*Stability Order in Metal Chelate Compounds. I. 4-Carboxy- and 4-Sulfocatechol Complexes**

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Irving and Williams⁽¹⁾ collected and examined the stability data of complexes formed with bivalent metal ions of the first transition series and put forward the stability order, manganese < iron < cobalt < nickel < copper > zinc. This order has been shown to hold substantially for nitrogen-type, nitrogen-oxygen-type and oxygen-type ligands. On the other hand, it is of much interest to find a place for the bivalent zinc in the stability order ranging from bivalent manganese through bivalent copper, since the Irving-Williams order does not provide any knowledge about the stability of zinc complexes in comparison with the other transition metal complexes.

Meanwhile, Mellor and Maley demonstrated the stability order for bivalent metal chelates with salicylaldehyde⁽²⁾ and ethylenediamine⁽³⁾ and placed zinc between iron and cobalt in the first transition series, i. e., copper>nickel>cobalt>zinc>iron>manganese. However, the general applicability of the Mellor-Maley order has not yet been established, and the higher stability of bivalent zinc complexes than the corresponding bivalent cobalt complexes has been frequently observed. It seems, therefore, that the stability of a zinc complex is quite dependent on the ligand properties and the character of the resulting coordinate bonds. In this connection, the catechol derivatives were selected in this investigation as ligands for the first transition metals as well as for

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* Contribution No. 37 from the Department of Organic Synthesis, Faculty of Engineering, Kyushu University.

1) H. Irving and R. J. P. Williams, *Nature*, **162**, 746 (1948); *J. Chem. Soc.*, **1953**, 3192.

2) D. P. Mellor and L. Maley, *Nature*, **159**, 370 (1947).

3) D. P. Mellor and L. Maley, ibid., **161**, 436 (1948).

alkaline earth metals, and the stability order was studied.

Experimental

Materials.—The bivalent metal nitrates, $Zn(NO_3)_2\cdot 6H_2O$, $Cu(NO_3)_2\cdot 3H_2O$, $Ni(NO_3)_2\cdot 6H_2O$, $Co(NO_3)_2\cdot 6H_2O$, $Mg(NO_3)_2\cdot 6H_2O$, $Ca(NO_3)_2\cdot 4H_2O$ and $Sr(NO_3)_2$, and manganese sulfate, $MnSO_4\cdot nH_2O$, are analytical reagents produced by the Wako Pure Chemical Industries, Ltd.

Reagent grade catechol of the Wako Pure Chemical Industries, Ltd. was purified by means of repeated recrystallization from benzene. Dotite Tiron (analytical grade) was used without further purification.

Preparation of Ligands.—*4-Carboxycatechol (Protocatechuic Acid).*—This catechol derivative was prepared from vaniline following the standard method reported by Pearl and Beyer[4] and was recrystallized from water. M. p. found, 203~204°C; reported, 199~200°C[4].

Found: C, 54.48; H, 4.00. Calcd. for $C_7H_6O_4$: C, 54.55; H, 3.92%.

Potassium Catechol-4-sulfonate.—This material was synthesized by the sulfonation of catechol[5] and was recrystallized from water as white platelets.

Found: C, 31.58; H, 2.39; K, 16.91. Calcd. for $C_6H_5O_5SK$: C, 31.57; H, 2.21; K, 17.13%.

Reagent Solutions.—Aqueous stock solutions of metal ions were standardized by the usual procedures of chelatometric titration[6]. Aqueous stock solutions of all the ligands were standardized by potentiometric titration with a standard base.

Potentiometric Measurements.—The apparatus and procedures for potentiometric titrations have been mentioned elsewhere[7].

Spectral Measurements.—The infrared spectra were measured by the KBr disk method with a Koken model DS-301 spectrophotometer equipped with sodium chloride optics.

Mathematical Treatment

Acid Dissociation Constants.—The equilibria and the dissociation constants involved in the dissociation process of catechol protons are:

$$H_2L \rightleftharpoons HL^- + H^+ \quad K_{H_2L}=\frac{[HL^-]\,[H^+]}{[H_2L]} \tag{1}$$

$$HL^- \rightleftharpoons L^{2-} + H^+ \quad K_{HL}=\frac{[L^{2-}]\,[H^+]}{[HL^-]} \tag{2}$$

If T_L represents the total concentration of ligand species and T_{OH} represents the total concentration of base added to the system, the following stoichiometric relations may hold:

$$T_L=[H_2L]+[HL^-]+[L^{2-}] \tag{3}$$

$$T_{OH}+[H^+]-[OH^-]=[HL^-]+2[L^{2-}] \tag{4}$$

Combination of Eqs. 1 through 4 results in:

$$1/K_{H\,L}=A\,K_{HL}+B \tag{5}$$

where

$$A=\frac{\{2T_L-T_{OH}-[H^+]+[OH^-]\}}{\{T_{OH}+[H^+]-[OH^-]\}[H^+]^2}$$

$$B=\frac{\{T_L-T_{OH}-[H^+]+[OH^-]\}}{\{T_{OH}+[H^+]-[OH^-]\}[H^+]}$$

Thus, when $1/K_{H_2L}$ is plotted graphically as a function of K_{HL} with values of A and B corresponding to experimental values of T_L, T_{OH}, and $[H^+]$, straight lines obtained from a number of experimental points are found to intersect at one point, which represents the simultaneous solution of K_{H_2L} and K_{HL} for the dibasic acid.

Chelate Stability Constants.—If the pH value of the system is maintained in an appropriate range so that the metal chelates formed are the 1:1 (ligand to metal) and the 2:1 chelates in significant concentrations, the equilibria involved in metal chelate formation may be expressed as:

$$M^{2+}+L^{2-}\rightleftharpoons ML \quad K_1=\frac{[ML]}{[M^{2+}]\,[L^{2-}]} \tag{6}$$

$$ML+L^{2-}\rightleftharpoons ML_2^{2-} \quad K_2=\frac{[ML_2^{2-}]}{[ML]\,[L^{2-}]} \tag{7}$$

The stoichiometric relationships involved in this system are represented as:

$$T_M=[M^{2+}]+[ML]+[ML_2^{2-}] \tag{8}$$

$$T_L=[H_2L]+[HL^-]+[L^{2-}] \\ +[ML]+2[ML_2^{2-}] \tag{9}$$

$$T_{OH}+[H^+]-[OH^-]=[HL]+2[L^{2-}] \\ +2[ML]+4[ML_2^{2-}] \tag{10}$$

where T_M indicates the total concentration of all the metal species. Equations 6 through 10 may by combined to give an equation for the evaluation of K_1 and K_2:

$$(F-1)K_1[L^{2-}]+(2F-1)K_1K_2[L^{2-}]^2=1 \tag{11}$$

where

$$F=T_M/\{T_L-[H_2L]-[HL^-]-[L^{2-}]\}$$

and

$$[L^{2-}]=\frac{\{2T_L-T_{OH}-[H^+]+[OH^-]\}K_{H_2L}K_{HL}}{\{2[H^+]^2+[H^+]K_{H_2L}\}}$$

Therefore, K_1 may be plotted as a function of K_1K_2, and one straight line may be drawn for each experimental point on the titration curve; the lines thus obtained are to intersect at one point if the metal chelate formations expressed by Eqs. 6 and 7 predominantly hold in the system. This method of evaluation is quite

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[4] I. A. Pearl, "Organic Syntheses", Vol. 29, 85 (1949); I. A. Pearl and D. L. Beyer, *Ind. Eng. Chem.*, **42**, 376 (1950).

[5] J. N. Rây and M. L. Dey, *J. Chem. Soc.*, **117**, 1407 (1920).

[6] K. Ueno, "Chelatometric Titration" (in Japanese), Nankodo, Ltd., Tokyo (1960).

[7] Y. Murakami, This Bulletin, **35**, 52 (1962).

similar to those mentioned for the determination of acid dissociation constants in the preceding section and for chelate stability constants elsewhere⁷⁾, and the intersect of the family of straight lines may provide the chelate stability constants, K_1 and K_2.

When more than three moles of ligand per gram-ion of metal are added to the titrating system and when an appropriate pH range is selected, the 3 : 1 (ligand to metal) chelate may be formed in a significant concentration, depending upon the coordination ability of the metal ion. Under such conditions, it was found in this investigation that reaction 6 was nearly completed and that reactions 7 and 12 are to be taken into consideration.

$$\mathrm{ML_2^{2-}} + \mathrm{L^{2-}} \rightleftharpoons \mathrm{ML_3^{4-}} \qquad K_3 = \frac{[\mathrm{ML_3^{4-}}]}{[\mathrm{ML_2^{2-}}]\,[\mathrm{L^{2-}}]} \qquad (12)$$

Then, an adequately modified form of Eq. 11 may be employed for the evaluation of the third stability constant, K_3.

Results and Discussion

Acid Dissociation Constants.—As the electron-withdrawing effect of a substituent group or groups in the catechol derivatives decreases in the order: Tiron, catechol-4-sulfonate, 4-carboxycatechol, catechol, an inflection region for the neutralization of the first catechol proton in their potentiometric titration curves becomes increasingly insignificant. Thus, the first and the second dissociation processes for Tiron do not overlap each other to any significant extent. On the other hand, those processes for catechol do overlap to a great extent, so the inflection region was not noticed.

A carboxy proton of 4-carboxycatechol is very acidic in comparison with other catechol protons, so the first dissociation process was separated clearly from the others in this case.

The acid dissociation constants of the catechol derivatives other than Tiron were calculated with the aid of Eq. 5 and are summarized in Table I.

TABLE I. ACID DISSOCIATION CONSTANTS OF THE CATECHOL DERIVATIVES

30±0.1°C, μ=0.10 M (KNO_3)

Ligand	pK_{H_3L}	pK_{H_2L}	pK_{HL}
Catechol		9.13	11.59
4-Carboxycatechol	4.38	8.67	11.94
Catechol-4-sulfonate		8.26	12.16
Tiron		7.54	12.26

It is of interest to consider the effect of electron-withdrawing substituents on the dissociation process of catechol protons among these four catechols. The two processes are conceivable in this case, as is shown in Chart 1. A sulfonate and a carboxylate substituent in the benzene ring introduce a pronounced electron-withdrawing effect at their para position. For example, a dissociation constant of the phenol proton of hydroxybenzoic acid has a very close connection with the position of a carboxy group, as may be seen in Table II⁸⁾.

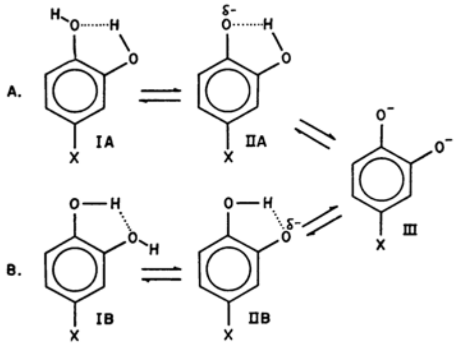


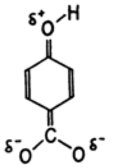
Chart 1. Dissociation processes of catechol-protons.

TABLE II. ACID DISSOCIATION CONSTANTS OF PHENOL DERIVATIVES⁸⁾

20°C, μ=0.1 M

Acid	pK_{H_2A}	pK_{HA}
Phenol		9.80
m-Hydroxybenzoic acid	3.96	9.61
p-Hydroxybenzoic acid	4.36	8.985

The carboxylate group transmits its strong electronic effect to its para position in the benzene ring through such resonance interaction as is indicated by structure IV, while this group shows only a weak inductive effect at its meta position, as may be understood from the data in Table II.



IV

As the pK_{HL} values in Table I indicate, the intramolecular hydrogen bond is strengthened as a ligand varies from catechol to Tiron in the order shown in the table. Because of the electrostatic nature of hydrogen bonding, the electrostatic potential ought to be increased in order to raise the strength of bonding. X being an electron-withdrawing group, an intramolecular hydrogen bond in IIA should be weakened

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8) A. V. Willi and J. F. Stocker, *Helv. Chim. Acta*, 38, 1279 (1955).

in comparison with catechol itself. This is, however, contrary to what is observed in this work. Therefore, IIB must be taken instead as a more favorable structure. As a result, process B in Chart 1 may be employed to elucidate the dissociation steps of the catechol protons. Meanwhile, the OH stretching vibrations involved in inter- and intramolecular hydrogen bonds were assigned, as Table III shows. The tendency of the OH frequency shift is in agreement with the change in pK_{HL} value except in the case of Tiron. The reason for the unexpected frequency shift in Tiron is not quite obvious at this moment.

TABLE III. STRETCHING VIBRATIONS OF CATECHOL-HYDROXY GROUPS

Frequency cm^{-1}	Ligand			
	Catechol	4-Carboxy-catechol	Catechol-4-sulfonate	Tiron
ν_{OH}	3320	3300	3165	3260
ν'_{OH}	3435	3440	3245	3475

ν_{OH}: Assignment of intramolecular hydrogen bonded OH vibration.

ν'_{OH}: Assignment of intermolecular hydrogen bonded OH vibration.

Interaction of Metal Ions with 4-Carboxycatechol. — Titration curves are illustrated in Fig. 1 for the 4-carboxycatechol chelates of magnesium(II), manganese(II), cobalt(II), nickel(II), copper(II) and zinc(II) for a 2 : 1 ratio of ligand to metal ion. The titration curve for the calcium(II) chelate is not shown in the figure because higher concentrations of ligand and metal ion were employed. The drifting behavior of the pH value was noticed for the manganese(II) chelate system during the measurement in the region of $-\log[H^+]$ value ranging from 7.2 to 8.1. A similar phenomenon was observed for the manganese-(II) kojate chelate system[7].

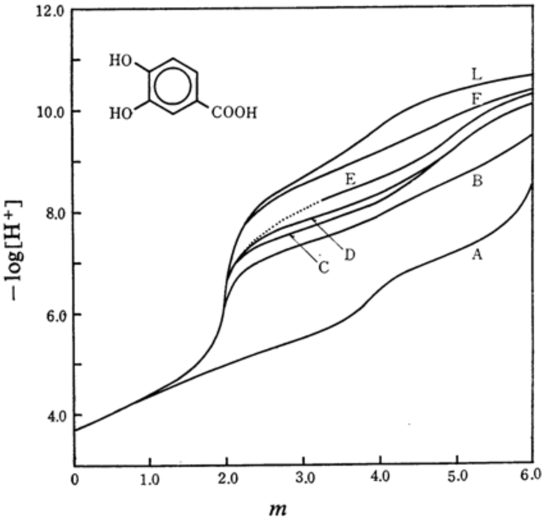

Fig. 1. Potentiometric titration of divalent metal chelates of 4-carboxycatechol in 0.10 M KNO_3 at 30°C, with 2 : 1 molar ratio of ligand to metal ion: A, Cu; B, Zn; C, Ni; D, Co; E, Mn; F, Mg; L, ligand alone; $T_M = 5.01 \times 10^{-4}$ M; m=moles of base added per gram-ion of metal. Dotted line indicates non-equilibrated region.

Potentiometric titrations for the 1 : 1 ratio of ligand to metal ion for calcium(II), magnesium(II), cobalt(II), nickel(II), copper-(II), and zinc(II) were also performed at the same ligand concentration. Precipitations were found at the end of the titrations of the cobalt(II), nickel(II) and zinc(II) chelate systems where all the protons of the catechols were nearly neutralized. These precipitations were probably caused either by disproportionation to the corresponding 2 : 1 chelate and metal hydroxide or by further hydrolysis reactions of the 1 : 1 chelate. The addition of a base to the copper(II) chelate system resulted in neither drifting of the pH values nor precipitation in the range of m values of up to 3.1 ($-\log[H^+] \approx 7.5$). This phenomenon is ascribed to the profound stability of the copper(II) chelate; this chelate could not undergo disproportionation reaction with the ease of other metal chelates.

In the case where more than two moles of ligand were present per gram-ion of metal, no precipitation was observed over the whole pH range of the titration.

As may be seen in Fig. 1, no obvious depression of pH was observed in the lower buffer region (m=0∼2.0), where the dissociation of a carboxy proton occurs predominantly, while only the titration curve of the copper-(II) chelate system demonstrates such a depression to some extent in the last part of this region. On the basis of these experimental facts, no appreciable chelation was expected in such a pH region expect for the copper(II) chelate system, and the carboxy group was not involved in complex formation with metal ions. It is also obvious from Fig. 1 that stability with respect to the metal ions increases in the order: magnesium(II)< manganese(II)<cobalt(II)∼nickel(II)<zinc(II) <copper(II). A small inflection at m=4 corresponding to the formation of the 1 : 1 chelate species and a rather steep inflection at m=6, which corresponds to the formation of the 2 : 1 chelate species, were observed only for the copper(II) system. The absence of such an inflection at m=4 suggests an appreciable overlapping of the two reactions producing the 1 : 1 and the 2 : 1 chelale species.

TABLE IV. STABILITY CONSTANTS OF THE METAL CHELATES OF CATECHOL DERIVATIVES

$30 \pm 0.1°C$, $\mu = 0.10$ M (KNO_3)

Ligand	Catechol		4-Carboxycatechol			Catechol-4-sulfonate			Tiron	
	$\log K_1$	$\log K_2$	$\log K_1$	$\log K_2$	$\log K_3$	$\log K_1$	$\log K_2$	$\log K_3$	$\log K_1$	$\log K_2$
Zn(II)	8.46	6.78	8.91	6.71		9.40	7.20		10.19	8.33
Cu(II)	12.52	9.66	12.79	9.81		13.29	10.23		13.99	11.17
Ni(II)			8.27	4.71	3.89	8.85	5.56	4.73		
Co(II)			7.96	5.40	4.06	8.54	5.86	3.08		
Mn(II)			7.22	5.06		7.87	4.66			
Mg(II)			5.67	4.17		6.27	4.14			
Ca(II)			3.71	2.65		4.40	3.59			
Sr(II)						3.61	—			

Interaction of Metal Ions With Catechol-4-sulfonate.—In Fig. 2 are shown titration curves for solutions containing a 2 : 1 ratio of ligand to metal ion. The metal ions employed in these measurements were strontium(II), calcium(II), magnesium(II), manganese(II), cobalt(II), nickel(II), copper(II) and zinc(II). No precipitates were observed throughout those titrations where ligand concentration exceeded two moles per gram-ion of metal. A drifting of the pH reading was also realized in the titration of the manganese(II) chelate system in the lower pH region ($-\log[H^+] < 8.2$). The stability order is obviously understood from these titration curves and arranged in the increasing order as: calcium(II) < magnesium(II) < cobalt(II) ~ nickel(II) < zinc(II) < copper(II). Again, a titration curve for the copper(II) system exhibits a significant inflection at $m=2$ and a steep one at $m=4$, corresponding to the formation of the 1 : 1 and 2 : 1 chelates respectively.

In titrations of solutions containing a 1 : 1 ratio of ligand to metal ion, pH drifting was observed to start for the transition metal chelate systems in the region where nearly all the catechol protons were neutralized ($m > 1.8$ in most cases). This drifting may be ascribed either to disproportionation to the 2 : 1 chelate and metal hydroxide or to the hydrolysis reaction of the 1 : 1 chelate in the same manner as has been mentioned for the 4-carboxycatechol chelates.

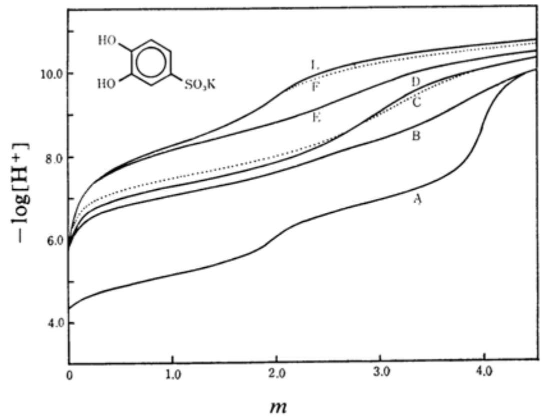

Fig. 2. Potentiometric titration of bivalent metal chelates of catechol-4-sulfonate in 0.10 M KNO_3 at 30°C, with 2 : 1 molar ratio of ligand to metal ion: A, Cu; B, Zn; C, Co; D, Ni; E, Mg; F, Ca; L, ligand alone; $T_M = 5.00 \times 10^{-4}$ M; m = moles of base added per gram-ion of metal.

Stability Constants.—The stabilty constants for the metal chelate compounds with catechol and its derivatives as ligands have been calculated by the aid of Eq. 11 and its modified forms. The constants thus estimated are listed in Table IV.

For the bivalent transition metal series, the stability order for the metal chelates with 4-carboxycatechol and catechol-4-sulfonate follows the sequence: manganese < cobalt ~ nichel < zinc < copper. The stability order, nickel(II) < zinc(II), seems to be rather unusual. This order has, however, been found occasionally in the literature in the past and may be ascribed to the following two main effects involved in chelation:

Structural Effects.—In most instances where the stability of metal chelates follows the sequence, nickel(II) > zinc(II), a lone pair of valence electrons in a donor atom is directed toward the metal ion, with which coordination is performed, thus forming a stable coordinate bond. However, the perturbation effect may be introduced if such a lone pair is located in a direction unfavorable for a coordinate bond formation, in which case the above sequence is reversed (zinc(II) > nickel(II)). In such a case the ionic size of the metal ion seems to be another factor controlling the stability order. 4-Hydroxybenzimidazole and its analogous compounds (V)[9] may be taken as ligands to elucidate this effect.

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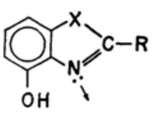
[9] T. J. Lane, C. S. C., A. Sam and A. J. Kandathil, *J. Am. Chem. Soc.*, **82**, 4462 (1960); T. J. Lane, C. S. C. and A. Sam, ibid., **83**, 2223 (1961).



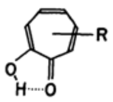
$X = NH, O, S$

V

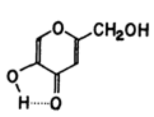
A lone pair of the donor nitrogen atoms in this case seems to have the greatest angular distribution toward external direction with respect to the coordinate bond. As a result this electron pair would have less overlapping with the bonding atomic orbital of a metal ion of smaller size.

Electronic Effects.—The stability of a metal chelate compound is certainly dependent on the electronic state of the donor atom. Thus, when a sulfur atom is involved in chelate ring formation as a donor atom, the stability is in favor of zinc chelates. For example, mercaptoacetic acid[10] and mercaptosuccinic acid[11] yielded the corresponding zinc chelates which were more stable than those of nickel.

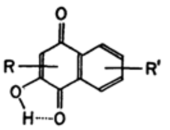
Even if the ligand species are limited to the nitrogen type, the oxygen type and the nitrogen-oxygen type, such a reversed order of stability for zinc and nickel chelates has been observed. However, such examples are found quite rarely to the best knowledge of the present authors. Tropolones (VI)[12] and kojic acid (VII)[13], as well as 2-hydroxynaphthoquinones (VIII)[13], were observed to form zinc chelates with a favorable stability. It is of much interest to find that all these ligand species accommodate the same chelating site, as is shown by structure IX:



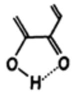
VI



VII



VIII



IX

The electronic configuration of whole ligand molecule and of the central ion, in addition to the electron delocalization effect through the coordinate bond formation, may come into play in these cases to control the stability of metal chelates thus produced.

The unusally high stability of zinc chelates in comparison with that of nickel chelates formed with 4-carboxy- and 4-sulfocatechol as well as with Tiron[12] must be associated to some extent with the electron delocalization through the interaction among zinc 3d orbitals, oxygen-orbitals not involved in σ-bonding, and π orbitals of the benzene ring. The configuration of these orbitals is depicted in Fig. 3.

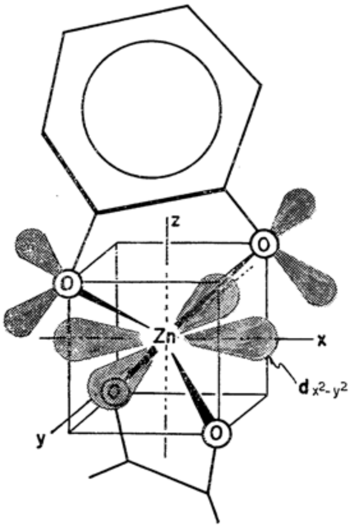


Fig. 3. Probable structure of the Zn(II)-catechol chelate with indication of metal d orbital and lone pair orbitals of oxygens.

The linear relationship between the basicity of the donor group (pK_{HL}) and the chelate stability ($\log K_n$) has been found to hold in a large portion of the literature reported so far. Thus, the weaker the acidity of the donor group, the more stable the chelate compound would be. In this investigation the stability constants for copper(II) and zinc(II) chelates with the four catechols were obtained, as is shown in Table IV. These data obviously prove the parallel relationship between the ligand basicity and the stability constant in agreement with the past observation only if the second pK value(pK_{HL}) is taken. In the opinion of the present authors, the basicity of both hydroxy groups in the ligand molecule should be taken into consideration, since both groups are involved in chelate ring formation. The value of ($pK_{H_2L}+pK_{HL}$), as a measure of ligand basicity, decreases in the order:

Catechol > 4-carboxycatechol > catechol-4-sulfonate > Tiron.

The stability order, however, is antiparallel to this order and is found in the sequence:

Tiron > catechol-4-sulfonate > 4-carboxycatechol > catechol.

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[10] D. L. Leussing, ibid., **80**, 4180 (1958).

[11] G. E. Cheney, Q. Fernando and H. Freiser, *J. Phys. Chem.*, **63**, 2055 (1959).

[12] J. Bjerrum, G. Schwarzenbach and L. G. Sillén, "Stability Constants, Part I. Organic Ligands", The Chemical Society, London (1956).

[13] H. Kido, W. C. Fernelius and C. G. Haas, Jr., *Anal. Chim. Acta*, **23**, 116 (1960).

In spite of the fact that the second catechol proton is involved in the intramolecular hydrogen bonding, the catechol group (two phenolate groups) certainly lowers its electron density as the 4-substituent group demonstrates a greater electron-withdrawing effect, thus indicating less basicity. The relationship between ligand basicity and chelate stability found in this study is certainly due to ligand nature. It seems that these ligand molecules introduced a more covalent character to the coordinate bonds, and that the resonance contribution of the substituent group made electron delocalization through the coordinate bonds more effective.

For alkaline earth metal ions, no peculiar stability order was observed in this work, and these chelates demonstrate much less stability than the corresponding transition metal chelates, as is shown in Table IV. The stability order, magnesium(II) > calcium(II) > strontium(II), is parallel to the reciprocal of the ionic size of the metal ions.

Meanwhile, the formation of such a hydrogen complex as MHL was noticed in this investigation in the region of relatively low pH value, as has also been observed elsewhere for the Tiron chelates in an aqueous system(12). A thorough investigation on this behavior has not yet been carried out. Investigations with other catechol derivatives, containing various 4-substituent groups, are under progress in these laboratories.

Summary

The stability constants of 4-carboxy- and 4-sulfocatechol chelates with bivalent transition metals and alkaline earth metals have been evaluated in aqueous media at 30.0±0.1°C and 0.10 M of ionic strength. The stability orders, manganese < cobalt ∼ nickel < zinc < copper for transition metal chelates and strontium < calcium < magnesium for alkaline earth metal chelates, have been found to hold in these catechol chelate systems. A unique stability sequence, nickel < zinc, has been discussed in terms of the electron delocalization effect, in which metal d orbitals, lone pair orbitals of catechol oxygens and π orbitals of the benzene ring are involved. A reverse relationship for ligand basicity and chelate stability was observed for copper(II) and zinc(II) chelates, and the stability of metal chelates was found to increase in the sequence; catechol < 4-carboxycatechol < catechol-4-sulfonate < Tiron. Substituent groups were considered to play an important role in this case.

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