m_f 2.55, p_f 46.9.

Discussion

To facilitate the discussion, pertinent data for the bromination, nitration, and mercuration of benzene and toluene in various solvents are summarized in Table IV.

The results of the present study reveal that trifluoroacetic acid is an excellent solvent for kinetic studies of the bromination reaction. There is no evidence for the complex kinetics observed in acetic acid,[6-8] for variation of the isomer distribution with the concentration of bromine,[10] or for competitive reaction of the halogen with the solvent. Consequently, the use of trifluoroacetic acid should make it possible to obtain partial factors for aromatic derivatives which are less reactive than benzene.

In addition to these advantages, trifluoroacetic acid exhibits some characteristics which should be discussed. First, the bromination of toluene and similar aromatics is far faster in trifluoroacetic acid than in acetic acid. For example, a comparison of the times required to achieve 10% completion in glacial acetic acid (12.9 × 10^6 min[9]) and in trifluoroacetic acid (5.2 × 10^3 min) at the same bromine concentration reveals a 2500-fold increase in rate in the halogenated solvent.

Moreover, the effect of the aqueous content of the solvent is considerably smaller in trifluoroacetic than in acetic acid. Thus an 18.5-fold increase in rate is noted for 87% aqueous trifluoroacetic acid, while there is a 150-fold increase for 85% aqueous acetic acid over the anhydrous material.[9] In both systems, the presence of the water does not appear to alter the toluene to benzene reactivity ratios.

Bromination in trifluoroacetic acid results in a decrease in the *ortho* isomer from the 32.9% realized in acetic acid[9] to 17.6%. Stock and Himoe proposed an effective halogenating species composed of a complex involving both the molecular halogen and the solvent in order to explain the marked influence of the solvent on the amount of substitution in the *ortho* position in the chlorination of toluene.[23] Such an explanation is consistent with the observed steric factor noted here for the bromination reaction. Possibly, trifluoroacetic acid would be helpful in preparations where it is desirable to synthesize *p*-bromoalkylbenzene with a minimum accompanying formation of the other isomers.

The simple second-order kinetics presumably also arise from participation of the solvent in the rate-determining step of the bromination reaction. In acetic acid, the second bromine molecule is believed to assist the reaction by associating with the leaving bromide anion (as Br_3^-), thus facilitating the formation of the σ complex. Presumably, in the present reaction trifluoroacetic acid, with its strong hydrogen-bonding capabilities, can serve this function, and bromine, present at relatively low concentrations, does not compete significantly.

It is also of interest that the reactivity ratio, k_T/k_B = 2580, is the highest which has been reported,[20] leading to a value of the Selectivity Factor of 3.10. This means that bromination in trifluoroacetic acid is extraordinarily sensitive to the electron supply of substituents. The reaction, therefore, should be especially valuable in investigating structural effects which are relatively small, such as secondary isotope effects.

The nitration reaction differs from bromination in that the toluene to benzene ratio, as well as the isomer distribution, both appear to be essentially independent of the medium.

On the other hand, the solvent is influential in the mercuration reaction. Again there is a decrease in the amount of substitution in the *ortho* position from 29.7% for the reaction in acetic acid to 12.2% in trifluoroacetic acid. Of major importance for the objectives of the present investigation is the observation that the reaction is very fast (the rate constant for the mercuration of benzene at 25° in trifluoroacetic acid is 690,000 times larger than the corresponding rate constant in acetic acid) and there is no indication of any side reaction with the solvent, such as complicates kinetic study of the less reactive aromatics in acetic acid.[14] Indeed, we have encountered no difficulties in utilizing the reaction in trifluoroacetic acid to establish the partial rate factors for the monohalobenzenes and their correlation by the Selectivity Relationship.[24]

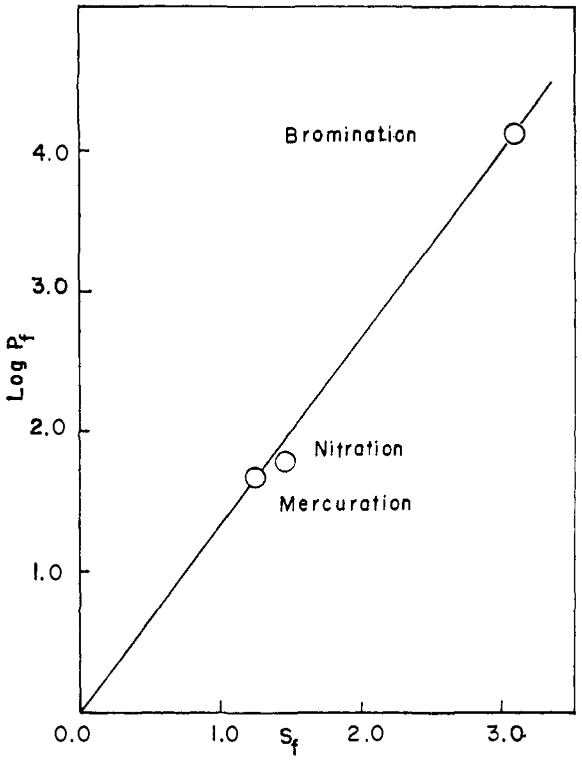

Figure 3. The bromination, nitration, and mercuration reactions of toluene in trifluoroacetic acid compared to the Selectivity Relationship as defined for 60 electrophilic substitution reactions.

Finally, some 60 reactions previously have been tested and shown to conform to the proposed Selectivity Relationship.[20,25] It therefore was of interest to ascertain whether the present reactions would also conform. Figure 3 shows that the three new reactions do conform to the correlation line defined by these 60 reactions.

In conclusion, then, trifluoroacetic acid promises to circumvent many of the difficulties now encountered in obtaining quantitative rate and isomer distribution data for the less reactive aromatics in the usual acetic acid medium.

Experimental Section

Materials. Benzene, toluene, and *p*-xylene were available from earlier studies and had purities exceeding 99.4 mole %. The bromotoluenes utilized as gas chromatographic standards possessed the following properties and purities (from cooling curves in mole %): *o*-bromotoluene, n^{20}_{D} 1.5561, 99.5%; *m*-bromotoluene, n^{20}_{D} 1.5525, 99.8%; *p*-bromotoluene, mp 26.7°, 99.8%.

Carbon disulfide was distilled from mercuric chloride and dried over calcium sulfate. In the initial experiments, bromine (J. T. Baker, purified grade) was extracted with aqueous sodium hydroxide, followed by distillation over phosphorus pentoxide. After experiments revealed that identical results were realized with the untreated material, the bromine was utilized directly in the later experiments.

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[23] L. M. Stock and A. Himoe, *Tetrahedron Letters*, No. **13**, 9 (1960). The selectivity of the reaction may be an even more important factor. Reactions of high selectivity appear to discriminate more effectively against the sterically hindered *ortho* position in favor of the *para:* private communication from L. M. Stock.

[24] H. C. Brown and R. A. Wirkkala, *J. Am. Chem. Soc.*, **88**, 1456 (1966).

[25] In recent years a considerable number of reactions have been reported by Dr. George A. Olah and his co-workers as not conforming to the Selectivity Relationship. All of these involve exceedingly fast reactions and there appears to be some question as to whether the deviations may not arise from the difficulties in mixing the reagents at adequate speed so that they become dispersed and dissolved before reaction occurs: W. S. Tolgyesi, *Can. J. Chem.*, **43**, 343 (1965).

Trifluoroacetic acid (Minnesota Mining and Manufacturing Co.) was purchased in large quantities and distilled through a fractionating column of 50 theoretical plates, bp 71.5° (741 mm). Analysis of the cooling curve indicated a purity of 99.5 mole %. Trifluoroacetic acid for the 87% aqueous solvent was prepared as described above and adding the calculated amount of water to yield 87% acid by weight.

Anhydrous nitric acid was prepared by the procedure used by Roberts.[26] Analysis of the cooling curve for the product, bp 17° (22 mm), indicated a purity of 99.2 mole %. The acid was stored in a cold room.

The isomeric nitrotoluenes were commercial materials further purified by distillation or recrystallization: *ortho*, n^{20}_{D} 1.5459; *meta*, n^{20}_{D} 1.5467; *para*, mp 51.5–52.0°.

Mercuric trifluoroacetate was prepared by a modification of the procedure used by Shearer and Wright.[27] To 100 ml of trifluoroacetic acid was added 10.8 g of mercuric oxide. The solution was stirred and cooled to 0°. The crystals were filtered off and dried overnight *in vacuo*, mp 165–167° (softening at 158°). Analysis for mercury, by titrating with standard thiocyanate, indicated 47.0%, calcd 47.0%.

Kinetics of Bromination. The procedure followed that described previously.[9] Aliquots of the reaction mixture were withdrawn at appropriate time intervals with fast delivery pipets and quenched in 5% excess potassium iodide. The resulting iodine solutions were immediately analyzed by titration with standard thiosulfate solution utilizing a starch indicator. Immediate titration was required to avoid air oxidation of the iodide. Blank experiments were run with standard solutions of bromine in trifluoroacetic acid; they indicated that the loss of bromine either by volatilization or by reaction with the solvent was negligible. Blackened flasks were used for the kinetic runs to avoid photochemical bromination of the side chain. Excellent second-order plots were realized (Figure 1).

Kinetics of Mercuration. In a typical experiment 25.0 ml of 0.02 *M* mercuric trifluoroacetate was quickly added to 25.0 ml of a 0.0200 *M* solution of the aromatic in trifluoroacetic acid, both preequilibrated at 25°. Aliquots were withdrawn at appropriate intervals and analyzed for mercuric ion by titration with standard thiocyanate solution with ferric ammonium sulfate as indicator. Excellent second-order plots were obtained in experiments carried out to 80% completion (Figure 2).

Competitive Nitration of Benzene and Toluene. In a typical experiment 25.0 ml of 0.100 *M* nitric acid (anhydrous) in trifluoroacetic acid was added to 25.0 ml of a solution which was 0.100 *M* in toluene and 0.50 *M* in benzene (and 0.05 *M* in iodobenzene as internal standard) and maintained at 25.0°. After 18 hr, the mixture was quenched in aqueous sodium hydroxide and the neutral organic constituents were extracted with carbon disulfide. Analysis was accomplished on a 2-m tricresyl phosphate–Celite column at 145°. Under these conditions the isomers and standard were widely separated (retention time in minutes): iodobenzene, 8; nitrobenzene, 16; *o*-, 20; *m*-, 26; *p*-nitrotoluene, 31.

Isomer Distribution in Bromination. In a typical experiment, 25.0 ml of 0.04 *M* bromine in trifluoroacetic acid was added to 25.0 ml of 0.08 *M* toluene in the same solvent and allowed to react at 25.0°. After an appropriate time interval, the solution was quenched in 1% aqueous sodium borohydride and the bromotoluenes were extracted with carbon disulfide. The isomeric composition was established on a Model 154D Perkin-Elmer gas chromatograph utilizing a 150-ft tricresyl phosphate capillary column at 110° in conjunction with a flame ionization detector. Excellent separation of the bromotoluenes was achieved. Utilizing standard solutions, it was established that as little as 0.5% of the *meta* isomer could be accurately detected in the presence of the *ortho* and *para* isomers. However, no *meta* isomer could be detected in the reaction mixture. The retention times in minutes were: *o*-, 21.2; *m*-, 22.6; *p*-bromotoluene, 23.0.

The data, summarized in Table V, established that the isomer distribution was not dependent on the bromine concentration.

Table V. Effect of Initial Bromine Concentration of the Isomer Distribution in Trifluoroacetic Acid at 25.0°

Bromine concn,[a] *M*	Product, %	
	ortho	*para*
0.0214	17.4	82.6
0.0408	17.2	82.8
0.0896	17.9	82.1
0.118	17.0	83.0
0.161	17.8	82.2

[a] Initial concentration of toluene, 0.201 *M*.

Isomer Distribution in Mercuration. In a typical experiment, 150.0 ml of 0.02 *M* mercuric trifluoroacetate in trifluoroacetic acid was added quickly to 150 ml of 0.02 *M* toluene in the same solvent, but at 25.0°. After an appropriate time interval, the reaction mixture was quenched in aqueous sodium bromide, maintaining a bromide ion to mercuric ion ratio of 2:1. The precipitated arylmercuric bromides were filtered and dried *in vacuo* over phosphorus pentoxide to constant weight. The bromides were obtained in yields of 95% theory. A sample of the tolylmercuric bromides was converted into the isomeric bromotoluenes by treatment with bromine in carbon disulfide. The carbon disulfide solutions were treated with sodium bisulfite, to remove excess bromine, and distilled water, and dried over calcium sulfate. Analysis was accomplished as described for bromination.

The data summarized in Table VI established the absence of isomerization as a significant complication in this system.

Table VI. Isomer Distribution for the Mercuration of Toluene in Trifluoroacetic Acid at 25.0° as a Function of the Per Cent Reaction and the Ratio of Aromatic to Mercury(II)

Molar ratio of ArH/Hg $(O_2CCF_3)_2$	Reaction, %	Isomer distribution, %		
		ortho	*meta*	*para*
4	20	12.0	8.6	79.4
	40	12.2	8.7	79.1
	60	12.8	8.4	78.8
	80	12.0	8.6	79.2
1	60	12.1	8.7	79.2
6	60	12.4	8.5	79.1
10	60	11.3	9.0	79.7
	Mean value	12.2	8.6	79.2

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(26) J. D. Roberts, J. K. Sanford, F. L. J. Sixma, H. Cerfontain, and R. Zagt, *J. Am. Chem. Soc.*, **76**, 4525 (1954).

(27) D. A. Shearer and G. F. Wright, *Can. J. Chem.*, **33**, 1002 (1955).