8. *The Kinetics and Mechanisms of Aromatic Halogen Substitution. Part II.* Partial Rate Factors for the Acid-catalysed Bromination of Toluene by Hypobromous Acid.*

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The ratio of isomers produced in the acid-catalysed bromination of toluene by hypobromous acid in aqueous dioxan as solvent has been determined, by the method of isotopic dilution, as: *ortho*-, 70·3%; *meta*-, 2·3%; *para*-, 27·4%; negligible side-chain substitution accompanies the reaction. Under the same conditions, the kinetic form for the bromination both of toluene and of benzene is $-d[BrOH]/dt = k[ArH][BrOH][H^+]$, toluene reacting 36·2 times faster than benzene. These results are discussed in conjunction with those established for other electrophilic substitutions.

RATES of nitration at the various positions in the aromatic nucleus, relative to those for benzene, have been determined for a number of monosubstituted derivatives of benzene. In contrast, there has been little study of other electrophilic substitutions. In the field of halogenations, there are some scattered observations from which estimates of some of the required isomer ratios can be made, particularly for *para*-substitution determined by molecular halogens (cf. de la Mare, *J.*, 1954, 4450). There are, however, no cases, so far as we are aware, in which complete analyses have been carried out under conditions in which the mechanism of halogenation has been determined, and hence no proper estimates of the partial rate factors, *ortho*-, *meta*-, and *para*- to any single substituent are yet available.

The isotope-dilution method is particularly suitable for the determination of these ratios, and can with proper safeguards be used for the estimation of quite small proportions of isomeric products. The present paper describes the use of this method in determining the proportions of isomers produced in the bromination of toluene, with hypobromous acid as source of electrophilic halogen, under catalysis by perchloric acid, in a mixture of dioxan and water at 25°. The conditions were chosen so that it could be established by kinetic methods that the reagent was a positively charged brominating species, either the brominium cation, Br^+, or the hypobromous acidium ion, $BrOH_2^+$.

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* Part I, *J.*, 1954, 1290.

EXPERIMENTAL

Materials and Methods.—Dioxan was refluxed with 2N-hydrochloric acid in a stream of nitrogen for 12 hr., and was then partially dried with solid sodium hydroxide. Peroxidic impurities were then removed by shaking with ferrous sulphate. The product was stored over ferrous sulphate in an atmosphere of nitrogen in the dark, and was distilled from sodium hydroxide when required. Toluene (sulphur-free) was fractionated; it had b. p. 110°/758 mm., n_D^{25} 1·4893. Benzene (" AnalaR ") was fractionated and had b. p. 80°/760 mm., n_D^{25} 1·5015. Hypobromous acid was prepared by shaking together bromine, water, and silver phosphate; the product was filtered, distilled under reduced pressure, shaken with carbon tetrachloride, centrifuged, and stored over mercuric oxide at 0°; it was used as soon as possible after preparation. Radioactive hypobromous acid was prepared similarly, irradiated ammonium bromide, supplied by A.E.R.E., Harwell, being introduced into the mixture of bromine and water before addition of the silver phosphate. All measurements of radioactivity were made with the isotope ^{82}Br, after complete decay of the shorter-lived isotope, ^{80}Br. Reference samples of the bromobenzoic acids were prepared by recrystallisation of commercial specimens; they had the following m. p.s : *ortho*-, 146·5°; *meta*-, 155°; *para*-, 251°. Reference samples of the bromotoluenes were prepared similarly, and had the following properties : *ortho*-, f. p. −25·8°; *para*-, f. p. 26·8°. Other reagents were of analytical-reagent quality.

Measurements of radioactivity were made with standard equipment. All counts were corrected for background (usually about 10 counts per min.), and for radioactive decay, as has been described elsewhere (cf. de la Mare, *J.*, 1955, 3196).

Kinetics of Disappearance of Hypobromous Acid.—The reactions were carried out in blackened bottles, and were followed iodometrically. Blank determinations were carried out accompanying each run, to allow a small correction to be made for the decomposition of hypobromous acid in the solvent. The following is an example of a typical kinetic run. From a solution of toluene (0·00799M), hypobromous acid (0·00133M), and perchloric acid (0·00320M), all in 50% dioxan (a mixture of equal volumes of dioxan and water, measured at room temperature), samples (25 ml.) were removed at intervals for titration against 0·00930N-sodium thiosulphate, with starch as indicator. A blank, with toluene omitted, was run side by side with this measurement.

Reaction			Blank		
Time (min.)	Titre (ml.)	10^2k_1 (min.$^{-1}$)	Time (min.)	Titre (ml.)	10^2k_1 (min.$^{-1}$)
0·0	7·17	—	0·0	7·84	—
5·38	5·85	3·78	5·10	7·68	0·40
10·67	4·88	3·61	11·30	7·52	0·37
15·12	4·23	3·49	17·60	7·40	0·33
19·55	3·66	3·44	27·20	7·33	0·25
27·40	2·95	3·24			

The quoted values of k_1, the first-order rate-coefficients for the disappearance of hypobromous acid, have been calculated by using the formula $k_1 = 2{\cdot}303 \log_{10} [a/(a-x)]/t$. They fall through the course of the reaction, partly because the rate is dependent on the concentration of toluene, and also partly because no allowance has yet been made for the rate of spontaneous decomposition of hypobromous acid. Since this reaction is of different kinetic form from the main reaction, the results quoted below are all initial second-order rate-coefficients, obtained in the following way. The initial values of k_1 were obtained by graphical extrapolation, and from these were subtracted the initial rate of decomposition of the blank. The resulting corrected initial first-order rate-coefficients were converted into second-order rate-coefficients by dividing by the concentration of aromatic compound. The latter are given in units l. mole^{-1} min.$^{-1}$, and all refer to a temperature of 25·0°. The following values show the results of varying the concentrations of reactants.

(i) Toluene, 0·0080M; $HClO_4$, 0·0032M :

BrOH (M)	0·0008	0·0013	0·0018
k_2 (l. mole^{-1} min.$^{-1}$)	4·30	4·46	4·25

(ii) $HClO_4$, 0·0032M; BrOH, *ca.* 0·0013M :

Toluene (M)	0·0050	0·0080	0·0090	0·0170
k_2 (l. mole^{-1} min.$^{-1}$)	4·50	4·46	4·34	4·35

(iii) BrOH, *ca.* 0·0013M; toluene 0·008—0·015M :

$HClO_4$ (M)	0·0016	0·0032	0·0048	0·0065	0·0081	0·0096
k_2 (l. mole^{-1} min.$^{-1}$)	1·7	4·4	6·4	8·6	10·6	12·3
k_2/H^+ (l.^{2} mole^{-2} min.$^{-1}$)	1060	1380	1330	1320	1310	1280

The results show very clearly that, at 25° in 50% dioxan as solvent, the kinetic form of the reaction is $-d[BrOH]/dt = k[ArH][BrOH][H^+]$. For toluene, the mean value of k is 1300 l.^{2} mole^{-2} min.$^{-1}$. For benzene, the same kinetic form was observed, as is shown by the following results, all under the same conditions of solvent and temperature:

(i) Benzene, 0·014M; $HClO_4$, 0·066M:

BrOH (M)	0·0009	0·00128
k_2 (l. mole^{-1} min.$^{-1}$)	2·44	2·24

(ii) $HClO_4$, 0·066M, BrOH, 0·0013M:

Benzene (M)	0·011	0·014	0·016
k_2 (l. mole^{-1} min.$^{-1}$)	2·39	2·24	2·37

(iii) BrOH, *ca.* 0·0013M; benzene, 0·011—0·016M:

$HClO_4$ (M)	0·027	0·044	0·066	0·088	0·111	0·133	0·141
k_2 (l. mole^{-1} min.$^{-1}$)	0·91	1·52	2·38	3·0	4·2	4·9	5·2
k_2/H^+ (l.$^{-2}$ mole^2 min.$^{-1}$)	33·7	34·6	36·4	34·1	37·9	36·8	36·9

From these values, for benzene, k = 35·9 l.^{2} mole^{-2} min.$^{-1}$ in 50% dioxan at 25°.

Proportions of Isomers Formed in the Bromination of Toluene.—(a) para-*Substitution.* Radioactive *p*-bromotoluene was prepared from *p*-toluidine by the Sandmeyer procedure, including with the hydrobromic acid and cuprous bromide *ca.* 3 g. of radioactive ammonium bromide. The product was crystallised several times from ethanol at low temperature, giving a material of m. p. 26·8°.

To a solution (8 l.) of hypobromous acid and perchloric acid (0·0130M) in 50% dioxan was added toluene (27·31 g.). After 6 min., the titre of a 25-ml. aliquot portion of the reaction mixture had fallen from 6·76 ml. of 0·1104N-$Na_2S_2O_3$ to 1·50 ml. In the same time, a blank solution had fallen in titre by 0·20 ml. The reaction was stopped by adding sodium formate and alkali. To 7700 ml., which, from the fall in titre corrected for blank decomposition, should have contained 14·7 g. of mixed bromotoluenes, were added 2·915 g. of radioactive *p*-bromotoluene. The resulting mixture was extracted with ether. The ether-extract was washed with water and fractionated. There were obtained 11 g. (63%) of crude bromotoluenes, b. p. 175—185°/760 mm., f. p. −10·9°. This material was redistilled twice, *ca.* 1 g. of distillate being rejected each time. The product then had f. p. −11·1°, and was crystallised twice from ethanol at low temperature. The product (1 g.) had m. p. 26·8°. The specific activity of this material was compared in ethanol with that of the original radioactive *p*-bromotoluene. The latter (0·00782M) gave a count of 129/min. The former (0·0281M) gave counts which, on interpolation to the same time, had a value of 195 counts/min. Hence the reaction mixture, after addition of radioactive material, contained 6·94 g. of *p*-bromotoluene, of which 4·02 g. (27·4%) had been produced in the reaction.*

(b) ortho-*Substitution.* The procedure was essentially that used for the *para*-isomer. The reaction mixture contained 0·0391M-toluene, 0·0181M-hypobromous acid, and 0·013M-perchloric acid. After reaction for 20 min., 11·63 g. of mixed bromotoluenes had been produced. To the reaction mixture were added 3·973 g. of radioactive *o*-bromotoluene, m. p. −25·9°, which had been prepared from *o*-toluidine. The recovered crude bromotoluenes (10 g.) were oxidised by 36 hours' refluxing with aqueous potassium permanganate. There were recovered 4 g. of bromobenzoic acids, m. p. 138°; these were recrystallised many times from water, with rejection of early fractions which consisted largely of *p*-bromobenzoic acid. There were finally obtained 1·3 g., m. p. 146·5°, unchanged in m. p. or in specific activity by further recrystallisation. The specific activity was determined in ethanol, and was compared with that of the original *o*-bromotoluene, and with that of a specimen of *o*-bromobenzoic acid, m. p. 146·5°, prepared from the latter by a similar oxidation. The values obtained were respectively, for a 0·382M-solution, 84·1, 254, and 260 counts/min. By using the mean specific activities of the two reference materials for calculation of the degree of dilution, it follows that 70·2% of *o*-bromotoluene was produced.

(c) meta-*Substitution.* It would be impracticable to use the above method for determining the % of *meta*-substitution, since the degree of dilution of the active sample would be too high. Instead, the reaction was carried out by using radioactive hypobromous acid. The reaction mixture contained initially 0·0516M-toluene, 0·00261M-hypobromous acid, and 0·013M-perchloric acid. After 20 min., its decrease in titre showed that 0·4554 g. of mixed bromotoluenes had been produced. The reaction was stopped, and to the mixture were added 9·67 g. of inactive *m*-bromotoluene. The crude mixture of bromotoluenes, isolated in the usual way, was oxidised

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* The f. p. of the crude bromotoluenes, in conjunction with the data of Van der Laan (*Rec. Trav. chim.*, 1907, **26**, 297) gives a value of 29·3%.

as described above. The resulting mixture of bromobenzoic acids was purified by fractional crystallisation, giving 1·5 g. of *m*-bromobenzoic acid, m. p. and mixed m. p. 155°. This material was still contaminated with traces of isomers of high specific activity. Successive crystallisations gave specific activities, expressed in counts/min. of an alkaline solution of 0·1603 g. in 15·0 ml. (0·0532M), of 168, 157, 150, 127, and 125. The limiting specific activity, on comparison with that of the original hypobromous acid, which had been converted into bromide ion for counting and had an activity of 708 counts/min. for a 0·000320N-solution, corresponds with the formation of 2·3% of *m*-bromotoluene.

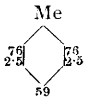
(d) *Side-chain substitution.* In the crude mixture of bromotoluenes isolated in one of the above reactions, benzyl bromide was estimated gravimetrically as silver bromide. There appeared to be produced in the bromination less than 0·01% of the product of side-chain substitution.

DISCUSSION

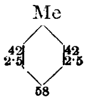
All the values given above are entirely independent; their sum, 99·9%, accounts for all the measured reaction within experimental error, and this is a partial check on the reliability of the values given. For the purposes of discussion, the following rounded-off values are adopted: *ortho*-, 70·3%; *meta*-, 2·3%; *para*-, 27·4%; side-chain, 0·0%.

The fact that side-chain substitution is nearly absent makes it certain that toluene is brominated in this reaction by an electrophilic process rather than by one involving bromine atoms. The kinetic form makes it clear that, as in investigations by other workers in similar conditions (Derbyshire and Waters, *J.*, 1950, 564; Shilov and Kaniaev, *Compt. rend. Acad. Sci. U.S.S.R.*, 1939, **24**, 890; Branch and Brynmor Jones, *J.*, 1954, 2317), the reagent is either Br^+ or $BrOH_2^+$.

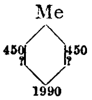
Combination of the relative rates of reaction of benzene and toluene with the above isomeric proportions gives the following values for the partial rate factors in the bromination of toluene. For comparison are given also values for nitration (Cohn, Hughes, Jones, and Peeling, *Nature*, 1952, **169**, 291), and, incompletely, for bromination by molecular bromine (Robertson, de la Mare, and Swedlund, *J.*, 1953, 782).



Br^+ or $BrOH_2^+$
(I)



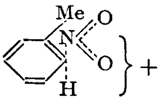
NO_2^+
(II)



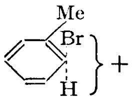
Br_2
(III)

The similarity between the results obtained for bromination with positive bromine and those available for nitration by the nitronium ion is remarkable. In both cases, the *meta*-position is activated by only a small factor, whereas the *para*-position is considerably more activated. Examination of the values for *ortho*-substitution suggests that there is somewhat more resistance to entry of the nitro- than to that of the bromo-group *ortho* to a methyl substituent. It is often considered (cf. Holleman, *Chem. Rev.*, 1925, **1**, 187) that steric hindrance is in general greater for *ortho*-bromination than for *ortho*-nitration; but this is a conclusion reached by consideration of data for molecular bromination as compared with ionic nitration. When both reactions are carried out with positively charged reagents, a different situation appears to arise, as shown by the present comparison.

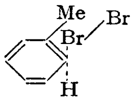
That steric hindrance should be greater for *ortho*-nitration than for *ortho*-bromination is not unreasonable if consideration is given to the most probable geometry of the transition state for nitration. The nitronium ion is linear, but, in reacting as an electrophilic reagent, its shape must be distorted towards that of the nitro-group. Its final most stable conformation is coplanar with the aromatic ring; and during the course of the reaction, while both the entering and the leaving group are still bound to the ring, repulsions involving the leaving hydrogen atom must not become too large. It follows that, as the nitro-group approaches the aromatic ring and displaces the proton downwards, so that the attacked carbon atom approaches the tetrahedral configuration (a type of transition state favoured by most writers on aromatic substitution; cf. Hughes, Ingold, and their co-workers, *J.*, 1937, 1257; 1941, 608), the nitro-group will tend to maintain itself so that its oxygen atoms lie parallel with the aromatic ring, as is indicated in formula (IV), the hydrogen atom lying below the entering group :



(IV)



(V)



(VI)

The effective radius of the nitro-group in the direction of the flanking *ortho*-methyl group is likely, therefore, to be greater than that of the spherical bromine substituent (formula V).

It seems, therefore, that the intrinsic reactivity of the position *ortho* to a methyl group is larger than that of the corresponding *para*-position. This is attributed essentially to the inductive influence of the substituent. Electrons are made available inductively more readily by electron-releasing substituents at the *ortho*- than at the *para*-position. In this connection there is no means of distinguishing between the inductive effect working through the bonding system and the same effect working directly through space; but analogy with the apparently greater selectivity of the *para*- than of the *ortho*-position for the acceptance of electrons by conjugative relay (cf. Waters, *J.*, 1948, 727; Hughes and Ingold, *J.*, 1941, 608; Bradfield, *Trans. Faraday Soc.*, 1941, **37**, 746) makes us think that the direct effect may be of some importance in these reactions.

The partial rate-factor for the bromination of toluene in the *para*-position, with molecular bromine as reagent, is 1990 (Robertson, de la Mare, and Swedlund, *loc. cit.*; de la Mare, *J.*, 1954, 4450). With this reagent, *para*-substitution predominates, accounting for 69% of the product. The contrast in proportion of *para*-substitution between molecular and ionic bromination might at first sight be considered to involve only differential steric hindrance, Br_2 being larger than Br^+. Consideration of models (cf. formula VI) suggests, however, that the eliminated bromide ion, coming from a bromine molecule, is unlikely to be in a situation where it would greatly be interfered with by an *ortho*-methyl group. It is considered probable, therefore, that the larger amount of *para*-substitution, found when molecular bromine is the reagent, is partly a reflection also of the relatively greater importance of conjugative electron-release with these molecular reagents.

De la Mare and Robertson (*J.*, 1948, 100) have proposed that inductive, as compared with electromeric, effects of substituents are called out more powerfully in electrophilic substitutions determined by formally positive than by comparable formally neutral reagents. This theory was developed from consideration of certain differences between nitration by the nitronium ion and halogenation by halogen molecules. A second factor requires consideration in regard to the latter reaction, namely, that the halogen molecule appears to be particularly effective in evoking electromeric electron release, and a theoretical interpretation of this fact has been given elsewhere (*J.*, 1949, 2871).

The present investigation represents a stage in an experimental approach towards a test of the theory by comparing reagents which, though of different charge-type, introduce the same group into the aromatic nucleus. The results, as indicated for example in comparisons between (I) and (III), are consistent with the theory outlined. Berliner and Berliner (*J. Amer. Chem. Soc.*, 1954, **76**, 6179) have, on the basis of independent experiments, reached similar theoretical conclusions. H. C. Brown and Nelson (*ibid.*, 1953, **75**, 6292) appear to take a similar view concerning the relatively greater importance of conjugative influences in halogenation than in nitration. It is surprising, therefore, that H. C. Brown and McGary (*ibid.*, 1955, **77**, 2310) should have so misunderstood the paper by Robertson, de la Mare, and Swedlund (*loc. cit.*) as to state that the latter authors regard as anomalous those differences, which they discuss, between these reactions. The theory set forth by the latter authors was regarded by them, and is regarded by the present writers, as being in accordance with the experimental results so far ascertained.

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