166. *The Activation Energy of Organic Reactions. Part I. Electronic Theories of Organic Chemistry from the Standpoint of Chemical Kinetics.*

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In this paper an attempt is made to correlate certain aspects of the electronic theory of organic reactions with the modern analysis of activation energy. The reactive centres in a molecule and in an attacking reagent are characterised *schematically* by effective charges which, according to sign, facilitate or oppose their mutual approach. Modification of the charges, by the introduction of substituents or by change of reagent, are thought of as adding algebraically extra classical electrostatic terms to the (largely non-classical) repulsion energies and to the bond energies involved in the energy of activation. Detailed consideration on this basis leads to the prediction of various regularities, which assist the interpretation of the experimental facts relating to the influence of substitution on reactivity.

THE influence of substituent atoms on the reactivity of organic compounds can be interpreted in an illuminating way by the theory of internal electron displacements of the two types, inductive and electromeric, which was first advanced in a generalised form by Robinson between 1919 and 1926 and developed by him and by Ingold and others (Hamilton and Robinson, J., 1916, **109**, 1029; Robinson, *ibid.*, p. 1038; Robinson and Robinson, J., 1926, 2204; Kermack and Robinson, J., 1922, **121**, 433; Robinson, *J. Soc. Chem. Ind.*, 1925, **44**, 456, 563; Allan, Oxford, Robinson, and Smith, J., 1926, 402; Robinson, " Outline of an Electrochemical Theory of the Course of Organic Reactions," 1932; Ingold and Ingold, J., 1926, 1310; Ingold, *Chem. Reviews*, 1934, **15**, 225).

From a totally different point of view the subject can be treated in terms of the ordinary conceptions of reaction kinetics such as activation energies, collision numbers, and probability factors. The two ways of approach are largely independent, but there is a certain common ground where they overlap, and it is obviously desirable that the ideas used in each should be expressible in terms of one another. The present paper attempts to contribute to this clarification.

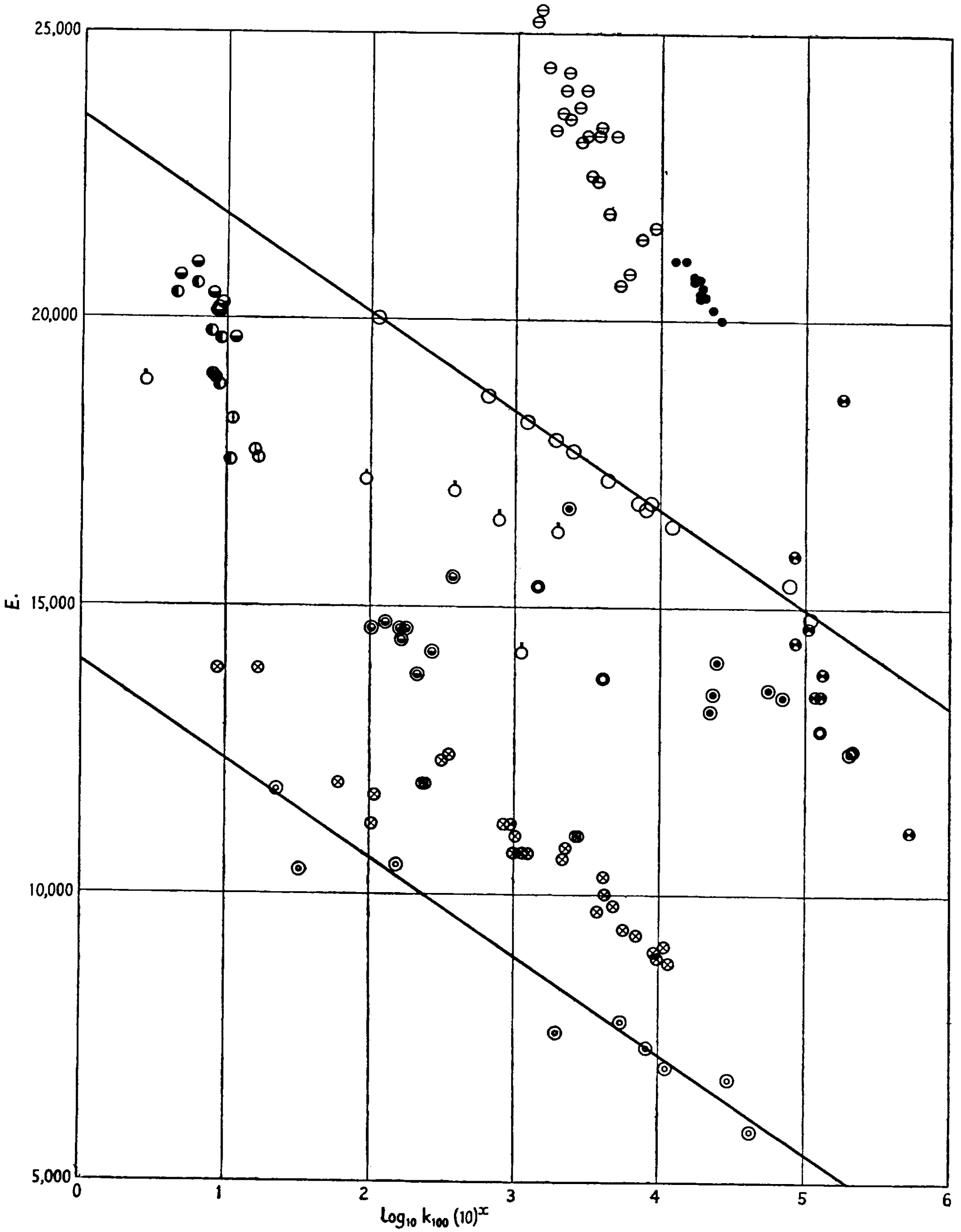
The treatment is a compromise between the purely non-physical approach of organic chemistry and the formally exact but complicated methods of the quantum-mechanical theory. The variations in certain *bond energies* and certain *interaction energies* between molecules are schematised by classical electrostatic terms. No attempt at application of rigid principles in calculating the energies is made, the main object being to show that certain interesting results follow from a consideration of the *balance* between the two *kinds* of energy terms referred to.

Electronic Theories of Organic Reactivity.—According to the modern theory, a substituent alters the reactivity of the parent compound by altering the availability of electrons at the point of reaction. According to Robinson, the total electronic effect may be divided into the general polar effect and the electromeric effect. The former is due to the unequal sharing of electrons between atoms, the latter to what is now called a resonance between possible electronic structures satisfying the octet rule. Both are permanent to a certain extent but also time-variable, especially the electromeric effect, the time-variability depending upon the demands of the attacking reagent. The sign of the charge produced by the substituent may be inferred from physical considerations such as dipole moments (see, *e.g.*, Sutton, *Proc. Roy. Soc.*, 1931, **133**, *A*, 668). The effect of a series of substituents in a given reaction generally follows the order predicted from the sign and magnitude of the induced charges: apparent anomalies can be explained in terms of a finer analysis of the relative importance of the general polar and electromeric effects. Reactions have been classified as class A or class B according as the reaction is facilitated by accession of electrons to or recession of electrons from the point of attack (Ingold and Rothstein, J., 1928, 1217). This terminology is convenient in classifying data, but gives no insight into the actual mechanism. In particular, it is impossible to predict to which class the reaction belongs, as was clearly pointed out by Oxford and Robinson for the case of hydrolysis (J., 1926, 384). Ingold has also classified reactions into types S_N1 and S_N2 according to whether a unimolecular ionisation or a bimolecular interaction with a reagent determines the rate. Much of his discussion is helpful for the purpose of this paper, though the point of view is different.

The present paper suggests possible lines along which the problem may be approached from the point of view of the activation energy and the various terms of which it is made up.

Reactivity and activation energy. The rate of a chemical reaction may be represented by the equation $k = PZe^{-E/RT}$, where E is the activation energy, Z the collision number, and P the probability that activated collisions shall result in reaction, being a measure of conditions other than activated collision which must be fulfilled. The order of magnitude of Z does not vary, and the question arises whether the changes of reactivity with which the electron-drift theories deal depend chiefly upon changes in E or upon changes in P. It now seems clear that changes in E are of primary importance. Naturally, if the substituent which alters the reactivity of a parent substance is very close to the seat of reaction, as, *e.g.*, in the hydrolysis of substituted acetic esters, then steric effects may distort the picture to some extent; and such a series of compounds is not so suitable for study as a series of *m*- or *p*-substituted aromatic compounds, where purely electronic effects will be more clearly in evidence. Fig. 1 shows most of the available data for series where E has been determined with reasonable accuracy. The method of representation is to plot $\log k_{100^\circ}$ against E for the reactions of a series. If changes in velocity from one reaction of the series to another are due to changes in E alone, then the slope of the line is $-2{\cdot}303\boldsymbol{R}T$. If the line has a greater slope than this, then the value of P is not constant for the series but increases with E. In the figure, k_{100° is multiplied by various powers of ten (indicated in the legend) to prevent confusion of the points belonging to different series. The following series may be said to show a constant value of P: halogenation of phenyl and tolyl ethers (Bradfield and Jones, J., 1928, 1006, 3073; 1931, 2903, 2907), benzoylation of amines (Williams and Hinshelwood, J., 1934, 1079), alkaline hydrolysis of benzoic esters (Ingold and Nathan, J., 1936, 222; Evans, Gordon, and Watson, J., 1937, 1430; Newling and Hinshelwood, J., 1936, 1357), alcoholysis of triarylmethyl chlorides (Nixon and Branch, *J. Amer. Chem. Soc.*, 1936, **58**, 492), reaction between substituted dimethylanilines and trinitroanisole (Hertel and Dressel, *Z. physikal. Chem.*, 1935, *B*, **29**, 178). In the esterification of benzoic esters the points are grouped too closely to allow a decision to be made. In the cases of acid hydrolysis of benzoic esters (Timm and Hinshelwood, Part III), alcoholysis of acyl chlorides (Branch and Nixon, *J. Amer. Chem. Soc.*, 1936, **58**, 2499), hydrolysis of arylsulphuric acids (Burkhardt, Horrex, and Jenkins, J., 1936, 1649), and the bromination of acetophenones (Evans, Morgan, and Watson, J., 1935, 17, 1167), P tends to increase as E increases. This effect is interesting but is of secondary importance, since for a series it is never large enough to outweigh changes in E. It has been explained tentatively on statistical principles as a general phenomenon which is to be expected when the average time required for a collision complex to complete its electronic rearrangements is large compared with the duration of a collision (Fairclough and Hinshelwood, J., 1937, 538). Whether this or another explanation is the correct one, there is little doubt that the phenomenon is due to a general cause not directly connected with the influence of substituents. According to the statistical theory referred to, the appearance or non-appearance

FIG. 1.



A ◎ *Benzoylation of amines ; $x = 4$.*

B ○ *Alkaline hydrolysis of ethyl benzoates in* $C_2H_5{\cdot}OH–H_2O$ *solvent ; $x = 4$.*

C ⭘ *Alkaline hydrolysis of ethyl benzoates in* $CH_3{\cdot}CO{\cdot}CH_3–H_2O$ *solvent ; $x = 4$.*

D ◉ *Alcoholysis of triarylmethyl chlorides ; $x = 3$.*

E ȯ *Reaction between substituted dimethylanilines and trinitroanisole ; $x = 5$.*

F ⊗ *Halogenation of phenyl and tolyl ethers ; $x = 3$.*

G ◎ *Esterification of benzoic acids ; $x = 4$.*

H ◐ *Acid hydrolysis of ethyl benzoates in* $C_2H_5{\cdot}OH–H_2O$ *solvent ; $x = 5$.*

I ◒ *Acid hydrolysis of ethyl benzoates in* $CH_3{\cdot}CO{\cdot}CH_3–H_2O$ *solvent ; $x = 5$.*

J ⦶ *Acid hydrolysis of methyl benzoates in* $CH_3{\cdot}OH–H_2O$ *solvent ; $x = 5$.*

K ⨂ *Alcoholysis of acyl chlorides ; $x = 5$.*

L ⊖ *Hydrolysis of arylsulphuric acids ; $x = 5$; E — 3,000 is plotted as ordinate.*

M ● *Bromination of acetophenones ;* k *in arbitrary units.*

of the effect in a given series of reactions depends upon the exact time relations involved in the reaction mechanism.

The conclusion may, therefore, be reached that the changes of reactivity which result from electronic displacements caused by substituents are due primarily to changes in the activation energy.

Factors determining the magnitude of activation energy. In order to form a picture of how substituents may alter activation energy, we first consider how the activation energy is made up in a simple system such as A + BC = AB + C. According to the Heitler–London theory of the interaction of atoms and molecules, BC will repel A. This repulsion prevents the close approach of A, and preserves BC from reaction. For the mechanism of activation two extreme cases are imaginable: (1) A is forced up against the repulsion of BC until it is so close that it competes for B on equal terms with C, which is finally expelled. (2) BC is given so much energy that the bond between B and C is disrupted, after which A and B can combine without further opposition. As the calculations of Eyring and Polanyi showed (*Z. physikal. Chem.*, 1931, *B*, **12**, 279), it is usually more economical for the reaction to proceed by a compromise between these two mechanisms, A being forced up against the repulsion and the bond between B and C being stretched at the same time until A and C can compete on equal terms for B. Thus we can regard the activation energy as being made up of two parts: that required to overcome the repulsion of the approaching reagent, and that required to weaken the existing bond. In extreme cases one or the other of these might conceivably be the only factor. In practice we know, of course, that sometimes, though not usually, dissociation of one reactant is the controlling step in a reaction. The general case is represented in Fig. 2.

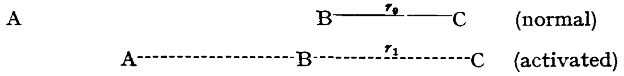
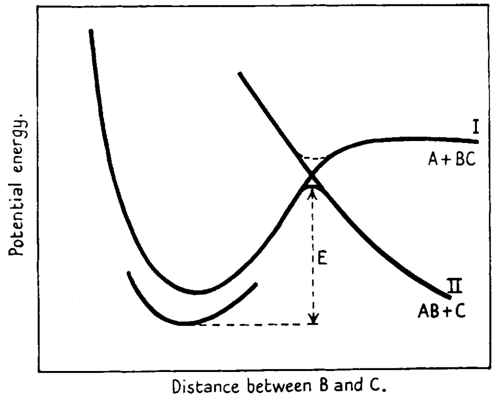


FIG. 2.

From the point of view of an Eyring–Polanyi diagram, four energies come into consideration: (1) the bond strength of the link BC, (2) the repulsion between A and BC, (3) the repulsion between AB and C, and (4) the bond strength of the link AB which is formed. Fig. 3 shows an energy diagram, which consists of two curves (cf. Evans and Polanyi, *Trans. Faraday Soc.*, 1938, **34**, 11). Curve I is a normal attraction curve with a minimum for any given distance between A and BC. As the distance between A and BC becomes smaller, this curve shifts upward on the diagram. Curve II is the repulsion curve for AB and C. The intersection of the two curves, slightly rounded off owing to resonance between two states, corresponds to the energy of the activated state, and the energy of activation is given by the vertical distance between the minimum of the BC attraction curve when A is at infinity and the intersection.

FIG. 3.



Of the energies enumerated above, positive increments in (1), (2), and (3) increase E, that in (1) by deepening the depression in curve I at all separations between A and BC, that in (2) by raising curve I without affecting the curve for infinite separation of A and BC, and that in (3) by the vertical displacement of curve II. On the other hand, a positive increment in (4) lowers the activation energy by lowering curve II, since a higher bond strength results in a lower potential energy of the system AB + C. In the terminology of Evans and Polanyi, (1), (2), and (3) are sources of inertia, (4) of driving force.

For the purpose of discussing the changes in activation energy caused by substituents, we shall make the following assumption, which seems reasonable as an approximation, *viz.*, that the additional charges appearing on given atoms as a result of electron displacements introduce an extra electrostatic term into the energy of the bond between the given atom and its neighbour, and that this term can be calculated as though it were entirely a classical Coulombic one. Just as the change in charge caused by a substituent on an atom which is a reaction centre is assumed to add or to subtract an extra electrostatic term to or from the bond energy, so also it adds or subtracts one to or from the repulsion energy of an approaching reagent. The main parts of both energies are, in fact, non-classical, but the *variations* due to the substituents will be treated here as ordinary electrostatic terms. This simple scheme appears capable of explaining a number of facts.

We may first consider in a qualitative way the effect of a substituent in the part B of the molecule depicted in Fig. 2. Suppose B contains a carbon atom attached to an electron-attracting group, such as a nitro-group. This group is thought of as conferring on the carbon atom a positive charge δe which is added algebraically to the charge which the atom bears in the unsubstituted compound. Suppose, for definiteness, that A is a negative ion and that C also is a negative centre. The positive charge added to B will therefore increase the strength of the bond BC. On the other hand, it will diminish the repulsion of the approaching A by superposing a Coulombic attraction on the normal force. In this way there are two opposing effects, one tending to increase and the other to decrease the activation energy. The bond strength of the product AB will be increased and the repulsive force between AB and C will be reduced. These factors also lower the activation energy. Thus there are three factors tending to lower the activation energy and one tending to raise it.

For our present purpose it is convenient, instead of considering all four terms separately, to consider the repulsion energy which must be overcome in bringing A up to the distance r of the transition state, and energy which must be utilised in stretching BC from the length r_0 to r_1; r and r_1 are functions of the four terms referred to above, but the regrouping into two terms will be convenient for an approximate treatment of the influence of substituents to be given later. We shall therefore speak of the activation energy as consisting of two parts: reagent repulsion energy, or simply *repulsion energy*, and *bond-stretching energy*.

In the light of this regrouping of the energy terms, we can say that in the example just considered the repulsive energy is lowered and the bond energy is increased. Conversely, an electron-repelling substituent will tend to decrease E by weakening the bond, and to increase it by increasing the repulsion energy. Since we know that reactions may occasionally involve the preliminary dissociation of a reactant, we see that repulsion energy and bond energy must vary widely and either might be the determining factor. In general, since the relative importance of the two factors varies from reaction to reaction, we are faced with an ambiguity, and no further predictions can be made without more detailed investigation. It might be expected that generally the change in the strength of the existing bond will be the less important since this is counterbalanced by three opposing changes, but this is not certain. Robinson has emphasised the fact that in additions to unsaturated systems and in benzene substitution the course of events is governed by the ease of approach of a positive (kationoid) reagent to a centre of available electrons in the molecule attacked. In these cases, evidently, modifications of the repulsive energy are of primary importance. In other reactions it can be seen that the changes in bond strength determine the influence of substituents on the course.

The following simple considerations show how the ambiguity can be to some extent resolved. We assume effective charges e_A, e_B, and e_C on A, B, and C respectively. The work done in bringing A up from infinity against the repulsion of BC to its position in the transition complex is given by

$$E_1 = W_1 - \int_{\infty}^{r} \frac{e_A e_B}{x^2} dx = W_1 + \frac{e_A e_B}{r} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where the second term represents the electrostatic part with which we are primarily concerned. Meanwhile, the charge on C has to be removed from the distance r_0 to the distance r_1, for which the work is given by

$$E_2 = W_2 - \int_{r_0}^{r_1} \frac{e_B e_C}{x^2} dx = W_2 - \frac{e_B e_C}{r_1}\left(\frac{r_1}{r_0} - 1\right) \quad . \quad . \quad . \quad . \quad . \quad (2)$$

In so far as the effect of the substituent on B can be schematised by a change δe_B in e_B, then the corresponding changes in activation energy are

$$\Delta E_1 = e_A \delta e_B / r \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

and

$$\Delta E_2 = -\frac{e_C \delta e_B}{r_1}\left(\frac{r_1}{r_0} - 1\right) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

These values are opposed to one another.

In an analogous way changes in e_A or e_C would yield similar formulæ.

The bond BC is mainly covalent, and consequently will be disrupted by a relatively small extension. The activation energy is a small fraction only of the bond strength. In general, therefore, r_1/r_0 will not exceed unity very greatly, and will probably be much less than 2; r_1 and r being of the same order of magnitude, it follows that for equal values of e_B and e_C, ΔE_2 will be less than ΔE_1. Thus the influence of the substituent on the activation energy will follow its influence on the repulsion of the reagent which approaches the active centre. This conclusion confirms that reached above from the consideration of the four energy terms. By considering how the various factors in these equations change as changes in the reactants are made, it is possible to arrive at various conclusions, of which the three following appear to be the most important. It must here be clearly stated that we are faced with two problems: that of determining the relative average magnitudes of the activation energies when comparing one reaction type with another, and that of determining the relative importance of the repulsion and bond energies when substituents are altered in either reactant. As will be seen, however, similar considerations can be applied in the solution of both problems.

As our first conclusion we re-state that arrived at above:

I. *There should be a general tendency for the influence of the substituent on the activation energy to follow the direction indicated by its effect on the attraction of the reagent to the seat of reaction.*

When, however, e_A becomes small, the relative importance of ΔE_1 diminishes, and finally ΔE_2 may predominate. We thus arrive at the second conclusion:

II. *The tendency referred to in* I *will weaken with the weakening or removal of any well-defined positive or negative centre in the attacking reagent. When such a centre has become weak enough, there will be a reversal of the effect, and the influence of the substituent will now be determined by its effect on the bond energy.*

A variation of this rule predicts the effect of changes in the charge of the central atom itself.

Another case in which a trend in this same sense occurs may be foreseen by considering the distances r and r_1. Most of the repulsive energy and most of the bond energy consists of parts which are (in our approximation) permanent and unchanged by the substituent, and these will vary greatly with change of the reagent A or of the molecule BC to be disrupted. Suppose we change from a given attacking reagent to another, the permanent repulsion of which by BC is much greater. Activation being a compromise between the two processes of forcing up the reagent and stretching the bond, the most economical reaction route will now be that involving a greater stretching of BC and a less intimate approach of A. Thus r_1 becomes greater *and* r greater. In the limit of extreme repulsion, the most economical mode of reaction would be by the complete disruption of BC. As we move in the direction of this limiting case the relative importance of the repulsion energy diminishes and that of the bond energy increases. This is reflected in an increase of $\Delta E_2/\Delta E_1$ as r and r_1 increase, the charges being assumed to remain the same. Thus we arrive at another principle.

III. *If the same molecule is attacked by two different reagents whose charges do not differ greatly, then as the total activation energy increases, it is influenced by substituents in the attacked molecule less and less in the sense predicted from the change in the repulsion of the reagent and may, for very large activation energies, become subject to influences parallel with those of the substituent on the bond strength.*

A converse rule can obviously be deduced for the case of the same reagent attacking different molecules of the type BC.

The above generalisations do not allow absolute predictions to be made; but starting from I—which is of some qualitative importance—the application of II and III and their variants appears to explain some interesting general trends in experimental data which are not easy to interpret otherwise.

In this discussion we have limited ourselves to consideration of a three-centre system A + BC. The centres need not of course be atoms, but merely molecular parts which retain their identity during reaction. In more complicated reactions it is frequently found that only three reactive centres are involved in the rate-determining step. When more than three centres are actually involved, treatment along these lines still aids in clarifying the situation, as we shall see, for example, in the hydrolysis of esters.

This necessitates a certain degree of schematisation, which we think is justified by its results, but which should be explicitly stated. For example, if water is an attacking agent and gives a hydroxyl to a positive carbon atom, we regard the water molecule as characterised by a smaller value of the negative e_A than an attacking hydroxyl ion, and we try to see what can be accounted for on this basis. Similarly we regard a weak tertiary base as having a smaller negative e_A than a strong base. We might, on the other hand, regard the system *base plus alkyl halide* as a four-centre system, and consider the development of negative charge on the nitrogen atom as a function of the activation of the base, the electron-pair which has to be loosened from the rest of the molecule itself constituting the fourth centre. This, as Dr. Sutton has pointed out to us, might be a very fruitful mode of approach, especially in those reactions which appear to be determined by the condition that electromeric effects render unshared electrons easily available on a given atom only at the call of the reagent. This problem is referred to later in connexion with the substitution of chlorobenzene, which we are hoping to investigate further.

In the meantime we may test the possibilities of the simple scheme.

Survey of Experimental Results.—The above considerations were developed primarily with the object of interpreting two sets of experimental results recently obtained in this laboratory (see following papers). One set refers to the formation of quaternary ammonium salts, the other to the hydrolysis of esters; other examples, however, are also discussed in this section.

As an example of Rule I may be taken the formation of quaternary ammonium salts. Here a pronounced rise in activation energy is found on passing from methyl iodide through ethyl to *iso*propyl iodide : it is attributable to the diminished positive charge on the carbon atom which attracts the approaching base. When we pass from a weak base like pyridine to a strong base like triethylamine, the activation energy falls.* We schematise the difference between the two bases by saying that the stronger base with its more readily available pair of electrons has a greater effective negative charge, *i.e.*, a greater value of e_A. (The measured dipole moments are of no help in characterising the bases from this point of view. At large distances, x, of a charge from a dipole of moment $\mu = ed$, the force is proportional to μ/x^3, but when x is small compared with d, the force tends to become proportional to e/x^2. For the close approach involved in chemical interaction the latter is probably nearer the truth.) Rule II allows us to interpret the changes in activation energy found when for a given iodide we go from one base to another, or for a given base from one iodide to another. Table I shows the changes of activation energy (for two solvents) accompanying these variations. It is seen that for methyl iodide the change in E on going from triethylamine to pyridine is greater than that for *iso*propyl iodide. For methyl iodide the factor e_B is larger than for *iso*propyl iodide, the positive charge on the carbon in the

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* Compare the fall in E found on passing to a stronger base in the reaction between substituted dimethylanilines and methyl picrate (Hertel and Dressel, *loc. cit.*).

latter having been diminished by the flow of electrons from the methyl groups, so that the change in e_A will make a larger change in the repulsion energy and, since changes in E are here determined largely by changes in this, will bring about a larger change in E itself. Similarly, the results show that on passing from one iodide to the other, the changes are greater for triethylamine than they are for pyridine : this is explained as due to the fact that the higher value of e_A for triethylamine makes changes in e_B have a greater influence on the repulsion term and therefore on E. Thus it seems that, not only the direction of the changes, but also their relative magnitudes can be interpreted in the light of the above principles.

TABLE I.

Formation of Quaternary Ammonium Salts.

(In each case the number in the first line refers to benzene solution, that in the second line to nitrobenzene.)

	MeI.	$Pr^{\beta}I$.		NEt_3.	C_5H_5N.
$E_{C_5H_5N} - E_{NEt_3}$	4600	900	$E_{Pr^{\beta}I} - E_{MeI}$	7400	3700
	3900	700		6300	3100

Among other reactions determined mainly by repulsion energy and only to a small extent by bond strength changes may be mentioned the benzoylation of amines, and the acid and alkaline hydrolysis of benzoic esters.

The bond-energy factor also seems less important than the repulsion energy in catalysed prototropic changes. Evans, Morgan, and Watson (J., 1935, 1167) find that the order of energies for the acid-catalysed prototropic change of substituted acetophenones varies in the direction governed by the attraction of the catalysing proton to the carbonyl oxygen, although this is the direction of increasing strength of attachment of the mobile hydrogen atom. Since the catalyst is charged and has a large effective e_A, this is what we should expect. In another triad prototropic system catalysed by negative ions (ethoxyl) the effect of substituents is the reverse of that found by Nathan and Watson, and thus still in the sense governed by attraction of the negative ion (Shoppee, J., 1933, 1117). But, as Shoppee points out, this case is unusual, since proton attachment and attraction of reagent change in the same sense. Most benzene substitutions probably follow the same rule, but the activation energies are not properly known for the nitration and sulphonation reactions.

We may now consider some interesting cases in which there is a transition from one type of behaviour to another in a way which can be understood in the light of the rules formulated above.

First, we may compare the alcoholysis of acyl chlorides (Branch and Nixon, *loc. cit.*) with the alcoholysis of triarylmethyl chlorides in ether–alcohol solution (Nixon and Branch, *loc. cit.*).* For the former reaction the trend of values is indicated by the following selection :

p-Nitrobenzoyl chloride	11,100	Benzoyl chloride	14,400
p-Chlorobenzoyl chloride	13,850	*p*-Methoxybenzoyl chloride	18,650

Here the introduction of a nitro-group, for example, diminishes the repulsion of the hydroxyl group in the approaching alcohol, while causing the chlorine to be held more tightly. The fact that the activation energy is lowered shows that the change in the repulsive term is the most important. With the alcoholysis of the triarylmethyl chlorides the trend is in the opposite direction :

Diphenyl-*p*-tolylmethyl chloride	12,450	*p*-Chlorotriphenylmethyl chloride ...	13,480
Triphenylmethyl chloride	13,420	*p*-Nitrotriphenylmethyl chloride ...	16,710

Here the energy of activation increases as the carbon–chlorine bond strength increases, although the repulsion of the approaching hydroxyl or ethoxyl is decreased. The origin of the difference would appear to lie in the fact that the carbonyl carbon of the acyl chlorides bears, through the influence of the oxygen, a larger positive charge than the central

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* A similarly contrasted behaviour is shown by the velocities of addition to pyridine of substituted benzyl bromides and substituted bromoacetophenones respectively (Baker, J., 1933, 1128).

carbon atom of the triphenylmethyl halides. It thus attracts the approaching group more powerfully, and in the transition state we have relatively close approach and relatively smaller bond stretching. The activation energy is therefore sensitive to changes in the repulsive term. In the triphenylmethyl halides there is relatively little attraction of the reagent; consequently, the repulsion is considerable, and the compromise reached in the transition state involves a greater proportion of energy as bond energy. Hence the variations in the latter govern the trend of the activation energies.

Interesting transitions are shown by the reactions of the alkyl halides with the following series of reagents: strong tertiary base, weak tertiary base, negative hydroxyl or alkoxyl ion, and water and alcohol molecules. As we have seen, the change from weak base to strong base can be represented as an increase in the effective value of e_A and results in greater dependence on the repulsion term. When we change the reagent attacking an alkyl halide from a tertiary base to a hydroxyl ion, the strength of the carbon–halogen bond is a constant, but the non-electrostatic part of the repulsion energy will change in a difficultly predictable way. We find, in fact, that the activation energy increases very markedly (*e.g.*, pyridine and ethyl iodide 15,800; triethylamine and ethyl iodide 11,400; ethyl iodide and sodium hydroxide 21,000). The increase may be due partly to an increased permanent repulsion of the reagent, but is probably also connected with changes in the repulsion between the products. In the quaternary ammonium salt formation the products are ions, whereas in the hydrolysis they are an ion and a neutral molecule:

$$\mathrm{NEt_3 + CH_3I = [NEt_3CH_3]^+ + I^-}$$
$$\mathrm{OH^- + CH_3I = CH_3{\cdot}OH + I^-}$$

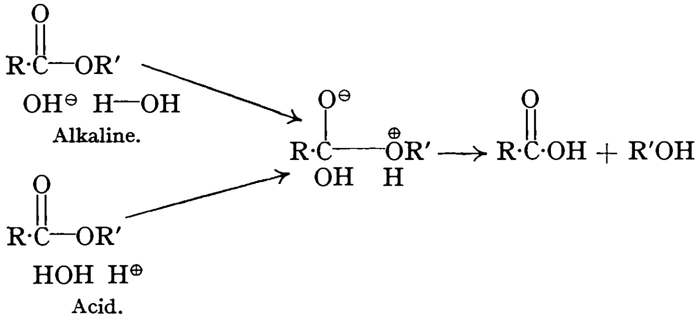
The total repulsion between the products may therefore be expected to be greater in the latter case, and this raises the activation energy by lifting curve II in Fig. 3 and so increasing the distance r_1. Without deciding which factor is more important, we can say that, since the activation energy is much greater, and since the bond to be stretched is the same, then the increase must be due to a change in the repulsive terms. Hence, in accordance with rule III, we should expect the bond energy to play a more important part. In view of the large increase in E this effect should be considerable. But at the same time we have changed from a base to a negative ion: this means a large increase in the effective charge of the reagent, e_A. In fact, the experimental results show that the bond strength and repulsion terms become of nearly equal importance, the activation energies of alkyl halides for reaction with hydroxyl ions or alkoxyl ions varying little as one changes from methyl to *iso*propyl (Grant and Hinshelwood, J., 1933, 258; Hughes, Ingold, and Shapiro, J., 1936, 225; Cooper and Hughes, J., 1937, 1183). Some values are: ethyl chloride 23,000 (in alcohol); *iso*propyl chloride 23,000 (in 80% aqueous alcohol); ethyl bromide 21,000 (alcohol); *iso*propyl bromide 20,760 (in 60% alcohol), 21,700 (80% alcohol), the changes of solvent being probably of minor importance in these examples.

These results are confirmed by those found for the reactions with sodium alkoxides in alcoholic solution, the mechanism being an attack of the OR⁻ ion on the halide (Segaller, J., 1913, **103**, 1421; 1914, **105**, 106; Haywood, J., 1922, **121**, 1904; Woolf, J., 1937, 1172). The following examples show the approximate constancy of E:

Iodide.	RI + PhONa.	RI + Ph·CH$_2$·ONa.
Methyl	22,120	20,570
Ethyl	22,000	21,860
*iso*Propyl	22,100	21,410

Since the two opposing effects nearly balance when the alkyl halide is attacked by hydroxyl, we should expect the bond-strength factor to be of predominant importance when we pass from hydroxyl to the water molecule as the attacking agent, the value of e_A being here much less. In fact, it is found that the attack by water on *iso*propyl and *tert.*-butyl halides is much easier than with methyl and ethyl halides, the change being in the sense of the change in bond strength. The accumulation of negative charge from the substituent alkyl groups loosens the halogen and should lower the activation energy. Hughes regards this as a change to a unimolecular mechanism in which the reaction is determined solely by the rate of ionisation of the halide, but on general grounds and in the light of fresh evidence which has appeared since Hughes's paper (Taylor, J., 1937, 1853), we should prefer to regard the change as one depending upon the lowered effective charge of the attacking water molecule. Unfortunately, we can only judge from the course of *velocities* in this case since with the *tert.*-butyl compounds the activation energies for the reaction with OH^- cannot be measured, and with the *iso*propyl compounds the proportion of hydrolysis by water under normal conditions is too small to allow E to be determined with much accuracy. The relative changes in velocity are, however, so marked that they may be taken provisionally as significant. (The large changes of PZ in passing from hydrolysis by alkali to hydrolysis by water are only to be expected, since one of the reactants becomes the solvent in the latter case.) Further, as already mentioned, in the alcoholysis of substituted triarylmethyl chlorides, which are in fact substituted alkyl chlorides, the trend of E is again governed by the bond strength.

In the hydrolysis of esters, the Lowry mechanism, which is generally accepted, makes the following postulates. In alkaline hydrolysis the hydroxyl ion becomes attached to the carbonyl carbon, whereas in acid hydrolysis the proton combines with the ethereal oxygen. The second step in either case involves the obtaining of a second ion from water to supplement the one previously derived from the acid or the alkali. The last step involves the breaking of the bond as shown :



The fact that the mean values of P are the same for both types supports the view that both mechanisms have a similar plan. The effect of substituents is in the same direction in each case, which shows that the charge on the carbonyl carbon matters in the same way in each. But in alkaline hydrolysis the charged ion attacks the carbon atom where the effect of the substituents is greatest, while the water attacks the oxygen where the effect of the substituents is damped down, whereas in acid hydrolysis it is the uncharged water which attacks the carbonyl, and the ion which attacks a point more remote from the substituent. Since the activation energies for acid and alkaline hydrolysis are different, although the bonds formed are identical, it is assumed that the repulsion terms govern the situation and that the attraction or repulsion of an ion is considerably greater than the attraction or repulsion of a water molecule, and further that the influence of the substituent decreases with its distance from the reaction centre.

The following table shows the change in activation emergy to be expected from an electron sink such as a nitro-group in the group R. One minus sign indicates a small lowering and two indicate a great lowering.

Change in activation energy to be expected on basis of approach of	Alkaline hydrolysis.	Acid hydrolysis.
(1) Hydroxyl to carbonyl	— —	nil
(2) OH of water to carbonyl	nil	—
(3) Hydrion to oxygen	nil	+
(4) H of water to oxygen	+	nil

On balance, the alkaline hydrolysis benefits most, which is consistent with the fact that the effect of the substituents is very much greater in alkaline than in acid hydrolysis. It is not surprising that (2) outweighs (3) enough to give a trend of the activation energies in acid hydrolysis in the same direction as in alkaline hydrolysis (see Part III, Fig. 1). Similar considerations explain why the average activation energies for alkaline hydrolysis are some thousands of calories lower than for acid hydrolysis.

That the facts relating to ester hydrolysis are thus consistent with the view that the repulsive energy is the governing factor, even when water is the agent which attacks the most important centre of charge, is in contrast with what has been said about the alkyl halide hydrolysis. The explanation, as in the transition from triarylmethyl to acyl chlorides, would appear to depend upon the fact that the carbonyl carbon is the seat of a much more important charge than the carbon of an alkyl halide : thus, close approach of a suitable reagent is encouraged, and the balance of the activation energy is shifted away from the bond-stretching term to the repulsive term, and changes in the latter become most significant.

With regard to the problem of benzene substitution, it is a pity that more data about energies of activation are not available. There is, however, little doubt that the attraction of the reagent is in most cases the predominant factor, and this would almost certainly be reflected in the measured activation energies. One point is, however, worth considering further. As is well known, the case of chlorobenzene is anomalous, *op*-substitution being found associated with a decreased reactivity compared with benzene. One explanation is that at the approach of the reagent an electromeric effect occurs, owing to easy polarisability, which renders electrons more easily available than would have been expected from the dipole moment. If this explanation is correct, one would expect a reaction depending upon a time-variable polarisation to be associated with an abnormal value of P. If the value of E proved to be abnormally large, it might suggest an alternative explanation, *viz.*, that with chlorobenzene substitution is governed by the loosening of the proton rather than by the approach of the reagent (in accordance with rule III above). Increased repulsion of the reagent would make the reaction slow, but the loosening of the proton would occur most readily at the *o*- and *p*-positions. This mechanism had been assumed by Hückel (*Z. physikal. Chem.*, 1937, *B*, **35**, 163) for benzene substitution generally, where it is not applicable, as Robinson has pointed out : but, in the light of what we have said, it may be admissible as the explanation of an apparent anomaly. All that can be said at the moment is that it would be interesting to investigate further the question of the activation energies involved in the further substitution of chlorobenzene and to compare the kinetics of this reaction carefully with that involved in the substitution of nitrobenzene.

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