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SOME RECENT DEVELOPMENTS IN REACTION RATE THEORY

BY HENRY EYRING AND RICHARD P. SMITH

Department of Chemistry, University of Utah, Salt Lake City, Utah

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A brief review of the status of theoretical calculations of reaction rates is given. New developments in organic reaction rate theory are discussed; particular attention is given the development of a theory for charge distributions in aliphatic molecules and the correlation of the calculated charge distributions with organic reaction rates. The reaction of sodium atoms with organic halides and the chlorination of aliphatic molecules are discussed in some detail. The parallelism between changes in electrical resistance and hardness of alloys is discussed in terms of electronic availability.

Modern reaction rate theory reduces most ordinary problems in reaction rates to problems in molecular structure and the potential of interaction between molecules. Specifically, the theory of absolute reaction rates, as formulated by Eyring¹ in 1935 for the general case where one or more molecules combine to form the activated complex has for the specific rate constant

$$k' = \kappa \frac{kT}{h} \frac{F^\ddagger}{F_A F_B \dots} e^{-E_0/RT} \frac{kT}{h} K^\ddagger \quad (1)$$

Here k' is the specific rate constant, R is the gas constant, h is Planck's constant, T is the absolute temperature, E_0 is the activation energy per mole of the reaction at absolute zero, κ is the "transmission coefficient," and $F^\ddagger$, F_A , F_B , etc., are the partition functions of the "activated complex" and of the reactants A, B, etc., respectively, per unit volume and $K^\ddagger$ is the equilibrium constant between reactants and activated complex. The "activated complex" is defined to be the configuration of the reactant atoms and/or molecules corresponding to maximum energy along the most favorable reaction path. The transmission coefficient allows for the possibility that not every system of reactant molecules reaching the top of the barrier (*i.e.*, the activated complex configuration) and moving along the coordinate of decomposition leads to reaction. For normal adiabatic reactions, such as those usually encountered by the organic chemist, this factor may satisfactorily be taken to be unity.

The theory of absolute reaction rates is, then, a statistical theory relating the very important quantity k' , the specific rate constant, to (a) statistical quantities, such as the average translational energy of a molecule ($(3/2)kT$) and partition functions $F^\ddagger$, F_A , F_B , etc.; (b) the transmission coefficient, which is primarily related to the shape of the "barrier,"

i.e., "hump" in the potential energy plotted as a function of the reaction coordinate, and which will not concern us here, the deviations of this factor from unity being negligible for the reactions of particular interest to us; and (c) the activation energy, which must be calculated quantum mechanically, estimated semi-empirically or empirically, or determined experimentally.

Equation (1) is often written in the quasi-thermodynamic forms

$$k' = \kappa \frac{kT}{h} e^{-\Delta F^\ddagger/RT} \quad (2)$$

$$k' = \kappa \frac{kT}{h} e^{\Delta S^\ddagger/R} e^{-\Delta H^\ddagger/RT} \quad (3)$$

where $\Delta F^\ddagger$ is the "free energy of activation," $\Delta S^\ddagger$ is the "entropy of activation," $\Delta H^\ddagger$ is the "heat of activation," (all per mole, referred to standard states which must be designated), and R is the gas constant. The heat of activation, $\Delta H^\ddagger$, is practically the same as the previously introduced activation energy, E_0 , the two differing essentially by RT for unimolecular gas reactions and for reactions in solution where the standard states are unit concentrations; for other types of reactions, the relationships are readily derived.²

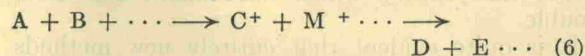
Equation (1) is derived for the rate process



Here species A and B, etc., unite to form the activated complex $C^\ddagger$ which breaks up to form D and E, etc. Thus the velocity of reaction is

$$v = k' (A) (B) \dots = C^\ddagger \kappa (kT/h) \quad (5)$$

The relation $v = C^\ddagger \kappa (kT/h)$ holds equally well for a reaction of the type



(2) S. Glasstone, K. J. Laidler and H. Eyring, "The Theory of Rate Processes," McGraw-Hill Book Co., Inc., New York, N. Y., 1941.

In this case

$$v = \kappa \frac{kT}{h} e^{-E_0/RT} \frac{F^\ddagger F_m \cdots (A)(B) \cdots}{F_A F_B (M) \cdots} = \kappa \frac{kT}{h} K^\ddagger \frac{(A)(B) \cdots}{(M) \cdots} = k' \frac{(A)(B) \cdots}{(M) \cdots} = C^\ddagger \kappa \frac{kT}{h} \quad (7)$$

Ordinarily the Arrhenius plot of the specific rate constant against $1/T$ yields a negative slope in the accustomed manner. This is, however, not necessary since $K^\ddagger$ like any equilibrium constant may possess a temperature maximum. Thus many biological reactions show a maximum with temperature ordinarily interpreted as the superposition on the customary Arrhenius speed-up with temperature rise of an accompanying enzyme inactivation. Alternatively one may simply say that $K^\ddagger$ shows a temperature maximum and that above this temperature maximum the activated complex is less energy rich than the constituents from which it is assembled. One cannot emphasize too much that $K^\ddagger$ must be expected to show just the complexities of any other equilibrium constant.

The main problems to be dealt with in calculating reaction rates then, are (a) calculation of the entropy of activation, and (b) calculation of the heat of activation (or energy of activation).

It is not difficult to estimate the entropy of activation with fair accuracy once the approximate configuration of the activated complex is known. This is fortunate not only for the sake of calculating the "frequency factor" (i.e., the coefficient of $e^{-\Delta H^\ddagger/RT}$) for a reaction, but this also provides us with a powerful tool for the elucidation of reaction mechanisms. Various forms for the activated complex of a reaction may be postulated, and the entropy of activation estimated for each. This is possible because masses and moments of inertia are the most important factors entering these calculations, other than universal constants. By comparing the various calculated entropies of activation with that which is observed, the mechanism of the reaction may be decided upon in many cases.² A particularly striking example is a reaction which we shall discuss more fully later in this paper: the reaction of sodium atoms with halides. When a sodium atom approaches a halide molecule, the valence electron of the sodium transfers to the halide, which promptly dissociates, the result being the formation of a sodium halide and a free atom or radical. Magee³ has shown that the very high frequency factors observed can be accounted for only by assuming a separation of five to seven Ångström units between the halide center of gravity and the sodium atom nucleus, so that the electron must prefer to jump from the sodium to the halogen even when quite a large separation exists.

Large, important areas in the field of reaction rate theory apparently would be in good condition, then, if means were available for calculating (or successfully estimating from empirical considerations) activation energies. This is the part of reaction rate theory which has caused the most trouble.

It is quite evident that entirely new methods must be found for determining activation energies

theoretically. In principle, straightforward quantum mechanical calculations should be used. However, by using this approach, it has so far been possible only to show that, for the simplest reaction, $H + H_2 \text{ para} = H_2 \text{ ortho} + H$, the activation energy is less than 19 kcal., while the experimental value is about 7 kcal. Thus it appears that this can only be a successful approach, as new approximations are found which will both simplify and improve the calculations.

An alternative approach was devised by Polanyi and Eyring⁴ which is usually known as the "semi-empirical" method for calculating activation energies. They used London's approximate formula for the energy E for four monovalent atoms, which is

$$E = Q - \{1/2(\alpha - \beta)^2 + (\beta - \gamma)^2 + (\gamma - \alpha)^2\}^{1/2} \quad (4)$$

Here Q represents the total "coulombic" binding, and α , β and γ are exchange interactions between various atoms. Following Sugiura's calculations² on the hydrogen molecule, the "coulombic" terms were assumed to be about 14% of the total binding, and the total binding energies between pairs of atoms were assumed to be satisfactorily approximated by means of Morse curves between the atoms. These approximations made possible the construction of potential surfaces, and these were sufficiently accurate for at least qualitative discussion of the nature of a chemical reaction; and, in many cases, the calculated activation energies were in good agreement with experiment.

The method described above for the calculation of activation energies is now seldom used, and the *a priori* calculation of activation energies is a task that few have ventured to try during the last decade. The reasons for this shyness on the part of chemists appear to be, first, that the "semi-empirical" method has been applied to most of the simple gas reactions with results ranging from poor to excellent, and no one is sure of how to consistently improve the calculations; and, second, the reactions which are at once most interesting and most numerous, namely, the reactions of organic chemistry, are not suited to treatment by the "semi-empirical" method. This latter fact is well illustrated by the poor results which have been obtained with what has been called the simplest of organic reactions, namely, the reaction of sodium atoms with organic halides. Here the agreement with experiment is very rough indeed. Furthermore, in this particular case, one is not at all sure of how to take account of the changing properties of, for example, the C-Cl bonds when calculating the energies of activation for a series of chlorides, such as CH_3Cl , CH_2Cl_2 , $CHCl_3$ and CCl_4 , where the activation energy differential is about 10 kcal.

It therefore seems evident that neither the Eyring-Polanyi method nor strict quantum mechanical methods can at present be very fruitful for solving the activation energy problem, in view of the difficulties involved and the large number of reactions the chemist is interested in. Hence a high degree of successful empiricism seems to be demanded.

An empirical but very successful method for qualitatively considering relative organic reaction rates

(3) J. L. Magee, *J. Chem. Phys.*, **8**, 687 (1940).

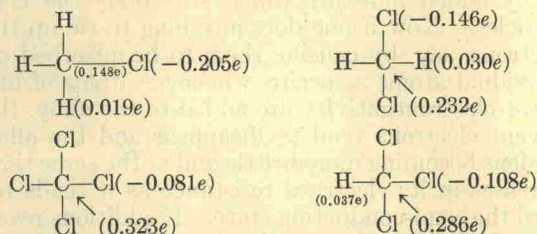
(4) H. Eyring and M. Polanyi, *Z. physik. Chem.*, **B12**, 279 (1931).

has been built up by the "electronic interpretations" school, led particularly by such English workers as Ingold, Robinson, Lowry and Lapworth. Simple concepts for discussing changes in electronic densities on various atoms in molecules due to substituent charges are used, and these charges are in turn qualitatively correlated with reaction rates and equilibria. In 1940 Ree and Eyring⁵ decided that here was a good place to start in attempting to attain a more quantitative treatment of organic reactions, and the result was the demonstration that the simple rules of the electronic school could equally simply be mathematically formulated and applied to the consideration of relative amounts of ortho, meta and para nitration of substituted benzenes.

The success of these calculations clearly demanded further explorations in this field. Efforts were begun in 1940 toward the development of a simple theory for estimating charge distributions in simple aliphatic molecules, such as methylene chloride. The war interrupted this work, but it has finally been continued in the recent paper by Smith, Ree, Magee and Eyring,⁶ wherein a simple, semi-empirical scheme is detailed for the calculation of charge distributions in aliphatic molecules. The validity of the method was demonstrated by the calculation of dipole moments of polysubstituted methanes and ethyl halides, using the moments of the methyl halides as the bases. A following paper by Smith and Eyring⁷ shows that the net charges thus calculated may be simply correlated with the activation energies for reactions of halides with sodium atoms, thereby lending support to the charge distribution theory and at the same time showing how charge distributions are easily correlated with reaction rates, at least for certain types of reactions.

For details of the charge distribution theory the reader is referred to the appropriate paper.⁶ There it was shown how, to the approximations used, atoms in molecules may be considered to have "net charges" associated with them, and these may be calculated by a simple scheme. It was found that certain moments were needed as bases, among them being the C-H bond moment in methane. This is certainly small, and the calculations based on the assumption that it is zero were satisfactory. All calculations presented in this paper are based upon this assumption.

The net charges for CH_3Cl , CH_2Cl_2 , CHCl_3 and CCl_4 were calculated to be as follows.



Here e is the negative charge of an electron. This series clearly portrays the main features of the "inductive effect," *i.e.*, the change in the moment

of a bond with the bond environment. As the carbon becomes more heavily substituted with chlorines, the latter take more electronic charge from the carbon, thereby increasing its effective nuclear charge, making further removal of charge more difficult. Hence two chlorines cannot remove twice as much charge as one, *i.e.*, the chlorines in CH_2Cl_2 have smaller net negative charges than has the chlorine in CH_3Cl , and so on.

In the reactions of the above molecules with sodium atoms, it is found that the activation energies decrease as we go through the series, the total change being about 9.5 kcal./mole. This seems qualitatively understandable when the net charges shown above are considered. As the chlorine atom becomes more negatively charged, its electron affinity decreases, and the electron from the sodium atom therefore is not transferred to the chlorine so easily. Remarkably enough, the plot of the net charges against the activation energies yields a straight line.⁷ Still more remarkable is the fact that if net halogen charges are divided by the polarizabilities of the carbon-halogen bonds, not only do the chlorides fall on a straight line (the polarizabilities of all C-Cl bonds are taken to be the same), but bromides and iodides are brought onto the same straight line. This relationship is so accurate that one wonders about the possibility of showing how it may be made to follow from theoretical considerations. So far, not much progress has been made in this direction, so that this remains as a challenge. A very rough argument that indicates how such a relationship might arise is as follows. Let us treat the "extra" charge on the halogen, *i.e.*, the halogen net negative charge, by the "particle in a box" model, using a one dimensional model for simplicity. If L is the length in which the particle may move, the ground-state energy of such a system is

$$E = h^2/8mL^2 \quad (5)$$

Suppose the available space is shortened an amount dL . The corresponding energy change is then

$$dE = -(h^2/4mL^3)dL \quad (6)$$

Suppose that, before the "loose" electron of the sodium atom can be transferred to the halogen atom, the "extra charge" of the halogen atom must be pushed over onto the carbon atom. This is equivalent to a reduction in L . If this reduction is constant, then eq. (6) shows the energy differential to be inversely proportional to L^3 for a unit of charge. Multiplying this by the fraction of a charge to be transferred, we arrive at a proportionality of energy differential to net charge divided by L^3 . Now L^3 has the same dimensions as polarizability, and might be expected to be proportional to the polarizability; hence a rough justification of our empirical relation. Similar arguments, made more precise, might lead to the desired relationship.

Two very different types of reactions, then, have so far yielded to treatment by the new methods, where other methods have failed. They are, (a) an electrophilic attack on a carbon atom by an ion (the nitration of substituted benzenes); (b), an electron-transfer reaction (reaction of sodium atoms with halides). Many important organic reactions are essentially of these types, and may be expected

(5) T. Ri (Ree) and H. Eyring, *J. Chem. Phys.*, **8**, 433 (1940).

(6) R. P. Smith, T. Ree, J. L. Magee and H. Eyring, *J. Am. Chem. Soc.*, **73**, 2263 (1951).

(7) R. P. Smith and H. Eyring, *ibid.*, **74**, 229 (1952).

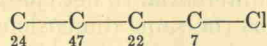
to yield to similar treatment. Other types, such as a dissociation reaction (acidic ionization) will be shown to be amenable to such treatment in a future paper.

In all the reactions discussed above, net charges residing on atoms are the fundamentally important factors. In another class of reactions, namely, free radical reactions, it is well known that not net charges, but rather charge availabilities, are the important factors. Our inductive effect theory is, as we shall now demonstrate, capable of providing indices of electron availability for various positions in molecules, and these can be correlated with rates of free-radical attack on various positions.

The reaction we shall consider is one for which many data have been assembled, namely, the free radical chlorination of aliphatic hydrocarbons and aliphatic chlorides. Ash and Brown⁸ have recently reviewed the data on this reaction. Here a chlorine atom comes up to a hydrogen atom in the chlorinated (or unsubstituted) alkane; an electron is pulled out of the C-H bond, so that an H-Cl bond may be formed, leaving a free radical.

In order to understand how the experimental results for this reaction may be explained, let us first consider *n*-butane. Here the secondary carbons are favored toward chlorination. In $(\text{CH}_3)_2\text{CHCH}_2\text{CH}_3$, the tertiary carbon is highly favored. These facts have previously been explained only by the suggestion that a methyl group may be considered to activate the adjoining carbon, though the nature of this activating influence is not elucidated. Our explanation is simply this: The more easily an electron can be pulled out of a given C-H bond to form the H-Cl bond, the lower the activation energy should be. The more easily a carbon atom can regain electronic charge from other bonds, the more willing it will be to give up a C-H bond electron. Carbon-carbon bonds will be much better suppliers of charge than carbon-hydrogen bonds, because of the greater longitudinal polarizability of the former. A primary carbon has only one C-C bond through which to partially make up charge deficit; a secondary carbon has the benefit of two C-C bonds; and a tertiary carbon has three. Hence the results mentioned above are readily explained.

We turn now to the chlorination of *n*-butyl chloride, which is a bit more complicated. Here we have not only the "reservoir" effect just considered, but superimposed on this is the inductive effect. The relative amounts of attack at the various carbons are as follows.¹



Numbering the positions 1, 2, 3, 4 from the left, we see that the "reservoir" effect will explain the greater amount of attack at position 2 over position 1. Carbons 3 and 4 have equally good "reservoirs," but they are already electron deficient because of the influence of the chlorine already present in the molecule.

To show that the above explanation will actually account for the trend shown, we have assumed that, in the activated state, the incomplete H-Cl bond

has removed about as much charge from the carbon concerned as a chlorine would remove if attached directly to the carbon. Then we may use the charge actually removed by a chlorine substituted in a position as a measure of the "electron availability" at that position. That is, we simply calculate charge distributions for the four compounds $\text{Cl}(\text{CH}_2)_4\text{Cl}$, $\text{CH}_3\text{CHCl}(\text{CH}_2)_2\text{Cl}$, $\text{CH}_3\text{CH}_2\text{CHClCH}_2\text{Cl}$ and $\text{CH}_3(\text{CH}_2)_2\text{CHCl}_2$. The charges we calculate to reside on the second chlorine then are, respectively, in units of 10^{-10} e.s.u., -1.056 , -1.129 , -1.024 , -0.799 . These figures parallel the amounts of substitution previously given very well. Similar calculations have been made for the chlorination of $\text{CH}_3(\text{CH}_2)_2\text{CHCl}_2$ and $\text{CH}_3(\text{CH}_2)_2\text{CCl}_3$. The results are tabulated below. For each molecule, the experimental amounts of substitution are given on the first line, and the charges a chlorine will remove are given on the second line (units of 10^{-10} e.s.u.).

C	C	C	C	X
24	47	22	7	Cl
-1.056	-1.129	-1.024	-0.799	
37	49	12	2	Cl ₂
-1.051	-1.071	-0.966	-0.618	
51	49	0	...	Cl ₃
-1.043	-1.058	-0.925	...	

Experiment shows carbons 1 and 2 in the last molecule to be about equally attacked, while our "electron availability indices" also become almost equal for these positions, as contrasted with the two other molecules. In other words, the strong inductive effect of the three chlorines seems to just counterbalance the different "reservoir" effects here.

It is intended to discuss this reaction in more detail elsewhere. Meanwhile, it is hoped that we have indicated how useful the simple concepts of our inductive effect theory can be for semi-quantitative understanding of diverse types of organic reactions.

One other concept which involves electronic availability serves to explain the parallelism between changes in the electrical resistance and in the hardness of alloys.⁹ One should think of conductance electrons as a solvent surrounding the positive atomic kernels holding them together and permitting them to slip past each other readily, providing there is sufficient electron solvent. A useful and close analogy is clay held together and made plastic by added moisture which surrounds the clay particles. Now if one does anything to tie up the electrons, say, by causing them to be adsorbed on individual atoms as occurs whenever atoms of different electronegativity are added to the alloy, the solvent electrons tend to disappear and the alloy hardens becoming more brittle and at the same time increases in its electrical resistance as it tends toward the semi-conducting state. If additions reach the point where compounds start precipitating out of the alloy, the situation becomes complex and the simple parallelism between hardness and resistance requires closer analysis. We will pursue this matter no further here.

(8) A. B. Ash and H. C. Brown, *Record Chem. Progress*, **9**, 81 (1948).

(9) R. F. Vines, "The Platinum Metals and Their Alloys," The International Nickel Co., 1941.

In reactions involving the fusion of more than one saturated molecule into an activated complex, electronic promotion is involved. This activation energy of promotion is lessened by coordination of the activated complex with a suitable electron acceptor. Metals as shown by their work functions

have long been recognized to have this catalytic virtue of temporarily accepting unwanted electrons. We have been able to mention only a few of the cases where electron displacement lowers activation energy. In most cases suitable quantitative theories are still much needed.

