U.S.P. grade) was added to a solution of 365 g (2.60 moles) of 71% perchloric acid (J. T. Baker, Analyzed reagent grade) in 1.0 l. of water. The oxide dissolved quickly as the mixture was swirled. The slightly warm reaction mixture was then filtered through a sintered-glass funnel, and the filtrate was concentrated to 250 ml by gentle warming on a water bath (bath temperature kept below 60°) and application of vacuum. The residue was permitted to cool to room temperature whereupon it solidified almost completely to a crystalline mass. The crystals were separated from the adhering mother liquor by filtration on a sintered-glass funnel; approximately 500 g of material was obtained in this way. This was recrystallized from about 50 ml water, and the product, colorless, regular hexagonal rods, was dried by centrifuging (weight, 300 g). *Anal.* Calcd for $Hg(ClO_4)_2 \cdot 6H_2O$: Hg^{II}, 39.52; ClO_4^-, 39.18; H_2O, 21.30. Found: Hg^{II}, 39.78; ClO_4^-, 39.27; H_2O, 21.72.

B. Analytical Methods. Water Analysis.—The Karl Fischer method using a methanol-based reagent was employed.[26] Titrations were done to a visual end point in 250-ml, glass-stoppered erlenmeyer flasks. No special precautions were taken to exclude atmospheric moisture during a titration since it was found that no appreciable error was introduced from this source during a reasonably rapid determination. Empty stoppered flasks did pick up moisture when allowed to stand in a normal laboratory atmosphere for 1 day or longer, and titration flasks were therefore dried in an oven at 110° just before use. The reagent was standardized daily against sodium acetate trihydrate (J. T. Baker, Analyzed reagent grade) which was stored in a hygrostat whose humidity was controlled by a saturated solution of potassium carbonate.[27]

It was found that acetic acid solutions of water, especially those containing dissolved acids or salts, gave high results and fading end points when analyzed with methanol-based Karl Fischer reagent. It is likely that this was the result of a water-producing esterification reaction between acetic acid and methanol; the error was corrected by dissolving these acetic acid solutions in at least two volumes of anhydrous pyridine and cooling the resultant solutions in ice just before titration.

Perchloric Acid Analysis.—Acetic acid solutions of perchloric acid were analyzed for strong acid by nonaqueous titration with sodium acetate in anhydrous acetic acid.[28] End points were determined visually using bromothymol blue indicator.

Mercury Analysis.—Mercury analyses were conducted by titration with standard aqueous potassium thiocyanate (J. T. Baker, Analyzed reagent grade) solution using ferric alum as an indicator.[29]

C. Kinetic Method.—Reaction mixtures were prepared by combining appropriate quantities of three different acetic acid solutions, one containing mercury(II) either as mercuric acetate or mercuric perchlorate, one containing perchloric acid, and the third containing benzene; all three solutions were allowed to equilibrate with the thermostated water bath (25.00 ± 0.02°) before they were mixed. Reactions were conducted in glass-stoppered flasks; 10-ml samples were removed at appropriate intervals of time and were quenched in equal volumes of water. Two to five milliliters of indicator solution (the quantity was adjusted to the mercury content of the sample) was added to the quenched samples, and the mixture was cooled to 10° in ice water. (Sharper end points were observed when titrations were conducted below 15°.) Titrations were carried out by adding 0.1 *N* thiocyanate solution as the sample was swirled in ice water; the first faint appearance of color was taken as the end point and blank corrections were found to be unneccessary. It was found that the color change could be discerned more clearly by playing a strong tungsten light at an oblique angle to the surface of the solution being titrated. Washings were kept to a minimum in order to avoid unnecessary dilution.

Registry No.—Perchloric acid, 7616-81-1; benzene, 71-43-2; sodium perchlorate, 7601-89-0; mercuric acetate, 1600-27-7; mercuric perchlorate, 7616-83-3.

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(27) I. M. Kolthoff and E. B. Sandell, "Textbook of Quantitative Inorganic Analysis," The Macmillan Co., New York, N. Y., 1953, p 141.

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Perchloric Acid Catalyzed Aromatic Mercuration in Acetic Acid Solution. II. The Substitution Process[1,2]

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The mercuration of benzene by acetatomercury(II) perchlorate ion pairs in acetic acid solution shows a large primary hydrogen isotope effect and the reaction is first order in the excess reactant. This indicates that aromatic substrate and electrophile combine rapidly and reversibly to form a σ-complex intermediate in low concentration, and that proton transfer from this intermediate is rate determining. The acetate group originally present in the electrophile is lost during the reaction to give phenylatomercury(II) perchlorate ion pairs as the final product. Acetate group loss may be concerted with proton transfer, the acetate group serving as the proton transfer agent in a cyclic transition state, or proton transfer may occur externally to a solvent molecule.

It is usually convenient to divide an electrophilic aromatic substitution reaction into two parts: generation of the electrophilic reagent and reaction of the electrophile with the aromatic substrate. In the first paper of this series,[3] we showed that mercuric acetate is the electrophilic reagent for uncatalyzed aromatic mercuration in acetic acid solution and that acetatomercury(II) perchlorate ion pairs and mercuric perchlorate ion triplets are the electrophiles in the perchloric acid catalyzed reaction. In this paper, we shall discuss the details of the reaction of these mercurating

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(1) Based in part upon a thesis submitted by J. F. Brennan to the Illinois Institute of Technology in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) This investigation was supported by Public Health Service Research Grant GM 09369-03 from the National Institute of General Medical Sciences.

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

agents with the aromatic substrate; most of our remarks will be directed at substitution by the acetatomercury(II) perchlorate ion pair which is the principal electrophile responsible for aromatic mercuration in acetic acid solution at moderate concentrations of perchloric acid.

The substitution of an electrophilic reagent for aromatic hydrogen is known to be a two-step reaction.[4,5] The electrophile (E^+) first combines with the aromatic substrate (ArH) to form an intermediate σ complex, $EArH^+$. Then hydrogen is transferred as a proton

$$E^+ + ArH \longrightarrow EArH^+ \qquad (1)$$

from the σ complex to a base (B). Either one of these

$$EArH + B \longrightarrow EAr + HB^+ \qquad (2)$$

reactions, or even some previous step which serves to generate the electrophile, can be rate determining, and one of the principal problems which must be solved in establishing the mechanism of an electrophilic aromatic substitution is determination of the slow step.

In the present case, aromatic mercuration, the reaction is kinetically first order in aromatic substrate.[3] This means that the transition state of the slowest step contains a molecule of aromatic substrate, and, consequently, no step prior to attack of the electrophile on the aromatic can be rate determining. The problem of identifying the rate-determining step is thus limited to establishing which of the two reactions represented by eq 1 and 2 is the slower. Two mechanistic criteria, kinetic isotope effects and base catalysis, can usually be applied to provide an answer to this question. Detection of base catalysis, however, is not always straightforward, especially when generation of the electrophile is itself an acid-base reaction. Since this is the case in the present situation, we have used the kinetic isotope effect to provide primary evidence to show which of the two substitution steps in aromatic mercuration is rate determining.

Results

The hydrogen-deuterium isotope effect on the mercuration of benzene was determined by measuring rates of reaction of benzene and benzene-d_6 under exactly the same conditions. Mercuric acetate at an analytical concentration of 0.051 M was the source of mercury(II); the reaction mixtures also contained perchloric acid and water at analytical concentrations of 0.32 and 0.23 M, respectively. Under these conditions, 85% of the mercury(II) is present as acetatomercury(II) perchlorate ion pairs and the rest is present as mercuric acetate; the concentration of free perchloric acid is 0.08 M. Essentially none of the mercuration reaction occurs through mercuric acetate, 90% takes place through acetatomercury(II) perchlorate ion pairs, and the rest takes place through mercuric perchlorate ion triplets. Since the conversion of mercuric acetate to acetatomercury(II) perchlorate ion pairs is nearly complete, the position of this equilibrium does not change very much during the course of the mercuration reaction and good second-order kinetic behavior was observed throughout these measurements.

The results of these experiments are presented in Table I; the kinetic isotope effect (k_H/k_D) is 6.0 ± 0.1 at 25°.[8]

TABLE I

RATES OF MERCURATION OF BENZENE AND BENZENE-d_6 IN ACETIC ACID SOLUTION AT 25°[a]

$k_H/k_D = 6.01 \pm 0.13^b$

Aromatic substrate	Concn (M) of HAr	10^2k_{obsd} (M^{-1} min^{-1})
C_6H_6	0.229	1.63
C_6H_6	0.229	1.68
C_6H_6	0.229	1.57
C_6H_6	0.189	1.70
		1.65 ± 0.029^b
C_6D_6	0.169	0.268
C_6D_6	0.169	0.284
C_6D_6	0.169	0.274
C_6D_6	0.169	0.273
		0.275 ± 0.0034^b

[a] By mercuric acetate, $[Hg^{II}]_{t=0} = 0.051$ M; $[H_2O]_{analyt} = 0.23$ M; $[HClO_4]_{analyt} = 0.32$ M. [b] Standard deviation of the mean value.

Discussion

Kinetic Isotope Effect.—The mercuration of benzene-d_6, under conditions where the acetatomercury(II) perchlorate ion pair is the principal electrophile, is six times slower than the mercuration of ordinary benzene. This is a large hydrogen/deuterium rate ratio, as large as the isotope effects usually found for aromatic substitution under conditions where other evidence shows that the second step of substitution (eq 2) is fully rate determining.[9] It may be concluded, therefore, that the slow step in the mercuration of benzene by acetatomercury(II) perchlorate ion pairs is proton removal from the σ-complex intermediate.[10]

The isotope effect by itself, however, does not fix the mechanism of the mercuration reaction, for it permits no conclusion to be drawn about the relative concentration of the σ complex. This species could either be a high-energy intermediate always present in low

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(4) For recent summaries of the evidence, see H. Zollinger, *Advan. Phys. Org. Chem.*, **2**, 164 (1964); E. Berliner, *Progr. Phys. Org. Chem.*, **2**, 253 (1964).

(5) Aromatic hydrogen exchange and nitration by nitronium ion salts were once thought to be exceptions to this general mechanism, and more elaborate reaction schemes were proposed for these two cases. These elaborations, however, are not consistent with the results of more recent investigations.[6,7]

(6) (a) A. J. Kresge and Y. Chiang, *J. Am. Chem. Soc.*, **81**, 5509 (1959); **83**, 2877 (1961); (b) *Proc. Chem. Soc.*, 81 (1961); (c) J. Colapietro and F. A. Long, *Chem. Ind.* (London), 1056 (1960); J. Schulze and F. A. Long, *J. Am. Chem. Soc.*, **86**, 331 (1964); (d) B. C. Challis and F. A. Long, *ibid.*, **87**, 1196 (1965).

(7) W. S. Tolgyesi, *Can. J. Chem.*, **43**, 343 (1965).

(8) This result was published in preliminary form: A. J. Kresge and J. F. Brennan, *Proc. Chem. Soc.*, 215 (1963).

(9) H. Zollinger, *Helv. Chim. Acta*, **38**, 1597, 1617, 1623 (1955); *Experientia*, **12**, 165 (1956).

(10) The isotope effect for mercuration by $HgOAc^+ClO_4^-$ alone is probably slightly less than the observed value ($k_H/k_D = 6.0$) for 90% reaction through $HgOAc^+ClO_4^-$ and 10% reaction through $Hg^{2+}(ClO_4^-)_2$. Since the isotope effect for uncatalyzed mercuration by $Hg(OAc)_2$ is 3.2,[11] it would seem that the isotope effect increases with increasing reactivity of the electrophile. But even if the effect for reaction through $Hg^{2+}(ClO_4^-)_2$ had the improbably high value of 10, the effect for $HgOAc^+ClO_4^-$ would still be 5.5. Although the mechanistic significance of small isotope effects is sometimes not clear, this is not true of large isotope effects[4,12] and there would seem to be little doubt that the present effect provides clear indication of carbon-hydrogen bond breaking in the rate-determining step.

(11) G. Goldman, Ph.D. Thesis, Purdue University, 1961; *Dissertation Abstr.*, **22**, 2209 (1961).

(12) F. H. Westheimer, *Chem. Rev.*, **61**, 265 (1961); J. Bigeleisen, *Pure Appl. Chem.*, **8**, 217 (1964).

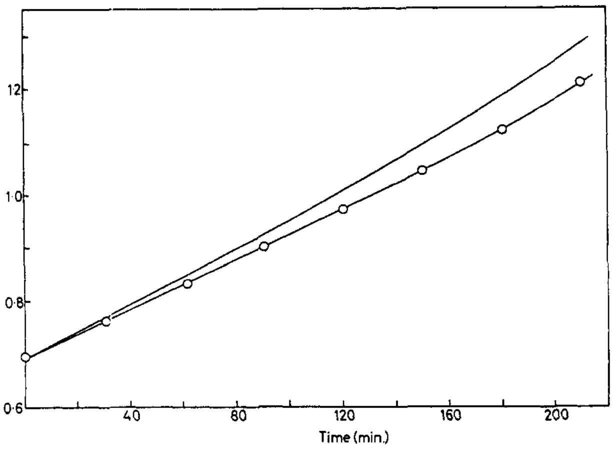

Figure 1.—Experimentally determined and calculated values of log $[C_6H_6]/[Hg^{II}]$: lower line, constant analytical perchloric acid concentration; upper line, analytical perchloric acid concentration increasing according to eq 5.

concentration, or, as has been observed in some cases,[13] it might be quasi-stable and present in appreciable concentrations at the early stages of the reaction. In the latter case, the process would not be kinetically first order in the reactant present in excess; in the limit of a σ complex much more stable than the substances from which it is formed, the reaction would be zero order in the excess reactant. Benzene was always present in considerable excess over mercury(II) both in the present study and in the investigations of the previous paper,[3] and in all cases the reaction was strictly first order in this reactant. This demands that the σ complex in mercuration be formed rapidly and reversibly; the gross mechanism for the substitution steps is therefore that shown in eq 3 and 4 with $v_{-1} >> v_1 > v_2$.

$$E^+ + C_6H_6 \underset{v_{-1}}{\overset{v_1}{\rightleftharpoons}} EC_6H_6^+ \qquad (3)$$

$$EC_6H_6^+ + B \xrightarrow{v_2} EC_6H_5 + HB^+ \qquad (4)$$

This analysis shows that the σ complex in mercuration reverts to reactants more readily than it produces substitution products. Such a situation is rare in electrophilic substitution for aromatic hydrogen; for the case of benzene, it has been observed only once before: $k_H/k_D = 1.7$ for the reaction of benzene with isopropyl alcohol and boron trifluoride at 0°.[14] It is of interest, therefore, to inquire into the reason for this behavior in the present case.

Steric hindrance to the introduction of the electrophile has most often been shown to be the cause of a partitioning of the σ complex which favors reactants over products.[4] Even here, however, there is evidence that another factor is operative, for, while there is a large isotope effect in the bromination of 1,3,5-tri-*t*-butylbenzene,[15] nitration of this substance does not show an isotope effect,[15] but nitration of the more crowded 2,4,6-tri-*t*-butylnitrobenzene does show one.[16] Similarly, the bromination of 3-bromodurene gives an isotope effect, but chlorination of the same substance does not.[17] This, together with the fact that the majority of the isotope effects found in aromatic substitution have occurred in sulfonations and iodinations, reactions which are reversible and in which, therefore, the carbon–electrophile bonds are weak, suggests that the relative strengths of the two bonds involved in σ-complex partitioning play a role in determining the course of this reaction. This explanation is, of course, consistent with the present case, for the carbon–mercury bond is known to be unusually weak.[18]

Constitution of the Product.—Electrophilic substitution for aromatic hydrogen is an acid-producing reaction. Because aromatic mercuration is also acid

$$E^+ + ArH \longrightarrow EAr + H^+ \qquad (5)$$

catalyzed, this rise in analytical acidity might cause rates of mercuration to increase as the reaction proceeds. Deviations from second-order kinetics consistent with this effect were in fact observed[3] under conditions of low acidity where the effect should be prominent, but these deviations were nevertheless ascribed to a different cause. At low acidities, the formation of acetatomercury(II) perchlorate ion pairs from mercuric acetate and perchloric acid is not complete.[3] As

$$Hg(OAc)_2 + HClO_4 \rightleftharpoons HgOAc^+ClO_4^- + HOAc \qquad (6)$$

mercury(II) is consumed during a kinetic run, some of the perchloric acid which had combined with mercuric acetate to form acetatomercury(II) perchlorate ion pairs is freed. This raises the concentration of free perchloric acid (but not the analytical acid concentration), and this, in turn, increases the fraction of mercury(II) which is positively charged thus accelerating the rate.

Figure 1 shows that the latter explanation of the deviations from second-order kinetics is essentially correct. The points represent experimentally determined values of log $([C_6H_6]/[Hg^{II}])$ for a run in which the initial analytical concentrations were $[HClO_4] = 0.200\ M$, $[Hg^{II}] = 0.100\ M$, $[C_6H_6] = 0.500\ M$, and $[H_2O] = 0.25\ M$. These data give a bimolecular rate constant at 75% reaction which is 20% greater than that at 0% reaction; they are correlated well by the lower line of Figure 1, which is calculated on the basis of a shift in the position of equilibrium of the reaction of eq 6 at a *constant analytical perchloric acid concentration*. The upper line of Figure 1, on the other hand, is calculated on the basis of an increase in analytical perchloric acid concentration according to the reaction of eq 5. This gives a bimolecular rate constant at 75% reaction which is 41% greater than that at 0% reaction, and it does not correlate the experimental data at all well.

Thus, although aromatic mercuration by acetatomercury(II) perchlorate ion pairs is formally an acid-producing reaction, the protons formed by substitution do not appear in the reaction mixture as strong acid. This situation can be accommodated only if, at some state of the reaction, the electrophile loses an acetate

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[13] E. Grovenstein, Jr., and U. V. Henderson, Jr., *J. Am. Chem. Soc.*, **78**, 569 (1956); L. G. Cannell, *ibid.*, **79**, 2927, 2932 (1957); M. Christen and H. Zollinger, *Helv. Chim. Acta*, **45**, 2057, 2066 (1962); V. A. Volodkin and V. V. Ershov, *Izv. Akad. Nauk. SSSR, Otd. Khim Nauk.*, 2022 (1962); B. T. Baliga and A. N. Bourns, *Can. J. Chem.*, **44**, 363, 379 (1966); ref 6b; ref 6d.

[14] G. A. Russell, *J. Am. Chem. Soc.*, **81**, 2017 (1959).

[15] P. C. Myhre, *Acta Chem. Scand.*, **14**, 219 (1960).

[16] P. C. Myhre and M. Beug, *J. Am. Chem. Soc.*, **88**, 1569 (1966).

[17] E. Baciocchi, G. Illuminati, and G. Sleiter, *Tetrahedron Letters*, 30 (1960).

[18] N. V. Sidgewick, "The Chemical Elements and Their Compounds," Oxford University Press, London, 1950, p 298; B. C. Gowenlock, J. C. Polanyi, and E. Warhurst, *Proc. Roy. Soc.* (London), **A218**, 269 (1953).

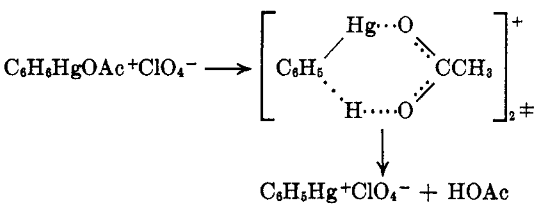
$$HgOAc^+ClO_4^- + C_6H_6 \longrightarrow C_6H_5Hg^+ClO_4^- + HOAc \quad (7)$$

residue to combine with the displaced proton. This furnishes a molecule of solvent which does not alter the acidity of the medium. Phenylmercuric acetate, therefore, is ionized in acetic acid solutions containing perchloric acid to approximately the same extent as is mercuric acetate, and the product of the mercuration reaction is the phenylatomercury(II) perchlorate ion pair.

Proton-Transfer Agent.—The rate-determining step in the reaction of benzene with positively charged mercury(II) in acetic acid solution is a proton-transfer reaction (eq 4). Free protons cannot exist in solution,[19] and, in a reaction such as this, they are always transferred to a base. In assigning a reaction mechanism for aromatic mercuration, therefore, it is of some significance to inquire what the proton transfer agent may be.

The only basic substances present in the reaction solution are mercuric acetate, water, and the solvent itself. Of these, the first two can be excluded as proton-transfer agents by considering uncatalyzed mercuration. This reaction shows a hydrogen isotope effect of 3,[11] and proton transfer must be at least partly rate determining. Consequently, an external base of sufficient strength to remove a proton from the σ complex would appear in the rate law. But the reaction is only first order in mercuric acetate,[20,21] and it has the same rate constant in 97% acetic acid (1.7 M water)[20] as in 99.5% acetic acid (0.3 M water).[21] If mercuric acetate and water do not serve as proton-transfer agents in uncatalyzed mercuration, they certainly cannot do so in the perchloric acid catalyzed reaction where they exist largely in their protonated forms.

This leaves only the solvent, acetic acid, to serve as an external base in the proton-transfer step of aromatic mercuration. The possibility cannot be excluded, however, that, as in some other aromatic substitutions,[22] proton removal may occur through a cyclic transition state in which an acetate residue present in the σ complex receives the proton. This transition


(8)

state presents an attractive route for ejection of the acetate group which, according to the arguments of the section above, must be lost before the final products are formed. If proton transfer occurs externally to the solvent, then this acetate group must either be lost before proton removal, giving a perhaps improbable dipositive intermediate, or after proton removal by subsequent ionization of first-formed phenylmercuric acetate.

Experimental Section

The kinetic method and materials used have already been described in the first paper of this series.[3] Benzene-d_6 (Volk, reagent grade) had a deuterium content of 99.5 atom %.

Registry No.—Perchloric acid, 7601-90-3; benzene, 71-43-2; benzene-d_6, 1076-43-3; acetatomercury(II) perchlorate ion, 7648-28-4.

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