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Kinetics and Mechanism of the Reactions of β-Isovalerolactone in Water[1]

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β-Isovalerolactone (I), stable in non-polar solvents, is rapidly decarboxylated in water, the decarboxylation rate being approximately doubled in 2.2 *M* perchloric acid with a catalysis linear in acid concentration. This lactone is hydrolyzed by hydroxyl ion at a slower rate than β-propio- or β-butyrolactone, but by water about a hundred times faster than the latter at 25° and by acid (following the Hammett H_0 function) about a thousand times faster than the secondary lactone. It is concluded that the mechanism of alkyl–oxygen fission makes its appearance in this tertiary lactone in both the water and the acid hydrolyses, and that the decarboxylation involves an initial ionic cleavage at the tertiary carbon atom. In water the yield of acid is 37%, of carbon dioxide 63% and of isobutylene 50%, with traces of *t*-butyl alcohol and diisobutylene. Most of the decarboxylation cannot be forestalled by strong nucleophilic competitors.

Introduction

β-Butyrolactone is attacked by neutral water at the β-carbon atom with inversion, while in acid or alkaline solutions its ring opening occurs at the carbonyl group by an ester hydrolysis mechanism.[2] The somewhat faster hydrolysis of β-propiolactone in aqueous sulfuric and perchloric acids follows the H_0 function, which fact is consistent with an $A_{Ac}1$ mechanism of hydrolysis.[3,4] With the recent availability of β-isovalerolactone from ketene and acetone[5] we have made a kinetic study of its hydrolytic behavior to learn how the tertiary character of the β-carbon atom influences the mechanism of lactone reactions.

Experimental

β-Isovalerolactone was provided by the B. F. Goodrich Co. Twice redistilled middle cuts were used, b.p. 58° (12 mm.), $n^{23}\text{D}$ 1.4092. The lactone was stored in a desiccator at 0–5° and used within a few days of distillation.

Dimethylformamide, du Pont practical grade, was dried over potassium hydroxide and distilled from fresh potassium hydroxide. Only the middle portion, boiling at 55° (21 mm.), was collected. A mixture of 50 cc. of this solvent with 50 cc. of water did not color phenolphthalein, and was rendered acid toward methyl red indicator by one drop of acetic acid.

Sodium benzenethiosulfonate was prepared by Dr. G. Lohaus from benzenesulfonyl chloride and sodium sulfide, according to the directions of Troeger and Linde,[6] and recrystallized from alcohol.

β-Carboxyethyl Benzenethiosulfonate.—Sodium benzenethiosulfonate (14.4 g., 0.073 mole) and β-propiolactone (5.45 g., 0.0755 mole) were dissolved in 50 ml. of methanol with cooling by tap water. After a few minutes one drop of the solution was acidified; the lack of any turbidity from decomposition of benzenethiosulfonic acid showed that the reaction was complete. The main solution was allowed to stand for one hour and then evaporated with a stream of air. The residue was dissolved in 40 ml. of cold water, 30 ml. of 6 *N* hydrochloric acid was added, and the solution extracted three times with 40-ml. portions of benzene. The benzene extracts were dried with sodium sulfate and filtered. Addition of 130 ml. of ligroin (60–90°) and seeding gave white crystals in a yield of 13.35 g. (74.4%), m.p. 70–74°. One recrystallization raised the melting point to 74–75°.

Anal. Calcd. for $C_9H_{10}O_4S_2$: C, 43.89; H, 4.09. Found: C, 44.01; H, 4.20.

Four grams (0.0162 mole) of β-carboxyethyl benzenethiosulfonate was dissolved in 30 ml. of 2 *N* sodium hydroxide and oxygen was bubbled through the solution for 1.5 hours. Acidification with 7 ml. of concentrated hydrochloric acid with ice-cooling and subsequent refrigeration for several hours gave fine crystals of bis-β-carboxyethyl disulfide, yield 1.55 g. (91%). Recrystallization raised the melting point to 154–156°.

Similar treatment of β-carboxyethyl thiosulfate with sodium hydroxide in water gave directly the disulfide melting at 150–153°. The yield was 40% after oxygenation for 1.5 hours, 55.5% after 24 hours of oxygenation, and 45% after one week. When the oxygenation was carried out on the steam-bath the yield of disulfide dropped to zero.

Determination of Products from Decomposition of β-Isovalerolactone.—In all the product studies the lactone was decomposed in a closed flask through which nitrogen was steadily bubbled and the effluent gas was carried through a suitable succession of traps and weighed absorption vessels. The reaction was started by dislodging a glass bucket containing a weighed amount of the lactone from a hook on the inside of a standard taper joint attached to the reaction flask. The nitrogen stream of about 1–2 large bubbles per second was maintained for 15 minutes before introducing the sample. The flask was then shaken vigorously to introduce the lactone and the system swept with nitrogen for 1.25 to 1.5 hours. Sweeping for more than one hour failed to increase the weight of the tared Ascarite tube in which the carbon dioxide was absorbed. Water was removed from the gas stream by a Dry Ice trap placed before Ascarite tubes; the efficiency of this trap was shown by the attainment of constant weight in the Ascarite tubes after about an hour of nitrogen sweeping. Chemical drying agents such as Anhydrone were avoided for their possible polymerizing effect on the olefin.[7]

For purposes of determining isobutylene among the products the absorption train consisted of an ice-cooled trap, an Ascarite tube and two weighed absorption tubes containing 96–98% sulfuric acid. The efficiency of this absorption system was shown by the very small gain in weight of the second sulfuric acid tube, *e.g.*, 0.7 mg., compared to 190.0 mg. in the first absorption tube. The sulfuric acid turned brown during absorption of the isobutylene and a layer of colorless oil collected on top.

For determination of the acid products of the hydrolysis of β-isovalerolactone the weighed lactone was allowed to stand with water in a closed system at 25° for two hours, which was forty times the half-life. The carbon dioxide was then removed by allowing a few milliliters of the solution to distil off under 20 mm. pressure from a bath at 50°. The solution was then titrated with standard sodium hydroxide, using phenolphthalein as an indicator.

The sum of the carbon dioxide content and the acid titer amounted to 100.2% of the theoretical, tending to confirm the purity of the lactone.

The acidic hydrolysis products were tested for unsaturation by the bromate–bromide titration of Pressman and Lu-

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[1] Presented in part at a Symposium of The Chemical Society on "Solvent Effects and Reaction Mechanism" at Queen Mary College, London, July 8, 1957.

[2] A. R. Olson and R. J. Miller, THIS JOURNAL, **60**, 2687 (1938).

[3] F. A. Long and M. Purchase, *ibid.*, **72**, 3267 (1950).

[4] C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 768.

[5] T. L. Gresham, J. E. Jansen, F. W. Shaver and W. L. Beears, THIS JOURNAL, **76**, 486 (1954).

[6] J. Troeger and O. Linde, *Arch. Pharm.*, **239**, 129 (1901).

[7] H. S. Lilley and G. L. Foster, *Nature*, **160**, 131 (1947).

cas[8] after an evacuation procedure to remove isobutylene. Pressman and Lucas established the rate of interconversion of β,β-dimethylacrylic acid and β-hydroxyisovaleric acid; such interconversion is much too slow to occur, under the conditions of our experiments, to any appreciable extent. The results in two experiments showed 1.2 and 1.4 mole %, respectively, of the acid product to be unsaturated. This amount is barely greater than the experimental error. This method tends to give high results on account of the substitution of bromine into β-hydroxyisovaleric acid.[8]

Isolation of Silver β-Hydroxyisovalerate from the Hydrolysis of β-Isovalerolactone.—β-Isovalerolactone (2.3 g., 0.023 mole) was dissolved in 100 ml. of distilled water and the solution allowed to stand for 1 hour. After evacuation to free the solution of carbon dioxide, it was neutralized to the phenolphthalein end-point with 4.1 ml. of 2.16 N sodium hydroxide. A few drops of nitric acid and 1.7 g. of silver nitrate in 10 ml. of water were then added, the solution heated to boiling, filtered hot, and cooled. The yield of white crystals amounted to 0.94 g. The amount expected from the sodium hydroxide titer was 1.87 g.; yield of silver salt, 50.2%. The silver salt is appreciably soluble in water.

Anal. Calcd. for $C_5H_9O_3Ag$: Ag, 48.0. Found: Ag (Volhard), 48.1, 48.1.

The Inequality between Carbon Dioxide and Isobutylene Found.—Only 50.3% of isobutylene was obtained from reactions yielding 63.3% of carbon dioxide. Several possible explanations of this were considered: (a) the formation of t-butyl alcohol, which would remain in the water phase; (b) formation of diisobutylene, which would be retained in the ice-trap; (c) formation of dimethylneopentylcarbinol; (d) a flaw in the analytical method.

An attempt was made to use Deniges reagent (50 g. of mercuric oxide in 200 ml. of sulfuric acid diluted to 1 liter)[9] to precipitate a solid derivative with t-butyl alcohol from the aqueous solution. A precipitate weighing from 3 to 6 mg. was obtained, which would account for only about 1% of the product as t-butyl alcohol.

By saturation of 50 ml. of the distillate from an aqueous hydrolysis with hydrogen chloride at ice temperature a product could be obtained which upon extraction into carbon tetrachloride gave a characteristic infrared spectrum. This spectrum was different from that of t-butyl chloride or of diisobutylene hydrochloride, but a product having the same spectrum could be produced by the treatment of either t-butyl alcohol or diisobutylene in aqueous solution with concentrated hydrochloric acid.

In another experiment 7 g. of β-isovalerolactone in 200 ml. of water at pH 6.8 was subjected to vacuum distillation until about 40 ml. had been collected. Saturation of this distillate with potassium carbonate and extraction with carbon tetrachloride yielded a solution which, on bromination, showed the infrared spectrum of diisobutylene dibromide.

Thus the indications are that small amounts of both t-butyl alcohol and diisobutylene may be in the hydrolysis product, but the amounts demonstrated do not account for the discrepancy in amount between carbon dioxide and isobutylene. There remains the possibility that the 96–98% sulfuric acid used in the absorption trap may have been too strong to retain the isobutylene quantitatively and that in consequence of hydride transfers as much as 20% of the olefin may have been converted into isobutane, isopentane and other volatile paraffins which escaped in the nitrogen stream.

Determination of k_{OH} (see derivation below).—For a run, a known amount of standard sodium hydroxide was added to a known volume of water, both carbonate free, in a 500-ml. round-bottomed flask and thermostated to 25.0°. A weighed sample of β-isovalerolactone in a small glass bucket was dropped in and the stoppered flask shaken vigorously. After two hours a known amount of standard sulfuric acid was added and the contents of the flask evacuated at 20 mm. and at 50° (bath temp.) until a small portion was distilled off, thus freeing the solution of carbon dioxide. The solution was then titrated with standard sodium hydroxide, using phenolphthalein indicator.

Standard solutions: 0.0957 N H_2SO_4, 0.1240 N NaOH

	Run 1	Run 2	Run 3
NaOH, ml.	25.00	20.00	15.00
Water (for diln.), ml.	100.00	100.00	100.00
Lactone, g.	0.2218	0.1430	0.1245
H_2SO_4, ml.	35.00	20.00	15.00
NaOH (back titrn.), ml.	5.34	2.71	2.27
a (NaOH, M)	0.02480	0.02067	0.01617
c_0 (lactone, M)	.01773	.01190	.01082
x ($CO_3^=$, M)	.00652	.00436	.00466
y ($C_4H_9OCOO^-$, M)	.01120	.00755	.00616
$2x + y$ (M)	.02425	.01626	.01547
k_{OH^-} (l. mole^{-1} sec.$^{-1}$)[a]	.221	.221	.219

[a] The value of k_{OH^-} was obtained from graphical solution of the equation, av. k_{OH^-} = 0.220 l. mole^{-1} sec.$^{-1}$.

Kinetic Measurements.—The decomposition of β-isovalerolactone was followed by manometric determination of the evolved carbon dioxide in an apparatus of the same design as was used recently in this Laboratory in the study of the Leuchs anhydrides.[10] The single outlet of the reaction vessel was sealed to a mercury manometer and the attainment of liquid–vapor equilibrium was promoted by a magnetic stirrer which was actuated through the flask and through the beaker containing the thermostated water. After evacuation of the system and thermal equilibration for 15 minutes the lactone was introduced by dislodging the glass bucket, as previously described. The flask was shaken to effect rapid solution, returned to the bath and the magnetic stirrer started. Because of the first-order kinetics, the zero point of time could be defined arbitrarily as that of the first pressure measurement.

In the acid solutions, it was found that the pressure reached a certain point and then dropped somewhat. This pressure drop could not be due to leakage, since the pressure inside the system was less than that outside. It was probably due to re-absorption of the isobutylene into the acidic solution which was capable of slowly hydrating it. The final pressure in these cases was estimated by graphical extrapolation and was usually within 1 mm. of the highest reading near the end of the run.

Results and Discussion

Reaction Products of β-Isovalerolactone in Water at 25°.—Carbon dioxide is immediately evolved on solution of β-isovalerolactone in water under neutral or acidic conditions. The carbon dioxide evolution from a 0.117 M solution of lactone in pure water amounted to 63.0% and from a 0.159 M solution in a $^1/_{30}$th M phosphate buffer of pH 6.8, the carbon dioxide evolved was 63.7%. The effect of the addition of perchloric acid up to 3.9 M upon the carbon dioxide yield is shown in Fig. 1 and the effect of added salt on the carbon dioxide yield is shown in Fig. 2. Concurrent with the decarboxylation is a hydrolysis to β-hydroxyisovaleric acid, which was identified as its silver salt and estimated quantitatively by titration with standard base, following complete reaction. Three determinations showed 37.4, 37.3 and 36.0% yields of β-hydroxyisovaleric acid, the average being 36.9%. Thus, normal hydrolysis is the only reaction competing with decarboxylation.

It would be expected that the carbon dioxide would be accompanied by an equal amount of isobutylene. The absorption of this product in concentrated sulfuric acid yielded only 50.3% in 3 runs and attempts to account for the rest led only to the detection of traces of t-butyl alcohol and uncertain amounts of diisobutylene. The fact that the decarboxylation, though not involving water directly as a reagent, takes place rapidly in aqueous solution and not at all in non-polar solvents, and the small

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(8) D. Pressman and H. J. Lucas, THIS JOURNAL, **62**, 2069 (1940).

(9) R. F. Robey and N. C. Robertson, *Anal. Chem.*, **19**, 310 (1947).

(10) P. D. Bartlett and R. H. Jones, THIS JOURNAL, **79**, 2153 (1957).

TABLE I

ACID-CATALYZED HYDROLYSIS AND DECARBOXYLATION OF β-ISOVALEROLACTONE, 25.0°[a]

Run	$HClO_4$ (M)	10^3k	10^3k_D	10^3k_H	$10^3k_{H_2O}a_{H_2O}$	10^3k_a	$4 + \log k_a$	$-H_0$
11 runs	0	3.67	2.32	1.35				
94	0.100	3.76	2.26	1.50	1.34	0.16	0.205	−1.0
95	.340	4.07	2.32	1.75	1.33	.42	.624	−0.61
163	.413	4.94	2.86	2.08	1.32	.76	.882	− .51
160	.827	6.04	2.96	3.08	1.30	1.78	1.251	− .03
161	1.240	7.77	3.27	4.50	1.28	3.22	1.508	.29
162	1.654	10.00	3.48	6.52	1.25	5.27	1.722	.49
96	1.92	12.10	3.68	8.42	1.23	7.19	1.857	.60
170	2.23	16.6	4.35	12.25	1.20	11.0	2.042	.74
164	2.341	18.0	4.49	13.6	1.19	12.4	2.094	.78
172	2.63	22.4	4.70	17.7	1.16	16.5	2.218	.90
165	2.931	30.2	5.35	24.8	1.13	23.6	2.374	1.03
173	3.24	35.7	5.07	30.6	1.09	29.5	2.470	1.17
174	3.24	39.8	5.65	34.2	1.09	33.1	2.520	1.17
175	3.44	44.3	5.55	38.8	1.06	37.7	2.577	1.26
176	3.44	47.2	5.90	41.3	1.06	40.2	2.605	1.26
177	3.65	51.5	5.46	46.0	1.04	45.0	2.654	1.36
178	3.65	55.3	5.87	49.4	1.04	48.0	2.682	1.36

[a] All rate constants in sec.$^{-1}$; k = total rate constant; k_D = rate constant for decarboxylation; k_H = rate constant for hydrolysis (both water and acid catalyzed); k_{H_2O} = rate constant for hydrolysis in neutral solutions; a_{H_2O} = activity of water, Robinson and Baker, *Trans. Proc. Roy. Soc. New Zealand*, **76**, 250 (1946); $k_a = k_H - k_{H_2O}a_{H_2O}$ acid-catalyzed rate constant; $-H_0 = \log h_0$, values from L. P. Hammett and M. A. Paul, THIS JOURNAL, **56**, 827 (1934).

but definite positive salt effect on this reaction, indicate that a separation of charge is involved in the mechanism of the decarboxylation.

Rate of Hydrolysis and of Decarboxylation.—A kinetic analysis (see section on kinetic equations below) shows that although carbon dioxide is produced only in the decarboxylation reaction, the first-order rate constant obtained by measuring carbon dioxide evolution is the total rate constant for disappearance of β-isovalerolactone and, therefore, is the sum of the decarboxylation and hydrolysis rate constants. Under each set of conditions it is possible to estimate the separate rate constants for decarboxylation and hydrolysis by a combination of the over-all rate constants and the fractional yield of carbon dioxide. This has been done in Table I where the over-all velocity constant in sec.$^{-1}$ is resolved into k_D, the rate constant for decarboxylation, and k_H, the rate constant for hydrolysis. Figures 3 and 4 now show the effects of neutral salt and of perchloric acid, respectively, on the rate of decarboxylation of β-isovalerolactone. The effects are of the same order of magnitude, making it possible that perchloric acid may influence the decarboxylation of the lactone only in its capacity as a strong electrolyte. However, the effect of acid is roughly linear up to 4 molar, unlike that of neutral salt.

On the other hand, the effect of strong acid upon the hydrolysis of β-isovalerolactone is a much more powerful one and is best shown by plotting the logarithm of the rate constant against the Hammett acidity function H_0 of the solution. Such a plot is shown in Fig. 5 along with the similar data reported by Long and Purchase[3] for β-propiolactone and the results of Olson and Miller,[2] plotted in corresponding fashion.[11] In deducing the value

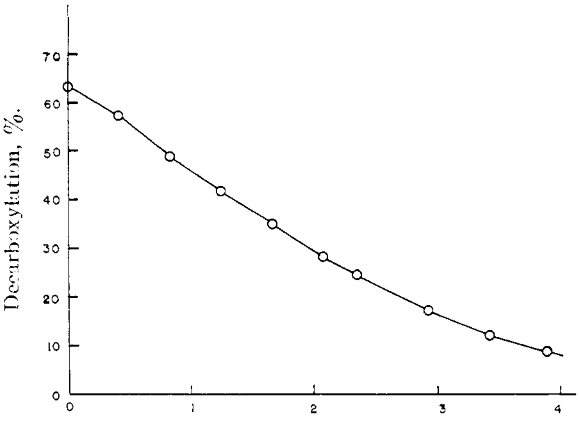

Fig. 1.—Effect of perchloric acid concentration on amount of decarboxylation of β-isovalerolactone.

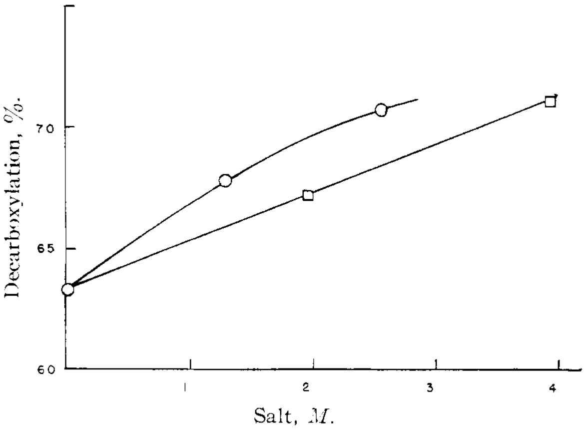

Fig. 2.—Effect of neutral salt on amount of decarboxylation of β-isovalerolactone: O, potassium nitrate; □, potassium chloride.

of k_a, which is plotted in Fig. 5, we have adopted the procedure of Long and Purchase, according to

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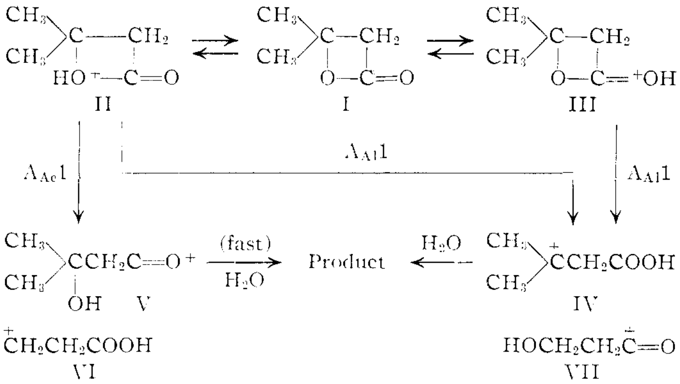
[11] In a similar plot, Long and Purchase[3] showed the line for β-butyrolactone as occurring *above* that for β-propiolactone. As we read the data of Olson and Miller, the points for the secondary lactone correspond to lower velocities than the corresponding ones for propiolactone and lie *below* the line for the latter.

which each observed rate constant is regarded as the sum of a rate due to water and a rate due to acid. From each experimental first-order rate constant, therefore, a value corresponding to the water rate is subtracted to obtain the value due to acid. Long and Purchase assumed that the rate due to water is the product of a water-rate constant by the activity of water and the correction accordingly decreases as the acid becomes more concentrated. We have followed this procedure, although we question the assumption on which it is based. Details of the correction procedure lose importance from the fact that in the strongly acid solutions where the magnitude of the correction is in question, the entire water-correction is only a few per cent. of the observed rate constant.

The lines in Fig. 5 are all drawn with unit slope; it is evident that the hydrolysis of β-isovalerolactone, like that of β-propiolactone, follows the H_0 function closely. This means that the rate of hydrolysis is controlled by the fraction of the lactone which is in the protonated form at equilibrium, and that the hydrolysis involves a first-order reaction of the protonated lactone, hence either the $A_{Ac}1$ or the $A_{Al}1$ mechanism.

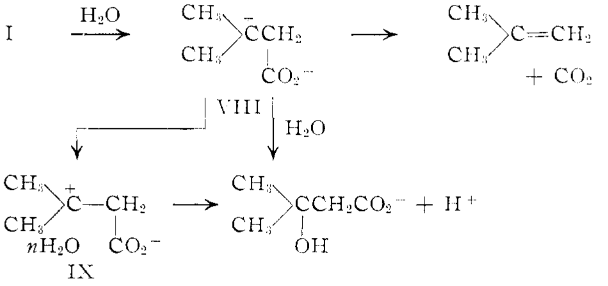


Protonation of β-isovalerolactone (I) can occur at either of the two oxygen atoms, leading to the two conjugate acids II and III, either one of which can undergo rate-determining cleavage by the $A_{Al}1$ mechanism to yield IV. Alternatively, II (but not III) can cleave by the $A_{Ac}1$ mechanism to yield V. In the case of β-propiolactone the counterparts of the intermediates IV and V are VI and VII, of which the former is quite improbable on account of its primary nature. This consideration and certain analogous cases of the $A_{Ac}1$ mechanism support Long and Purchase's assignment[3] of this mechanism to the case of β-propiolactone.

In the case of β-isovalerolactone an alkyl–oxygen cleavage is not so easily ruled out, since the tertiary β-carbon atom can well accommodate the positive charge in the intermediate IV. If the mechanism remained unchanged on going from propiolactone to isovalerolactone, one might expect β-butyrolactone to occupy something of a median position, with respect to its rate of hydrolysis, between propiolactone and the tertiary homolog. As seen from Fig. 5, there is a retardation from the primary to the secondary lactone, but a thousandfold increase in rate from the secondary to the tertiary. We interpret this to mean that in the tertiary lactone for the first time the $A_{Al}1$ mechanism becomes important and completely outstrips the $A_{Ac}1$ process which is relatively insensitive to substitution at the β-position of the lactone.[12]

Mechanism of the Decarboxylation.—Whereas β-isovalerolactone is stable indefinitely alone or in non-polar organic solvents, water rapidly brings about decarboxylation as the principal reaction. The main products, carbon dioxide and isobutylene, do not result from chemical reaction with water, and the conclusion seems clear that water produces this decarboxylation by acting as an ionizing solvent. An attractive possibility would be the formation of the dipolar ion VIII in a form involving exterior solvation by water, but no separation between the positive and negative centers, as in Winstein's "intimate ion pair."[13] One form of stabilization of this intermediate consists in the severance of the C–C bond liberating carbon dioxide and isobutylene, while another might be the reaction of the positive center with water to produce β-hydroxyisovalerate ion. If this reaction were of the nature of a direct displacement, all substitution reagents should be able to compete with the formation of carbon dioxide, and a really strong nucleophile should substantially reduce the carbon dioxide yield. Two pieces of evidence seem to indicate that this is not the case. Chloride ion up to 4 *M*, if anything, slightly increases the fraction of decarboxylation. In the presence of the rather strong nucleophile, ammonium dithiocarbamate, Gresham, Jansen, Shaver and Beears[5] obtained the related thiono-keto-thiazine in a yield of 34.3%, corresponding almost exactly to our yield of hydroxyacid in neutral solution with no diversion of material from decarboxylation.

On the other hand, an experiment with a 4.3 *M* solution of sodium thiosulfate gave ambiguous results. The yield of carbon dioxide was lowered to 52%, the lowest in any of our experiments, and the first-order rate constant was 13.5 × 10^{-3} sec.$^{-1}$, more than twice as great as in the presence of 4 *M* potassium chloride. However, since sodium thiosulfate is a unibivalent salt this would not be an unexpected effect for it to have upon a reaction strongly subject to kinetic salt effects. We can at least say that both β-isovalerolactone and the



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[12] The $A_{Al}1$ mechanism appears also in tertiary esters; S. G. Cohen and A. Schneider, THIS JOURNAL, **63**, 3382 (1941).

[13] S. Winstein, E. Clippinger, A. H. Fainberg and G. C. Robinson, *ibid.*, **76**, 2597 (1954); S. Winstein, E. Clippinger, A. H. Fainberg, R. Heck and G. C. Robinson, *ibid.*, **78**, 328 (1956).

dipolar ion VIII, in sharp contrast to β-propio- and butyrolactones, are quite insensitive to attack by the thiosulfate ion. These facts could be accommodated within a Winstein sequence in which the externally solvated dipolar ion VIII undergoes about half cleavage and half conversion into the solvent separated dipolar ion IX. The species IX in turn may both cleave and suffer attack by water and other nucleophilic reagents. The fate of VIII is only slightly influenced by solutes. Attempts to avoid dipolar intermediates altogether fail to account for the unique role of water in promoting the decomposition of the lactone into products in which water is not involved.

The effect of perchloric acid upon the rate of the decarboxylation (Fig. 4) is of a quite different form from its effect upon the hydrolysis, as well as being of a much lower order of magnitude. If this is not an electrolyte effect, it could be a weak "specific oxonium ion catalysis." A reaction in which the carboxyl group is directly displaced by a hydrogen ion would perhaps account at the same time for the mild enhancement of the decarboxylation rate by acid and for a non-equivalence in the amounts of carbon dioxide and isobutylene, with more *t*-butyl alcohol being formed than would arise from the hydration of the product isobutylene under the conditions.

It is obvious that, whereas the dipolar ions VIII and IX can stabilize themselves by the C–C cleavage that leads to decarboxylation, the protonated species II and III cannot do so; therefore strong acid increases the hydrolysis out of proportion to the decarboxylation.

β-Isovalerolactone appeared to be stable in dimethylformamide solution, but underwent decarboxylation in formamide at 26° with $k_D = 1.11 \times 10^{-4}$ sec.$^{-1}$, about 5% of the water rate.

Kinetic Equations.—Let

c = concentration of lactone, moles/l.
x = moles/l. of lactone decarboxylated at time t
y = moles/l. of lactone hydrolyzed at time t
k_D = rate constant for decarboxylation
k_H = rate constant for hydrolysis

Let subscripts 0 and ∞ denote conditions at the beginning and end of the reaction, respectively. Then

$$x = \frac{k_D}{k_D + k_H}(c_0 - c) = x_\infty - \frac{k_D}{k_D + k_H}c$$

whence

$$c = \frac{k_D + k_H}{k_D}(x_\infty - x)$$

Therefore

$$dx/dt = k_Dc = (k_D + k_H)(x_\infty - x)$$

and since

$$\ln \frac{x_\infty}{x_\infty - x} = (k_D + k_H)t$$

and x is proportional to the pressure p of carbon dioxide, it follows that

$$\ln \frac{p_\infty}{p_\infty - p} = (k_D + k_H)t$$

Thus the manometric method, though measuring only carbon dioxide, gives the *total* rate constant $k_D + k_H$. The separate values of these constants are determined by combining the measurement of carbon dioxide yield with that of the rate, since

$$(\% \text{ yield of } CO_2) = 100\frac{k_D}{k_D + k_H}$$

In considering the reaction in strong base, the following additional quantities enter. Each carbon dioxide molecule reacts with two hydroxyl ions to yield carbonate ions at concentration x, consuming $2x$ hydroxyl ions. Each hydroxyisovaleric acid molecule consumes one hydroxyl ion in neutralization. Therefore

$$dx/dt = k_D(c_0 - x - y)$$
$$dy/dt = k_H(c_0 - x - y) = k_{H_2O}(c_0 - x - y) + k_{OH^-}(c_0 - x - y)(a - 2x - y)$$

where k_{H_2O} and k_{OH^-} are the first-order rate constant for hydrolysis by water and the second-order rate constant for hydrolysis by hydroxyl ion, respectively, and a is the initial concentration of hydroxyl ion. Then

$$dy/dx = \beta(a + \alpha - 2x) - \beta y$$

where $\alpha = k_{H_2O}/k_{OH^-}$ and $\beta = k_{OH^-}/k_D$. By integration

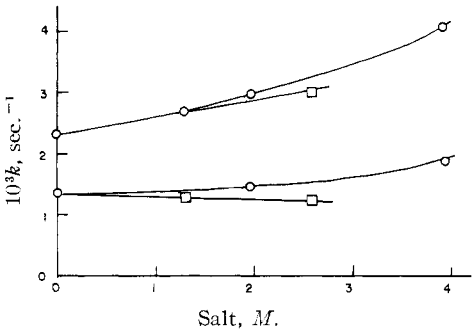

Fig. 3.—Effect of neutral salt on rate constant for decarboxylation (upper curves) and hydrolysis (lower curves): ○, potassium chloride; □, potassium nitrate.

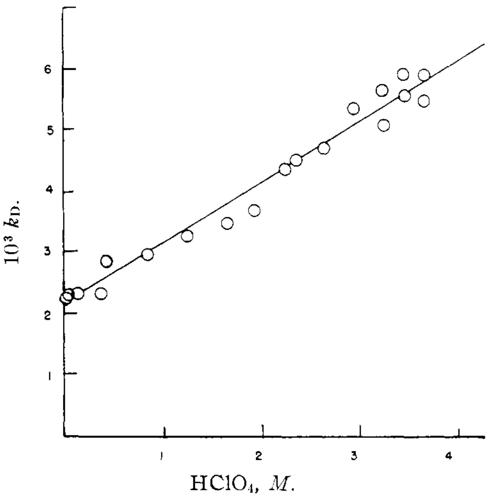

Fig. 4.—Effect of perchloric acid concentration on rate of decarboxylation of β-isovalerolactone.

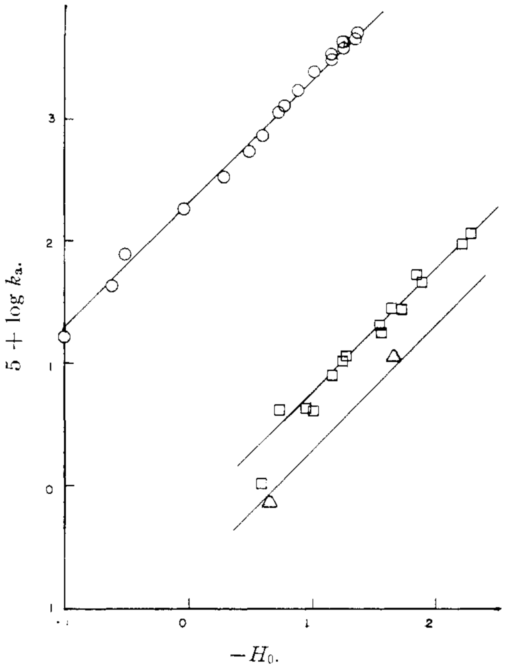

Fig. 5.—Effect of acidity on rate constant of hydrolysis of β-isovalerolactone (upper line, circles), β-propiolactone (middle line, squares) and β-butyrolactone (lower line, triangles).

$$y = a + \alpha - 2x + \frac{2}{\beta} - \left(a + \alpha + \frac{2}{\beta}\right) e^{-\beta x}$$

At the end of a reaction between a known amount of lactone and a known amount of sodium hydroxide solution, the β-hydroxyisovaleric acid can be determined by titration, the carbon dioxide by difference, and hence α and β can be determined, leading to a measurement of k_{OH^-} from only product ratios and the known values of k_D and k_{H_2O}. Three determinations at different concentrations of sodium hydroxide yielded $k_{OH^-} = 0.220 \pm 0.001$ l. mole^{-1} sec.$^{-1}$.

Table II compares the values of k_{H_2O}, k_a/h_0 and k_{OH^-} for β-propio-, β-butyro- and β-isovalerolactones.

The sequence of values of k_{OH^-} is that to be expected on the basis of a normal mechanism of attack by hydroxyl ion on the carbonyl group in each case.

TABLE II

RATE CONSTANTS IN WATER AT 25° FOR β-LACTONES

Lactone	k_{H_2O}, sec.$^{-1}$	k_{OH^-}, l./mole sec.	k_a/h_0, l./mole sec.
β-Propio-[3]	5.6×10^{-5}	1.2	5.8×10^{-6}
β-Butyro-[2]	1.4×10^{-5}	0.82	$\sim 2.3 \times 10^{-6}$
β-Isovalero-	1.35×10^{-3}	0.22	2.0×10^{-3}

Other Reactions of β-Isovalerolactone.—In agreement with Gresham, Jansen, Shaver and Beears, who found that aqueous ammonia and methylamine yielded only amides in reaction with β-isovalerolactone, we obtained no amino-acid from the reaction with *n*-butylamine in dioxane solution.

Sodium benzenethiosulfonate in methanol at room temperature and in dimethylformamide for two days gave no reaction with β-isovalerolactone, although with β-propiolactone the reaction in methanol at room temperature was over in a few minutes, giving a 74% yield of the expected β-carboxyethyl benzenethiosulfonate. This ester, relatively stable in neutral and acidic solutions, is cleaved quantitatively by alkali. After bubbling oxygen through an alkaline solution of the thioester, bis-β-carboxyethyl disulfide was isolated in 91% yield.

The effect of a β-substituent in β-propiolactone upon the rate of reaction with thiosulfate was determined by a few measurements on β-caprolactone which, for reasons of solubility, could not be run in pure water. Both this lactone and β-propiolactone were studied in a solution consisting of 75% dimethylformamide and 25% water. The rate constants were 1.39×10^{-3} and 1.1 l./mole sec., respectively, showing a retarding effect of about a thousandfold due to the propyl group. The fact that β-propiolactone reacts with thiosulfate in this solvent about six times faster than in water is probably associated with a lower degree of hydration of the thiosulfate ion.

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