A SEMIQUANTITATIVE EXTENSION OF THE ELECTRONIC THEORY OF THE ENGLISH SCHOOL

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Of the many attempts to apply the electron theory to problems of organic reactivity, the most successful and hence the most widely used is the one developed chiefly by the English school of organic chemists (1). According to this theory all chemical reactions are considered to be generalized oxidation-reduction reactions in the sense that a necessary condition for reaction is the bringing together of an electron-rich center of sufficiently low electronegativity and an electron-poor center of sufficiently high electronegativity; or one may say that no reaction can possibly occur unless the nucleophilic centers and the electrophilic centers have, respectively, sufficiently high nucleophilic and electrophilic reaction tendencies (2). It is also considered that in all slow reactions the ratecontrolling step consists of the union of the most strongly electrophilic with the most strongly nucleophilic center unless such a union can be classified as a "neutralization" in the generalized sense of G. N. Lewis (3), in which event it involves no activation energy. Finally, substituents may alter the speed of a reaction by altering the electron density at the reaction site by five different modes of electron displacement: the I_s, I_d, E, M, and D effects (1).

The weakness of the English theory lies in the fact that it is a qualitative theory and thus is not only unable to predict which of the various opposing electron-displacement effects is the largest but is also unable to predict the effect of substituents on a reaction whose mechanism is not known or, alternatively, whose membership in class A or class B (4) has not been established by actual experiment. The desirability of an extension of the theory in a more quantitative direction is obvious.

The purpose of this paper is to consider the possibility of making a priori estimates of reaction mechanism by a semiquantitative extension of Lapworth's ideas on nucleophilic and electrophilic reaction tendencies. Such a method could also be used to predict the relative speeds of sufficiently similar reactions involving unsubstituted compounds. No attempt will be made here to discuss the sister-problem of establishing more quantitative methods for dealing with the five electron displacement effects.

The problem whose solution we seek has already been developed extensively under the title of the transition state theory or, as it is sometimes called, the theory of absolute reaction rates (5). However, the mathematical complexities of this theory are discouraging to the average organic chemist, who needs some simpler method of attack. Such a simplified method will now be outlined, but the organic chemists for whom it is developed must remember that simplification is usually achieved only through a compensating loss of accuracy.

According to the Lapworth theory, adopted by the English school, nucleo-

philic and electrophilic reaction tendencies of atoms in molecules are to be judged by their tendencies to form covalencies. Just how these tendencies are to be measured was apparently never definitely decided, nor were they ever quantitatively defined. Sometimes they are measured in terms of ionization constants or reduction potentials, sometimes by electronegativity differences deduced from the periodic table, sometimes by observing the speed of a reaction, etc. It seems to the author, however, that they could logically be defined as the ΔF or ΔH of covalency formation between two neutral radicals or atoms, when a "non-ionic mechanism" is concerned, or between two ions when the

IONIZATION ENERGIES (7)			
KCAL./MOLE	ATOM	KCAL/MOLE	
311.8	Р	251.2	
258.5	S	237.4	
333.7	Cl	298.5	
312.3	Br	272.0	
399.7	I	244.3	
	IONIZATION E KCAL./MOLE 311.8 258.5 333.7 312.3 399.7	KCAL./MOLE ATOM 311.8 P 258.5 S 333.7 Cl 312.3 Br 399.7 I	

TABLE IIONIZATION ENERGIES (7)

	IADDI	5 11	
	ELECTRON AFFINIT	TIES OF ATOMS ^a	
ATOM	KCAL./MOLE	ATOM	KCAL./MOLE
Н	17.5	Р	3.4
С	31.6	S	47.5
Ν	0.9	Cl	85.3
0	87.6	Br	81.55
\mathbf{F}	91.2	I	72.6°

^a Unless otherwise designated, these values were taken from reference (8). The factor 23.05 was used to convert electron-volts into kcal./mole.

^b This is the value of Mayer and Helmholz (9). Glockler and Calvin (10) report 88 ± 3.4 kcal. while Piccardi (11) reports 86.7 kcal.

^c See Mayer (12).

mechanism is "ionic." Only examples of the latter mechanism will be considered in this paper.

Since tables of bond energies $(-\Delta H)$ are in existence, while no corresponding values exist for the free energies of bond formation, it will be convenient to measure "tendencies for covalency formation" by means of the values of ΔH for the formation of normal covalent bonds from their gaseous ions. Such a table (see Table III) can easily be constructed by combining data on bond energies (6), electron affinities (Table II), and ionization potentials (Table I). This is illustrated by the following calculation.

$C^+ + e \rightarrow C$	(ioniz. pot.)	$\Delta H =$	-258.5	kcal.
$Cl^- \rightarrow Cl + e$	(electron aff.)	$\Delta H =$	85.3	
$\mathrm{C}+\mathrm{Cl}\rightarrow\mathrm{C}\mathrm{Cl}$	(bond energy)	$\Delta H =$	-66.5	
$C^+ + Cl^- \rightarrow C - C$	Ī	ΔH_{C^+}	$c_{1-} = -2$	239.7 kcal

By means of Table III it is easy to see, for example, that C^- is more nucleophilic than O^- . This is shown by the following figures:

X^+	ΔH_{C-X^+}	ΔH_{O-X^+}	
$\overline{\mathrm{H}^{+}}$	-367 kcal.	-334 kcal.	
C^+	-285	-241	
Cl^+	-270	-260	
O^+	-350	-259	

But we cannot make the comparison for two ions bearing opposite charges because the two cannot be combined separately with the same reference ion. Moreover, it sometimes happens that more than one bond needs to be considered in order to predict the more probable reaction path. All in all, it would seem best to judge the most probable reaction path by comparing the summation of ΔH for all bonds made and broken in the rate-controlling step. If this sum-

TABLE III

HEAT EFFECTS IN THE GAS PHASE FORMATION OF BONDS FROM IONS IN KCAL./MOLE

BOND	IONS	$\Delta H_{A^+ B^-}$	BOND	IONS	$\Delta \mathbf{H}_{\mathbf{A^{+} B^{-}}}$
H-C H-N H-O H-Cl H-Br H-I C-C	H+, C- H+, N- H+, O- H+, Cl- H+, Br- H+, I- C+, C- C+, N-	$\begin{array}{r} -367.5 \\ -394.6 \\ -334.4 \\ -329.2 \\ -317.6 \\ -310.6 \\ -285.5 \\ -306.2 \end{array}$	C—I C—I N—Cl N—Cl O—Cl Cl—Cl Br—Br I—I	C+, I- C-, I+ N-, Cl+ N+, Cl- O-, Cl+ Cl+, Cl- Br+, Br- I+ I-	$\begin{array}{r} -231.4 \\ -258.2 \\ -336.0 \\ -286.8 \\ -260.2 \\ -271.0 \\ -236.6 \\ -207.9 \end{array}$
C—O C—O C—Cl C—Cl C—Br C—Br	C+, O- C-, O+ C+, Cl- C-, Cl+ C+, Br- C-, Br+	$\begin{array}{r} -300.2 \\ -240.9 \\ -350.7 \\ -239.7 \\ -333.4 \\ -231.0 \\ -294.4 \end{array}$	C=C C=N C=0 P-Cl P-Cl P-H	C ⁺	$\begin{array}{r} -207.9\\ (-268.3)\\ +2.3\\ (-249.9)\\ -228.7\\ -357.9\\ -371.4\end{array}$

mation were made correctly, taking into account the interaction between the bonds involved, the value of ΔH finally obtained should be the heat of activation¹ (ΔH^{\dagger}). Such calculations can be made with fair accuracy for simple compounds on the basis of the theory of absolute reaction rates. However, it is the purpose of this paper to show that, if these interactions are neglected and a simple summation is made of the ΔH values for the bonds made and broken, the results give a reasonably safe guide for comparing reactions involving unsubstituted, unconjugated compounds and hence form a semiquantitative extension of the electronic theory of the English school. Thus for the reactions

$$A + BC \rightleftharpoons A \cdots B \cdots C \rightarrow A - B + C$$

and
$$D - E + F - G \rightleftharpoons D \cdots E \cdots F \cdots G \rightarrow D + E - F + G$$

¹ Note that such a summation for all bonds made and broken in the entire reaction (not merely in the rate-controlling step) would give the value of ΔH for the reaction (not ΔH^{\ddagger}).

we could define the quantity ΔH^{\ddagger} by the respective equations:

$$\Delta \mathbf{H}^{\ddagger} = \Delta \mathbf{H}_{AB} - \Delta \mathbf{H}_{BC}$$
$$\Delta \mathbf{H}^{\ddagger} = \Delta \mathbf{H}_{EF} - \Delta \mathbf{H}_{DE} - \Delta \mathbf{H}_{FG}$$

and

where ΔH_{AB} represents the change in heat content attending the formation of the bond A—B in the gaseous molecule AB from the gaseous ions A⁺ and B⁻ or A⁻ and B⁺, etc. Which pair of ions is involved in a given case may be indicated by the alternative symbols $\Delta H_{A^+B^-}$ or $\Delta H_{A^-B^+}$. Such a calculation assumes that all of the energy of the bond being formed finds its way into the bonds being broken and that all of the bonds concerned are completely formed or completely broken. Neither assumption is correct. However, Ri and Eyring (13) state that in general, bonds being made or broken in a critical complex are about ten per cent longer than normal bonds. This indicates that there is at least a uniformity in this regard, and that the proposed summation of heat effects should, roughly speaking, do equal violence to the calculated values of ΔH^{\ddagger} for different reactions, if they are not too different, thus giving the same sequence of ΔH^{\ddagger} values as would obtain for the true values of ΔH^{\ddagger} . Of course the relative probabilities of the two reactions are not determined by the relative heats of activation, but by the relative free energies of activation (ΔF^{\ddagger}) . Thus the sequence of values of ΔH^{\ddagger} may not parallel the sequence of probabilities unless the entropy terms (ΔS^{\dagger}) are either small or equal. The latter is apt to be the case when the reactions are similar, *i.e.*, when they involve the same number of reactant and product molecules of about the same complexity, and when their transition states, as pictured above, involve the same number of dotted line bonds.

Since the proposed method aims at nothing more profound than establishing a sequence of the relative probabilities of different conceivable rate-controlling steps, the calculations will be still further simplified by omitting from consideration all of the ΔH terms for bonds which would occur in both or all of the reactions being considered, and which would accordingly cancel out when the final comparison is made. The resultant values of ΔH will be referred to as "comparative heats of activation" ($\Delta H_{com}^{\ddagger}$). The remainder of this paper will be devoted to examples showing how these simply calculated values of $\Delta H^{\ddagger}_{com}$, involving no kinetic data, can be used to determine: (a) the mechanism of a reaction, and (b) the relative speeds of reactions of the same type.

A. The addition of halogens to ethylene. In order to make an a priori determination of the mechanism of any reaction, it is convenient to start by formulating the different rate-controlling steps which conceivably could occur. In this case there are four:

I. An electrophilic attack by the halogen molecule [polarized by the glass walls of the reaction vessel (14)] on the carbon atom of the ethylene molecule:

$$\begin{array}{rcl} H_2 C = & CH_2 + Cl_2 \rightleftharpoons H_2 \stackrel{-}{\underset{C}{\rightrightarrows}} H_2 \stackrel{-}{\underset{C}{\rightrightarrows}} H_2 & \rightarrow & H_2 CCl \cdot \stackrel{-}{\underset{C}{C}} H_2 + Cl \stackrel{-}{\underset{C}{\square}} \\ & & \downarrow \\ & & \downarrow \\ & & \downarrow \\ & & \downarrow \\ & & Cl \stackrel{-}{\underset{C}{\square}} \end{array}$$

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Here the transition state is represented as involving the simultaneous formation of a C^--Cl^+ bond and the rupture of the Cl^--Cl^+ bond and one-half of the double bond, *i.e.*, it is represented as a typical displacement reaction (15). II. A nucleophilic attack by halogen on carbon:

+ -- --

$$\begin{array}{rcl} \mathrm{H_2C}{=}\mathrm{CH_2} \ + \ \mathrm{Cl_2} \ \rightleftharpoons \ \mathrm{H_2C}{=}\mathrm{CH_2} \ \to \ \mathrm{CH_2Cl}{\cdot}\mathrm{CH_2} \ + \ \mathrm{Cl^+} \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\$$

III. A nucleophilic attack by halogen on hydrogen, leading to substitution: $H_{2}C=CH_{2} + Cl_{2} \rightleftharpoons H_{2}C=C^{-}-H^{+}-Cl^{-}-Cl^{+} \rightarrow$ $H_{2}C=CH + HCl + Cl^{+}$

IV. A nucleophilic attack by halogen on carbon, leading to substitution:

$$\begin{array}{rcl} H_2 C = & CH_2 \ + \ Cl_2 \ \rightleftharpoons \ H_2 C = & CH_2 \ + \ H_2 C = & CH_2 \ + \ H_2 C = & CH_2 \ + \ H_2 \ + \ Cl_2 \ & CH_2 \ + \ H_2 \ + \ Ch_2 \ & CH_2 \ + \ H_2 \ + \ Ch_2 \ & CH_2 \ + \ H_2 \ + \ Ch_2 \ & CH_2 \ + \ H_2 \ + \ Ch_2 \ & CH_2 \ + \ H_2 \ + \ Ch_2 \ & CH_2 \ + \ H_2 \ + \ Ch_2 \ & CH_2 \ + \ H_2 \ + \ Ch_2 \ & CH_2 \ + \ H_2 \ + \ Ch_2 \ & CH_2 \ & CH_2 \ + \ H_2 \ + \ Ch_2 \ & CH_2 \$$

On the basis of these equations we may now easily calculate the values of ΔH^{\ddagger} . $(\Delta H^{\ddagger})_{I} = \Delta H_{C^{-}Cl^{+}} - \Delta H_{C^{+}=C^{-}} - \Delta H_{Cl^{-}Cl^{+}} = -333 + 268 + 271 = 206$ kcal. $(\Delta H^{\ddagger})_{II} = \Delta H_{C^{+}Cl^{-}} - \Delta H_{C^{-}=C^{+}} - \Delta H_{Cl^{-}Cl^{+}} = -240 + 268 + 271 = 299$ $(\Delta H^{\ddagger})_{III} = \Delta H_{H^{+}Cl^{-}} - \Delta H_{C^{-}H^{+}} - \Delta H_{Cl^{-}Cl^{+}} = -329 + 367 + 271 = 309$ $(\Delta H^{\ddagger})_{IV} = \Delta H_{C^{-}Cl^{+}} - \Delta H_{C^{-}H^{+}} - \Delta H_{Cl^{-}Cl^{+}} = -333 + 367 + 271 = 305$

Since $(\Delta H^{\ddagger})_{I}$ has the smallest value, it is apparent that: (a) I represents the most probable mechanism; (b) the reaction will lead to addition in preference to substitution (at least if substitution involves an ionic mechanism, which it probably does not); and (c) ethylene is the nucleophilic reagent in this reaction, which may accordingly be placed in class A of the Ingold-Rothstein classification, *i.e.*, electron-releasing substituents in the ethylene molecule should facilitate the reaction. Similar calculations for the addition of bromine or iodine lead to the same conclusion, which is in complete accord with the known facts.

The next check on our rough method of calculation will be to see if it is capable of predicting the well established order of velocities of halogen addition to olefins, viz, $Cl_2 > Br_2 > I_2$. For these reactions we have, from consideration of Eq. I:

For Cl₂: $\Delta H_{com}^{\ddagger} = \Delta H_{C^-Cl^+} - \Delta H_{Cl^-Cl^+} = -333 + 271 = -62$ kcal.

For Br₂:
$$\Delta H_{com}^{\sharp} = \Delta H_{C^-Br^+} - \Delta H_{Br^-Br^+} = -294 + 236 = -58$$
 kcal.

For I₂: $\Delta H_{com}^{\ddagger} = \Delta H_{C^{-}I^{+}} - \Delta H_{I^{-}I^{+}} = -258 + 207 = -51$ kcal.

These figures give the correct order of velocities. It is unfortunate, however, that the value of the electron affinity of bromine is in grave doubt (9).

B. The addition of hydrogen halides to olefins. First it must be determined

whether the rate-controlling step is an electrophilic attack by hydrogen ion, or a nucleophilic attack by halide ion, on the carbon atom of the olefin.

I.

$$R_{2}C = CR_{2} + HX \rightarrow R_{2}C = CR_{2}$$

$$H \rightarrow X$$
II.

$$R_{2}C = CR_{2} + HX \rightarrow R_{2}C = CR_{2}$$

$$X \rightarrow H$$

$$(\Delta H^{\ddagger})_{I} = \Delta H_{C^{-}H^{+}} - \Delta H_{H^{+}X^{-}} - \Delta H_{C^{-}=C^{+}}$$

$$(\Delta H^{\ddagger})_{II} = \Delta H_{C^{+}X^{-}} - \Delta H_{H^{+}X^{-}} - \Delta H_{C^{-}=C^{+}}$$

Therefore, for any given halogen hydride:

$$(\Delta H_{com})_{I} = \Delta H_{C^{-}H^{+}} = -367.5 \text{ kcal.}$$

 $(\Delta H_{com})_{II} = \Delta H_{C^{+}X^{-}} = -239.7 \text{ for HCl}$
 -231.0 for HBn
 -231.4 for HI

It is concluded, therefore, that reaction I represents the rate-controlling step. The next problem is to make a comparison of the relative speeds of addition of the different hydrogen halides. It is evident from the above that $\Delta H_{com}^{\ddagger} = -\Delta H_{H^+X^-}$ for this purpose.

For HCl: $\Delta H_{com}^{\ddagger} = -\Delta H_{H^+Cl^-} = 329.2$ kcal.

For HBr: $\Delta H_{com}^{\ddagger} = -\Delta H_{H^+Br^-} = 317.6$

For HI: $\Delta H_{com}^{\ddagger} = -\Delta H_{H^+I^-} = 310.6$

The predicted order of velocity (neglecting entropy factors) thus turns out to be: HI > HBr > HCl, which is in complete accord with the well known facts.

C. The hydrolysis of the chlorides of nitrogen and phosphorus. The hydrolysis of NCl₃ yields HOCl while that of PCl₃ yields HCl. This perplexing difference in behavior between two sister elements has been a standing challenge to theorists, and it is interesting to discover to what extent our method of calculation is able to meet the challenge.

We may simplify the problem by making the calculations on the basis of pure water as the reactant. Then, since the concentrations of H_3O^+ and OH^- ions are very low, we may assume water as the most probable attacking reagent. Now regardless of whether the attack is made by hydrogen or oxygen atoms of water, the H—OH bond must become ruptured, and hence this energy factor will cancel out. We may then consider H^+ and OH^- as the attacking reagents for purposes of comparison.

There are four possible modes of attack, since there are two possible attacking ions and two possible points of attack. These four possibilities may be formulated as follows, using X to represent either P or N.

I. $\operatorname{XCl}_3 + \operatorname{H}^+ \rightleftharpoons \operatorname{H} \cdots \operatorname{XCl}_2 \cdots \operatorname{Cl} \to \operatorname{HXCl}_2 + \operatorname{Cl}^+$

II. $\operatorname{XCl}_3 + \operatorname{H}^+ \rightleftharpoons \operatorname{Cl}_2 \operatorname{X} \cdots \operatorname{Cl} \cdots \operatorname{H} \to \operatorname{Cl}_2 \operatorname{X}^+ + \operatorname{HCl}_2 \operatorname{X}^+$

III.
$$\operatorname{XCl}_3 + \operatorname{OH}^- \rightleftharpoons \operatorname{Cl}_2 \operatorname{X} \cdots \operatorname{Cl} \to \operatorname{Cl}_2 \operatorname{XOH} + \operatorname{Cl}^-$$

IV.
$$XCl_3 + OH^- \rightleftharpoons Cl_2 X \cdots Cl \cdots OH \rightarrow Cl_2 X^- + HOCl$$

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The calculations of the corresponding values of $\Delta H_{com}^{\ddagger}$ may now easily be made. If X is taken to be phosphorus, then:

$$\begin{split} (\Delta H^{\ddagger}_{com})_{I} &= \Delta H_{H^{+}P^{-}} - \Delta H_{P^{-}Cl^{+}} = -13.5 \text{ kcal.} \\ (\Delta H^{\ddagger}_{com})_{II} &= \Delta H_{H^{+}Cl^{-}} - \Delta H_{P^{+}Cl^{-}} = -100.5 \text{ kcal.} \\ (\Delta H^{\ddagger}_{com})_{III} \text{ Data unavailable} \end{split}$$

 $(\Delta H_{com}^{\ddagger})_{IV} = \Delta H_{O^-Cl^+} - \Delta H_{P^-Cl^+} = 97.7 \text{ kcal.}$

The relative probabilities of the three mechanisms for which data are available turns out to be II > I > IV. If we may assume that all three chlorine atoms are removed by the same mechanism, we are thus led to the result that PCl_3 should yield HCl and H_3PO_3 on hydrolysis.

If the corresponding calculations are made for NCl₃, the values of ΔH_{com}^{I} for cases I, II, and IV are found respectively to be -58.6, -43.4, and +76.8 kcal. Thus mechanism I is most probable in this case, and we would predict that NCl₃ would yield HOCl and NH₃ on hydrolysis.

Our assumption that all three chlorine atoms are removed by the same mechanism is justified by qualitative considerations. Thus, if the first chlorine atom is replaced by hydrogen, the lone pair of the resulting $HXCl_2$ is all the more available for coordination with another proton (mechanism I), and XH_3 will ultimately result. But if mechanism II results in the replacement of Cl⁻ by OH⁻, the resultant HOXCl₂ will be only slightly more basic than XCl₃, since the $-I_s$ effect of hydroxyl is only slightly less than that of chlorine. In view of the large difference in $\Delta H_{com}^{\ddagger}$ (-13.5 compared to -100.5 kcal.) which is found between mechanisms I and II in this case, it is hardly likely that this slight alteration would cause an inversion of mechanism in the second or third step.

D. The hydrolysis of alkyl halides. A very large amount of experimental work has been done in an effort to establish the mechanism of the hydrolysis of alkyl halides. Due chiefly to the work of Hughes, Ingold, and their collaborators (16), it now appears that methyl and ethyl halides show a strong tendency to hydrolyze by a bimolecular mechanism involving a nucleophilic attack by hydroxyl ion on carbon, while tertiary butyl halides tend to hydrolyze by a unimolecular mechanism involving the solvolytic production of carbonium ions. Isopropyl halides occupy an intermediate position, usually involving a mechanism compounded of sizeable proportions of both the unimolecular and bimolecular reactions. The mechanism obtaining in any case is, however, decidedly dependent on conditions, and it has been observed that increasing alkalinity of solution favors the bimolecular reaction (17), while increasing acidity seems to favor the unimolecular mechanism. Thus, although the normal mode of reaction of primary alkyl halides is bimolecular, it was found (18) that the hydrolysis

of n-butyl bromide in formic acid containing a small proportion of water is mainly unimolecular.

It is hardly to be expected that our crude method could be a completely reliable guide in a border line case like the hydrolysis of alkyl halides, but its general implications are reliable as shown by the following calculations.

The three following mechanisms are conceivable if the hydrolysis takes place in basic solutions, in which, of course, the hydronium ion concentration is very low.

I. A nucleophilic attack by hydroxyl ion on carbon.

$$CH_{3}X + OH^{-} \cdot Aq \rightleftharpoons HO \cdots CH_{3} \cdots X + Aq \rightarrow CH_{3}OH + X^{-} + Aq$$

Aq stands for water of hydration, which is presumably lost on entering the transition state.

II. An electrophilic attack by hydrogen on halogen.

$$CH_3X + HOH \rightleftharpoons H_3C \cdots X \cdots H \cdots OH \rightarrow CH_3^+ + HX + OH^-$$

III. An electrophilic attack by hydrogen on carbon.

$$CH_3X + HOH \rightleftharpoons HO \cdots H \cdots CH_3 \cdots X \rightarrow OH^- + CH_4 + X^+$$

The corresponding values of ΔH^{\ddagger} may now be calculated for the case where X = Cl.

$$\begin{split} (\Delta \mathrm{H}^{\ddagger})_{\mathrm{I}} &= \Delta \mathrm{H}_{\mathrm{C}^{+}\mathrm{O}^{-}} - \Delta \mathrm{H}_{\mathrm{C}^{+}\mathrm{C}\mathrm{I}^{-}} - \Delta \mathrm{H}_{\mathrm{Aq}\cdot\mathrm{OH}^{-}} = -\Delta \mathrm{H}_{\mathrm{Aq}\cdot\mathrm{OH}^{-}} - 1 \text{ kcal.} \\ (\Delta \mathrm{H}^{\ddagger})_{\mathrm{II}} &= \Delta \mathrm{H}_{\mathrm{H}^{+}\mathrm{C}\mathrm{I}^{-}} - \Delta \mathrm{H}_{\mathrm{C}^{+}\mathrm{C}\mathrm{I}^{-}} - \Delta \mathrm{H}_{\mathrm{H}^{+}\mathrm{O}^{-}} = 145 \text{ kcal.} \\ (\Delta \mathrm{H}^{\ddagger})_{\mathrm{III}} &= \Delta \mathrm{H}_{\mathrm{C}^{-}\mathrm{H}^{+}} - \Delta \mathrm{H}_{\mathrm{H}^{+}\mathrm{O}^{-}} - \Delta \mathrm{H}_{\mathrm{C}^{-}\mathrm{C}\mathrm{I}^{+}} = 300 \text{ kcal.} \end{split}$$

Obviously, there is no chance of a hydrocarbon being formed (III). The value for the heat of hydration of the hydroxyl ion is not known, but it could hardly be much more than 100 kcal., since the corresponding value for chloride ion is 92.1 kcal. (19). Thus, mechanism I is clearly favored, which is in accord with experiment.

Having thus established the mechanism, we may now calculate ΔH_{com}^{\dagger} for RCl and RBr. Taking $\Delta H_{com}^{\dagger} = \Delta H_{C^+X^-}$, we get the values 239 and 231 kcal. for chlorides and bromides, respectively. The experimental activation energies for the hydrolysis of ethyl chloride and bromide fall in the same order, *viz.*, 23 and 21 kcal., respectively (20).

If the hydrolysis is carried out in an acid solution, the above three mechanisms become respectively:

I.
$$CH_3X + HOH \rightleftharpoons H_3C - OH \rightarrow CH_3OH + H^+ + X^-$$

 $X H$

II.
$$CH_3X + Aq \cdot H^+ \rightleftharpoons H_3C - X - H^+ + Aq \rightarrow CH_3^+ + HX + Aq$$

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III. $CH_{3}X + Aq \cdot H^{+} H_{3}C - X + Aq \rightarrow CH_{4} + X^{+} + Aq$ $\stackrel{|}{H^{+}}$ $(\Delta H^{\ddagger})_{I} = \Delta H_{C^{+}C^{-}} - \Delta H_{C^{+}C^{-}} - \Delta H_{H^{+}O^{-}} = 333 \text{ kcal.}$ $(\Delta H^{\ddagger})_{II} = \Delta H_{H^{+}C^{-}} - \Delta H_{C^{+}C^{-}} - \Delta H_{Aq \cdot H^{+}} = 164 \text{ kcal.} (19)$

$$(\Delta \mathbf{H}^{\ddagger})_{\mathrm{III}} = \Delta \mathbf{H}_{\mathbf{H}^{+}\mathbf{C}^{-}} - \Delta \mathbf{H}_{\mathbf{C}^{-}\mathbf{C}\mathbf{I}^{\ddagger}} - \Delta \mathbf{H}_{\mathrm{Aq}^{+}\mathbf{H}^{\ddagger}} = 219 \text{ kcal. (19)}$$

These figures show mechanism II to be the favored mechanism. This is at least in accord with the trend experimentally observed in acid solutions.

E. Cyanhydrin formation with aldehydes. Calculations will now be made to determine whether this reaction is favored by basic or acidic solutions, and whether the aldehyde exhibits electrophilic or nucleophilic properties.

In an acid solution, either HCN or H_3O^+ could be the attacking reagent. Of these two, H_3O^+ is favored, because it would call the electromeric effect of the carbonyl group into play more strongly than would the uncharged HCN; moreover, H_3O^+ is the stronger acid, and hence would lose its proton more easily. In a basic solution the attack would be more apt to be made by CN^- or $OH^$ ions, because of their high concentrations, and to other factors which the calculations below will make clear. Accordingly, there are three possible rate controlling steps to be considered.

I.
$$CH_3CHO + H_3O^+ \rightleftharpoons CH_3C \rightleftharpoons O-H^+-OH_2$$

 \downarrow
H

II.
$$CH_{3}CHO + CN^{-}(Aq) \rightleftharpoons CH_{3}C \rightleftharpoons O + Aq$$

III.
$$CH_{3}CHO + OH^{-}(Aq) \rightleftharpoons CH_{3}C \Longrightarrow O + Aq$$

In calculating the corresponding values of $\Delta H^{\ddagger}_{com}$, $\Delta H_{C^{+}=0^{-}}$ may be omitted since it is common to all three. Thus we may write:

$$\begin{aligned} (\Delta H_{com}^{\ddagger})_{I} &= \Delta H_{O^{-}H^{+}} - \Delta H_{Aq \cdot H^{+}} = -334 + 253 = -81 \text{ kcal.} \\ (\Delta H_{com}^{\ddagger})_{II} &= \Delta H_{C^{+}CN^{-}} - \Delta H_{Aq \cdot CN^{-}} = -285 - 75 = -360 \text{ kcal.}^{2} \\ (\Delta H_{com}^{\ddagger})_{III} &= \Delta H_{C^{+}O^{-}} - \Delta H_{Aq \cdot OH^{-}} = -241 - \Delta H_{Aq \cdot OH^{-}} \end{aligned}$$

Since the value of $\Delta H_{Aq\cdot OH^-}$ is not known, the calculations do not make clear whether the hydroxyl or cyanide ion will lead the attack, but the use of any reasonable value for $\Delta H_{Aq\cdot OH^-}$ at least clearly establishes the electrophilic char-

² Bichowsky and Rossini (21) give the value of Qf for $CN^{-}(Aq)$ as -34.9 kcal.mole⁻¹. The conversion of this value to the basis used by Rice (19) for the heats of hydration of ions gives: $\Delta H_{Aq \cdot CN^{-}} = 74.7$ kcal.mole.⁻¹.

acter of the aldehyde in basic solutions, (*i.e.*, either II or III is more probable than I), and indicates that more facile addition is to be expected in basic than in acidic solutions, all of which is in accord with experiment (22). If our previous guess that $-\Delta H_{Aq \cdot OH^-}$ is of the order of magnitude of -100 kcal., then $\Delta H_{com}^{t} = ca. - 141$ kcal. for III, and the CN⁻ ion is indicated as the attacking ion.

F. Reactions of ethers with halogen hydrides, etc. Three possible mechanisms may be considered.

I. An electrophilic attack by H on oxygen.

$$\begin{array}{c} \mathrm{CH}_{3}\mathrm{OCH}_{3} + \mathrm{HX} \rightleftharpoons \mathrm{CH}_{3}\mathrm{O} - \mathrm{CH}_{3} \to \mathrm{CH}_{3}\mathrm{OH} + \mathrm{X}^{-} + \mathrm{CH}_{3}^{+} \\ \downarrow \\ \mathrm{H} - \mathrm{X} \end{array}$$

II. An electrophilic attack by H on C.

 $CH_3OCH_3 + HX \rightleftharpoons X \cdots H \cdots CH_3 \cdots OCH_3 \rightarrow CH_4 + X^- + OCH_3^+$

III. A nucleophilic attack by X on C.

$$CH_{3}OCH_{3} + HX \rightleftharpoons H_{3}C - OCH_{3} \rightarrow CH_{3}X + H^{+} + OCH_{3} - I_{3} + I_{3}C + I$$

The most probable mechanism may now be predicted by calculating the corresponding values of ΔH^{\ddagger} for the case in which HX is HI.

$$\begin{aligned} (\Delta H^{\ddagger})_{I} &= \Delta H_{H^{+}O^{-}} - \Delta H_{C^{+}O^{-}} - \Delta H_{H^{+}I^{-}} &= 218 \text{ kcal.} \\ (\Delta H^{\ddagger})_{II} &= \Delta H_{H^{+}C^{-}} - \Delta H_{C^{-}O^{+}} - \Delta H_{H^{+}I^{-}} &= 295 \\ (\Delta H^{\ddagger})_{III} &= \Delta H_{C^{+}I^{-}} - \Delta H_{C^{+}O^{-}} - \Delta H_{H^{+}I^{-}} &= 321 \end{aligned}$$

Similar calculations made for HBr and HCl show that in all cases mechanism I is the most probable. Incidentally, the calculations make it amply clear why the reaction cannot lead to the formation of a hydrocarbon and an alkyl hypochlorite (II).

The next step is to decide which of the halogen hydrides should be most reactive. For this purpose we may calculate $\Delta H_{com}^{\dagger} = -\Delta H_{H^+X^-}$. We thus get the following values for ΔH_{com}^{\dagger} : 311 for HI, 318 for HBr, 329 for HCl, 334 for H₂O, and 334 for HOR. It is thus predicted that HI is the most reactive, which is in accord with experience, although concentrated aqueous solutions are used experimentally, while our calculations were made for the gas-phase reaction. It is well known that ethers are practically unreactive with water and alcohols at room temperature. Furthermore, the hydrolysis is said to be accelerated by hydrogen ions and not by hydroxyl ions, which is in accord with the nucleophilic properties established for the ethers by our rough calculations.

G. Reactions of alcohols with halogen hydrides. The formulation of this reaction is exactly like the preceding, and the calculated values are the same. This means that the predicted order of reactivity is HI > HBr > HCl, which is in accord with common knowledge of the reactions involving the anhydrous gases.

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In accord with the nucleophilic properties of the alcohols in these reactions, it would be predicted that an increase in the basicity of the oxygen atom would aid the reaction, and hence that the order of reactivity should be tertiary > secondary > primary, which is in accord with common knowledge.

CONCLUDING REMARKS

Many chemists believe that the natural complexity of organic compounds must of necessity introduce such insuperable mathematical difficulties that organic chemists need expect no practical aid from physical chemistry in predicting the paths which are pursued by organic reactions. Perhaps they are right, but the above discussion gives one the right to hope, at least, that simple considerations of the energy involved in making and breaking valence bonds will prove to be a step forward. Unfortunately, the simplifications employed above were not rigorously justified, but they do seem to follow logically from Lapworth's theory of electrophilic and nucleophilic reaction tendencies, and hence at least may be said to constitute a semiguantitative extension of that theory. It is also unfortunate that it was necessary to use the ΔH rather than the ΔF of bond formation as a measure of the tendency to form covalencies, since the former can only lead to estimations of activation energy, while the latter would lead to estimations of reaction velocity. Moreover, the vagaries of solvation make it difficult to apply the theory with confidence to reactions in solution. Nevertheless, the success enjoyed in all of the examples thus far investigated justifies the tentative conclusion that this simple method is a safe guide if applied to the comparison of sufficiently similar reactions of the "ionic" type which are not complicated by mesomeric effects or polar substituents. These limitations make the method chiefly of use in predicting the mechanism and hence the reaction path followed by unsubstituted reactants. With these facts established one may usually proceed safely by applying the customary methods of the English school to predict the effects of substituents.

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