

The Halogenation of Phenolic Ethers and Anilides. Part XVII. An Investigation into the Additive Effects of Substituents in Benzyl Phenyl Ethers.*

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Kinetic studies of the nuclear chlorination of aromatic ethers of a wide variety of types have revealed that differences in rate arising from constitutional changes may be accounted for satisfactorily by variations in the energy of activation, with the substituents contributing in an additive manner.

In an attempt to delineate the extent of such behaviour, and to assess what departures from additivity are to be expected when polar groups are in close proximity to one another, rate constants have been determined for a series of benzyl phenyl ethers in which polar substituents occupy the *ortho*-positions of both the benzyl and phenyl groups.

THE earlier kinetic studies in this series have shown the nuclear chlorination of aromatic ethers to be an eminently suitable reaction for the study of the influence of substituents on reactivity. In part, this is to be attributed to the method of chlorination developed by Orton and King (*J.*, 1911, **99**, 1360), whereby a known amount of chlorine can be liberated at will by the addition of hydrochloric acid to a chloramine in acetic acid, and, of equal importance, to the fact that the kinetics of the chlorination of ethers of wide variety are singularly free from complicating secondary reactions. From the accumulated rates of substitution, a remarkable degree of uniformity has been revealed in the effects of substituents on reactivity. Only in those ethers which contain one or more alkyl groups in the nucleus which undergoes substitution has any significant departure (of the order of 10–15%) from the strict constancy of velocity ratios been observed. As a result, it has been possible to analyse the data in terms of the equation $k = PZ \cdot e^{-E/RT}$, and to demonstrate that the differences in rate which arise from constitutional changes may be accounted for satisfactorily by variations in the energy of activation, changes in the entropy term P being almost negligible by comparison (cf. *J.*, 1942, **418**, 676). When these relations had been established for ethers of the simple type $p\text{-RO}\cdot\text{C}_6\text{H}_4\cdot\text{X}$ (where R and X were varied

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independently), series of ethers based on substituted cresols, xylenols, and hydroxybenzophenones, and on dihydroxydiphenyl sulphones and hydroxydiphenyls, were examined. In all these series the same pattern of behaviour was observed. Once the constancy of velocity ratios had been firmly established, however, for a wide range of ethers, it was of interest to try to delineate the extent of this behaviour by investigating compounds where some departure from additivity might be expected.

The present investigation constitutes a first attempt to reveal these departures. One condition which would be expected to militate against additivity is the presence in the molecule of two or more polar groups in close proximity to each other, for kinetic studies of a number of reactions have shown that the presence of *ortho*-substituents is generally conducive to anomalous results. The first compounds chosen were substituted benzyl phenyl ethers with polar substituents in the *ortho*-positions of both the benzyl and the phenyl group, since these afford opportunity for the operation and interplay of polar factors.

Tables 1—3 record the velocity constants for the series of 2-nitro-, 2-chloro-, 2-methyl-, 2:6-dichloro-, and 2:4:6-trimethyl-benzyl ethers, while in Tables 4 and 5 velocity ratios for *ortho*-substituted benzyl ethers of *ortho*-substituted phenols are compared with those for the same *ortho*-substituted benzyl ethers of phenols which have no *ortho*-substituents. Unfortunately, in some series, the benzyl ethers were liquids which proved extremely difficult to purify to the degree required in this study, and, in these series, the crystalline *p*-nitrobenzyl ethers were used as a standard of reference. In such cases, the ratio of the rate constants for the *o*-nitrobenzyl ether and the *p*-nitrobenzyl ether was multiplied by the value of k/k^* where k refers to *p*-bromophenyl 4-nitrobenzyl ether and k^* to *p*-bromophenyl benzyl ether.

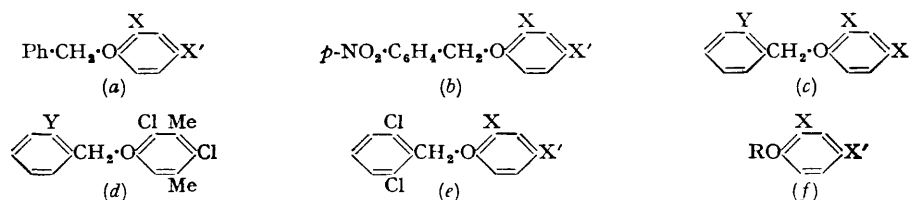


TABLE 1. Benzyl and *p*-nitrobenzyl ethers. Velocity coefficients for the chlorination of ethers of the types (a) and (b).

X	X'	k_{20}	X	X'	k_{20}
	Type (a)			Type (b)	
H	F	1.56	H	Cl	0.193
H	Cl	0.840	Me	Br	0.490
H	Br	0.805	Br	C_2H_5	0.976
Me	Cl	2.33	Br	Pr ^a	0.739
Me	Br	2.16	Br	Bu ^t	0.393
Br	Me	3.99	Br	CH_2Bu^t	0.333
Br	CH_2Bu^t	1.58			

TABLE 2. *o*-Substituted benzyl ethers. Velocity coefficients for the chlorination of ethers of the types (c) and (d).

Type (c)				Type (d)			
X	X'	Y	k_{20}	X	X'	Y	k_{20}
H	F	NO ₂	0.300	Br	Bu ^t	NO ₂	0.336
H	Cl	NO ₂	0.178	H	Cl	Cl	0.335
Me	Cl	NO ₂	0.362	Me	Br	Cl	0.897
Me	Br	NO ₂	0.392	Br	Me	Cl	1.60
Br	Me	NO ₂	0.802	H	Br	Me	1.10
Br	Et	NO ₂	0.899	Me	Br	Me	3.29
Br	Pr ^a	NO ₂	0.650	Br	Me	Me	4.58
Br	CH_2Bu^t	NO ₂	0.257				
Y				H	Me	Cl	NO ₂
k_{20}				7.09	10.3	2.97	1.23

TABLE 3. 2 : 6-Dichlorobenzyl ethers. Velocity coefficients for the chlorination of ethers of the type (e).

X	H	Me	Br
X'	Cl	Cl	Bu ^t
k_{20}	0.275	0.859	0.697

TABLE 4. Relative directive powers of the group $\text{O}\cdot\text{CH}_2\cdot\text{C}_6\text{H}_4\text{Y}$ in ethers of types (c) and (d). Values of $100k/k^*$, where k refers to group $\text{O}\cdot\text{CH}_2\cdot\text{C}_6\text{H}_4\text{Y}$ and k^* to group $\text{O}\cdot\text{CH}_2\text{Ph}$.

X	X'	Y				X	X'	Y			
		H	<i>o</i> -Me	<i>o</i> -Cl	<i>o</i> -NO ₂			H	<i>o</i> -Me	<i>o</i> -Cl	<i>o</i> -NO ₂
H	F	100	—	—	20.0	Br	Bu ^t	100	—	—	18.0
H	Cl	100	—	39.9	21.0	Br	CH ₃ Bu ⁱ	100	—	—	16.3
H	Br	100	137	—	—	Me	Br	100	142	41.6	16.8
Br	Me	100	116	40.3	20.1	Me	Cl	100	—	—	15.5
Br	Et	100	—	—	19.3	Dichloroxylyl ethers		100	137	41.8	17.4
Br	Pr ⁿ	100	—	—	18.5						

Throughout, the solvent was 99% acetic acid (containing 1 ml. of water per 100 ml. of acetic acid), the concentrations of reagents were: ether 0.0225; chlorine 0.0075; hydrochloric acid 0.0375 mole/l.; and the velocity coefficients are expressed in l. mole⁻¹ min.⁻¹ at 20°.

Discussion.—It is seen from the Tables that the 2-chlorobenzyl ethers in all series give the same value for the relative directive power—the maximum variation here is only from 39.9 to 41.8. This means that there is neither significant interaction in these compounds between the groups, nor appreciable hindrance to the approach of the reagent.

In the 2-nitrobenzyl ethers, on the other hand, this is not the case, for all the values (Table 4) of the relative directive power of the 2-nitrobenzyloxy group are lower than the value of 21 obtained in the *p*-chlorophenyl 2-nitrobenzyl ether. The lowest value, 15.5, is found for an ether having an *o*-methyl group in the nucleus in which substitution occurs. The differences here, 15.5 to 21.0, are sufficiently large to be significant (cf. Part X, *J.*, 1941, 272, Table 5), and to indicate some departure from additivity.

In the 2-methylbenzyl series, the lowest value, 115.7, is found in the 2-bromo-4-methylphenyl 2-methylbenzyl ether, which has a bromine atom in the *ortho*-position of the phenyl nucleus. The 2 : 6-dichlorobenzyl ether of *p*-chlorophenol has a directive power relative to that of the benzyl ether of 32.7, while that of the 2-chlorobenzyl ether of *p*-chlorophenol is 39.9. The deactivating effects of the two chlorine atoms are evidently not additive, for the influence of the second chlorine is small compared with that of the first.

TABLE 5. Relative directive powers of the 2 : 6-dichlorobenzyl- and benzyloxy-group in ethers of type (f). Values of $100 k/k^*$, where k and k^* refer to these two groups respectively.

X	H	Me	Br
X'	Cl	Cl	Bu ^t
$100 k/k^*$	32.7	36.8	37.2

In the two 2 : 6-dichlorobenzyl ethers which have *ortho*-substituents in the phenyl group—in one a methyl group, and in the other a bromine atom—the values of the relative directive power of the dichlorobenzyl- and benzyloxy-group, 36.8 and 37.2, are appreciably higher than the value 32.7 found for *p*-chlorophenyl 2 : 6-dichlorobenzyl ether.

The 2 : 4 : 6-trimethylbenzyl ethers are chlorinated so fast that it was impossible to obtain accurate figures for the velocity constants. The approximate values (350) found for *p*-chloro- and *p*-bromo-phenyl trimethylbenzyl ether are so much higher than the value of 4.83 for *p*-chlorophenyl 2 : 4-dimethylbenzyl ether that it must be concluded that rapid chlorination of the benzyl group occurs under the influence of the activating methyl groups, and that this masks the true reactivity of the phenyl group.

EXPERIMENTAL

Purification of Acetic Acid.—Acetic acid was purified by distillation from 2% of chromium trioxide ("AnalaR"), followed by redistillation from 0.2% of naphthalene-2-sulphonic acid and the theoretical amount of "AnalaR" acetic anhydride (Orton and Bradfield, *J.*, 1927, 983). Head and tail fractions were rejected, and the final distillate had m. p. 16.4°; this corresponds to 99.9% purity. The measurements were carried out in 99% acetic acid. This medium was stable to chlorine, and the difficulties experienced in Part XVI (*loc. cit.*) were not encountered.

Determination of Velocity Constants.—All measurements were made at $20^\circ \pm 0.02^\circ$. The procedure adopted was the same as in the earlier parts. The mean velocity constants obtained in different experiments did not differ by more than 3%.

The concentrations of ether and chlorine were always in the ratio 3 : 1. To ensure purity, solid ethers were crystallised at least four times, usually from benzene, ethanol, or acetic acid, and liquid ethers were fractionally distilled until a constant value was obtained for the velocity coefficient. This was found to be a more reliable criterion of purity than the more usual physical constants.

Materials.—Benzyl phenyl ethers were prepared by dissolving the phenol in a solution of one molecular proportion of sodium in absolute alcohol, adding one molecular proportion of the benzyl chloride in alcohol, and refluxing the mixture in a water-bath for 3–6 hr. The solid ethers were obtained on addition of water, after the bulk of the alcohol had been removed by distillation; the low-melting and liquid ethers were extracted with ether. The ether extract was washed free from phenol, and the benzyl ethers were crystallised or distilled.

2-Nitrobenzyl chloride was obtained from 2-nitrobenzyl alcohol by thionyl chloride in refluxing pyridine. It melted at 49.5° after crystallisation from acetic acid.

2-Methylbenzyl chloride, b. p. $192^\circ/760$ mm., was prepared in the same way from 2-methylbenzyl alcohol.

2 : 6-Dichlorobenzyl chloride was obtained by the chlorination of 2 : 6-dichlorotoluene, and the product, after distillation and crystallisation, had m. p. 35°.

3-Bromo-4-ethylphenol. Commercial *p*-hydroxyacetophenone was reduced (Clemmensen) to *p*-ethylphenol which was brominated in acetic acid with 1 mol. of bromine. The purified product had b. p. $110^\circ/10$ mm.

3-Bromo-4-*n*-propylphenol. Clemmensen reduction of *p*-hydroxypropionophenone gave *p*-*n*-propylphenol, which was brominated to the required product, b. p. $130^\circ/20$ mm.

3-Bromo-4-*tert*.-butylphenol. *p*-*tert*.-Butylphenol, in glacial acetic acid, was stirred during the dropwise addition of 1 mol. of bromine. The product obtained after fractionation had b. p. $120^\circ/15$ mm.

4-Bromo-*o*-cresol (OH = 1). *o*-Cresol was brominated in carbon tetrachloride at 0°. The product had m. p. 62–63°.

Those ethers which are new are listed.

Substituted benzyl phenyl ethers

Subst. in Ph	Subst. in CH ₂ Ph	M. p.	Found (%)		Formula	Required (%)	
			C	H		C	H
<i>p</i> -Br	2-Me	62°	60.6	4.6	C ₁₄ H ₁₃ OBr	60.6	4.7
<i>p</i> -Cl	2 : 6-Cl ₂	55	54.7	3.1	C ₁₃ H ₉ OCl ₃	54.3	3.1
2 : 4-Cl ₂	2-NO ₂ *	126	52.4	3.1	C ₁₃ H ₉ O ₃ NCl ₂	52.4	3.0
2 : 4-Cl ₂	2 : 6-Cl ₂ *	127	48.2	2.5	C ₁₃ H ₈ OCl ₄	48.4	2.5
4-Cl-2-Me	—	40	72.0	5.4	C ₁₄ H ₁₃ OCl	72.3	5.6
4-Cl-2-Me	2-NO ₂	110	60.6	4.4	C ₁₄ H ₁₃ O ₃ NCl	60.5	4.3
4-Br-2-Me	2-Me	28	62.1	5.3	C ₁₅ H ₁₅ OBr	61.9	5.2
4-Cl-2-Me	2 : 6-Cl ₂	54	55.8	3.8	C ₁₄ H ₁₁ OCl ₃	55.7	3.7
2-Br-4-Me	2-Me	48	62.0	5.3	C ₁₅ H ₁₅ OBr	61.9	5.2
2-Br-4-Bu [†]	2 : 6-Cl ₂	107	52.9	4.2	C ₁₇ H ₁₇ OCl ₂ Br	52.6	4.4
2 : 4-Cl ₂ -3 : 5-Me ₂	2-Me	86	65.5	5.6	C ₁₆ H ₁₆ OCl ₂	65.1	5.4
2 : 4-Cl ₂ -3 : 5-Me ₂	2-NO ₂	132	55.0	3.8	C ₁₅ H ₁₃ O ₃ NCl ₂	55.2	4.0

* The solubility of these two ethers in 99% acetic acid at 20° was too low to enable any measurements to be made.

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