52. *Kinetics and Mechanism of Aromatic Halogenation by Hypohalous Acids. Part IV.* Chlorination of Aromatic Ethers by Hypochlorous Acid in 75% Acetic Acid.*

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Reactions of hypochlorous acid in 75% acetic acid with several *p*-alkoxybenzoic acids and with *p*-chloroanisole and methyl anisate have been surveyed. The kinetics and mechanism are similar to those for anisic acid (Part III). The effect of structure upon reactivity is discussed in terms of the constants of the rate equation for *n*-alkyl and *iso*alkyl groups, and for nuclear substituents.

CHLORINATION of *p*-anisic acid * by hypochlorous acid in 75% acetic acid involves a non-ionic chlorinating species and an active form of *p*-anisic acid. The chlorinating species was tentatively identified as acetyl hypochlorite, and the active form as the hydrated anisic acid molecule, the bulk of the phenolic ether being present as unreactive complex of anisic and acetic acids. We now give a less detailed survey of the reactions of hypochlorous acid with a number of *p*-alkoxybenzoic acids and with *p*-chloroanisole and methyl anisate.

EXPERIMENTAL

The methods used for the purification of acetic acid and for the preparation of hypochlorous acid, and also the technique of initial-rate measurements were described in Part III. Values of r_0 are expressed in moles of HOCl used per litre per second.

The *p*-alkoxybenzoic acids were prepared from *p*-hydroxybenzoic acid by Brynmor Jones's [1] method. The products were recrystallised several times from acetic acid and from benzene to constant m. p.

p-Chloroanisole was prepared from *p*-anisidine by diazotisation and Sandmeyer reaction; it was isolated by steam distillation and purified by repeated distillation under reduced pressure. A commercial sample of methyl anisate was recrystallised several times from ethanol until it gave consistent results in kinetic measurements.

DISCUSSION

Kinetics of the Reaction of Hypochlorous Acid with Aromatic Ethers in 75% Acetic Acid at 20°.—Dependence of initial rate r_0 on ether concentration was examined for four *p*-alkoxybenzoic acids and for *p*-chloroanisole and methyl anisate (Table 1). In all

TABLE 1. *The dependence of r_0 on ether concentration.*

	(*a*) *p*-Ethoxybenzoic acid			(*b*) *p*-*n*-Propoxybenzoic acid		
10^3[ether] (M)	2·5	4	5	2·5	4	5
$10^6 r_0$	2·36	3·92	4·88	2·55	3·88	4·78
$10^4 r_0$/[ether]	9·44	9·80	9·76	10·2	9·70	9·56
	[HOCl] = 0·00654M.			[HOCl] = 0·00536M.		
	(*c*) *p*-*n*-Butoxybenzoic acid			(*d*) *p*-*iso*Propoxybenzoic acid		
10^3[ether] (M)	2	4		2	3·5	5
$10^6 r_0$	2·18	4·40		3·24	5·64	8·02
$10^4 r_0$/[ether]	10·9	11·0		16·2	16·1	16·0
	[HOCl] = 0·00553M.			[HOCl] = 0·00577M.		
	(*e*) *p*-Chloroanisole			(*f*) Methyl *p*-anisate		
10^3[ether] (M)	5	7	10	5	8	10
$10^6 r_0$	3·50	5·05	7·12	2·03	3·18	4·30
$10^4 r_0$/[ether]	7·00	7·21	7·12	4·06	3·98	4·30
	[HOCl] = 0·00455M.			[HOCl] = 0·005M.		

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* Part III, preceding paper.

[1] Brynmor Jones, *J.*, 1935, 1874.

cases a first-order dependence was found, as for anisic acid. There is no reason to doubt that other *p*-alkoxybenzoic acids would show the same behaviour.

Dependence of rate on hypochlorous acid concentration was examined for eight *p*-alkoxybenzoic acids and for *p*-chloranisole and methyl anisate. The results are shown in Figs. 1—3, those for anisic acid being included for comparison. (To facilitate comparison the results are plotted for an ether concentration of 0·01M. The concentrations used in the actual measurements were as follows: anisic acid and methyl anisate 0·01; *p*-ethoxy-, *p*-*n*-propoxy-, *p*-*iso*propoxy-, *p*-*iso*butoxy-, and *p*-*iso*pentyloxy-benzoic acids, and *p*-chloroanisole 0·005; *p*-*n*-butoxy-, *p*-*n*-pentyloxy-, and *p*-*n*-hexyloxy-benzoic acids 0·004.) As in the case of anisic acid the relation

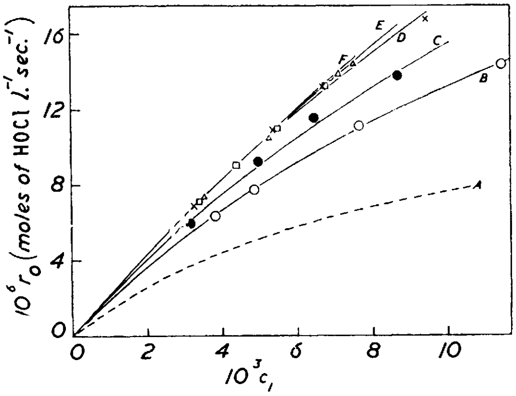
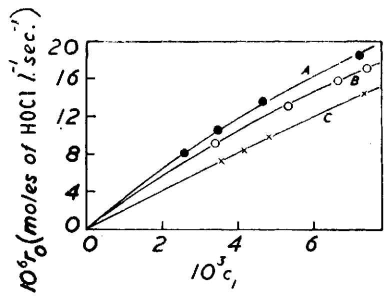


FIG. 1. *The dependence of initial rate r_0 on hypochlorous acid concentration c_1 for* p-n-*alkoxybenzoic acids.*

Ether concentration = 0·01M.

A. Broken line: curve for anisic acid from Part III.
B. ○ p-*Ethoxybenzoic acid.*
C. ● p-n-*Propoxybenzoic acid.*
D. × p-n-*Butoxybenzoic acid.*
E. △ p-n-*Pentyloxybenzoic acid.*
F. □ p-n-*Hexyloxybenzoic acid.*

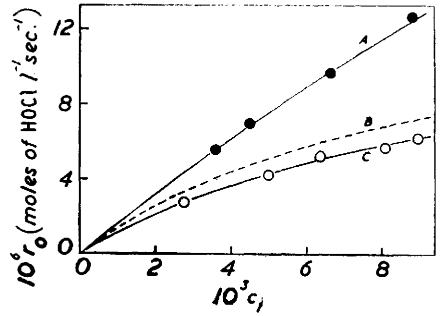
FIG. 2. *The dependence of initial rate r_0 on hypochlorous acid concentration c_1 for* p-iso*alkoxybenzoic acids.*



Ether concentration = 0·01M.

A. ● p-iso*Propoxybenzoic acid.*
B. ○ p-iso*Butoxybenzoic acid.*
C. × p-iso*Pentyloxybenzoic acid.*

FIG. 3. *The dependence of initial rate r_0 on hypochlorous acid concentration c_1 for* p-*substituted anisoles.*



Ether concentration = 0·01M.

A. ● p-*Chloroanisole.*
B. Broken line: curve for anisic acid from Part III.
C. ○ *Methyl anisate.*

$$r_0 = Ac_1c_2/(1 + Bc_1) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

is applicable, where c_1 is the concentration of hypochlorous acid, c_2 is the concentration of ether, and A and B are constants. The values of A and B for each compound are shown in Table 2, and the curves in Figs. 1—3 are drawn with these values of A and B.

The influence of 0·05M-sodium perchlorate, perchloric acid, and sodium acetate was examined for *p*-ethoxy-, *p*-*iso*propoxy-, and *p*-*n*-butoxy-benzoic acids and for *p*-chloroanisole and methyl anisate. The effects of these electrolytes varied somewhat with the ether but not with discernible regularity, so only the overall position is of interest. For the five compounds, 0·05M-sodium perchlorate increased r_0 on the average by 14% (range 8—19%), and 0·05M-perchloric acid by 16% (range 9—24%); 0·05M-sodium acetate decreased r_0 by 7% (range 4—10%). For anisic acid the effects were in the same direction and the corresponding values were 11, 20, and 2%. Thus in all cases sodium perchlorate and perchloric acid exert small and comparable catalytic effects, and sodium acetate exerts slight inhibition.

The kinetics for higher *p*-alkoxybenzoic acids, and for *p*-chloroanisole and methyl anisate thus closely resemble those for anisic acid. The reaction mechanism is therefore probably the same in all cases, and the constants A and B may be identified with k_1k_3f/k_2 and k_3f/k_2 respectively, where k_1 gives the rate at which unreactive complexes break down to hydrated ether molecules, k_2 the rate of formation of the complexes, and k_3 the rate of reaction between hydrated ether molecules and acetyl hypochlorite present in concentration fc_1.

The Influence of Structure upon Reactivity.—A full discussion of this topic requires knowledge of k_1, k_2, and k_3. k_1 can be calculated as the ratio A/B, and the values are recorded in Table 2. The constant B gives the values of k_3f/k_2, and since f can be assumed independent of the aromatic compound, changes in B reflect changes in k_3/k_2. The individual values of k_3 and k_2 are not known. Suggestions about k_3 can, however, be made by analogy with other halogenation reactions of aromatic ethers, and hence some indication of the effect of structure on k_2 can be obtained. It is also of interest to discuss the values of A as a measure of overall reactivity. The effect of structure will be discussed with regard to *n*- and *iso*-alkyl groups, and nuclear substituents. Since the values of A and, in particular, B are not known with any great precision, discussion can only be general in character.

TABLE 2. *The constants in the rate expression for the chlorination of aromatic ethers by hypochlorous acid in 75% acetic acid.*

	A	$B = k_3f/k_2$	10^3k_1
p-Methoxybenzoic acid	0·155	102	1·52
p-Ethoxybenzoic acid	0·200	51	3·92
p-*n*-Propoxybenzoic acid	0·217	40	5·43
p-*n*-Butoxybenzoic acid	0·232	29	8·0
p-*n*-Pentyloxybenzoic acid	0·223	20	11·2
p-*n*-Hexyloxybenzoic acid	0·220	16	13·7
p-*iso*Propoxybenzoic acid	0·352	48	7·3
p-*iso*Butoxybenzoic acid	0·311	45	6·9
p-*iso*Pentyloxybenzoic acid	0·215	11	19·6
p-Chloroanisole	0·169	22	7·7
Methyl *p*-anisate	0·126	91	1·39

n-*Alkyl groups.* Table 2 shows that k_1 increases very markedly with chain length. At the same time B, and hence k_3/k_2, decreases. Now it seems likely that k_3 will rise to a maximum at about *n*-butyl, for the reactivity changes in this way in various electrophilic substitution reactions of aromatic ethers. Relative reactivities in halogenation reactions are summarised in Table 3. If k_3 indeed rises with chain length to *n*-butyl, it is evident that k_2 rises even more rapidly. Hence both k_1 and k_2 probably rise with chain length. Until more is known about the active and unreactive forms of the ether it would be premature to attempt to explain the changes in k_1 and k_2 by reference to electronic or steric effects.

The relative values of A can be compared with the relative reactivities in other reactions of aromatic ethers (Table 3). The effect of chain length found in the present work is not so pronounced as that found in the other reactions, but in all cases the effect of alkyl groups of moderate size is almost independent of chain length. There is some indication in the values of A that beyond a certain point the reactivity falls slightly with chain length. Such a fall has been observed with rather longer chains in the other halogenation reactions, particularly in that involving molecular chlorine, where the reactivity is 218 for *n*-heptyl and 201 for *n*-cetyl.

If the effect of structure upon k_3 is comparable with the effect on reactivity in other halogenation reactions, then it would appear that k_1/k_2 decreases somewhat with increase in chain length, with the result that the effect on A of the change in k_3 is partially compensated.

iso*Alkyl groups.* Table 2 shows that in the series of *iso*alkyl groups k_1 generally increases and k_3/k_2 decreases with chain length, as in the series of *n*-alkyl groups. The small irregularity in the values of k_1 is probably due to the value of B for the *iso*butyl compound being too high. There is no apparent general relationship of the values of k_1 and k_3/k_2 to those of the straight-chain isomers, and the uncertainty in the values makes any detailed discussion unwise.

TABLE 3. *Relative reactivities in the halogenation of aromatic ethers.*

R:	Me	Et	Pr^n	Bu^n	n-C_5H_{11}	n-C_6H_{13}	Pr^i	Bu^i	*iso*-C_5H_{11}
(*a*) Chlorination by Cl_2 in 99% acetic acid [2]	100	199	223	223	221	221	440	216	—
(*b*) Bromination by HOBr in 75% acetic acid [3]	100	200	225	230	232	—	296 to 396	271	262
(*c*) Chlorination by HOCl in 75% acetic acid	100	129	140	150	144	142	227	201	139

In (*a*) and (*b*) the values given are the mean values of 100 $k^{\text{OR}}_{\text{XY}}/k^{\text{OMe}}_{\text{XY}}$, referring to second-order velocity constants in various series of aromatic ethers 1 : 2 : 4-$RO{\cdot}C_6H_3XY$. Except in the case of Pr^i in (*b*) the values vary only slightly with the nature of the nuclear substituents X and Y.

In (*c*) the values given are those of A for the *p*-alkoxybenzoic acids, that for Me being taken as 100.

Table 3 shows that the *iso*propyl group greatly enhances overall reactivity as measured by A. If the effect of this group is compared with that observed in other halogenation reactions, it is seen that in the reactions with molecular chlorine and with hypochlorous acid the ratio Pr^i/Et is greater than Et/Me, but the opposite is found with hypobromous acid.

If the relative values of A for the *iso*alkyl chains are compared with the relative reactivities for the other reactions, it appears quite general for reactivity to increase in the order *iso*-$C_5H_{11} < Bu^i < Pr^i$. The relationship to the straight chains varies. In the hypobromous acid reaction all the *iso*alkyl compounds are more reactive than their straight-chain isomers; in the reaction with molecular chlorine there is the relationship $Bu^n > Bu^i$, and in the reaction with hypochlorous acid n-$C_5H_{11} >$ *iso*-C_5H_{11}.

Nuclear substituents. When the carboxyl group of anisic acid is replaced by methoxycarbonyl, both k_1 and k_3/k_2 fall slightly (Table 2). When the carboxyl group is replaced by chlorine, k_1 rises greatly and k_3/k_2 falls greatly.

The order of reactivity measured by A is $CO_2Me < CO_2H < Cl$. The effect of the carboxyl group was not studied in the work on hypobromous acid, but the order $CO_2H < CO_2Me < Cl$ was observed in the reaction with molecular chlorine.[4] This sequence can be interpreted in terms of electron-releasing power increasing in the same order. The slightly different order found for the reaction with hypochlorous acid is presumably due to the complexity of the quantity A.

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[2] Brynnmor Jones, *J.*, 1935, 1831.

[3] Branch and Brynmor Jones, *J.*, 1955, 2921.

[4] Bradfield and Brynmor Jones, *J.*, 1928, 1006; 1931, 2903.