49. *Mechanism of, and Constitutional Factors controlling, the Hydrolysis of Carboxylic Esters. Part VIII. Energies Associated with Induced Polar Effects in the Hydrolysis of Substituted Benzoic Esters.*

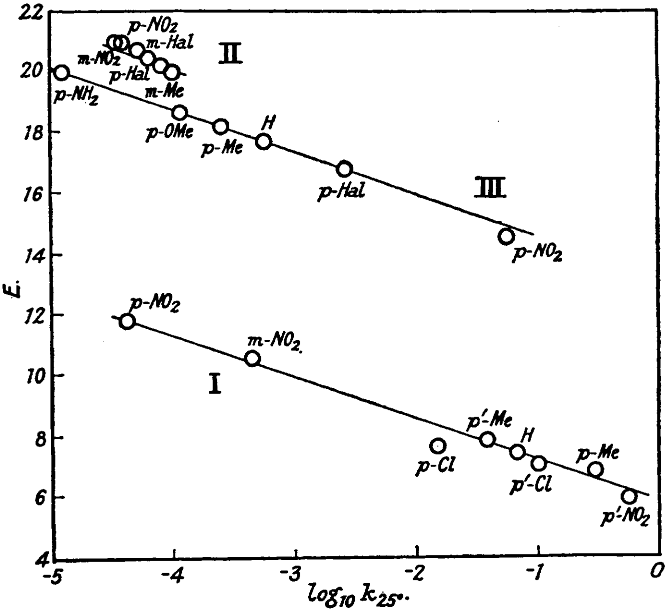
By CHRISTOPHER K. INGOLD and WILFRED S. NATHAN.

IT is a tacit assumption of the electronic theory of organic reactions that a substituent in modifying the availability of electrons at the site of a reaction thereby alters the energy of activation (*Chem. Reviews*, 1934, **15**, 227). The experimental examination of this proposition has already been taken up by several authors, using the only practicable method, *viz.*, analysis of the effects of constitution on reaction rate into effects on B and E in the Arrhenius equation $k = Be^{-E/RT}$ $(= PZe^{-E/RT})$. First, Bradfield and Jones (J., 1928, 1006, 3073; 1931, 2903, 2907) showed that in the nuclear halogenation of phenol ethers the changes of rate are controlled, mainly at least, by changes of critical energy which the substituents influence in an additive manner. Secondly, Nathan and Watson (J., 1933, 217, 890, 1248) showed that a similar assumption for aromatic side-chain reactions would lead to a simple connexion between the dipole moment of a group and its effect on the critical energy; however, Evans, Morgan, and Watson (J., 1935, 1168) measured Arrhenius critical energies for the acid-catalysed bromination of nuclear-substituted acetophenones and observed deviations which they regarded as sufficiently serious to deserve a special interpretation. Thirdly, Williams and Hinshelwood showed that the effect of nuclear substituents on the rate of benzoylation of anilines is, in fact, controlled almost wholly by the effect on E; however, in other studies by Hinshelwood, Winkler, and Legard, in which no use is made of the principle of isolating induced polarity from local effects by interposing the electrically conducting benzene ring between the substituent and the reaction zone, marked changes in both B and E were found (J., 1934, 1079; 1935, 587, 1147, 1588).

We have confined ourselves to the case in which induced polar effects may be assumed to be isolated from local disturbances: we have studied the alkaline hydrolysis of *p*-substituted benzoic esters, and have investigated in the usual way the dependence of changes in the absolute rate on variations of B and of E. Before considering our own results, however, we wish further to discuss the two prior investigations (one published during the progress of our experiments, and the other after their completion) in which the conditions and methods are similar to ours; for it has been suggested that these researches reveal a noteworthy difference of result, inasmuch as in Williams and Hinshelwood's experiments on the benzoylation of anilines the plot of E against $\log_{10}k$ approximated to a straight line of that slope ($-$ 2·303RT) which corresponds to constancy in B, whereas in Evans, Morgan, and Watson's experiments on the bromination of acetophenones no such plot was obtained. We take the view, however, that it is asking altogether too much of the Arrhenius equation to anticipate a linear plot of the right slope for the acetophenone experiments because of the smallness of the range of velocities. It is pointed out in another connexion (following paper) how unsatisfactory the conclusions can be which follow from an *exact* identification of Arrhenius's B and E, both of which are functions of temperature, with quantities implicitly considered to be functions of structure alone: such an identification is justified only when the differences in question are large. Now Williams and Hinshelwood had a range of variation of 1 : 10^4 in k, and hence the Arrhenius equation was adequate to establish the conclusion which these authors drew, *viz.*, that the changes of rate are correlated essentially with changes in the energy of activation. On the other hand, in Evans, Morgan, and Watson's experiments the extreme range of k was only 1 : 3, and the Arrhenius equation was therefore, in our opinion, not a sufficiently refined instrument of analysis.

Our results agree with those of Williams and Hinshelwood, but we made our range of variation of velocity as large as we could, *viz.*, 1 : 5000. The corresponding extreme range of the factor B was only 1 : 2·5, so that almost the whole of the variation of rate was accounted for by the alterations of E.

Effect of nuclear substituents on second-order rate constants of aromatic side-chain reactions.



[E is in kg.-cals., and $k_{25°}$ in l./g.-mol./sec. The lines represent B = constant.]

Series I : Benzoylation of anilines in benzene (W. and H.). Rate $\propto[\mathrm{Ar{\cdot}NH_2}][\mathrm{Ar{\cdot}COCl}]$. Substitution in aniline nucleus represented by *m*- and *p*-, and in benzoyl chloride nucleus by *p*′-.

Series II : Hydrion-catalysed bromination of acetophenones in 75% acetic acid (E., M., and W.). Rate $\propto[\mathrm{H^{\cdot}}][\mathrm{Ar{\cdot}COMe}]$. The points for the separate halogens are so closely grouped that only mean points are given, one for the *m*- and one for *p*-halogens.

Series III : Saponification of benzoic esters in 85% ethyl alcohol (this paper). Rate $\propto[\mathrm{OH'}][\mathrm{Ar{\cdot}CO_2Et}]$. The closely grouped points for the separate halogens are represented by a mean point.

In the figure the three aromatic side-chain reactions, (I) the benzoylation of anilines, (II) the hydrion-catalysed bromination of acetophenones, and (III) the saponification by hydroxide ion of ethyl benzoates, are compared with respect to the influence of nuclear substituents on k and on E and B : E is plotted against $\log_{10}k_{25°}$ on the same scale for the three reactions, and in each case a straight line of the slope which signifies the invariance of B is drawn through the point for the unsubstituted compound. It will be observed that the deviations of the points from the reference lines are comparable in the three cases; in particular, it is not apparent that the data for the acetophenone reaction are qualitatively distinct from, or in demonstrable conflict with the general trend of, the other results. Of course, if the acetophenone points are plotted on a scale large enough to make their locus as long as those which relate to the other two reactions, the deviations look very great.

The data for the saponification of benzoic esters are summarised in the following table, where the second-order rate constants at 25° are in l./g.-mol./sec. The sequence of groups is normal except amongst the halogens, where, however, the differences of rate are not of a kind to which we should ascribe simple constitutional significance. The *p*-methoxy-group, although electron-attracting, is in its right place in the series for the reason already explained in relation to the strengths of the substituted benzoic acids (J., 1933, 1124); a *m*-methoxy-group would fall, of course, between H and *m*-Cl. Evidently, the reaction requires the recession of electrons, as we should expect from its electronic nature.

p-Substituent.	$10^5k_{25^\circ}$.	*E* (cals.).	$10^{-9}B$.	*p*-Substituent.	$10^5k_{25^\circ}$.	*E* (cals.).	$10^{-9}B$.
NH_2	1·27	20,000	5·42	Cl	237	16,800	4·93
OMe	11·5	18,650	5·38	I	278	16,700	4·93
Me	25·1	18,200	5·73	Br	289	16,800	5·82
H	55·0	17,700	5·32	NO_2	5670	14,500	2·30

EXPERIMENTAL.

Materials.—Ethyl benzoate and its *p*-amino-, *p*-methoxy-, *p*-chloro-, *p*-bromo-, and *p*-nitro-derivatives were purchased, and the *p*-iodo-derivative was prepared from the amino-compound. All the liquid esters were purified by repeated fractionation, considerable head and tail fractions being neglected. The crystalline amino- and nitro-esters were crystallised from ethyl alcohol repeatedly, and further purified by partial freezing. In some preliminary experiments the medium was " 50% " aqueous alcohol, *i.e.*, 50 g. of absolute ethyl alcohol made up to 100 c.c. with water. In the main series the medium was " 85% " aqueous alcohol; this was made up by weight (about 5 l.) from carefully dehydrated and fractionated absolute alcohol, and its density indicated a concentration by weight of 84·988%.

Measurements.—The thermostats could be set to 0·05°. The ester (0·1*M*) was weighed and made up to the appropriate volume at the thermostat temperatures. A few drops of 60% sodium hydroxide (to become 0·005*M*) were delivered from a micropipette into a dry flask in the thermostat and the ester solution was added and well shaken. Pipettes stored in a jacket in the thermostat were used to withdraw samples, which were run into aqueous hydrochloric acid and titrated, the acid solutions being kept at — 5° and subsequently warmed to the room temperature if they could not be titrated at once. As the measured concentration falls off with time substantially according to an exponential law under the conditions chosen, no error should arise through the finite time of delivery of the pipette (a simple calculation shows this), but the precaution was taken, nevertheless, to employ an especially rapid pipette for the faster reactions. The nozzle was widened to give delivery in 7 secs., and the top was provided with a 3-way tap, the extra branch of which contained a suitable air-leak; by means of this device the setting, which was observed from above with the use of an inclined mirror, could be done very rapidly. A 15-c.c. micro-burette was employed, which could be read to 0·01 c.c., although the end-point was estimated to be liable to an error of 0·05 c.c. The titrations, which were done in approximately 33% alcohol with bromothymol-blue as indicator, were facilitated in some cases by the addition of a little carbon tetrachloride to dissolve crystalline or viscous esters. Carbon dioxide-free reagents were used, and all end-points in a run were matched against the initial end-point, which for each run was matched against a permanent colour standard. It was verified that *p*-aminobenzoic acid, the weakest of the acids formed in the hydrolyses, could be accurately titrated.

Results.—Preliminary experiments (not recorded) were made to determine the best method of calculating the rate constants, and it was ultimately decided to use a modification of Guggenheim's method (*Phil. Mag.*, 1926, 2, 538), in which each result is used once only; in our modification each result is used once and given a weight proportional to its accuracy, *i.e.*, to the titre. Other preliminary experiments (below) showed that neutral-salt effects are small at the dilutions used.

Ethyl benzoate in " 50% " alcohol at 25·0°. Effect of neutral salts.

$[KOH]_{t=0}$ (= [KOH] + [KOBz])	0·005	0·005	0·010	0·010
[NaCl]	—	0·005	0·010	0·020
Total μ	0·005	0·010	0·020	0·030
10^3k_2 (l./g.-mol./sec.)	1·30	1·32	1·32	1·32

A few experiments only were carried out in order to confirm the linearity of the usual logarithmic plot based on the Arrhenius equation, as this has previously been so very thoroughly established for ester hydrolysis in aqueous solution. The three following results fit the Arrhenius equation quite accurately.

Ethyl benzoate in 50% *ethyl alcohol.*

Temp.	25·0°	40·0°	50·0°
10^3k_2 (l./g.-mol./sec.)	1·33	9·32	20·00

The main series of results relate to " 85% " ethyl alcohol as solvent and the temperatures 25·0° and 50·0° (in one case 40°). The constants are summarised below. Those relating to the nitro-compound are less accurate than the others on account of the rapidity with which this ester undergoes hydrolysis.

p-*Substituted ethyl benzoates in* 85% *ethyl alcohol.*

(10^3k_2 in l./g.-mol./sec.)

p-Group	NH_2	OMe	Me	H	Cl	I	Br	NO_2
25·0°	0·0127	0·115	0·251	0·550	2·37	2·78	2·89	56·7
50·0°	0·172	1·31	2·71	5·56	21·3	24·8	25·9	183 *

* Temp. = 40·0°.

In the last table the rate constants are calculated relatively to those of the unsubstituted ester, and compared in this form with the figures derived by McCombie and Scarborough (J., 1915, **107**, 156) for hydrolysis in absolute ethyl alcohol at 30° and by Kindler (*Annalen*, 1926, **450**, 1) for hydrolysis in 87·83% (weight) aqueous ethyl alcohol at 30·0°.

Ratios (k_2^R/k_2^H) *of rate constants for* p-*substituted ethyl benzoates.*

p-Group (R)	NH_2	OMe	Me	[H]	Cl	I	Br	NO_2
Temp. 25°	0·0231	0·208	0·456	1·00	4·31	5·06	5·25	103·1
,, 50°	0·0308	0·232	0·480	1·00	3·78	4·39	4·57	—
McC. and S. (30°)	—	—	0·506	1·00	3·83	4·76	4·31	—
K. (30°)	0·0233	0·214	0·467	1·00	4·33	5·09	4·94	103·9

UNIVERSITY COLLEGE, LONDON.

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