294. *Studies of the* ortho-*Effect. Part III. Alkaline Hydrolysis of Benzoic Esters.*

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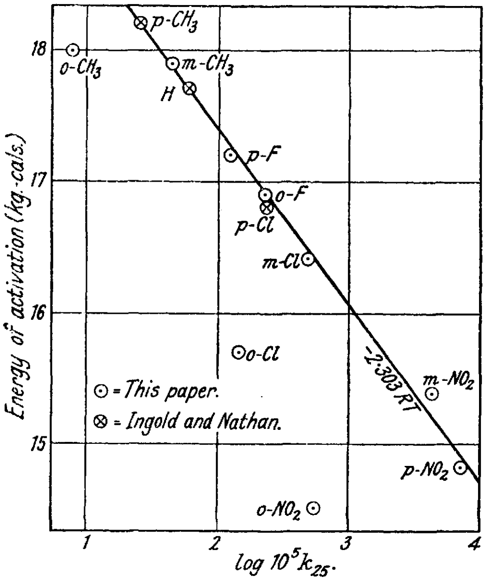
It has been found by Ingold and Nathan (J., 1936, 222) that the effect of a *p*-substituent upon the alkaline hydrolysis of ethyl benzoate is to change the energy of activation, the *P* factor of the kinetic equation not being influenced to any extent. The results described below show that the same remark applies to *m*-substituents, but that a group in the *o*-position leads to a relatively low velocity of hydrolysis by decreasing the *P* factor. The suggestion is made that this is due to a reduction in the facility with which the activated complex (formed by the ester and hydroxyl ion as the first step in the complete change) breaks down to give the products.

It has now become evident that the mere comparison of velocity coefficients determined at a single temperature may throw but little light upon the influences governing reactivity, and may in some cases, indeed, lead to incorrect conclusions. In order to extract the information which a study of reaction speeds is capable of yielding, the velocity coefficient must be analysed into its component parts. Hinshelwood (this vol., p. 635; compare Hinshelwood and Winkler, J., 1936, 371) has given ample justification for the treatment of reaction velocity problems on the basis of the collision theory, and for the use of the equation $k = PZe^{-E/RT}$, where E is the energy of activation and P represents the proportion of the sufficiently energised collisions which actually lead to the formation of the reaction products. The collision method is "not really at a fundamental disadvantage" as compared with the thermodynamic treatment of Polanyi and others, and it has the advantage of providing a simple physical picture of the reaction. It attributes changes in velocity to variations in E, in P, or in both (Z does not change seriously from an average value of about $2{\cdot}8 \times 10^{11}$), and the determination of these two quantities for a series of reactions may be regarded as a satisfactory method of attacking problems such as those relating to the influence of substituent groups upon reactivity.



In at least three instances, *viz.*, the chlorination of phenolic ethers (Bradfield *et al.*, *Chem. and Ind.*, 1932, **51**, 254, and references there cited), the benzoylation of anilines (Williams and Hinshelwood, J., 1934, 1079), and the alkaline hydrolysis of ethyl benzoates (Ingold and Nathan, J., 1936, 222), it has been shown that the differences in velocity accompanying constitutional changes are to be ascribed, almost entirely at least, to variations in the energy of activation, P being altered but little. Ingold and Nathan point out that, in these reactions where substituents influence the energy of activation almost exclusively, "induced polar effects may be assumed to be isolated from local disturbances." Such is the case, for example, in the reaction which they studied, *viz.*, the alkaline hydrolysis of *p*-substituted ethyl benzoates. The same applies to the corresponding *m*-substituted esters, and we have now shown that, here again, the value of P is almost constant. Such constancy is indicated most clearly by a linear plot of E against log k, the straight line having a slope of $-\ 2{\cdot}303RT$; this theoretical line is shown in the figure, and it will be seen that the points relating to the *m*-substituted ethyl benzoates, as well as those for the isomeric *p*-substituted esters, approximate to it very closely.

When the substituent is in the *o*-position, however, a different state of affairs arises. The *o*-substituted esters are hydrolysed, as a rule, much more slowly than their *m*- and *p*-isomerides, as has been shown by Kindler (*Annalen*, 1928, **464**, 278) and others. We have determined the rates and energies of activation of the alkaline hydrolysis of a number of these esters, and the points relating to them are included in the figure. Our results are summarised below.

Alkaline Hydrolysis of Benzoic Esters, $X\cdot C_6H_4\cdot CO_2Et$, *in* 85% *Alcohol.*

X.	10^3k_{50}.	10^3k_{35}.	10^3k_{25}.	10^2P.	E (cals.).	X.	10^3k_{50}.	10^3k_{35}.	10^3k_{25}.	10^2P.	E (cals.).
H	6·28	1·68	0·621	2·17	17,700	*m*-CH_3	4·57	1·18	0·433	2·13	17,900
o-CH_3	0·809	0·207	0·0776	0·45	18,000	*m*-Cl	39·6	11·8	4·77	1·82	16,400
o-F	21·0	5·81	2·32	2·13	16,900	*m*-NO_2	—	100	42·9	3·08	15,400
o-Cl	11·0	3·38	1·39	0·17	15,700	*p*-F	12·0	3·20	1·26	1·92	17,200
o-NO_2	38·8	12·75	5·41	0·08	14,500	*p*-NO_2	—	162	72·0	1·86	14,800

(In the above table, k is the bimolecular velocity coefficient expressed in l./g.-mol.-sec., and P is calculated from the kinetic equation on the assumption that $Z = 2\cdot 8 \times 10^{11}$.)

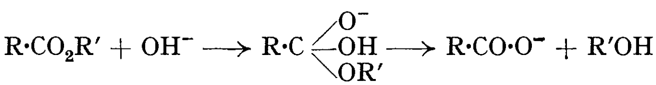
Three interesting facts emerge from our study of the alkaline hydrolysis of *o*-substituted benzoic esters :

1. The hydrolysis of ethyl *o*-fluorobenzoate does not reveal the operation of any factors which are not observed in the *m*- and the *p*-substituted ester; in the plot of E against log k, this ester gives a point lying on the theoretical line.

2. For the remaining *o*-substituted esters, the values of E are not very different from those obtained for their *m*- and *p*-isomerides. On the whole, they show a tendency to be slightly *lower*, that for ethyl *o*-chlorobenzoate definitely so.

3. The *o*-esters, except the *o*-fluoro-ester, give values of P which are *smaller* by about a power of 10 than those found for the others. The lower velocity observed when a substituent is introduced into the *o*-position is therefore to be attributed to a decrease in the proportion of energised collisions which actually lead to the reaction products.

Hinshelwood and Winkler (*loc. cit.*) have directed attention to several causes which might reduce the value of the P factor for reactions in solution. It has long been recognised that when two molecules collide with the necessary energy, the formation of the transition complex may still require the fulfilment of definite phase and orientation conditions. But even when all these demands are satisfied, and the molecules have actually " got to grips," the consummation of the reaction is yet dependent upon the existence of the right conditions for the breakdown of the complex to give the products. Hinshelwood has suggested, for example (*Trans. Faraday Soc.*, 1936, **32**, 970), that it may be necessary for solvent molecules to be suitably placed for the removal of energy from the complex. We believe that, in catalysed reactions, P may depend very largely upon the fulfilment or otherwise of the conditions necessary for the transformation of the complex into the actual products, *i.e.*, for the completion of the second stage in a scheme such as the following : $A + \text{Catalyst} \longrightarrow [A, \text{Catalyst}] \xrightarrow{B} \text{Products} + \text{Catalyst}$. The alkaline hydrolysis of an ester may be formulated



$$R\cdot CO_2R' + OH^- \longrightarrow R\cdot C\begin{cases} O^- \\ OH \\ OR' \end{cases} \longrightarrow R\cdot CO\cdot O^- + R'OH$$

and the velocity depends, *inter alia*, upon the probability that the complex will break down to give anion and alcohol; the possible intervention of a solvent molecule at this stage, as suggested by Newling and Hinshelwood (J., 1936, 1357), does not influence the argument.

The relatively small values of P observed in the alkaline hydrolysis of *o*-substituted ethyl benzoates *might* be due to a decrease in the proportion of fruitful collisions between ester and hydroxyl ion, but since, in acid-catalysed esterification, *o*-substituents actually cause an increase in P (Hinshelwood and Legard, J., 1935, 592), we do not regard this as probable. In a mechanism of esterification suggested by Evans, Morgan, and Watson (J., 1935, 1171), the acid, after activation by the catalyst, co-ordinates with a molecule of alcohol, whereas in alkaline hydrolysis the complex releases an —OR group (see scheme above; cf. Polanyi and Szabo, *Trans. Faraday Soc.*, 1934, **30**, 508); we suggest, therefore, that the "*ortho*-effect" observed in these hydrolyses arises from the operation of some factor which reduces the facility with which the products are formed from the complex, but also assists the co-ordination with a molecule of alcohol (in esterification processes). The possible nature of this factor is considered in Part I.

EXPERIMENTAL.

Materials.—The ethyl benzoate after fractionation had b. p. 103°/20 mm. The three ethyl nitrobenzoates were purchased, and purified by recrystallisation to constant m. p.; m. p.'s, o-NO_2, 30·5°; m-NO_2, 42°; p-NO_2, 57°. The ethyl *o*- and *m*-toluates and -chlorobenzoates were prepared from the corresponding acids by the usual esterification process and fractionated at least three times; b. p.'s, o-CH_3, 110°/17 mm.; m-CH_3, 110°/20 mm.; *o*-Cl, 130°/20 mm.; *m*-Cl, 121°/20 mm. Ethyl *p*-fluorobenzoate was prepared from ethyl *p*-aminobenzoate as described by Schiemann and Winkelmüller ("Organic Syntheses," Vol. 13, p. 52), b. p. 105°/30 mm., m. p. 26° (cf Dippy and Williams, J., 1934, 1466). Ethyl *o*-fluorobenzoate was obtained by esterification of *o*-fluorobenzoic acid, also prepared by the Balz–Schiemann method, according to the details given by Dippy and Williams (*loc. cit.*), b. p. 105°/10 mm. All liquid esters were fractionated immediately before use, considerable head and tail fractions being neglected.

Velocity Measurements.—The aqueous-alcoholic medium employed was prepared as follows. Ethyl alcohol after being shaken with silver oxide was kept over freshly baked lime, from which it was subsequently distilled. This alcohol was suitably diluted with conductivity water; observed density of medium, $d_{4^\circ}^{20^\circ}$ 0·8314, corresponding to 84·8% of alcohol by weight. Errors due to possible non-reproducibility of the medium were avoided by preparing a large stock. The stock solution of alkaline hydrolysing agent consisted of $N/5$-sodium hydroxide ("Analar") in this medium. In the kinetic measurements the ester and sodium hydroxide were used in equivalent amounts, and the bimolecular velocity coefficients were calculated from the equation $k_2 = (1/t) \,.\, x/(a - x)a$. At the dilutions used (0·05M) this procedure was found to be more satisfactory than that of Ingold and Nathan (*loc. cit.*), who employed excess of ester.

The ester was weighed out accurately in a 100-ml. stoppered flask, and made up to 75 ml. with 84·8% alcohol, at the temperature of the bath. 25 Ml. of sodium hydroxide in 84·8% alcohol at the same temperature were added, and the flask well shaken. Zero time was taken at half delivery of the alkali. At suitable intervals, 10 ml. of reaction mixture were withdrawn, added to 10 ml. of cooled $N/15$-hydrochloric acid, and titrated with $N/20$-sodium hydroxide, bromothymol-blue being used as indicator. Each end-point was matched against a colour standard consisting of a freshly prepared solution of 15 ml. of $M/30$-sodium benzoate in 15 ml. of 50% aqueous alcohol containing the same amount of indicator as used in the titration. Except for the more rapid reactions of the nitrobenzoic esters, we estimate the accuracy of the velocity coefficients as ± 1·5%. The Arrhenius straight line was followed accurately in every case.

We thank Messrs. Imperial Chemical Industries Ltd. for financial assistance.

TECHNICAL COLLEGE, CARDIFF. [*Received, June 22nd*, 1937.]