# The Uncatalysed and the Metal-Ion Catalysed Decarboxylation of Oxaloacetic Acid

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The decomposition of oxaloacetic acid in aqueous solution into pyruvic acid and carbon dioxide is an example of the ketonic decomposition exhibited by β-keto carboxylic acids in general. From a kinetic study of the decarboxylation of a,a-dimethyl acetoacetic acid [1], the author of the present paper concluded that, in the decomposition of β-keto carboxylic acids, the keto-form of the acid (or its anion) decomposes spontaneously into carbon dioxide and an enol (or enolate ion) which, by a consecutive reaction, is transformed into the stable ketone. In the decarboxylation of oxaloacetic acid, we should therefore expect that the keto-form of the acid (or its uni- or divalent anion) decomposes spontaneously into carbon dioxide and an enol-form of pyruvic acid (or a corresponding anion) which, by a consecutive reaction, is transformed into ordinary pyruvic acid:

$$HOOC-CH_2-CO-COOH \rightarrow CO_2 + CH_2=COH-COOH \qquad (1)$$

$$CH_2=COH-COOH \rightarrow CH_3-CO-COOH \qquad (2)$$
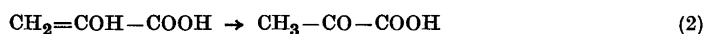
Steinberger and Westheimer [2] have confirmed this mechanism for the decarboxylation of a,a-dimethyl oxaloacetic acid.

The decarboxylation of oxaloacetic acid has been studied by biochemists [3-10] who have found that the rate of the spontaneous reaction depends upon the pH of the solution and has a maximum when pH is about 4, and that the reaction is catalysed (1) by enzymes, (2) by primary amines (like the decarboxylation of all other β-keto carboxylic acids), and (3) by certain metal ions (unlike the decomposition of β-keto monocarboxylic acids, but like that of some di- and tri-carboxylic acids, e.g. acetonedicarboxylic acid and oxalosuccinic acid).

In the present paper, the decarboxylation of oxaloacetic acid has been studied from a purely physico-chemical point of view. It was the object of the work to find out which molecular species (undissociated acid, uni- and divalent

oxaloacetate ion, and metal complexes of these ions) decompose spontaneously, and to give a quantitative interpretation of the rates from velocity constants for each of the unstable molecules. For that purpose, the uncatalysed reaction was examined in solutions of potassium and hydrogen chloride and in acetate buffers. The metal-ion catalysis was studied in solutions of potassium and hydrogen chloride containing in addition zinc chloride or cupric nitrate. In order to interpret the results in a satisfactory way, it was desirable to have better data for the dissociation constants of oxaloacetic and pyruvic acid than those already available. The dissociation constants of the two acids were therefore measured by means of the glass electrode. The results of these measurements have recently been published [11]. A preliminary report of some of the results of the kinetic study and the conclusions drawn from them has already been given [12].

Materials and experimental method. Oxaloacetic acid was prepared and purified in the same way as in the paper on the electrometric determination of the dissociation constants [11]. The molecular weight found by alkalimetry varied from 132.1 to 132.5 (calc. 132.1). The other chemicals were of analytical purity. The water, hydrochloric acid, and acetic acid were redistilled in an all-glass apparatus. Sodium acetate and cupric nitrate were recrystallised. The kinetic measurements were carried out at the temperature 37.0° C. The reaction was followed by observing the pressure above the solution by means of an apparatus described earlier [13]. Since P, the difference between the final pressure reading and the reading at the time t minutes after the start, is proportional to the concentration x of oxaloacetic acid present in the solution at the time t, we may write $P = \varphi x$. The constant φ may be calculated by means of the equation $P_o = \varphi x_o$, where P_o and x_o are the initial values of P and x.

UNCATALYSED DECOMPOSITION IN SOLUTIONS OF HYDROGEN AND POTASSIUM CHLORIDE

Three series of measurements were carried out. Within each series the total concentration s of hydrogen and potassium chloride was kept constant at 0.050, 0.100, and 0.200 molar, respectively, while the concentration h of hydrogen chloride was varied between s and zero. The oxaloacetic acid is in these solutions present partly in the form of undissociated acid (H_2Ox) and partly as univalent ion (HOx^-) and divalent ion (Ox^{--}). The velocity of decarboxylation may be written as follows

$$-\frac{dx}{dt} = k_o[H_2Ox] + k_1[HOx^-] + k_2[Ox^{--}]$$
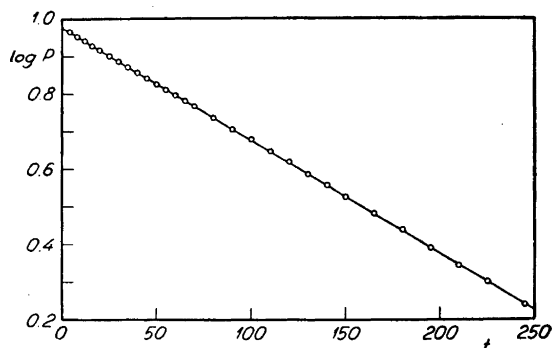$$= [k_o + (k_1 - k_o)\alpha_1 + (k_2 - k_o)\alpha_2]x$$

Fig. 1. Decomposition of oxaloacetic acid in 0.05 molar potassium chloride at 37.0° C. The diagram shows that the reaction obeys the first-order law.

where k_o, k_1, and k_2 are velocity constants for the spontaneous decarboxylation of the molecules H_2Ox, HOx^-, and Ox^{--}, while α_1 and α_2 are degrees of dissociation into the ions HOx^- and Ox^{--}, respectively. If we presuppose that the velocity constants k_o, k_1, and k_2 are not equal, the reaction will be of first order only if α_2 and α_1, and consequently also the hydrogen ion concentration, are constant during the reaction. In that case, the first-order constant for the total reaction will be

$$k = k_o + (k_1 - k_o)\alpha_1 + (k_2 - k_o)\alpha_2 \tag{3}$$

The measurements showed that the reaction followed the first-order law for all the solutions listed in Table 1. In order to demonstrate this we take as an example one of the solutions where the greatest deviation from the first-order law might be expected, namely 0.050 molar potassium chloride without hydrogen chloride. In Fig. 1, $\log P$ for the reaction in this solution has been plotted against t. The first-order law is obeyed since all the points fall close to a straight line. The numerical value of the slope is $k^* = 0.4343\ k$.

In Table 1 are given the composition of the solutions examined, their ionic strengths I, and the degrees of dissociation of oxaloacetic acid calculated by means of the dissociation constants. The subscripts o and ∞ denote that the values are, respectively, initial and final (that is, corresponding to a solution x_o molar with respect to the *keto*-form of pyruvic acid). In calculating the dissociation constants of oxaloacetic acid (K_1 and K_2) and pyruvic acid (K_{HPy}), the following formulae have been used:

$$-\log K_1 = 2.450 - 1.038\sqrt{I} + 0.86\ I \tag{4}$$

$$-\log K_2 = 4.359 - 2.076\sqrt{I} + 1.61\ I \tag{5}$$

$$-\log K_{HPy} = 2.420 - 1.038\sqrt{I} + 0.92\ I \tag{6}$$

The formulae have been found to hold [11] at the temperature 37° C for sodium chloride solutions, but it has been shown that it makes very little difference whether the solutions contain sodium or potassium chloride. It is seen from Table 1 that the initial and final values of a_1 are practically the same. The magnitude of a_1 during the reaction cannot be calculated since both the dissociation constant and the life-time of the enol-form of pyruvic acid are unknown,

Table 1. Decomposition of oxaloacetic acid (initial concentration x_0 molar) at 37.0° C in the solvent: h molar hydrogen chloride, (s—h) molar potassium chloride.

x_0	h	I	a_{10}	$a_{1\infty}$	a_2	$k*10^3$	$k*10^3$ calc.
Series 1 (s = 0.050):							
0.01514	0.0499	0.0515	0.0969	0.0968	0.0002	0.764	0.765
0.01514	0.03985	0.0518	0.1170	0.1168	0.0003	0.900	0.893
0.01533	0.02496	0.0526	0.1671	0.1666	0.0006	1.206	1.213
0.01515	0.00996	0.0543	0.2799	0.2782	0.0021	1.926	1.932
0.01514	0.00498	0.0554	0.3486	0.3466	0.0037	2.370	2.371
0.01508	0.00000	0.0570	0.4446	0.4432	0.0071	2.999	2.992
Series 2 (s = 0.100):							
0.01508	0.0998	0.1009	0.0581	0.0581	0.0001	0.523	0.521
0.01515	0.0499	0.1016	0.1077	0.1076	0.0003	0.845	0.839
0.01521	0.03985	0.1020	0.1294	0.1292	0.0004	0.969	0.978
0.01510	0.01994	0.1033	0.2118	0.2112	0.0012	1.487	1.506
0.01508	0.00498	0.1058	0.3681	0.3671	0.0048	2.517	2.513
0.01506	0.00000	0.1073	0.4612	0.4610	0.0089	3.133	3.120
Series 3 (s = 0.200):							
0.01518	0.1995	0.2005	0.0336	0.0336	0.0000	0.374	0.369
0.01514	0.1493	0.2007	0.0443	0.0443	0.0001	0.443	0.437
0.01518	0.0998	0.2010	0.0646	0.0646	0.0001	0.568	0.568
0.01512	0.0664	0.2014	0.0932	0.0932	0.0002	0.747	0.752
0.01512	0.0499	0.2018	0.1188	0.1187	0.0004	0.914	0.916
0.01537	0.03316	0.2026	0.1633	0.1630	0.0008	1.182	1.202
0.01520	0.02492	0.2031	0.1992	0.1989	0.0012	1.413	1.434
0.01515	0.01246	0.2045	0.2905	0.2900	0.0031	2.027	2.022
0.01534	0.00499	0.2062	0.3844	0.3844	0.0061	2.676	2.632
0.01500	0.00249	0.2068	0.4287	0.4295	0.0082	2.942	2.923
0.01525	0.00000	0.2077	0.4744	0.4764	0.0110	3.215	3.226
0.00762	0.00000	0.2049	0.5819	0.5875	0.0214	3.807	3.946
0.01223	0.00000	0.2067	0.5088	0.5117	0.0136	3.406	3.454
0.02041	0.00000	0.2093	0.4305	0.4316	0.0083	3.012	2.935
0.03015	0.02490	0.2057	0.1857	0.1851	0.0011	1.401	1.345
0.03015	0.00000	0.2118	0.3742	0.3739	0.0057	2.662	2.565

but from the fact that the first-order law holds we conclude that α_1 is practically the same all the time. It may be added that it has been found [11] that solutions of oxaloacetic acid which had been left for 24 hours at 37° C to complete decarboxylation, when measured with the glass electrode, gave the same e.m.f. (average deviation 0.0002 volts) as solutions of the same composition prepared directly from pyruvic acid. As seen from Table 1, α_2 is, for all the solutions examined, very small compared with α_1. Its variation during the reaction is therefore negligible.

The velocity constants k^* found from the measurements are given in the next to the last column of Table 1. In order to test equation 3 we calculate the last and very small term of this equation from $k_2^* = 1.8 \times 10^{-3}$ found in the next part of this paper and a preliminary value of k_o^*. We then plot $k^* - (k_2^* - k_o^*)\alpha_2$ against α_1 for all the solutions within each of the three series. The points fall for each series close to a straight line from which the constants k_o^* and $(k_1^* - k_o^*)$ are determined. The values of k_o^* and k_1^* found in this way are given in Table 2. It is seen that both velocity constants are nearly inde-

Table 2. Velocity constants for the spontaneous decomposition of undissociated oxaloacetic acid (k_0^*) and the univalent oxaloacetate ion (k_1^*) at the temperature 37.0° C.

Series	s	$k_0^* 10^3$	$k_1^* 10^3$
1	0.050	0.147	6.53
2	0.100	0.148	6.56
3	0.200	0.153	6.57

pendent of the salt concentration, and that the univalent ion decomposes about 44 times as fast as the undissociated acid. When the values of k_o^* and k_1^* given in Table 2 and $k_2^* = 1.8 \times 10^{-3}$ are introduced into equation 3 we calculate the values of k^* presented in the last column of Table 1. The agreement with k^* found directly from the measurements is good when x_o is about 0.015. For the last five solutions in the table, where x_o is either smaller or greater than 0.015, the difference between the calculated and measured values of k^* is somewhat greater than that corresponding to the usual experimental error.

UNCATALYSED DECOMPOSITION IN ACETATE BUFFER SOLUTIONS

Experiments were carried out in solutions of acetic acid (a molar) and sodium acetate (b molar). In three series of measurements, b was nearly 0.1, 0.2, and 0.3, respectively, while a within each series varied from about 0.1 to a little more than 0.6. In these solutions, the oxaloacetic acid is nearly completely dissociated into uni- and divalent ions; only from 0 to 2 % is undisso-

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ciated. Since, further, k_o is much smaller than k_1 and k_2, the contribution of the undissociated acid to the total rate of decomposition is negligible. We may therefore express the velocity as follows

$$-\frac{dx}{dt} = (k_1\alpha_1 + k_2\alpha_2)\ x \tag{7}$$

The reaction does not obey the first-order law since α_1 and α_2 vary during the decomposition. We shall attempt to compute the constant

$$k_\infty = k_1\alpha_{1\infty} + k_2\alpha_{2\infty} \tag{8}$$

from the measurements.

The degrees of dissociation α_1 and α_2 may be calculated when the dissociation constants of acetic acid (K_{HAc}), oxaloacetic acid, and pyruvic acid for the respective solutions are known. It is, however, sufficient to know the ratio

Table 3. *Dissociation constants of acetic acid (K_{HAc}), pyruvic acid (K_{HPy}), and oxalo-acetic acid (K_1 and K_2) at 37° C in s molar sodium chloride.*

s	$K_{HAc}10^5$	$K_{HPy}10^3$	K_110^3	K_210^4	K_{HAc}/K_2
0.1	2.79	6.55	6.19	1.37	0.204
0.2	3.06	7.24	6.95	1.77	0.173
0.3	3.20	7.45	7.24	1.97	0.162

Table 4. *Decomposition of oxaloacetic acid (initial concentration x_0 molar) at 37° C in the solvent: a molar acetic acid, b molar sodium acetate.*

x_0	a	b	α_{10}	$\alpha_{1\infty}$	α_{20}	$\alpha_{2\infty}$	$k_\infty*10^3$
Series 1:							
0.01526	0.6257	0.0996	0.609	0.594	0.368	0.386	4.745
0.01503	0.4173	0.0997	0.526	0.503	0.461	0.486	4.170
0.01503	0.2084	0.0997	0.382	0.348	0.612	0.648	3.407
0.01510	0.1042	0.0997	0.264	0.222	0.734	0.776	2.870
0.02004	0.1042	0.0997	0.298	0.240	0.699	0.758	2.892
0.01015	0.1042	0.0997	0.232	0.206	0.766	0.793	2.824
Series 2:							
0.01522	0.6263	0.1994	0.389	0.374	0.605	0.620	3.794
0.01503	0.4171	0.1994	0.304	0.288	0.692	0.710	3.285
0.01503	0.2086	0.1994	0.191	0.173	0.808	0.826	2.725
0.01501	0.1042	0.1992	0.118	0.101	0.882	0.899	2.331
Series 3:							
0.01501	0.6257	0.2991	0.278	0.267	0.720	0.731	3.329
0.01518	0.3128	0.2991	0.169	0.157	0.831	0.842	2.690
0.01526	0.1042	0.2991	0.074	0.064	0.926	0.936	2.210

K_{HAc}/K_2 accurately; the other constants are of minor importance in the calculation. Since the constants are not known accurately enough for a complete analysis of the results, we shall use them only where no great accuracy is essential. The initial and final values of α_1 and α_2 given in Table 4 have been computed from the dissociation constants presented in Table 3. The constants listed pertain to sodium chloride solutions with the same sodium ion concentration as the acetate buffers. K_1, K_2, and K_{HPy} have been calculated from formulae 4—6, while K_{HAc} has been estimated on the basis of the determinations of Harned and Hickey[14].

By means of equation 8, equation 7 may be written as follows

$$- \frac{dx}{dt} = (k_\infty + k_1(\alpha_1 - \alpha_{1\infty}) - k_2(\alpha_{2\infty} - \alpha_2))x \tag{9}$$

We introduce the approximation that α_1 and α_2 vary linearly with x:

$$\alpha_1 - \alpha_{1\infty} = \beta_1 x \quad \text{and} \quad \alpha_{2\infty} - \alpha_2 = \beta_2 x$$

where the constants β_1 and β_2 may be calculated from the equations

$$\alpha_{10} - \alpha_{1\infty} = \beta_1 x_0 \quad \text{and} \quad \alpha_{2\infty} - \alpha_{20} = \beta_2 x_0$$

When we further use the abbreviation

$$\gamma = (\beta_1 k_1 - \beta_2 k_2)/k_\infty \varphi \tag{10}$$

equation 9 may be written as follows

$$- \frac{dx}{dt} = k_\infty (1 + \varphi \gamma x) x$$

By integration and change to decadic logarithms is obtained

$$- k_\infty^* t = \log x - \log(1 + \varphi \gamma x) + \text{const.}$$

If we introduce $P = \varphi x$, we obtain

$$- k_\infty^* t = \log P - \log(1 + \gamma P) + \text{const.} \tag{11}$$

In the calculation of γ by means of equation 10, we use k_1^* found in the previous part of this paper and preliminary values of k_2^* and k_∞^*. The constant

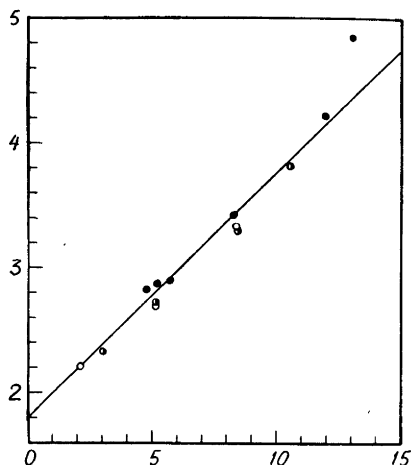Fig. 2. Decomposition in acetate buffer
solutions. Abscissa: X defined by equation
14; ordinate: $k_\infty^*/(a_{1\infty} + a_{2\infty})$. Filled
circles refer to series 1, half-filled circles to
series 2, and open circles to series 3.

k_∞^* is finally found graphically by means of equation 11. The results are given in the last column of Table 4.

We shall now test equation 8 and evaluate k_2^*. We assume that the ratio K_{HAc}/K_2 is constant within each of the three series of measurements, but make no assumption of its exact numerical value. When we remember that

$$\frac{K_{HAc}}{K_2} = \frac{[Ac^-]_\infty}{[HAc]_\infty} \frac{a_{1\infty}}{a_{2\infty}} \tag{12}$$

we may show that equation 8 is identical with the following equation

$$\frac{k_\infty^*}{a_{1\infty} + a_{2\infty}} = k_2^* + \frac{K_{HAc}}{K_2} X \tag{13}$$

where

$$X = \frac{[HAc]_\infty}{[Ac^-]_\infty} \left(k_1^* - \frac{k_\infty^*}{a_{1\infty} + a_{2\infty}} \right) \tag{14}$$

According to equation 13, a plot of $k_\infty^*/(a_{1\infty} + a_{2\infty})$ against X should, for each series, give a straight line from which k_2^* may be obtained by extrapolation to $X = 0$ while the slope is equal to K_{HAc}/K_2. In the calculation of $k_\infty^*/(a_{1\infty} + a_{2\infty})$, it is accurate enough to use the values of $a_{1\infty}$ and $a_{2\infty}$ given in Table 4 since their sum is nearly unity. The plot is shown in Fig. 2 where the filled circles represent series 1, the half-filled circles series 2, and the open circles series 3. All the points except one (corresponding to the first solution

in Table 4) fall rather close to the straight line drawn, from which we obtain by extrapolation $k_2^* = 1.80 \times 10^{-3}$. The slope of the straight line is K_{HAc}/K_2 = 0.197. The points for series 1 alone would give a little more, those for series 2 and 3 a little less than this value. There is a moderately good agreement between the values of the ratio determined from kinetic measurements on acetate buffers and those estimated for sodium chloride solutions and presented in Table 3.

CATALYSIS BY ZINC IONS

Experiments were carried out in solutions of hydrogen chloride, potassium chloride, and zinc chloride (c molar). The total ionic strength was always 0.200. The reaction followed the first-order law. The composition of the solutions examined and the velocity constants k^* found are given in Table 5. The hydrogen ion concentrations and degrees of dissociation α_1 and α_2 have been computed by means of dissociation constants calculated from equations 4—6 ($I = 0.200$). The kinetic results are shown graphically in Fig. 3. It is seen that there is a linear relation between the velocity constant and the concentration of zinc chloride when the hydrogen ion concentration is constant, and that the effect of the zinc ions increases rapidly with decreasing hydrogen ion concentration. The zinc ion catalysis may be explained quantitatively

Table 5. Decomposition of oxaloacetic acid (initial concentration x_0 molar) at 37° C in the solvent: h molar hydrogen chloride, c molar zinc chloride, (0.200 − h − 3c) molar potassium chloride.

| x_0	h	$c10^3$	$[H^+]$	α_1	α_2	k^*10^3	k^*10^3 calc.
0.01506	0.1798	3.32	0.1804	0.0371	0.0000	0.415	0.414
0.01514	0.1798	6.64	0.1804	0.0371	0.0000	0.445	0.436
0.01523	0.1498	16.61	0.1505	0.0441	0.0001	0.592	0.588
0.01521	0.0998	6.64	0.1008	0.0645	0.0001	0.686	0.686
0.01514	0.0998	13.27	0.1008	0.0645	0.0001	0.799	0.805
0.01514	0.0999	19.96	0.1008	0.0645	0.0001	0.921	0.925
0.01519	0.0999	26.58	0.1008	0.0645	0.0001	1.026	1.044
0.01509	0.0500	6.64	0.0518	0.1183	0.0004	1.282	1.291
0.01517	0.0500	13.27	0.0518	0.1182	0.0004	1.676	1.669
0.01523	0.02500	6.63	0.02809	0.1984	0.0012	2.541	2.529
0.01502	0.02500	13.27	0.02805	0.1986	0.0012	3.630	3.635
0.01525	0.00998	6.64	0.01493	0.3164	0.0037	5.38	5.38
0.01504	0.00999	13.27	0.01489	0.3171	0.0037	8.47	8.59
0.01512	0.00499	1.361	0.01099	0.3851	0.0060	3.75	3.70
0.01517	0.00499	3.32	0.01101	0.3846	0.0060	5.28	5.23
0.01529	0.00500	6.64	0.01105	0.3838	0.0060	7.85	7.79
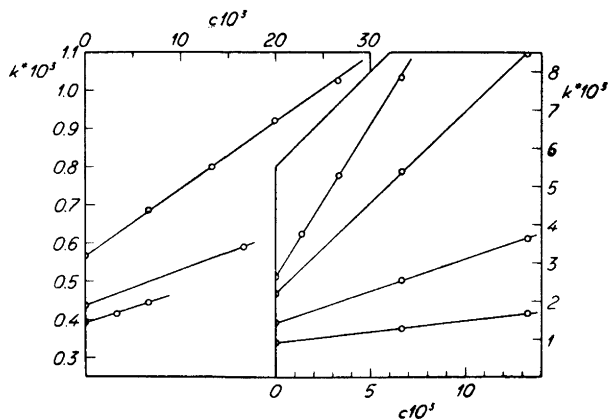
Fig. 3. Catalysis by zinc ions (c molar) and its dependence upon the hydrogen ion concentration. In the seven groups of solutions shown in the diagram, $[H^+]$ was, respectively, (left side of the diagram, taken from the bottom) 0.180, 0.150, and 0.101, (right side, from the bottom) 0.0518, 0.0281, 0.0149, and 0.0110.

when it is assumed that unstable complexes of the composition ZnOx and ZnHOx$^+$ are formed in the solutions. The velocity of decarboxylation will then be given by the expression

$$k_0 \ [H_2Ox] + k_1[HOx^-] + k_2[Ox^{--}] + k_3[ZnOx] + k_4[ZnHOx^+] \qquad (15)$$

The concentrations of the unstable complexes are determined by the equilibria

$$Zn^{++} + HOx^- \rightleftharpoons ZnOx + H^+ \qquad (16)$$

$$Zn^{++} + HOx^- \rightleftharpoons ZnHOx^+ \qquad (17)$$
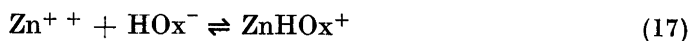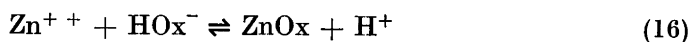
When K_3 and K_4 denote the mass-action constants for the equilibria 16 and 17, respectively, the two last terms of expression 15 may be written

$$k_3K_3[Zn^{++}][HOx^-][H^+]^{-1} + k_4K_4[Zn^{++}][HOx^-]$$

If [ZnOx] and [ZnHOx$^+$] are negligible compared with c, we may set $[Zn^{++}] = c$. From expression 15 we then obtain

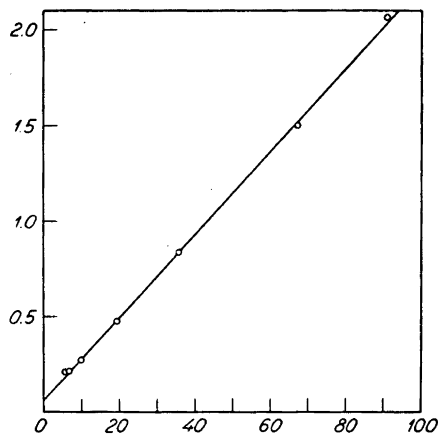$$k = k_u + k_3K_3c\alpha_1[H^+]^{-1} + k_4K_4c\alpha_1 \qquad (18)$$

Fig. 4. Catalysis by zinc ions. Abscissa:
$[H^+]^{-1}$; *ordinate:* $(k^* - k_u^*) / c a_1$

where k_u is the contribution to k from the uncatalysed reaction:

$$k_u = k_0 + (k_1 - k_0)a_1 + (k_2 - k_0)a_2 \tag{19}$$

Equation 18 may also be written in the following way

$$(k^* - k_u^*)/ca_1 = k_3^* K_3 [H^+]^{-1} + k_4^* K_4 \tag{20}$$

In Fig. 4, mean values of $(k^* - k_u^*)/ca_1$ for each of the seven groups of solutions examined have been plotted against $[H^+]^{-1}$. The points fall close to a straight line which shows that the explanation given above, including the assumption that $[Zn^{++}] = c$, is valid. From the straight line we find

$$k_3^* K_3 = 0.0217 \quad \text{and} \quad k_4^* K_4 = 0.063$$

Since the concentrations of the unstable zinc complexes are small compared with c, we can only determine the products of the velocity and complexity constants but not the constants separately. In the last column of Table 5 are given the values of k^* calculated by means of equation 18 when the values found for $k_3^* K_3$ and $k_4^* K_4$ are introduced and k_u^* is computed by means of equation 19 and the values of k_0^*, k_1^*, and k_2^* found earlier. There is a good agreement between k^* calculated from the formula and k^* found directly from the measurements.

CATALYSIS BY CUPRIC IONS

Experiments were carried out in solutions of hydrogen chloride, potassium chloride, and cupric nitrate (c molar). The sum of the concentrations of hydrogen and potassium chloride was in three series of experiments 0.050, 0.100, and 0.200, respectively. Table 6 and 7 show the composition of the solutions examined, their ionic strengths and hydrogen ion concentrations, and the degrees of dissociation α_1 and α_2 of the oxaloacetic acid, computed by means of the dissociation constants calculated from equations 4—6. It was found that cupric ions have a much greater catalytic effect than zinc ions, and that the reaction follows the first-order law only when the hydrogen ion concentration is sufficiently high. It will be shown that the kinetic results may be explained quantitatively when it is assumed that unstable complexes of the composition CuOx and CuHOx$^+$ are formed in the solutions. The velocity of decarboxylation may then be written in the following way

$$- \frac{dx}{dt} = k_u x + k_3[\text{CuOx}] + k_4[\text{CuHOx}^+] \tag{21}$$

where k_u is defined by equation 19. The concentrations of the unstable complexes are given by the mass-action expressions

$$[\text{CuOx}] = K_3 \, [\text{Cu}^{++}] \, [\text{HOx}^-] \, [\text{H}^+]^{-1} \; = K_3 \, [\text{Cu}^{++}] \, \alpha_1 x \, [\text{H}^+]^{-1} \tag{22}$$

$$[\text{CuHOx}^+] = K_4 \, [\text{Cu}^{++}] \, [\text{HOx}^-] = K_4 \, [\text{Cu}^{++}] \, \alpha_1 x \tag{23}$$

From equations 22 and 23, we find

$$[\text{Cu}^{++}] = c/(1 + \beta x) \tag{24}$$

where we have used the abbreviation

$$\beta = K_3 \, \alpha_1[\text{H}^+]^{-1} + K_4 \, \alpha_1 \tag{25}$$

As x approaches zero, [Cu^{++}] will approach c, and the reaction will approach a first-order course with the velocity constant

$$k = k_u + k_c \tag{26}$$

where

$$k_c = k_3 K_3 c \alpha_1[\text{H}^+]^{-1} + k_4 K_4 c \alpha_1 \tag{27}$$

We shall find an expression for k by means of the pressures observed during the reaction. The differential equation 21 may, by means of equations 23—26, be written as follows

$$- \frac{dx}{dt} = \left(k_u + \frac{k_c}{1 + \beta x}\right)x = kx\left(1 - \frac{k_c}{k} \frac{\beta x}{1 + \beta x}\right)$$

Upon integration, it is found that

$$kt = \ln x + \frac{k_c}{k_u} \ln \left(1 + \frac{k_u}{k} \beta x\right) + \text{const.}$$

or, introducing $P = \varphi x$ and changing to decadic logarithms,

$$k^*t = \log P + \frac{k_c}{k_u} \log \left(1 + \frac{k_u \beta}{k \varphi} P\right) + \text{const.} \tag{28}$$

Since $P = P_0$ when $t = 0$, we obtain from equation 28

$$k^*t = \log \frac{P_0}{P} + \frac{k_c}{k_u} \log Y \tag{29}$$

where

$$Y = \frac{1 + \frac{k_u \beta}{k \varphi} P_0}{1 + \frac{k_u \beta}{k \varphi} P} \tag{30}$$

Instead of equations 29 and 30, we may write

$$\log Y = \frac{k_u}{k_c}\left(k^*t - \log \frac{P_0}{P}\right) \tag{31}$$

$$Y - 1 = \frac{k_u \beta}{k \varphi} (P_0 - PY) \tag{32}$$

When β is sufficiently small, that is (since, as we shall see, the last term of equation 25 is small) when $[H^+]$ is sufficiently high, equation 28 may be written as follows

$$k^*t = \log P + 0.4343 \frac{k_c \beta}{k \varphi} P + \text{const.} \tag{33}$$

Table 6. Decomposition of oxaloacetic acid (initial concentration x_0 molar) at 37.0° C in the solvent: h molar hydrogen chloride, c molar cupric nitrate, (s—h) molar potassium chloride.

x_0	h	$c10^3$	I	$[H^+]$	a_1	a_2	$k*10^3$	$k*10^3$ calc.
Series 1 (s = 0.050):								
0.01490	0.0499	0.100	0.0518	0.0513	0.0971	0.0002	1.338	1.356
0.01517	0.0499	0.249	0.0522	0.0514	0.0972	0.0002	2.243	2.227
0.01519	0.0499	0.498	0.0530	0.0514	0.0973	0.0002	3.700	3.676
0.01514	0.0499	0.996	0.0543	0.0514	0.0977	0.0002	6.57	6.567
0.01495	0.0250	0.100	0.0529	0.0275	0.1673	0.0006	3.026	3.082
Series 2 (s = 0.100):								
0.01510	0.0998	0.100	0.1012	0.1007	0.0581	0.0001	0.668	0.670
0.01510	0.0998	0.599	0.1027	0.1007	0.0583	0.0001	1.410	1.413
0.01504	0.0998	0.997	0.1039	0.1007	0.0585	0.0001	2.018	2.004
0.01506	0.0998	1.996	0.1069	0.1007	0.0586	0.0001	3.456	3.466
0.01515	0.0499	0.996	0.1046	0.0515	0.1082	0.0003	6.125	6.124
Series 3 (s = 0.200):								
0.01493	0.1995	0.100	0.2008	0.2000	0.0336	0.0000	0.410	0.404
0.01512	0.1996	0.996	0.2035	0.2001	0.0337	0.0000	0.719	0.716
0.01517	0.1996	1.996	0.2065	0.2001	0.0337	0.0000	1.049	1.062
0.01516	0.1493	0.100	0.2010	0.1500	0.0443	0.0000	0.501	0.499
0.01517	0.1494	0.996	0.2037	0.1501	0.0444	0.0000	1.041	1.039
0.01508	0.1494	1.996	0.2067	0.1501	0.0444	0.0000	1.649	1.640
0.01507	0.0998	0.100	0.2013	0.1008	0.0647	0.0001	0.686	0.699
0.01514	0.0998	0.204	0.2016	0.1008	0.0647	0.0001	0.834	0.834
0.01512	0.0998	0.498	0.2025	0.1008	0.0647	0.0001	1.220	1.215
0.01516	0.0998	0.997	0.2040	0.1008	0.0647	0.0001	1.865	1.858
0.01516	0.0998	1.993	0.2070	0.1008	0.0648	0.0001	3.116	3.142

The solutions examined may, according to their hydrogen ion concentrations, be divided into two groups, presented in Tables 6 and 7, respectively. In the first group, the hydrogen ion concentration is so high that the reaction approximately follows the first-order law, while there is a pronounced deviation from this law in the second group. In the first group, the velocity constants $k*$ are calculated by means of formula 33, where the small second term on the right side is estimated from preliminary values of $k*$, k_c^*, and β. The constants $k*$ found in this way are given in the next to the last column of Table 6. The velocity constants k_u^* for the uncatalysed reaction in the same solutions are calculated by means of equation 19 and the values of k_0^*, k_1^*, and k_2^* found earlier in this paper. When k_u^* is subtracted from $k*$, we

Table 7. Decomposition of oxaloacetic acid (initial concentration x_0 molar) at 37.0° C in the solvent: h molar hydrogen chloride, c molar cupric nitrate, (s — h) molar potassium chloride. The complexity constant K_3 has been computed from the kinetic data.

x_0	h	$c10^3$	I	$[H^+]$	α_1	α_2	$k*10^3$ calc.	K_3
Series 1 (s = 0.050):								
0.01527	0.00996	0.0249	0.0544	0.01434	0.2791	0.0021	3.400	2.16
0.01504	0.00996	0.0996	0.0546	0.01427	0.2801	0.0021	7.869	2.03
0.01523	0.00498	0.0996	0.0557	0.01042	0.3474	0.0037	12.36	1.98
0.01515	0.00498	0.1991	0.0560	0.01040	0.3483	0.0037	22.38	2.04
Series 2 (s = 0.100):								
0.01508	0.00996	0.0996	0.1049	0.01459	0.2992	0.0028	7.176	1.74
0.01507	0.00996	0.1992	0.1052	0.01460	0.2989	0.0028	12.24	1.83
0.01506	0.00498	0.0996	0.1061	0.01069	0.3680	0.0048	11.04	1.66
Series 3 (s = 0.200):								
0.01515	0.01246	0.0498	0.2046	0.01697	0.2906	0.0031	3.697	1.28
0.01515	0.01246	0.0996	0.2048	0.01697	0.2906	0.0031	5.376	1.32
0.01506	0.00996	0.0996	0.2053	0.01488	0.3181	0.0038	6.384	1.26
0.01514	0.00499	0.0100	0.2062	0.01101	0.3856	0.0061	3.314	1.16
0.01515	0.00499	0.0249	0.2062	0.01101	0.3856	0.0061	4.341	0.94
0.01514	0.00499	0.0498	0.2063	0.01101	0.3856	0.0061	6.055	1.22
0.01515 [a]	0.00498	0.0996	0.2064	0.01101	0.3856	0.0061	9.49	1.28
0.01525	0.00498	0.1991	0.2067	0.01104	0.3850	0.0061	16.27	1.16
0.01523	0.00249	0.0249	0.2069	0.00923	0.4270	0.0082	5.152	1.05

[a] The kinetic data for this solution are shown in Fig. 5.

obtain k_c*. In order to test equation 27, we proceed in the same way as in the discussion of the zinc ion catalysis. When $k_c*/c\alpha_1$ is plotted against $[H^+]^{-1}$, the points fall, for each of the three series of solutions with nearly constant ionic strength, close to a straight line whose intercept on the ordinate axis has a small positive value. This shows that the cupric ion catalysis can nearly completely be explained by the spontaneous decarboxylation of the complex CuOx, while decarboxylation of the complex CuHOx+ gives only a small, if any, contribution to the catalysis. A further analysis of the data shows that we get the best agreement with equation 27 when we for k_3*K_3 and k_4*K_4 choose the values given in Table 8 at the ionic strengths stated. When they are used for the calculation of $k*$ by means of equations 26 and 27, the values given in the last column of Table 6 are obtained. In the calculation, k_3*K_3
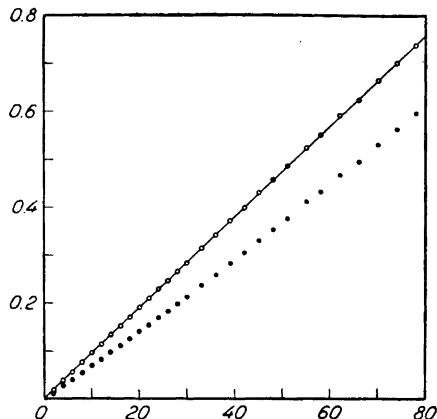
Fig. 5. Catalysis by cupric ions. Kinetic data for the solution marked a in Table 7. Abscissa: t in minutes; ordinate: (filled circles) log (P₀/P), (open circles) log (P₀/P) + (k_c/k_u)logY.

has been corrected for the effect of small differences in ionic strength by means of the following formula derived from the data in Table 8:

$$- \Delta\log \ (k_3{}^*K_3) = 2.076 \ \Delta\sqrt{I} - 1.80 \ \Delta I$$

A comparison of the last two columns of Table 6 shows that there is a satisfactory agreement between k^* calculated by means of formulae 26 and 27 and k^* found directly from the measurements.

The composition of the second part of the solutions examined, those with the lowest hydrogen ion concentrations, is given in Table 7. If the cupric ion concentration were constant during the decomposition and equal to c, the reaction would follow the first-order law with the velocity constant k^*. Values of k^*, calculated by means of equations 26 and 27 and the constants found above, are given in the next to the last column of Table 7. The actual rate was always lower than that calculated from the assumption that $[Cu^{++}] = c$. This is shown for one of the solutions in Fig. 5, where the filled circles represent $\log (P_0/P)$ plotted against the time t in minutes. If the assumption were valid, $\log (P_0/P)$ should be equal to k^*t and the points fall close to the straight line shown in the diagram. From the deviation, it is possible to estimate K_3. We calculate Y by means of equation 31 and plot $Y-1$ against PY. In agreement with equation 32, the points fall close to a straight line. From the slope of this line, we compute β. K_3 is finally calculated by means of equation 25 where we neglect the last term. It is reasonable to do this, since, as we have seen, $k_4{}^*K_4$ is much smaller than $k_3{}^*K_3 [H^+]^{-1}$ while $k_4{}^*$ is probably at least of the same order of magnitude as $k_3{}^*$. On proceeding in this way, we find for the experiment shown in Fig. 5 that $\beta = 44.8$ and $K_3 = 1.28$. When we, for the same experiment, calculate Y by means of equation 30, setting $\beta = 44.8$,

Table 8. Cupric and zinc ion catalysis in the decarboxylation of oxaloacetic acid at 37.0° C.

Catalyst	Series	I	$k_3^*K_3$	$k_4^*K_4$	K_3	k_3^*	$\dfrac{(CuOx)}{(Cu^{++})\,(Ox^{--})}$
Cu^{++}	1	0.053	3.05	0.7	2.03	1.50	1.88×10^4
Cu^{++}	2	0.104	2.50	0.57	1.74	1.44	1.25×10^4
Cu^{++}	3	0.206	1.96	0.50	1.20	1.63	0.67×10^4
Zn^{++}		0.200	0.0217	0.063			

introduce the values found for Y into equation 29, and plot the sum of the two
terms on the right side of the equation against t, we obtain the open circles
shown in Fig. 5. They all fall close to the straight line already drawn. This
shows that the value 1.28 for the complexity constant K_3 satisfactorily explains
the deviations from the course we should expect if the cupric ion concentration
were all the time equal to c. The values of K_3 found for the respective solutions
are given in the last column of Table 7. Average values of K_3 for each of the
three series of experiments are given in Table 8 together with k_3^* calculated
by means of K_3 and the known values of $k_3^*K_3$. As we should expect, K_3
decreases considerably with increasing ionic strength. The accuracy of K_3
is, however, too small, and the salt concentration too high, to justify an
extrapolation to zero ionic strength by means of Debye-Hückel's law. We
should expect k_3^*, the velocity constant for the spontaneous decarboxylation
of the complex CuOx, to be nearly independent of the salt concentration. The
irregular variations found are probably due to inaccuracy in the determination.
The mean value for all the three series, $k_3^* = 1.52$, corresponds to a time of
half-completion amounting to 12 seconds. The mass-action constant for the
equilibrium

$$Cu^{++} + Ox^{--} \;\rightleftarrows\; CuOx$$
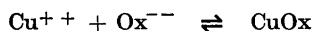
is equal to K_3/K_2. In the last column of Table 8 are given the values computed
for it. In the last line of the table are shown the values of $k_3^*K_3$ and $k_4^*K_4$
found in the zinc ion catalysis.

THE MECHANISM OF THE METAL-ION CATALYSIS

Metal-ion catalysed decarboxylation has been found only for di- and tri-
carboxylic acids. The decarboxylation of monocarboxylic acids may even be
retarded by metal ions. Let us compare the decarboxylations of oxaloacetic
and nitroacetic acid. It has been shown [15] that the mechanism of the latter
reaction is analogous to that of the decarboxylation of β-keto carboxylic acids.

The *nitro*-form of the univalent nitroacetate ion decomposes spontaneously into carbon dioxide and the anion of *aci*-nitromethane. It was suggested [15] that an electron displacement in the molecule towards the nitro (or keto) group is the reason why the bond is broken and carbon dioxide set free. The effect of metal ions on the decarboxylation of nitroacetic acid has been studied by the author of this paper [16]. It was found that both the undissociated nitro-acetic acid and metal ion complexes of the nitroacetate ion are stable. It is reasonable to assume that a metal ion bound directly to the carboxylate group will hinder the displacement of electrons towards the nitro group and therefore stabilize the molecule. A divalent oxaloacetate ion, on the other hand, may bind a metal ion either to the carboxyl group having the keto group in β-position or to the stable carboxyl group in the other end of the molecule. In both cases, the metal ion will probably also be linked to the keto group forming a chelate compound. While the metal ion in the former case stabilizes the molecule, it will, in the latter case, owing to the electric attraction emanating from it, enlarge the displacement of electrons from the un-stable carboxylate group towards the keto group, and therefore make the molecule less stable. Since the probability for a decarboxylation in this way may be increased a great number of times, it is not surprising that it greatly outweighs the stabilizing effect.

An important contribution to the understanding of the metal-ion catalysis in the decarboxylation of dicarboxylic acids has been given by Steinberger and Westheimer [2] who have examined the decomposition of dimethyloxaloacetic acid, $HOOCCOC(CH_3)_2COOH$, and its monoester, $C_2H_5OOCCOC(CH_3)_2COOH$. They have shown that heavy metal ions catalyse the former, but not the latter reaction. Their explanation of the mechanism of the metal-ion catalysis is essentially the same as that given above.

SUMMARY

The uncatalysed decarboxylation of oxaloacetic acid was examined at $37.0°$ C in solutions of potassium and hydrogen chloride and in acetate buffer solutions. It was found that both undissociated oxaloacetic acid (H_2Ox) and the uni- and divalent ion (HOx^- and Ox^{--}) decompose spontaneously. The velocity may therefore be expressed by the sum

$$v_u = k_0 \, [H_2Ox] + k_1 \, [HOx^-] + k_2 \, [Ox^{--}]$$

The velocity constants k_0, k_1, and k_2 were determined.

The zinc and cupric ion catalysis in the decarboxylation of oxaloacetic acid was examined at $37.0°$ C in solutions of potassium and hydrogen chloride containing in addition zinc chloride or cupric nitrate. It was shown that the catalysis may, for the greatest part, be explained by the spontaneous decarboxylation of a complex of the composition MeOx (where Me is either Zn or Cu), but also the spontaneous decarboxylation of the complex $MeHOx^+$ contributes to the reaction. When K_3 and K_4 denote mass-action constants for the equilibria

$$Me^{++} + HOx^- \rightleftharpoons MeOx + H^+ \text{ and } Me^{++} + HOx^- \rightleftharpoons MeHOx^+$$
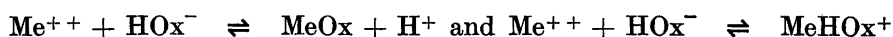
the velocity may be expressed by the following sum

$$v = v_u + k_3 [MeOx] + k_4 [MeHOx^+]$$
$$= v_u + k_3K_3 [Me^{++}] [HOx^-] [H^+]^{-1} + k_4K_4 [Me^{++}] [HOx^-]$$

The products k_3K_3 and k_4K_4 were determined both for the zinc and the cupric ion catalysis. For the latter, the two constants k_3 and K_3 were also determined separately.

The mechanism of the uncatalysed and the metal-ion catalysed decarboxylation was discussed, and it was explained why metal ions catalyse the decarboxylation of di-, but not of mono-carboxylic acids.

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