266. *The Halogenation of Phenolic Ethers and Anilides. Part IX. The Influence of Fluorine and of Alkyl Groups.*

By Brynmor Jones.

Earlier papers in this series (*e.g.*, J., 1928, 1006; J., 1935, 1831, 1835) have recorded the velocities of chlorination at 20° of several series of aromatic ethers of the general type *o*- and *p*-$C_6H_4X{\cdot}OR$, where R was usually an alkyl or substituted-benzyl group and X a polar substituent. Two such substituents were chlorine and bromine. In view of the interest attaching to the relative influence of the halogens on the reactivity of organic compounds, velocity coefficients are now reported for eleven ethers where X is a fluorine atom, and, in the *p*-halogeno-series, it is found that the reactivities of analogous ethers are in the ratio F : Cl : Br = 191 : 100 : 103. Similar velocity measurements have been made for three *p*-fluoro-anilides.

The influence of alkyl substituents in the benzyl radical on the velocity of chlorination of ethers of the types $C_6H_4X{\cdot}O{\cdot}CH_2{\cdot}C_6H_4{\cdot}$Alkyl and $C_6H_4X{\cdot}O{\cdot}CH_2{\cdot}C_6H_3Me_2$ (where X is F or Cl) has also been investigated. The velocities decrease in the order 2 : 4-Me_2 > 3 : 4-Me_2 > *p*-alkyl, the influence of Me, Et, Pr^β and Bu^γ as *p*-substituents being identical.

The comparative velocities of chlorination now determined are recorded in Tables I and II. The measurements were carried out by the method employed in previous papers, and the velocity coefficients calculated from the usual expressions for a bimolecular reaction, the unit of time again being minutes.

Table I.

Velocity coefficients for the chlorination of substances of the types *o*- and *p*-$C_6H_4X{\cdot}OR$ in 99% acetic acid, at 20°.

$[Cl_2] = 0{\cdot}0075$; [ether] = 0·0225; [HCl] = 0·0375.

X = *p*-F; R =	*k.*	X = *o*-F; R =	*k.*	X = *p*-Cl; R =	*k.*	X = *o*-Cl; R =	*k.*
CH_2Ph	1·58	CH_2Ph	3·61	CH_2Ph	0·837	*p*-$C_6H_4Me{\cdot}CH_2$	4·21
p-$C_6H_4Me{\cdot}CH_2$	2·23	*p*-$C_6H_4Me{\cdot}CH_2$	4·91	*p*-$C_6H_4Me{\cdot}CH_2$	1·165	*p*-$C_6H_4Et{\cdot}CH_2$	4·23
p-$C_6H_4Et{\cdot}CH_2$	2·18	*p*-$C_6H_4Br{\cdot}CH_2$	2·09	*p*-$C_6H_4Et{\cdot}CH_2$	1·16	*p*-$C_6H_4Bu^\gamma{\cdot}CH_2$	4·21
p-$C_6H_4Cl{\cdot}CH_2$	0·960	*p*-$C_6H_4(NO_2){\cdot}CH_2$	0·771	*p*-$C_6H_4Pr^\beta{\cdot}CH_2$	1·19	*m*-$C_6H_4Me{\cdot}CH_2$	4·35
p-$C_6H_4Br{\cdot}CH_2$	0·913			*p*-$C_6H_4Bu^\gamma{\cdot}CH_2$	1·15		
p-$C_6H_4(NO_2){\cdot}CH_2$	0·329			2 : 4-$C_6H_3Me_2{\cdot}CH_2$	4·83		
$CH(CH_3)_2$	10·5			3 : 4-$C_6H_3Me_2{\cdot}CH_2$	1·95		

Table II.

Velocity coefficients for the chlorination of substances of the type *p*-$C_6H_4F{\cdot}NHAc$ in 99% acetic acid, at 20°.

$[Cl_2] = 0{\cdot}02$; [HCl] = 0·0475.

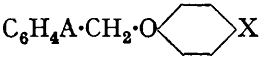
Concn. of anilide	0·02	0·04	0·06
Mol. proptn. of anilide	1	2	3
Ac = $CH_3{\cdot}CO$	0·362	0·386	0·410
$C_6H_5{\cdot}CO$	0·324	—	—
$C_6H_5{\cdot}SO_2$	0·194	0·196	0·201

Discussion of Results.—The existence of the same additive relationships for the present series of ethers as for those investigated in earlier papers was anticipated from their structural similarity, and this is confirmed by the velocity ratios given in Tables III and IV, where a number of ratios recorded in Part VI are included for comparison.

Fluoro-ethers and -anilides. Comparison of the new data for the rates of chlorination of fluoro-ethers and -anilides with those given in previous papers for the corresponding chloro- and bromo-compounds gives several new ratios, and shows (1) that *p*-fluoro- and *p*-chloro-anilides undergo chlorination at almost identical rates, (2) that for *o*-halogeno-ethers the ratio of F : Cl : Br is 432 : 370 : 436, and (3) that the corresponding ratio for *p*-halogeno-ethers is 191 : 100 : 103. It is clear from these ratios that the relative effects of the three halogens are different in the three series examined. In the first two series,

TABLE III.

Relative directive powers of the groups $C_6H_4A{\cdot}CH_2{\cdot}O$ in compounds of the types



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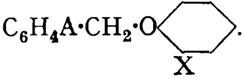

Values of $100k_X^{OCH_2{\cdot}C_6H_4A}/k_X^{OCH_2Ph}$

A =	H.	*p*-Me.	*p*-Et.	*p*-Pr$^\beta$.	*p*-Bu$^\gamma$.	*p*-F.	*p*-Cl.	*p*-Br.	*p*-NO$_2$.
X = *p*-F	100	141	138	—	—	—	61	58	20·8
p-Cl	100	139	139	143	138	81	58	58	20·8
p-Br	100	138	—	—	—	—	61	—	20·8
o-F	100	136	—	—	—	—	—	58	21·3
o-Cl	—	140	141	—	140	83	62	—	21·4
o-Br	—	—	—	—	—	—	60	—	21·0

TABLE IV.

Relative influences of F, Cl, Br in compounds of the types *o*- and *p*-$C_6H_4X{\cdot}OR$. Values of $100k_X^{OR}/k_{p\text{-}Cl}^{OR}$.

X =	*p*-F.	*o*-F.	*p*-Cl.	*o*-Cl.	*p*-Br.	*o*-Br.
R = CH_2Ph	189	431	100	—	102	—
p-$C_6H_4Me{\cdot}CH_2$	191	421	100	360	100	—
p-$C_6H_4Et{\cdot}CH_2$	—	—	100	364	—	—
p-$C_6H_4Bu^\gamma{\cdot}CH_2$	—	—	100	365	—	—
p-$C_6H_4F{\cdot}CH_2$	—	—	100	368	—	—
p-$C_6H_4Cl{\cdot}CH_2$	196	—	100	381	106	441
p-$C_6H_4Br{\cdot}CH_2$	189	432	100	383	—	—
p-$C_6H_4(NO_2){\cdot}CH_2$	189	443	100	369	102	431

however, difficulties of interpretation arise owing to (*a*) basicity in the orienting acetamido-group, and (*b*) the fact that in the *o*-halogeno-ethers two positions are available for substitution, and consequently, for a complete and satisfactory interpretation of the velocity data, knowledge of the rate of entry at each position would be essential. In the *p*-halogeno-ethers, on the other hand, uncertainties of interpretation are avoided since chlorination occurs only in the *o*-position to the group OR. The greater facilitation of nuclear chlorination by fluorine in this series, as shown by the ratio 191 : 100 : 103 for F : Cl : Br, shows that it is, in effect, far less powerfully electron-attractive than either chlorine or bromine.

Influence of alkyl groups. The data recorded in Table I are confined to the influence of various alkyl substituents in the benzyl radical on the rates of chlorination of ethers of the type $C_6H_4X{\cdot}O{\cdot}CH_2{\cdot}C_6H_4{\cdot}$Alkyl and $C_6H_4X{\cdot}O{\cdot}CH_2{\cdot}C_6H_3Me_2$, where X is fluorine or chlorine. That the introduction of a methyl group into the benzyl radical increases the velocity of substitution in accordance with its known inductive effect was shown in Part VI, the directive power of the benzyloxy-group being increased from 100 to 148, 151, and 140 by an *o*-, *m*-, and *p*-methyl substituent respectively. For other alkyl groups the present data show (1) that all alkyl substituents increase the velocity of chlorination, and that with a single *p*-alkyl substituent this increase is identical for the four groups Me, Et, Pr$^\beta$, Bu$^\gamma$; (2) that the introduction of a second methyl group into the benzyl radical produces a further increase in the reactivity, this being very marked in the 2 : 4-*dimethylbenzyl ether*, which undergoes chlorination approximately 2·5 times as fast as the 3 : 4-*isomer*. The exact magnitude of this difference in the reactivity of the two isomeric dimethylbenzyl ethers is a little uncertain, since the velocity coefficients for the 2:4-dimethyl ether show a small upward drift, and are therefore less trustworthy than those for other ethers (cf. experimental section).

The influence of the various alkyl substituents on the directive power of the benzyloxy-group may be summarised as follows :

H.	*o*-Me.	*m*-Me.	*p*-Me.	*p*-Et.	*p*-Pr$^\beta$.	*p*-Bu$^\gamma$.	2 : 4-Me$_2$.	3 : 4-Me$_2$.
100	148	151	140	139	143	139	577	233

The effects of alkyl groups are, in general, so much alike that it is not surprising that in the present system all *p*-alkyl substituents should influence the velocity of chlorination to the same degree.

EXPERIMENTAL.

Velocity Measurements.—The method of determining the velocity coefficients and the precautions taken to ensure accurate values were the same as in previous papers. Each ether was crystallised at least thrice from ethyl alcohol or glacial acetic acid, and the following random selection of examples illustrates the constancy, after further purification, of the mean values of the velocity coefficients in single experiments. (1) *o*-Fluorophenyl benzyl ether had $k = 3{\cdot}63$ and 3·58 after three crystallisations from ethyl alcohol, and $k = 3{\cdot}60$ and 3·62 after two further crystallisations from the same solvent. (2) *o*-Fluorophenyl *p*-nitrobenzyl ether, after two crystallisations from ethyl alcohol and one from glacial acetic acid, had $k = 0{\cdot}768$, and after two additional crystallisations from ethyl alcohol, $k = 0{\cdot}774$. (3) For *p*-fluorophenyl *p*-methylbenzyl ether $k = 2{\cdot}225$ after four crystallisations from ethyl alcohol, and $k = 2{\cdot}23$ after an additional crystallisation.

To ensure that the experimental conditions were the same as in previous work, velocities of chlorination of two ethers, for which values have already been published, were redetermined, with the following results: *p*-chlorophenyl *p*-methylbenzyl ether had $k = 1{\cdot}18$, formerly 1·15—the mean value 1·165 is recorded in Table I, and is employed in calculating the values given in Table II—and the corresponding *o*-chloro-ether had the values 4·21 and 4·20 respectively.

Materials.—*o*- and *p*-Fluorophenol were prepared by the methods of Bennett, Brooks, and Glasstone (J., 1935, 1822): *o*- and *p*-anisidine were converted into *o*- and *p*-fluoroanisole (b. p. 156—158° and 174—175° respectively) by Balz and Schiemann's method (*Ber.*, 1927, **60**, 1186), and these in turn were demethylated by heating with anhydrous aluminium chloride. The *o*-fluorophenol had b. p. 151—153°, and the *p*-compound, after distillation, solidified; m. p. 48° after two crystallisations from ligroin (b. p. 40—60°).

p-*Alkylbenzyl chlorides.* *p*-Methylbenzyl chloride was obtained by chlorination of boiling *p*-xylene, the fraction of b. p. 180—200° being further fractionated under reduced pressure, and the specimen of b. p. 79—83°/15 mm. used for the preparation of the ethers. *m*-Methylbenzyl chloride was prepared similarly from *m*-xylene. Since all the ethers were solids which were repeatedly crystallised, it was not necessary to purify the chlorides to a very high degree.

p-Ethyl- and *p*-*iso*propyl-benzyl chlorides were prepared from purchased specimens of ethyl- and *iso*propyl-benzene respectively by Sommelet's method (*Compt. rend.*, 1913, **157**, 1445), the procedure and yields of product being similar to those recorded by Baker and Nathan (J., 1935, 1844). Both chlorides were colourless liquids, and the specimens used in the preparations had b. p. 106—110°/15 mm. and 116—118°/22 mm., respectively.

p-tert.-*Butylbenzyl bromide.* *p*-*tert.*-Butyltoluene was prepared by Verley's method (*Bull. Soc. chim.*, 1898, **19**, 67), and converted by direct bromination into *p*-*tert.*-butylbenzyl bromide. The colourless fraction, b. p. 130—133°/14 mm. (86 g. from 82 g. of toluene), was frozen thrice, and the final product was a white solid, m. p. 15°.

2 : 4- and 3 : 4-Dimethylbenzyl chlorides were also prepared by Sommelet's method from *m*- and *o*-xylene respectively. The colourless fractions of b. p. 118—120°/13 mm. and 105—115°/13 mm., respectively, were employed.

p-Chlorobenzyl chloride, prepared by chlorination of boiling *p*-chlorotoluene, had m. p. 29° after crystallisation from (a) acetic acid, and (b) ligroin (b. p. 40—60°). *p*-Bromobenzyl bromide was prepared similarly by bromination of *p*-bromotoluene.

The ethers were prepared by standard methods from the parent phenol and the appropriate benzyl chloride or bromide.

p-*Fluorophenyl Ethers.*—The *benzyl ether*, prepared from *p*-fluorophenol, alcoholic potassium hydroxide, and benzyl chloride, crystallises from alcohol as colourless prisms, m. p. 55·5° (Found: C, 76·9; H, 5·4. $C_{13}H_{11}OF$ requires C, 77·2; H, 5·5%). The p-*methyl*- and the p-*ethyl-benzyl ether* crystallise similarly, m. p. 69° (Found: C, 77·5; H, 5·8. $C_{14}H_{13}OF$ requires C, 77·75; H, 6·1%), and m. p. 65° (Found: C, 78·1; H, 6·5. $C_{15}H_{15}OF$ requires C, 78·2; H, 6·6%), respectively. The p-*chloro*- and the p-*bromo-benzyl ether* also crystallise as colourless prisms, m. p. 58° (Found: C, 66·1; H, 4·2. $C_{13}H_{10}OClF$ requires C, 66·0; H, 4·3%), and m. p. 66° (Found: C, 55·5; H, 3·7. $C_{13}H_{10}OBrF$ requires C, 55·5; H, 3·6%), respectively.

The o- and p-*nitrobenzyl ethers*, prepared from commercially pure specimens of the corresponding nitrobenzyl chlorides and *p*-fluorophenol in sodium ethoxide, melt at 62° and 74·5° respectively after two crystallisations from acetic acid and one from alcohol (Found, for *p*-compound: C, 63·0; H, 4·0. Found, for *o*-compound: C, 62·9; H, 4·2. $C_{13}H_{10}O_3NF$ requires C, 63·2; H, 4·1%).

* All micro-determinations by Dr. A. Schoeller.

The iso*propyl ether*, prepared from a specially purified sample of *p*-fluorophenol, alcoholic potassium hydroxide, and *iso*propyl bromide, had b. p. 73°/18 mm. (Found: C, 70·8; H, 7·3. $C_9H_{11}OF$ requires C, 70·1; H, 7·2%).

o-*Fluorophenyl Ethers.*—The *benzyl ether*, after three crystallisations from ethyl alcohol, melts at 42° (Found: C, 77·3; H, 5·5. $C_{13}H_{11}OF$ requires C, 77·2; H, 5·5%). The p-*methyl*- (Found: C, 77·6; H, 5·9. $C_{14}H_{13}OF$ requires C, 77·75; H, 6·1%) and p-*bromo-benzyl ether* (Found: C, 55·5; H, 3·6. $C_{13}H_{10}OBrF$ requires C, 55·5; H, 3·6%), both of m. p. 66°, crystallise from alcohol as colourless prisms. The p-*nitrobenzyl ether* crystallises as soft yellow prisms, m. p. 84·5° (Found: C, 63·1; H, 4·0%).

p-*Chlorophenyl Ethers.*—The *p*-methylbenzyl ether had m. p. 97° (cf. Part VI). The p-*ethylbenzyl ether* crystallises from alcohol as colourless prisms, m. p. 82·5° (Found: C, 72·8; H, 6·1. $C_{15}H_{15}OCl$ requires C, 73·0; H, 6·1%). The p-iso*propylbenzyl ether* (Found: C, 73·8; H, 6·7. $C_{16}H_{17}OCl$ requires C, 73·7; H, 6·6%) and the p-tert.-*butylbenzyl ether* (Found: C, 74·2; H, 7·0. $C_{17}H_{19}OCl$ requires C, 74·3; H, 7·0%) crystallise similarly; m. p. 79·5° and 92°, respectively.

The 2 : 4-*dimethylbenzyl ether*, m. p. 81°, crystallises well from ethyl alcohol (Found: C, 73·2; H, 6·2. $C_{15}H_{15}OCl$ requires C, 73·0; H, 6·1%). Unlike those of the other ethers examined, its velocity coefficient shows a steady rise of approximately 10% over the usual range of 35—60% change when equimolecular proportions of ether and chlorine are employed, and this discrepancy, although diminished, is not completely eliminated even with 3 mols. of ether. The cause of this upward drift in the velocity coefficient is unknown, but it is noteworthy that the 3 : 4-dimethylbenzyl ether gives a satisfactory velocity coefficient under all conditions. It appears, therefore, that the drift observed with the 2 : 4-dimethyl ether is to be associated with the presence of a methyl group in the *o*-position—a tentative suggestion is that the hydrogen of the methylene group is rendered reactive to chlorine.

The 3 : 4-*dimethylbenzyl ether* melts at 89° (Found: C, 73·0; H, 6·2%).

o-*Chlorophenyl Ethers.*—The *p*-methylbenzyl ether crystallises from alcohol as colourless prisms, m. p. 76° (cf. Part VI), and the p-*ethyl*, m. p. 79° (Found: C, 73·2; H, 6·2%), and p-tert.-*butyl*, m. p. 63° (Found: C, 74·2; H, 6·9%), homologues crystallise similarly. The m-*methylbenzyl ether* was first obtained as a colourless liquid, b. p. 183°/13 mm., which deposited crystals on long standing, and these after three crystallisations from alcohol melt at 77° (Found: C, 72·2; H, 5·6. $C_{14}H_{13}OCl$ requires C, 72·3; H, 5·6%).

p-*Fluoroaniline and* p-*Fluoro-anilides.*—*p*-Nitroaniline was converted into *p*-fluoronitrobenzene by Balz and Schiemann's method (*loc. cit.*), the decomposition of the diazonium borofluoride being carried out according to Bennett, Brooks, and Glasstone (*loc. cit.*). The purified *p*-fluoronitrobenzene was then reduced by West's method (J., 1925, **127**, 494), and the resulting *p*-fluoroaniline had b. p. 184—186°. From this the following three anilides were prepared; they were purified by repeated crystallisation from ethyl alcohol or glacial acetic acid: *p*-Fluoroacetanilide and benz-*p*-fluoroanilide melt at 152° and 184° respectively; *benzenesulphon*-p-*fluoroanilide* melts at 110° (Found: C, 57·7; H, 4·3. $C_{12}H_{10}O_2NFS$ requires C, 57·4; H, 4·2%).

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