CCLXXV.—*The Mechanism of, and Constitutional Factors controlling, the Hydrolysis of Carboxylic Esters. Part IV. Hydrolytic Stability Maxima of Some Dihydroxypropyl Esters of Aliphatic Acids.*

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This paper is a sequel to Part II (J., 1930, 1039) which recorded hydrocatalytic data for the hydrolysis of a series of esters, $R\cdot CO_2R'$, in which R' was varied whilst R was kept constant. We here submit similar data for a series of esters, $R_1\cdot CO_2R_1'$, in which R_1' is kept constant whilst R_1 is varied. In the former series, the groups R' were alkyl groups; and in the present series, the groups R_1 are also alkyl groups, in each ester identical with one of the groups R' of the former series. In the earlier series, dihydroxyethyl was selected as the constant radical R, in order to ensure that the esters should be readily soluble in water over a wide range of variation of R'; and in the present series, for similar reasons, dihydroxypropyl is the chosen form of the constant radical R_1'. Actually, it was found that *iso*propylidene-dihydroxypropyl esters, which are more easily purified than the parent dihydroxypropyl esters, are rapidly hydrolysed to the latter under the conditions of the dynamical investigation, and that this reaction can be completed before the first time-reading is taken; we therefore found it convenient to use *iso*propylidene derivatives throughout, but we regard the results as relating to the dihydroxypropyl parents.

The method of measurement and computation, which is designed to yield the hydrocatalytic data free from disturbance due to primary and secondary buffer effects, was described in Part II. It consists, in brief, of determining the v–$[H^{\cdot}]$–u relation * experimentally, and then expressing it in a form which permits the deduction of the $\{v\text{–}[H^{\cdot}]\}_{u=0}$ relation by extrapolation. Six esters of the form indicated above were examined in this way, and a consideration of the results, which are given in the experimental portion, is included in the more general discussion contained in Part V. There is one point, however, which may be noted here.

When the v_0–$[H^{\cdot}]$ functions were used to calculate k_H, it was observed that, for the four esters for which R_1 was a n-alkyl group, this quantity varied irregularly with homology. The nature of the variation may be expressed in the statement that if log k_H is plotted against the number of carbon atoms in R_1, a line joining the points would pass through a maximum at the second member and an

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* For nomenclature, see Part II (*loc. cit.*).

inflexion near the third. Direct measurements of k_H were therefore made for the four esters at two temperatures both differing considerably from that to which the v_0–[H˙] relations apply. These showed that, for all four esters, k_H exhibits the normal kind of variation with temperature, the log k_H–$(1/T)$ functions having nearly rectilinear form; furthermore, both sets of four measurements reproduced the anomaly revealed originally by the v_0–[H˙] functions (see Table VI). Despite this, but consistently with the considerations advanced in Part I (J., 1930, 1032), the values of p_H^* exhibit no such anomaly (see below and Part V).

EXPERIMENTAL.

(A) *Materials.*—As explained above, the dihydroxypropyl esters were used in the form of their *iso*propylidene derivatives, which were prepared by Fischer's method (*Ber.*, 1920, **53**, 1596) in accordance with details illustrated by the following example: A mixture of redistilled quinoline and freshly prepared, carefully fractionated *iso*propylideneglycerol (1 mol. each) was treated below 0° with pure freshly distilled propionyl chloride. After being kept overnight at 0°, the mixture was treated with ice and extracted with ether. The extract was washed at 0° as rapidly as possible successively with a slight excess of dilute sulphuric acid, a further small amount of the same reagent, water, dilute sodium hydrogen carbonate, and several portions of water. It was dried by shaking with anhydrous sodium sulphate, and the final fractionation of the ester (b. p. 98—99°/10 mm.) was controlled by quantitative saponification (Found: $C_2H_5{\cdot}CO{\cdot}$, 30·46, 30·20. Calc. for $C_9H_{16}O_4$: 30·33%).

(B) *Hydrolytic Stability Maxima. Method.*—The experimental method was essentially that described in Sections (B), (C), and (D) of the experimental portion of Part II (*loc. cit.*), except that a different procedure was followed in the preparation of the solutions for dynamical measurement. The object of the change was to bring about a complete elimination of the *iso*propylidene group before commencing the study of the fission of the acyl group; and for this purpose advantage was taken of the fact that the separation of the *iso*propylidene group is rapidly effected by acids, but not by alkalis, whereas the acyl group is rapidly split off by alkalis, but only slowly by acids. As, however, the rate of fission of the acyl groups by acids is not negligible, it is necessary to ensure that the amount of this fission which occurs under the conditions established to hydrolyse the *iso*propylidene residue is small enough to be included in the amount which it is intended to bring about in order to establish the buffer conditions to which the experiment relates. The following example illustrates the matter.

*iso*Propylidenedihydroxypropyl acetate (49·377 g.) was placed in the graduated flask A (Part II, *loc. cit.*) together with about 400 c.c. of water. The mixture was brought to 55°, shaken with 26·34 c.c. of 1·0034*N*-hydrochloric acid for 4 minutes, mixed with 44·04 c.c. of 0·9746*N*-sodium hydroxide, placed in the thermostat, and diluted to the calibration mark. This procedure is known to satisfy the necessary conditions for the following reasons. The *iso*propylidene ester is insoluble in water and remains unaffected by prolonged shaking with it at 55°; the dihydroxypropyl ester is, of course, readily soluble in water. Therefore when, within 1 minute from the time of the addition of hydrochloric acid, dissolution of the ester became complete, it may be assumed that conversion into the dihydroxypropyl ester was substantially complete. To give an ample safety margin, more than four times this period is allowed; and this procedure does not violate the second condition, *viz.*, that the liberation of acetic acid shall be sufficiently small, because it is possible to estimate, from the data of Section (E), that the acid liberated could not, under the conditions stated, amount to more than 1 mol. %, and in this experiment the intention is to liberate altogether about 6 mols. % in order to establish the buffer conditions. The subsequently added sodium hydroxide first neutralises the hydrochloric and acetic acids, and then makes up the total concentration of sodium acetate to the required value (3*N*/100) by the almost instantaneous hydrolysis of a further quantity of the dihydroxypropyl ester. Very shortly after the addition of the alkali, the solution passes through the neutral point and becomes faintly acid. From the data given it can be calculated that, at the moment of neutrality (supposing the volume to have been adjusted), the molar concentration of the dihydroxypropyl ester is 0·4960; and that, from this moment onward, the buffer salt concentration (c) is 0·0300.

(C) *Hydrolytic Stability Maxima. Results.*—In these measurements it was found convenient to use more dilute buffers than were employed in those described in Part II, and our normal practice was to use three buffer series with salt concentrations 0·03, 0·02, and 0·01. This gives a convenient separation of the v–p_H curves and renders the v–c curves capable of linear extrapolation. As illustration, the data for dihydroxypropyl acetate are assembled in Table I and plotted in Fig. 1 (full-line curves).

The figure shows that, as c increases, the minimal velocity increases and becomes displaced towards regions of lower hydrogen-ion concentration. From these curves the v–c curves can be plotted. They are shown in Fig. 2 for each 0·1 p_H unit from 4·4 to 5·4, and it is seen that points corresponding to the same p_H lie on a straight line. Since the salt effects must approximate still more closely to linearity as c is further diminished, these lines may be produced to the axis $c = 0$, the intercepts on which will yield velocities pertaining to the buffer-free medium. These velocities are shown by means of the broken curve in Fig. 1, and are compared in Table II with the requirements of equation (16) of Part II, in which the values used are $h_0 = 1{\cdot}23 \times 10^{-5}$, $u_0 = 0{\cdot}85 \times 10^{-5}$, $w_0 = 0{\cdot}00 \times 10^{-5}$.

Fig. 1.

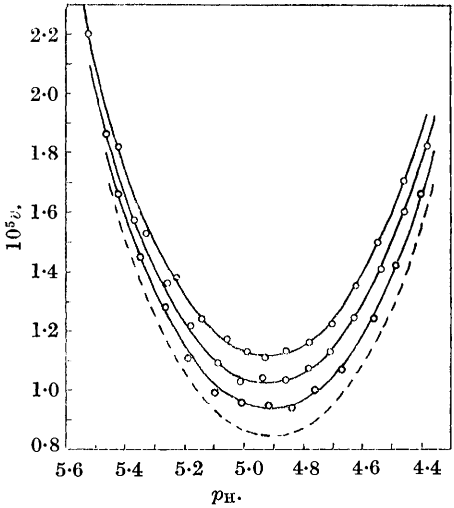


TABLE I.

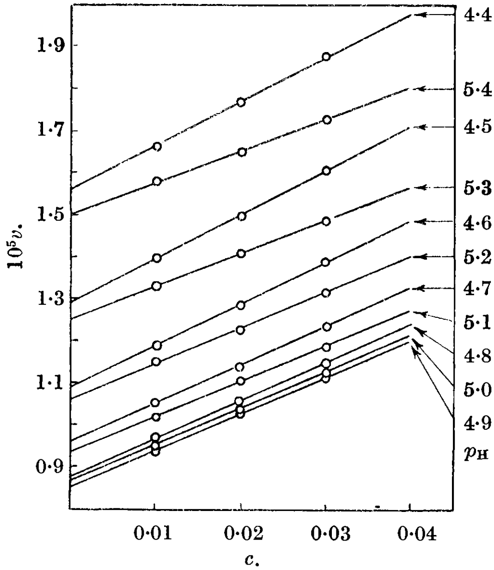
$c = 0{\cdot}0100$.		$c = 0{\cdot}0200$.		$c = 0{\cdot}0300$.	
p_H.	10^5v.	p_H.	10^5v.	p_H.	10^5v.
5·42	1·66	5·46	1·86	5·52	2·20
5·35	1·45	5·37	1·57	5·42	1·82
5·27	1·28	5·26	1·36	5·33	1·53
5·19	1·11	5·18	1·22	5·23	1·38
5·10	0·99	5·09	1·09	5·12	1·24
5·01	0·96	5·01	1·03	5·06	1·17
4·92	0·95	4·94	1·04	4·99	1·13
4·84	0·94	4·86	1·03	4·93	1·11
4·76	1·00	4·78	1·07	4·86	1·13
4·67	1·07	4·71	1·13	4·78	1·16
4·56	1·24	4·63	1·24	4·70	1·22
4·49	1·42	4·54	1·41	4·62	1·35
4·40	1·66	4·46	1·60	4·54	1·50
—	—	4·38	1·82	4·46	1·70

From the limiting slope at high p_H's, and the rate of increase of slope at low p_H's, of the curves in Fig. 2, it is possible to make rough

TABLE II.

$p_{\rm H}$	5·40	5·30	5·20	5·10	5·00	4·90	4·80	4·70	4·60	4·50	4·40
10^5v_0	1·50	1·25	1·06	0·93	0·86	0·85	0·88	0·96	1·09	1·29	1·55
10^5v_0 (calc.)	1·50	1·24	1·06	0·93	0·87	0·85	0·87	0·96	1·09	1·28	1·57
Diff.	±0·00	+0·01	±0·00	±0·00	−0·01	±0·00	+0·01	±0·00	±0·00	+0·01	− 0·02

FIG. 2.



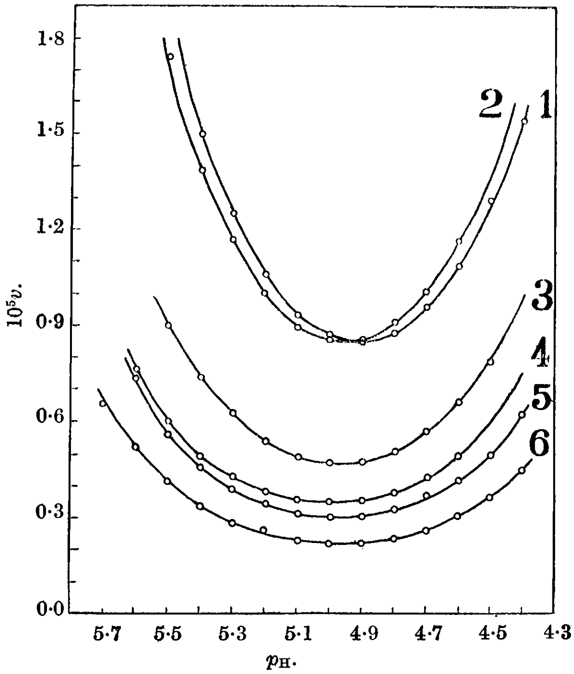
estimates (see Part II) of k_m and k_a. It appears that k_m is of the order of 10^{-6} and k_a of the order of 10^{-4}.

The v–$p_{\rm H}$ data ($v \times 10^5$) for the complete series of the esters investigated are summarised in Table III, and the extrapolated velocity values ($v_0 \times 10^5$) for buffer-free solutions are given in Table IV and shown graphically in Fig. 3.

The curves shown in conjunction with the data in Fig. 3 are the graphs of equation (16) of Part II for certain assumed values of the parameters u_0, h_0, and w_0. The values of w_0 are in all cases very small (of order not greater than 10^{-7}) and the curves are not sensitive to their absolute magnitudes; it is sufficient in practice to ascribe to w_0 the uniform value of zero. The adopted values of u_0 and h_0 correspond to the co-ordinates of the minima of the curves. They are given in Table V together with the corresponding values of $p_{\rm H}^*$ and $k_{\rm OH}/k_{\rm H}$.

Although the above figures are calculated by the method of Part II, it must be remembered that their significance is different from that attaching to the previous data. There it was noted that the velocities, even those pertaining to the buffer-free medium, relate, not to water as solvent, but to a $\frac{1}{2}M$-solution of ester in water. In the present case, the buffer-free solvent is at once a $\frac{1}{2}M$-solution of ester, a $\frac{1}{2}M$-solution of acetone, and a $0{\cdot}05M$-solution of sodium chloride. The remarks in Part II on the subject of solutes present in uniform concentration throughout the series of measurements apply without essential change to the present case.

FIG. 3.



1 = *Acetate*.
2 = *Propionate*.
3 = n-*Butyrate*.
4 = iso*Butyrate*.
5 = n-*Valerate*.
6 = iso*Valerate*.

(D) *Catalytic Coefficients for Hydrion. Method.*—These are calculable by known formulæ from the results tabulated in the preceding section, but in order to determine whether the peculiar position of the propionate, as revealed by these calculations, is an accidental result of the choice of temperature, direct determinations of k_H for the acetate, propionate, n-butyrate, and n-valerate were made at two other temperatures differing considerably from each

TABLE III.

100 c =	1	2	3	1	2	3	1	2	3
Ester	Acetate.			Propionate.			n-Butyrate.		
p_H.									
5·5	—	—	—	1·78	1·87	1·94	0·94	0·99	1·03
5·4	1·58	1·65	1·73	1·47	1·56	1·63	0·79	0·84	0·88
5·3	1·33	1·41	1·49	1·25	1·34	1·42	0·67	0·71	0·76
5·2	1·15	1·23	1·32	1·09	1·18	1·26	0·59	0·63	0·68
5·1	1·02	1·11	1·19	0·99	1·07	1·16	0·54	0·59	0·64
5·0	0·95	1·04	1·13	0·94	1·03	1·12	0·52	0·57	0·62
4·9	0·94	1·03	1·12	0·95	1·03	1·13	0·52	0·57	0·63
4·8	0·97	1·06	1·15	1·00	1·08	1·17	0·56	0·61	0·66
4·7	1·05	1·14	1·24	1·10	1·19	1·29	0·63	0·68	0·73
4·6	1·19	1·29	1·39	1·26	1·36	1·46	0·72	0·78	0·83
4·5	1·40	1·50	1·61	—	—	—	0·83	0·89	0·94
4·4	1·66	1·66	1·88	—	—	—	—	—	—
Ester	*iso*Butyrate.			n-Valerate.			*iso*Valerate.		
p_H.									
5·7	—	—	—	—	—	—	0·69	0·72	0·75
5·6	0·79	0·82	0·85	0·75	0·78	0·80	0·55	0·58	0·61
5·5	0·63	0·66	0·69	0·59	0·61	0·64	0·44	0·47	0·50
5·4	0·52	0·55	0·58	0·49	0·51	0·54	0·36	0·39	0·42
5·3	0·45	0·48	0·51	0·42	0·45	0·48	0·31	0·34	0·37
5·2	0·41	0·44	0·47	0·37	0·40	0·43	0·27	0·30	0·33
5·1	0·39	0·42	0·45	0·34	0·37	0·40	0·26	0·28	0·32
5·0	0·38	0·41	0·44	0·33	0·36	0·39	0·25	0·28	0·31
4·9	0·39	0·42	0·46	0·34	0·37	0·39	0·25	0·28	0·32
4·8	0·41	0·44	0·48	0·35	0·38	0·42	0·27	0·30	0·33
4·7	0·46	0·49	0·53	0·39	0·42	0·46	0·30	0·33	0·36
4·6	0·52	0·56	—	0·45	0·48	0·51	0·34	0·37	0·40
4·5	—	—	—	0·53	0·56	0·60	0·40	0·44	0·48
4·4	—	—	—	0·66	0·69	0·73	0·48	0·52	—

TABLE IV.

p_H	5·7	5·6	5·5	5·4	5·3	5·2	5·1	5·0	4·9	4·8	4·7	4·6	4·5	4·4
Ester.														
Acetate	—	—	—	1·50	1·25	1·06	0·93	0·86	0·85	0·88	0·96	1·09	1·29	1·55
Propionate	—	—	1·72	1·39	1·17	1·00	0·90	0·85	0·86	0·91	1·01	1·17	—	—
n-Butyrate	—	—	0·90	0·74	0·62	0·54	0·49	0·47	0·47	0·51	0·57	0·66	0·78	—
*iso*Butyrate	—	0·77	0·60	0·49	0·42	0·38	0·36	0·35	0·36	0·38	0·43	0·49	—	—
n-Valerate	—	0·74	0·56	0·46	0·39	0·34	0·31	0·30	0·30	0·33	0·37	0·42	0·50	0·62
*iso*Valerate	0·66	0·52	0·41	0·33	0·28	0·26	0·23	0·22	0·22	0·23	0·26	0·31	0·37	0·45

TABLE V.

Ester.	$u_0 \times 10^6$.	$h_0 \times 10^6$.	p^*_H.	$k_{OH}/k_H \times 10^{-2}$.
Acetate	8·5	12·3	4·910	8·90
Propionate	8·5	11·0	4·960	7·10
n-Butyrate	4·7	10·7	4·970	6·85
*iso*Butyrate	3·5	9·9	5·005	5·75
n-Valerate	3·0	10·7	4·970	6·85
*iso*Valerate	2·2	10·6	4·975	6·60

other and from that of the measurements recorded above. As the source of hydrions, $0{\cdot}1N$-hydrochloric acid was used, and this was relied on to complete the elimination of the *iso*propylidene residue before the commencement of the time-readings. As a control on the fulfilment of this condition, the velocities were computed in a way which would at once reveal any initial disturbance due to its not being satisfied, *viz.*, by plotting the logarithm of the ester concentration against time; in all cases accurate straight lines were obtained. In some cases the experiments were repeated in the presence of $0{\cdot}05M$-sodium chloride. This was done in order to justify comparison of the results with those recorded in Section (C), but it was found, in fact, that the addition of sodium chloride in this concentration made no perceptible * difference to the velocities.

(E) *Catalytic Coefficients for Hydrion. Results.*—These are recorded in the cols. 2, 3, and 4 of Table VI, from which it is apparent that at all these temperatures the propionate is hydrolysed more rapidly than its lower and higher homologues. These results, when plotted as $\log_{10}k_{\text{H}}$ against $1/T$, show that the equation $\log_{10}k_{\text{H}} = A - B/T$ is very approximately fulfilled, and the argument of Part V will suggest reasons for supposing that in this equation A is primarily a steric function of constitution, whilst B is fundamentally a polar function. Accordingly, it seems of interest to calculate these constants, and this has been done from the data for the two extreme temperatures (25° and 70°). The numbers are in Table VI, cols. 5 and 6. It will be seen that the peculiarity of the propionate disappears when these numbers are considered, both sets of figures showing unidirectional variation with homology. The critical energy increment can, of course, be calculated in the usual way ($E = 4{\cdot}571B$ g.-cals./g.-mol.). These matters were passed over in the introduction because it is hoped to discuss, in a later paper and on a broader basis, the constitutional significance of the high-temperature values, and the temperature derivatives, of velocities.

TABLE VI.

	k_{H}.				
Temp.	25°.	55°.	70°.		B
Ester.				A.	(°Abs.).
Acetate	$4{\cdot}10 \times 10^{-4}$	$4{\cdot}85 \times 10^{-2}$	$3{\cdot}47 \times 10^{-1}$	20·91	6650
Propionate	4·79 ,,	5·45 ,,	3·89 ,,	20·81	6600
n-Butyrate	2·93 ,,	3·00 ,,	2·19 ,,	20·10	6500
n-Valerate	2·24 ,,	2·09 ,,	1·38 ,,	19·37	6330

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* The difference is probably under 1%, the presumable limit of precision of the measurements of k_{H}.