propyl esters, and those for the branched butyl esters are generally lower than those for primary butyl esters. The variations among the isomeric butyl lactates are much greater, however, than are the differences between members of the corresponding butyl acetates and benzoates. Nevertheless, in all cases a pronounced minimum in the *PZ* factor among the butyl esters is encountered with the *s*-butyl compound. Examination of Fisher–Hirschfelder models reveals the possibility that more mechanical interference with the approach of the attacking hydroxyl group to the carbonyl carbon may be offered by a *s*-butyl ester than by other butyl esters and that the low *PZ* factors may be subject to interpretation on this basis.

A comparison of the data for ethyl, *n*-propyl, β-methoxyethyl and β-chloroethyl lactates demonstrates that substitution of a β-hydrogen atom of the ethyl group of ethyl lactate produces no significant effect of E_a. The rate increases resulting from β-methoxy and β-chloro substitution are caused by increased *PZ* factors.

DEPARTMENT OF CHEMISTRY
CARNEGIE INSTITUTE OF TECHNOLOGY
PITTSBURGH 13, PENNSYLVANIA

The Hydrolysis of Some Alkyl Lactates. II. "Neutral" and Acid Hydrolyses[1]

BY A. ALBERTO COLON, KENNETH H. VOGEL AND J. C. WARNER

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An investigation of the kinetics of the acid hydrolyses of certain alkyl and substituted alkyl lactates, initiated several years ago,[2] has now been completed, and the effects of lengthening, of branching and of substituting the alkyl carbon chain upon the activation energies and frequency factors are reported in this paper. Studies on the "neutral" hydrolyses of some *n*-alkyl lactates are also reported.

Experimental Method

The sources and methods of purification of the lactic esters, the preparation and care of reagents and solutions and the precision of thermostatic controls were described in the preceding paper.[3] To start a hydrolysis a Victor Meyer bulb containing a known amount of ester was placed in a flask together with the amount of standard hydrochloric acid (acid hydrolysis) or water ("neutral" hydrolysis) necessary to give the desired ester concentration. In the case of the *n*-alkyl lactates, each solution was allowed to reach the temperature of the thermostat before the bulb was broken, but with most of the other lactates the bulb was broken *in* the catalyzing acid before the flask was placed in the thermostat. Aliquot portions of solutions of the *n*-alkyl esters were discharged into sufficient standard sodium hydroxide solution to neutralize just the catalyzing hydrochloric acid. Aliquot portions of solutions of the other lactates were discharged onto washed cracked ice. Excess acid (acid hydrolysis) or total acid ("neutral" hydrolysis) was titrated with standard sodium hydroxide solution using cresol red indicator. Time was measured with an electric stop-watch.

Second-order rate constants for the acid hydrolyses were evaluated from the slopes of plots of log $1/(a - x)$ *vs.* time in accordance with the pseudo first-order rate equation

$$k = \frac{2.303}{ct} \log \frac{1}{a - x} + \text{constant}$$

in which a represents the initial concentration of ester, x the concentration of lactic acid at time t, and c the essentially constant total acid concentration. Second-order rate constants for the "neutral" hydrolyses were evaluated from the slopes of the plots of log $(a^{1/2} + x^{1/2})/(a^{1/2} - x^{1/2})$ *vs.* time in accordance with the rate equation

$$k = \frac{2.303}{(ab)^{1/2}t} \log \frac{a^{1/2} + x^{1/2}}{a^{1/2} - x^{1/2}} + \text{constant}$$

in which a is the initial concentration of ester and x the concentration of acid formed at time t; the value of b, the ionization constant of lactic acid, was taken from the work of Martin and Tartar.[4] This rate equation is obtained by integrating: $dx/dt = k(a - x)(bx)^{1/2}$. The units of all rate constants are liters/mole^{-1} min.$^{-1}$.

Results and Discussion

In Table I, the second-order rate constants (k), activation energies (E_a), and *PZ* factors for the acid hydrolyses of nine lactic esters are given. Table II shows similar data for the "neutral" hydrolyses of four *n*-alkyl lactates.

TABLE I

ACID HYDROLYSES

Lactate	$10^3k_{30°}$	$10^3k_{40°}$	$10^3k_{50°}$	E_a, cal.	$PZ \times 10^{-8}$ (using $k_{30°}$)
Methyl	9.48	20.11		14150	1.55
Ethyl	10.01	20.69		13700	0.77
n-Propyl[a]	9.73	20.35		13700	0.72
n-Butyl	8.70	18.27		14000	1.04
Isobutyl	10.61	23.97	51.13	15300	11.47
s-Butyl	5.41	11.95	26.07	15300	5.66
t-Butyl	6.75	22.46	81.18	24200	1.77×10^7
2-Methoxyethyl	8.39	17.69		14050	1.15
2-Chloroethyl	5.63	12.15		14500	1.61

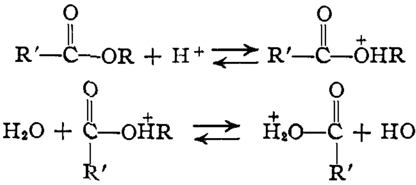
[a] $k_{60°} = 7.899 \times 10^{-2}$.

TABLE II

"NEUTRAL" HYDROLYSES

Lactate	$10^3k_{40°}$	$10^3k_{60°}$	E_a, cal.	$PZ \times 10^{-8}$ (using $k_{40°}$)
Methyl	25.90	118.08	15700	23.10
Ethyl	23.77	113.30	16200	47.49
n-Propyl	22.66	111.50	16500	73.42
n-Butyl	38.28	186.70	16400	105.5

With the exception of the case of *t*-butyl lactate, the pseudo first-order kinetics and the similarity among activation energies and *PZ* factors for the acid hydrolyses of the lactic esters listed in Table I are consistent with the mechanism proposed by Day and Ingold[5] (termed "bimolecular acid hydrolysis with acyl–oxygen fission" and labeled A′2) and by Roberts[6] (labeled II).



$$\mathrm{R'{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}OR} + \mathrm{H^+} \rightleftharpoons \mathrm{R'{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}\overset{+}{O}HR}$$

$$\mathrm{H_2O} + \mathrm{\underset{\underset{\displaystyle R'}{|}}{\overset{\overset{\displaystyle O}{\|}}{C}}{-}\overset{+}{O}HR} \rightleftharpoons \mathrm{H_2\overset{+}{O}{-}\underset{\underset{\displaystyle R'}{|}}{\overset{\overset{\displaystyle O}{\|}}{C}}} + \mathrm{HOR}$$

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[1] Abstracted from theses submitted by A. A. Colon and K. H. Vogel to the Committee on Graduate Degrees, Carnegie Institute of Technology, in partial fulfillment of the requirements for the D.Sc. degree.

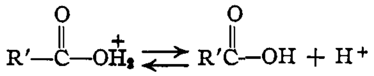
[2] A. A. Colon and J. C. Warner, *Bol. oficial asoc. quim. Puerto Rico*, **2**, No. 2, 15 (1943).

[3] K. H. Vogel and J. C. Warner, THIS JOURNAL, **75**, 6072 (1953).

[4] A. W. Martin and H. V. Tartar, *ibid.*, **59**, 2672 (1937).

[5] J. N. E. Day and C. K. Ingold, *Trans. Faraday Soc.*, **37**, 686 (1941).

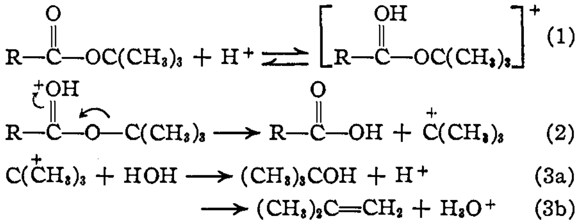
[6] I. Roberts, *Ann. N. Y. Acad. Sci.*, **39**, 375 (1940).



$$R'-\overset{O}{\overset{\|}{C}}-\overset{+}{O}H_2 \rightleftharpoons R'\overset{O}{\overset{\|}{C}}-OH + H^+$$

This series of reversible processes involves first a fast attachment of hydrogen ion to the alkyl oxygen atom of the ester, forming an oxonium ion. In a slow step, the electrophilic carbonyl atom of the oxonium ion is then attacked by a water molecule and a molecule of alcohol is expelled. The resulting oxonium ion rapidly loses a proton to form a carboxylic acid.

The *PZ* factor for the acid hydrolysis of *t*-butyl lactate is about 10^7 times larger than those for the other lactates, and the energy of activation is about 9 kcal./mole greater than the values for the remaining esters. Palomaa, *et al.*,[7] and Drushel and Dean[8] have measured rate constants for the acid hydrolyses of some alkyl acetates. Activation energies and *PZ* factors calculated from their data disclose that these values for the reaction involving *t*-butyl acetate exceed the values for the other acetic esters by about the same margin as that observed in our work on the lactic esters. It is therefore reasonable to assume that the mechanism for the acid hydrolysis of *t*-butyl esters is different from that which characterizes the acid hydrolysis of primary and secondary alkyl esters. Cohen and Schneider[9] have shown that *t*-butyl 2,4,6-trimethylbenzoate undergoes acid-catalyzed methanolysis by alkyl–oxygen fission and have reported evidence suggesting *t*-butyl esters suffer alkyl–oxygen fission on acid hydrolysis. Their mechanism for the alcoholysis is readily adapted to the hydrolysis of *t*-butyl esters.



$$\begin{aligned}
&R-\overset{O}{\overset{\|}{C}}-OC(CH_3)_3 + H^+ \rightleftharpoons \left[R-\overset{OH}{\overset{\|}{C}}-OC(CH_3)_3\right]^+ && (1)\\
&R-\overset{+OH}{\overset{\|}{C}}-O-C(CH_3)_3 \longrightarrow R-\overset{O}{\overset{\|}{C}}-OH + \overset{+}{C}(CH_3)_3 && (2)\\
&\overset{+}{C}(CH_3)_3 + HOH \longrightarrow (CH_3)_3COH + H^+ && (3a)\\
&\qquad\qquad\qquad\;\; \longrightarrow (CH_3)_2C{=}CH_2 + H_3O^+ && (3b)
\end{aligned}$$

This process involves the rapid reversible addition of a proton to the acyl oxygen atom of the ester, forming an oxonium ion which yields the carboxylic acid by the slow irreversible loss of the *t*-butylcarbonium ion. The latter may then be converted by water to *t*-butyl alcohol or through the loss of a proton to isobutylene; recent evidence[10] suggests that alcohol formation 3a should predominate over olefin formation 3b under the chosen conditions. It seems probable that steps 2 and 3 are not actually separate and distinct but are the components of a concerted process.

Comparison of the data for the acid hydrolyses of the *n*-alkyl lactates (Table I) and the data reported by Palomaa[7,11] and by Salmi[12] for the corresponding acetates demonstrates that increasing the length of the primary alkyl chain has little effect on the activation energy or the *PZ* factor for this reaction. However, sensible effects of chain branching may be observed. Branching by methyl at the β-position (isobutyl lactate) brings about an approximately tenfold increase in *PZ*, which is sufficient to cause a slight increase in the rate constants despite a simultaneous increase in E_a. Branching by methyl at the α-position (*s*-butyl lactate) likewise effects increases in both E_a and *PZ;* but in this case the former predominates, and the rate constants decrease. Substitution of a β-hydrogen atom in the ethyl group of ethyl lactate by a methyl, an ethyl, or a methoxy group brings about only very small progressive decreases in the velocity constants. Substitution by a β-chlorine atom brings about a somewhat larger decrease in rate, the result of an increased E_a.

The kinetic behavior of the four *n*-alkyl lactates on "neutral" hydrolysis (Table II) is in harmony with the assumption that the major reaction is really an acid hydrolysis in which the catalyzing acid is hydronium ion produced by the dissociation of the lactic acid formed during the reaction. However, the failure of the individual rate constants, E_a, and *PZ* values to agree with the values determined for the same compounds on acid hydrolysis suggests that the "neutral" hydrolysis is in fact a composite reaction of which the major component is acid hydrolysis but of which a hydrolysis reaction or reactions of some other type, possibly an internal displacement, also form a part. The anomalous behavior of *n*-butyl lactate in this series also suggests the operation of a competing hydrolysis reaction different from either acid or alkaline hydrolysis. Table II shows little change in velocity constants from methyl through *n*-propyl lactates on "neutral" hydrolysis. There is a progressive increase in both E_a and *PZ* through this series of compounds. However, the rate constants increase substantially in passing to *n*-butyl lactate, an effect caused largely by an increased *PZ* factor, as E_a is held constant. No such rate maximum for *n*-butyl lactate is found in either the acid or the alkaline hydrolysis.

Department of Chemistry
Carnegie Institute of Technology
Pittsburgh 13, Pennsylvania

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The Hydrolysis of Some Alkyl Lactates. III. Ethyl O-Acetyllactate and O-Acetyllactic Acid[1]

By A. Alberto Colon, Kenneth H. Vogel, Robert B. Carlin and J. C. Warner

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A number of investigations have been reported[2,3] on the kinetics of the hydrolysis of diesters in which the ester linkages are equivalent, but few studies have been made on diesters in which the linkages are not structurally equivalent. For this reason an investigation of the kinetics of the alkaline, acid and "neutral" hydrolyses of the diester, ethyl O-

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[1] Abstracted from theses by A. A. Colon and K. H. Vogel presented to the Committee on Graduate Degrees, Carnegie Institute of Technology, in partial fulfillment of the requirements for the D.Sc. degree.

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