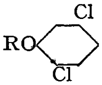
114. *The Halogenation of Phenolic Ethers and Anilides. Part XIV.* m-*Substituted Phenyl Ethers.*

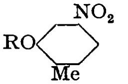
By Brynmor Jones.

Velocity coefficients for the chlorination of aromatic ethers of the type m-$C_6H_4X\cdot OR$, and for certain disubstituted ethers, where chlorination can occur simultaneously in more than one position, are recorded. Although the reactions are composite in character, it is found that the relative directive powers of OR groups obtained from a ratio of velocity coefficients are very similar to those found in ethers of the type p-$C_6H_4X\cdot OR$, where chlorination results in the formation of a single homogeneous product.

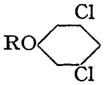
The series of ethers examined are of the type m-$C_6H_4X\cdot OR$, where $X = NO_2$, CO_2H, Cl, or F, and the types (I), (II), and (III). In each measurement an excess of ether was employed, the usual expression for a bimolecular reaction giving satisfactory velocity coefficients in all cases. The mean values are in Table I. The medium is again "the 99% acetic acid containing 1 c.c. of water per 100 c.c. of acetic acid," the concentrations are in g.-mol./l., and the time in minutes.



(I.)



(II.)



(III.)

Table I.

Velocity coefficients for the chlorination of compounds in 99% acetic acid, at 20°.

Type m-$RO\cdot C_6H_4\cdot CO_2H$: $[Cl_2] = 0·0075$; $[HCl] = 0·0375$.

Concn. of ether	0·0225	0·0150		0·0225	0·0150		0·0225	0·0150
Mol. ratio, $[\text{ether}]/[Cl_2]$	3	2		3	2		3	2
R =	*k.*		R =	*k.*		R =	*k.*	
CH_3	1·63	1·67	$C_6H_{13}{}^a$	—	3·54	$[CH_2]_2Ph$	2·01	2·08
C_2H_5	3·24	3·31	$C_7H_{15}{}^a$	—	3·45	$[CH_2]_3Ph$	2·75	2·81
$C_3H_7{}^a$	3·48	—	$C_8H_{17}{}^a$	—	3·49	p-$C_6H_4F\cdot CH_2$	0·909	0·950
$C_3H_7{}^\beta$	6·37	6·37	$C_9H_{19}{}^a$	—	3·45	p-$C_6H_4Cl\cdot CH_2$	—	0·722
$C_4H_9{}^a$	3·56	3·66	$C_{12}H_{25}{}^a$	—	3·38	p-$C_6H_4Br\cdot CH_2$	—	0·692
$C_5H_{11}{}^a$	3·40	3·55	$CH_2\cdot Ph$	1·14	—			

Type m-$C_6H_4X\cdot OR$: $[Cl_2] = 0·02$; $[\text{ether}] = 0·10$; $[HCl] = 0·0475$.

X =	R =	$k \times 10^2$.	X =	R =	$k \times 10^2$.
NO_2	CH_3	0·534	NO_2	C_2H_5	1·06
$[Cl_2] = 0·0075$; $[\text{ether}] = 0·0075$; $[HCl] = 0·0375$.					
Cl	CH_3	75·8	F	o-$C_6H_4(NO_2)\cdot CH_2$	52·7
,,	CH_2Ph	52·7			

Type (I) : $[Cl_2] = 0·0075$; $[HCl] = 0·0375$.

Concn. of ether	0·0225	0·0150		0·0225	0·0150
Mol. ratio, $[\text{ether}]/[Cl_2]$	3	2		3	2
R =	*k.*		R =	*k.*	
CH_2Ph	0·320	0·336	p-$C_6H_4Br\cdot CH_2$	0·189	—
p-$C_6H_4Me\cdot CH_2$	—	0·458	m-$C_6H_4F\cdot CH_2$	—	0·172
p-$C_6H_4F\cdot CH_2$	0·246	0·256			

Type (II) : $[Cl_2] = 0·02$; $[\text{ether}] = 0·10$; $[HCl] = 0.0475$.

R =	$k \times 10^2$.	R =	$k \times 10^2$.	R =	$k \times 10^2$.
CH_3	1·23	C_2H_5	2·44	CH_2Ph	0·834

Type (III) : $[Cl_2] = 0·0075$; $[HCl] = 0·0375$.

Concn. of ether	0·0225	0·0075		0·0225	0·0075
Mol. ratio, $[\text{ether}]/[Cl_2]$	3	1		3	1
R =	*k.*		R =	*k.*	
CH_3	8·15	8·48	p-$C_6H_4Br\cdot CH_2$	3·70	3·83

For a complete understanding of any electrophilic benzene substitution reaction, knowledge is required of the total velocity of substitution and of the relative rates of reaction at the individual reactive centres, the latter being obtained usually from an analysis of the proportions of the isomerides formed. In the kinetic studies of the nuclear chlorination of aromatic ethers so far reported, the necessity of obtaining data for the proportions of isomerides did not arise, since in the great majority of ethers only one product is formed and the velocity coefficient is itself a direct measure of the reactivity at a particular carbon atom. In the present series this is no longer the case; *e.g.*, 2 : 5-dichlorophenyl ethers have two, and the m-alkoxybenzoic acids three, reactive centres in the molecule, and a measure of their separate contributions to the reactivity as well as the total velocity of chlorination becomes essential. Interruption of this work makes it impossible to complete the present investigation by a study of the proportions, and it seems desirable therefore to place on record the data so far obtained and the tentative conclusions arising therefrom.

The interpretation of the results for compounds such as *m*-alkoxybenzoic acids where, in theory, three positions are available for substitution is simplified to a certain extent by the fact that, in practice, only two isomerides are formed. Holleman and his co-workers ("Die direkte Einführung von Substituenten in den Benzolkern," Leipzig, 1910) have shown that *m*-chlorobenzoic acid on nitration gives the 6- and the 2-nitro-3-chlorobenzoic acid in the ratio 93 : 7, and that *m*-bromobenzoic acid gives 89% and 11% respectively of the corresponding bromonitrobenzoic acids. Similarly, Beyer (*Rec. Trav. chim.*, 1921, **40**, 621) found that the chlorination of *m*-hydroxybenzoic acid in glacial acetic acid yields the 6-chloro- and the 2-chloro-3-hydroxybenzoic acids [see also Mazzara (*Gazzetta*, 1899, **29**, i, 376), who obtained the same two acids by the action of sulphuryl chloride]. An accurate estimation of the relative amounts of the two chlorohydroxybenzoic acids was not made, but it is clear from Beyer's work that the 6-chloro-acid is the chief product, with the 2-chloro-acid forming approximately 30% of the total. An approximate analysis carried out in the present work indicates that in the chlorination of *m*-methoxybenzoic acid the 6-chloro-3-methoxybenzoic acid is the chief product.

Further light is thrown on the significance of the present data by the demonstration by Miss Mabel L. Hemming, employing the method reported in J., 1936, 1231, that in the chlorination of anisole, phenetole, and certain substituted phenyl benzyl ethers in acetic acid the *o*/*p* ratio is almost unaltered by changes in the OR group. This result suggests that in the above *m*-substituted phenyl ethers changes in the alkoxy-group would probably not alter to any appreciable degree the relative reactivity at the 2- and the 6-position, and at the 4- and the 6-position in such ethers as those of 2 : 5-dichlorophenol. If this is so, then a general correspondence would be expected between the relative directive powers of OR groups in the present series of compounds and those recorded in earlier papers for compounds of the simpler type *p*-$C_6H_4X \cdot OR$ where only one product is formed. The velocity ratios in Table II show this correspondence.

TABLE II.

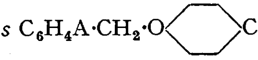
Relative directive powers of the groups OR *in compounds of the types* m- *and* p-$RO \cdot C_6H_4 \cdot CO_2H$.

Values of $100k^{OR}_{CO_2H}/k^{OMe}_{CO_2H}$.

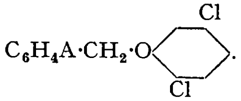
R =	CH_3.	C_2H_5.	$C_3H_7^{\alpha}$.	$C_3H_7^{\beta}$.	$C_4H_9^{\alpha}$.	$C_5H_{11}^{\alpha}$.	$C_6H_{13}^{\alpha}$.	$C_7H_{15}^{\alpha}$.	$C_8H_{17}^{\alpha}$.	$C_9H_{19}^{\alpha}$.	$C_{12}H_{25}^{\alpha}$.
m-CO_2H …………	100	198	214	382	219	211	212	207	209	207	202
p-CO_2H …………	100	198	215	444	221	218	216	213	207	203	202

R =	CH_2Ph.	$[CH_2]_2Ph$.	$[CH_2]_3Ph$.	*p*-$C_6H_4F \cdot CH_2$.	*p*-$C_6H_4Cl \cdot CH_2$.	*p*-$C_6H_4Br \cdot CH_2$.
m-CO_2H …………	70	124	169	56	43	41
p-CO_2H …………	70	119	171	59	45	44

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



and



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

A =	H.	*p*-Me.	*p*-F.	*p*-Br.	*m*-F.
p-Chloro-series ……………………	100	138	81	58	47
2 : 5-Dichloro-series ………………	100	136	77	59	51

Comparison of the velocity coefficients in Table III shows that the deactivating substituents F, Cl, CO_2H, and NO_2 exert a smaller effect in the *m*- than in the *p*-position on the overall rate of chlorination, the influence of position being most noticeable in the case of fluorine and least noticeable in that of the strongly polar nitro-group.

TABLE III.

Substituent :	H.	F.	Cl.	CO_2H.	NO_2.
k, *m*-substituted anisole ………………	*ca.* 900	*ca.* 380	76·0	1·60	0·0053
k, *p*- ,, ,, ………………	*ca.* 900	2·32	1·23	0·444	0·0029

The effect of both number and position of chlorine atoms is exemplified by the comparison of *o*-, *m*-, and *p*-chloroanisoles and 2 : 4-, 2 : 5-, and 3 : 5-dichloroanisoles, for which the velocity coefficients are respectively, 4·44, 76·0, 1·23, 0·0031, 0·46, and 8·15.

EXPERIMENTAL.

The measurements of the velocity coefficients of chlorination were carried out at 20° as usual. The procedure of crystallising each ether at least three times from ethyl alcohol, glacial acetic acid, or, in some cases, from benzene was followed, and the satisfactory nature of the velocity coefficients when the ether : chlorine ratio was 3 : 1 or 2 : 1 is illustrated by the data in Table IV.

TABLE IV.

m-Methoxybenzoic acid.

[ether] = 0·0225; $[Cl_2]$ = 0·0075; [HCl] = 0·0375.

Time, mins.	Titre, c.c.	*k*.	Time, mins.	Titre, c.c.	*k*.
0	7·50	—	24·35	3·42	1·60
13·00	4·85	1·60	30·00	2·88	1·62
17·68	4·16	1·62		Mean	1·61

[ether] = 0·0150; $[Cl_2]$ = 0·0075; [HCl] = 0·0375.

Time, mins.	Titre, c.c.	*k*.	Time, mins.	Titre, c.c.	*k*.
0	7·50	—	42·60	3·12	1·67
22·20	4·57	1·67		Mean	1·67
32·10	3·79	1·66			

m-*n*-Butoxybenzoic acid.

[ether] = 0·0225; $[Cl_2]$ = 0·0075; [HCl] = 0·0375.

0	7·50	—	8·917	3·90	3·58
5·433	4·93	3·65	12·33	3·12	3·58
				Mean	3·60

[ether] = 0·0150; $[Cl_2]$ = 0·0075; [HCl] = 0·0375.

0	7·50	—	15·68	3·62	3·65
10·13	4·56	3·68	19·10	3·16	3·66
				Mean	3·66

2 : 5-Dichlorophenyl benzyl ether.

[ether] = 0·0150; $[Cl_2]$ = 0·0075; [HCl] = 0·0375.

0	7·50	—	72·35	5·37	0·335

[ether] = 0·0150; $[Cl_2]$ = 0·0075; [HCl] = 0·0375.

96·80	4·83	0·336	132·2	4·18	0·337
				Mean	0·336

Materials.—The analyses marked by an asterisk were carried out by the author; the remainder were micro-determinations by Dr. Ing. A. Schoeller or Messrs. Weiler and Strauss.

m-*Alkoxybenzoic acids.* These were prepared from *m*-hydroxybenzoic acid by the method employed earlier for the preparation of the isomeric *p*-alkoxybenzoic acids (J., 1935, 1834, 1874). Pure specimens were assured by crystallising each acid three times from glacial acetic acid. Three of the acids, the methoxy-, ethoxy-, and *n*-propoxy-, m. p.'s 104—105°, 137°, and 71—72°, respectively, had been prepared by Cohen and Dudley (J., 1910, **97**, 1737) by alkylation of the hydroxy-ester and subsequent hydrolysis. The present method is more economical since it does not involve the formation, and consequent hydrolysis, of the esters. The methoxy-, ethoxy-, and *n*-propoxy-benzoic acids crystallised from glacial acetic acid in long colourless prisms, m. p. 105°, m. p. 137° (Found : * C, 64·7; H, 6·1. Calc. : C, 65·1; H, 6·1%), and m. p. 74°, respectively. The iso*propoxybenzoic acid*, m. p. 96° (Found : * C, 66·5; H, 6·4. $C_{10}H_{12}O_3$ requires C, 66·7; H, 6·7%), and the n-*butoxybenzoic acid*, m. p. 62° (Found : * C, 68·1; H, 7·0. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·3%), crystallised similarly. The n-*amyloxybenzoic acid* crystallised from glacial acetic acid in clusters of colourless, elongated prisms, m. p. 72° (Found : * C, 69·6; H, 7·6. $C_{12}H_{16}O_3$ requires C, 69·2; H, 7·8%). From the same solvent, the n-*hexyloxybenzoic acid*, m. p. 71° (Found : * C, 70·5; H, 8·0. $C_{13}H_{18}O_3$ requires C, 70·3; H, 8·2%), the n-*heptyloxybenzoic acid*, m. p. 80° (Found : * C, 71·0; H, 8·3. $C_{14}H_{20}O_3$ requires C, 71·1; H, 8·5%), the n-*octyloxybenzoic acid*, m. p. 73° (Found : * C, 72·0; H, 8·5. $C_{15}H_{22}O_3$ requires C, 71·9; H, 8·9%), and the n-*nonyloxybenzoic acid*, m. p. 84° (Found : * C, 72·9; H, 9·0. $C_{16}H_{24}O_3$ requires C, 72·7; H, 9·2%), crystallised in clusters of colourless plates. The n-*dodecyloxybenzoic acid* had m. p. 91° (Found : * C, 74·8; H, 9·8. $C_{19}H_{30}O_3$ requires C, 74·5; H, 9·9%).

m-*Benzyloxybenzoic acid* crystallised from glacial acetic acid in clusters of colourless prisms, m. p. 134° (Found : * C, 73·5; H, 5·1. $C_{14}H_{12}O_3$ requires C, 73·7; H, 5·3%), whereas m-(p'-*fluorobenzyloxy*)*benzoic acid*, m. p. 148° (Found : C, 68·05; H, 4·4. $C_{14}H_{11}O_3F$ requires C, 68·0; H, 4·5%), the p'-*chloro-acid*, m. p. 170° (Found : C, 64·0; H, 4·4. $C_{14}H_{11}O_3Cl$ requires C, 63·8; H, 4·2%), and the p'-*bromo-acid*, m.p. 179° (Found : C, 55·1; H, 3·1. $C_{14}H_{11}O_3Br$ requires C, 54·8; H, 3·6%), crystallised from acetic acid in colourless plates.

m-*β-Phenylethoxybenzoic acid*, m. p. 110° (Found : C, 74·2; H, 5·9. $C_{15}H_{14}O_3$ requires C, 74·3; H, 5·8%), and m-*γ-phenyl*-n-*propoxybenzoic acid*, m. p. 118° (Found : C, 74·9; H, 6·2. $C_{16}H_{16}O_3$ requires C, 75·0; H, 6·3%), crystallised similarly.

2 : 5-*Dichlorophenyl ethers.* 2 : 5-Dichlorophenol, m. p. 58°, was prepared by standard methods by the following sequence of reactions : *p*-dichlorobenzene ⟶ 2 : 5-dichloronitrobenzene ⟶ 2 : 5-dichloroaniline ⟶ 2 : 5-dichlorophenol. Its *benzyl* ether, m. p. 58° (Found : * Cl, 27·8. $C_{13}H_{10}OCl_2$ requires Cl, 28·1%), crystallised from ethyl alcohol in clusters of colourless rhombs, and the p-*fluorobenzyl* ether, m. p. 86° (Found : C, 57·6; H, 3·4. $C_{13}H_9OFCl_2$ requires C, 57·6; H, 3·4%), and the m-*fluorobenzyl* ether, m. p. 79° (Found : C, 57·1; H, 3·4%), crystallised similarly. The p-*bromobenzyl* ether had m. p. 77° (Found : C, 47·3; H, 2·7. $C_{13}H_9OCl_2Br$ requires C, 47·0; H, 2·7%), and the p-*methylbenzyl* ether m. p. 58° (Found : * Cl, 26·4. $C_{14}H_{12}OCl_2$ requires Cl, 26·6%).

3 : 5-*Dichlorophenyl ethers.* The 3 : 5-dichlorophenol, m. p. 65°, was a specimen kindly supplied by Dr. A. W. Chapman and prepared by the following series of reactions : *p*-nitroaniline ⟶ 2 : 6-dichloro-*p*-nitroaniline ⟶ 3 : 5-dichloronitrobenzene ⟶ 3 : 5-dichloroaniline ⟶ 3 : 5-dichlorophenol. Methylation by means of methyl sulphate gave 3 : 5-dichloroanisole, which crystallised from ethyl alcohol in colourless, slender prisms, m. p. 40—41° (Found : C, 47·2; H, 3·3. Calc. : C, 47·5; H, 3·4%).

3 : 5-*Dichlorophenyl* p-*bromobenzyl ether* crystallised from alcohol in colourless plates, m. p. 68° (Found : C, 47·1; H, 2·8. $C_{13}H_9OCl_2Br$ requires C, 47·0; H, 2·7%).

4-*Nitro*-o-*tolyl ethers*. These were prepared from a purchased specimen of *p*-nitro-*o*-cresol, m. p. 116°. The methyl ether, m. p. 74°, the ethyl ether, m. p. 60° (Found : * C, 60·0; H, 6·0. Calc. : C, 59·7; H, 6·1%), and the n-*propyl* ether, m. p. 51° (Found : C, 61·5; H, 6·7. $C_{10}H_{13}O_3N$ requires C, 61·5; H, 7·1%), crystallised from ethyl alcohol in colourless slender prisms. The *benzyl* ether, m. p. 79° (Found : * C, 69·5; H, 5·3. $C_{14}H_{13}O_3N$ requires C, 69·1; H, 5·4%), and the p-*methylbenzyl* ether, m. p. 110° (Found : * C, 70·5; H, 6·2. $C_{15}H_{15}O_3N$ requires C, 70·0; H, 5·9%), crystallised from alcohol in clusters of colourless prisms.

m-Fluorophenol was prepared by the decomposition of the diazonium salt of *m*-fluoroaniline, which was itself prepared from *m*-nitroaniline *via* *m*-fluoronitrobenzene by Balz and Schiemann's method (*Ber.*, 1927, **60**, 1186; cf. Bennett, Brooks, and Glasstone, J., 1935, 1822). The phenol gave with *o*-nitrobenzyl chloride in the usual way m-*fluorophenyl* o-*nitrobenzyl ether*, which crystallised from ethyl alcohol in slender yellow prisms, m. p. 53° (Found : * N, 5·69. $C_{13}H_{10}O_3NF$ requires N, 5·67%). These crystals were very sensitive to sunlight, and soon darkened.

m-*Chlorophenyl benzyl ether* crystallised from alcohol in colourless, slender prisms, m. p. 65° (Found : C, 71·3; H, 5·0. $C_{13}H_{11}OCl$ requires C, 71·4; H, 5·1%). The methyl, ethyl, and benzyl ethers of *m*-nitrophenol had m. p.'s 39°, 36°, and 58° respectively.

THE UNIVERSITY, SHEFFIELD, 10.

[*Received, June 28th*, 1943.]