Perchloric Acid Catalyzed Aromatic Mercuration in Acetic Acid Solution. III. Relative Reactivity of Aromatic Substrates[1]

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The rates of perchloric acid catalyzed mercuration of a number of aromatic substrates covering a range of 2 × 10^5 in relative reactivity fall in the normal order expected for electrophilic aromatic substitution, and approximate additivity of substituent effects holds for several methyl-substituted benzenes. This indicates that there is a unity of reaction mechanism and that proton loss from the σ-complex intermediate is rate determining in all cases. These data for catalyzed mercuration obey the selectivity relationship just as do those for uncatalyzed mercuration, even though the catalyzed reaction is both more rapid and more discriminatory than the uncatalyzed reaction. An explanation is suggested for this inversion of the relationship usually found between reactivity and discriminatory ability in electrophilic aromatic substitution.

The first two papers of this series[3,4] dealt mainly with the mercuration of benzene in acetic acid solution. In this paper, we present the results of a study of the rates of mercuration of other aromatic substrates carried out for the purpose of comparing perchloric acid catalyzed mercuration with other electrophilic aromatic substitution reactions.

Aromatic mercuration in acetic acid solutions containing perchloric acid may occur through substitution by either one of two electrophiles: acetatomercury(II) perchlorate ion pairs or mercuric perchlorate ion triplets.[3] It is difficult, for practical reasons, to isolate one or the other of these reactions, so we chose instead to conduct this investigation under conditions which fixed the relative concentrations of the two electrophiles within narrow limits. When benzene is the aromatic substrate, these standard conditions allow 75% of the mercuration reaction to occur through substitution by acetatomercury(II) perchlorate ion pairs and the rest through substitution by mercuric perchlorate ion triplets.

In the mercuration of benzene by acetatomercury(II) perchlorate ion pairs, attack of the electrophile on the aromatic substrate is rapid and reversible, and proton loss from the low-concentration σ-complex intermediate is rate determining; this is very probably also the mechanism for the mercuration of benzene by mercuric perchlorate ion triplets.[4] This mechanistic homogeneity need not, of course, be preserved in the mercuration of other aromatic substrates by these two electrophiles, for changes in substrate reactivity may influence the free energies of activation of the two substitution steps in different ways. Insofar as a change in rate-determining step would be reflected in an abrupt deviation from normal structure–reactivity relationships, however, the data to be presented below show that mechanistic homogeneity is preserved.

Results

Standard Conditions.—Rates of mercuration were measured at 25° in acetic acid solution at an analytical perchloric acid concentration of 0.50 *M* and an analytical water concentration of 0.20 *M*. Mercury(II) was supplied as mercuric acetate at initial, analytical concentrations of either 0.050 or 0.025 *M*; in a few cases of very rapid reaction, this was lowered to 0.010 *M*. [Lower concentrations could not be used because the titrimetric determination of mercury(II) became inaccurate.] The initial concentrations of aromatic substrate ranged from 0.50 to 0.050 *M*; care was taken to keep the aromatic in sufficient excess over mercury(II) to avoid polysubstitution. Under these conditions, the rate of mercuration of benzene is not very sensitive to small changes in the acidity of the medium,[3] and it was found that control of the analytical perchloric acid concentration within the limits ±0.01 *M* and the analytical water concentration within the limits ±0.03 *M* was sufficient to hold rate variations to ±1%. The standard conditions employed were therefore set at $[HClO_4]_{analyt} = 0.50 \pm 0.01\ M$ and $[H_2O]_{analyt} = 0.20 \pm 0.03\ M$.

Under these conditions 95% of the mercury(II) exists as acetatomercury(II) perchlorate ion pairs and 5% exists as mercuric acetate; these proportions are not very sensitive to the total mercury(II) concentration. The concentration of free perchloric acid is 0.27 *M* when the total mercury(II) concentration is 0.050 *M*, and 0.31 *M* when the total mercury(II) concentration is 0.010 *M*; with benzene as the aromatic substrate, this increase in acidity causes the portion of the mercuration reaction which occurs through substitution by mercuric perchlorate ion triplets to rise very little (from 24 to 27%). Consequently, the deviations from second-order kinetics sometimes encountered[3] are not to be expected, and good compliance with second-order kinetic laws was observed through this study.

Rates of Mercuration.—Second-order rate constants, based on the disappearance of aromatic substrate and total mercury(II), were measured over 2 to 3 half-lives. Kinetic runs were carried out at least in duplicate, and more determinations were made for benzene than for other aromatic substrates. These data (Table I) provided a general precision in rate constant of 2–3% (average deviation) which was reduced to less than 1% in the case of benzene. The precision of the relative rates based on benzene, therefore, is of the order of the precision in the rate constants themselves.

Product Isomer Distribution.—The composition of the product in the mercuration of toluene was determined under kinetic conditions by converting pre-

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[1] Directive Effects in Aromatic Substitution. LX.

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[3] A. J. Kresge, M. Dubeck, and H. C. Brown, *J. Org. Chem.*, **32**, 745 (1967).

[4] A. J. Kresge and J. F. Brennan, *ibid.*, **32**, 752 (1967).

TABLE I

RATES OF AROMATIC MERCURATION UNDER STANDARD CONDITIONS OF PERCHLORIC ACID AND WATER CONCENTRATION IN ACETIC ACID SOLUTION AT 25°[a]

Aromatic substrate	10^2k_{obsd} (M^{-1} min^{-1})[b]	Rel rate
Benzene	2.56 ± 0.02	1.00
Toluene	23.2 ± 0.1	9.1
Ethylbenzene	19.8 ± 0.1	7.7
Isopropylbenzene	18.2 ± 0.7	7.1
t-Butylbenzene	16.3 ± 0.3	6.4
n-Propylbenzene	18.6 ± 0.8	7.3
Isobutylbenzene	17.5 ± 0.4	7.8
sec-Butylbenzene	20.0 ± 0.4	6.8
Fluorobenzene	0.962 ± 0.002	0.38
Chlorobenzene	0.136 ± 0.002	0.053
Bromobenzene	0.120 ± 0.002	0.047
Iodobenzene	0.109 ± 0.005	0.045
Biphenyl	10.7 ± 0.2	4.2
Nitrobenzene	0.00106 ± 0.00004	0.00041
Phenylmercuric acetate	1.77 ± 0.02	0.69
Naphthalene	31.4 ± 0.3	12.3
o-Xylene	82 ± 3	32
m-Xylene	230 ± 7	90
p-Xylene	32.3 ± 0.4	12.6

[a] Standard conditions: $[HClO_4]_{analyt}$ = 0.50 ± 0.01 M $[H_2O]_{analyt}$ = 0.20 ± 0.03 M. [b] Average values of at least duplicate determinations; error limits are average deviations.

cipitated tolylmercuric bromides into tolyl bromides and analyzing the resultant mixtures by infrared spectrophotometry.[5] Since the product distribution changes with time, samples were removed at various times and the initial composition was estimated by extrapolation (Table II).

TABLE II

ISOMER DISTRIBUTION IN THE PRODUCT OF THE MERCURATION OF TOLUENE UNDER STANDARD CONDITIONS OF PERCHLORIC ACID AND WATER CONCENTRATION IN ACETIC ACID SOLUTION AT 25°[a]

Time	%	Product compn		
(min)	reaction	% *ortho*	% *meta*	% *para*
63	85	24.0	8.4	67.6
18	70	21.6	7.5	70.9
9	50	20.5	8.9	70.6
0	0	19.4[b]	8.3[b]	72.3[b]

[a] $[HAr]_{t=0} = 0.50\,M$; $[Hg^{II}]_{t=0} = 0.050\,M$; $[HClO_4]_{analyt}$ = 0.50 ± 0.01 M; $[H_2O]_{analyt}$ = 0.20 ± 0.03 M. [b] Estimated by extrapolating values for finite reactions times.

Discussion

Relative Reactivities.—The data of Table I show that electron-supplying groups in the aromatic substrate facilitate perchloric acid catalyzed aromatic mercuration and that electron-withdrawing groups retard this reaction. This is the normal order of substituent effects found in electrophilic aromatic substitutions such as nitration and halogenation where formation of the σ complex is known to be rate determining and proton loss from this intermediate is known to be rapid.[6] The reaction mechanism for aromatic mercuration is of course different: σ-complex formation is rapid and proton loss is rate determining.[4] The slow step here is a reaction which will be retarded by electron-supplying groups and accelerated by electron-withdrawing groups, but, even so, the effect of substituents on the rate of the over-all reaction can be expected to be the same as that for the electrophilic aromatic substitutions which operate through the other reaction mechanism. This is because, for reaction by either mechanism, the substituent has more positive charge with which to interact at the rate-determining transition state than it did in the initial state. An analysis of mercuration in terms of the pseudo-equilibrium forming the σ complex and of the rate of the slow step converting this intermediate to products leads to this same conclusion. The σ complex contains a full positive charge in the formerly aromatic ring, whereas, in the transition state of the slow step, some of this positive charge has been lost to the attacking base. Electron supply through substituents will therefore aid the equilibrium process more than it will hinder the rate process, and a normal electrophilic order will prevail.

Of all the aromatic substrates listed in Table I, nitrobenzene is the least reactive by a considerable margin: it is mercurated only 1/2500 as fast as benzene. Since this appears to be the first instance in which direct rate data have been obtained for so inert an aromatic in a substitution reaction of electrophile for hydrogen, it is of interest to determine how well the observed rate compares with that predicted by the modified Hammett equation.[7] Values of ρ^+ calculated from the *m*-methyl and *p*-methyl partial rate factors for catalyzed mercuration presented in the section below are −5.37 and −5.13, respectively; using the average of these (−5.25) and standard values of σ^+ for the nitro group,[7] the *m*-nitro partial rate factor can be estimated at 2.9×10^{-4} and the *p*-nitro partial rate factor can be estimated at 0.7×10^{-4}. Since it is unlikely that very much *ortho* substitution occurs in the mercuration of nitrobenzene, a reasonable prediction of its relative rate of reaction can be made on the basis of *meta* and *para* substitution alone. The value so obtained (6.5×10^{-4}) agrees well with the observed quantity (4.1×10^{-4}), considering that this calculation is based on rate data which differ by a factor of 22,000.

This good compliance with the modified Hammett equation indicates that the mechanism of catalyzed mercuration is the same for benzene, toluene, and nitrobenzene, and this, in turn, can be used to argue that the reaction mechanism is the same for all the substrates of Table I. In the mercuration of benzene, σ-complex formation is rapid and proton loss from this intermediate is slow.[4] Electron-withdrawing substituents in the aromatic substrate should facilitate proton loss, making this step more rapid and thus shifting the mechanism toward one in which this step is fast and σ-complex formation is slow. The fact that such a change in reaction mechanism has not happened in the case of nitrobenzene, the aromatic with the most strongly electron-withdrawing substituent of all the substrates in Table I, means that it could not have occurred in any of the other cases.

Partial Rate Factors for Substitution in Toluene and the Xylenes.—When the isomer distribution in the product (Table II) and the relative rate of reaction (Table I) for the mercuration of toluene are

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(5) (a) H. C. Brown and C. W. McGary, Jr., *J. Am. Chem. Soc.*, **77**, 2300 (1955); (b) *ibid.*, **77**, 2306 (1955).

(6) P. B. D. de la Mare and J. H. Ridd, "Aromatic Substitution," Butterworth and Co. (Publishers) Ltd., London, 1959; R. O. C. Norman and R. Taylor, "Electrophilic Substitution in Benzeneoid Compounds," Elsevier Publishing Co., Amsterdam, 1965.

(7) L. M. Stock and H. C. Brown, *Advan. Phys. Org. Chem.*, **1**, 35 (1963).

combined in the usual way, the following values are obtained for the partial rate factors for the perchloric acid catalyzed reaction at 25°: *ortho*, 5.27; *meta*, 2.26; *para*, 39.3. These do not differ in any significant way from partial rate factors which have been measured for the reaction of toluene with other electrophiles;[7] they may therefore be considered to be normal values. Like the others, they can be interpreted in terms of weak, inductive electron release to all positions coupled with a somewhat stronger but still weak conjugative electron release to the *ortho* and *para* positions. In all probability, a steric effect also operates to reduce the rate of reaction at the *ortho* positions.

These partial rate factors can be used to calculate rates of reaction in polymethylbenzenes. When this is done for the three xylenes and the results are compared with experiment, moderately good agreement is found: the average difference between observed and calculated values is 21% (Table III). With these same three substrates, somewhat better agreement is reported for uncatalyzed mercuration[8] and for halogenation by chlorine[9] and by bromine;[10] here the average differences between observed and calculated values are 17, 13, and 8%, respectively. But these differences are of the same order of magnitude as those found in catalyzed mercuration, and additivity of substituent effects can be said to hold approximately in all these cases.

TABLE III

COMPARISON OF OBSERVED AND CALCULATED RELATIVE RATES OF MERCURATION OF THE XYLENES UNDER STANDARD CONDITIONS OF PERCHLORIC ACID AND WATER CONCENTRATIONS IN ACETIC ACID SOLUTION AT 25°[a]

Aromatic substrate	Rel rate: Obsd	Rel rate: Calcd[b]	100 × (obsd − calcd)/obsd
Benzene	1.00	1.00	. . .
Toluene	9.1	9.1	. . .
o-Xylene	32.1	33.7	−5.0
m-Xylene	89.9	74.6	+17.0
p-Xylene	12.6	7.4	+41.3
			Av 21.1

[a] Standard conditions: $[HClO_4]_{analyt} = 0.50 \pm 0.01$ *M*; $[H_2O]_{analyt} = 0.20 \pm 0.03$ *M*. [b] Calculated using the partial rate factors: $o_f = 5.27$, $m_f = 2.26$, $p_f = 39.3$.

Comparison of Catalyzed and Uncatalyzed Aromatic Mercuration.—Table IV, in which relative rates for uncatalyzed and perchloric acid catalyzed aromatic mercuration are compared, shows that substituents in the aromatic have a considerably greater effect on the rate of the catalyzed reaction than they do on the rate of the uncatalyzed process: the spread in relative rate in the former case is nearly twice that in the latter. This difference in discriminatory power was noted before[5b] when it was shown that perchloric acid alters the selectivity of the electrophile in aromatic mercuration without affecting the reaction's adherence to the selectivity relationship.[7] The new data for toluene obtained under the conditions of the present study obey this relationship just as do the data for uncatalyzed mercuration[5b] and the previous data for the catalyzed reaction at a lower acidity.[5a] The selectivity factor (S_f) for catalyzed mercuration under the present conditions is 1.240; that for the uncatalyzed reaction is 1.014.[7] This difference in selectivity factor indicates that the catalyzed reaction is the more discriminatory process, and this, of course, is consistent with the fact that ρ^+ in the modified Hammett equation[7] for catalyzed mercuration under the present conditions (−5.25) is more negative than ρ^+ for the uncatalyzed reaction at the same temperature (−4.00).[7]

$$\log p_f = b \log(p_f/m_f) = bS_f$$

TABLE IV

COMPARISON OF RELATIVE RATES OF CATALYZED AND UNCATALYZED AROMATIC MERCURATION

Aromatic substrate	Rel rate: Cat[a]	Rel rate: Uncat[b]
Benzene	1.00	1.00
t-Butylbenzene	6.4	4.00[c]
Toluene	9.0	6.5[d]
Fluorobenzene	0.38	0.72[e]
Chlorobenzene	0.053	0.100[e]
Bromobenzene	0.047	0.090[e]

[a] In acetic acid solution at 25°: $[HClO_4]_{analyt} = 0.50 \pm 0.01$ *M*; $[H_2O]_{analyt} = 0.20 \pm 0.03$ *M*. [b] In glacial acetic acid solution at 25°. [c] H. C. Brown and M. Dubeck, *J. Am. Chem. Soc.*, **81**, 5608 (1959). [d] Reference 5b. [e] H. C. Brown and G. Goldman, *J. Am. Chem. Soc.*, **84**, 1650 (1962).

It is usually the case in electrophilic aromatic substitution by closely related electrophiles that the more discriminatory reagents are the less reactive species. Aromatic halogenation provides a number of examples in support of this principle: molecular halogenating agents are more discriminating electrophiles than the corresponding positive halogen species, and molecular halogens are also less reactive than positive halogens; bromine is more selective and also reacts more slowly than chlorine.[6,7] These differences receive a logical explanation in reasoning such as that expressed in the Hammond postulate:[11] with the more reactive reagents, the transition state occupies an earlier position along the reaction coordinate and reaction occurs with less help from, and therefore less discrimination by, the aromatic substrate. In aromatic mercuration, however, the converse is true: catalyzed mercuration is more rapid than uncatalyzed mercuration (in the case of benzene at 25°, by a factor of nearly 10^4 [3]) and it is also the more discriminatory reaction.

The more rapid reaction need not, of course, always be the less discriminatory process. In most electrophilic aromatic substitutions, formation of the σ complex is rate determining. In such a reaction, an increase in rate will, by the Hammond postulate, make the rate-determining transition state more like the initial state and less like the σ complex. Since the σ complex occupies the point along the reaction coordinate at which the discriminatory power of the aromatic is at its maximum, this change will make the reaction less selective. In an aromatic substitution in which proton removal from the σ complex is rate determining, however, an increase in reaction rate produced by a lowering of the free energy of the rate-determining transition state will make this transition state more like the initial state and *more like the σ complex as well*, for now

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[8] H. C. Brown and C. W. McGary, Jr., *J. Am. Chem. Soc.*, **77**, 2310 (1955).

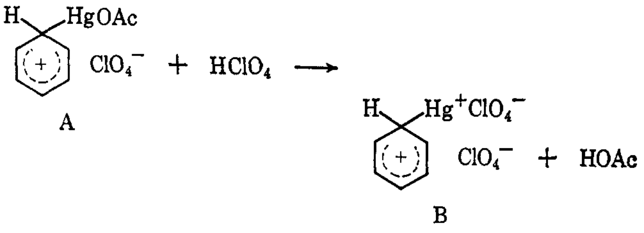
[9] H. C. Brown and L. M. Stock, *ibid.*, **79**, 5175 (1957).

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

[11] G. S. Hammond, *ibid.*, **77**, 334 (1955).

the σ complex lies between this transition state and the initial state. In this case, therefore, an increase in reaction rate will have a different effect on discriminatory ability: it will make the reaction more selective.

It is not immediately apparent how this general explanation applies to the particular case of catalyzed and uncatalyzed aromatic mercuration. The principal effect of the perchloric acid catalyst in mercuration must be to raise the free energy of the initial state by converting mercuric acetate into the less stable and more reactive electrophiles, acetatomercury(II) perchlorate ion pairs and mercuric perchlorate ion triplets. This will affect the first step of substitution, σ-complex formation, but it will not change very much the energetics or transition state structure of the proton-removal step. It is possible, however, that perchloric acid has the additional effect of promoting the ionization of the σ complex so that proton loss in catalyzed mercuration actually occurs through 1-mercury(II)-benzenonium perchlorate ion triplets (B) rather than through 1-acetatomercury(II)benzenonium perchlorate ion pairs (A). The inductive effect of the positively charged mercury substituent in B should facilitate proton removal and make this a lower energy route to products. This would also have the effect of shifting the transition state for this step toward the σ complex and thus making catalyzed mercuration the more selective process.



It can be argued that a doubly charged species such as B would be highly unstable and its formation would therefore be improbable, but this is mitigated by the fact that the two positive charges in B are separated by a saturated carbon atom. It is also a fact that a mercury substituent in benzene has little effect on the rate of further reaction under conditions of catalyzed mercuration (Table I) where this group is known to exist at least partly as Hg^+.[4] This could be interpreted as indicating that Hg^+ has little electron-withdrawing inductive effect and therefore cannot accelerate the rate of proton loss appreciably. Under the conditions of catalyzed mercuration, however, the further substitution of benzene may be occurring through reaction of the phenylmercuric acetate which is in equilibrium with phenylatomercury(II) perchlorate ion pairs, and the latter species may well be resistant to further mercuration.

We are currently engaged in further research designed to test this hypothesis.

Experimental Section

The materials used, other than those listed below, and the kinetic method employed were those already described in the first paper of this series.[3]

Aromatic Substrates.—**Toluene** was J. T. Baker, Analyzed reagent grade. The alkylbenzenes were NBS standard hydrocarbon samples of the following purity: **ethylbenzene**, 0.04 ± 0.02 mole % impurity; **isopropylbenzene**, 0.07 ± 0.03 mole % impurity; ***t*-butylbenzene**, 0.06 ± 0.03 mole % impurity; ***n*-propylbenzene**, 0.25 ± 0.08 mole % impurity; **isobutylbenzene**, 0.13 ± 0.09 mole % impurity; ***sec*-butylbenzene**, 0.12 ± 0.06 mole % impuirty; ***o*-oxylene**, 0.010 ± 0.007 mole % impuirity; ***m*-xylene**, 0.07 ± 0.03 mole % impurity; and ***p*-xylene**, 0.06 ± 0.03 mole % impurity. **Fluorobenzene** (Eastman Kodak, White Label grade) was dried over calcium hydride and was fractionally distilled; a center cut of constant refractive index ($n^{20}{}_D$ 1.4652) was used. **Chlorobenzene** was a highly purified sample kindly furnished by Dr. F. Jensen. **Bromobenzene** was Eimer and Amend, tested purity reagent grade, Lot No. 452803, fp −31.053 ± 0.002°. **Iodobenzene** (Eastman Kodak, White Label grade) was dried over calcium hydride and was fractionally distilled at reduced pressure. Just prior to use, a center cut of constant refractive index ($n^{20}{}_D$ 1.6196) was washed with aqueous sodium bisulfite, dried over calcium chloride, and distilled rapidly at atmospheric pressure. **Biphenyl** (Paragon) was recrystallized to constant melting point (68.2–68.6° cor) from methanol. **Nitrobenzene** was a highly purified sample kindly furnished by Dr. H. Young. **Phenylmercuric acetate** was prepared by heating under reflux for 20 hr a solution of 130 g (0.41 mole) of mercuric acetate (B and A, reagent grade) and 400 ml (350 g, 4.5 moles) of benzene (thiophene-free) in 1.0 l. of acetic acid (B and A, reagent grade). The reaction mixture was then concentrated *in vacuo* to 0.5 l. and this was poured into 1.0 l. of distilled water. The heavy, white, granular precipitate was collected by filtration, washed twice with water, and dried. This was then added to 0.75 l. of benzene (thiophene-free), and the resulting suspension was heated to boiling and was filtered while hot. The cooled filtrate deposited colorless, needle-shaped crystals. These were collected and were recrystallized from benzene (yield 38 g, 25%), mp 150.8–151.5° cor. *Anal.* Calcd for $C_8H_8HgO_2$: Hg^{II}, 59.57. Found: Hg^{II}, 59.25. **Naphthalene** was J. T. Baker, Analyzed reagent grade.

Isomer Distribution in Toluene.—The product composition in the mercuration of toluene was determined by the method already described.[5]

Registry No.—Perchloric acid, 7601-90-3; benzene, 71-43-2; toluene, 108-88-3; ethylbenzene, 100-41-4; isopropylbenzene, 98-82-8; *t*-butylbenzene, 98-06-6; propylbenzene, 103-65-1; isobutylbenzene, 538-93-2; *sec*-butylbenzene, 135-98-8; fluorobenzene, 462-06-6; chlorobenzene, 108-90-7; bromobenzene, 108-86-1; iodobenzene, 591-50-4; biphenyl, 92-52-4; nitrobenzene, 98-95-3; phenylmercuric acetate, 62-38-4; naphthalene, 91-20-3; *o*-xylene, 95-47-6; *m*-xylene, 108-38-3; *p*-xylene, 106-42-3; acetatomercury(II) perchlorate, 7601-92-5.

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