738. The Interaction of Transition-metal Ions with Oxaloacetic Acid. Part III.* Kinetics of the Catalysed Decarboxylation.

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The kinetics of decarboxylation of oxaloacetic acid in the presence of bivalent ions of calcium, manganese, cobalt, nickel, and zinc have been studied manometrically. Catalysis and inhibition of the reaction are related to the nature and stability of the chelate compounds formed under different conditions.

QUANTITATIVE studies of the kinetics of decarboxylation of oxaloacetic acid have shown that the undissociated acid and the two anions undergo first-order decomposition,[1,2] and that catalysis by metal ions can be related to the formation of a chelate compound, which also loses carbon dioxide in a first-order reaction.[3] A study of the reactions catalysed by copper and zinc ions indicated that the catalytically important species was a compound of the type MA, where M^{2+} and A^{2-} represent metal and substrate ions.[1] The catalytic power of transition-metal ions in the decomposition of acetonedicarboxylic acid follows the thermodynamic stability of the corresponding malonates.[4] A similar correlation has been established between the catalytic effect of rare-earth ions in the decarboxylation of oxaloacetic acid and the stability of chelate compounds of rare-earth oxaloacetates.[5] These studies have been extended to the metal ions of the first transition series. Thermo-dynamic association constants have been obtained,[6] and catalytic rate coefficients have now been measured.

EXPERIMENTAL

Weighed samples of oxaloacetic acid were dissolved in the requisite amounts of water, standard hydrochloric acid, and potassium chloride solution. After addition of the metal chloride solution, the reaction mixture (5 ml.) was run into the gas-evolution apparatus, which was evacuated, sealed, and placed in a water thermostat maintained at $36.9° \pm 0.03°$. Decarboxylation was then followed manometrically as previously described.[5] With very fast reactions a modified apparatus was used. A magnetically operated plunger supported a bucket containing oxaloacetic acid above the appropriate solution. The apparatus was evacuated and sealed, and the reaction was started by withdrawing the plunger into a sidearm. An oxalo-acetic acid concentration of $0.03M$ produced a suitable rise in the mercury manometer. 80—90% of reaction was generally followed and the rate coefficients were obtained from first-order plots, the infinity readings being taken after 10 half-times of reaction. " AnalaR " materials and " grade A " volumetric glassware were used.

RESULTS AND DISCUSSION

A series of experiments were designed to study the kinetic behaviour of the chelate com-pounds MA. In the range of pH and metal-ion concentration used the concentration of the species MAH^+ is small, as indicated [6] potentiometrically; however, a kinetic contribution from this species could be detected in some cases.

Catalysis.—In the appropriate concentration range the rate of decarboxylation is given by the equation

$$d[CO_2]/dt = -dc_a/dt = k_u c_a + k[MA] + k'[MAH^+] \quad . \quad . \quad , \quad . \quad , \quad (1)$$

where k_u, k, k' are first-order rate coefficients.

This equation is applied when the concentration of chelate compound is so small that the

* Part II, preceding paper.
[1] Pedersen, *Acta Chem. Scand.*, 1952, **6**, 285.
[2] Gelles, *J.*, 1956, 4736
[3] Gelles and Hay, *ibid.*, 1958, 3673.
[4] Prue, *ibid.*, 1952, 2331.
[5] Gelles and Clayton, *Trans. Faraday Soc.*, 1956, **52**, 353.
[6] Gelles and Salama, preceding paper.

concentration of free metal ion can be taken as equal to the total concentration of metal, c_m, and the concentration of free oxaloacetate as equal to the total concentration of oxaloacetic acid, c_a.

α_1 and α_2, the degrees of dissociation of oxaloacetic acid into the ions HA^- and A^{2-} respectively, are given by the equations

$$\alpha_1/(1 - \alpha_1 - \alpha_2) = K_1^c/[H^+], \text{ and } \alpha_2/(1 - \alpha_1 - \alpha_2) = K_1^c K_2^c/[H^+]^2 \quad . \quad . \quad (2)$$

where $K_1^c(= 6\cdot19 \times 10^{-3})$ and $K_2^c(= 1\cdot37 \times 10^{-4})$ are the concentration ionisation constants of oxaloacetic acid [1] at ionic strength 0·1. The concentration association constants at ionic strength 0·1 are defined by the equations

$$K_{MA}^c = [MA]/[M^{2+}][A^{2-}] \text{ and } K_{MAH^+}^c = [MAH^+]/[M^{2+}][HA^-] \quad . \quad . \quad (3)$$

Then, from eqns. (1) and (3) we obtain

$$d[CO_2]/dt = k_u c_a + k K_{MA}^c[M^{2+}][A^{2-}] + k' K_{MAH^+}^c[M^{2+}][HA^-] \quad . \quad . \quad (4)$$

and by substitution for $[A^{2-}]$ and $[HA^-]$ from eqns. (2)

$$k_{obs} = k_u + k K_{MA}^c c_m (K_2^c \alpha_1/[H^+]) + k' K_{MAH^+}^c c_m \alpha_1 \quad . \quad . \quad . \quad . \quad (5)$$

where k_{obs} is the observed first-order rate coefficient. Hence

$$(k_{obs} - k_u)/(K_2^c \alpha_1 c_m) = k K_{MA}^c[H^+]^{-1} + k' K_{MAH^+}^c/K_2^c \quad . \quad . \quad . \quad (6)$$

A plot of $(k_{obs} - k_u)/(K_2^c \alpha_1 c_m)$ against $[H^+]^{-1}$ will give a straight line of slope $k K_{MA}^c$ and intercept $k' K_{MAH^+}^c/K_2^c$.

TABLE 1. *Rate coefficients for the uncatalysed reaction.*

(Concentrations are in moles/l.; $10^2 c_a = 3\cdot00$.)

$10^2[HCl]$	0·255	0·500	1·00	2·00	2·50	5·00
$10^2[H^+]$	1·23	1·39	1·75	2·56	2·99	5·30
α_1	0·334	0·307	0·261	0·1945	0·1715	0·1048
α_2	0·00373	0·00303	0·00200	0·00104	0·00079	0·00027
$10^4 k_u$ (sec.$^{-1}$)	0·91	0·84	0·725	0·555	0·495	0·325

TABLE 2. *Catalysis by transition metal ions at 36·9°.*

($c_a = 0\cdot03$, $I = 0\cdot1$.)

Zn^{2+}

$10^2[H^+]$	1·39	1·39	1·75	1·75	2·99	2·99	5·30	
$10^3 c_m$	5	7·5	5	10	10	20	15	
$10^4 k_{obs}$	1·98	2·65	1·48	2·18	1·08	1·80	0·672	
R	542	574	422	407	249	278	161	

Ni^{2+}

$10^2[H^+]$	1·75	1·75	2·56	2·56	2·99	2·99	5·30	5·30
$10^3 c_m$	5	10	5	10	10	20	10	15
$10^4 k_{obs}$	1·86	2·88	1·13	1·73	1·38	2·21	0·649	0·851
R	636	602	432	441	377	365	226	244

Co^{2+}

$10^3[H^+]$	1·75	1·75	2·56	2·56	2·99	2·99	5·30	
$10^3 c_m$	5	15	10	20	10	20	15	
$10^4 k_{obs}$	1·25	2·30	1·11	1·65	0·874	1·36	0·576	
R	294	294	208	205	161	184	117	

Mn^{2+}

$10^2[H^+]$	1·23	1·23	1·23	1·23	1·39	1·39	1·39	
$10^3 c_m$	15	20	25	25	15	20	25	
$10^4 k_{obs}$	1·31	1·42	1·54	1·57	1·11	1·21	1·28	
R	58·2	55·8	55·0	57·6	42·8	44·0	41·8	

$10^2[H^+]$	1·75	1·75	2·99	2·99	2·99	5·30		
$10^3 c_m$	15	20	20	20	20	15		
$10^4 k_{obs}$	0·94	1·00	0·585	0·595	0·600	0·347		
R	39·6	38·5	19·3	21·3	22·4	10·2		

Ca^{2+}

$10^2[H^+]$	1·23	1·23	1·39	1·39	1·75	1·75	2·99	2·99
$10^3 c_m$	25	25	15	20	20	25	10	20
$10^4 k_{obs}$	1·025	1·045	0·908	0·921	0·790	0·805	0·504	0·522
R	10·1	11·8	10·8	9·6	9·1	8·95	5·1	5·7

The measurement of rate coefficients for the uncatalysed reaction, and the calculation of α_1, α_2, and k_u have been described.[1, 2] The relevant data on the uncatalysed reactions at ionic strength 0·1 are collected in Table 1. The values of α_1, α_2, [H⁺], and k_u will be unchanged in the presence of metal ions if [M²⁺] can be taken as equal to c_m. Potentiometric data indicate the concentration range in which this assumption is justified.[6]

The kinetic data for catalysis by transition-metal ions are summarised in Table 2. The quantity $(k_{obs} - k_u)/(K_2{}^c\alpha_1 c_m)$ is represented by R, and is calculated by using the values of α_1 and k_u given in Table 1.

Figs. 1 and 2 show plots of R against 1/[H⁺]. Individual rate coefficients are known with an accuracy of ± 2—3%, but R involves a difference $(k_{obs} - k_u)$, which becomes quite small for catalysis by manganese and calcium ions. In view of this the linearity of the plots can be considered very satisfactory. No systematic variation of R with concentration of metal ion could be detected, at any given concentration of hydrogen ion. This supports the prediction from the known [6] association constants, that [M²⁺] $\sim c_m$ under the present conditions. The small positive intercepts on the ordinate indicate that the species MAH⁺ makes some kinetic
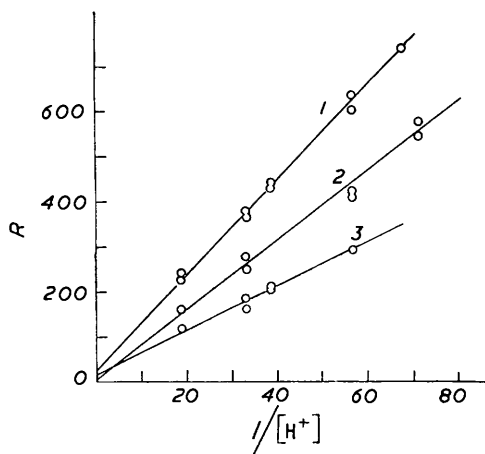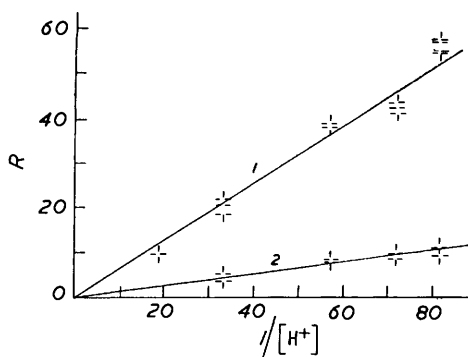
FIG. 1. *Catalysis:* (1) Ni²⁺, (2) Zn²⁺, (3) Co²⁺.

FIG. 2. *Catalysis:* (1) Mn²⁺, (2) Ca²⁺.

contribution to the rate of decarboxylation. The coefficients $kK_{MA}{}^c$ for the species MA are obtained from the slope of these plots. The thermodynamic association constants at 25°, K_{MA}, have been measured.[6] The concentration association constants $K_{MA}{}^c$ at 36·9° and ionic strength 0·1, can be estimated from activity coefficients calculated from the Davies equation, and a constant entropy of association calculated from thermodynamic data on copper oxalo-acetate at 37° [1] and 25° [6]: It is found that $K_{MA}{}^c \approx 0.143\,K_{MA}$. The rate coefficients $kK_{MA}{}^c$, and approximate rate constants k for decarboxylation of the chelate compounds MA are given in Table 3.

TABLE 3. *Rate constants for chelate compounds* MA *at* 36·9° *and ionic strength* $I = 0.1$.

	Ca²⁺	Mn²⁺	Co²⁺	Zn²⁺	Ni²⁺	Cu²⁺
$kK_{MA}{}^c$	0·14	0·65	4·8	7·6	10·7	706 [1]
$10^2 k$ (approx.)	0·24	0·65	2·4	3·1	2·3	6·6

In the study of catalysis by metal ions it is usual to determine the catalytic rate coefficient $kK_{MA}{}^c$. This coefficient provides a measure for the effect of metal ion on the rate of reaction; it is a composite measure of the concentration of chelate compounds formed $(K_{MA}{}^c)$, and of their reactivity (k). A parallelism between the rate coefficients $kK_{MA}{}^c$ and the association constants $K_{MA}{}^c$ is to be expected and is indeed found.

Comparison can be made between the rate constants, k, and the association constants for oxaloacetates and oxalates listed in Table 4 of the preceding paper.

The association constants, $K_{MA}{}^c$, for the oxaloacetates refer to both ketonic and enolic form

of the complex MA, and only the former undergoes decarboxylation.   The proportion of enol has been determined[3] for each metal ion.   The association constants corresponding to the formation of only the ketonic complex can thus be calculated.   Division of the rate coefficients $kK_{MA}{}^c$ (Table 3) by these ketonic association constants will give rate constants corresponding to the active ketonic complexes.   However, the general conclusions from a comparison of rate constants and association constants are not altered by using constants for the active ketonic complex instead of the overall constants.   Comparison will therefore be made between the overall rate constants given in Table 3 and the overall association constants.[6]   It is seen that the rate constants k do not follow the order of association constants.

The interaction of metal ion and substrate in the transition state of decarboxylation might resemble that in the initial state (a).   In that case a parallelism between rate constant and association constant for oxaloacetates would be expected

$$k = GK_{MA}{}^\alpha \qquad \ldots \ldots \ldots \ldots \ldots \quad (7)$$

$$\log k = \alpha \log K_{MA} + \log G \quad \ldots \ldots \ldots \quad (8)$$

or

$$\log kK_{MA} = (\alpha + 1) \log K_{MA} + \log G \quad \ldots \ldots \quad (9)$$

Fig. 3 shows a logarithmic plot of the rate constants k against the thermodynamic association constants for oxaloacetates.   It is seen that the reactivity of the nickel, and particularly of the
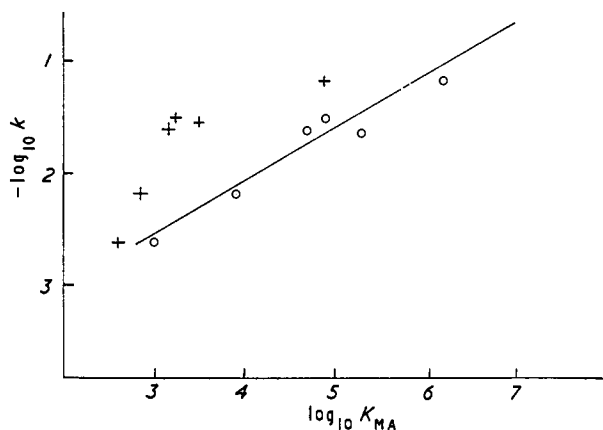

FIG. 3.   *Variation of rate constants k with association constants K_{MA} for:* $+$ *oxaloacetates, $\bigcirc$ oxalates.*

copper chelate compounds, is considerably lower than expected from a linear free energy relation. Allowance for the formation of a catalytically inactive enolic form does not change the relation significantly.

(a)   (b)

If the transition state of reaction corresponds more closely to (b) than to (a) the interaction between metal ion and substrate should be similar to that in metal oxalates, which have considerably higher association constants than the oxaloacetates.[6]

A logarithmic plot (Fig. 3) of the rate constants k against the thermodynamic association constants for the oxalates is approximately linear.   The two plots indicate the strength of the interaction of metal ion and substrate in the transition state of decarboxylation, which appears to resemble structure (b).

Inhibition.—There is potentiometric evidence for the formation of the chelate compounds M_2A^{2+} at high concentration of metal ion.[6]   The structure of this complex is discussed in the preceding paper.   The kinetics of decarboxylation at low concentrations of chelate compound could be interpreted without contribution from the species M_2A^{2+}; a significant retardation, observed at high concentrations of copper ion, is being investigated.

At high values of pH enols are formed which are not decarboxylated.[3] At pH 13, $\alpha\alpha$-di-methyloxaloacetic acid decomposes, but no carbon dioxide is evolved by oxaloacetate or copper oxaloacetate. Studies of the inhibition of this reaction are being continued.

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