

GENERAL DISCUSSION

Dr. A. E. Bradfield (*London*) said, in introducing the paper: In the substitution reactions of benzene derivatives there is a consistency and regularity in the relation between reactivity and structure which is much more obvious than it is, for example, in aliphatic substitution and elimination reactions. There is every reason to believe that the familiar processes of nitration, sulphonation and halogenation proceed by simple bimolecular mechanisms, free from intrusions of unimolecular mechanisms. This conclusion is reached from a consideration of the observed regularities rather than from a detailed knowledge of the reaction kinetics, for experiment has shown that often these aromatic substitution reactions are by

no means simple kinetically, with the result that even the nature of the substituting entities is to some extent conjectural. In spite of this gap in our knowledge, it has been possible in this field to raise some of the observed regularities to the approximately quantitative level, and it is of interest to examine a few further examples of these regularities.

It has been shown that the effects of NO_2 , Hal., H and CH_3 attached to ring II of substituted alkoxybenzophenones, or to the benzyl group of benzyloxyphenols, may be correlated by means of the linear logarithmic relationship with the effects of the same substituents on the rates of such reactions as, for example, the hydrolysis of esters of substituted benzoic acids. When these same substituents are attached to the phenolic nucleus undergoing chlorination, they exert very much more powerful effects on the speed of the reaction. For instance, while *p*-nitroanisole chlorinates very slowly and *p*-chloroanisole at a moderate speed, anisole (with a *p*-hydrogen atom) and *p*-tolyl methyl ether chlorinate with such extreme rapidity that the reaction cannot be followed by ordinary methods. However, values for the relative effects of NO_2 , Cl, H and CH_3 attached to carbon 2 of phenolic ethers on the rate of chlorination at carbon 4, may be derived by combining the data for the relative effects of (1) H and Cl in 4-chloro- and 2:4-dichloroanisole, (2) Cl and NO_2 in 2-chloro-4-methyl and 2-nitro-4-methyl anisole, and (3) H and CH_3 in 4-bromoanisole and 2-methyl-4-bromoanisole, respectively. The values so obtained (denoted by r_2) are shown in the first line of Table IV. It should be noted that the combination of these ratios to give the complete sequence involves the assumption that the relative effects of groups attached to carbon 2 are independent of the group attached to carbon 4. This assumption is an extension of the rule of additivity of *E*-terms discussed in the paper. Comparison with the relative effects on the speed of chlorination of the same groups in the *m'*-position of alkoxybenzophenones (values denoted by r_{Bp} , line 2) shows that in the former case the range of speeds is greater by no less than 10^5 than in the latter. The following relationship exists between the values of r_2 and r_{Bp} :

$$\log r_{\text{Bp}} = 0.0988 \log r_2. \quad (1)$$

The values of r_{Bp} calculated by this expression are shown in the third line of Table V.

TABLE V

	NO_2 .	Cl.	H.	CH_3 .
r_2 . . .	1.00	2.40×10^2	4.60×10^4	3.20×10^5
r_{Bp} . . .	1.00	1.77	2.86	3.50
r_{Bp} (calc.) .	1.00	1.72	2.89	3.50

Similarly the values of r_2 may be connected with $r_{\text{Benz.}}$, representing the relative rates of chlorination of *m'*-substituted benzyl ethers by means of the expression:

$$\log r_{\text{Benz.}} = 0.128 \log r_2. \quad (2)$$

The agreement here (Table VI) is not quite so good as in the previous case, and with the CH_3 group, a definite divergence occurs.

TABLE VI

	NO_2 .	Cl.	H.	CH_3 .
$r_{\text{Benz.}}$. . .	1.00	1.91	4.29	6.49
$r_{\text{Benz.}}$ (calc.)	1.00	2.02	3.95	5.06

The effects of these groups (as *m*-substituents) on the rates of hydrolysis of benzoic esters cover a range intermediate between the two extremes considered above. Table VII shows in line 1 the relative rates of ester hydrolysis, r_H , while line 2 shows the values of r_H calculated from the expression :

$$\log r_H = -0.3945 \log r_2 \quad (3)$$

It will be seen that again the experimental and calculated values for the methyl group are not in good agreement.

TABLE VII

	NO ₂	Cl	H	CH ₃
r_H	1.00	0.111	0.0145	0.0101
r_H (calc. from 3)	1.00	0.115	0.0145	0.0068
r_H (calc. from 4)	1.00	0.122	—	0.0091

From the existing data, values for the effects of substituents attached to carbon 4 of the phenolic nucleus can only be obtained for NO₂, Cl, and CH₃. From the figures obtained, *viz.*, 1.00, 4.10×10^2 , 6.75×10^3 , values of r_H calculated by the expression :

$$\log r_H = -0.350 \log r_4 \quad (4)$$

are shown in line 3 of Table VII.

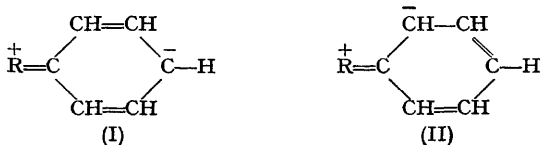
Both in the benzyl ethers and the alkoxybenzophenones, and also in the phenolic nucleus, the substituents are so placed that they are unable to initiate directly electromeric changes assisting the substitution reaction, and it would seem that it is the polarisation induced by the substituents which is the determining factor and which exhibits this regularity. It has been pointed out that the partial rate factors for the *para* nitration of toluene, benzene and the halogenobenzenes show an *approximately* linear relationship to the effects of CH₃, H and Hal. in the alkoxybenzophenones. This signifies, perhaps, that the major differences in speeds of nitration are primarily determined by polarisation effects. Polarizability, which is here possible, probably plays a more important part in determining the relative rates of *ortho* versus *meta* or *para* substitution.

Attention may be drawn to another point of interest in connection with the relative effects of alkyl groups attached to phenolic oxygen. As is to be expected, for chlorination, bromination and nitration, the rate measurements place the alkyl groups in a sequence corresponding to the operation of the general inductive effect. When attached to carbon 4 of the phenolic nucleus, the differences between the effects of the various alkyl groups on the speed of chlorination of ethers are smaller than when they are attached to oxygen, and, moreover, the sequence is now Me < Et > Pr > Bu > Amyl. The effect is still essentially a polarisation effect, but in contrast to the previous case, the mesomeric polarisation opposes the inductive effect differentially as between one group and another, so that not only is the ratio Et/Me reduced from 1.99 to 1.21, but also the ethyl group represents a maximum in the series. A precisely similar sequence is theoretically to be expected for the effects of alkyl groups attached in the *p*-position to the benzyl ring of benzyl ethers, but with the already diminished differences enormously reduced. It is not surprising, therefore, that Brynmor Jones found that in this case no differences are experimentally detectable.

Dr. W. A. Waters (Durham) said : The *meta* dibromination of benzene at high temperatures is probably a reaction of bromine atoms since (a) thermal dissociation of molecular bromine is possible under these

circumstances and (b) the polar substitution laws do not hold and one finds that the *meta/para* ratio is 2/1, which is the figure deduced from collision probabilities.¹ The low percentage of *ortho* substitution may be due, in part, to steric effects, but the production of rather a low percentage of the *ortho* isomer is a general feature of aromatic substitution, which is particularly evident in the polar substitution of compounds containing *ortho/para* directing groups. With these compounds the *ortho/para* ratio never rises to the statistical value of 2/1.

A symmetry factor conditioning energy levels in the mesomeric structures of aromatic compounds may be operative here. Thus a symmetrical form (I) may well have a lower energy content than an unsymmetrical form (II) in which the bulk of the aromatic ring lies to one side of the developed polar charges. Should this be so then the probability of the activated state being symmetrical, and largely (I) would be greater than for it being largely (II).



Dr. Bradfield, in reply, said: I agree with Waters's remarks. Hypotheses concerning the magnitude of the *ortho/para* ratio can, of course, be "inverted" for the consideration of *meta* substituting compounds, since these contain substituents which deactivate the *para* position more than the *ortho* position.

Prof. C. K. Ingold said: I wish to support Waters's and Bradfield's arguments with respect to the importance of the symmetry factor on the *ortho/para* ratio, though I think this factor affects the transition probability more than the energy of Waters's quinonoid structures (I) and (II), *i.e.*, of excited states approximating to these structures. The probability is as important as the energy in determining the capacity of the system for the perturbations needed to form the transition states of substitutions.²

Dr. Gwyn Williams (*London-Bristol*) (*communicated*): Benford and Ingold³ have pointed out that the agent in nitration is probably a molecule of the type $X-NO_2$, where X is an electron attracting group and the NO_2 group is positively polarised. As a logical extension, the nitronium cation should be a potent nitrating agent,⁴ if the conditions of reaction allow it to exist. In connection with Bradfield and Jones's comments upon the nature of the nitrating agent in aromatic nitration, it is therefore interesting to note that Russian authors⁵ have recently supported the view that the nitrating agent is a nitronium cation.

Hantzsch⁶ emphasised that the strong mineral acids differ in acid strength and determined the order $HClO_4 > H_2SO_4 > HNO_3$; and Kolthoff and Willman⁷ deduced the same order from conductivity

¹ Cf. Waters, *This vol.*, p. 772.

² Cf. Hughes and Ingold, *J. Chem. Soc.*, 1941, 612.

³ *J. Chem. Soc.*, 1938, 929.

⁴ Cf. Brewin and Turner, *ibid.*, 1928, 334; P. V. Youle, Ph.D. Thesis, Sheffield, 1937.

⁵ Ussanowitsch, *J. Gen. Chem. Russia*, 1940, 10, 219; Ussanowitsch and Abidov, *ibid.*, 223; Ussanowitsch and Glouchov, *ibid.*, 227; Ussanowitsch and Sushkevitch, *ibid.*, 230; Ussanowitsch, *Acta Physicochim. U.R.S.S.*, 1935, 2, 239.

⁶ Hantzsch and Weissberger, *Z. physikal. Chem.*, 1927, 125, 251; Hantzsch and Voigt, *Ber.*, 1929, 62, 975; Hantzsch and Langbein, *Z. anorg. chem.*, 1932, 204, 193; Hantzsch, *ibid.*, 1932, 205, 163.

⁷ Kolthoff and Willman, *J. Amer. Chem. Soc.*, 1934, 56, 1007. Cf. Hall, *Chem. Reviews*, 1931, 8, 191.

measurements in acetic acid, in which nitric acid behaves as a weak electrolyte. Hantzsch⁸ also established the existence of nitronium cations by isolating crystalline nitronium perchlorates $[\text{NO}(\text{OH})_2]^+\text{ClO}_4^-$ and $[\text{N}(\text{OH})_3]^{++}(\text{ClO}_4)_2^{--}$ and by showing⁹ that, on electrolysis of nitronium perchlorate in nitromethane solution, nitric acid accumulated at the cathode. Nitronium bisulphate was shown to exist in nitric-sulphuric acid mixtures.⁸ The nitronium perchlorates correspond to the crystalline hydroxonium perchlorate $[\text{OH}_3]^+\text{ClO}_4^-$.¹⁰

Applying these considerations to nitrating acids, Ussanowitsch and co-workers⁵ point out that aromatic nitration is facilitated by mixing nitric acid with substances (e.g., H_2SO_4) towards which it acts as a base and hindered by mixture with substances (e.g. water, nitrobenzene) towards which it acts as an acid. They conclude that nitrate ions do not nitrate aromatic compounds and that the nitrating agent is the nitronium cation. On the other hand, the nitration of aliphatic compounds¹¹ is assisted by addition of water or acetic acid and here they consider the nitrating agent to be the nitrate ion.

Experimentally, the authors have examined the nitration of toluene at 90° , in nucleus and side-chain, by nitric acid mixed with varying proportions of each of a number of solvents. Increasing proportion of monochloroacetic acid and ethyl nitrate, towards which nitric acid displays no acid or basic function, lowers the yields of both side-chain and nuclear nitrated products obtained in a given time; but increasing proportion of acetic acid and nitrobenzene lowers the yield of nitrotoluenes and increases that of phenylnitromethane; whilst sulphuric and trichloroacetic acids direct nitration almost exclusively into the nucleus. Nitric acid evidently acts as an acid towards acetic acid and nitrobenzene, and as a base towards sulphuric acid; but the conclusion that it acts as a base towards trichloroacetic acid may be in conflict with the results of Hantzsch,⁸ according to which trichloroacetic acid is a weaker acid than nitric acid.

Dr. H. O. Jenkins (*communicated*): The influence of substituents on the alkaline hydrolyses of a series of *p*-substituted ethyl benzoates has been examined previously by plotting the energy of activation *E* against the calculated electrostatic potential ψ due to the substituent dipole, at the carbon atom to which the ester grouping is attached.¹² The changes in energies of activation have been referred to differences in the amounts of work required to bring up hydroxyl ions against dipole fields, and the usual mechanism of alkaline ester hydrolysis given some quantitative support.

In a private communication Bradfield has invited me to apply this method to the study of the effect of substituents attached to the phenolic nucleus undergoing chlorination in the *m*-position to the substituent. The data therefore of Bradfield and Jones for the relative effects of the NO_2 , Cl, H, and CH_3 groups attached to carbon 2 of the anisole nucleus on the rate of chlorination at carbon atom 6 has been taken, and plotted against the electrostatic potential at carbon 6 due to each substituent dipole at carbon 2. As the above-mentioned authors have explained, the data of the complete sequence are partly derived using the well-established law of additivity of *E* terms. It is $\log r_2$ (see Bradfield's Introduction) which is plotted against ψ , the justification for this being the approximate constancy of the *PZ* term of the Arrhenius expression. The flat curve I is obtained, but the departure from linearity is not great (although it may well be a real effect (see Fig.) considering the range of r_2

⁸ Hantzsch, *Ber.*, 1925, **58**, 941.

⁹ Hantzsch and Berger, *ibid.*, 1928, **61**, 1328.

¹⁰ Volmer, *Annalen*, 1924, **440**, 200.

¹¹ Konowalow, *Ber.*, 1895, **28**, 1852; Markownikoff, *ibid.*, 1899, **32**, 1441; 1900, **33**, 1905.

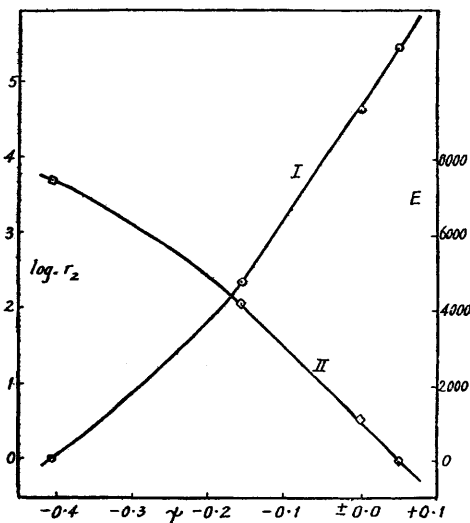
¹² Jenkins, *J.C.S.*, 1939, 1780.

which is 10^5 . Similar graphs could be drawn for the effects of substituents attached to carbon atom 4 of the phenolic nucleus, and to represent the relative rates of chlorination of substituted alkoxybenzophenones and benzyl ethers. Again using equations of the form

$$\ln k_{\text{Me}} - \ln k_{\text{NO}_2} = \frac{E_{\text{NO}_2} - E_{\text{Me}}}{RT}$$

relative energies of activation have been calculated for the anisole series with the substituents at carbon 2. These are given in the Table and plotted in Curve II.

As is to be expected a flat curve is also obtained. The main point of interest, however, lies in the difference of 7360 cal. when the substituent is changed from NO_2 to CH_3 , which provides a guide as to the mechanism of the reaction. Since the substituents are not in a position to directly initiate electromeric changes affecting the reaction, Bradfield drew the conclusion that it is the polarisation induced by them which is the determining factor affecting the relative rate, and this is supported by the present method of treating the re-



sults. The usual statement, however, as to the mechanism of the chlorination of phenolic ethers in 99 % acetic acid surely needs some modification. In the hydrolyses of *p*-substituted ethyl benzoates $E_{\text{Me}} - E_{\text{NO}_2}$ was found experimentally to be 3700 cal. The corresponding difference 7360 cal. in the chlorination example is of the same order of magnitude, and the inference is that the attacking body is again an ion and not a partially polarised chlorine molecule, *i.e.* a dipole,

Substituent.	E (cal.)	ρ .
NO_2 . .	7360	- 0.408
Cl . .	4180	- 0.158
H . .	1130	\pm 0.000
CH_3 . .	0	+ 0.050

which would provide an insignificant work term. The ion would also have to be positive in sign. It is realised that the chlorination reactions are more complex than the hydrolyses, but there is a similarity in the effects of substituents which implies some similarity in mechanism.

Dr. Brynmor Jones (Sheffield), in reply, said: In the earlier stages of the kinetic study of the chlorination of phenolic ethers it was expected that the observed regularity in the relative effects of groups attached to the oxygen atom and of substituents in the nucleus would only be maintained within a narrow range of ethers. Subsequent extension of the work to include a wide variety of ethers has so far, however, brought to light only minor anomalies.

The regularities have been explained by assuming that for all the compounds examined the term P of the expression $k = PZe^{-E/RT}$ remains constant, and further, that each group contributes a characteristic quota to the critical energy increment. That the influence of groups is, in fact,

mainly on *E* was shown by Bradfield, Jones and Spencer in 1931 when a study of the velocities of chlorination at 20° and 35° was made.

Latterly attention has been turned to a re-examination of the question of the constancy of the term *P* with a view to determining the precision with which the earlier conclusion may be applied to the much wider range of ethers since investigated.

At present results are available only for ethers of the simple type *p*-RO . C₆H₄ . X, where R is an alkyl or benzyl group and X is F, Cl, NO₂ or CPh. For the ten ethers of this type selected for detailed study, the energies of activation, calculated from the rates of chlorination measured at five temperatures between 15° and 35°, vary from 9,600 to 14,300 cal. On plotting log₁₀ *k* against *E*, it is found that the series of approximately equally spaced points all fall on or very near to a line of slope $-2.303RT$. Up to the present the only disubstituted ether examined is 2 : 4-dichloroanisole, and this, too, gives a point on the line.

These new measurements (a fuller account of which will be published elsewhere) fully confirm the original conclusion, *viz.*, that the influence of substituents is to be ascribed almost entirely to changes in the energy of activation.

It is proposed later to extend this investigation to di- and poly-substituted phenolic ethers.
