

assuming again the presence of a constant amount of withheld reagent, the major portion of the residue shows a hydrogen content of 5%. This points to the presence of heavy styrene polymers on the catalyst in agreement with the previous evidence that lighter polymers were present in the liquid product. Despite the evidence of Goldwasser and Taylor¹² that under certain conditions styrene does not lower catalyst activity, we find it difficult to avoid the conclusion that styrene polymers destroy the activity of the catalyst for the straightforward dehydrogenation of cyclohexane to benzene. Entirely different is the behavior of octenes and of methylcyclopentane; the amount of residue is nearly twenty times that from the cyclohexanes. The assumption previously made that a constant small amount of feed is retained in the reaction tube would predict the low hydrogen content observed here. Most of the residue is, like that from paraffins, carbon rather than tar-like hydrocarbons.

It appears likely that the carbon is produced by side reactions involving extensive dehydrocondensation of linear and cyclic diene polymers. One can then explain by a common mechanism the catalyst poisoning of such apparently unrelated hydrocarbons as ethylbenzene, octenes, cyclopentanes and ethylene.¹⁰ The more or less refractory nature of styrene polymers leads to little actual carbonization but instead leaves appreciable amounts of strongly adsorbed aromatic hydrocarbon as such in the residue. When di-

(12) Goldwasser and Taylor, *THIS JOURNAL*, **61**, 1260 (1939).

luted with cyclohexane, *n*-heptane gave almost as much residue as alone. Added toluene had the exceptional effect of decreasing the hydrogen content of the residue. These results with mixed reagents are not readily explained by the generalizations derived from the pure hydrocarbons. Further work on mixtures and kinetic treatment of the data are necessary.

Conclusions

1. Representative hydrocarbons of all classes have been dehydrogenated over chromic oxide catalysts under identical high-rate, high-temperature conditions.

2. Cyclohexanes are converted to aromatics for extended periods and practically no residual products are formed.

3. Paraffins are much less rapidly converted than cyclohexanes, the activity of the catalyst steadily decreases, and elementary carbon is deposited. Olefins are more readily converted than paraffins, but the activity decline and carbon deposition are far more pronounced.

4. Cyclopentanes are slowly dehydrogenated, but closely resemble olefins in depositing large amounts of carbon.

5. Simple methylated aromatic hydrocarbons are unaffected, but alkyl aromatics with longer side-chains, such as ethylbenzene, are slowly dehydrogenated to products which strongly poison the catalyst. The residue probably responsible consists of tar rather than elementary carbon.

WHITING, INDIANA

RECEIVED MAY 11, 1940

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 758]

The Hydration of Unsaturated Compounds. VIII. The Rate of Hydration of β,β -Dimethylacrylic Acid; the Rates of Dehydration and Decarboxylation of β -Hydroxyisovaleric Acid

By DAVID PRESSMAN AND H. J. LUCAS

Introduction

In order to determine the effect of various substituents upon the heat of hydration of the ethylenic double bond, a number of compounds must be studied. It is reasonable to believe that the influence of the substituent may be exerted through two principal effects. One, which is the inductive effect, is shown by all substituents. The other, which affects the double bond character through resonance, is exhibited by only certain

substituents. In addition there is bound to be a certain interaction between these two effects.

It is the purpose of the present hydration studies to evaluate the two principal effects and their interactions. The heats of hydration are determined from equilibria or kinetic data as in previous work.^{1,2,3} A study is being made also of the kinetics and mechanism of the hydration and

(1) W. F. Eberz and H. J. Lucas, *THIS JOURNAL*, **56**, 1230 (1934).

(2) S. Winstein and H. J. Lucas, *ibid.*, **59**, 1461 (1937).

(3) D. Pressman and H. J. Lucas, *ibid.*, **61**, 2271 (1939).

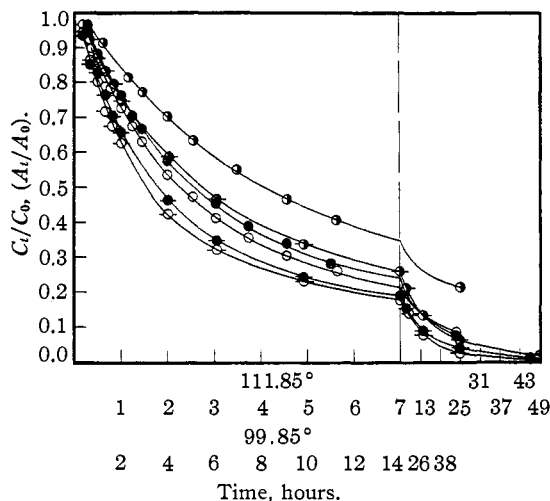


Fig. 1.—Plot against time of fraction of β,β -dimethylacrylic acid remaining, C_t/C_0 , (A_t/A_0), in hydration experiments.

	(H ⁺), normal	μ , normal	C ₀ , molar
99.85°			
○	1.000	1.0	0.00828
●	0.544	1.0	.00686
●	.480	2.1	.00806
111.85°			
○	1.010	1.0	0.00860
●	0.544	1.0	.00690
●	.480	2.1	.00749

dehydration reactions and data are being obtained for a correlation of structural effects upon reaction velocities and heats of activation of the hydration and dehydration reactions. At the same time the influence of acid and base catalysts and of the ionic strength upon these two reactions is being observed. Since the heat of hydration of crotonic acid has been determined already, it was desirable to extend the study of the hydration of unsaturated compounds to include that of β,β -dimethylacrylic acid and its equilibrium with β -hydroxyisovaleric acid. No reference has been found concerning either the hydration of β,β -dimethylacrylic acid or the dehydration of β -hydroxyisovaleric acid.

The plan of work was to obtain the heat of hydration from the kinetic constants of the hydration of the unsaturated acid and of the dehydration of the hydroxy acid and also from the equilibria between the two acids at two temperatures in dilute perchloric acid solution as in previous work. However, the decarboxylation of β -hydroxyisovaleric acid to *t*-butyl alcohol under the conditions of the experiments is a complication which does not permit a direct measurement of the equilibria.

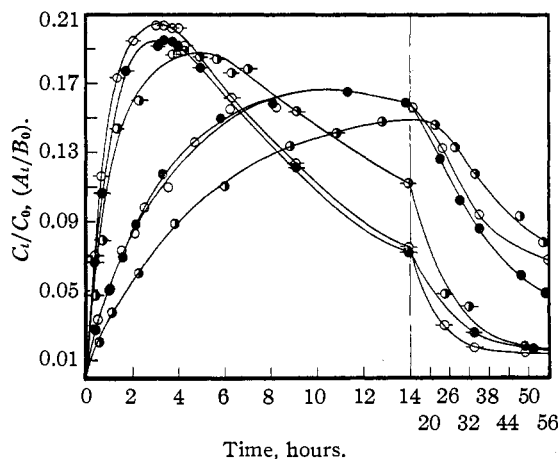


Fig. 2.—Plot against time of fraction of initial β -hydroxyisovaleric acid present as dimethylacrylic acid, C_t/C_0 , (A_t/B_0), in dehydration experiments.

	(H ⁺), normal	μ , normal	C ₀ , molar
99.85°			
○	0.985	1.0	0.01520
●	.528	1.0	.01590
●	.466	2.1	.01422
111.85°			
○	0.994	1.0	0.01640
●	.527	1.0	.01705
●	.463	2.1	.01691

Decarboxylation in aqueous solution has not been reported for either β -hydroxybutyric acid or β -hydroxyisovaleric acid. Indeed, the great stability of the equilibrium between the former and crotonic acid is definite evidence that it could decarboxylate only at an infinitesimal rate in 2 *N* perchloric acid at a temperature of 100°. However, two homologs of the β -hydroxyisovaleric acid, namely, α -methyl- β -hydroxyisovaleric acid⁴ and α,α -dimethyl- β -hydroxyisovaleric acid,⁵ decarboxylate in hot aqueous solution to yield dimethylethylcarbinol and dimethylisopropylcarbinol, respectively. In spite of the decarboxylation reaction, the hydration and dehydration constants along with the decarboxylation constants could be determined from the kinetic data obtained in the hydration and dehydration experiments.

The hydration studies were carried out at hydrogen ion concentrations of approximately 0.3, 0.5 and 1.0 *N* at an ionic strength of 1.0 *N*, and at ionic strengths of 0.6, 1.0 and 2.06 *N* at a hydrogen ion concentration of approximately 0.5 *N*. The dehydration and acid catalyzed decarboxyla-

(4) Giljarow, *J. Russ. Phys.-Chem. Soc.*, **28**, 501 (1896).

(5) S. Reformatsky and B. Plesconogoff, *Ber.*, **28**, 2839 (1895).

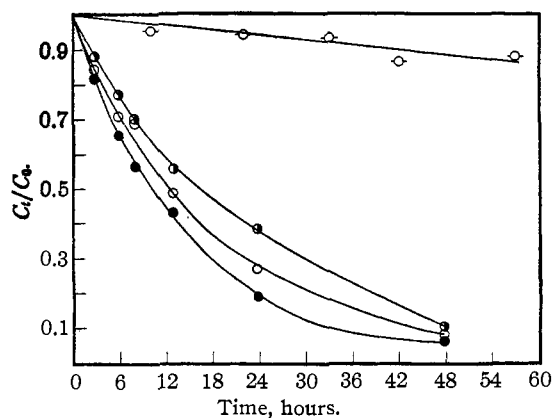


Fig. 3.—Decarboxylation of β,β -dimethylacrylic acid and of β -hydroxyisovaleric acid at 111.85° in absence of perchloric acid. Plot against time of fraction of organic acid remaining, C_i/C_0 .

	μ , normal	C_0 , molar
β,β -Dimethylacrylic acid		
○	0.0	0.01158
β -Hydroxyisovaleric acid		
●	0.0	0.0202
○	1.0	.0250
●	2.1	.0237

tion studies were carried out at ionic strengths of 1.0 and 2.0 N with a hydrogen ion concentration of approximately 0.5 N , and at hydrogen ion concentrations of approximately 0.5 and 1.0 N at an ionic strength of 1.0 N .

Decarboxylation constants were also determined independently at ionic strengths 0.0, 1.0 and 2.0 N , but in the absence of added perchloric acid. These values were found to be quite different from those determined in the perchloric acid solutions, indicating that there are two mechanisms of decarboxylation.

The hydration studies were carried out at 82.45, 99.85 and 111.85° while the dehydration and decarboxylation studies were carried out at the two higher temperatures only. Perchloric acid rather than nitric or a hydrohalic acid was used since nitric acid has a decided oxidizing action at the elevated temperatures and hydrogen halides might add to the ethylenic linkage.

Kinetics

Typical curves for the hydration of β,β -dimethylacrylic acid and for the dehydration of β -hydroxyisovaleric acid are shown in Figs. 1 and 2, respectively. Here C_i/C_0 , the fraction of the original acid either saturated or unsaturated, which is present as the unsaturated acid, is plotted

against time. Since both hydration and dehydration curves approach the axis asymptotically, it is evident that eventually all of the dimethylacrylic acid and hence all of the hydroxyisovaleric acid disappears. In the curves for the dehydration (Fig. 2), the β,β -dimethylacrylic acid concentration passes through a maximum value and then decreases as the β -hydroxyisovaleric acid is removed by irreversible decarboxylation. Typical decarboxylation curves for β -hydroxyisovaleric acid in the absence of perchloric acid are shown in Fig. 3 where C_i/C_0 , the fraction of the original β -hydroxy acid present, is plotted against time. Since the fraction remaining approaches zero, all the acid decarboxylates eventually. The slow change in the value of C_i/C_0 for β,β -dimethylacrylic acid (Fig. 3) indicates that this decarboxylation reaction is negligible compared with the decarboxylation of the hydroxy acid.

The straight line character of the plot of $\log_{10} C_0/C_i$ indicates that the hydration of β,β -dimethylacrylic acid initially is first order with respect to the unsaturated acid (Fig. 4). Moreover, the equality in the slopes of these curves for runs at the same hydrogen ion concentration and ionic

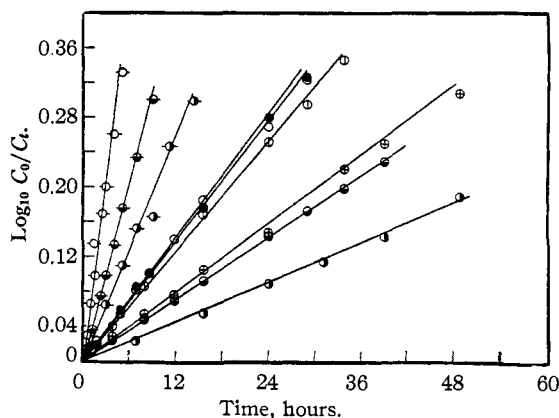
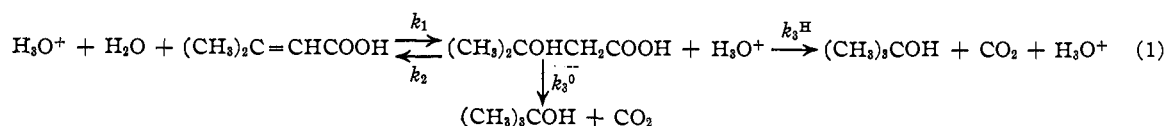


Fig. 4.—Plot against time of $\log_{10} C_0/C_i$ for the hydration of β,β -dimethylacrylic acid.

	(H^+) , normal	μ , normal	C_0 , molar
82.45°			
○	1.000	1.0	0.00973
●	1.000	1.0	.00414
⊕	0.544	1.0	.00984
⊙	.302	1.0	.01015
⊖	.610	0.6	.00878
⊗	.480	2.1	.00920
99.85°			
○	1.000	1.0	0.00516
●	0.302	1.0	.00883
⊖	.601	0.6	.00875

strength, but for different initial concentrations of β,β -dimethylacrylic acid, indicates the same thing. The reaction therefore is pseudounimolecular. The increase in slopes of the plots with increasing hydrogen ion concentration and increasing ionic strengths shows the dependence of the rate constant upon these quantities. That the hydration is first order with respect to the hydrogen ion concentration can be seen from a comparison of the slopes of the curves for different hydrogen ion concentrations in Fig. 4, for the slope is doubled when the hydrogen ion concentration is



doubled. On the other hand, the kinetics of the dehydration cannot be determined in as simple a manner. However, the dehydration for the time being may be assumed to be first order with respect to the hydroxy acid and first order with respect to the hydrogen ion concentration, analogous to the dehydration of β -hydroxybutyric acid³ and of aldol.² It will be shown later in this paper that such an assumption is justified.

The decarboxylation of β -hydroxyisovaleric acid in the absence of perchloric acid also appears to be first order with respect to the hydroxy acid since plots of $\log_{10} C_0/C_t$ against time (Fig. 5) are straight lines. However, the decarboxylation is catalyzed by hydrogen ion, as shown later. The

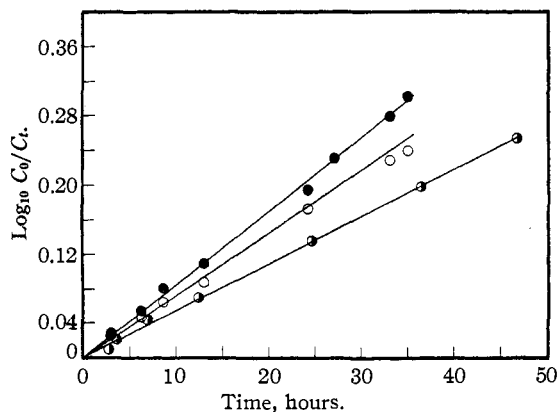


Fig. 5.—Plot against time of $\log_{10} C_0/C_t$ for the decarboxylation of β -hydroxyisovaleric acid at 99.85° in the absence of perchloric acid.

	μ , normal	C_0 , molar
○	0.0	0.0187
◻	1.0	.0250
●	2.1	.0237

acid catalyzed reaction is assumed to be proportional to the hydroxy acid concentration and to the hydrogen ion concentration. The decarboxylation of β,β -dimethylacrylic acid in the perchloric acid solution is assumed to be negligible since it is negligible in the absence of the inorganic acid. The final products of all these reactions are tertiary butyl alcohol and carbon dioxide. These were actually shown to be present by an analysis of the reaction mixture.

Mathematical Treatment.—The reactions under investigation are as follows:

Here k_1 , k_2 , k_3^0 , k_3^{H} are the pseudo-unimolecular hydration, dehydration, uncatalyzed decarboxylation, and acid catalyzed decarboxylation constants respectively, with dimension, hour⁻¹. The apparent pseudo-unimolecular decarboxylation constant, k_3 , in the presence of acid is the sum of the acid catalyzed and uncatalyzed reactions, equation 2

$$k_3 = k_3^0 + k_3^{\text{H}} \quad (2)$$

Using A to represent the concentration of β,β -dimethylacrylic acid, B , of β -hydroxyisovaleric acid, and C , of t -butyl alcohol, the time rate of change of these concentrations is given by equations 3, 4 and 5.

$$dA/dt = k_2B - k_1A \quad (3)$$

$$dB/dt = k_1A - (k_2 + k_3)B \quad (4)$$

$$dC/dt = k_3B \quad (5)$$

These equations integrate to give the following expressions where the subscripts 0 and t indicate the concentrations at time initial and time t , respectively.

In the special case where $B_0 = 0$ and $C_0 = 0$ at $t_0 = 0$

$$A_t/A_0 = \frac{(k_1 + \beta)e^{\alpha t} - (k_1 + \alpha)e^{\beta t}}{(\beta - \alpha)} \quad (6)$$

and in the case where $A_0 = 0$ and $C_0 = 0$ at $t_0 = 0$

$$A_t/B_0 = \frac{k_2}{\alpha - \beta} (e^{\alpha t} - e^{\beta t}) \quad (7)$$

where

$$\alpha = \frac{-(k_1 + k_2 + k_3) + \sqrt{(k_1 + k_2 + k_3)^2 - 4k_1k_3}}{2} \quad (8)$$

$$\beta = \frac{-(k_1 + k_2 + k_3) - \sqrt{(k_1 + k_2 + k_3)^2 - 4k_1k_3}}{2} \quad (9)$$

Since the hydration and dehydration reactions were followed by analysis for unsaturation, A_t , the concentration of the β,β -dimethylacrylic acid alone was determined. The value of A_t/A_0 or A_t/B_0 could be determined experimentally since known amounts of β,β -dimethylacrylic acid or β -hydroxyisovaleric acid were present initially. Hence equations 6 and 7, which determined values of A_t/A_0 and A_t/B_0 , were those used in the evaluation of the constants, k_2 and k_3 .

Evaluation of the Hydration Constant, k_1 .—Since k_1 happens to be larger than k_2 , and k_3 is very close to k_2 in magnitude, the actual rate of dehydration of β -hydroxyisovaleric acid is always small compared to the actual rate of hydration of the β,β -dimethylacrylic acid in those experiments where dimethylacrylic acid is the starting material. Therefore, it is possible to obtain the hydration constant, k_1 , from the initial slope of the plot of $\log_{10} A_t/A_0$ against t for the hydration of the unsaturated compound with an error of less than 1% due to the reverse reaction. These plots are straight lines at least up to 0.4 hydrated as shown in Fig. 4. It will be noticed that the intercept on the abscissa is positive. This is due to the time lag in reaching the thermostat temperature. The specific hydration constants, k_1 , for hydration experiments are tabulated in Table I.

TABLE I								
RATE CONSTANTS FOR HYDRATION OF β,β -DIMETHYLACRYLIC ACID								
(H ⁺), normal	μ , normal	A_0 , molar	k_1 , hr. ⁻¹	$\frac{k_1}{(H_3O^+)}$	Relative γk_1	$-\alpha$	$-\beta$	
82.45°								
1.000	1.0	0.00973	0.0265	0.0265	1.000			
1.000	1.0	.00414	.0255	.0255	0.963			
0.544	1.0	.00984	.01525	.0280	1.059			
.302	1.0	.01015	.00865	.0287	1.082			
.610	0.6	.00878	.0137	.0224	0.845			
.480	2.1	.00920	.0235	.0490	1.85			
99.85°								
1.000	1.0	0.00828	0.165	0.165	1.000	0.0365	0.226	
1.000	1.0	.00516	.165	.165	1.000			
0.544	1.0	.00686	.0930	.171	1.038	.0268	.131	
.302	1.0	.00883	.0530	.176	1.068			
.610	0.6	.00875	.0844	.138	0.836			
.480	2.1	.00806	.151	.314	1.901	.0392	.214	
111.85°								
1.010	1.0	0.00860	0.507	0.507	1.00	0.126	0.789	
0.544	1.0	.00690	.300	.552	1.09	.0970	.485	
.480	2.1	.00749	.449	.935	1.84	.145	.705	

Calculation of the Dehydration and Decarboxylation Constants, k_2 and k_3 . **Evaluation of α and β .**—On the other hand, it is not practical to calculate the dehydration constant, k_2 , from the initial slope of the dehydration curve since the

decarboxylation is taking place at a comparable rate and the equilibrium lies well on the hydrated side. The most useful equation for the determination of both the dehydration constant, k_2 , and the decarboxylation constant, k_3 , is equation 7. A plot of A_t/B_0 against $(e^{\alpha t} - e^{\beta t})$ is a straight line with the slope $k_2/(\alpha - \beta)$ when the correct values of α and β are used. Since A_t/B_0 passes through a maximum, the straight line plot reaches a maximum value of A_t/B_0 and of $(e^{\alpha t} - e^{\beta t})$ and then returns upon itself.

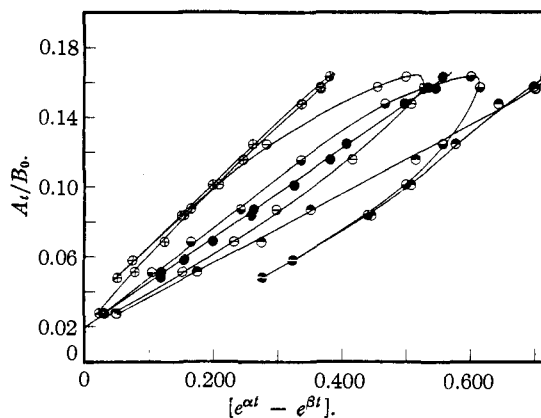


Fig. 6.—Effect of variation in α and β on a plot of A_t/B_0 against $(e^{\alpha t} - e^{\beta t})$ for dehydration experiment. (H^+) = 0.466 N, μ = 2.1 N, T = 99.85°.

	$-\alpha$	$-\beta$
●	0.038	0.208
○		(chosen value)
⊙	.023	.258
⊖	.023	.158
⊕	.053	.258
⊗	.053	.158

Figure 6 demonstrates the effect of variations of α and β on a plot of A_t/B_0 against $(e^{\alpha t} - e^{\beta t})$. From the slope of this straight line, a value of k_2 can be calculated since

$$\text{slope} = k_2/(\alpha - \beta) \quad (10)$$

from α , β and k_1 a value of k_3 can be calculated by equation 11.

$$\alpha\beta = k_1 k_3 \quad (11)$$

Another relation which must be satisfied is that the sum of the rate constants is equal to the negative of the sum of α and β , equation 12.

$$(k_1 + k_2 + k_3) = -(\alpha + \beta) \quad (12)$$

Different values of α and β were used until a straight line plot was obtained according to equation 7 and until equation 12 was satisfied. Although many straight lines are possible with the experimental data, only one has a slope which will yield a satisfactory pair of values for α and β .

TABLE II
 RATE CONSTANTS FOR DEHYDRATION OF β -HYDROXYISOVALERIC ACID

(H ⁺), normal	μ , normal	B_0 , molar	$-\alpha$	$-\beta$	Slope	k_1 , hr. ⁻¹	k_2 , hr. ⁻¹	k_2 , hr. ⁻¹	Σk	$(-\alpha$ $-\beta)$	$\frac{k_2}{(H_3O^+)}$	Relative γ/k_2	t maximum Calcd. hr.	Obsd. hr.	K
99.85°															
0.985	1.0	0.01520	0.036	0.223	0.256	0.1626	0.0480	0.0494	0.2600	0.259	0.0487	1.000	9.8	9-11	3.39
.528	1.0	.01590	.026	.127	.257	.0904	.0260	.0361	.1536	.153	.0493	1.011	15.7	14-20	3.47
.466	2.1	.01422	.038	.208	.259	.1470	.0442	.0538	.2450	.246	.0948	1.950	10.0	9-11	3.32
111.85°															
0.994	1.0	0.01640	0.125	0.780	0.314	0.499	0.2056	0.196	0.901	0.905	0.207	1.000	2.8	2.5-3.5	2.42
.527	1.0	.01705	.094	.470	.320	.291	.1202	.152	.563	.564	.228	1.10	4.3	3-4	2.41
.463	2.1	.01691	.140	.680	.325	.434	.1785	.222	.834	.830	.386	1.85	2.9	2.5-3.5	2.43

The hydroxy acid is added to the perchloric acid in the form of a silver salt, and since it is largely un-ionized in the strongly acid solution, a correction must be made in the hydrogen ion concentration to account for the hydrogen ion concentration decrease due to the formation of the un-ionized organic acid. The hydration constants, k_1 , used in these calculations were values determined from the initial slopes of the hydration experiments corrected for the new hydrogen ion concentration. The constant is proportional to the hydrogen ion concentration.

The time, t , is corrected in each case for the average time of warming to the thermostat temperature as determined by abscissa intercepts of the plot of $\log_{10} A_0/A_t$ against t for the hydration of the unsaturated acid, although this is four minutes for the runs at 111.85°, it comes out to be ten minutes at 99.85°. This can be accounted for

easily by the fact that when the solutions were placed in the thermostat an extra heater was turned on to help provide the heat required to bring the cold solutions to temperature. Apparently, heat was supplied faster in the case of the runs at the higher temperatures. Since the runs at one temperature were all made at the same time, the same time lag would occur for all the rates at that temperature. The positive intercepts, 0.02, on the ordinates of the plots of A_t/B_0 against $(e^{\alpha t} - e^{\beta t})$ are nearly equal in the different runs. This is due to the fact that a little of the silver is reduced, since a slight amount of dark precipitate formed in the reaction tubes. This subsequently reacted during bromination to use bromine and thus a high value for the concentration of the unsaturated compound resulted. Of course, more silver is reduced in the tubes which are heated longer but uniform bromination of the same amount of the free silver takes place in each determination.

Evaluation of α and β by Other Methods.—

The constants α and β can be obtained also from the plot of A_t/A_0 against $[(k_1 + \alpha)e^{\beta t} - (k_1 + \beta)e^{\alpha t}]$. This is a straight line with the slope $1/(\alpha - \beta)$. However, this is not so sensitive to variations in α and β as is the plot from equation 12 for it is sensitive only when the unsaturated acid has largely disappeared. However, these points are the least accurate. Figure 7 shows the effect of variations of α and β on a plot of A_t/A_0 against $[(k_1 + \alpha)e^{\beta t} - (k_1 + \beta)e^{\alpha t}]$. The same corrections in time are made here as in the calculations concerning the dehydration experiments. Table I contains the values of α and β used in these calculations. The slopes and the calculated values of $1/(\alpha - \beta)$ are equal to each other from the nature of the point at zero time. Since the unsaturated acid is added to the aqueous perchloric acid solution as such, it does not remove any acid and hence the values of α and β are higher

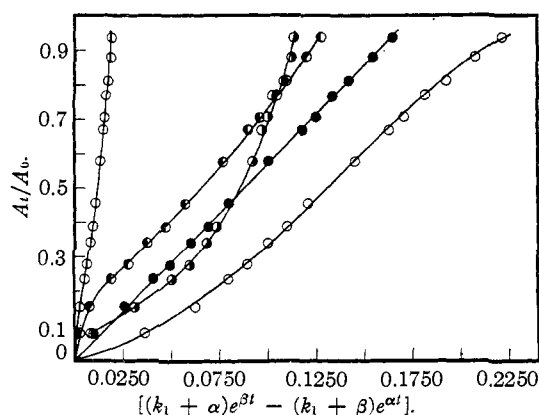


Fig. 7.—Effect of variation in α and β on a plot of A_t/A_0 against $[(k_1 + \alpha)e^{\beta t} - (k_1 + \beta)e^{\alpha t}]$ for hydration experiment. (H⁺) = 0.480 N, μ = 2.1 N, T = 99.85°.

	$-\alpha$	$-\beta$
●	0.039	0.214
○		(chosen value)
◐	.023	.258
◑	.023	.158
◒	.053	.258
◓	.053	.158

here than in the corresponding dehydration runs where a lower hydrogen ion concentration resulted from the addition of the silver salt of the organic acid to the same perchloric acid solution. For the small differences in the hydrogen ion concentrations in the hydration and dehydration runs the values of α and β are proportional to the hydrogen ion concentrations of the solutions.

Another check on the values of α and β can be obtained from the position of the maxima in the dehydration curves. The maximum lies at the point where the rate of change of the dimethylacrylic acid concentration is zero, equation 13.

$$d(A_i/B_0)/dt = 0 \quad (13)$$

At the maximum, the values of the time is given in equation 14.

$$t = 2.30 \log_{10} (\beta/\alpha)/(\beta - \alpha) \quad (14)$$

Table II contains the value of t , observed and calculated, for the maxima in the different runs. The satisfactory agreement here, as well as the fact that each set of values of α and β is satisfactory (Tables I and II), proves that the method of treatment is reliable.

Calculation of the Decarboxylation Constants, k_3^H and k_3^0 .—The decarboxylation constant obtained above is the apparent decarboxylation constant, k_3 . The value for the uncatalyzed reaction, k_3^0 , can be obtained from the slope of the plot of $\log_{10} C_0/C_t$ against time, Fig. 5, for the decarboxylation in a solution not containing perchloric acid.⁶ The catalyzed decarboxylation constant, k_3^H , is then the difference between the apparent constant and the uncatalyzed constant at the same ionic strength, equation 2. The values of the constants for the different decarboxylation runs are found in Tables III and IV.

TABLE III
DECARBOXYLATION RATE CONSTANTS IN THE ABSENCE OF PERCHLORIC ACID

μ , normal	B_0 , molar	k_3^0 , hr. $^{-1}$	Relative $\gamma_{k_3^0}$
		99.85°	
0.0	0.0187	0.0122	0.775
1.0	.0250	.0157	1.00
2.1	.0237	.0195	1.24
		111.85°	
0.0	0.0202	0.0461	0.835
1.0	.0250	.0555	1.000
2.1	.0237	.0720	1.30
0.0	.012 ^a	.002	

^a β, β -Dimethylacrylic acid.

(6) The first five figures have been so formed as to present all the experimental data available in an easily accessible form without an excessive number of plots and tables.

Effect of Hydrogen Ion Concentration and Ionic Strength on the Reaction Rate Constants

Hydration Rate Constant.—According to the Brönsted theory, the hydration rate is expressed by equation 15

$$\text{hydration rate} = k''(\text{H}_2\text{O})(\text{H}_3\text{O}^+)(\text{C}_5\text{H}_8\text{O}_2)\gamma_{\text{H}_2\text{O}}\gamma_{\text{H}_3\text{O}^+} / \gamma_{\text{C}_5\text{H}_8\text{O}_2} / \gamma_{\text{C}_5\text{H}_8\text{O}_2 \cdot \text{H}_2\text{O} \cdot \text{H}_3\text{O}^+} \quad (15)$$

Usually the assumption is made that the activity coefficients of the positive ions cancel each other. However, since even the un-ionized β, β -dimethylacrylic acid activity is affected by ionic strength, it is quite likely that the large positive intermediate complex ion also should be similarly affected and thus its activity coefficient should be a function of the ionic strength different from that of the hydronium ion. Even the activity coefficient of water is calculated to decrease by about 8% when the solution is made 2 *N* in sodium perchlorate. Hence the activity coefficients may all be grouped together in the term γ_{k_1} , since the individual activity coefficients are not known well enough to be discussed. The rate then can be expressed by equation 16

$$\text{hydration rate} = k_1'(\text{H}_3\text{O}^+)(\text{C}_5\text{H}_8\text{O}_2)\gamma_{k_1} \quad (16)$$

where k_1' contains the water concentration, which is practically the same for the different solutions and $k_1'(\text{H}_3\text{O}^+)\gamma_{k_1}$ is the experimentally determined k_1 . Indeed, γ_{k_1} already has been shown to be different from the activity coefficient of the unsaturated compound, $\gamma_{\text{unsat.}}$, in the case of the hydration of isobutene.⁷ There, the γ_{k_1} was compared with the activity coefficient of isobutene for different ionic strengths as determined by distribution experiments and found to differ by 10 and 40% at ionic strengths of 1 and 2 *N*, respectively. This shows that γ_{k_1} for the hydration rate increases more rapidly with ionic strength than the activity of the butene. It can be seen therefore that the ratio $\gamma_{\text{H}_2\text{O}}\gamma_{\text{H}_3\text{O}^+} / \gamma_{\text{C}_5\text{H}_8\text{O}_2 \cdot \text{H}_2\text{O} \cdot \text{H}_3\text{O}^+}$ must increase with ionic strength. The activity of water acts in the opposite direction, however, decreasing with increasing ionic strength. Therefore, the ratio $\gamma_{\text{H}_3\text{O}^+} / \gamma_{\text{C}_5\text{H}_8\text{O}_2 \cdot \text{H}_2\text{O} \cdot \text{H}_3\text{O}^+}$ must increase with ionic strength. The same most likely holds true for dimethylacrylic acid.

The observed rate constant divided by the hydronium ion concentration, $k_1/(\text{H}_3\text{O}^+)$, should then be proportional to γ_{k_1} . The values of $k_1/(\text{H}_3\text{O}^+)$ for the various experiments are in Table I. The hydronium ion concentration, (H_3O^+) ,

(7) H. J. Lucas and W. F. Eberz, *THIS JOURNAL*, **56**, 460 (1934).

is taken to be the same as the hydrogen ion concentration. As an aid in comparing the effect of the different ionic strengths and hydrogen ion concentrations on γ_{k_1} at different temperatures, there are also tabulated the ratios of γ_{k_1} to the γ_{k_1} at ionic strength of 1.0 *N* and hydrogen ion concentration of 1.0 *N* at the same temperature. This ratio determines the γ_{k_1} in various solutions relative to a standard γ_{k_1} in 1 *N* hydrogen ion concentration and 1 *N* ionic strength. This is termed the relative γ_{k_1} of the reaction rate constant. It is fairly constant for any one solution over the different temperatures. Figure 8 shows that the relative γ_{k_1} values of the hydration constant for solutions of hydrogen ion concentration approximately 0.5 *N* increase rapidly as the ionic strength increases. The relative γ_{k_1} is almost doubled by raising the ionic strength from 1 to 2 *N*. The increase of γ_{k_1} with ionic strength also has been observed in the hydration of other unsaturated compounds.^{1,2,7,8}

In the reactions carried out at the same ionic strength but at different hydrogen ion concentrations, the replacement of hydrogen ion by sodium ion increases the values of the relative γ_{k_1} of the reaction rate. This is due to the specific difference of the two ions in their effect on the activity of dimethylacrylic acid. This difference in action has been noticed chiefly in oxygenated compounds, crotonaldehyde, crotonic acid, and dimethylacrylic acid, where the oxonium forma-

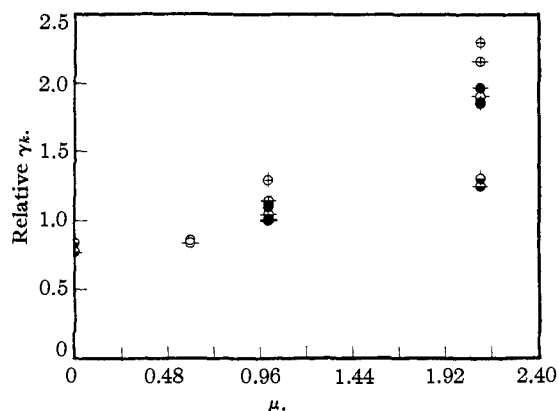


Fig. 8.—Plot of relative γ_k against ionic strength at approximately 0.5 *N* hydrogen ion concentration.

Relative γ_k for	82.45°	99.85°	111.85°
Hydration	○	○	○
Dehydration		●	●
Decarboxylation (acid catalyzed)		⊖	⊖
Decarboxylation (uncatalyzed)		⊖	⊖

(8) H. J. Lucas and Y. Liu, *THIS JOURNAL*, **56**, 2138 (1934).

tion is appreciable. A more extended analysis of these effects in other systems is being made.

Dehydration Rate Constant.—The Brönsted expression for the dehydration rate constant is similar to that of the hydration rate except that water does not enter the expression, equation 17

$$\text{dehydration rate} = k_2'(\text{H}_3\text{O}^+)(\text{C}_5\text{H}_{10}\text{O}_3)\gamma_{\text{H}_3\text{O}^+}\gamma_{\text{C}_5\text{H}_{10}\text{O}_3}/\text{C}_5\text{H}_{10}\text{O}_3\text{H}_3\text{O}^+ \quad (17)$$

From assumptions equivalent to those made for the hydration rate, this reduces to the expression

$$\text{dehydration rate} = k_2'(\text{H}_3\text{O}^+)(\text{C}_5\text{H}_{10}\text{O}_3)\gamma_{k_2} \quad (18)$$

where $k_2'(\text{H}_3\text{O}^+)\gamma_{k_2} = k_2$ as experimentally measured. The values of $k_2/(\text{H}_3\text{O}^+)$, which are directly proportional to γ_{k_2} , are tabulated in Table II along with the relative γ_{k_2} values for the different solutions. The latter values are plotted in Fig. 8 to show the variation of the relative γ_{k_2} with ionic strength at a hydrogen ion concentration of approximately 0.5 *N*. These variations are quite similar to those for the hydration experiments as are the variations occurring when hydrogen ion is replaced by sodium ion.

Decarboxylation Rate Constant.—The decarboxylation in the presence of perchloric acid must take place by two mechanisms, one acid catalyzed and the other not. The fact that this is a true hydrogen ion catalysis is indicated by the fact that the decarboxylation rate in 0.5 *N* perchloric acid is four times that in water, whereas the change in the concentration of the un-ionized acid ($K_A = 10^{-5}$) is only 2%.

The uncatalyzed decarboxylation rate, k_3^0 , is itself a function of the ionic strength, Table III. Therefore the hydroxy-acid does not decarboxylate unimolecularly in an unsolvated form, since then the rate constant would be essentially independent of the ionic strength. Either the acid must react with water or the anion must decarboxylate. If the latter is the case the rate con-

TABLE IV
DECARBOXYLATION CONSTANTS OF β -HYDROXYISOVALERIC ACID IN PERCHLORIC ACID SOLUTIONS

(H ⁺), normal	μ , normal	k_3 hr. ⁻¹	k_3^{H}	$\frac{k_3^{\text{H}}}{[\text{H}_3\text{O}^+]}$	Relative $\gamma_{k_3^{\text{H}}}$
99.85°					
0.985	1.0	0.0494	0.0337	0.0342	1.00
.528	1.0	.0361	.0204	.0386	1.13
.466	2.1	.0538	.0343	.0735	2.15
111.85°					
.994	1.0	0.196	0.140	0.141	1.00
.527	1.0	.152	.096	.182	1.29
.463	2.1	.222	.150	.324	2.30

stant, k_3^0 , would be a function of the ionic strength since dissociation and hence the anion concentration are also functions of that quantity. An experiment to test the decarboxylation of the anion was carried out by heating a concentrated solution of calcium β -hydroxyisovalerate at 100° for three days in a sealed tube. Since no *t*-butyl alcohol was formed, the anion cannot be the material which decarboxylates. Therefore, the uncatalyzed decarboxylation mechanism must be the reaction of the un-ionized acid with water.

The Brönsted expression for the reaction of β -hydroxyisovaleric acid with water is given by equation 19:

$$\text{decarboxylation rate} = k_3^0(\text{C}_5\text{H}_{10}\text{O}_3) = \frac{k_3^0(\text{H}_2\text{O})(\text{C}_5\text{H}_{10}\text{O}_3)\gamma_{\text{H}_2\text{O}}\gamma_{\text{C}_5\text{H}_{10}\text{O}_3}}{\gamma_{\text{C}_5\text{H}_9\text{O}_3}\gamma_{\text{H}_2\text{O}}} \quad (19)$$

The activity coefficients and hence the observed rate constant, k_3^0 , are functions of the ionic strength.

In Table IV are shown the decarboxylation constants, observed at different ionic strengths, hydrogen ion concentrations and temperatures. The decarboxylation constant for the acid-catalyzed reaction, k_3^{H} , is actually the difference between the observed constant, k_3 , and the constant at zero hydrogen ion concentration, k_3^0 , but at the same ionic strength, neglecting the difference in the effect of a hydrogen and sodium ion on $\gamma_{k_3^0}$ of the uncatalyzed reaction. The Brönsted equation for the acid catalyzed decarboxylation is similar to equation 20, the expression for the dehydration reaction. The values of k_3^{H} corrected for the hydrogen ion concentration and also the values of the relative $\gamma_{k_3^{\text{H}}}$ for the different solvents are in Table IV and Fig. 8. It can be seen that these values are somewhat greater than those for the hydration and dehydration reactions.

The relatively low effect of ionic strength on the un-ionized decarboxylation reaction is due to the fact that the other cases deal with positive ions and it would be reasonable to expect a larger effect of ionic strength on ions than on electrically neutral substances.

Equilibrium Constants.—The theoretical equilibrium constants which would determine the final concentrations of the two organic acids if decarboxylation were not taking place can be calculated as the quotient of the hydration and dehydration rate constants. These values are in Table II. The effects of both hydrogen ion concentration and ionic strength on the dehydration and hydration rate constants are essentially the

same within experimental error. Thus there is no definite shift in the observed equilibria with salt as was observed in the aldol-crotonaldehyde² and the β -hydroxybutyric acid-crotonic acid⁸ equilibria. The effect of salt can be seen to be practically the same at the different temperatures.

Thermochemistry

In Table V are the heats of activation for the hydration, dehydration, non-catalyzed decarboxylation, and the acid catalyzed decarboxylation. Most of the hydration runs were made at three temperatures. The values for the heat of activation were obtained from the slopes of the plots of the $\log_{10} k_1$ against the reciprocal of the absolute temperature (Fig. 9). The activation energy is

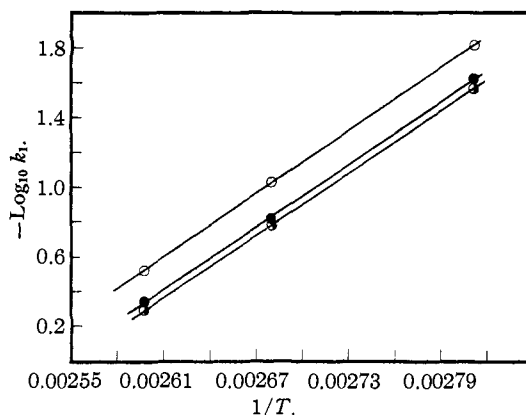


Fig. 9.—Plot of $\log_{10} k_1$ against $1/T$ for the hydration of β,β -dimethylacrylic acid.

	(H ⁺), normal	μ , normal
○	1.000	1.0
●	0.544	1.0
●	.480	2.1

independent of ionic strength and hydrogen ion concentration since the straight line curves are parallel. The dehydration and decarboxylation runs were made at only two temperatures. The

TABLE V
THERMAL CONSTANTS OF THE HYDRATION, DEHYDRATION AND DECARBOXYLATION REACTIONS

(H ⁺), normal	μ , normal	Q_1 , Fig. 9, kcal.	Q_1 , 82.45- 99.85° kcal.	Q_1 , kcal.	Q_2 , kcal.	Q_3^0 , kcal.	Q_3^{H} , kcal.	ΔH of hydration, kcal.
1.0	1.0	27.3	28.1	26.8	34.7	30.2 ^a	33.8	-7.9
0.5	1.0	27.4	27.4	28.0	36.6		37.0	-8.6
.3	1.0		27.5					
.5	2.1	27.6	28.2	26.0	33.6	31.2 ^a	35.3	-7.6
.6	0.6		27.5					
.0	.0					31.8 ^a		
Average			27.7	26.9	35.0	31.1 ^a	35.4	-8.1
		Temperature coefficient for 100-110°						
		2.58	3.42	2.98	3.47			

^a (H⁺) = 0.

heats of activation were calculated from the rate constants by the Arrhenius equation.

In Table V also are the values of the heat of hydration calculated as the difference between the activation energies of the hydration and dehydration reactions. The average is 8.1 kcal. An analysis of the effect of structure on the heat of hydration will be made in a future communication.⁹

Interfering Reactions

Dehydration of Tertiary Butyl Alcohol.—The dehydration of *t*-butyl alcohol with the formation of isobutene is inappreciable even at 111.85° since at equilibrium the concentration of the alcohol is 100 times that of butene if the heat of hydration in aqueous solution remains constant at 11.6 kcal. since the equilibrium constant of (C₄H₉OH)/(C₄H₈) is 4000 at 35°. The presence of butene in the vapor is evidenced by its odor. The butene concentration in the vapor when the tube is opened is very low and is calculated to be of the order of 0.2 mm., for most of the butene in the vapor at the high temperature would hydrate at room temperature before the tube was opened since it has been shown⁷ that in 1 *N* nitric acid butene hydrates 90% in one-half hour at a temperature of 25°. A calculation cannot be made as to the fraction of the system in the vapor phase since it would be proportional to the volume of the space above the solution, which varied from 1 to 15 ml. In any case the analyses of the last tubes of a run for unsaturation showed negligible bromine absorption, indicating that the butene either hydrated on cooling or was lost in the pouring of the solution and the butyl alcohol present did not brominate.

Lactone Formation.—According to Gerhke and Willrath,¹⁰ β -hydroxybutyric acid loses water

(9) Table V of hydration paper number VII of the thermal data concerning the heat of hydration of crotonic acid³ should read

(H ⁺)	μ	Heats of activation		- ΔH , kcal.	Temp. coefficient 90-100°	
		Q ₁	Q ₂		Hyd.	Dehyd.
1.06	2.06	20.1	25.4	5.3	2.11	2.57
2.06	2.06	20.2	25.6	5.4	2.12	2.60

Thus the heat of hydration of crotonic acid is 5.4 kcal. instead of 10.1 kcal. as previously stated. This is 0.6 kcal. lower than the heat of hydration of crotonaldehyde rather than 4 kcal. higher. Since it has been shown that one would expect crotonaldehyde to lose more resonance energy than crotonic acid in the hydration reaction, the small difference in the heats of hydration of the aldehyde and acid must be due to another property of the carboxyl and aldehyde groups which would decrease relatively the heat of hydration of the acid. This may be due to the different inductive effects of the carboxyl and carbonyl group. This problem is being investigated further with respect to various other hydration reactions.

(10) M. Gerhke and H. H. Willrath, *Z. physik. Chem.*, **A142**, 301 (1929).

to form a compound of lower free carboxyl content, a 0.1 *M* solution at 100° having 4.5% of the carboxyl groups bound. It has been shown that if the formation of a lactone is the cause, dilution would have no effect on this value.³ From the stabilizing effect of methyl groups on small rings¹¹ one would expect β -lactone formation to be favored in β -hydroxyisovaleric acid over β -hydroxybutyric acid. The formation of the lactone would increase the values k_2 and k_3 for dehydration and decarboxylation. Since the small change would roughly be the same for the two temperatures it cancels out in the important calculation of the heat of hydration. Any bimolecular esterification would be negligible at the high dilutions prevailing.

Experimental

β , β -Dimethylacrylic Acid.— β , β -Dimethylacrylic acid was prepared according to a modification of the method of Barbier and Leser¹² from the chloroform reaction of mesityl oxide. Into a liter of 1.5 *N* sodium hydroxide solution was passed 185 g. (2.6 mole) of chlorine with cooling, and to this 75 g. (0.77 mole) of mesityl oxide (Eastman Kodak Company product redistilled through Vigreux column and boiling at 126-128° uncor.) was added with vigorous mechanical stirring, at first in a steady stream until about 25% was added which brought the reaction mixture to the boiling point under a reflux. The rest was added dropwise to maintain the temperature at about 60°. There was no residual hypochlorite. The aqueous solution was neutralized with 300 ml. of 6 *N* sulfuric acid and then acidified with 200 ml. more. At first a large amount of carbon dioxide was evolved. A white oil separated and crystallized on cooling. The mother liquor was extracted with four 200-ml. portions of ether. The residue on evaporation was combined with the original crystals and the mixture recrystallized from hot water, yielding large individual needle-like crystals. The yield was 30 g. (0.34 mole), 44%. The crystals were recrystallized again from hot water, m. p. 66.5-67.5° cor. Analysis for unsaturation by bromination showed 1.02 double bonds per mole.

Silver β -Hydroxyisovalerate.— β -Hydroxyisovaleric acid was prepared from diacetone alcohol by the chloroform reaction. To a solution of 320 g. (8 moles) of sodium hydroxide in 1.5 liters of water was added, with cooling, 230 g. (3.1 moles) of chlorine, and then 100 g. (0.85 mole) of diacetone alcohol with vigorous stirring. The reaction mixture became hot and the chloroform distilled out as it was formed. The slight excess of chlorine was removed by sodium bisulfite and the solution was decomposed with 1250 ml. of 6 *N* sulfuric acid. The solution was extracted with eight 1-liter portions of ether which were subsequently extracted with a thin paste of 20 g. of calcium hydroxide in 200 ml. of water. The lime extract was diluted to 400 ml., filtered, and carbonated until the solution was just neutral to phenolphthalein. A clear solution

(11) C. K. Ingold, *Ann. Report Chem. Soc.*, **22**, 127 (1925).

(12) P. Barbier and G. Leser, *Bull. soc. chim.*, [3] **33**, 815 (1905).

was obtained by filtering hot with the aid of "hyflow" diatomaceous earth. Crystals of calcium β -hydroxyisovalerate separated after concentration to 250 ml. These weighed 9 g. (0.03 mole) when dried in vacuum over phosphoric anhydride at 70° but were contaminated with chloride. On adding the calcium salt to a solution of 34 g. of silver nitrate in 500 ml. of boiling water, silver β -hydroxyisovalerate precipitated immediately. To the mixture 3 g. of "hyflow" was added, and the mixture filtered hot. The light gray crystals which separated on cooling were filtered off and the original precipitate of the silver salt was extracted twice more with the mother liquor. The combined crystals of three such extractions (only a little precipitated the third time) were recrystallized out of 800 ml. of boiling water. The solid was a very light gray. The crystals were quite stable and were dried at 78° over phosphorus pentoxide; yield, 8.5 g. (0.04 mole). *Anal.* Calculated for $C_5H_8O_3Ag$: Ag, 48.1. Found: (by Volhard method), Ag, 48.0.

Perchloric Acid Solutions of Constant Ionic Strength.—The solutions of different acidity were made merely by adding different amounts of solid sodium hydroxide to portions of a perchloric acid solution of known concentration. The change in volume caused by this addition was neglected. No correction was applied for the effect of temperature on the volume since the change in volume from 82 to 110° is only 2%. The equilibrium constant is not affected by the volume change. These solutions then had the same ionic strength (within 2%) but different acid concentrations.

Method of Performing Hydrations and Dehydrations.—Dimethylacrylic acid solutions were made up to approximate concentration with standard perchloric acid and analyzed volumetrically by bromination. β -Hydroxyisovaleric acid solutions were made up to exact volume with the perchloric acid solution from a known weight of silver β -hydroxyisovalerate. 15.00 ml. aliquots of these solutions were pipetted into test-tubes with constricted necks and sealed off. They were then placed in an oil thermostat at temperatures of 82.45 ± 0.05 , 99.85 ± 0.05 , or $111.85 \pm 0.05^\circ$. Tubes were removed at different time intervals and quenched in ice water. The tip of the tube was broken and the contents washed into the flask used for analysis. The tubes in the latter part of any one run showed an appreciable pressure of carbon dioxide and evolved a very slight odor of isobutene on opening.

Method of Analysis.—This was essentially the same as that described previously.³ The bromination of the β,β -dimethylacrylic acid took place as rapidly as bromine was liberated with the result that bromination was complete as soon as the bromine color appeared. That the brominated product is stable is shown by the fact that the analysis does not change when 125% excess bromine is present for five minutes after the first appearance of the bromine color. The β -hydroxyisovaleric acid seemed to substitute about 0.5% when brominated under the conditions of the experiment.

Method of Performing Decarboxylations.—The solution of β,β -dimethylacrylic acid was made up by dissolving an approximate amount of the solid in pure water and standardizing the solution volumetrically. Solutions of the β -hydroxyisovaleric acid were made by adding a known

amount of the silver salt to an exactly equivalent amount of perchloric acid solution. The reaction was carried out in sealed tubes similar to that of the dehydration. The solutions were analyzed by titration with a standard sodium hydroxide solution to the phenolphthalein end-point with boiling to remove carbon dioxide as the end-point was approached. The silver ion was first precipitated by the addition of 5 ml. of one-half saturated sodium chloride since otherwise silver hydroxide would form before the phenolphthalein end-point was reached.

Isolation of *t*-Butyl Alcohol as the Decarboxylation Product.—Five grams of β,β -dimethylacrylic acid and 20 ml. of 2 *N* perchloric acid were sealed in a tube and heated at 100° for twenty hours. The pressure was released from time to time. At the end of that period some light oil seemed to be separating. The aqueous phase was separated, neutralized to phenolphthalein with sodium hydroxide and then distilled. The first portion of the distillate was saturated with potassium carbonate and the 1 ml. of oil which separated was dried with the carbonate. The boiling point was 80.0° uncor. When 0.25 ml. of this substance was mixed with 1.5 ml. of HCl-ZnCl₂ reagent,¹³ 0.25 ml. of a second oil which boiled at 50.5° uncor. was obtained. The constants in the literature for *t*-butyl alcohol and chloride are 82.9 and 51°, respectively.

The oil which separated in the original reaction mixture probably was polymerized isobutene for a similar oil was observed to separate when 5 ml. of *t*-butyl alcohol and 20 ml. of 2 *N* perchloric acid were heated under similar conditions.

Attempted Decarboxylation of Calcium β -Hydroxyisovalerate.—Twenty ml. of an aqueous solution containing about 10 g. of calcium β -hydroxyisovalerate was heated at 100° in a sealed tube for sixty hours. The mixture was distilled through a 2-ft. (61-cm.) Vigreux column with a reflux condenser. Only enough alcohol was present to give the first few drops a faint odor of *t*-butyl alcohol but no alcohol separated on saturating these drops with potassium carbonate. If the ion decarboxylates, one would expect essentially complete decomposition, even under milder conditions.

Summary

The acid catalyzed hydration of β,β -dimethylacrylic acid to β -hydroxyisovaleric acid was investigated in aqueous perchloric acid and sodium perchlorate solutions of hydrogen ion concentrations varying from 0.3 to 1.0 *N* and ionic strengths varying from 0.3 to 2.0 *N* at temperatures of 82.45, 99.85 and 111.85°.

The acid catalyzed dehydration of β -hydroxyisovaleric acid to β,β -dimethylacrylic acid was investigated in various perchloric acid and sodium perchlorate solutions at 99.85 and 111.85°.

The interpretation of the data of the hydration and dehydration reactions was complicated by the simultaneous decarboxylation of the β -hydroxyisovaleric acid to form *t*-butyl alcohol. The

(13) H. J. Lucas, THIS JOURNAL, 52, 802 (1930).

acid catalyzed decarboxylation was investigated under the same conditions as the acid catalyzed dehydration.

A mathematical treatment was developed to handle a system of reactions of the type $A \rightleftharpoons B \rightarrow C$, where the reaction rate constants are comparable.

The acid catalyzed hydration, dehydration and decarboxylation reactions are first order with respect to the organic acid concentration and first order with respect to the hydrogen ion concentration.

The reaction rate constants of these three reactions increase rapidly with ionic strength and slowly when sodium ion replaces hydrogen ion at constant ionic strength.

The uncatalyzed decarboxylation of β -hydroxyisovaleric acid in distilled water and in aqueous

sodium perchlorate solutions was investigated at 99.85 and 111.85°. The reaction is first order with respect to the organic acid. The constant is somewhat smaller than the constant for the acid catalyzed decarboxylation, and increases moderately with ionic strength. Decarboxylation involves the free acid and not the anion.

The rate of decarboxylation of β,β -dimethylacrylic acid in pure water is negligible compared to that of β -hydroxyisovaleric acid.

The heat of activation of the hydration of β,β -dimethylacrylic acid essentially is not a function of ionic strength or hydrogen ion concentration.

For the hydration of dimethylacrylic acid, ΔH is -8.1 kcal. The correct value for crotonic acid is -5.4 kcal.

PASADENA, CALIFORNIA

RECEIVED MAY 7, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, CORNELL UNIVERSITY MEDICAL COLLEGE, AND THE GEORGE WASHINGTON UNIVERSITY SCHOOL OF MEDICINE]

A Simple Laboratory Method for Obtaining Preparations Containing Pressor and Oxytocic Activity from the Posterior Lobe of the Pituitary Gland

BY GEORGE W. IRVING, JR.,¹ AND VINCENT DU VIGNEAUD

The observation recorded in a previous paper² that practically all of the pressor and oxytocic activity contained in posterior lobes could be removed in the press juice obtained by subjecting the ground glands to high pressure in a hydraulic press, suggested to us that this method might be utilized for the extraction of the principles from glands on a preparative scale. Dry-ice frozen posterior lobes were thawed, ground with sand and subjected to pressure in a hydraulic press. The juice obtained, together with several washes of the sandy residue, was acidified with acetic acid. The mixture was heated for ten minutes in a boiling water-bath to precipitate inactive protein. The clear solution obtained by centrifugation was concentrated by evaporation in a stream of clean air at room temperature. The active material was precipitated from the concentrated solution by saturation with sodium chloride as described by Kamm and his associates.³ The dried salt-cake was extracted with

98% acetic acid, and the active material was precipitated from the acetic acid solution by means of ether and petroleum ether. This final product, which will be referred to as "ether precipitate," is a chalk-white, non-hygroscopic, water-soluble powder. It contains from 9 to 10 units of pressor and oxytocic activity per mg.

A comparison of the yield of active material obtained by the above procedure with the yields recorded in the literature for the extraction of acetone desiccated glands, shows that the present method compares favorably with previous procedures. Both Kamm, *et al.*,³ and Stehle and Fraser⁴ report that commercial acetone desiccated posterior lobes contain 1 unit of each activity per mg. They were able to obtain from this material a crude product which contained 80 to 90% of the initial activity. On this basis 1 kg. of fresh glands (approximately 160 g. of acetone desiccated powder) would yield by the procedures of Kamm, *et al.*, or Stehle and Fraser, a crude preparation containing about 135,000 units of each activity. By the procedure outlined in this paper, 1 kg. of frozen glands yields 13 g. of ether precipitate

(1) (a) Parke, Davis and Company Research Fellow. (b) Present address: The Rockefeller Institute for Medical Research, New York, N. Y.

(2) Irving and du Vigneaud, *J. Biol. Chem.*, **123**, 485 (1938).

(3) Kamm, Aldrich, Grote, Rowe and Bugbee, *THIS JOURNAL*, **50**, 373 (1928).

(4) Stehle and Fraser, *J. Pharmacol.*, **55**, 136 (1935).