[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

THE RELATION OF STRUCTURE, AFFINITY AND REACTIVITY IN ACETAL FORMATION. I[1]

BY HOMER ADKINS AND ELMER WADE ADAMS

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A knowledge of the relationship between the structure of organic compounds and their reactivity would seem to lie at the basis of any rational explanation of important phenomena. Such problems as the relationship of the constitution of substances to their physiological action, or of the processes involved in the elaboration of products in plant or animal tissue, possibly must wait for their solution upon a thorough knowledge of the relationship of structure to those factors which determine the course, extent and rate of reactions.

"Reactivity" is a word in regard to whose meaning there is considerable confusion. There are two distinct phases to the problems of reactions. The one phase has to do with the extent to which a reaction goes, with the affinity manifested by the radicals that are joined in the reaction, and in a certain sense with the strength of the linkage that is set up. This phase of reactivity is a function of the true equilibrium constant and is quantitatively expressed in terms of calories calculated from the thermodynamical equation, $\Delta F = -RT \ln K$, where ΔF is the decrease in free energy, R the gas constant (1.98), T the absolute temperature and $\ln K$ the natural logarithm of the equilibrium constant.[2]

The other phase of reactivity has to do with the speed of the reaction. Michael wished to restrict the term reactivity to the first phase, but most chemists when they have realized that there are two unrelated phases to the problem, have used the term in connection with the speed of the reaction. It seems wiser to accept the commoner usage, and in this series of papers the term affinity will be used when the first phase of the problem is discussed, and the term reactivity or ease of reaction when the latter phase, having to do with the speed of a reaction, is considered.

Michael,[3] Hill and Hibbert,[4] Hibbert and Timm[5] and Conant and Kirner[6] have recently published papers that review the more important of the previous papers on the general problem of reactivity.

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[1] This paper is based upon Part II of a dissertation submitted by Mr. Adams in partial fulfilment of the requirements for the degree of Doctor of Philosophy. H. A.

[2] Lewis and Randall, "Thermodynamics," McGraw-Hill Book Co., New York, **1923**, p. 294.

[3] Michael, THIS JOURNAL, **41**, 393 (1919).

[4] Hill and Hibbert, *ibid.*, **45**, 3108 (1923).

[5] Hibbert and Timm, *ibid.*, **46**, 1283 (1924).

[6] Conant and Kirner, *ibid.*, **46**, 232 (1924). Norris and Steward, Washington Meeting, American Chemical Society, April, 1924.

One way of studying the relationship between the structure of organic compounds and the affinity manifested at a given linkage, is to note the relationship between the structure and the ionization or affinity constant of organic acids. Numerous pieces of work along this line culminated in the notable papers of C. G. Derick,[7] who made a study of the polarity of elements and radicals measured in terms of a logarithmic function of the ionization constant. He defines a positive element or radical as one increasing hydroxyl ionization when substituted for a hydrogen of water and a negative element or radical as one which, when substituted for the hydrogen of water, increases the hydrogen ionization. He points out that the free energy change rather than the total energy change is a true measure of chemical affinity; also, that since the free energy of ionization is a logarithmic function of the ionization constant, the relative positivity and negativity of groups may be stated in terms of a logarithmic function of the ionization constant. He noted many interesting facts and applications of the relationship between the structure and the ionization of acids.

Conclusions as to the relationship of structure and affinity which are based upon observations of the relationship between the structure and the ionization of acids would appear to be of questionable value for interpreting organic processes. The factors which promote the separation of a positive electron (hydrogen ion) from a molecule may have little relationship to those factors which weaken or strengthen the linkages of carbon–carbon and of carbon–oxygen. Ionization of any type appears to play but an unimportant role in organic reactions. Then, too, the ionization of an acid is now considered by leading physicists and chemists to be due in part to the solvation of the ions;[8,9] hence, factors that affect solvation but not affinity relationships would affect the degree of ionization. Positivity and negativity must now be regarded as the shifting of electrons away from or towards a given point in the molecule.[10]

An experimental method of measuring the effect of structure upon the manifested affinity of carbon–carbon and especially of carbon–oxygen linkages has been urgently needed. It seems possible to do this by noting the effect of structure in changing the equilibrium point in the reversible reaction, $2\,ROH + R'CHO \rightleftharpoons R'CH(OR)_2 + H_2O$. Fortunately we can also follow the rate of the reaction in either direction and hence correlate with the affinity relations the equally important phase of reactivity that has to do with the speed of the reaction. It is possible in this reaction to compare the relative positivity and negativity of groups as affecting a typical organic reaction, one which does not involve ionization.

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[7] Derick, THIS JOURNAL, **33**, 1152–1181 (1911).

[8] Sir J. J. Thomson, "Electron in Chemistry," Franklin Institute, Philadelphia, **1923**, p. 76.

[9] Latimer and Rodebush, THIS JOURNAL, **42**, 1425 (1920).

[10] Lewis, *ibid.*, **38**, 782 (1916).

A comprehensive study of these relationships is under way in this Laboratory. This first paper of the series is concerned with cases where R is methyl, ethyl, *n*-propyl, *iso*propyl, *n*-butyl, *iso*butyl, *sec.*-butyl, *tert.*-butyl, *iso*pentyl, *tert.*-pentyl, benzyl or phenylethyl, and where R′ is methyl, ethyl, propyl, *n*-pentyl, *iso*propyl, phenyl-vinyl, phenyl or furfuryl. The reaction mixtures contained 1 mole of the alcohol, 0.091 mole of the aldehyde and 0.000465 g. of hydrogen chloride. The excess of alcohol was used to prevent the separation of water. Preliminary

TABLE I

SUMMARY OF DATA[a]

Acetal	% Conv.	Vol. cc.	K_E	ΔF	$k_v \times 10^3$
Methyl acetal	93.80	45.60	0.0859	1452	1.02
Ethyl acetal	90.72	63.00	.0730	1549	2.37
n-Propyl acetal	90.22	79.70	.0950	1464	2.11
*iso*Propyl acetal	58.55	80.50	.0075	2895	5.52
n-Butyl acetal	92.86	97.06	.1519	1115	2.68
*iso*Butyl acetal	92.80	97.68	.1526	1112	1.93
sec.-Butyl acetal	64.00	97.57	.0115	2641	4.64
tert.-Butyl acetal	31.20	100.15	.0015	3867	11.34
*iso*Pentyl acetal	21.17	114.03	.0064	2989	
tert.-Pentyl acetal	21.25	113.75	.0006	4353	16.99
Phenylethyl acetal	87.45	124.25	.0972	1389	2.38
Benzyl acetal	69.30	108.85	.0179	2380	2.16
Methyl butylal	96.44	48.62	.1707	1046	0.83
Ethyl butylal	91.68	68.09	.0918	1413	1.91
n-Propyl butylal	93.78	82.75	.1542	1106	1.62
*iso*Propyl butylal	59.25	83.53	.0082	2844	2.66
n-Butyl butylal	97.65	100.09	.5575	245	1.50
*iso*Butyl butylal	96.32	100.07	.3455	629	0.84
Ethyl propylal	89.04	64.60	.0608	1657	2.09
*iso*Propyl propylal	49.47	82.05	.0044	3217	3.72
Ethyl *iso*butylal	83.54	66.33	.0195	2340	1.56
*iso*Propyl*iso*butylal	37.41	83.77	.0019	3694	5.01
Methyl furfurylal	60.83	48.14	.0040	3271	(14)
*iso*Propyl furfurylal	24.45	83.04	.0007	4336	(300)
Ethyl furfurylal	39.75	66.14	.0018	3728	(100)
Ethyl heptal	30.58	70.70	.0010	4106	(400)
*iso*Propyl heptal	19.58	88.30	.0004	4612	(600)
Ethyl cinnamal	36.35	69.46	.0016	3810	(300)
*iso*Propyl cinnamal	19.00	86.90	.0005	4636	(1500)
Ethyl benzal	36.33	67.32	.0017	3787	(100)
*iso*Propyl benzal	15.65	84.76	.0002	4944	(500)
Ethyl-*m*-nitrobenzal	41.80	69.00	.0022	3618	(200)

[a] The experimental errors are of such a magnitude that the calculation of ΔF is possibly not accurate within 50 calories. The error may be larger than this when the percentage conversion is very high, as in the case of butyl and *iso*butyl butylal. The velocity constant k_v seems to be accurate within 8%. The method used for its calculation is questioned by Waddell, Ostwald and others.

work had indicated that the amount of the catalyst used would give a rate of reaction that could be readily followed. Later experience proved that with certain aldehydes the rate was too rapid for accurate measurement.

The data obtained are summarized in Table I. The percentage conversion of the aldehyde to the acetal is given in Col. 1, the volume of the reaction mixture in Col. 2, the equilibrium constant calculated from these data in Col. 3, the decrease in free energy in Col. 4 and the velocity constant times 10^3 in Col. 5. It is to be noted that the value for the decrease in free energy expressed in calories is always a positive number. The greater the value of ΔF the less is the affinity between the radicals that are joined together to form the acetal. For example, the value of ΔF for the formation of *n*-propyl butylal is +1106 calories. This means that in order to convert two moles of *n*-propanol and one mole of butyric aldehyde into one mole of *n*-propyl butylal and one mole of water, 1106 calories of energy must be put into the system.

The value of ΔF for *iso*propyl butylal is +2844 calories. This means that 1738 more energy units must be used to convert completely two moles of *iso*propanol into the butylal than was required with *n*-propanol. Of the two propyl groups, *n*-propyl must have had an affinity greater by 1738 calories for the aldehyde radical. The figure 1738 is thus a measure of the difference in the affinity of the two propyl groups for butylal formation.[11]

The decrease in free energy for the reaction of eleven alcohols with acetaldehyde is plotted in Fig. 1. Since a decrease in ΔF indicates an increase in affinity, the values have been so plotted that affinity increases in going up on the graph. There is seen to be a great variation in the affinity values when different alcohols react with acetaldehyde. If the straight-chain alcohols are considered, there is a slight decrease in affinity in going from methyl to ethyl, and a slight rise in going to propyl. Butyl shows an affinity value higher by 434 calories than does ethyl. In fact, *n*-butanol and *iso*butanol show the highest affinity values of any of the alcohols used. *iso*Propanol has an affinity value lower than *n*-propanol by 1431 calories. A similar lowering of affinity values is found when *sec.*-butanol is compared with *n*-butanol. The effect in lowering affinity values, when the hydrogens of the carbinol carbon are replaced by carbon, is further shown in the affinity value of the *tert.*-butanol, the value being 1226 calories lower than for the *sec.*- and

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[11] Dr. Farrington Daniels has pointed out that if the "effective" concentrations of reactants are not the same as those analytically determined, the conclusions as to affinity based on the observation of the equilibrium point are not entirely valid. If the activity of the water varies greatly in the different alcohols, the value of ΔF would be affected. However, variation in the activity of water would not affect the comparison of different aldehydes with the same alcohol.

2752 lower than for the *n*-butanol. The effect of replacing a hydrogen of methyl with a phenyl group is to lower the affinity by 926 calories. If

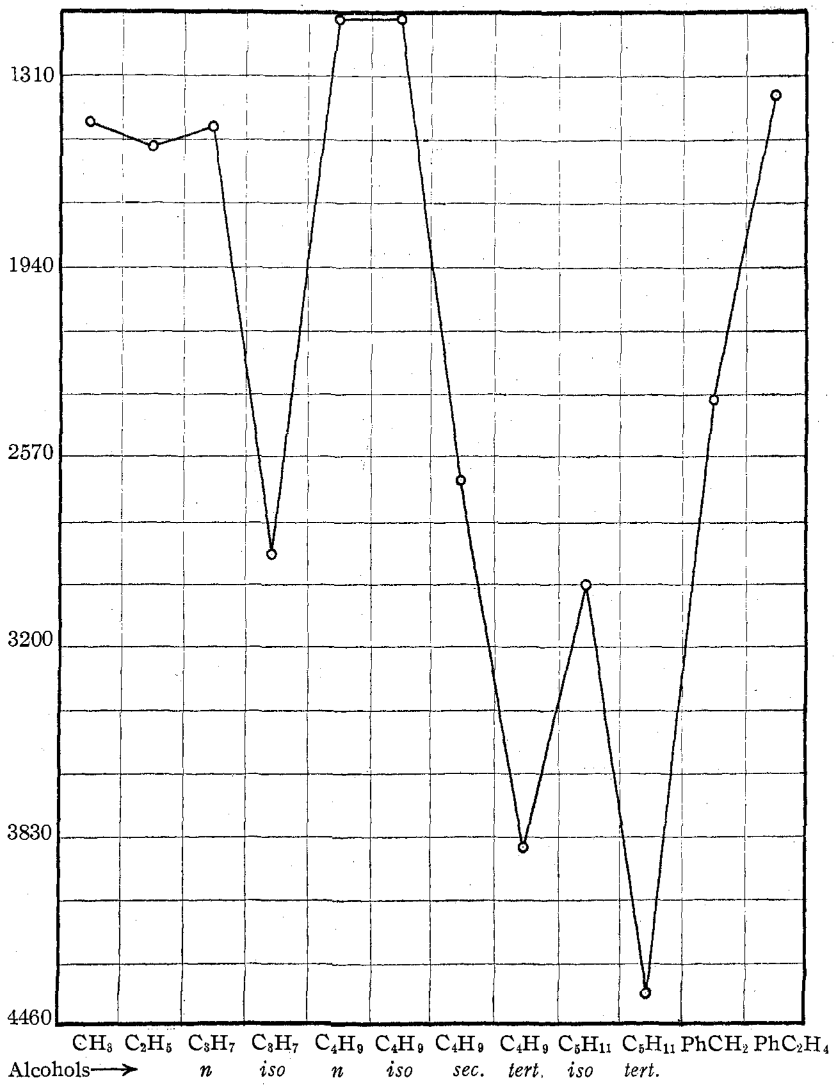

Fig. 1.—Variations in affinity with changes in the alcohol reacting with acetaldehyde.

The values for the decrease in free energy (ordinates) for various alcohols (abscissae) in their reaction with acetaldehyde are plotted. Data from Table I.

the phenyl group is moved one carbon away from the carbinol group as in β-phenylethyl alcohol, it no longer has the "negative" effect of lowering the affinity, but actually increases it slightly. (This is not in accord with Derick's ideas gained from a study of the ionization of organic acids.)

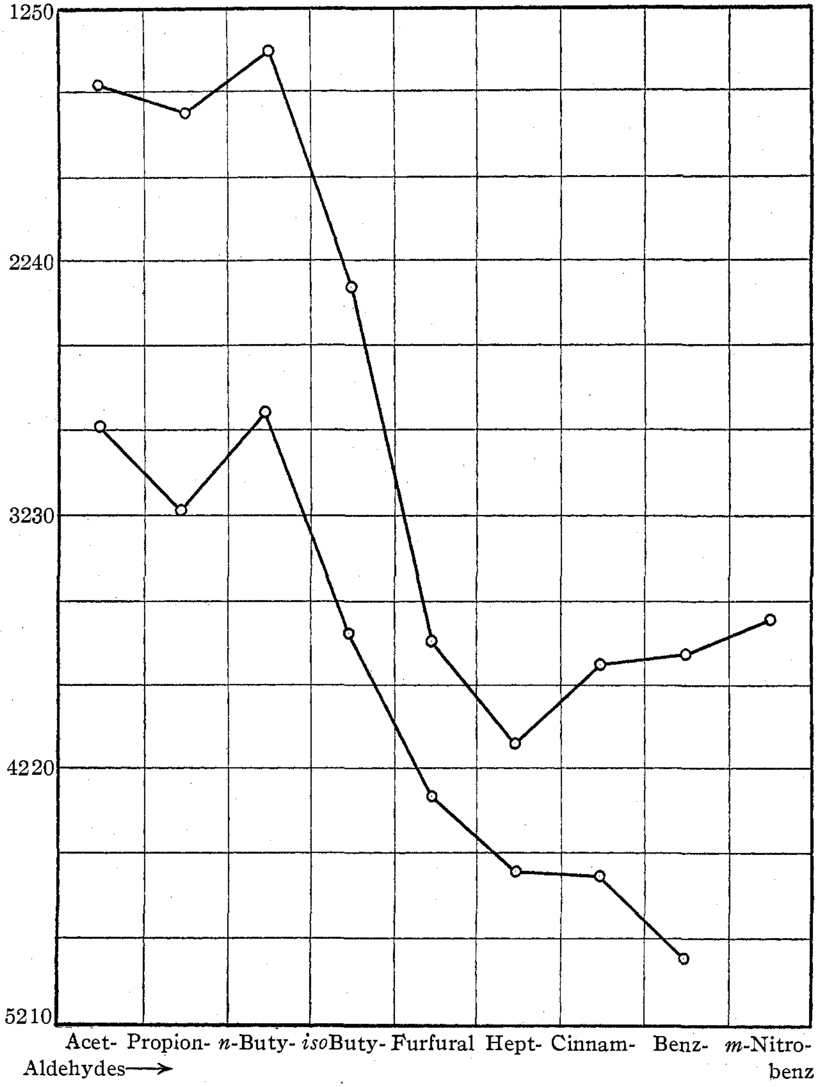

Fig. 2.—Variations in affinity with ethanol and *iso*propanol in their reaction with various aldehydes.

The values for the decrease in free energy (ordinates) for ethanol (upper curve) and *iso*propanol (lower curve) in their reaction with various aldehydes (abscissas) are plotted. Data from Table I.

The decrease in free energy for the reactions of ethanol and *iso*propano with nine aldehydes is plotted in Fig. 2. The four carbon straight chain compound, butyraldehyde, again shows the highest affinity value of all the aldehydes studied. In the case of the alcohols, branching of the chain at the 2 carbon of the alcohol (*iso*butanol and *n*-butanol) had little effect; in the case of the aldehydes (*iso*butyric and *n*-butyric) branching at the 2 carbon decreases affinity values by 927 and 850 calories. The similarity in the affinity values for cinnamic aldehyde, benzaldehyde and furfural is possibly due to the fact that in each case there is a double bond between the 2 and 3 carbon atoms of the aldehyde. A most unexpected result was the low affinity value manifested by heptaldehyde. It behaves like the aromatic or unsaturated aldehydes. It is worthy of note that while there is about 1400 calories difference between the affinity values of ethyl and *iso*propyl for the first four aldehydes plotted, the difference is very much less for the other aldehydes.

The velocity constants for the reactions of nine alcohols with acetaldehyde, and of five alcohols with butyraldehyde are plotted in Fig. 3. It is apparent that butyraldehyde is less reactive than is acetaldehyde. There is an enormous difference in the rate with which different alcohols react. Methanol and *n*-butanol, which have the highest affinity values, that is, react to the greatest extent, are the slowest to react. The secondary alcohols react the most rapidly of those whose rates are plotted. The tertiary alcohols react so rapidly that their velocity constants cannot be conveniently plotted in the same graph with the other alcohols. It may be recalled that in the case of these alcohols there was less driving force than for any others. A phenyl group on either the 1 or 2 carbon atoms of an alcohol has little effect upon the rate of reaction, though it greatly lowers affinity when it is on the 1 carbon atom. It has a large effect in promoting the rate of the reaction when it is attached directly to the aldehyde group. The rates of reaction for furfural, benzaldehyde, *m*-nitrobenzaldehyde, cinnamic aldehyde and heptaldehyde are enormous as compared with acetic, propionic, butyric and *iso*butyric aldehydes. In fact, the rates were too rapid for accurate measurement under our experimental conditions.

Michael[12] was the first to point out that there was no connection between the two phases of the problem of reactions. The results here presented show conclusively that Professor Michael was correct in his conclusions. A reaction may be very rapid, but the affinity between the attached radicals may be low, or the reverse of this may be true. He suggested that the extent of a reaction is determined by the affinity of the attached radicals, while the rate of a reaction depends on "the quantity and quality of the free chemical energy in the carbonyl group; that is, on its magnitude and on its affinity relations to the component parts of the addenda." Not all chemists attach the same meaning

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[12] Michael, THIS JOURNAL, **41**, 393 (1919).

to the words used in the quotation, and Professor Michael's meaning is perhaps not clear. In any case, it seems desirable to have a more concrete conception of what is meant by "affinity" and "free chemical energy."

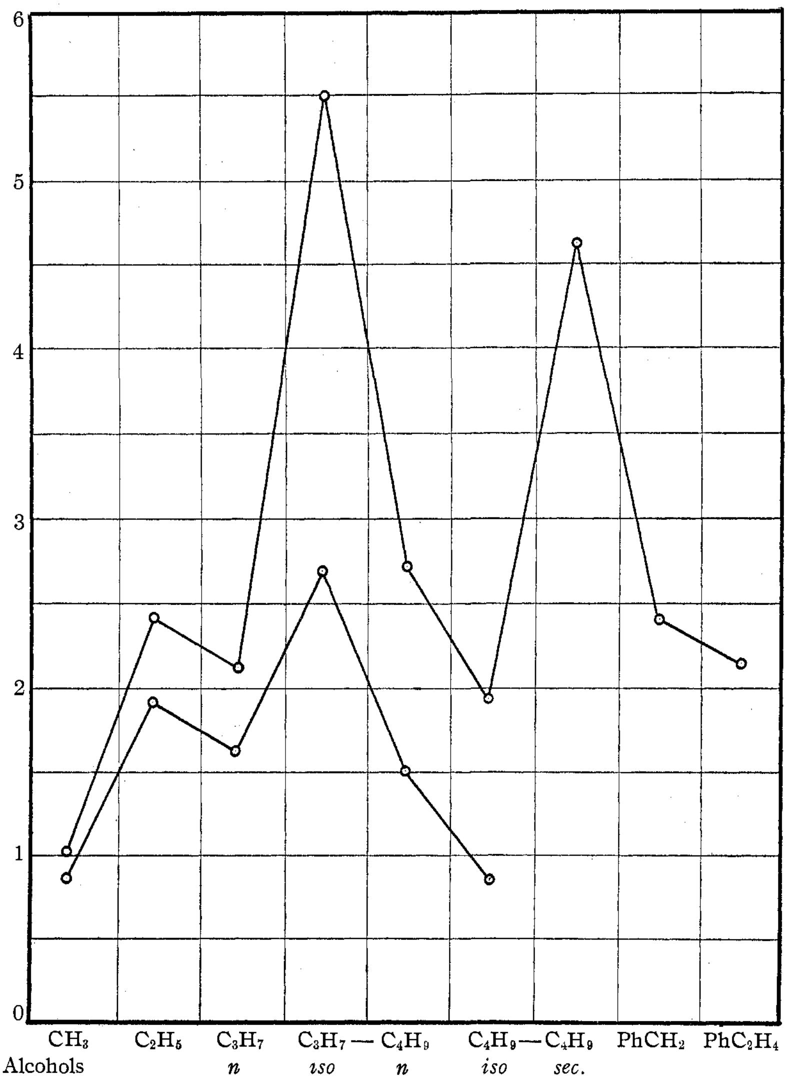

Fig. 3.—Variations in rates of reaction with changes in structure.

The velocity constants multiplied by 1000 (ordinates), for the formation of acetals between acetaldehyde and various alcohols (abscissas) are shown in the upper curve. Similar data for the formation of butylals are shown in the lower curve. Data from Table I.

The term affinity may be defined in terms of energy relationships but in view of the marvelous success of the structural theory of Kekulé and van't Hoff it seems worth while to attempt to define it in structural terms.[13] Since linkage is now considered to be a sharing of electrons, the stability of a linkage is determined by the stability of the electronic system (of the compound) which that linkage necessitates. In a reversible reaction, the equilibrium point indicates the relative stability of the electronic systems on the right and the left hand side of the equation. Consider these two reactions:

$$2(CH_3)_2CHOH + CH_3CHO \rightleftharpoons CH_3CH[OCH(CH_3)_2]_2 + H_2O \quad (1)$$
$$2CH_3CH_2CH_2OH + CH_3CHO \rightleftharpoons CH_3CH(OCH_3CH_2CH_3)_2 + H_2O \quad (2)$$

The first goes 90% to the right, the second 58% under the same conditions. The arrangement of electrons in the *iso*propyl group is such that it is more difficult (by 1431 calories) to get the electrons (*i. e.* their orbits) into the position where a linkage may be formed than it is in the case of the *n*-propyl group. *Conversely, one may hope to find something about the effect of different substituents upon electron arrangement through a study of the equilibrium points of such reactions as that under investigation.*

On the basis of the theory of the mechanism of reactions recently advanced[14] the ease or speed with which a reaction takes place is partially dependent upon the ease or extent to which the electronic system of a compound must be dislocated, through the intervention of the catalyst, before reaction may ensue. Now the ease or extent to which a given electronic system must be dislocated (from the state in which it exists in the pure compound) before it forms a new product bears no relationship whatsoever to the relative stability of the electronic systems on the two sides of the equation. Yet this relative stability determines the *extent* of the reaction.

It should be possible to assign electronic structures to organic molecules as we have hitherto assigned the relative position of atoms. As the structural theory of Kekulé brought order out of chaos in so far as the *classification of compounds* goes, so it appears that the assignment of electronic structure may bring *order and systematization into our knowledge of reactions.*

Calculations and Experimental Methods

The reagents for this work were of the same grade as previously described.[15] The acetaldehyde in this case was sealed in 5cc. samples under anhydrous conditions, as described by Child.[16]

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[13] Compare Lewis, "Valence and the Structure of Atoms and Molecules," Chemical Catalog Co., New York, **1923**, p. 20–21.

[14] Adkins and Nissen, This Journal, **46**, 137 (1924).

[15] Adams and Adkins, *ibid.*, **47**, 1358 (1925).

[16] Child and Adkins, *ibid.*, **45**, 3020 (1923).

The reaction was carried out in Pyrex test-tubes (25 × 3.5 cm.). The tubes were provided with a sampling device as described by Child. The reaction containers were immersed in a thermostat held at 25° ± 0.2°.

The concentrations of the reagents in most experiments were 0.091 mole of the aldehyde and one mole of the alcohol, the latter containing 0.0004650 g. of HCl. In a few instances the amounts of alcohol, aldehyde and catalyst were less, although the same relative proportions were always preserved when reactivities and affinities were to be compared.

The catalyst was in all cases made up by passing hydrogen chloride through concentrated H_2SO_4 into the alcohol. Ten cubic centimeter samples of this were then analyzed for chlorine by the Volhard method. Calculations were made as to the proper dilution necessary to obtain a concentration of 0.0016275 g. of HCl per mole of the alcohol. When two parts of this concentration were employed with five parts of alcohol containing the aldehyde, it is readily seen that the final concentration of catalyst was 0.0004650 g. of HCl per mole of alcohol. There were two reasons for this method of making up the catalyst. In the first place, it was found by preliminary tests that about 0.0004 g. of HCl per mole of alcohol, with the concentrations of aldehyde and alcohol employed, was the maximum that could be used and keep the rate of all the reactions to be studied, sufficiently slow so that they could be conveniently followed. Secondly, it was found advisable to put the aldehyde into the alcohol before the addition of the catalyst, for in some cases a considerable heat of solution was developed. After this aldehyde-alcohol solution was brought down to 25°, the alcoholic solution of the catalyst was added.

A typical procedure for an experiment was as follows: five-sevenths of a mole (32.9 g.) of absolute ethyl alcohol was weighed out into the Pyrex test-tube held in an ice-bath. The 5cc. sample of acetaldehyde was added and the stopper carrying a thermometer and the sampling device fitted on at once. When the temperature was observed to have subsided to 25° the two-sevenths mole of alcohol containing 0.001627 g. of hydrogen chloride per mole was added, the stopper replaced, and the test-tube immediately placed in the thermostat. The stopper was sealed at once with collodion. Five-cc. samples were taken at the desired intervals for titration by the modified Seyewetz-Bardin method. The analytical methods have been described in the previous paper and by Child.[16]

The accuracy of duplication of the runs made was tested upon both dimethyl and diethyl acetal by redehydration of the alcohols and by making up new catalyst. This second set of data checked very closely with the original averages. Assuming that there might be some variation in the concentration of catalyst as employed, runs were made with diethyl acetal using twenty-five per cent. of hydrogen chloride in excess of the normal amount. This gave very little acceleration of the rate. Since our determinations of hydrogen chloride could not have varied by more than 1% or 2% it is obvious that inaccuracies due to this cause must be insignificant.

The retrograde-reactions were run upon diethyl and di-*iso*propyl acetals and upon diethyl butylal. Again, ethyl acetal is given as typical: 0.091 mole of pure acetal (10.74 g.) was weighed into the reaction tube. With this were then placed 0.091 mole of water (1.64 g.) and 24.48 g. of alcohol. This was brought to 25° in the thermostat and then 13.16 g. of alcohol containing 0.0016275 g. of hydrogen chloride per mole was added, making the concentration of hydrogen chloride per mole of alcohol present 0.0004650 g., the same as in the synthetic reaction. Five-cc. samples were taken from time to time for analysis.

The Use of Two Moles of Alcohol and One Mole of Aldehyde.—In the case of five acetals the percentage conversion was determined and the equilibrium point calculated in experiments where 2 moles of the alcohol and one mole of the aldehyde were allowed to react. The percentage conversions and the equilibrium constant are given after the name of the acetal: methyl acetal 52%, 0.0834; ethyl acetal 49.8%, 0.0804; *iso*propyl acetal 30%, 0.0127; methyl butylal 54.4%, 0.1260; *iso*propyl butylal 26%, 0.0088.

The equilibrium constants have been calculated according to the formula

$$\frac{\mathrm{C} \times \mathrm{D}}{\mathrm{B} \times \mathrm{B} \times \mathrm{A}} = K_E$$

where A, B, C and D represent moles per liter at equilibrium of aldehyde, alcohol, acetal and water, respectively.

The decrease in free energy was calculated according to the equation:

$$\Delta F = -(1.986)\ (298)\ (2.3025)\ (\log K)$$

The velocity constants were calculated on the basis that this is a bimolecular, reversible reaction. The formula used was

$$\frac{2.302}{(a-b)t} \log \frac{(a-x)b}{(b-x)a} = k_v$$

where a and b represent moles of alcohol and aldehyde, respectively, transformed at equilibrium and x the change in aldehyde concentration after a given time t in minutes.

This method of calculation of velocity constants was suggested to the authors by Cohen.[17] It is referred to by Mellor,[18] defended by Muller,[19] and condemned as having no theoretical basis by Waddell[20] and Ostwald.[21] In its favor may be advanced the fact that by its use "constants" were obtained while other equations were not satisfactory in this respect. The agreement among the calculated values for k_v is indicated by the following figures: Dimethyl acetal for the first 95 minutes: 0.86, 1.01, 1.01, 1.06, 1.08; av., 1.02. Di-*iso*propyl acetal: 5.74, 5.12, 5.63, 5.33, 5.80. Diethyl butylal: 2.19, 1.99, 2.00, 1.87, 1.81. Diethyl acetal: 2.47, 2.23, 2.31, 2.30, 2.54, 2.37, 2.38, 2.42.

The change in aldehyde concentration (x) after any given time does not represent the change in concentration from the beginning of the reaction. It represents, rather, the change after the first five or ten minutes. With certain of these aldehydes, which were run after concentrations of reagents and catalyst had been chosen in the earlier work, it was found that the rate of conversion was too rapid for accurate measurement. The reactions in some cases, especially with the furfurylals, heptals, cinnamals and benzals, were found to be almost complete by the time it was possible to make the first titration. In these cases, the constants were also calculated from the beginning of the reaction in order, at least, to get a rough approximation for comparison with the earlier experiments carried out on the lower members in the aliphatic series. The values for the velocity constant bracketed in the table are, at best, approximations.

The "velocity constant" does not give a *complete* picture of the velocity, for in most cases it is only "constant" for the first sixty or eighty minutes of the reaction. For since water is a marked "poison" for the reactions it cuts down the rate as it accumulates. This effect is entirely apart from its effect in reversing the reaction. It seems necessary to give the percentage conversion of aldehyde after a few intervals of time (in hours) in order to present completely the facts as to the rates of the reaction. The percentage conversions have all been duplicated within 1% or 2%, using the same reagents and many of them with different samples of reactants.

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[17] Cohen, "Organic Chemistry," Longmans, Green and Co., New York, **1919**, vol. 1, p. 308.

[18] Mellor, "Chemical Statics and Dynamics," Longmans, Green and Co., New York, **1904**, p. 91.

[19] Muller, *Bull. soc. chim.*, [3] **19**, 337 (1898).

[20] Waddell, *J. Phys. Chem.*, **3**, 41 (1899).

[21] Ostwald, "Lehrbuch der Allgemeinen Chemie," **1896–1902**, vol. 2, pt. 2, p. 257.

Table II

Rate of Formation of Acetals

Acetals

	Time	0.17	0.50	1.58	2.58	7.0	27	120			
Methyl	%	3.3	13.1	31.4	39.4	62	84	93.8			
	Time	0.09	0.17	0.50	0.75	1.00	1.5	3.42	8.5	120	
Ethyl	%	10.2	15	29.6	36	41.7	51.3	68	80.6	90.7	
	Time	0.17	0.33	0.75	1.25	2.42	8.0	25	240		
n-Propyl	%	15.6	20.5	29.2	37.8	48.8	68.5	85.1	90.2		
	Time	0.09	0.25	0.50	0.75	1	1.25	3.42	6.5	15	25
*iso*Propyl	%	5.5	11.7	15.7	21.9	24.8	29.0	42.2	49.5	54	58.6
	Time	0.17	0.50	1.5	2.67	5.0	12	24	120		
n-Butyl	%	14.2	27.6	44	53.1	63.1	80	89	92.8		
	Time	0.13	0.25	0.50	0.75	1.0	1.33	2.42	4.0	25	120
*iso*Butyl	%	10.1	16.3	18.6	22.6	26.6	30.4	41.4	50.8	83.2	92.8
	Time	0.17	0.50	1.0	1.83	3.87	27				
sec.-Butyl	%	18.7	29.3	35.5	43	53.3	64	64			
	Time	0.08	0.25	0.75	1.25	17	120				
tert.-Butyl	%	3.0	5.7	10.5	13.5	23.6	31.2				
	Time	0.17	0.33	0.67	1.50	48					
tert.-Pentyl	%	10.2	12.4	14.7	16	21.2					
	Time	0.17	0.50	3							
*iso*Pentyl	%	12.3	17.3	20.7	(Not duplicated)						
	Time	0.25	0.67	2.25	10.5	48					
β-Phenylethyl	%	20.6	29.5	46	74.3	87.4					
	Time	0.20	0.67	2.25	12	24					
Benzyl	%	14.5	20.4	33.8	61.5	69.3					

Butylals

	Time	0.17	0.33	0.75	1.05	2.25	15	22	120	
Methyl	%	8.0	12.8	20.5	24.4	36.5	72.3	86	96.5	
	Time	0.08	0.25	0.75	1.92	3.0	8	24	120	
Ethyl	%	13.2	20	30.2	40	55	75	88	91.7	
	Time	0.17	0.50	1.0	1.75	4.67	25	120		
n-Propyl	%	10.5	19.9	25.8	34.6	50.2	79	93.8		
	Time	0.17	0.50	0.82	1.92	7	26	120		
*iso*Propyl	%	10.4	16	19.6	27.8	40	52	59.2		
	Time	0.17	0.50	0.83	2	4	13	24	120	
n-Butyl	%	19.5	26.4	31.9	45.7	55	73	81	97.6	
	Time	0.17	0.50	0.83	1.08	2.5	7.33	15.5	27	120
*iso*Butyl	%	10	14.2	17.3	20	28.3	46.6	63.3	77.2	96.3

Propylals

	Time	0.17	0.33	1.0	1.5	3.25	6.75	25	72
Ethyl	%	11.7	17.9	32.9	39.6	56	69.9	85.7	89
	Time	0.18	0.50	1.0	1.58	4.33	15	24	
*iso*Propyl	%	3.7	9.6	14.5	19.2	32	45	49.5	

*iso*Butylals

	Time	0.17	0.33	0.75	1.58	5.33	24	48
Ethyl	%	9.3	13.8	22	32.4	52.3	76	83.5
	Time	0.17	0.50	0.75	1.33	5.0	15	48
*iso*Propyl	%	4	8.3	10.5	13.5	25	32	37.4

Furfurylals

	Time	0.17	0.33	0.75	4
Methyl	%	19.5	29	40.2	60
	Time	0.18	0.50	1.0	6
Ethyl	%	29.2	32.7	35	39.7
	Time	0.18	2.3	6.0	
*iso*Propyl	%	18.4	23.2	24.4	

TABLE II (*Concluded*)

		HEPTALS					CINNAMALS			
	Time	0.10	0.33	67	23	96	0.08	0.18	0.83	4
Ethyl	%	21.9	25.2	26	28.5	30.6	19.8	32.3	33.8	36.3
	Time	0.10	0.58	5	96		0.08	0.17	48	
*iso*Propyl	%	13.3	16.3	17.6	19.6		17.5	18.3	19	

		BENZALS			
	Time	0.08	0.33	0.58	1.5
Ethyl	%	4.3	27	34.4	36.3
	Time	0.08	0.50	24	
*iso*Propyl	%	9.66	14.2	15.6	

		m-NITRO BENZAL				
	Time	0.08	0.50	1.0	1.75	48
Ethyl	%	26.5	35.2	38.8	40.7	41.8

		HYDROLYSIS OF TWO ACETALS						
	Time	0.17	0.42	1.25	3.08	7.0	24	48
*iso*Propyl	%	97.2	96	94.7	91.3	86.4	69	63
	Time	0.17	0.67	1.5	3.42	7.25	32	
Ethyl	%	99.2	97.4	95.8	95.0	92.1	90.7	

Summary

A method has been developed for the measurement of the effect of substituents in either alcohols or aldehydes, upon the affinity and speed of reaction in the formation of acetals. This method involves the determination of the rate and percentage conversion of the aldehyde and alcohol into an acetal. Thus, in a series with a single aldehyde and various alcohols, the difference is between the affinity for hydrogen of the alkoxy group and for the radical R C H =. The method gives a measure of the positivity and negativity of substituents in a typical organic reaction that does not involve ionization. The results have been expressed in terms of the decrease of free energy, since this gives a quantitative statement of the changes in affinity with changes in the structure of alcohols or aldehydes, provided the "effective" concentrations are those analytically determined.

The affinity and reactivity relationships have been studied for 32 acetals derived from various combinations of methanol, ethanol, the two propanols, the four butanols, two pentanols, phenyl methanol and phenyl ethanol with furfural, benzaldehyde, *m*-nitro benzaldehyde, acetic, propionic, butyric, *iso*butyric, heptylic and cinnamic aldehydes.

It has been found that the affinity values decrease very markedly when carbon atoms are substituted for hydrogen on the carbinol carbon atom. Such substitution on the 2 carbon atom of alcohols has little effect, while it decreases the affinity value if the substitution is on the 2 carbon atom of an aldehyde. If a hydrogen on the carbinol carbon is replaced by phenyl, that negative group reduces affinity, but if phenyl replaces a hydrogen on the 2 carbon atom of ethanol there is little change in affinity relationships. The highest affinity values are obtained when there are four carbon atoms on either the alcohol or aldehyde side of the acetal. The aldehydes which have a double bond in the 2-3 position, such as benzaldehyde, cinnamic aldehyde and furfural, have a very low affinity in the acetal reaction.

Methanol shows the slowest rate of reaction of all the alcohols. Next to it in order of reactivity is *n*-butanol. The secondary alcohols and especially the tertiary alcohols show a very much higher rate of reaction. Butyraldehyde reacts more slowly than does acetaldehyde or any other aldehyde studied. Furfural, benzaldehyde and cinnamic aldehyde apparently react hundreds of times more rapidly then do the lower aliphatic aldehydes. Heptaldehyde is *apparently* like these aldehydes both in rate of reaction and in affinity values.

Michael's speculation that there is no necessary relationship between the extent of a reaction and its velocity has been completely substantiated.

The results are in harmony with the conceptions that the extent of a reaction is determined by the relative stability of the electronic systems that are represented on the right and left hand sides of the equation, while the rate of a reaction is in part dependent upon the ease or extent to which the electronic system of a given compound must be dislocated by the catalyst before reaction may ensue. There appears to be no correlation between these two characteristics of a compound or a reaction.

MADISON, WISCONSIN

[CONTRIBUTION FROM THE BUREAU OF CHEMISTRY, UNITED STATES DEPARTMENT OF AGRICULTURE]

A METHOD FOR THE ESTIMATION OF HYDROGEN SULFIDE IN PROTEINACEOUS FOOD PRODUCTS[1]

BY L. H. ALMY

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Hydrogen sulfide is one of the end products resulting from the action of many varieties of bacteria on organic material containing protein. Though the presence in protein of sulfur-containing compounds other than cystine has been hinted at, it is generally recognized that this amino acid is the chief source of hydrogen sulfide formed during the putrefaction of flesh products.

A large number of bacteria produce hydrogen sulfide from protein containing the cystine linkage, and it is probable, therefore, that among the organisms causing decomposition of any flesh product will be found one or more of these hydrogen sulfide formers. Indeed, Rettger[2] states that "Hydrogen sulfide is, no doubt, one of the first substances which are split

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[1] This paper was presented before the Division of Biological Chemistry at the Washington Meeting of the American Chemical Society, April, 1924.

[2] Rettger, *J. Biol. Chem.*, **2**, 71 (1906–7).