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

THE RATE OF SYNTHESIS AND HYDROLYSIS OF CERTAIN ACETALS

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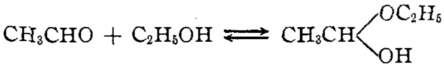
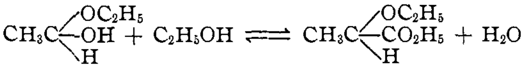
In a previous publication upon the relationship of the structure of alcohols and aldehydes to their reactivity in acetal formation,[1] a comparison of the rates of reaction was made upon the basis of "velocity constants" calculated according to the equation $k = \frac{2.302}{(a_e - b_e)t} \log \frac{(a_e - x)b_e}{(b_e - x)a_e}$, where a_e and b_e represented the concentration of alcohol and aldehyde, respectively, at equilibrium and x the change in aldehyde concentration in time, t. As pointed out by the authors,[2] this empirical expression of Muller's has no justification except in the fact that for the first hour of the reaction fairly consistent "constants" are obtained, and that, apparently, by its use one may compare rates of reactions going to very different equilibrium points.

The treatment of the experimental results has been somewhat facilitated by the conclusion from the measurements of the refraction indices and densities of mixtures of certain alcohols and aldehydes,[3] that in some cases one molecule of alcohol reacts immediately with one molecule of aldehyde to form a hemiacetal.



$$CH_3CHO + C_2H_5OH \rightleftharpoons CH_3CH\begin{matrix}OC_2H_5\\OH\end{matrix}$$

The synthetic reaction whose rate is studied is then that of the hemiacetal with alcohol



$$CH_3C\begin{matrix}OC_2H_5\\OH\\H\end{matrix} + C_2H_5OH \rightleftharpoons CH_3C\begin{matrix}OC_2H_5\\CO_2H_5\\H\end{matrix} + H_2O$$

The reaction may then be treated as a bimolecular reversible reaction and the expression $dx/dt = k_1 (a-x)(b-x)\text{-}k_2X^2$ applied to the experimental results, where k_1 is the rate of the synthetic reaction, k_2 the rate of the reverse reaction, a and b the initial molar concentrations per liter of alcohol and hemiacetal, respectively, and x is the molar conversion of hemiacetal at time, t. k_1 or k_2 may be expressed in terms of the other and of the equilibrium constant, since $k_1/k_2 = K$, the value of K being calculated from the expression

$$K = \frac{\text{concn. acetal} \times \text{concn. water}}{\text{concn. alcohol} \times \text{concn. hemiacetal}}$$

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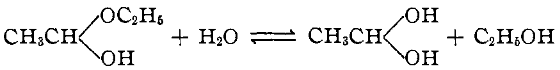
[1] Adkins and Adams, THIS JOURNAL, 47, 1368 (1925).

[2] Ref. 1, p. 1378.

[3] Adkins and Broderick, THIS JOURNAL, 50, No. 2 or 3 (1928).

However, there is good reason for suspecting that hemiacetal reacts with water to form aldehydrol as well as with alcohol to give an acetal.



$$CH_3CH\begin{cases}OC_2H_5\\OH\end{cases} + H_2O \rightleftharpoons CH_3CH\begin{cases}OH\\OH\end{cases} + C_2H_5OH$$

A consideration of the three reactions shows that if the equilibrium point of the last reaction noted is quite far to the right, there will be no material reversal of the acetal reaction during the early stages of synthesis because little water will be present; and that the concentration of the aldehyde at any time, t, will not be $b - x$, but $b - 2x$, for every molecule of acetal formed means one molecule of water formed which would then convert a molecule of hemiacetal into aldehydrol. The concentration of the alcohol will remain constant, because every molecule of alcohol going to acetal will be replaced by a molecule of alcohol resulting from the hydrolysis of hemiacetal. The differential equation then becomes

$$\frac{dx}{dt} = k_1'(a)(b - 2x)$$

or

$$k_1' = \frac{dx}{dt} \cdot \frac{1}{a(b - 2x)}$$

The rates of formation of methyl, ethyl, *iso*propyl and butyl acetals and the rate of hydrolysis of *iso*propyl acetal have been very carefully measured, using reagents of high purity, specially designed apparatus and a refined technique for analysis. The percentage of aldehyde (hemiacetal) found was plotted against time and a smooth curve drawn. Tangents were drawn to the curve at 2, 3, 6, 12, 18, 24, 30, 50, 75 and 100 minutes, and from the slopes of these tangents the values of dx/dt were calculated in molar concentration per minute. The values of k_1, k_2 and k_1' were obtained by substituting in the differential equation the values of dx/dt so found, the values of x as analytically determined and of a and b as calculated from the initial concentrations.

The data from which the curves were constructed represented in each case the results of several runs and on the average represented about 20 determinations. Very few of the experimental points were more than 1.0% off the curve representing the average. The concentration at equilibrium was checked after several days, although in general it was reached in from 24 to 36 hours. The values obtained during the first three or four minutes of the reaction are of doubtful reliability.

A summary of the numerical results is given in Table I. After the name of each acetal is given the per cent. conversion at equilibrium and the initial concentration in moles per liter of aldehyde and alcohol (or of acetal, alcohol and water in the hydrolytic reaction). The values of the tangents and the moles of aldehyde reacted are given for intervals from 2 to 100 minutes. The calculated value of k_1 or k_2 and k_1' are then given.

The values for the equilibrium constant, disregarding the formation of any hemiacetal, and the corresponding values of $-RT \ln K$ are as follows

Methyl acetal $K = 0.1033$ $-RT \ln K = +1340$
Ethyl acetal $K = .0744$ $-RT \ln K = 1540$
Butyl acetal $K = .1850$ $-RT \ln K = 994$
*iso*Propyl acetal $K = .00769$ $-RT \ln K = 2876$

TABLE I

THE RATE OF SYNTHESIS OF METHYL, ETHYL, *iso*PROPYL AND BUTYL ACETALS AND OF THE HYDROLYSIS OF *iso*PROPYL ACETAL[a]

Time, min.	2	3	6	12	18	24	30	50	75	100
Methyl acetal 94.7% (2.000 moles of CH_3CHO, 21.886 moles of CH_3OH)										
dx/dt	0.0503	0.0443	0.0328	0.0244	0.0174	0.0143	0.0133	0.0087	0.0062	0.0031
Moles react.	.120	.164	.280	.446	.564	.662	.740	.942	1.12	1.21
$k_1 \times 10^4$	13.5	12.2	9.7	8.1	6.3	5.6	5.6	4.4	3.9	2.2
$k'_1 \times 10^4$	14.3	13.3	11.4	11.1	9.9	10.4	12.9			
Ethyl acetal 90.9% (1.43 moles of CH_3CHO, 15.71 moles of C_2H_5OH)										
dx/dt	0.0405	0.0303	0.0198	0.0123	0.0103	0.0090	0.0070	0.0041	0.0029	0.0023
Moles react.	.114	.144	.224	.314	.379	.436	.486	.600	.665	.743
$k_1 \times 10^4$	21.7	18.2	11.8	8.0	7.1	6.8	5.5	4.4	2.9	2.7
$k'_1 \times 10^4$	23.6	18.6	14.1	11.3	10.8	11.2	10.7	12.5		
*iso*Propyl acetal 59.5% (1.075 moles of CH_3CHO, 12.35 moles of *iso*-C_3H_7OH)										
dx/dt	0.0158	0.0129	0.0085	0.0060	0.0048	0.0043	0.0037	0.0030	0.0020	0.0014
Moles react.	.045	.061	.102	.159	.192	.219	.243	.306	.370	.409
$k_1 \times 10^4$	13.7	11.4	8.0	5.9	5.1	4.9	4.4	4.0	3.3	2.7
$k'_1 \times 10^4$	14.3	11.1	8.7	7.2	7.3	6.1	5.7	5.8	5.4	5.0
Butyl acetal 95.8% (0.851 moles of CH_3CHO, 10.44 moles of C_4H_9OH)										
dx/dt	0.0179	0.0136	0.0087	0.0059	0.0046	0.0034	0.0032	0.0023	0.0014	0.0011
Moles react.	.034	.047	.090	.128	.161	.186	.206	.257	.308	.341
$k_1 \times 10^4$	22.8	17.6	12.1	8.6	7.1	5.5	5.2	4.2	2.8	2.3
$k'_1 \times 10^4$	23.8	18.9	10.3	9.1	7.5	7.7	7.1	6.4	6.8	6.7
*iso*Propyl acetal 40.5% (1.25 moles of acetal, 9.91 moles of *iso*-C_3H_7OH, 1.247 moles of H_2O)										
dx/dt	.....	.....	0.0073	0.0072	0.0068	0.0066	0.0062	0.0042	0.0024	0.0013
Moles react.	.....	.....	.044	.088	.131	.169	.208	.317	.396	.439
$k_2 \times 10^3$	.....	.....	5.2	5.7	6.0	6.6	7.1	7.3	6.7	7.0

[a] The concentration of the catalyst was 0.000465 g. of hydrogen chloride per mole of alcohol in the synthetic reactions and five times that amount in the hydrolysis of *iso*propyl acetal.

The chief point of difference between the experimental results obtained by Adams and those described in this paper is with respect to the faster rate with which methanol reacts with acetaldehyde. However, this does not affect the validity of the conclusion that methanol has a lower reactivity during the initial stages of the reaction than does ethanol. However, it is greater than for butanol and *iso*propanol.

The method used in this paper for the evaluation of the reaction rates from the experimental results does change the conclusion reached by

Adkins and Adams that *iso*propyl alcohol is more reactive than the primary alcohols. The values of k_1 and k_1' given in the table must lead one to the conclusion that *iso*propyl alcohol is less reactive than the three primary alcohols studied, although the differences between the four alcohols are not great.

A consideration of the values of k_1 given in the table shows that they rapidly decrease as the synthetic reaction proceeds. The values of k_1' are very much more constant and after the first two or three time intervals are quite constant over a period of from 30 to 60 minutes. The assumption made in the calculation of k_1' is of course justifiable and approximates the truth only in the early stages of the reaction, as it ignores any hydrolysis of acetal and assumes that the active concentration of aldehyde is decreasing twice as fast as the formation of acetal. The limiting point of this assumption is the conversion of 50% of the aldehyde to acetal. The values of k_1' are seen to be constant for a much longer interval in the case of *iso*propyl acetal than for those acetals which reach an approximately 50% conversion in a shorter time. The values of k_1' lend support to the hypothesis outlined above with regard to aldehydrol formation. The rapid decreases in the values of the constants during the first few minutes are certainly due in a large part to the poisoning effect of water upon the catalyst. The values of k_1' reach a constant value more slowly in the case of *iso*propyl acetal than with the other acetals. This is understandable because any given concentration of water is reached more slowly in the synthesis of this acetal than with the others; so that the amount of change in k_2 during the period under consideration is relatively small and the value is fairly constant in the period from 24 to 100 minutes. It should be noted that while the values of k_2 for the hydrolytic reaction are roughly ten times those of the synthetic reaction, this is because the concentration of the catalyst is five times as great. With the same concentration of catalyst the rate of the hydrolytic reaction is a small fraction of that for the synthetic reaction. This is further evidence of the poisoning effect of water upon the catalyst.

An inspection of the curves showing percentage conversion of aldehyde against time, even more than an examination of the values given in the table, will lead one to the conclusion that the true reaction rates are individualistic and irregular. For example, if one notes the time required for the reaction to go half-way to equilibrium this is found to be about 50 minutes for methanol, an hour for ethanol and *iso*propanol, and two or three hours for butanol. Yet the one reaching this point the soonest (methanol) has a lower value k_1' than for ethanol, while butanol requires more than twice as long to reach the half-way point, this too in spite of the fact that the equilibrium points are quite close together. Four and a half minutes are required for 10% of the aldehyde to react with methanol, three minutes for ethanol and about six minutes for the *iso*propanol and butanol. A comparison of these figures leads to a somewhat different picture of the relative reactivities.

The authors do not believe that the lack of conformity of the experimental curves representing the aldehyde conversion to any precise mathematical pattern is due to impurity of reagents or errors in procedure or analysis. The results have been repeatedly checked by using different sets of reagents under different conditions, using a technique that can be demonstrated to be very accurate.

Experimental

The alcohols were repeatedly dried over fresh lime until the last portion of lime showed no visible crumbling effect at the end of 24 hours' refluxing. (Some ethanol thus dried was refluxed with aluminum ethoxide for 24 hours, but showed no precipitate of aluminum hydroxide. The alcohol so dried was identical in reactivity with that dried over lime only.) The final distillation was performed very carefully, a 46cm. Vigreux column used, the first and last 500 cc. of a 3000cc. lot being discarded and the product protected at all times by guard tubes. The boiling point range was always less than 0.2°.

Acetaldehyde was fractionated from a commercial product through a 46cm. Vigreux condenser surrounded by a water jacket. The vapors before condensation were passed through a 22cm. horizontal column of calcium chloride. Ice water was circulated through the condensers and about the column. All connections were made with paraffined corks. The distillation was discontinued when the temperature of the vapors rose above 21°. The process was repeated three times, the final product being sealed in 5cc. portions in test tubes.

Di-*iso*Propyl Acetal.—In a 2.5 liter bottle were placed 1100 g. of *iso*propyl alcohol of commercial grade and 200 g. of specially prepared calcium chloride. The whole was then shaken mechanically for several hours until most of the calcium chloride was dissolved. The mixture was then cooled to near 0° and 425 g. of acetaldehyde of commercial grade was added slowly so as to prevent immediate mixing. The bottle was then securely stoppered to resist pressure and the contents were thoroughly shaken. Considerable heat was evolved. The mixture was allowed to stand for twenty-four hours with occasional shaking. At the end of this time no aqueous layer was observed to have formed. The material was filtered through dry potassium carbonate into a flask. It was then distilled under diminished pressure. No very definite fractions could be collected at this time but it was divided into two parts, of which the lower contained most of the alcohol and some aldehyde while the higher was richer in the acetal. The temperature was never allowed to rise above 50°. The average pressure maintained was 25 mm. of mercury. A large quantity of solid material, 200–300 g., remained as residue. The two fractions of liquid collected were then fractionated several times. A fraction boiling at 125.5 to 126.5° was collected as di-*iso*propyl acetal. This weighed 251 g. and represented a yield of 18.7%. By making a wider cut the yield could have been increased 3 to 4%, but a less pure product would have been obtained. The pure material was found to have a specific gravity of 0.8128 (25°).

The calcium chloride was prepared by treating the commercial grade with dry hydrogen chloride at 250 to 300°. A flask containing the material was placed in an oil-bath and kept at that temperature. Hydrogen chloride was passed through for five to six hours. It was then swept clear of any excess by carbon dioxide. This gave the normal salt, whereas the commercial grade is often slightly alkaline.

Catalyst.—Hydrogen chloride generated by adding concentrated sulfuric acid to moist sodium chloride was conducted through a sulfuric acid gas-washing bottle into a bottle containing 150 to 200 cc. of the alcohol for which the catalyst was intended. The alcohol used had been purified in the manner described above. After a considerable quantity had bubbled through, it was allowed to come to room temperature. It was then analyzed for chlorine content by the Volhard method. Having determined the concentration of hydrogen chloride in this way, a quantity was diluted up to the proper concentration for the reaction. For convenience, the concentration was so chosen that on adding 1.0 cc. of the catalyst for the reaction mixture, the final concentration was 0.000465 g. of hydrogen chloride per mole of alcohol present. This was the concentration used by Adams. The bottle containing the catalyst thus prepared was protected from the light by covering with glazed paper. It was then inserted into the apparatus as illustrated in Fig. 1.

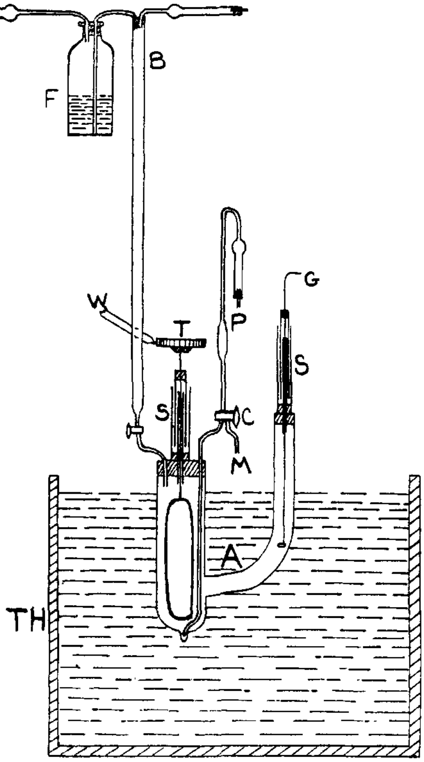


Fig. 1.

It was found that the catalyst diminishes in value as time goes on, if exposed to light, and it seems probable that it does so to a slight extent even when protected. For this reason, the catalyst was always used within a few days after making up. A sample unprotected from the light, which contained 0.21107 g. of hydrogen chloride per 10 cc., was found at the end of six weeks of exposure to contain 0.19198 g. per 10 cc. The depreciation, therefore, was about 10% for that period of time. Very probably some of the hydrogen chloride was converted to the alkyl chloride.

The reaction flask A in Fig. 1 was kept in the thermostat TH but may be removed independently of the remaining apparatus should accidental breaking of the stirrer T occur or should mercury from either of the seals gain entrance. The stirrer T was propelled by a current of air W working against a fan which was attached at the outer end. The flask A was washed with three 75cc. portions of anhydrous alcohol after each experiment. This was introduced through the side arm of A, from which the mercury seal S had been temporarily removed, and was withdrawn through the pipet P into a trap. This procedure was then repeated using 75 cc. portions of anhydrous ether. The pipet P was then connected to a source of air under pressure, the air having been previously passed through a sulfuric acid gas-washing bottle. The air was allowed to pass through at a moderate rate for fifteen to twenty minutes when all of the ether vapors had been removed and the flask was completely dry and filled with an atmosphere of dry air. The aldehyde sample was then put in place in the side arm of A with the finely drawn tip going through the loop of G. It was allowed to rest in this position until the alcohol was added. The connection of the mercury seal with the arm was carefully made with collodion. The required quantity of alcohol was forced into the buret B from the flask F by means of an aspirator connected to the drying tube. That part of the buret below its stopcock was filled from the previous experiment. The rubber connections to the drying tubes were shut off by pinchcocks when not in use in order to prevent the action of any vapor from the bottle F upon the calcium chloride in the drying tubes. An identical arrangement for introducing the catalyst was used but is not illustrated by Fig. 1. The alcohol was allowed to flow into the flask. The aldehyde was then released by raising the support G and allowing the tube to fall against the bottom of the arm, thus breaking the capillary tip. The stirrer was working vigorously, meanwhile, so that it was immediately mixed with the alcohol as it flowed into A. In this way the effect of the vapor pressure of the aldehyde on the mercury seals was rapidly diminished. The temperature was allowed to come to 25°. A 5.0cc. sample was then withdrawn into the pipet P through the three-way stopcock C. The sample was allowed to flow into the titration flask F, Fig. 2, through M, Figs. 1 and 2.

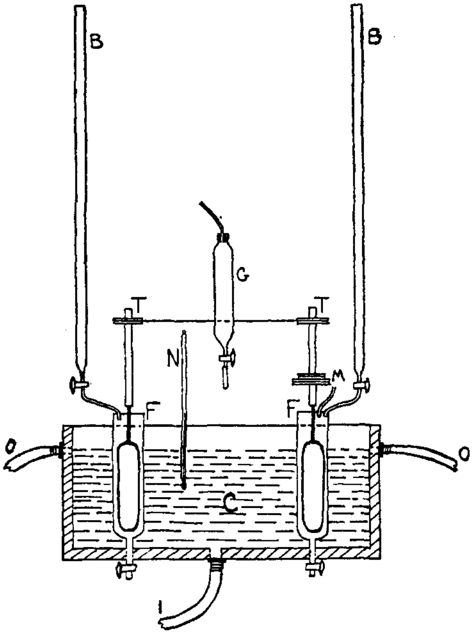


Fig. 2.

The titration flask F, Fig. 2 contained 40 cc. of 10% sodium sulfite maintained at 2 to 3° by a circulating bath C through which ice water was passed in through I and out at O. The aldehyde was determined by titrating the alkalinity developed. This is the Seyewetz-Bardin method described by Child. The amount of alkali formed is equivalent in moles to the available aldehyde and hemiacetal in the sample. The titration flask F on the left was for holding the blank. The stirrers T were operated by a motor at such a speed that good mixing was obtained. The buret G was for measuring out quantities of sodium sulfite from a stock solution immersed in an ice-salt waterbath. The titration must be performed slowly. The acid was allowed to run from the buret B at an average rate of 4 cc. per minute. The volume of liquid in the two flasks was equalized by adding distilled water gradually to the blank so that the temperatures and volumes were identical at the end-point. When the color of the liquid in the two flasks had reached the same degree of intensity when compared by observation against a light background behind the bath C, whose rear and forward faces are of transparent glass, the end-point had been reached and the reading on the buret B on the right was taken.

When the titration for the original concentration had been completed, the catalyst was added through a buret B which was graduated accurately to 0.01 cc. The stirrer T was working vigorously, meanwhile, to insure rapid and thorough mixing. Only 1 cc. of the catalyst was added so that the time consumed never exceeded thirty seconds. The mid-point of this period of time was taken as the initial time in all calculations of the rate. The time was carefully noted by means of a stopwatch with a second hand. Samples were withdrawn at the desired intervals of time and titrated in a manner identical with that described above. The time at which the meniscus of the sample passed a given point on the pipet P, Fig. 1, in discharging, was chosen as the time the sample was taken. Since a titration at the beginning requires ten to fifteen minutes, it was necessary to combine the results of several runs in order to obtain sufficient data for the first hour or so.

The concentrations at the beginning of the reaction were always so regulated that 0.091 mole of aldehyde and 0.000465 g. of hydrogen chloride were present for each mole of alcohol.

It is essential that the reaction mixture be free from mercury. It has been found that mercury diminishes the rate very appreciably.

Summary

The rate of reaction of acetaldehyde with methyl, ethyl, *iso*propyl and *n*-butyl alcohols has been very accurately determined using reagents of very high purity. The curve representing the disappearance of aldehyde is in each case somewhat different for each alcohol so that the quantitative differences between reactivities are somewhat dependent upon the method of comparison. There are, however, no very large differences in the reactivities of the four alcohols for acetal formation.

The values of the reaction velocity constant have been calculated upon the assumption that the reaction under investigation is a bimolecular reversible reaction in which a molecule of hemiacetal reacts with a molecule of alcohol to form a molecule of acetal and of water. The values of k_1 so calculated fall off steadily in the period from 2 to 100 minutes, in some cases to one-tenth of their first value.

The values of the reaction velocity constants have also been calculated upon the assumption that the water formed in the acetal reaction is largely consumed in the hydrolysis of hemiacetal. The constants so obtained are quite consistent after the first few minutes of reaction and a study of them lends confirmation to the assumptions upon which they are based.

The values of the reaction velocity constant for the hydrolytic reaction increase somewhat as the reaction proceeds, but are fairly consistent during the period of 24 to 100 minutes. When the concentration of catalyst used in the hydrolytic reaction is the same as in the synthesis, the reaction rate is very much slower.

The decrease in the velocity constant as the synthesis proceeds, the increase as the hydrolysis proceeds and the lowered rate of hydrolysis as compared with rate of synthesis (in the early stages of each) are all three believed to be due to the poisoning effect of water.

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