

A Kinetic Study of the Fe(III)-Catalyzed Aquation of Bis(malonato)Diaquochromate(III) Ion

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The bis(malonato)diaquochromate(III) ion, $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$ in acidic solution hydrolyzes to give $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)^+ + 1$. This reaction is catalyzed by ferric ion and the rate law for this cation catalyzed-aquation in a $\text{HClO}_4/\text{NaClO}_4$ medium, $I = 1.00\text{M}$, is $-d[\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-]/dt = (k_1[\text{Fe}^{3+}] + k_2[\text{H}^+])[\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-]$ where $k_1(25^\circ\text{C}) = 4.72 \times 10^{-5} \text{ M}^{-1}\text{sec}^{-1}$ ($\Delta H^\ddagger = 22.5 \text{ Kcal/mol}$, $\Delta S^\ddagger = -2.58 \text{ eu}$) and $k_2(25^\circ\text{C}) = 4.75 \times 10^{-5} \text{ M}^{-1}\text{sec}^{-1}$ ($\Delta H^\ddagger = 21.2 \text{ Kcal/mol}$, $\Delta S^\ddagger = -7.13 \text{ eu}$). Rapid preequilibrium association of basic Cr-bound oxygen with Fe^{3+} , followed by rate-determining ring opening, is proposed to account for the k_1 hydrolysis pathway.

Introduction

Reactions of chromium(III) oxalate complexes and chromium(III) malonate complexes have been extensively studied.²⁻¹⁴ Aquations of bis(oxalato)diaquochromate(III), $\text{Cr}(\text{C}_2\text{O}_4)_2^{3-}$, and bis(malonato)diaquochromate(III), $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$ ¹⁰⁻¹⁴ have been investigated in the acidic media and these reactions are known to be acid-catalyzed. The presence of acid is expected to facilitate the opening of chelate ring which is postulated as the rate determining step. Metal ion catalysis of aquation⁶ and isomerization¹⁵ of bis(oxalato)diaquochromate(III) ion have been also studied. Both in aquation and isomerization, it is suggested that a direct attack of the cation on the chelated oxalate forms a five coordinated intermediate with only one end of the oxalate bound to chromium in the first step reaction.

No studies of the metal ion catalyzed aquation of analogous malonate system have been done.

Before beginning the work reported here, we attempted to find evidence for the reaction shown below and reaction is



cation-catalyzed. No rapid ultraviolet or visible spectral change occurred upon mixing $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2(\text{H}_2\text{O})_2^-$ with Fe^{3+} but slow changes in absorbance at 563 nm were observed, and were identified with reaction 1.

We also reexamined the acid-catalyzed aquation of $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$. The investigation of this reaction was prompted by the fact that the results of four previous investigations¹⁰⁻¹³ are different considerably in the observed rate constants which are medium-dependent. Furthermore, the rate of this reaction is important in interpreting the results of Fe^{3+} -catalyzed aquation of $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$.

Experimental Section

Reagents. Bis(malonato)diaquochromate(III) was prepared from reagent grade potassium dichromate and malonic acid as described by Palmer¹⁶. Reaction mixture of potas-

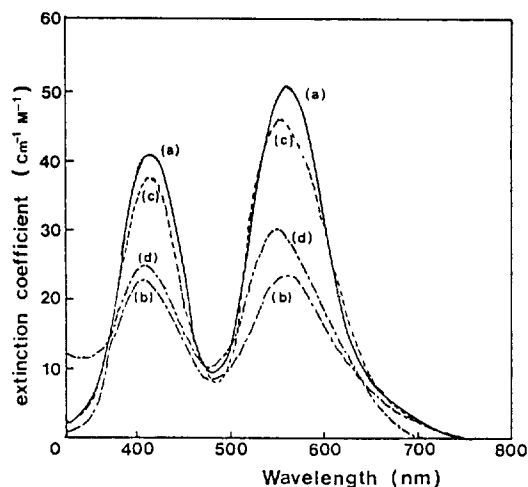


Figure 1. Absorption spectra of (a) *cis*- $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$, (b) *trans*- $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$, (c) equilibrium solution of *cis*-*trans* isomers, and (d) $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)^+$ ions.

sium dichromate(0.05 mole) and malonic acid(0.40 mole) was allowed to react and to isomerize for more than 10 hours in 0.15l of water at about 50°C . The equilibrium solution is dominantly in the *cis*-form.¹²

Solutions of $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$ were isolated by ion-exchange chromatographic techniques developed elsewhere¹⁷; equilibrium solution was used to charge of column of anion exchange resin(Dowex-1-X8, 50-100 mesh) in the chloride form at about 10°C . The column was washed with 0.01M NaClO_4 and was eluted with 0.10M NaClO_4 . A purple band formed at the top of the column was eluted and was separated from the other band remaining at the top of the column. Chromatographic behavior of this purple band implies that this species is negatively and singly charged and is equilibrium mixture of *trans*-*cis* isomers of $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$ where the *cis*-isomer is the principal isomer. Optical spectra of *trans*-isomer, *cis*-isomer and equilibrium mixture are shown in Figure 1. Potassium *trans*-bis(oxalato)diaquoch-

romate(III) and Potassium *cis*-bis(oxalato)diaquochromate(III) were obtained by fractional crystallization of equilibrium mixture. Successive small yields of the crystalline, less soluble *trans* salts were induced by overnight refrigeration of the equilibrium *cis*-*trans* solution. More soluble *cis* salts were also isolated from the condensed equilibrium solution. Anal. Cald. for *cis* isomer of $\text{K}[\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2(\text{H}_2\text{O})_2]3\text{H}_2\text{O} \cdot \text{Cr}$, 13.51%; C, 18.71%; H, 3.64%. Found: Cr, 13.51%; C, 18.95%; H, 2.93%.

Chromium contents of complexes were determined by conversion to CrO_4^{2-} with alkaline peroxide followed by spectrophotometric analysis of CrO_4^{2-} produced ($\epsilon_{373} = 4815$).¹⁸

Hexaquoiron(III) perchlorate, $\text{Fe}(\text{ClO}_4)_3$ was prepared from solutions of ferric chloride in perchloric acid by heating to remove hydrogen chloride. After the solution failed to produce a visible precipitation in a chloride test with silver ion, two successive crystallizations from concentrated perchloric acid were done. Iron(III) solution was prepared from the iron(III) perchlorate and perchloric acid. The concentrations of Fe(III) in acidic iron(III) perchlorate solution was determined by the direct titration with standard Na_2EDTA solution using Variamine blue (4-methoxy-4'-aminodiphenylamine) as an indicator.¹⁹ The acidity of the iron(III) perchlorate solution was determined by allowing an aliquot of the solution to pass through an ion-exchange column containing Dowex 50W-X8 cation exchange resin (H^+ -form, 50-100 mesh). For each iron(III) ion in the original solution, three hydrogen ions were eluted. By subtracting the acidity due to the iron(III) from the total acidity of the eluate, the acidity of the original solution were calculated. Water used in all reactions was doubly distilled and sodium perchlorate was purchased from Fluka Co. and recrystallized before use. Atomic absorption spectroscopy was also utilized for the analysis of chromium(III) and iron(III) contents of some spent reaction mixture.

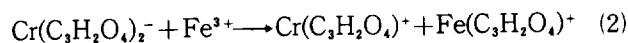
Rate Measurements. The rate of reaction 1 was measured spectrophotometrically by observing the decrease in absorbance at 563nm. The absorbance measurements were done with a Shimadzu UV 250 UV-Visible spectrophotometer. The bis(malonato)diaquochromate(III) solution used in the rate measurement was actually the *trans*-*cis* mixture solution isolated by chromatographic techniques described above. The solution was prepared at least 24 hr before kinetic run, to ensure that *cis*-*trans* equilibrium was achieved. The ionic strength was adjusted to the 1.00M in all reaction mixtures. Rate measurements at 45°C were carried out in a stopped silica cell placed in the thermostated cell compartment. Solution reacting at 25°C and 35°C were kept in an opaque, thermostated water bath, outside the spectrophotometer, except during periodic absorbance measurements. Light was excluded to prevent possible photodecomposition of malonate species. The temperature was maintained with less than 0.2°C variation as measured by a calorimetric thermometer graduated in 0.01°C units. Pseudo first-order rate constants were evaluated by using the conventional $\log(A-A_\infty)$ vs. time plots. The reactions were followed for at least 5 half times. The plots were linear for 4 or more half times for most experiments.

Results

Table 1. Spectral data for the chromium(III) complexes prepared in this work

Complex	Absorption peak (λ_{max} , nm)		Corresponding extinction coefficients $\text{M}^{-1} \text{cm}^{-1}$		Reference
$\text{Cr}(\text{H}_2\text{O})_6^{3+}$	417	589	15	14	24
<i>cis</i> - $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$	418	565	42.1	50.8	12
<i>cis</i> - $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$	417	565	40.6	50.8	this work
<i>trans</i> - $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$	401	555	20.3	17.6	12
<i>trans</i> - $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$	409	560	22.9	23.4	this work
$\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)^+$	410	558	25.0	30.3	this work
<i>trans</i> - <i>cis</i> mixture of $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$ at equilibrium	416	563	37.7	45.9	this work

Stoichiometry. The stoichiometry indicated by equation 1 was observed in the following ways; to confirm that only one malonate is lost from the *trans*-*cis* $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$, a spent reaction mixture was passed through Dowex 50W-X8 ion exchange resin. The column was first rinsed with 0.1M NaClO_4 and the collected eluate ($\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)^+$) was analyzed for chromium(III) content. About 94% of $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_5^{2-}$. This collected eluate, which contains +1 charged chromium species, $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)^+$, does not contain monomalonatoion(III), $\text{Fe}(\text{C}_3\text{H}_2\text{O}_4)^+$. However, K_1 value for the formation of $\text{Fe}(\text{C}_3\text{H}_2\text{O}_4)^+$ is very large²⁰ and the absorbance at 300 nm increases as the aquation reaction proceeds. The increase of absorbance at 300 nm might be attributed to the formation of $\text{Fe}(\text{C}_3\text{H}_2\text{O}_4)^+$ and the stoichiometry of the iron(III) catalyzed aquation can be described by equation 2.



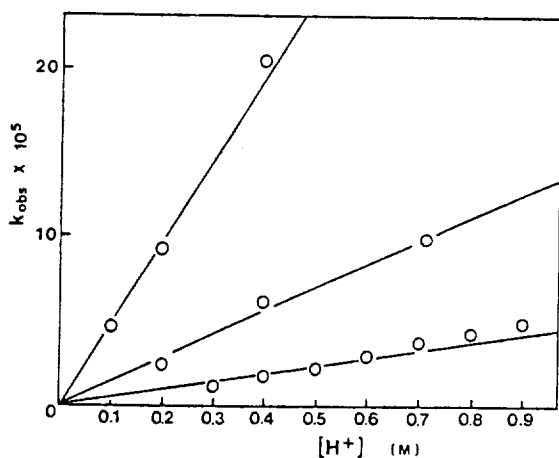
The column was also rinsed with 1M HClO_4 and then eluted with 3M HClO_4 after $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$ was completely removed from the resin. The 3M HClO_4 solution should have contained any Cr^{3+} that was formed but chromium could not be detected in the 3M HClO_4 and further aquation of $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)^+$ to Cr^{3+} does not occur. Spectrophotometric data of chromium(III) ions considered in this work are summarized in Table 1 and are shown in Figure 1. As mentioned in experimental parts, the bis(malonato)diaquochromate(III) solution used in the rate measurements was the *trans*-*cis* mixture solution contained mainly of the *cis*-isomers. From the spectral data of *trans*- and *cis*-isomers, % of the *cis*-form in the equilibrium solution at 25°C was calculated to be about 82%.

Acid Catalyzed Aquation of Bis(malonato)diaquochromate(III). Kinetic results obtained for the acid-catalyzed aquation of $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$ are summarized in Table 2. The dependence of k_{obsd} on $[\text{H}^+]$ follows the equation $k_{obsd} = k_2[\text{H}^+]$, where k_2 is the second-order rate constant and agrees with the rate expression reported by Frank and Huchital.¹² Acid dependencies of k_{obsd} are shown in Figure 2. Activation parameters are evaluated from the temperature dependency on the rate constants (see Figure 4). Activation parameters obtained in our studies are $\Delta H_2^\ddagger = 21.2 \text{ Kcal/mol}$,

Table 2. Observed and calculated rate constants for acid-catalyzed of $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$ at 1.00M ionic strength^a

[H ⁺] ^b	Temp. (°C)	$k \times 10^6 \text{ sec}^{-1}$	
		obsd.	calcd.
0.30	25	12.4	14.2
0.40	25	18.3	19.0
0.50	25	23.4	23.8
0.60	25	30.1	28.5
0.70	25	37.5	33.2
0.80	25	42.5	38.0
0.90	25	48.4	42.8
0.20	35	24.6	27.8
0.40	35	61.5	55.6
0.50	35	97.3	97.3
0.10	45	46.7	48.2
0.20	45	93.0	96.4
0.40	45	205	193

^a Ionic strength was maintained at 1.0M using NaClO_4 as supporting electrode. ^b The initial $[\text{H}^+]/[\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-]$ ratio was always 10 or greater.

**Figure 2.** Acid dependencies on the observed rate constants, k_{obsd} for the aquation of $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$.

and $\Delta S_2^\ddagger = -7.13 \text{ eu}$. The results of Frank and Huchital¹² are also listed in Table 2 for the comparison purposes.

Fe(III)-catalyzed Aquation of Bis(malonato)diaquo-chromate(III) in Acidic Media. Reaction 1 was found to conform to the rate law given equation 1. Since $[\text{Fe(III)}]$ and $[\text{H}^+]$ were always at least tenfold greater than $[\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-]$, first order behavior was observed with $k_{obsd} = k_1[\text{Fe}^{3+}] + k_2[\text{H}^+]$.

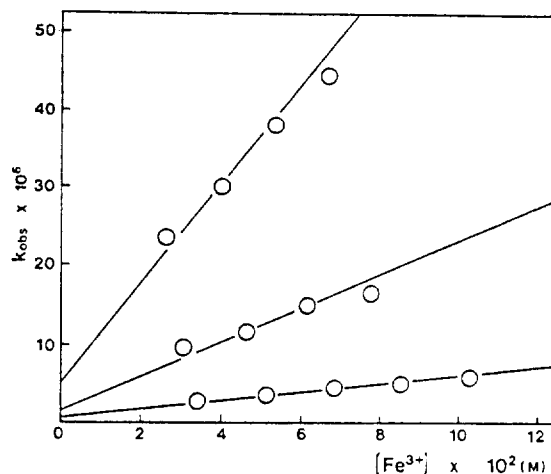
$$d[\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-]/dt = k_{obsd}[\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-]$$

The measured rate constants for each experiments at $[\text{H}^+] = 0.01\text{M}$ and other conditions are listed in Table 3. In the reaction mixtures, however, the actual concentration of Fe^{3+} was less than the total iron(III) concentration, $[\text{Fe(III)}]$, owing to the hydrolysis of iron(III). Total iron(III) concentration was corrected by subtracting concentrations of hydrolyzed species, using the data reported by Milburn.²¹ This corrections are indicated in the Table 3.

Table 3. Observed and calculated rate constants for Fe(III) catalyzed aquation of $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$ in acidic media^a

[H ⁺]	Total [Fe(III)] $\times 10^2\text{M}^b$	[Fe ³⁺] $\times 10^2\text{M}$	Temp. (°C)	$k \times 10^6 \text{ sec}^{-1}$	
				obsd.	calcd.
0.01	4.00	3.43	25	2.51	2.38
0.01	6.00	5.15	25	3.42	3.34
0.01	8.00	6.87	25	4.45	4.29
0.01	10.0	8.58	25	4.94	5.24
0.01	12.0	10.3	25	5.81	6.20
0.01	4.00	3.10	35	9.60	8.33
0.01	6.00	4.64	35	11.5	11.8
0.01	8.00	6.19	35	15.0	15.2
0.01	10.0	7.74	35	16.3	18.7
0.20	8.00	7.88	35	36.6	45.4
0.40	4.00	3.97	35	60.6	64.5
0.40	8.00	7.94	35	68.6	73.4
0.70	4.00	3.98	35	106	106
0.01	4.00	2.67	45	23.4	21.8
0.01	6.00	4.01	45	30.2	30.4
0.01	8.00	5.34	45	38.1	38.8
0.01	10.0	6.68	45	44.6	47.4

^a Ionic strength was maintained at 1.0M using NaClO_4 as supporting electrode. ^b The initial $[\text{Fe(III)}]/[\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-]$ ratio was always 10 or greater.

**Figure 3.** Fe^{3+} ion dependencies on the observed rate constants, k_{obsd} for the aquation of $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$.

The acid dissociation of iron(III) was particularly important at high temperature and low acid concentration that we have to take it account in deriving a rate law in terms of Fe^{3+} ion. The data were fitted to equation 3 and to the absolute rate theory equation, using a least-squares program. The average deviation between k_{calcd} and k_{obsd} was 6.9%. The result of one experiment was deleted from the final calculation because of an excessive difference between k_2 value obtained as an intercept of the plot of k_{obsd} vs $[\text{Fe}^{3+}]$ and k_2 value obtained from the study of acid dependency on the rate. The experiment that was deleted was done at 35°C and $[\text{Fe}^{3+}] = 1.55 \times 10^{-2}\text{M}$. The dependence of k_{obsd} on the $[\text{Fe}^{3+}]$ are shown in Figure 3. The activation parameters obtained

Table 4. Rate Parameters for the Aquation of $\text{cis}-\text{Cr}(\text{C}_2\text{O}_4)_2^-$ and $\text{cis}-\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$

Forms of Rate term	$k(25^\circ\text{C})\text{M}^{-1}\text{sec}^{-1}$	$\Delta H^\ddagger(\text{Kcal}\cdot\text{M}^{-1})$	$\Delta S^\ddagger(\text{eu})$	Ref.
$k[\text{H}^+][\text{cis}-\text{Cr}(\text{C}_2\text{O}_4)_2^-]$	2.6×10^{-6}	24	-5	3
$k[\text{Fe}^{3+}][\text{cis}-\text{Cr}(\text{C}_2\text{O}_4)_2^-]$	1.0×10^{-3}	24	9	6
$k[\text{H}^+][\text{cis}-\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-]$	6.50×10^{-5}	21.8 ± 0.4	-4.7 ± 0.1	12
$k[\text{H}^+][\text{cis}-\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-]$	4.75×10^{-5}	21.2 ± 2.6	-7.1 ± 0.1	this work
$k[\text{Fe}^{3+}][\text{cis}-\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-]$	5.56×10^{-6}	22.5 ± 2.2	-2.6 ± 0.1	this work

from the least-squares fitting procedures are $\Delta H_1^\ddagger = 22.5$ Kcal/mol, and $\Delta S_1^\ddagger = -2.58$ eu (see Figure 4). The calculated value of k_1 at 25°C is $5.56 \times 10^{-6}\text{M}^{-1}\text{sec}^{-1}$.

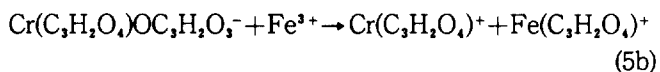
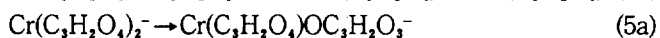
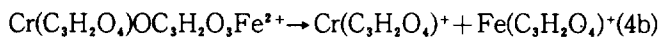
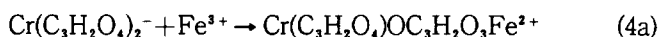
The contribution to the k_{obsd} value from k_2 pathway is comparable to k_1 pathway and activation parameters for two different reaction pathway are very similar (see Table 4). In order to learn whether the k_1 term in equation 3 represents a general or a specific cation effect, the substitutionally inert species Cr^{3+} was added to one reaction mixture, containing equimolar Fe^{3+} and Cr^{3+} , was the same as for a mixture that was identical, except that it did contain Cr^{3+} ion.

Discussion

Four studies on the acid-catalyzed aquation of the $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$ have been made previously and the observed rate constants were reported to have the following dependencies on acid concentration; (a) $k_{\text{obsd}} = 2.33 \times 10^{-3}[\text{H}^+](45^\circ\text{C})^{10}$, (b) $k_{\text{obsd}} = 3.20 \times 10^{-4}[\text{H}^+] + 9.5 \times 10^{-3}[\text{H}^+](50^\circ\text{C})^{13}$, (c) $k_{\text{obsd}} = 4.20 \times 10^{-5} + 3.6 \times 10^{-4}[\text{H}^+](45^\circ\text{C})^{14}$, and (d) $k_{\text{obsd}} = 7.22 \times 10^{-4}[\text{H}^+](45^\circ\text{C})^{12}$. Our values for k_{obsd} at 45°C is $4.82 \times 10^{-4}[\text{H}^+]$. The magnitude of k_{obsd} value and the absence of acid-independent reaction pathway, i.e. the k_0 term, observed in our investigation are in agreement with the observation made by Frank and Huchitals.¹² Although it is quite likely that the k_0 term is not zero, the least-squares analysis of the data yields $k_0 \approx 10^{-7}\text{sec}^{-1}$ which is essentially zero within the errors of computation.

Rates of aquation of $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$ are definitely medium dependent and the large variations in the observed rate constants among reported results might be attributed at least in part to the differences in reaction medium they employed.

Possible mechanisms for the Fe^{3+} -catalyzed aquations of $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$ include equations 4 and 5.



Since it is quite unlikely that $\text{trans}-\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$ is for more reactive than the dominant cis -isomer we did not propose metal-catalyzed isomerization from cis -isomer to trans -isomer, followed by the fact aquation of trans -isomer. The failure of the inert hexaquo chromium(III) ion to catalyze the aquation is in accord with our suggestion that the catalytic metal ion must coordinate to the leaving malonate. Similar mechanisms have been suggested for the Fe^{3+} -catalyzed aquation of analogous oxalate complex.⁶

In each of reactions 4 and 5, the bonds to leaving malonate

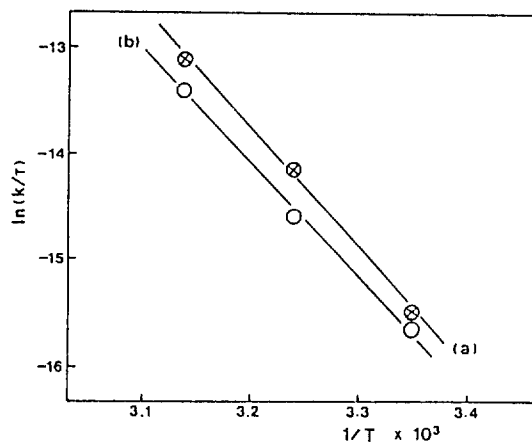


Figure 4. Plots of $\ln(k/T)$ vs. $1/T$ for the acid-catalyzed reaction path (b) and Fe^{3+} -catalyzed reaction path (a) for the aquation of $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$.

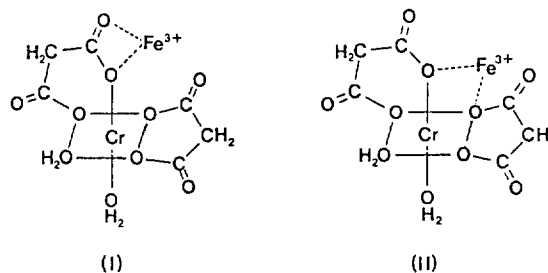


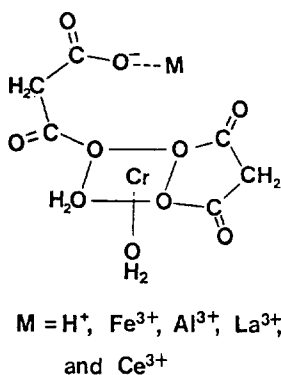
Figure 5. Proposed activated complexes in the Fe^{3+} -catalyzed aquation pathway of $\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$.

nate are singly broken, so that a monodentate intermediate is formed. The effect of Fe^{3+} in mechanism expressed by reaction 4 is to break the first-oxygen bond and then to help to break the second. The effect of Fe^{3+} in the mechanism expressed by reaction 5 is to break only the second bond. We prefer mechanism expressed by reaction 4 because only the first chromium-oxygen bond is broken in the isomerization of $\text{trans}-\text{Cr}(\text{C}_3\text{H}_2\text{O}_4)_2^-$, yet the reaction is catalyzed by acid. We also suggest that if reaction 4a occurs, and catalytic role of cation and proton is similar, both aquation and isomerization are logical consequences.

As mentioned above, in studies of both acid catalyzed^{3,4,12-14} and metal catalyzed isomerization,^{6,15} protons or catalytically active metal ions are assumed to make a direct attack of the malonate or oxalate, forming five coordinated intermediate with only one end of oxalate or malonate bound to chromium (see Figure 6). The chelate effect may be lost when the ring opens, and it might be expected that malonate would escape as it is bound to catalytic metal ion. In the

Table 5. Equilibrium Constants for the Reaction $M^{n+} + L^{-2} \rightleftharpoons ML^{(n-2)+}$ where L^{-2} is Oxalate or Malonate Ion

Metal	Ligand	Temp. (°C)	Log of equilibrium constants	Medium	Reference
H ⁺	oxalate	25	K ₁ = 3.57	1.0 M(NaClO ₄)	25
Al ³⁺	oxalate	25	K ₁ = 4.85	1.0 M(NaClO ₄)	27
Ce ³⁺	oxalate	20	K ₁ = 4.49	1.0 M(NaClO ₄)	28
La ³⁺	oxalate	25	K ₁ = 4.3	1.0 M(NaClO ₄)	29
Fe ³⁺	oxalate	25	K ₁ = 7.54	0.5 M(NaClO ₄)	23
Cr ³⁺	oxalate	25	K ₁ = 5.34, K ₂ = 5.17	0.1 M(NaClO ₄)	30
H ⁺	malonate	25	K ₁ = 5.11	0.1 M(NaClO ₄)	26
Fe ³⁺	malonate	25	K ₁ = 7.46	0.5 M(LiClO ₄)	20
Cr ³⁺	malonate	25	K ₁ = 7.06, K ₂ = 5.79	0.1 M(NaClO ₄)	31

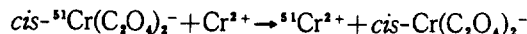
**Figure 6.** Five coordinated intermediate possibly formed in the acid- or iron-catalyzed isomerization and aquation reactions.

Fe³⁺-catalyzed aquation of Cr(C₂O₄)₂⁻, Fe(C₂O₄)⁺ is reported to be formed as a reaction product.⁶ The result of the formation of Fe(C₂O₄)⁺, instead of isomerization which has been shown the presence of other trivalent cations such as Al³⁺, La³⁺ and Ce³⁺, is possibly due to the great affinity of the Fe³⁺ ion toward oxalate ligand or malonate ligand, (see Table 5), and/or to the fact that the chromium system was already at equilibrium with respect to isomerization at the beginning of each reaction. The catalytic effect of acid or metal cations on the aquation of Cr(C₂O₄)₂⁻ or Cr(C₃H₂O₄)₂⁻ seems to be observed when the formation constant K₁ for $M^{n+} + L^{-2} \rightleftharpoons ML^{(n-2)+}$ (M = H⁺ or metal ion and L = oxalate or malonate ion) is greater or comparable to the formation constant K₂ for $CrL^+ + L^{-2} \rightleftharpoons CrL_2^-$. We could not isolate Fe(C₃H₂O₄)⁺ chromatographically as an aquation product, But the K₁ value for the formation of Fe(C₃H₂O₄)⁺ is quite large (K₁ = 10^{7.46} at 25 °C and I = 0.50M)²⁰ and is comparable to that for the formation of Fe(C₂O₄)⁺ (k₁ = 10^{7.54} at 25 °C and I = 0.50M).²³ The absorbance at ~300nm gradually increases as the aquation of Cr(C₃H₂O₄)₂⁻ proceeds in the presence of Fe³⁺. So, it is plausible to suggest that Fe(C₃H₂O₄)⁺ might be formed in the aquation of Cr(C₃H₂O₄)₂⁻.

The reason why we could not isolate Fe(C₃H₂O₄)⁺ from the reaction product chromatographically might be due to the fact that kinetic lability of Fe(C₃H₂O₄)⁺ on the cationic resin leads to the formation of higher charged iron species.

As shown in Table 4, Activation parameters of acid catalyzed aquation and Fe³⁺-catalyzed aquation are similar, which is expected from the fact that the activated complexes are quite similar. The less negative entropy of activation for

the Fe³⁺-catalyzed pathway is consistent with either of proposed mechanisms and reflects the greater charge of Fe³⁺. The position of Fe³⁺ attack is no the type question answered by kinetic data only. It seems useful to consider some reasonable possibilities, however. the attack could occur at either of the chromium bound oxygen atom, or at the unbound oxygen atoms of the coordinated malonate as shown in Figure 5.



Huchital's study²² of the chromium(II) catalyzed *trans*-*cis* isomerization of Cr(C₂O₄)₂⁻ suggested that electron transfer between chromium(II) and chromium(III) complexes occurs by both oxalate ligands as simultaneous bridging groups, and based on the isotope tracer studies using labeled *trans*- and *cis*-Cr(C₂O₄)₂⁻, demonstrated a transfer of ⁵¹Cr activity from chromium(II) to chromium(III) for the *cis*-complexes. Exchange of activity for the following reaction occurs on the same time scale as the isomerization.

Huchital finally concluded that Cr²⁺ can not bond to more than one oxygen atoms on each coordinated oxalate. This behavior of Cr²⁺ suggest that Fe³⁺ may also form an intermediate of type(II) in Figure 5.

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The synthesis and some biological properties of 7 β -[2-(Z)-(2-aminothiazole-4-yl)-2-(N-substituted carbonyl)ethoxyiminoacetamido]-3-vinyl-3-cephem-4-carboxylic acid are described. The effect of substituents on the carbamoyl group in the 7-side chain were investigated in order to improve antibacterial activities. Two of these new orally active β -lactam derivatives showed wide expanded antimicrobial activities against Gram-positive and Gram-negative bacteria, including *Pseudomonas aeruginosa*, as well as good stability to β -lactamases.

Introduction

Since the discovery of penicillins more than sixty years ago¹, the β -lactam family has grown enormously to include a wide variety of structural types². In 1945, a sardinian bacteriologist, Brotzu found a strain of *Cephalosporium acremonium* which produced antibiotic material with a broader spectrum of activity³. But the early developed compounds possessed a relatively narrow spectrum of activity and the weakness of resistance caused by β -lactamase appeared to be a serious problem. However the use of 6-aminopenicillanic acid(6-APA) and 7-aminocephalosporanic acid(7-ACA) as a synthetic intermediate enabled a large scale production and afforded a wide range of compounds with a broad spectrum of activity. In spite of their high antibacterial activity and their broad antimicrobial spectrum, some bacterial species or strains are not inhibited at concentrations sufficient of successful chemotherapy. They are usually not effective against some clinically important bacteria, including *Pseudomonas* and some *Proteus* species⁴. It was not until 1980 when cefotaxime, a semisynthetic cephalosporin prepared by direct acylation of 7-ACA by 2-(2-aminothiazole-4-yl)-2-syn-methoxyiminoacetic acid, was avail-

able for clinical use⁵. It has a high antibacterial activity against all tested strains of Gram-positive and Gram-negative aerobic and facultatively anaerobic bacteria. The syn-methoxyimino(generally alkoxyimino) group is known to play an important role in the stability to the β -lactamase-releasing Gram-negative bacteria. In contrast to the remarkable improvements of the injectable β -lactam antibiotics, progress has been less evident among the oral β -lactam antibiotics such as the cephalosporins. Cefixime, developed by Fujisawa, would be the most potent antibiotics and is characterized by displacement of the 3-acetoxymethyl group in cefotaxime with vinyl moiety. It shows also a relatively high antibacterial activity against Gram-positive and Gram-negative bacteria⁶.

Results and Discussion

Recently many new β -lactam antibiotics modified with 7 β -[2-(2-aminothiazole-4-yl)-2-(substituted carbamoyl-methoxyimino)acetamido]group at the C-7 position and with various heteroaromatics at the C-3 position are reported⁷. In the course of our extensive research on the modification of cephalosporin, efforts has been focused on synthesizing new