

experimental error in the analysis. At 75° a 20 to 1 molar ratio of toluene to mercuric acetate was used to avoid possible errors arising from dimercuration.

Rate of Mercuration.—The reaction mixtures were prepared precisely as described above for determining the isomer distribution in the mercuration of toluene at 25°. At intervals of time, aliquots were removed and treated with sodium bromide solution to precipitate the arylmercuric bromide. These precipitates were collected in sintered glass funnels, dried, and weighed. Excellent second-order rate data were obtained over 80% reaction. Typical rate data are shown

in Fig. 4 for two runs involving benzene and toluene. The data are for the first kinetic study for each hydrocarbon listed in Table III.

The reaction also was followed by the change in ionic mercury concentrations. The agreement in the ratio of the rates of toluene and benzene, obtained by the two procedures, was excellent.

The rate constants for the mercuration of benzene and toluene are summarized in Table III.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF PURDUE UNIVERSITY]

The Effect of Perchloric Acid on the Reactivity Ratio and Isomer Distribution in the Mercuration of Benzene and Toluene. Modification of the Activity and Selectivity of an Electrophilic Substituting Agent^{1,2}

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A study has been made of the reaction of benzene and toluene with mercuric acetate in glacial acetic acid and in the presence and absence of perchloric acid and sodium perchlorate. As previously reported by Westheimer and co-workers, the presence of perchloric acid results in an enormous enhancement of the rate of reaction (the rate of mercuration of toluene at 25° proceeds 2000-fold faster in the presence of 0.095 *M* perchloric acid). On the other hand, sodium perchlorate results in a relatively minor increase (the rate of mercuration at 25° proceeds 5-fold faster in the presence of 0.092 *M* sodium perchlorate). From the rates of reaction of benzene and toluene with mercuric acetate at several temperatures, the toluene/benzene reactivity ratios are determined to be 5.0, 4.3 and 3.6 at 50°, 70° and 90°, respectively. The results indicate that the attacking species in the uncatalyzed reaction is a less selective agent than that involved in the perchloric acid-catalyzed reaction. The uncatalyzed reaction of toluene with mercuric acetate at 50° produces the monosubstituted isomers with the distribution: *ortho*, 30.7; *meta*, 13.2; and *para*, 56.1%. At 70° the distribution is: *ortho*, 32.0; *meta*, 14.5; and *para*, 53.5%. At 90°, the distribution is: *ortho*, 32.5; *meta*, 15.7; and *para*, 51.8%. These distributions are in accord with the linear relationship previously proposed to account for isomer distribution in toluene substitutions.

In an earlier paper a linear relationship was proposed to correlate the "selectivity" of electrophilic substituting agents and the observed isomer distribution in toluene⁴ and other monosubstituted aromatics.⁵ It was suggested that the "activity" or "selectivity" of electrophilic substituting agents might be modified by the presence or absence of catalytic agents.⁴ The present investigation was undertaken to examine the validity of this prediction.

It was shown previously by Westheimer and his co-workers that the reaction of benzene with mercuric acetate in 97% acetic acid is strongly catalyzed by perchloric acid. For example, the presence of 0.05 *M* perchloric acid results in a 1000-fold increase in the second order rate constant.⁶ We have demonstrated recently that this perchloric acid-catalyzed mercuration of benzene and toluene obeys the proposed linear relationship between relative reactivity and isomer distribution.⁵ It therefore appeared that a study of the effect of the uncatalyzed mercuration reaction on the toluene/benzene reactivity ratio and the isomer distribution in toluene should provide a suitable test for the proposal that catalysts might affect these quantities. Accordingly, a study was made of the uncatalyzed reaction of benzene and toluene at several temperatures.

(1) Directive Effects in Aromatic Substitution. V.

(2) Based upon a thesis submitted by C. W. McGary, Jr., in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(3) Purdue Research Foundation Fellow, 1952-1953; American Cyanamid Corp. Fellow, 1953-1954; Research assistant on a grant from the National Science Foundation, 1954.

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

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

(6) R. M. Schramm, W. Klapproth and F. H. Westheimer, *J. Phys. Colloid Chem.*, **55**, 843 (1951).

Results

Rates of Mercuration of Benzene and Toluene.—The reactions were followed by determining the decrease in the mercuric ion concentration with time by titrating the residual mercuric ion with thiocyanate. However, deviations were observed in the second-order kinetics. Investigation of these irregularities revealed that mercuric acetate was undergoing a reaction with the solvent resulting in a loss of mercuric ion at a rate comparable to that involved in the mercuration of benzene. This loss of mercuric ion with time was not altered by a careful purification of the solvent which included distillation from sodium dichromate followed by distillation from mercuric acetate. Even with this purified solvent there was observed, after three hours of reflux, a decrease of 50% in the original titer for mercuric ion.

From the observation that the rate of loss of mercuric ion is not altered by the careful purification of the solvent, it appears certain that the reaction is not due to the presence of an impurity. Although we did not investigate the exact nature of the side reaction, it appears from these observations as well as related observations reported in the literature, that the loss of mercuric ion must result from a reaction of mercuric ion with either acetate ion or with acetic acid.⁷⁻⁹ A number of experiments invariably led to a maximum loss of 50% of the original titer. It therefore appears that the

(7) R. E. Vollrath, *ibid.*, **62**, 1310 (1940).

(8) N. V. Subba Rao and T. R. Seshadi, *Proc. Indian Acad. Sci.*, **11A**, 23 (1940); *C. A.*, **34**, 3677 (1940).

(9) F. C. Whitmore, "Organic Compounds of Mercury," The Chemical Catalog Company, Inc. (Reinhold Publ. Corp.), New York, N. Y., 1921, p. 141.

reaction must involve the formation of one carbon-to-mercury bond for each mercuric ion present.

The side reaction followed simple first-order kinetics. The rate constants at 50, 70 and 90° were measured (Table I).

TABLE I
RATES OF REACTION OF BENZENE AND TOLUENE WITH MERCURIC ACETATE IN GLACIAL ACETIC ACID

Temp., °C.	Reactant ^a	Rate constant $k_2 \times 10^4$, 1. mole ⁻¹ min. ⁻¹	Relative rate toluene/benzene
50.0	Benzene	0.450	5.0
	Toluene	2.26	
	Blank	0.057 ^b	
70.2	Benzene	3.43	4.3
	Toluene	14.8	
	Blank	0.62 ^b	
90.5	Benzene	21.1	3.6
	Toluene	76.2	
	Blank	4.8 ^b	

^a Concentration of benzene and toluene, $0.93 \pm 0.02 M$; concentration of mercuric acetate, $0.095 M$. ^b First order rate constants in units of min.⁻¹.

The following procedure permitted correction of the rate data for the mercuration of the aromatics with the consequent determination of the rate constants for the uncatalyzed reaction of benzene and toluene with mercuric acetate. A large molar excess of aromatic was utilized to increase the rate of the mercuration reaction, while decreasing the relative amount of mercuric ion disappearing in the side reaction. A pseudo first-order plot was made of the data. The first-order rate constant obtained in this way was corrected by subtraction of the first-order rate constant for the side reaction. The second-order constant was then obtained by dividing the corrected first-order constant by the average concentration of benzene over the range followed. The correction for the side reaction amounted to only 10% at 50° and 25% at 90° for benzene. In the case of toluene the correction was much smaller. The data are summarized in Table I.

It was observed that the rate constant increases linearly with the concentration of perchloric acid until the acid is present in equimolar concentration with the mercuric acetate. The increase then becomes much more gradual (Fig. 1). The presence of sodium perchlorate results in a much smaller effect upon the reaction rate (Fig. 1).

The rate of reaction of mercuric acetate with benzene in the presence of sodium perchlorate is far slower than that observed by Westheimer and his co-workers⁶ for the corresponding reaction of mercuric perchlorate under similar conditions. It therefore must be concluded that the presence of acetate ion, from the mercuric acetate, must greatly reduce the rate of the mercuration reaction.

The rate constants are summarized in Table II.

Isomer Distribution in Toluene.—The mercuration of toluene was carried out with mercuric acetate in glacial acetic acid at 50, 70 and 90° in the same manner as used in the kinetic measurements. Aliquots were quenched at various time intervals. The products were then precipitated from solution as the tolyl mercuric bromides and

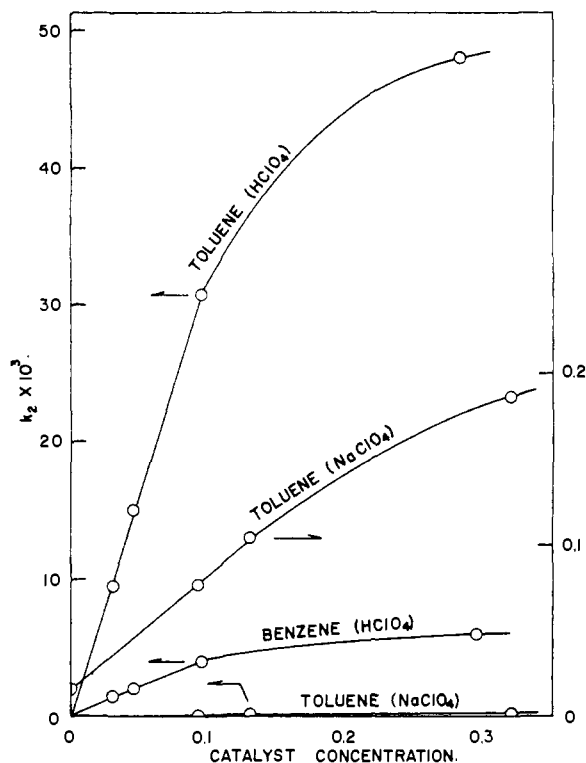


Fig. 1.—Variation in the rates of mercuration with concentration of catalyst.

these were converted to the isomeric tolyl bromides by reaction with bromine in carbon disulfide suspension. The resulting solutions of the tolyl bromides were analyzed directly by infrared absorption.⁵

TABLE II
THE EFFECT OF PERCHLORIC ACID AND SODIUM PERCHLORATE ON THE RATE OF REACTION OF BENZENE AND TOLUENE WITH MERCURIC ACETATE IN GLACIAL ACETIC ACID AT 25°

Concentration, M Hydrocarbon	Mercuric acetate	Catalyst HClO ₄	NaClO ₄	Rate constant $k_2 \times 10^4$, 1. mole ⁻¹ min. ⁻¹
Benzene				
0.930	0.095			0.0248 ^a
.638	.098	0.0300		14.0
.868	.094	.0460		21.0
.585	.092	.095		40 ^b
1.960	.196	.294		60 ^b
Toluene				
0.930	0.095			0.159 ^a
.854	.095		0.092	.77
.859	.095		.130	1.04
.866	.088		.320	1.86
.624	.095	.0300		95
.854	.092	.0460		150
.478	.091	.095		307 ^b
1.900	.190	.285		480 ^b

^a Extrapolated from rate data at 50, 70 and 90° (Table IV). ^b Reference 5.

The reactions were not carried further than 60–70% completion to minimize possible complications from the formation of polymerized products

and isomerization of the product.⁵ In no case was any isomerization observed over this limited range of reaction. The results are summarized in Table III.

TABLE III

VARIATION IN THE ISOMER DISTRIBUTION WITH TEMPERATURE IN THE REACTION OF TOLUENE WITH MERCURIC ACETATE IN GLACIAL ACETIC ACID

Temp., °C.	Isomer distribution, %		
	<i>Ortho</i>	<i>Meta</i>	<i>Para</i>
50	30.7	13.2	56.1
70	32.0	14.5	53.5
90	32.5	15.7	51.8

Discussion

It was previously reported that the relative reactivity in the mercuriation of toluene and benzene at 25° in the presence of 0.29 *M* perchloric acid is

term is so large that the others may be considered negligible.

In a reaction in which substitution at low temperatures is predominantly in the *para* position, such as the mercuriation reaction here considered, we can write $k_t \approx k_p$. However, at very high temperatures the rates in the isomeric positions approach equality, and $k_t \approx 5k_p$. Obviously, then, if $\log k_p$ is linear in $1/T$, $\log k_t$ cannot also be linear in this quantity.

Therefore, in order to calculate the rate constants and relative rates at 25° it was considered necessary to calculate the frequency and activation energy terms for the partial rates. The results are given in Table IV. The heats and entropy of activation were calculated by the method of Cagle and Eyring.¹¹ Derived data for the total rate of reaction for benzene and toluene are included in Table IV

TABLE IV

PARTIAL RATE CONSTANTS AND DERIVED DATA FOR THE REACTION OF BENZENE AND TOLUENE WITH MERCURIC ACETATE IN GLACIAL ACETIC ACID

Compound	25.0°	Partial rate constant $k_2 \times 10^4$, l. mole ⁻¹ min. ⁻¹		90.5°	E_{act} , kcal./mole	$\log A^a$	ΔH^\ddagger , kcal./mole	ΔS^\ddagger , cal./deg.
		50.0°	70.2°					
Benzene	0.00413	0.075	0.571	3.52	22.2	9.781	21.6	-23.5
Toluene, <i>ortho</i>	.0236	.347	2.37	12.4	20.6	9.496	20.0	-25.4
Toluene, <i>meta</i>	.00923	.149	1.07	5.98	21.3	9.592	20.7	-24.9
Toluene, <i>para</i>	.0949	1.27	7.92	39.5	19.9	9.531	19.3	-25.0
Benzene ^b	.0248	0.450	3.43	21.1	22.2	10.659	21.6	-19.6
Toluene ^c	.159	2.26	14.8	76.2	20.3	10.091	19.7	-22.6

^a Calculated for k in units of l. mole⁻¹ min.⁻¹. ^b Data for all six positions in benzene. ^c Approximate values for total rate constants.

8.0.⁵ Because of the slowness of the uncatalyzed reaction examined in the present study it was inconvenient to measure the rates at 25°. It appeared that the desired rate data might be obtained from a simple Arrhenius treatment of the rate data at 50, 70 and 90°.

In this way Hinshelwood and his co-workers have reported rates and energies of activation for the sulfonation of a series of aromatic derivatives.¹⁰ However, it should be apparent that the Arrhenius expression should express the temperature variation of a rate constant only for a single reaction. Substitution in the isomeric positions of a monosubstituted benzene constitutes three different reactions, each with its own rate constant and its own energy of activation. Therefore the Arrhenius equation can be applied only to each of the isomeric positions involved in the substitution.

The difficulties may be rendered clearer by the following treatment. Applying the Arrhenius equation to k_t^o , k_t^m and k_t^p , the partial rate constants for each of the three different isomeric positions in toluene, we have

$$\begin{aligned} k_t^o &= A^o e^{-E_o/RT} \\ k_t^m &= A^m e^{-E_m/RT} \\ k_t^p &= A^p e^{-E_p/RT} \end{aligned}$$

The total rate of reaction will be

$$k_t = 2k_t^o + 2k_t^m + k_t^p$$

and this will have the form

$$k_t = A e^{-E/RT}$$

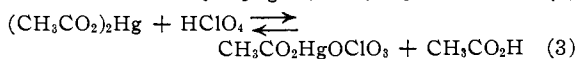
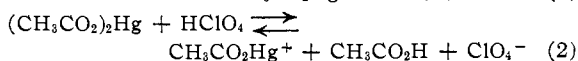
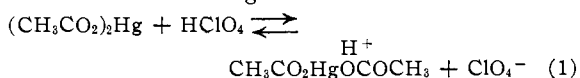
only if the A and E_{act} terms are identical or if one

(10) F. J. Stubbs, C. D. Williams and C. N. Hinshelwood, *J. Chem. Soc.*, 1065 (1948).

to permit comparison of results obtained by this approximate treatment.

The calculations lead to a toluene/benzene reactivity ratio of 6.4 for the uncatalyzed reaction at 25° as compared to the value of 8.0 previously obtained for the catalyzed reaction.^{5,12} Indeed a comparison of the relative rates reveals a regular change in the reactivity ratio with increasing concentration of the catalysts from the 6.4 value to the 8.0 value at 0.29 *M* perchloric acid (Fig. 2).

It is noteworthy that the change in reactivity ratio is linear up to the point where the molar concentration of the perchloric acid becomes equal to that of the mercuric acetate. This suggests that the perchloric acid reacts almost completely with the mercuric acetate in a 1:1 ratio. Possible reactions of this kind might be



Westheimer and his co-workers considered the possibility that equilibrium 2 might be involved.

(11) F. W. Cagle, Jr., and H. Eyring, *THIS JOURNAL*, **73**, 5628 (1951).

(12) In the previous paper toluene/benzene ratios of 8.0 and 7.8 were observed for solutions 0.29 and 0.099 *M* in perchloric acid. At the time we did not recognize that the ratio would be a sensitive function of the perchloric acid concentration and considered the variation to represent merely experimental uncertainty in the rate data. Consequently an average figure of 7.9 for the reactivity ratio was adopted and utilized.

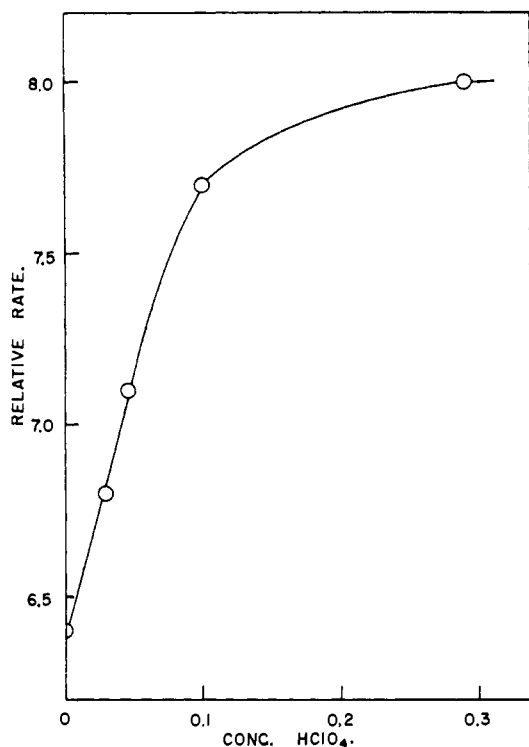


Fig. 2.—Variation in the relative rate of toluene to benzene with concentration of perchloric acid.

However, they observed that in an electrometric titration there was no evidence that mercuric acetate was neutralized by perchloric acid. Unfortunately, their conditions were such that one cannot extend their results to our system. Thus they used 0.04 *N* perchloric acid in 97% acetic acid for the titration. Since the aqueous content of the solvent corresponds to a solution 1.5 *M* in water, it is evident that the water may have reacted preferentially with the acid.

In the absence of the perchloric acid catalyst the reactivity ratio at 25° is 6.4 as compared to 8.0 for the catalyzed reaction. According to the relationship previously proposed, the uncatalyzed reaction should be less selective and result in a lower ratio of *para/meta* substitution. At 50, 70 and 90° the reactivity ratio decreases to 5.0, 4.3 and 3.6, respectively. It is gratifying to note that the observed isomer distribution corresponds closely with the proposed linear relationship (Fig. 3).

It was pointed out previously that the iodine-catalyzed reaction of bromine with toluene is a highly selective reaction with a toluene/benzene reactivity ratio of approximately 470/1. In this reaction negligible amounts of the *meta* isomer are formed.¹³ It was suggested that the use of a highly electrophilic catalyst should decrease the selectivity and increase the amount of substitution occurring in the *meta* position.⁴

One experiment was carried out to test this conclusion. Toluene reacted with bromine at 30° in the presence of an equimolar quantity of alu-

(13) Robertson recently has calculated from partial rate factors that the amount of *meta* isomer formed should be approximately 0.26%; P. W. Robertson, *J. Chem. Soc.*, 1267 (1953).

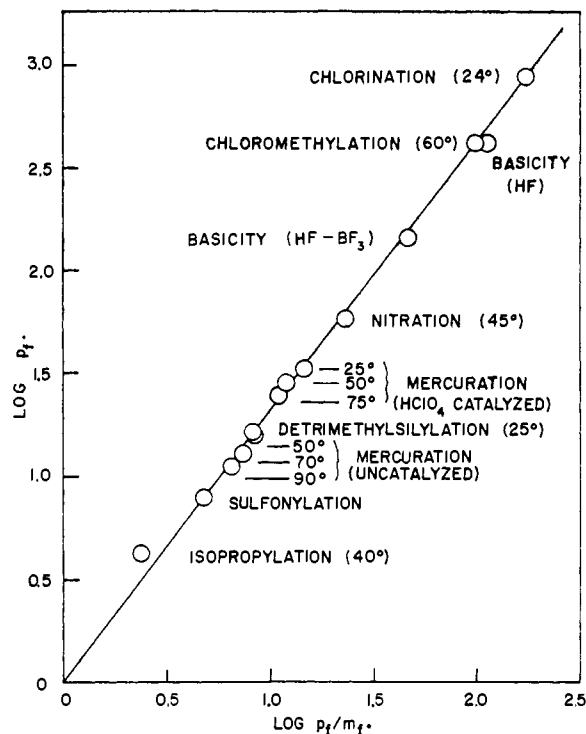


Fig. 3.—Relationship between the "activity" of the reagent and the degree of meta substitution, in terms of the partial rate factors.

minum bromide. The reaction mixture was quenched immediately and the isomer distribution determined by infrared analysis. The observed distribution is: *ortho*, 20%; *meta*, 30%; and *para*, 50%. Unfortunately, time did not permit an examination of the question of possible isomerization under the reaction conditions. The reaction time was so short, approximately 30 seconds, that such isomerization appears improbable. However, until this question is settled the results must be accepted with caution.

It may be concluded that the results on the catalyzed and uncatalyzed reactions of benzene and toluene with mercuric acetate definitely support the conclusion that catalysts can alter both the reactivity ratio and the isomer distribution in electrophilic aromatic substitutions. The results with such catalyzed reactions appear to follow the proposed linear relationship governing isomer distribution in toluene substitutions.

Experimental Part

Materials.—C.P. benzene and toluene were dried over calcium hydride and distilled through a 50-plate column. Constant-boiling center cuts were collected and used in the rate studies. Anhydrous sodium perchlorate was prepared from 70% perchloric acid (Baker, reagent) and sodium carbonate (Baker, reagent) with the excess water being removed under vacuum at room temperature.

Glacial acetic acid (Baker and Adamson, reagent) which had been refluxed over sodium dichromate and then mercuric acetate, gave the same rate constants when used as solvent as did the unpurified material. Therefore, the glacial acetic acid was used directly without purification. It was shown also that small quantities of water did not alter the rates appreciably in mercuration of aromatics without catalyst and therefore no attempt was made to exclude atmospheric air. All other chemicals used were commercial reagent grades.

Rates of Mercuration.—Mercuric acetate was dissolved in sufficient glacial acetic acid to make a 0.1 *M* solution. This solution and the aromatic were measured and mixed at 25°, the reaction being very slow at this temperature. Then, 10-ml. aliquots were removed and sealed off in thin glass bulbs and were placed in the appropriate constant temperature bath. After a period of five minutes, a bulb was quenched as the initial point. The reaction was followed by determining the decrease in the mercuric ion concentration by titration with standard thiocyanate using ferric alum indicator. The rate constants were reproducible to a precision of less than 3% and are summarized in Table I.

The reactions involving perchloric acid and sodium perchlorate were followed similarly. The results in which the perchloric acid was less than 0.09 *M*, were somewhat less precise since the second-order rate constants dropped off in the latter stages of the reaction. Data are summarized in Table II.

Mercuration of Toluene.—At 50°, 77 ml. (0.72 mole) of toluene was added to a 500-ml. round bottomed flask con-

taining 300 ml. of a 0.24 *M* (0.072 mole) mercuric acetate solution in glacial acetic acid. Aliquots were removed with a 50-ml. pipet and quenched in an equal volume of water. The product was then converted to a mixture of bromotoluenes and analyzed by infrared as described previously.⁵

The mercuration in glacial acetic acid at 70 and 90° was carried out similarly except that 154 ml. of toluene was added, thus raising the toluene-to-mercuric acetate ratio to twenty. The data together with those at 50° are reported in Table III.

Bromination of Toluene.—A homogeneous solution of 4.0 ml. (0.037 mole) of toluene and 3.3 g. (0.0062 mole) of aluminum bromide (prepared from bromine and aluminum and distilled) was prepared in a small flask. To this solution at 30°, 1.0 g. (0.0062 mole) of bromine was added. The reaction was quenched immediately in ice-water and was analyzed by infrared.

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The Rates of Mercuration of the Monoalkyl- and the Polymethylbenzenes. Calculation of Relative Reactivities for the Mercuration Reaction^{1,2}

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The rates of mercuration of the polymethylbenzenes and a series of monoalkylbenzenes have been measured using mercuric acetate in glacial acetic acid at 50°. The relative reactivities of the polymethylbenzenes may be calculated with the assumption of additivity of the partial rate factors with a mean deviation of 12%. By taking into account steric factors involving substitution in the *ortho* position, the rate constants can be calculated with a mean deviation of 6%. The rate of mercuration decreases from toluene to ethyl-, isopropyl- and *t*-butylbenzene with the latter compound undergoing mercuration at a rate 36% less than that of toluene. The decrease in rate appears to be only slightly greater than can be accounted for by a decrease in substitution in the *ortho* position. It is concluded that mercuration is a reaction of low selectivity which shows only low discrimination between hydrogen and methyl as substituents in benzene, as well as between methyl and *t*-butyl.

It was shown previously by Condon that the relative reactivities of the polymethylbenzenes in halogenation could be calculated by the use of partial rate factors calculated from data for toluene.⁴ The relative rates calculated in this way agreed with the available experimental data within a factor of 2.

In the preceding paper the partial rate factors for the mercuration of toluene were determined.⁵ The mercuration reaction exhibits simple second-order kinetics. The rates of mercuration can be measured readily with a precision of 2–3%. This reaction therefore offered a promising method for determining the relative reactivities of the polymethylbenzenes to provide a test of the generality of the treatment utilized by Condon.⁴ Accordingly, a study was made of the rates of reaction of mercuric acetate in acetic acid with the three xylenes and all of the higher methylbenzenes.

In the bromination reaction, toluene has been reported to react five times as fast as *t*-butylbenzene.⁶ The decreased reactivity of *t*-butylbenzene was attributed to the decreased importance of hy-

perconjugation as the α -hydrogen atoms are replaced by methyl groups. However, in the case of nitration⁷ and isopropylation,⁸ the decreased reactivity is small and appears to be due entirely to the decreased substitution in the *ortho* position. These two seemingly contradictory sets of data have been considered to be anomalous.⁹ It therefore appeared of interest to examine the behavior of toluene, ethyl-, isopropyl- and *t*-butylbenzene in the mercuration reaction.

Results and Discussion

Mercuration of Alkylbenzenes.—The rates of mercuration of a series of alkylbenzene derivatives were determined, using the uncatalyzed reaction with mercuric acetate in glacial acetic acid at 50°. The reaction was followed by quenching aliquots at various time intervals and titrating with standard thiocyanate. The reactions followed second-order kinetics, first in both aromatic and mercuric acetate, and were carried out to 30–70% completion. The rate constants were reproducible to better than 3%. The results are summarized in Table I.

The Methylbenzene Series.—In Table II, columns one and two, the experimental reactivity

(1) Directive Effects in Aromatic Substitution. VI.

(2) Based upon a thesis submitted by C. W. McGary, Jr., in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(3) Purdue Research Foundation Fellow, 1952–1953; American Cyanamid Corp. Fellow, 1953–1954. Research assistant on a grant from the National Science Foundation, 1954.

(4) F. E. Condon, *THIS JOURNAL*, **70**, 2265 (1948).

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

(6) E. Berliner and F. Berliner *ibid.*, 1195 (1949).

(7) H. Cohn, E. D. Hughes, M. H. Jones and M. A. Peeling, *Nature*, **169**, 291 (1952). The authors report that the rates of substitution in the *meta* and *para* positions of *t*-butylbenzene are slightly greater than in toluene.

(8) F. E. Condon, *THIS JOURNAL*, **70**, 2265 (1948).

(9) P. W. Robertson, P. B. D. de la Mare and B. E. Swedlund, *J. Chem. Soc.*, 782 (1953).