A Correlation of Reaction Rates

BY GEORGE S. HAMMOND

While there is no completely general correlation between the rates and free energies of chemical reactions there are many instances in which the most stable products are formed at the most rapid rates from a series of similarly constituted reactants. In certain other reactions, the less stable products seem to be formed at the more rapid rates with considerable regularity. In the latter cases it appears that the transition states are formed with the minimum amount of reorganization of the reactants. By invoking a simple postulate one can decide whether the reactants or products or neither are good structural models for estimating the influence of structural variations on the free energies of transition states. Several examples of the application of the postulate are presented.

Chemists have long been plagued by the lack of any general correlation between reaction rates and the positions of chemical equilibria. In many instances highly exothermic reactions are exceedingly slow because the over-all changes are so complex that the transformations can only occur by stepwise processes which involve at least one endothermic stage. However, even when one-step reactions, or the rate-controlling steps of complex reactions, are compared it is found that there is no general relationship between the free energies of the reactions and their rates. However, there are a sufficient number of such one-step, or elementary, processes in which a close parallelism is observed between rates and equilibria (either measured or inferred) to render it imperative that the scope of such relationships be given careful consideration. We have found that a rather simple postulate aids considerably in estimating the degree of correlation which is to be expected in a given reaction. The same concept leads to an understanding of another class of reactions in which the ultimate thermodynamic consequences have little influence on relative reaction rates.

The postulate can be stated in the following way. *If two states, as for example, a transition state and an unstable intermediate, occur consecutively during a reaction process and have nearly the same energy content, their interconversion will involve only a small re-*

organization of the molecular structures. Thus, if a bond which is being broken during the process is nearly covalent in the first state it will be stretched by an arbitrarily small amount in going to the second. If a bond is being made from two particles which are kinetically free in the first state there will be only a loose association between the two in the second. Furthermore, other changes in molecular geometry, such variations in bond angles, will also be limited to small changes.[1]

The value of the postulate derives from its application to elementary processes which are either highly exothermic or highly endothermic. In highly exothermic steps it will be expected that the transition states will resemble reactants closely and in endothermic steps the products will provide the best models for the transition states. This last observation follows directly from the observation that if a highly endothermic process has a detectable rate it cannot involve any large excess activation energy.[2] The application to exothermic reactions is slightly less general since it is conceivable that a highly exothermic step can involve a large activation energy. However, the postulate applies to fast, exothermic reactions and, by the principle of microscopic reversibility, to any reactions which have a finite rate in the reverse direction.

Three extreme cases are represented by the schematic potential energy diagrams shown in Fig. 1. Curve A represents the destruction of a highly reactive species and B depicts the formation of a high energy intermediate. In the first case, going from the reactants to the transition state involves little progress along the reaction coördinate and in the second the same is true of the conversion of the transition state to the products.[3] Curve C repre-
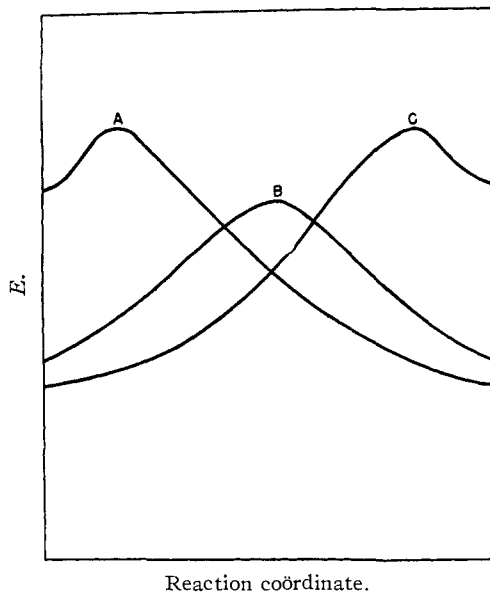
Reaction coördinate.

Fig. 1.

(1) It will be noticed that the postulate deals directly with potential energy rather than free energy relationships. Translational entropy changes and to some extent solvation entropies are essentially uncontrolled by the postulate. For example, if two ions A^+ and B^- are brought together to form a transition state in a process which involves only a small activation energy, translational entropy will be lost no matter how loosely the two particles are in the transition state. Furthermore, some changes in the electrostriction of the solvent also will result if the two ions are brought close enough to permit interaction of their electrostatic fields.

(2) In keeping with the qualitative nature of the discussion, we refer to large and small energy differences. Since most reactions which have observable rates at ordinary temperatures have activation energies of 15–30 kcal. per mole, a value of 20 kcal. would certainly be considered large for the over-all energy change in the reaction.

(3) In a sense the postulatory basis of this discussion is the view that curves such as those shown in Fig. 1 can be drawn with confidence since the conclusions become obvious from consideration of the curves. It should be explicitly stated, however, that the curves may be constructed from two potential functions of an ordinary sort and that situations such as that shown in Fig. 2 are unlikely to arise.

sents a typical thermally balanced process in which the transition state has no close analog of conventional chemical structure.

Applications. Production of Free Radicals, Carbanions and Carbonium Ions.—It is observed experimentally that the recombination reactions of atoms and free radials do not involve activation energies of more than a few kilocalories[4] and that in solution rates of such reactions may even become diffusion controlled.[5] Such behavior indicates, by the principle of microscopic reversibility, that the dissociation of molecules to give high energy atoms and radicals fits curve B which is close to the semi-theoretical curve originally described by Morse.[6] It is to be expected, therefore, that structural variations which effect a decrease in the dissociation energy will be reflected nearly quantitatively in a decrease in the rate of decomposition. The assumption that little excess activation energy is involved in such dissociation reactions constitutes the basis of the familiar kinetic method for the determination of bond dissociation energies.[7]

In a similar manner it is observed that the rates of production of carbonium ions from alkyl halides and similar substances generally may be correlated with the expected variations in the free energies of the ionization reactions.[8] The fact that curve B describes such reactions was rationalized at an early stage in the development of the theory of displacement reactions.[9] The practical result is the confidence which most chemists place in predictions of the relative rates of unimolecular solvolysis reaction on the basis of such factors as the variations in the resonance energies of the ions produced and the relief of steric strain which accompanies the conversion of a tetrahedral molecule into a planar ion.

A third reaction type in which unstable intermediates are produced is the removal of protons from weak, pseudo acids to form carbanions. As a rough generalization it may be stated that there is a parallelism between acidity and the rate of proton removal by bases.[10] Since these reactions are rather highly endothermic, one would anticipate that such a relationship should exist.

Reactions of Carbonium Ions and Carboniums.—A reaction in which a highly reactive ion is destroyed in a very fast reaction is, in a sense, the converse of the cases just discussed and should be described by curve A in Fig. 1. According to the postulate the products should be structurally quite different from the transition states and, therefore, there should be no regular tendency for the most stable products to be produced the most rapidly in competitive reactions. There are many examples which show that this frustration of thermodynamics does occur frequently. For example, it has been

(4) S. Glasstone, K. J. Laidler and H. Eyring, "The Theory of Rate Processes," McGraw–Hill Book Co., Inc., New York, N. Y., 1941, p. 131.

(5) K. J. Laidler, "Chemical Kinetics," McGraw–Hill Book Co., Inc., New York, N. Y., 1950, p. 118.
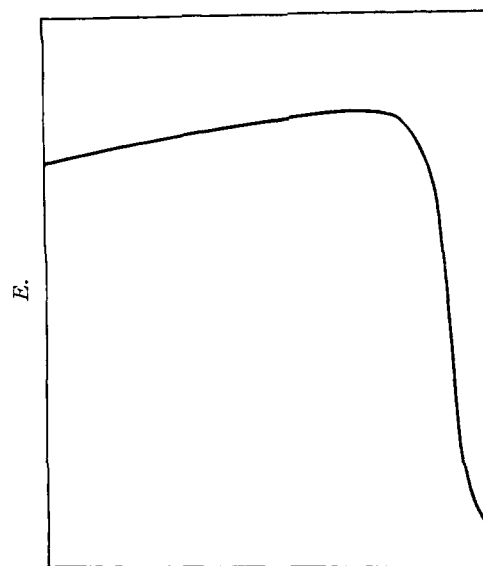
(6) P. M. Morse, *Phys. Rev.*, **34**, 57 (1929).

(7) E. T. Butler and M. Polanyi, *Trans. Faraday Soc.*, **39**, 19 (1943).

(8) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, Chapt. VII.

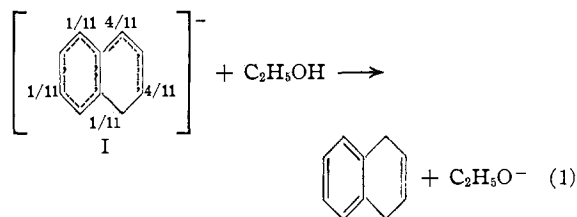(9) R. A. Ogg and M. Polanyi, *Trans. Faraday Soc.*, **31**, 607 (1935).

(10) C. K. Ingold, ref. 8, pp. 537–566.

Reaction coördinate.

Fig. 2.

known for many years that the reduction of naphthalene with sodium and alcohol gives 1,4-dihydronaphthalene[11] although this product is unstable with respect to its conjugated 1,2-dihydro isomer. Many similar observations have been made concerning the partial reduction of other unsaturated compounds by alkali metals in liquid ammonia.[12] The naphthalene reduction will be discussed in detail as it is representative of the entire class of reactions. It is likely that the product is formed by the neutralization of the unsaturated anion I. The approximate charge

$$
\begin{bmatrix} \text{1/11} \; \text{4/11} \\ \text{1/11} \qquad \text{4/11} \\ \text{1/11} \end{bmatrix}^- + \; C_2H_5OH \longrightarrow
$$

I

$$
+ \; C_2H_5O^- \quad (1)
$$

distribution in the ion, as calculated by the method of zero energy molecular orbitals,[13] is indicated. One should consider reactions in which the proton is added to each of the five centers of negative charge. We can imagine three idealized situations in transition states in which the new C–H bond is made increasingly short. These cases are: (1) at very long distances the stability of the transition states will be determined by the interaction of the O–H dipole with the geometric center of charge density in the ion and the proton will probably be deposited most readily near that center; (2) at somewhat shorter distances the attractive interaction will still be described properly as a charge–dipole interaction but the position of maximum stability will be determined in part by the formal charge on the particular carbon atom to which

(11) E. Bamberger and W. Lodter, *Ber.*, **26**, 1833 (1893); F. Straus and L. Lemmel, *ibid.*, **46**, 232 (1913).

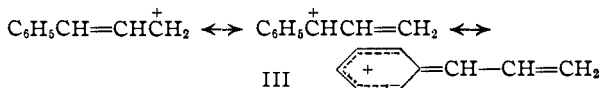(12) A. Birch, *Quart. Revs.*, **4**, 69 (1950).

(13) H. C. Longuet-Higgins, *J. Chem. Phys.*, **18**, 265 (1950).

the bond is being formed; and (3) at very short C–H distances the covalent character of the new bond will become important and the stability of the various transition states will become closely related to the stability of the corresponding products. In the problem at hand, case 3 can be eliminated immediately on two counts. First, the most stable product is not formed and, second, the large exothermicity of the reaction requires that the transition state occur at a point at which little progress has been made in bond formation. Distinguishing between cases 1 and 2 is much more difficult since either might be considered a "loose" transition state as demanded by our postulate. If case 1 obtains one should expect to produce some II since the bridgehead carbon atom is close to the center of

II
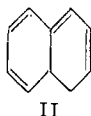
charge density. That this product is not found does not rigorously exclude case 1 as the formation of III might be rapidly reversible because of the instability of the compound. Since the formal charge densities at positions 1 and 3 are equal, it is to be expected that the relative rates of reaction at those positions will be determined solely by the fact that position 1 is closer to the other centers of negative charge.

It will be evident that similar results should be observed in reactions which destroy unsaturated cations. The experimental evidence is, however, much less clean cut. A particularly appropriate case for study should be the cation III produced by the solvolysis of cinnamyl or phenylvinylcarbinyl compounds. One would expect reactive nucleophilic reagents to attach themselves to the cation by

$$C_6H_5CH{=}CH\overset{+}{C}H_2 \longleftrightarrow C_6H_5\overset{+}{C}HCH{=}CH_2 \longleftrightarrow$$

III $\langle \overset{+}{} \rangle{=}CH{-}CH{=}CH_2$

way of loose transition states in which electrostatic forces provide most of the binding energy between the reactants. Since the secondary position is the closer of the two exocyclic positions to the center of charge density in the ion we would expect to produce notable amounts of the less stable phenylvinylcarbinyl compounds in the irreversible reactions of the cation. In the majority of the reactions which have been studied the destruction of the carbonium ion is reversible so that equilibration occurs with the consequent production of the conjugated cinnamyl derivatives.[14,15] However, it is noteworthy that the hydrolysis,[16] alcoholysis[16] and acetolysis[17] of cinnamyl chloride give some of the unconjugated products. Braude[18] has criticized the view[14] that the rearranged products are produced by way of the phenylallyl cation. His objection is based upon the fact that, " . . . the thermodynam-

ically less stable, deconjugated products are produced from cinnamyl and other halides; if the mesomeric carbonium ions were formed, the positive charge would be expected to remain concentrated at $C\alpha$ [the primary position]." This objection must be considered invalid since, (1) the thermodynamic stability of the products is not pertinent to the question according to our postulate and (2) the distribution of positive charge in the ion should correspond to the distribution of negative charge in I.

A further complication in studying the products of carbonium ion reactions is the familiar overlapping of S_N1 and S_N2 mechanisms. In order for the line of reasoning presented above to hold it is necessary that the carbonium ion have a sufficiently long lifetime to acquire the indicated charge distribution.[19]

The Role of Intermediate Complexes in Reactions.—An outstanding area of confusion in the field of reaction mechanisms is found in the evaluation of the importance of complexes of various types which may be formed between reactants. There are two ways in which information, gained either by experiment or inference, as to the stability of complexes can be of aid in the discussion of reaction rates. If one can measure independently the equilibrium constant for the formation of the complex, or of a similar complex in a closely related system, a close correspondence between the formation constants and the reaction rates will be expected *if the structure of the complex is similar to that of the transition state.* In the more likely event that some type of addition complex which is similar in structure to the transition state can be *imagined* the (perhaps hypothetical) complex may well provide a concrete basis for the discussion of relative reactivities. The role of postulate is that of enabling one to use discrimination in the choice of the complexes which will serve as useful models for transition states.

Electrophilic aromatic substitution represents a reaction in which there has been extensive discussion of the possible importance of complexes formed from the electrophile and the aromatic substrate. Dewar has suggested[20] that π-complexes are formed in the course of the reactions and that their formation may even be rate determining. The description of the complexes is rather vague since it is implied that they may have large heats of formation despite the fact that complexes which he cites as examples have been found[21] to have low heats of formation. Recently the loose complexes of aromatic compounds have been regularly referred to as π-complexes. Although some point is frequently made of the role of these complexes in substitution reactions,[22] the fact that their heats of formation are small in comparison with the heats of activation for substitutions indicates that they are not in general good models for the transition states. They

(14) A. G. Catchpole, E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, 8 (1949).

(15) A. G. Catchpole and E. D. Hughes, *Trans. Faraday Soc.*, **37**, 629 (1941).

(16) J. Meisenheimer and J. Link, *Ann.*, **479**, 211 (1930).

(17) J. Meisenheimer and G. Beutter, *ibid.*, **508**, 58 (1933).

(18) E. A. Braude, *Quart. Revs.*, **4**, 69 (1950).

(19) It would be more accurate to speak of the time required to achieve an arrangement of the solvation shell corresponding to the charge distribution in the free ion.

(20) M. J. S. Dewar, "The Electronic Theory of Organic Chemistry," Oxford University Press, London, 1949, p. 168.

(21) H. C. Brown and W. J. Wallace, This Journal, **75**, 6279 (1953).

(22) L. N. Ferguson, *Chem. Revs.*, **50**, 47 (1952).

represent small shoulders on the potential energy surface which should be located close to the uncomplexed reactants as is shown by the point labeled B in Fig. 3.

In Fig. 3 a saddle point corresponding to a metastable intermediate is shown at point D. The most successful accounts of the problem of relative reactivity in aromatic substitution have been based upon models for the transition state of the rate-determining step which have a configuration closely related to IV, a conceivable reaction intermediate in which the carbon atom undergoing substitution has been converted to a tetrahedral configuration.[23] If such an intermediate exists and has a heat of forma-

<center>H　X　IV</center>
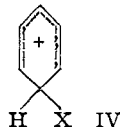
tion similar to the activation energy for the substitution reactions *it should be closely related to both the transition states,* C and E, through which it is formed and destroyed. The conversion of C to the intermediate would require only a small reorganization, such as a slight tightening of the C–X bond. Similarly, a small extension of the C–H bond should bring the intermediate to the top of the second barrier. If this is the case two important conclusions can be drawn. First, since both C and E are close to the intermediate configuration it will make little difference in the discussion of relative reactivities whether the formation or destruction of IV is rate determining. Second, and conversely, it will be exceedingly difficult to establish, by the use of conventional arguments based upon relative reactivities, which step is rate limiting. It will also be equally difficult to demonstrate that a real intermediate is actually formed although the conclusion that, if the reaction involves a single step, the transition state must resemble the (hypothetical) intermediate will remain as a useful guide to the study of such reactions.

Melander has recently reported[24] that no kinetic isotope effect is observed in aromatic nitration and bromination when tritium is substituted for hydrogen in the aromatic substrate at the site of the reaction. This brilliant piece of work merits very careful evaluation. The absence of an isotope effect shows that the zero point energies associated with the bending and stretching of the C–H bond are not changed significantly in going from the reactants to the transition state. Such an observation is usually transformed into the categorical conclusion that the bond to hydrogen is not being broken in the rate-controlling step of the reaction. This is not necessarily a proper conclusion in all cases. In a highly exothermic reaction, such as the removal of a proton from IV, the isotope effect might be undetectably small merely because only a slight weakening of the C–H bond would bring the intermediate to the second transition state. Such a case has been reported recently by Lewis and Boozer[25]

(23) C. K. Ingold, ref. 8, Chapt. 5.
(24) L. Melander, *Arkiv. Kemi.*, **2**, 213 (1950).
(25) E. S. Lewis and C. E. Boozer, THIS JOURNAL, **76**, 791 (1954); C. E. Boozer and E. S. Lewis, *ibid.*, **76**, 794 (1954).

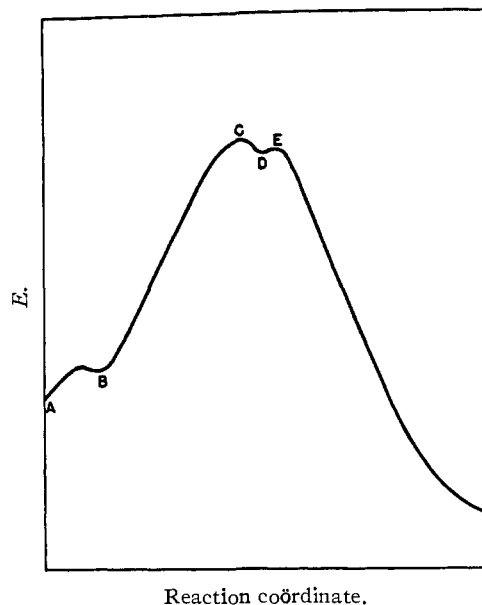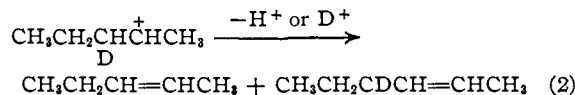<center>Reaction coördinate.</center>

<center>Fig. 3.</center>

who observed no isotope effect in the loss of protons (or deuterons) from partially deuterated secondary amyl cations. It is also noteworthy in this connection that Shiner[26] did observe a small isotope effect in a similar, but less exothermic, reaction, the

$$\overset{+}{CH_3CH_2CHCHCH_3} \xrightarrow{\;-H^+ \text{ or } D^+\;}$$

<center>D</center>

$$CH_3CH_2CH=CHCH_3 + CH_3CH_2CDCH=CHCH_3 \quad (2)$$

removal of protons (or deuterons) from partially deuterated *t*-amyl cations.

Since the tritium experiments do not demonstrate unequivocally that C–H bond breaking is not involved in the rate-determining steps of aromatic nitration and bromination they do not demonstate that intermediates such as IV are formed during the course of these reactions. On the other hand, it cannot be emphasized too strongly that the failure of the work to establish the timing of the reactions in an unequivocal manner does not detract from their value. It is clearly shown that the breaking of the C–H bond cannot have made much progress in the transition states. This is a matter of no small importance in understanding the reactions. The decision as to whether or not there is a non-isolable intermediate of high energy is trivial since the real objective is to obtain information concerning the configuration of the transition state in the slow step of the reaction irrespective of precisely what that step may be.[27] Melander also found
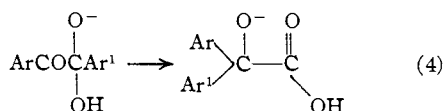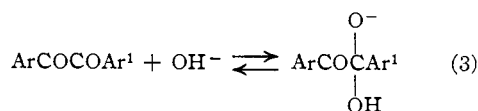
(26) V. J. Shiner, *ibid.*, **75**, 2925 (1953).
(27) It could be maintained that Melander's results cast some doubt on the possible existence of IV as a high energy intermediate. It would be reasonable to expect some loosening of the C–H bond in IV since the carbon atom has changed from the trigonal to the tetrahedral configuration and since some additional loosening should occur because of hyperconjugation of the C–H bond with the positively charged, unsaturated system. This last effect would be analogous to the loosening of the β C–H bonds in solvolysis of aliphatic compounds.[25,26] The absence of an isotope effect would, therefore, imply that the transition states are actually displaced considerable from configuration IV in the direction of the reactants. If this is true it would either mean that there is a fairly deep depression in the potential surface at the intermediate or that the intermediate is avoided altogether.

that an isotope effect was observed in aromatic sulfonation. This is accounted for readily if the intermediate V is formed. Since the intermediate in this case would be neutral it might have unusual

H   SO₃⁻   V
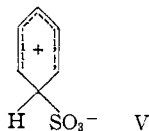
stability and the removal of a proton from it might involve considerable weakening of the C–H bond before the transition state is reached. Again it is possible that the intermediate is a fiction since the same description of the transition state could be arrived at without reference to it.

A last example will be discussed briefly since it illustrates the useful application of the postulate in a concrete manner. The benzilic acid rearrangement of an unsymmetrical benzil can be formulated as a stepwise process in the manner

$$ArCOCOAr^1 + OH^- \rightleftharpoons ArCOC\overset{\overset{\displaystyle O^-}{|}}{\underset{\underset{\displaystyle OH}{|}}{C}}Ar^1 \quad (3)$$

$$ArCOC\overset{\overset{\displaystyle O^-}{|}}{\underset{\underset{\displaystyle OH}{|}}{C}}Ar^1 \longrightarrow \underset{Ar^{1\prime}}{\overset{Ar}{>}}C\overset{\overset{\displaystyle O^-}{|}}{\underset{\underset{\displaystyle OH}{}}{}}{-}\overset{\overset{\displaystyle O}{\|}}{C}\overset{}{\underset{\displaystyle OH}{\diagdown}} \quad (4)$$

Alternatively, the Ar group could migrate from

ArC(O⁻)(OH)COAr.¹ Relative migratory aptitudes of two groups would be determined by influence of substituents on the two equilibrium constants and the two velocity constants. Furthermore, the effects in the two steps should tend to compensate since substituents which promote the formation of the tetrahedral structure at the adjacent carbonyl group should also tend to slow down migration of an aryl group from that position. The prediction of the over-all effect can, however, be made unambiguously. Since the adduct ion can be considered as an unstable intermediate the structure of the transition state in reaction 4 will be closely related to it. Therefore, the dominating influence on the over-all reaction rate will be that predicted for reaction 3 alone. It has recently been found, by the use of isotopic carbon to distinguish between the carbonyl groups, that the direction of rearrangement of unsymmetrical benzils is in accord with this prediction.[28]

Acknowledgment.—The author is much indebted to friends, too numerous to mention, who have read this manuscript and made many important suggestions as to its composition. Particular mention should be made of the contribution which has been made in this way by Professor John D. Roberts who suggested among other things the application of the postulate to the benzilic acid rearrangement.

(28) J. D. Roberts, D. R. Smith and C. C. Lee, THIS JOURNAL, **73**, 618 (1951).

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The Dissociation of Sterically Hindered Acids

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The ionization constants of a series of highly hindered aliphatic acids have been measured and it was found that the accumulation of bulky groups in the vicinity of the carboxyl function has a pronounced acid weakening influence. This is interpreted as indicating that the dominant effect is the shielding of the carboxylate ions from solvation. The commonly encountered view that acid strengthening effects observed in some hindered systems is due to the compression of the acidic proton is criticized. Two factors, steric hindrance to solvation and steric inhibition of resonance, are sufficient to give a qualitative account of steric effects on the strength of proton acids.

Because a number of sterically hindered acids were made available to us¹ we have measured the ionization constants in order to assess the effect of steric hindrance in unconjugated systems. The measurements were carried out by potentiometric titration in "50 per cent." methanol–water with a glass electrode and a calomel reference electrode. The solvent was chosen as representing the best available compromise based upon the slight solubility of the acids in water and the non-ideal behavior of electrolytes in non-aqueous solvents. It is anticipated that the unknown correction for the difference in the junction potential from that in-

volved in the use of the same electrodes in water is small and constant throughout the series and that the data in Table I represent a reasonable approximation to the *relative* thermodynamic dissociation constants. For comparison data previously reported² for the acidity constants of other aliphatic acids in a similar medium are summarized in Table II. While the values for benzoic acid do not check well between the two series of measurements this difference may be due to a medium effect as the earlier works did not specify the way in which their solvent was prepared. Another possible source of the discrepancy between the two series of measurements may be found in the fact that different electrode systems, involving different variations in the junction potentials, were used in the two investigations. It is evident, however, that the usual

(1) The acids were made available for the purpose of this study by Prof. M. S. Newman. Most of the compounds were originally a part of the chemical collection of the late F. C. Whitmore. The exact history of the samples is unknown, but it is inferred that they were prepared by the methods described in the various references given in the Experimental section.

(2) W. L. Bright and H. T. Briscoe, J. Phys. Chem., **37**, 787 (1933).