Kinetics and Mechanism of Aromatic Halogenation by Hypohalous Acids. Part II.* Directive Effects of Substituents in the Bromination of Aromatic Ethers by Hypobromous Acid.

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A kinetic study of the bromination of a wide range of aromatic ethers by hypobromous acid in 75% acetic acid has shown that the relative directive influences of *n*-alkoxy-groups are in close agreement with the values found earlier in the chlorination of similar ethers in 99% acetic acid.

The effects of substituents both in the alkyl group and in the phenyl nucleus on the rate of bromination have been studied. With halogen substituents the rates decrease in the order F > Br > Cl, a result which provides additional evidence for a mesomeric electron release in the halogens which is greater in fluorine than in bromine and chlorine. Experiments on iodo-ethers were complicated by the intrusion of a secondary reaction between the iodine atom and the hypobromous acid.

ONCE it had been established that the bromination of aromatic ethers, such as *p*-nitro-anisole and *p*-nitrophenetole, by hypobromous acid in 75% acetic acid is a reaction of the first order with respect to each of the reactants (cf. Part I *), and well suited to accurate measurement, it became possible to extend the kinetic study to a wide variety of mono-, di-, and poly-substituted aromatic ethers, and to analyse the rate constants obtained in terms of the parameters of the modified Arrhenius equation, $k = PZ \exp (-E/\mathbf{R}T)$. This makes it possible to enlarge existing knowledge of the rates of nuclear substitution and also affords an opportunity to compare the reactivity of a carefully selected family of compounds with different electrophilic reagents—in this case the chlorine molecule and the brominium ion Br⁺, or its solvated form, H_2OBr^+. Earlier attempts to study bromination in 50% acetic acid with bromine were complicated by the formation of HBr_3, the reaction undergoing a marked retardation as hydrogen bromide was liberated or when it was added initially (cf. *J.*, 1929, 2810).

The rate constants now obtained for the bromination of a variety of phenyl ethers by hypobromous acid in 75% acetic acid solution at 20°, are summarised in Tables 1 and 2. In all cases the reaction was of the second order, and satisfactory constants were obtained over 80—90% of the reaction range.

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TABLE 1. *Rate constants for the reaction of the ethers* 1 : 2 : 4-RO·C$_6$H$_3$XY *with hypobromous acid in* 75% *acetic acid.* Values of $k_{20°}$ (l. mole^{-1} sec.$^{-1}$).

X	Y	R: Me	Et	Pr^n	Bu^n	Am^n	Pr^i	Bu^i	Am^i	CH$_2$Ph
H	NO$_2$	0·162	0·330	0·353	0·360	0·359	0·642	—	—	0·113
Cl	Cl	0·283	0·566	0·634	0·645	0·652	1·034	—	—	0·205
Br	Br	0·373	0·747	0·852	0·860	0·880	1·36	1·01	0·974	0·265
Cl	CO$_2$Et	0·0648	0·130	0·145	0·153	0·153	0·224	—	—	—
Br	CO$_2$Et	0·0881	0·177	0·200	0·205	0·206	0·319	—	—	—
Cl	CO$_2$Me	0·0626	0·124	0·140	—	—	0·208	—	—	—
Br	CO$_2$Me	0·0840	0·166	0·192	—	—	0·305	—	—	—
CO$_2$Me	Cl	0·256	—	—	—	—	0·840	—	—	—
CO$_2$Me	Br	0·345	0·686	—	—	—	1·02	—	—	—

X	Y	R: [CH$_2$]$_2$Br	[CH$_2$]$_3$Br	p-NO$_2$·C$_6$H$_4$·CH$_2$	o-NO$_2$·C$_6$H$_4$·CH$_2$	CH$_2$·CO$_2$H *	[CH$_2$]$_2$CO$_2$H	CHMe·CO$_2$H
Cl	Cl	0·0455	0·160	—	—	0·0230	0·136	0·0274
H	F	—	—	—	15·6	9·5	—	—
H	Cl	—	—	11·7	9·5	4·1	35	5·0
H	Br	—	—	—	—	5·6	51	—

* Methyl ester = 0·102.

TABLE 2. *Rate constants for the reaction of di- and poly-substituted phenyl ethers* (conditions as in Table 1).

Series	R: Me	Et	CH$_2$Ph	CH$_2$·CO$_2$H	CHMe·CO$_2$H
2 : 6-Dichlorophenyl	—	—	—	—	0·003
2 : 6-Dibromophenyl	0·008	—	—	—	—
2 : 4-Dichloro-3 : 5-xylyl	—	—	—	3·1	—
4-Chloro-2-nitro-3 : 5-xylyl	0·742	1·42	0·493	—	—

The values of the relative directive powers derived from these rate constants are given in Tables 3 and 4. The effects of variations in the alkyl of the alkoxy-group upon the rates of bromination of the ethers RO·C$_6$H$_3$XY are expressed in the form $100k_{XY}^{OR}/k_{XY}^{OMe}$, where k_{XY}^{OR} and k_{XY}^{OMe} are the rates of substitution of 1 : 2 : 4-RO·C$_6$H$_3$XY and of the corresponding methyl ether, respectively.

TABLE 3. *Relative directive influences of alkyl groups in the bromination of ethers* 1 : 2 : 4-RO·C$_6$H$_3$XY *by hypobromous acid in* 75% *acetic acid.* Values of $100k_{XY}^{OR}/k_{XY}^{OMe}$.

X	Y	R: Et	Pr^n	Pr^i	Bu^n	Bu^i	Am^n	Am^i	Octyl^n
H	NO$_2$	204	219	396	223	—	223	—	218
Cl	Cl	201	224	365	228	—	231	—	—
Br	Br	200	229	366	231	271	236	262	—
Cl	CO$_2$Et	201	224	345	236	—	236	—	—
Br	CO$_2$Et	201	227	362	233	—	234	—	—
Cl	CO$_2$Me	198	224	331	—	—	—	—	—
Br	CO$_2$Me	198	229	362	—	—	—	—	—
CO$_2$Me	Cl	—	—	328	—	—	—	—	—
CO$_2$Me	Br	199	—	296	—	—	—	—	—
	Mean	200	225	—	230	271	232	262	218
Mean values in chlorination *		199	223	440	223	216	221	—	207

* Brynmor Jones, *J.*, 1935, 1832.

Discussion.—The influences of alkoxy-groups on the rates of reaction are in the order n-PrO > EtO > MeO. This sequence was to be expected from the studies on chlorination, but the data in Table 3 show a striking similarity between the values in the two reactions (Brynmor Jones, *J.*, 1935, 1831). Although bromination and chlorination are analogous processes, it could not be foreseen that the relative directive effects of so wide a range of alkoxy-groups would be so similar, especially since in bromination in 75% acetic acid the attacking reagent is either the brominium ion or the solvated cation H$_2$OBr$^+$ (Branch and Brynmor Jones, *J.*, 1954, 2317), while in chlorination it is the chlorine molecule. By contrast, bromination of the ethers p-RO·C$_6$H$_4$X in 50% acetic acid containing an excess of hydrogen bromide gave values of MeO : EtO : Pr^{i}O of 100 : 231 : 711 (cf. *J.*, 1929, 2810),

while in the nitration of the ethers p-RO·C$_6$H$_4$·OMe the values were 100 : 164 : 180 (Robinson and Smith, *J.*, 1926, 392).

As in chlorination, there is a point when further increase in the chain length of the group R is accompanied by a slight fall in the directive effect of the alkoxy-group. This is shown here at the octyl ether, but in chlorination the decrease becomes more marked as the chain is lengthened to cetyl (Brynmor Jones, *loc. cit.*). In the nitration of quinol ethers, on the other hand, the cetyl ether has the highest reactivity of all the *n*-alkyl ethers.

The effect of branching in the alkyl chain is, in general, very similar in both halogenation reactions. Progressive substitution of the methyl group results in substantial increases in the rates of reaction. The *iso*propoxy-group, however, is unique among alkoxy-groups in that its directive influence not only varies in the same reaction from one series of ethers to another, but also in that the values differ appreciably from one reaction to another (cf. *J.*, 1938, 1854; 1954, 1775).

All attempts to prepare a *tert.*-butyl ether in the state of purity demanded by this kind of investigation failed because of decomposition during distillation, and no firm value of the rate constants could be obtained.

The influence of an electron-attracting bromine atom and of a carboxyl group in modifying the directive power of an alkoxy-group is shown in Table 4. These values reveal a difference in relative directive powers of the O·[CH$_2$]$_n$·Z groups in passing from the simple p-substituted ethers to the 2 : 4-disubstituted compounds. This was not observed in chlorination when the alkoxy-groups were the simple ones.

TABLE 4. *Effect of electron-attracting substituents in the alkyl group.* Values of $100k_{XY}^{OR}/k_{XY}^{OMe}$ for the compounds ArO·[CH$_2$]$_n$·Z.

Z	Ether	$n = 1$	$n = 2$	Z	Ether	$n = 1$	$n = 2$
CO$_2$H	p-Chlorophenyl	6	52	CO$_2$H	2 : 4-Dichlorophenyl	8	48
,,	p-Bromophenyl	6	55	CH$_2$Br	2 : 4-Dichlorophenyl	16	59

The results in this table illustrate too the familiar " damping effect " of saturated hydrocarbon chains on the transmission of the influence of a polar substituent (Ingold, *Ann. Rep.*, 1926, **23**, 134). This effect can be measured by the percentage change in directive power which occurs in passing from, for instance, ArO·[CH$_2$]$_n$·Et to ArO·[CH$_2$]$_n$·Pr^i.

TABLE 5. *The damping effect of hydrocarbon chains on the transmission of an inductive effect; relative directive powers in the ethers* 1 : 2 : 4-RO·C$_6$H$_3$XY. Values of $100k_{XY}^{OR}/k_{XY}^{OMe}$.

R:	Me	Et	Pr^i	Pr^n	Bu^i	Bu^n	Am^i
	100	200	366	225	271	228	236
Increase, %, in directive power			83		20		3·5

The values for this increase are similar to those for the percentage of *m*-isomer formed in the nitration of Ar·[CH$_2$]$_n$·$\overset{+}{N}$Me$_3$ (Ingold, *Rec. Trav. chim.*, 1929, **48**, 805).

The benzyl ethers studied have directive powers close to the mean value found in chlorination (Table 6); the types contained a single powerful deactivating nitro-group, two halogen atoms, or a nitro-group and a halogen atom. The directive influences of the substituted benzyloxy-group in the few p-halogenophenyl ethers examined (Table 7) were also in fair agreement with previous values, although the rate of bromination of these ethers is extremely rapid, and the results have not therefore the same accuracy as those for ethers having lower rates of substitution.

Effect of Nuclear Substituents.—The very high reactivities of monosubstituted ethers with hypobromous acid in 75% acetic acid make it impossible to measure directly the relative effects of most p-substituents, but the required values may be obtained from the measured rates for certain 2 : 4-disubstituted ethers if the simple additive relation, $k_X^{OR}/k_X^{OR} = k_X^{OMe}/k_X^{OMe}$, is assumed to exist between the effects of substituent groups.

For example, the rates of bromination of p-chlorophenoxy- and 2 : 4-dichlorophenoxy-acetic acids are 4·1 and 0·023 l. mole^{-1} sec.$^{-1}$, respectively, and, since that of 2 : 4-dichloro-anisole is 0·283, the calculated value for p-chloroanisole is 50·4 l. mole^{-1} sec.$^{-1}$. From the

values thus calculated (Table 8) it is seen that the relative rates are in the same order as that for chlorination, namely, $NO_2 < CO_2Me < CO_2Et < Cl < Br < F(<H)$.

The order calculated for the halogens, $Cl < Br < F$, has been confirmed by direct measurements (Table 9), and it affords additional evidence for a mesomeric electron release increasing from bromine to fluorine.

TABLE 6. *Relative directive influence of the benzyl group in the ethers* $ArO \cdot CH_2Ph$. Values of $100 k^{O \cdot CH_2Ph}/k^{OMe}$.

Ar	Bromination by HOBr	Chlorination
p-Nitrophenyl	70	—
2 : 4-Dichlorophenyl	72	68 *
2 : 4-Dibromophenyl	71	64 *
4-Chloro-2-nitro-3 : 5-xylyl	67	—

* Cf. *J.*, 1931, 2903.

TABLE 7. *Relative directive powers of groups in the ethers* (I) $p\text{-}RO \cdot C_6H_4X$ *and* (II) $1 : 2 : 4\text{-}RO \cdot C_6H_3X_2$.

R :	$p\text{-}NO_2 \cdot C_6H_4 \cdot CH_2$	$o\text{-}NO_2 \cdot C_6H_4 \cdot CH_2$	$CH_2 \cdot CO_2H$	$[CH_2]_2 \cdot CO_2H$	$CHMe \cdot CO_2H$
(I; X = F)	—	15	9	—	—
(I; X = Cl)	21	17	8	61	19
(I; X = Br)	—	—	8	64	—
(II; X = Cl)	—	—	8	48	9

TABLE 8. *Calculated velocity constants for bromination of the ethers* $p\text{-}MeO \cdot C_6H_4X$.

X :	F	Cl	Br	CO_2Me	CO_2Et	NO_2
k_{20} (l. mole^{-1} sec.$^{-1}$)	108	50·4	68	11·1	11·5	0·16

TABLE 9. *Relative directive influences of the halogens.* Values of $100\ k_X^{OR}/k_{Cl}^{OR}$.

Series	Substituent Br	F	Series	Substituent Br	F
2 : 4-Disubstituted-phenyl alkyl ethers	135	—	2-Chloro-4-halogenoanisoles	130	—
p-Halogenophenoxyacetic acids	137	232	2-Bromo-4-halogenoanisoles	132	223
p-Halogenophenyl *o*-nitrobenzyl ethers	—	170 (approx.)	*p*-Halogenoanisoles (calc.)	135	217

EXPERIMENTAL

The acetic acid and hypobromous acid used in the kinetic experiments were purified by the methods given in Part I.

Most of the alkyl phenyl ethers were prepared by the following method. To the phenol (1·0 mole) in *cyclo*hexanone, anhydrous potassium carbonate (5—8 moles) and the alkyl iodide (1·2 moles) were added, and the solution was refluxed until a heavy sediment settled (usually 1—3 hr.). The sediment was filtered off and washed with acetone, and, after removal of the solvents from the filtrate, the residue was diluted with water and extracted with ether. The ether extract was washed successively with sodium hydroxide solution, water, sulphuric acid, and water, and dried (Na_2SO_4). The ether was then removed and the aromatic ether fractionated under reduced pressure. The physical constants of the ethers (and analyses in the case of new compounds) are recorded in Table 10.

2-Bromoethyl 2 : 4-*dichlorophenyl ether*, b. p. 134°/2 mm., was prepared in 50% yield by refluxing 2 : 4-dichlorophenyl and excess of potassium carbonate with ethylene dibromide in acetone (Found : C, 35·65; H, 2·6. $C_8H_7OCl_2Br$ requires C, 35·6; H, 2·6%). Appreciable quantities of 1 : 2-bis-(2 : 4-dichlorophenoxy)ethane, m. p. 134°, were also obtained.

3-Bromopropyl 2 : 4-*dichlorophenyl ether*, b. p. 148°/2 mm., was prepared similarly (Found : C, 38·0; H, 3·6. $C_9H_9OCl_2Br$ requires C, 38·1; H, 3·5%). Here only a trace of 1 : 3-bis-(2 : 4-dichlorophenoxy)propane, m. p. 94°, was isolated.

β-2 : 4-Dichlorophenoxypropionic acid, prepared by refluxing β-chloropropionic acid with 2 : 4-dichlorophenol in aqueous potassium hydroxide, had m. p. 93° after two crystallisations from alcohol.

Commercial samples of 2 : 4-dichlorophenoxyacetic acid, m. p. 146°, methyl 2 : 4-dichlorophenoxyacetate, m. p. 43°, and α-2 : 4-dichlorophenoxypropionic acid, m. p. 117°, were crystallised several times from methyl alcohol.

Methyl and ethyl 3-chloro-4-hydroxybenzoate (m. p.s 106° and 77°, respectively) gave the methyl and ethyl 4-alkoxy-3-chlorobenzoates by the standard methods.

3-Bromo-4-hydroxybenzoic acid, m. p. 156°, was obtained from *p*-hydroxybenzoic acid by the action of bromine in acetic acid; the methyl and ethyl 3-bromo-4-hydroxybenzoates had m. p. 107° and m. p. 102°, respectively. The methyl and ethyl 4-alkoxy-3-bromobenzoates (Table 10) were prepared by alkylation of these esters by standard methods.

5-Chloro-2-hydroxybenzoic acid, m. p. 172°, was prepared by the chlorination of salicylic acid in chloroform with dichloramine-T. The methyl ester melted at 47°, and the ethyl ester at 25°.

Salicylic acid and bromine in acetic acid gave 5-bromo-2-hydroxybenzoic acid, m. p. 165°; methyl ester, m. p. 60°. Alkylation of the 5-chloro- and 5-bromo-esters gave the 2-alkoxy-5-halogenobenzoates.

Most of the remaining ethers (Table 11) were either purchased or were available from previous studies. All were crystallised at least twice from alcohol. 2-Bromo-4-fluoroanisole, b. p. 87°/3 mm., was prepared by adding bromine in acetic acid (8 g. in 50 c.c.) during

TABLE 10. *Physical constants of the ethers* 1 : 2 : 4-RO·C₆H₃XY.

X	Y	R	M. p.	B. p./mm.	Found (%) C	Found (%) H	Formula	Reqd. (%) C	Reqd. (%) H
H	NO$_2$	Me	52·5°	—	—	—	—	—	—
,,	,,	Et	59	—	—	—	—	—	—
,,	,,	Pr^n	—	126°/2	—	—	—	—	—
,,	,,	Bu^n	32	148/5	—	—	—	—	—
,,	,,	n-Amyl	—	147/2	63·3	7·2	C$_{11}$H$_{15}$O$_3$N	63·2	7·1
,,	,,	n-Octyl	—	219/14	—	—	—	—	—
,,	,,	CH$_2$Ph	106	—	—	—	—	—	—
NO$_2$	NO$_2$	Me	29	229/760	—	—	—	—	—
,,	,,	Et	32	237/760	—	—	—	—	—
,,	,,	Pr^n	—	109/4	52·9	5·0	C$_9$H$_{10}$OCl$_2$	52·7	4·9
,,	,,	Pr^i	—	94/2	52·7	5·0	C$_9$H$_{10}$OCl$_2$	52·7	4·9
,,	,,	Bu^n	—	121/3	54·7	5·4	C$_{10}$H$_{12}$OCl$_2$	54·9	5·5
,,	,,	Bu^i	—	148/12	54·9	5·6	C$_{10}$H$_{12}$OCl$_2$	54·9	5·5
,,	,,	n-Amyl	—	228/760	57·1	6·0	C$_{11}$H$_{14}$OCl$_2$	56·8	6·0
,,	,,	*iso*Amyl	—	157/10	—	—	—	—	—
,,	,,	CH$_2$Ph	61	—	—	—	—	—	—
Br	Br	Me	61	—	—	—	—	—	—
,,	,,	Et	53	—	—	—	—	—	—
,,	,,	Pr^n	—	140/7	37·0	3·5	C$_9$H$_{10}$OBr$_2$	36·8	3·4
,,	,,	Pr^i	—	139/6	—	—	—	—	—
,,	,,	Bu^n	—	169/8	39·1	3·9	C$_{10}$H$_{12}$OBr$_2$	38·9	3·9
,,	,,	Bu^i	—	158/5	39·0	3·9	C$_{10}$H$_{12}$OBr$_2$	38·9	3·9
,,	,,	n-Amyl	—	178/8	40·8	4·2	C$_{11}$H$_{14}$OBr$_2$	40·9	4·4
,,	,,	*iso*Amyl	—	182/10	41·1	4·3	C$_{11}$H$_{14}$OBr$_2$	40·9	4·4
,,	,,	CH$_2$Ph	68	—	—	—	—	—	—
Cl	CO$_2$Me	Me	93	—	—	—	—	—	—
,,	,,	Et	48	168/12	56·3	5·1	C$_{10}$H$_{11}$O$_3$Cl	56·0	5·1
,,	,,	Pr^n	—	182/12	58·1	5·7	C$_{11}$H$_{13}$O$_3$Cl	57·8	5·7
,,	CO$_2$Et	Me	76	—	—	—	—	—	—
,,	,,	Et	51	—	—	—	—	—	—
,,	,,	Pr^n	—	179/7	59·3	6·3	C$_{12}$H$_{15}$O$_3$Cl	59·3	6·2
,,	,,	Bu^n	—	186/8	60·8	6·6	C$_{13}$H$_{17}$O$_3$Cl	60·7	6·6
,,	,,	n-Amyl	24	190/7	62·1	6·9	C$_{14}$H$_{19}$O$_3$Cl	61·9	7·05
Br	CO$_2$Me	Me	94	—	44·2	3·7	C$_9$H$_9$O$_3$Br	44·1	3·7
,,	,,	Et	46	177/15	46·0	4·1	C$_{10}$H$_{11}$O$_3$Br	46·3	4·25
,,	,,	Pr^n	—	192/7	47·3	5·0	C$_{11}$H$_{13}$O$_3$Br	48·0	4·8
,,	CO$_2$Et	Me	73	—	—	—	—	—	—
,,	,,	Et	60	—	—	—	—	—	—
,,	,,	Pr^n	35	179/5	49·8	5·2	C$_{12}$H$_{15}$O$_3$Br	50·2	5·2
,,	,,	Bu^n	—	190/8	51·3	5·6	C$_{13}$H$_{17}$O$_3$Br	51·7	5·65
,,	,,	n-Amyl	28	224/7	53·5	5·9	C$_{14}$H$_{19}$O$_3$Br	53·3	6·0
CO$_2$Me	Cl	Me	—	148/9	—	—	—	—	—
,,	,,	Et	—	156/9	56·5	5·3	C$_{10}$H$_{11}$O$_3$Cl	56·0	5·1
,,	Br	Me	38	168/15	—	—	—	—	—
,,	,,	Et	48	160/8	—	—	—	—	—

1 hr. to *p*-fluoroanisole (7 g.; prepared by the Balz–Schiemann method from *p*-anisidine) and powdered sodium acetate (10 g.) in a minimum of glacial acetic acid. 2-Bromo-4-chloroanisole, prepared similarly, had b. p. 95°/2 mm. 4-Bromo-2-chloroanisole was obtained by slowly adding a solution (7 g. in 50 c.c.) of dichloramine-т in acetic acid, with cooling, to *p*-bromoanisole in acetic acid (9·3 g. in 50 c.c.). After 24 hr., the solution was diluted with water and the solid crystallised from methyl alcohol.

TABLE 11. *Miscellaneous phenyl ethers.*

	M. p.	k_{20} (l. mole^{-1} sec.$^{-1}$)
p-Fluorophenoxyacetic acid	106°	9·5
p-Chlorophenoxyacetic acid	157	4·1
p-Bromophenoxyacetic acid	158	5·6
α-*p*-Chlorophenoxypropionic acid	116	5·0
β-*p*-Chlorophenoxypropionic acid	138	38
β-*p*-Bromophenoxypropionic acid	146	51
p-Fluorophenyl *o*-nitrobenzyl ether	62	15·6
p-Chlorophenyl *o*-nitrobenzyl ether	69	9·5
p-Chlorophenyl *p*-nitrobenzyl ether	102	11·7
Benzyl 4-chloro-2-nitro-3 : 5-xylyl ether	105	0·493
2-Bromo-4-fluoroanisole	(b. p. 87°/3 mm.)	0·829
2-Bromo-4-chloroanisole	(b. p. 95°/2 mm.)	0·349
4-Bromo-2-chloroanisole	69	0·296
p-Nitrophenyl *n*-octyl ether	26	0·349