SOME RELATIONS BETWEEN REACTION RATES AND EQUILIBRIUM CONSTANTS

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The idea that there is some sort of relationship between the rate of a reaction and the equilibrium constant is one of the most persistently held and at the same time most emphatically denied concepts in chemical theory. Many organic chemists accept the idea without question and use it, frequently with considerable success, but practically every treatise on physical chemistry points out that such a relationship has no theoretical basis and that it is in fact contradicted in many familiar cases. The contradiction is however more apparent than real. It is certainly true that there is no universal and unique relation between the rate and the equilibrium of a reaction; it is equally true that there frequently is a relation between the rates and the equilibrium constants of a group of closely related reactions. It is the purpose of this paper to review the known examples of this kind of relationship, to point out the quantitative form which it assumes, and to state certain limitations to its application.

This quantitative form is the one which was first observed by Brönsted (9, 6) and his coworkers in the study of reactions which show general acid-base catalysis. These are second-order reactions between an acid catalyst HA and a substrate S

$$HA + S \rightarrow Products + HA \tag{I}$$
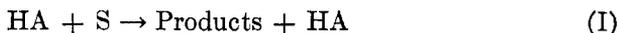
in which the acid is regenerated (and similar reactions in which the catalyst is a base). The rates of such reactions, for acid catalysts of a particular charge type, are related to the ionization constants of the acids by the equation

$$k = GK^x \tag{1a}$$

or
$$\log k = x \log K + \log G \tag{1b}$$

where k is the rate constant, K is the ionization constant, and G and x are constants.

This is obviously a relation between rates and equilibrium constants;

it is certainly not one between the rates and the equilibrium constants of the series of reactions I, whose equilibria are completely independent of the nature, the concentration, and even of the very presence of the catalyst HA. However it is overwhelmingly probable that this reaction takes place in steps, and Pedersen's (39, 40, 41) illuminating analysis suggests strongly that these steps are the following

$$HA + S \rightleftarrows SH^+ + A^- \tag{IIa}$$

$$SH^+ + A^- \rightarrow Products + HA \tag{IIb}$$
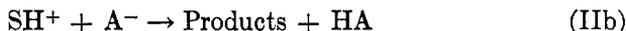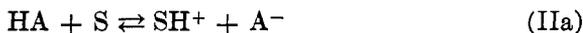
Reaction IIb is presumably so rapid that the measured rate is that of IIa alone, which is nothing more nor less than an acid–base reaction like the reaction of ammonia and hydrogen chloride[1]

$$HCl + NH_3 \rightleftarrows NH_4^+ + Cl^- \tag{III}$$

The equilibrium constants of the series of reactions of type IIa obtained by varying HA while keeping S constant are of thermodynamic necessity proportional to the ionization constants (measured in the same medium) of the series of acids HA. If this mechanism for the catalyzed reaction is correct, the relationship represented by equation I is indeed a relationship between the rates and the equilibrium constants of the same series of reactions, namely the series IIa. It is therefore strong evidence for the validity of the mechanism that the same quantitative relationship holds for numerous reactions which are clearly analogous to the step IIa and not at all to the total reaction I.

This appears especially well in the reaction of trimethylamine with a series of methyl esters of carboxylic acids (27). The general reaction

$$RCOOCH_3 + N(CH_3)_3 \rightarrow RCOO^- + N(CH_3)_4^+ \tag{IV}$$

consists simply in the transfer of a positively charged methyl group from the ester to the base. Figure 1 shows a plot of the logarithms of the reaction rate constants, k, against the logarithms of the ionization constants, K, of the acids whose esters were used.[2] The straight line is of course a

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[1] The widely held opinion that a reaction like IIa must be practically instantaneous is due to a quite unwarranted extrapolation from an experience which has been limited to relatively strong bases. The point has been well discussed by Pedersen (40, 41), but it may be added that Conant and Wheland (11) have actually observed simple acid–base reactions whose rates are measurable.

[2] This differs from the plots previously published by the inclusion of a point for salicylate from unpublished work of Pfluger, and in the fact that the ionization constants at 100°C. have been estimated for all the acids. In the case of phthalic and p-nitrobenzoic acids this estimate is based upon an application and extrapolation of the equation of Harned and Embree (28); in the case of lactic acid upon the behavior of other aliphatic acids.

graph of equation 1, which is seen to hold reasonably well, although by no means as exactly as it does in the catalytic reactions.

It would clearly be preferable to compare the rates of the series of reactions IV with the equilibrium constants of the same series of reactions, or, what would be entirely equivalent, with the equilibrium constants for the transfer of methyl ion from one acid radical to another.

$$RCOOCH_3 + R'COO^- \rightleftarrows RCOO^- + R'COOCH_3 \qquad (V)$$

Although it is entirely conceivable that these may be accessible to measurement they are not at present known. Lacking them the ionization con-
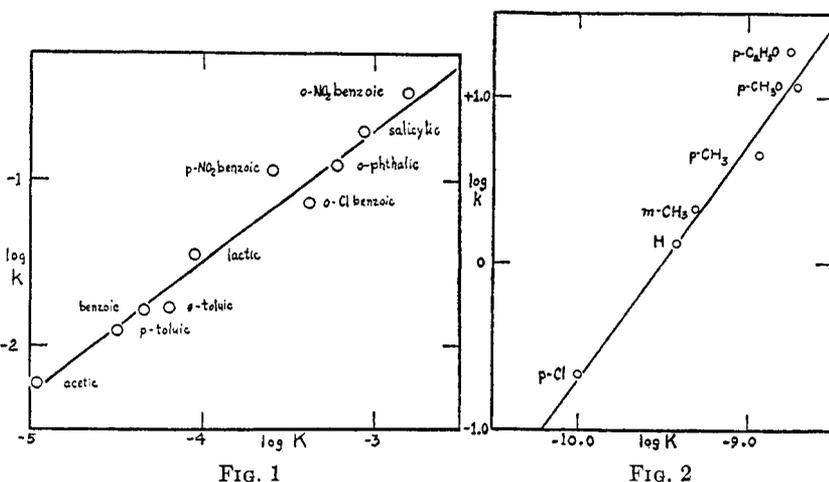
FIG. 1. Reaction of trimethylamine with methyl esters of carboxylic acids (Hammett and Pfluger).

FIG. 2. Reaction of dinitrochloronaphthalene with para and meta derivatives of aniline (van Opstall).

stants should be a good substitute, since they are proportional to the equilibrium constants of the series of reactions.

$$RCOOH + N(CH_3)_3 \rightleftarrows RCOO^- + N(CH_3)_3H^+ \qquad (VI)$$

which differ from reactions IV, whose rates are measured only in the fact that a hydrogen ion is transferred instead of a methyl ion.[3]

[3] There is a certain difficulty involved in the fact that the ionization constants are functions of the solvent used. In the case of the catalytic reaction it has been demonstrated by Brönsted, Nicholson, and Delbanco (8) that much better agreement is obtained if the ionization constants are measured in the solvent in which the reaction rates are determined. The constants used in figure 1 are those measured in

The next four figures represent similar plots for four reaction series in which the base rather than the ester is varied. Here again the comparison is between the rates of a series of reactions in which a positively charged
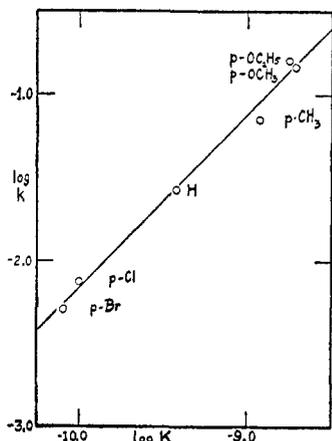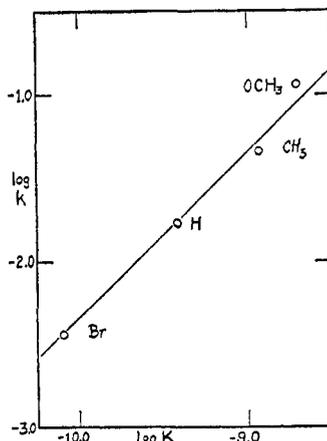
FIG. 3.   FIG. 4.

FIG. 3. Reaction of methyl iodide with para derivatives of dimethylaniline (Davies and Lewis).

FIG. 4. Reaction of trinitrocresol methyl ether with para derivatives of dimethylaniline (Hertel and Dressel).
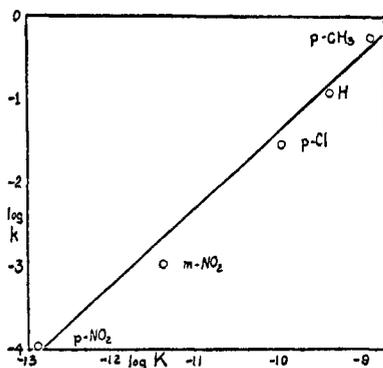
FIG. 5. Reaction of benzoyl chloride with para and meta derivatives of aniline (Grant and Hinshelwood).

water, but some preliminary measurements of Pfluger indicate that constants measured in methyl alcohol would give no better agreement. It is on the whole probable that the deviations due to the use of ionization constants instead of the equilibrium constants of the series of reactions IV are of about the same magnitude as the differences in relative strengths of a series of acids in different solvents.

organic group is transferred and the equilibrium constants of a series in which hydrogen ion is transferred. That is to say the K's in these plots are ionization constants of bases.[4]

Figure 2 is based upon the reaction rate data of van Opstall (44) for the series of reactions obtained by varying the group R in the equation

$$ClC_{10}H_5(NO_2)_2 + H_2NC_6H_4R \rightarrow Cl^- + C_{10}H_5(NO_2)_2\overset{+}{N}H_2C_6H_4R \quad (VII)$$
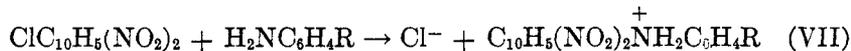
Figure 3 is based upon the data of Davies and Lewis (12) for the series

$$ICH_3 + (CH_3)_2NC_6H_4R \rightarrow I^- + (CH_3)_3\overset{+}{N}C_6H_4R \quad (VIII)$$
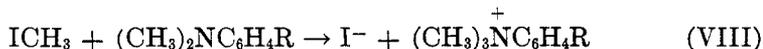
Figure 4 is based upon the data of Hertel and Dressel (29) for the series

$$(NO_2)_3(CH_3)C_6HOCH_3 + (CH_3)_2NC_6H_4R$$
$$\rightarrow (NO_2)_3(CH_3)C_6HO^- + (CH_3)_3\overset{+}{N}C_6H_4R \quad (IX)$$
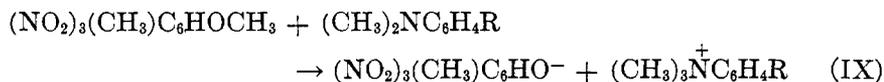
and figure 5 upon that of Grant and Hinshelwood (19) for the series[5]

$$ClCOC_6H_5 + H_2NC_6H_4R \rightarrow Cl^- + C_6H_5CO\overset{+}{N}H_2C_6H_4R \quad (X)$$
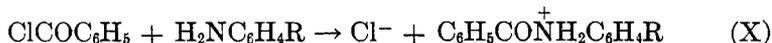
The agreement is about as good as in the case of the trimethylamine reaction (reaction IV), but only because a limitation was recognized which was not necessary in that case. These plots contain no points for ortho-substituted aniline derivatives, which react in fact at rates which are an order of magnitude slower than would be predicted from the strengths of the bases (43). The phenomenon is an obvious and indeed a familiar example of steric hindrance, for the organic chemist has long appreciated the fact that the reactions of ortho-substituted aniline derivatives are slower than they ought to be. The present correlation of rate and base strength seems to offer a definite criterion of the magnitude of the steric hindrance. It should also be noted that no correlation of rate and base strength is possible if comparisons are made between primary and tertiary amines, between aliphatic and aromatic amines, or even between dimethylaniline and diethylaniline derivatives.

A very similar situation appears in the case of the alkaline hydrolysis of esters. As was previously pointed out (27), there is no correlation whatsoever between the rates of hydrolysis of esters in general and the strengths

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[4] In the case of the reactions represented in figures 3 and 4 they are the ionization constants of the bases $RC_6H_4NH_2$ rather than those of the bases $RC_6H_4N(CH_3)_2$, because the base strengths of the dimethylaniline derivatives are not known.

[5] The ionization constants have been taken for the most part from the valuable compilations of Hall (21) and of Hall and Sprinkle (22). The value for p-nitroaniline is that of Hammett and Paul (26), and that for m-nitroaniline the one given by Farmer and Warth (17).

of the corresponding acids. But figure 6A shows that the correlation is quite satisfactory when para- and meta-substituted derivatives of benzoic acid alone are considered, and figure 6B shows that a similar correlation is obtained for ring-substituted derivatives of phenylacetic acid.[6] For a given acid strength the rate of hydrolysis of a phenylacetic ester is an order of magnitude faster than that of a benzoic ester. On the other hand the rates for ortho-substituted benzoic esters are so small that their representative points lie completely off this plot (30). This is of course a well-known example of steric hindrance.

It is an obvious generalization that correlations of this sort between the reaction rates and the equilibrium constants of a series of reactants will succeed only when the substitutions take place in a part of the molecule sufficiently removed from the point at which the reaction occurs. Unfortunately this "sufficient removal" is difficult of quantitative definition, and it varies from one reaction type to another. Thus an ortho substitution which exhibits a marked steric hindrance in the alkaline hydrolysis of esters has little if any effect of this sort in the reaction of the same esters with trimethylamine (27).

No such steric hindrance effects have so far been observed in acid or basic catalysis where the comparison is presumably between the rates and equilibrium constants of the same reaction series (IIa), even though some of the bases studied in the recent work of Brönsted, Nicholson, and Delbanco (8) on the nitramide reaction in m-cresol would be likely to exhibit the phenomenon if it exists.[7] It is therefore entirely possible that the steric hindrance effects would play a less important part in the reactions in which methyl or other organic groups are transferred if a direct comparison of rate and equilibrium constants in these reactions were to be made. In other words, it may be that the steric hindrances represent as much a failure of the relationship between the equilibrium constants of the methyl and hydrogen reactions as they do a failure of the relationship between rate and equilibrium constant in the methyl reaction.

The reactions thus far considered are of the type

$$AB + C \rightarrow A + BC \qquad\qquad (XI)$$

This may be called a substitution in the sense that the radical C substitutes for the radical A in its combination with B. In the basic catalysis and in reactions VII, VIII, IX, and X the group C is varied to obtain the series of reactions for which a correlation is obtained. In the acid catalysis and in the trimethylamine reaction (reaction IV) a similar correlation is obtained

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[6] The rate constants are taken from the valuable papers of Kindler (30).

[7] This is especially true of the use of o-chloroaniline and of the direct comparison of aniline, monomethylaniline, and dimethylaniline.

for changes in the nature of the group A.   Since the mechanism of ester hydrolysis is[8]

$$C_2H_5OCO \cdot R + OH^- \rightarrow C_2H_5O^- + HOCO \cdot R \qquad (XII)$$
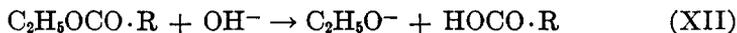
this series of reactions is of the third possible type, that obtained by variation of the B component.   Such a variation does not produce (31) and would not be expected to produce any large changes in equilibrium constants, because the affinity for HO^- and for $C_2H_5O^-$ must be similarly affected by the substitution.   There are, however, large changes in reaction rate and these correlate satisfactorily, as figure 6 shows, with the
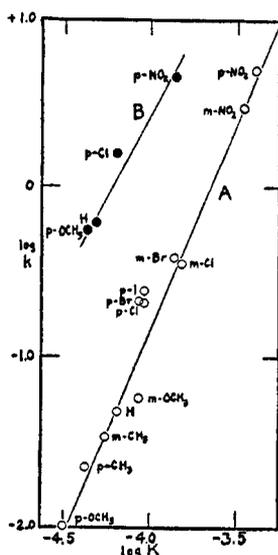
Fig. 6. Alkaline hydrolysis of (A) para and meta derivatives of ethyl benzoate and (B) para derivatives of ethyl phenylacetate (Kindler).

equilibrium constants of a quite different series of reactions, those of ionization.   This result is a rather surprising one, because the ionization reaction

$$RCOOH + H_2O \rightleftarrows RCOO^- + OH_3^+ \qquad (XIII)$$
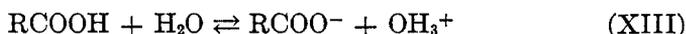
involves the separation of an anion $RCOO^-$, while the ester hydrolysis involves the transfer from one group to another of a positively charged

[8] This follows from a number of considerations (27), but most clearly from the recent work of Polanyi and Szabo (42), in which the bridge oxygen was demonstrated to go with the alkyl group by carrying out the reaction in water containing an increased concentration of O^{18}.

acyl group, RCO^+. The bonds broken are of a very different nature, but the experiment shows that their strengths are similarly affected by changes in the group R, provided these changes occur at a sufficient distance from the carboxyl group.

The same situation appears even more strikingly in the case of racemization reactions. These consist, as has been convincingly shown by Polanyi (3, 35) and by Olson (36, 37, 38), in a substitution of one group on an asymmetric carbon atom by another completely identical group, but with accompanying inversion of the configuration of the asymmetric carbon.

$$Br^- + R_2\!\!\overset{R_1}{\underset{R_3}{>}}\!\!C\!\!-\!\!Br \rightarrow Br\!\!-\!\!C\!\!\overset{R_1}{\underset{R_3}{<}}\!\!R_2 + Br^- \qquad (XIV)$$

$$\qquad\qquad d \qquad\qquad\qquad\qquad l$$
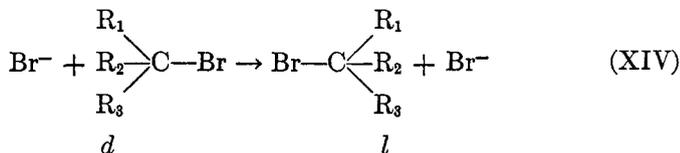
While the equilibrium constant is necessarily unity for all such reactions, the rates vary greatly with changes in the B component or in the identical
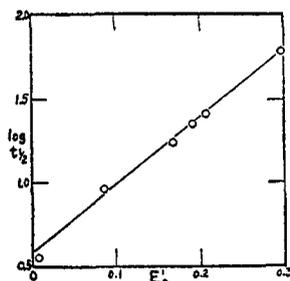
FIG. 7   FIG. 8

FIG. 7. Autoxidation of reduced indicator dyes (Barron)
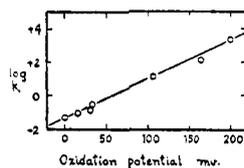
FIG. 8. Reaction of a series of quinones with dihydrophenyllutidinedicarboxylic ester (Dimroth).

A and C components. There is therefore no correlation whatsoever between the rates and the equilibria of reactions of type XIV. It is, however, to be expected that the racemization rates should correlate with the rates of other reactions involving the same groups or perhaps, as in the case of ester hydrolysis, with suitable equilibrium constants.

Equation 1 has also been found to apply to reactions of a different type, to oxidation–reduction reactions. In fact, the first observation of this relationship in any reaction except an acid or basic catalysis seems to be that of Barron (2). He found a linear relation between the logarithms of t_i, the time required for 50 per cent oxidation by oxygen of various reduced

dyes of the oxidation indicator type, and the molar oxidation potentials, E_0', of the dyes. Since the latter are proportional to the logarithms of the equilibrium constants of the oxidation–reduction reactions, this relationship is equivalent to equation 1. Figure 7 is taken from his work.

Dimroth (14) in an extensive series of investigations found that the same relation holds for the reactions of a series of quinone derivatives with an organic reducing agent. An example is given in figure 8, the reducing agent being dihydrophenyllutidinedicarboxylic ester. The agreement is equally good with other reducing agents, and also for the oxidation of a series of derivatives of hydroquinone by hexanitroazobenzene.

Chow (10) has found that the catalytic effect of such oxidant–reductant systems as ferricyanide–ferrocyanide upon the rate of autoxidation of linseed oil is similarly determined by the oxidation potential of the catalyst system.

Finally Frumkin (18) has made an interesting suggestion which relates the problem of the current–voltage relation in electrochemical reactions to the present one. It is known (4, 5), for instance, that the rate of hydrogen evolution on an electrode, measured of course by the current I, is related to the polarization potential ΔE by the equation[9]

$$RT \ln I = \tfrac{1}{2} F \Delta E + \text{const.} \qquad (2)$$

Frumkin suggests that increasing the negative polarizing potential increases the affinity of the electrode for hydrogen ion and is equivalent to the substitution in an acid–base reaction of a stronger base for a weaker one. The change in ionization constant K of the hypothetical base is given by

$$RT \ln K = -F \Delta E + \text{const.} \qquad (3)$$

so that the polarization equation becomes

$$\ln I = -\tfrac{1}{2} \ln K + \text{const.} \qquad (4)$$

The $\tfrac{1}{2}$ coefficient in this equation is equivalent to the coefficient x which appears in equation 1. The same factor, $\tfrac{1}{2}$, is found in the polarization equation for the electrochemical reaction (24)

$$\text{Quinone} + 2H^+ + 2e \rightleftarrows \text{Hydroquinone}$$
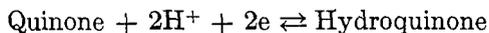
and also in the rate equations for some reactions in which the equivalent of a polarization is obtained by varying the concentration of a metal in an amalgam (7, 13, 18, 25).

[9] This is true only at relatively high overvoltages, where the rate-determining process seems to be the reaction $H + e \rightarrow H$ alone, and not at lower overvoltages where the reaction $2H \rightleftarrows H_2$ determines the rate (23).

There are a number of corollaries to the existence of the relationships represented by equation 1. One of the most obvious is the conclusion that the rate constants k_1 of one series of reactions should be related to the constants k_2 of another similar series by the equation

$$\log k_1 = x \log k_2 + \text{const.} \tag{5}$$

Figure 9 shows the application of this expectation to the work of Baker (1) on substituted benzyl halides. k_1 is the rate of reaction of various derivatives of benzyl bromide with pyridine.

$$BrCH_2C_6H_4R + C_5H_5N \rightarrow Br^- + RC_6H_4CH_2\overset{+}{N}C_5H_5 \tag{XV}$$
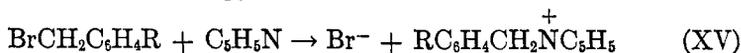
k_2 is the rate of the hydrolysis of the same benzyl bromide derivatives.

$$BrCH_2C_6H_4R + H_2O \rightarrow HOCH_2C_6H_4R + H^+ + Br^- \tag{XVI}$$

A correlation of this sort is an argument in favor of a fundamental similarity in the mechanisms of the reactions compared, and may therefore
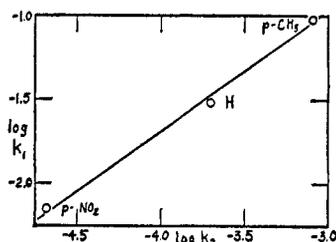
FIG. 9. Reaction of derivatives of benzyl bromide with pyridine and with water (Baker).

be of considerable assistance in the diagnosis of reaction mechanisms. Conversely, a failure of such a correlation is evidence of some difference in mechanism (27). Such an argument has been used in the comparison of the mechanisms of the reaction of an ester with trimethylamine and with hydroxyl ion. The trimethylamine reaction necessarily splits the ester on the alcohol side of the ether oxygen.

$$RCOOCH_3 + N(CH_3)_3 \rightarrow RCOO^- + N(CH_3)_4^+$$
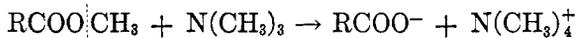
From the fact that steric hindrance due to ortho substitution is so much more significant in the hydrolysis reaction than in the reaction with trimethylamine, it was concluded that the hydrolysis takes place at a point in the molecule nearer the ortho substituent, and probably involves a split on the acid side of the ether oxygen.[8]

$$RCOOCH_3 + OH^- \rightarrow RCOOH + OCH_3^-$$
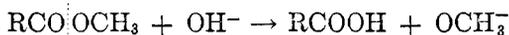
It is an important feature of the material cited in this paper that reaction rates in the type reaction

$$AB + C \rightarrow A + BC$$
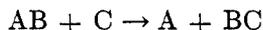
have been found to depend upon the equilibrium constant and hence upon the standard free energies of dissociation of both AB and BC. In the acid catalysis and in reaction IV the rate is dependent upon the free energy of the bond being broken (AB); in the basic catalysis and in reactions VII, VIII, IX, and X, it depends upon the free energy of the bond being formed (BC). There seems to be only one mechanism which leads simply and clearly to the expectation that the rate of a substitution reaction should be affected both by the bond being broken and by that being formed. This is the one proposed by London (32), Polanyi (3, 33, 34, 35), Eyring (16), and Olson (36, 37, 38), in which the combination of C with B proceeds simultaneously with the dissociation of A from B, and in which the height of the potential energy peak which must be overcome at the expense of the mutual kinetic energy of AB and C if reaction is to occur is a function among other things of the energies of dissociation of both AB and BC.

Unfortunately it has not so far been possible to develop this rather vague relation between the height of the potential energy peak and the dissociation energies into the definite and simple relation between the reaction rate and the free energy of dissociation which appears in equation 1. The recent attempt in this direction of Ogg and Polanyi (34), like the earlier attempts of Gurney (20) and of Erdey-Gruz and Volmer (15) to derive the polarization equation (2), leads only to a parallelism between rate and equilibrium, and is entirely incompetent to predict the exact linearity of the relation shown in equation 1b. This relation is in fact too widespread in its applicability and too exact in the more favorable cases for a test of its validity to be accounted for as the first-order approximation of a complicated function.

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