766. *The Halogenation of Phenolic Ethers and Anilides. Part XVIII.** *A Kinetic Method for the Determination of the* ortho/para-*Ratios for Aromatic Ethers.*

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The proportion of *ortho*- and *para*-isomers formed in the chlorination of a number of aromatic ethers has been determined by a kinetic method.

The classical methods of determining the proportions of isomers formed in an electrophilic aromatic substitution reaction, such as nitration, involve the examination of such physical properties as freezing point, solubility, or density. Although they have frequently been employed with success, and have been the means whereby much of the knowledge relating to the orientating and the directive effects of substituents has been obtained, they necessitate the isolation and purification of the products and, as a result, they are often laborious and at times uncertain.

The present method of analysis of the amounts of *o*- and *p*-isomers formed in nuclear chlorinations, which depends on the difference in the rates of further substitution of the two isomers, permits a rapid estimation of the proportions without isolation of the separate

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* Part XVII, *J.*, 1955, 2772.

isomers or indeed of the mixture. The method, first developed by Brynmor Jones [1] for anilides, has now been applied to a range of aromatic ethers. Its success depends largely on the controlled initial chlorination of the phenyl ether to the mixture of monochloro-derivatives without any dichlorination, for the presence of even a small amount of the highly reactive unsubstituted ether would result in a rapid initial rate of chlorination, and lead to a high and erroneous value for the proportion of the more reactive *ortho*-compound. This is apparent from the rates of chlorination of anisole and its chloro-derivatives. The respective rates at 20° are : anisole *ca.* 800, *o*-chloroanisole 4·44, *p*-chloroanisole 1·23, 2 : 4-dichloroanisole 0·0032. Clearly, the accuracy of the method cannot be affected by the gradual accumulation of the dichloro-compound in the reaction mixture, but, with so great a difference in the reactivity of anisole and its *o*- and *p*-chloro-derivatives, a trace of unsubstituted anisole would lead to an erroneous result. The presence of dichlorinated ether is excluded by the method employed, especially since dichlorination is so much slower. The mixtures are also believed to be free from significant amounts of unchlorinated ether, partly because of the degree of control that is possible in the method of preparing them and partly because of the good agreement found earlier [1] between the *ortho*/*para* ratios obtained by this method and those found by other procedures.

The sensitivity of the method depends on the magnitude of the difference in reactivity of the two isomers—in the case of anisole on the rate constants 4·44 and 1·23. Mixtures of the two isomers will have rates of substitution between these limits, the exact value depending on the composition of the mixture. Such a mixture of *o*- and *p*-isomers, obtained by controlled chlorination of an unsubstituted phenyl ether with 1 mol. of chlorine, may therefore be analysed by determining its rate of further substitution, whereupon the coincidence of its velocity with that of a mixture of known composition is observed.

An assessment of the accuracy of this method of analysis has been made [1] by comparing the values of the *ortho*/*para* ratios obtained with those found by other methods.

The proportions of *o*- and *p*-isomers found for three alkyl ethers, two phenoxy-acids, and four substituted benzyl ethers are given in the annexed Table.

Ether	*ortho*/*para* Proportion	Ether	*ortho*/*para* Proportion
Anisole	21 : 79	*p*-Ethylbenzyl phenyl ether	27 : 73
Phenetole	20 : 80	*p*-*tert.*-Butylbenzyl phenyl ether	27 : 73
Phenyl *iso*propyl ether	21 : 79	*p*-Chlorobenzyl phenyl ether	28 : 72
Phenoxyacetic acid	16 : 84	*p*-Nitrobenzyl phenyl ether	28 : 72
α-Phenoxypropionic acid	17 : 83		

For these ethers, which fall into three groups, the *ortho*/*para* ratios are essentially the same within any one group. Changes in constitution, such, for example, as anisole to phenyl *iso*propyl ether, and from *p*-ethylbenzyl phenyl ether to *p*-nitrobenzyl phenyl ether do not change the ratio, although they are accompanied by substantial variations in the rates of reaction.

EXPERIMENTAL

Acetic acid was purified by distillation as described in Part XVII. The distillate had m. p. 16·4°, corresponding to 99·9% purity. The measurements were carried out in 99% acetic acid stable to chlorine.

Method of Determination of ortho/para *Ratios.*—For the initial chlorination of an ether to a mixture of *o*- and *p*-isomers, the following procedure was adopted. To 1 mole of the ether dissolved in purified acetic acid in a 100 ml. flask were added 1 mole of chlorine in the form of dichloroamine-T and the amount of water necessary to dilute the acid to 99%. Hydrochloric acid (1/30 mole) was added to initiate chlorination : it produces a low concentration of chlorine which maintains itself throughout the process and prevents the occurrence of a high local concentration and the possibility of disubstitution. When all the chlorine had reacted, an amount of pure silver acetate equivalent to the hydrochloric acid (+5% excess) was added. It is essential for the success of the method that the hydrochloric acid used in the first stage of the chlorination should be removed from solution before proceeding further. When the silver chloride precipitated had settled, a 25 ml. portion of the solution was withdrawn from the flask

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[1] Brynmor Jones, *J.*, 1936, 1231.

and the velocity of further substitution was determined in the same way as were the rates of chlorination of mixtures of known composition of the two isomers. The alternative of filtering off the silver chloride was rejected, because of the hygroscopic nature of the medium.

At concentrations greater than 1/30-molar, silver chloride has a catalytic effect on the reaction, but control experiments showed that the presence of this low concentration of silver chloride during reaction of any of these ethers had no effect on the rate constant.

The rates of chlorination of the mixtures were determined by the standard methods used in this series of investigations. The proportions of isomers in the " unknown " mixture were obtained by comparing titres at identical times and not by a comparison of velocity coefficients. Since the mixture consists of two isomers of different reactivity, velocity coefficients obtained from the usual expression for a bimolecular reaction decrease gradually as the reaction progresses.

As an example of the method, the titrations relating to *p*-nitrobenzyl phenyl ether are tabulated. The titres for the " unknown " mixture are seen to fall between those for the mixture containing 27% and those for the mixture containing 30% of *ortho*-isomer, giving a result of 28% of *ortho*-chloro-derivative in the product of chlorination of *p*-nitrobenzyl phenyl ether.

" Unknown " mixture		Artificially prepared mixtures			
ortho (%)	—	20	23	27	30
Time (min.)	Titre (ml.)	Titre (ml.)	Titre (ml.)	Titre (ml.)	Titre (ml.)
0	7·25	7·25	7·25	7·25	7·25
120	5·70	5·82	5·77	5·71	5·68
130	5·58	5·67	5·61	5·59	5·56
140	5·48	5·59	5·56	5·49	5·46

Materials.—The ethers were prepared by standard methods, particular care being taken to ensure freedom from impurities.

Solids were recrystallised until the rate of chlorination remained unchanged on further purification, and liquids were fractionally distilled under reduced pressure several times.

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