Complexing Behavior of Kojic Acid with Metal Ions. I. Mg(II) and Mn(II) Chelates[*1,*2]

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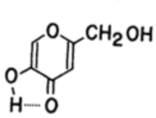
In recent years, the investigation of the metal complexes of tropolone and its derivatives has been in much progress and has brought about the information that these organic compounds form metal complexes of much greater stability than those of β-diketones of comparable acidity. Since kojic acid (I) forms a five-membered chelate ring with hydrogen or metal ion, which is the same as tropolone, it was expected that kojic acid would react with metal ions to produce metal chelates or relatively high stability. Thus, Fernelius and his coworker[1] have carried out an investigation on this subject and found out that kojic acid forms metal chelates whose stabilities were greater than, or at least equal to, those of β-diketones of the same acidity.



I

To avoid such an ambiguity brought about by their use of non-aqueous solvent[1] (50% dioxane) for the determination of the stability constants, it was intended in this work to employ an aqueous system to clarify the interaction between kojic acid and metal ions.

Experimental

Reagents.—Kojic acid was purchased from the Tokyo Kasei Kogyo Co., Ltd., and was purified by sublimation in vacuo: m. p. 156∼156.6°C; reported 154∼156°C[1], 154°C[2].

This purified substance was used to prepare an aqueous stock solution which was standardized by potentiometric titration with standard base. Analytical grade $Mg(NO_3)_2\cdot 6H_2O$ and $MnSO_4\cdot nH_2O$, purchased from the Wako Pure Chemical Industries, Ltd., were used to make up stock solutions and standardized by the usual technique of chelatometric titration[3].

Potentiometric Measurements.—An HRL Model P pH meter (made by the Horiba Instruments Inc., Kyoto) with extension glass and calomel electrodes was used to measure hydrogen ion concentration after being calibrated with acetic acid buffer as well as standard hydrochloric acid and sodium hydroxide. Measurements were carried out at 25.0 ±0.1°C, and the ionic strength was maintained at approximately 0.10 M with potassium nitrate. Solutions under investigation were kept in a nitrogen atmosphere by circulation of purified nitrogen through the jacketed titration cell.

Mathematical Treatment

In this investigation, metal species were found to exist in three forms: $M(H_2O)_4{}^{2+}$, $MA(H_2O)_2{}^{+}$, and MA_2. Therefore, the solution equilibria may be expressed in terms of the following equations:

$$HA \rightleftarrows H^+ + A^- \qquad K_D = \frac{[H^+]\,[A^-]}{[HA]} \tag{1}$$

$$M(H_2O)_4{}^{2+} + A^- \rightleftarrows MA(H_2O)_2{}^+ + 2H_2O$$

$$K_1 = \frac{[MA^+]}{[M^{2+}]\,[A^-]} \tag{2}$$

$$MA(H_2O)_4{}^+ + A^- \rightleftarrows MA_2 + 2H_2O$$

$$K_2 = \frac{[MA_2]}{[MA^+]\,[A^-]} \tag{3}$$

in which M represents a metal ion and HA indicates an undissociated form of a ligand.

The amount and distributing ratio of these chelate species may be calculated from the equilibrium relationships and the stoichiometric relations shown in the following paragraph.

If T_A and T_M represent the total concentration of the ligand species and of the metal species respectively, then

$$T_A = [HA] + [A^-] + [MA^+] + 2\,[MA_2] \tag{4}$$

$$T_M = [M^{2+}] + [MA^+] + [MA_2] \tag{5}$$

T_{OH}, the hydroxide added to a solution during the titration, introduces the relationship:

$$[H^+] - [OH^-] + T_{OH} = [A^-] + [MA^+] + 2\,[MA_2] \tag{6}$$

From Eq. 5 in combination with equilibrium relations 2 and 3, it results in

$$\frac{T_M}{[M^{2+}]} = 1 + K_1\,[A^-] + K_1K_2\,[A^-]^2 \tag{7}$$

[*1] Contribution No. 19 from Department of Organic Synthesis, Faculty of Engineering, Kyushu University.

[*2] Presented at the 14th Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1961.

1) B. E. Bryant and W. C. Fernelius, *J. Am. Chem. Soc.*, **76**, 5351 (1954).

2) F. Challenger, T. Klein and T. K. Walker, *J. Chem. Soc.*, **1929**, 1498.

3) K. Ueno, "Chelatometric Titration" (in Japanese), Nankodo, Ltd., Tokyo (1960), pp. 274, 278.

The combination of Eqs. 1, 4 and 6 gives

$$[A^-]=\frac{K_D}{[H^+]}\left\{T_A-[H^+]+[OH^-]-T_{OH}\right\} \qquad (8)$$

The quantity of free metal ion M^{2+} may be shown in terms of T_A, [HA], $[A^-]$, K_1 and K_2 from Eqs. 2, 3 and 4:

$$[M^{2+}]=\frac{T_A-[HA]-[A^-]}{K_1[A^-]+2K_1K_2[A^-]^2} \qquad (9)$$

Thus, substitution of the relationship 9 into Eq. 7 results in the final equation:

$$(F-1)[A^-]K_1+(2F-1)[A^-]^2K_1K_2=1 \qquad (10)$$

where

$$F=\frac{T_M}{T_A-[HA]-[A^-]}$$

Equation 10 means that K_1 may be plotted as a function of K_1K_2 corresponding to each experimental point on the titration curve. The intercept on the vertical axis is $1/(F-1)[A^-]$ and that on the horizontal axis is $1/(2F-1)[A^-]^2$. Straight lines obtained from a number of experimental points are to intersect at one point, which represents the solution of the simultaneous equations. The ordinate at this point is equal to K_1 and the abscissa is equal to K_1K_2. This method was employed for the determination of stability constants of the magnesium chelates. There is another graphical method for the evaluation of K_1 and K_2 employing Eq. 10. Equation 10 may be rewritten as

$$\alpha=K_1+K_1K_2\beta \qquad (11)$$

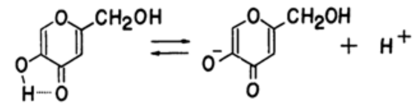
where

$$\alpha=1/(F-1)[A^-];\quad \beta=(2F-1)[A^-]/(F-1)$$

Thus if chelate formation reactions shown by Eqs. 2 and 3 occur, when α is plotted against β, a straight line is obtained the slope of which is equal to K_1K_2 and in which the intercept at $\beta=0$ is equal to K_1. This alternate method was used for the evaluation of the stability constants of the manganese chelates.

Results and Discussion

Kojic Acid.—Potentiometric titration of kojic acid provides only one sharp inflection which corresponds to the following dissociation:



The pK value of 7.68 is much smaller than the value of 9.40 obtained by Bryant and Fernelius[1] in 50% aqueous dioxane. This difference in pK value is to be expected because an acidic proton of an organic compound is more labile in aqueous system than in mixed aqueous systems.

Interaction of Mg(II) Ion with Kojic Acid.—Titration curves are illustrated in Fig. 1 for the kojate chelates of Mg(II) at 1 : 1 and 2 : 1 ratios of ligand to metal ion. In both titrations the total concentration of kojic acid was maintained constant.

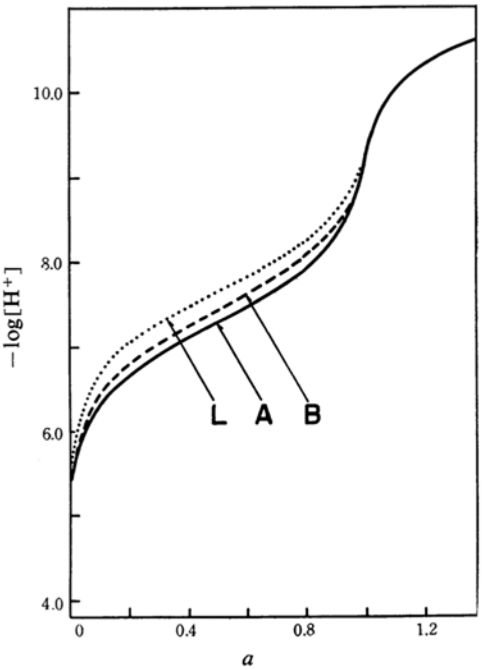


Fig. 1. Potentiometric titration of Mg(II)-kojate chelates at the total ligand concentration of 2.20×10^{-3} M, with these molar ratios of ligand to metal ion: A, 1 : 1; B, 2 : 1; L, ligand (kojic acid) alone; *a* = moles of base added per mole of ligand; $t=25°C$; $\mu=0.1$ (KNO_3).

The apparent depression of the titration curves in the buffer region indicates the formation of the metal chelate species. The titration curve for the 2 : 1 ratio behaves similarly to that for the 1 : 1 ratio, thus suggesting the simultaneous formation of MgA and MgA_2. No precipitates were found throughout the titrations. Mg(II) ion undergoes hydrolysis in accordance with the equation:

$$Mg^{2+}+H_2O \rightleftarrows Mg(OH)^++H^+$$

However, the contribution of such a reaction is expected to be negligible in the buffer region where the two chelate formation reactions take place, for the K value is as much as $10^{-12.8}$ at 30°C and $\mu=0.1$[4].

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4) S. Chaberek, Jr., R. C. Courtney and A. E. Martell, *J. Am. Chem. Soc.*, **74**, 5057 (1952).

TABLE I. STABILITY CONSTANTS OF THE METAL CHELATES

Metal ion	Ligand	Temp., °C	μ	pK_D	log K_1	log K_2
Mg(II)	Kojic acid (HA)	25	0.10	7.68	2.92	2.19
	Acetylacetone[a] (HA)	30	→0	8.95	3.63	2.54
	Tiron[b] (H_2A)	20	0.1	7.66	1.98	
Mn(II)	Kojic acid (HA)	25	0.10	7.68	3.95	2.83
	Acetylacetone[a] (HA)	30	→0	8.95	4.18	3.07

K_D=first dissociation constant; $K_1=\frac{[MA]}{[M][A]}$; $K_2=\frac{[MA_2]}{[MA][A]}$

K_1 value for the Tiron chelate is shown for equilibrium: $\frac{[MHA]}{[M][HA]}$

a) See Ref. 5; b) See Ref. 6

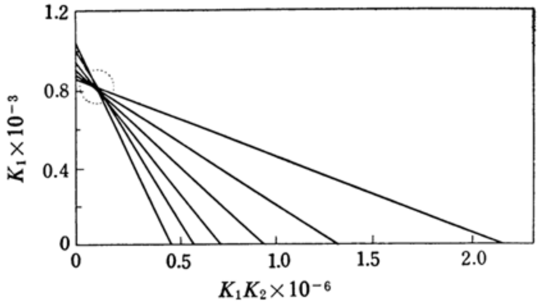


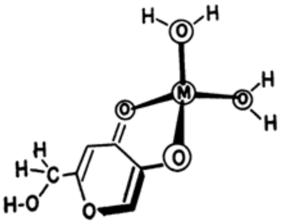
Fig. 2. Graphical determination of the formation constants for Mg(II)-kojate system.

In order to evaluate the formation constants of the chelates, Eq. 10 was employed and K_1 and K_2 values were obtained graphically in Fig. 2. All the straight lines intersect satisfactorily at one point which verifies the formation of the two chelate species, MgA^+ and MgA_2.

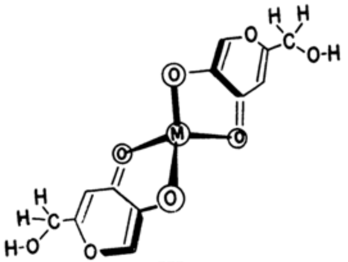
Although such differences were not critical, very slight deviations in K_1 and K_2 values, which depended upon the ligand to metal ratio, were noticed. Nevertheless, K_1 and K_2 values with reasonable accuracy may be obtained from 1:1 and 2:1 titration curves respectively. The values thus estimated are shown in Table I.

Formation of a tetracoördinated Mg(II) complex with tetrahedral configuration utilizing its $3s3p^3$ orbitals has been widely accepted. The 1:1 and 2:1 chelates probably have the structures indicated by II and III respectively.

The stability of the kojate chelate of Mg(II) may be compared with those of other Mg(II) chelates having a similar configuration of the chelate ring.

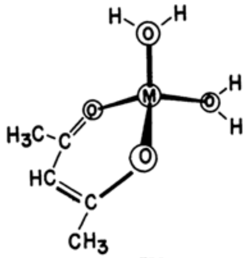


II

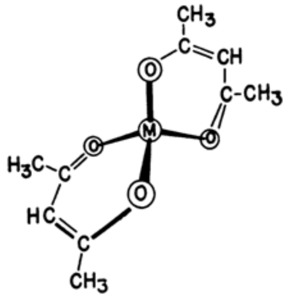


III

Acetylacetone forms chelates with Mg(II)[5] the structure of which are shown by IV and V. These formation constants for IV and V are slightly greater than those for the corresponding kojate chelates. These formation constants of slightly greater values for the acetylacetonate complexes may be considered



IV



V

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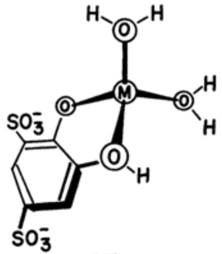
[5] R. M. Izatt, W. C. Fernelius and B. P. Block, *J. Phys. Chem.*, 59, 80 (1955).

due to the higher basicity of the enol group and the resonance stabilization of the heterocyclic chelate ring, while such resonance stabilization is prohibited for the kojate complexes.

Meanwhile, the Tiron chelate⁶⁾ indicated by VI is obtained with smaller stability in comparison with the kojate chelate in spite of the fact that both kojic acid and the first phenol group of Tiron have almost the same magnitude of dissociation constants. Thus, this difference in stability is solely due to the difference in donor property of alcoholic oxygen and carbonyl oxygen toward Mg(II) ion.



VI

Interaction of Mn(II) Ion with Kojic Acid.— A family of titration curves for solutions containing various amounts of kojic acid per mole of Mn(II) ion are shown in Fig. 3. Distinctive inflections were observed at *m* values corresponding to the complete neutralization of protons liberated from kojic acid.

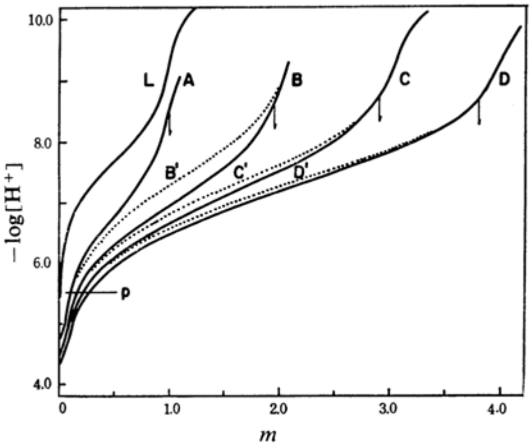


Fig. 3. Potentiometric titration of Mn(II)-kojate chelate system at the total metal concentration of 1.14×10^{-3} M, with these molar ratios of ligand to metal ion: A, 1 : 1; B, 2 : 1; C, 3 : 1; D, 4 : 1; L, ligand (kojic acid) alone; *m*=moles of base added per mole of metal ion; $t=25°C$; $\mu=0.1(KNO_3)$. Dotted curves represent superimposition of two titration curves: B′, A+L; C′, B+L; D′, C+L. Arrows indicate points where pH drifting became noticeable, while titration curves below p represent non-equilibrated data.

The color of the titrating solutions was pale yellow and slightly deepened as pH went up. Precipitation was observed at very high pH beyond inflection regions. In all cases, the solutions did not come to equilibrium immediately in the $pH(-\log[H^+])$ region below 5.5 and above 8.5. Thus, experimental titration curves lying between these pH values were actually used in pursuing the chelating behavior of kojic acid with the metal ion.

Curves obtained by superimposition of the titration curve of free kojic acid on adequate experimental titration curves are shown, together with experimental titration curves for solutions containing the same total concentrations of metal ion and ligand. The depression of pH is significant for the 2 : 1 ratio, and such depression decreases as the molar ratio of the ligand increases. However, such phenomena are not adequate enough to verify the chelate species formed at different molar ratios of kojic acid to Mn(II) ion.

As a first step in determining the Mn(II)-kojate chelate species, 1 : 1 titration curves were obtained over a four-fold concentration range as shown in Fig. 4.

The hydrolytic tendency of manganese(II) ion indicated by the equation:

$$Mn^{2+}+H_2O \rightleftarrows Mn(OH)^{+}+H^{+}$$

does not seem to influence the complexing behavior of this metal ion with the ligand under

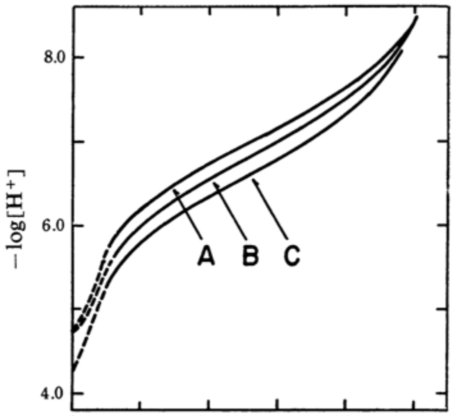


Fig. 4. Potentiometric titration of 1 : 1 Mn(II)-kojate chelate system: A, 5.68×10^{-4} M; B, 1.14×10^{-3} M; C, 2.28×10^{-3} M; *m*=moles of base added per mole of metal ion; $t=25°C$; $\mu=0.1(KNO_3)$. Dotted lines indicate non-equilibrated data.

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6) G. Schwarzenbach and A. Willi, unpublished results; J. Bjerrum, G. Schwarzenbach and L. G. Sillén, "Stability Constants, Part I Organic Ligands", the Chemical Society, London (1956), p. 45.

experimental conditions of the present investigation since the K value is as small as $10^{-10.6}$ at 30°C and $\mu=0.1$[4].

Mathematical treatment of the data employing Eq. 11 yielded the plots shown in Fig. 5. Good conformity with a straight line was obtained, and the slight fluctuation from the straight line for the data of lower concentration does not seem to disturb the evaluation of the formation constants. The same mathematical treatment performed for the titration curves of solutions containing 2 : 1 and 3 : 1 molar ratios of ligand to metal ion results in a satisfactory linear relationship as indicated in Fig. 6. With the same reason as mentioned above for the interaction of Mg(II) ion with the ligand, K_1 value was evaluated from the calculated data shown in Fig. 5 while K_2 value was determined from the data in Fig. 6. The results are summarized in Table I.

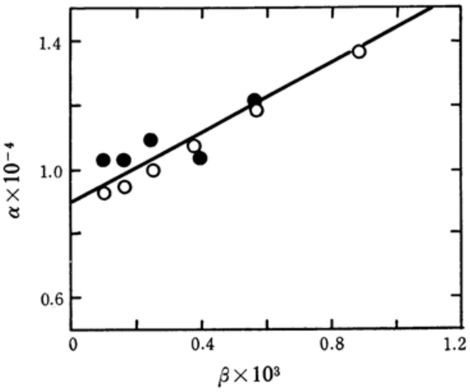

Fig. 5. Graphical determination of the formation constants for Mn(II)-kojate chelate system from titration data obtained for Mn(II)/kojic acid=1 in connection with Eq. 11. Concentrations of metal ion : ○, 2.28×10^{-3} M ; ●, 1.14×10^{-3} M.

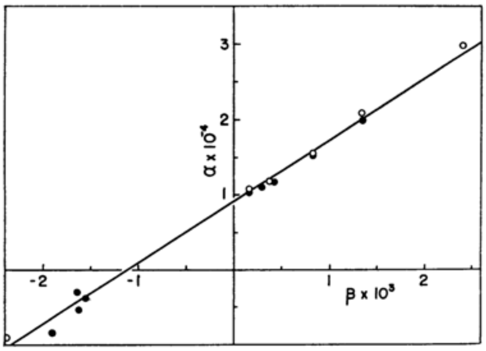

Fig. 6. Graphical determination of the formation constants for Mn(II)-kojate chelate system from titration data obtained for ligand to metal ratios : ○, 2 : 1 ; ●, 3 : 1.

Satisfactory linear relationship in Fig. 6 provides the conclusive support for the formation of a chelate species containing two moles of ligand per mole of metal ion and not more than two moles of ligand. Manganese(II) ion could be expected to form a hexacoördinated chelate compound having octahedral configuration. In the case of hexacoördinated manganese(II) ion, the metal ion should utilize its $3d^24s4p^3$ atomic orbitals for the coördinate bond formation. Such a five-membered chelate ring formation that takes up two oxygens as donor atoms toward manganese(II) ion does not seem to supply enough energy to transfer the five 3d electrons into three degenerate t_{2g} orbitals. Instead, $4s4p^3$ atomic orbitals of manganese(II) ion could be utilized for the formation of four chelate bonds in the atmosphere of weak ligand field produced by kojate ion. The structures of Mn(II)-kojate chelates may be represented by II and III having tetrahedral configuration.

Mn(II)-kojate chelates possess slighly greater values of formation constant than Mg(II)-kojate chelates as observed in other Mn(II) chelates involving oxygen atoms as donor atoms[7].

In conclusion, manganese(II) ion frequently behaves like magnesium(II) ion with a similar magnitude of chelate formation constants in aqueous system in spite of the fact that manganese(II) ion is a member of the first transition series.

Summary

Chelating tendencies of kojic acid toward divalent magnesium and manganese ions have been investigated in aqueous media at 25.0 ±0.1°C and 0.10 M of ionic strength. In spite of the difference in their electronic configurations, both metal ions formed similar chelate compounds and indicated an optimum coördination number of four. Both metal ions formed kojate chelates whose stabilities are nearly equal to the corresponding metal chelates of β-diketones of the same acidity.

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[7] J. Bjerrum, G. Schwarzenbach and L. G. Sillén, Loc. cit.