TABLE III

DETERMINATION OF $K_{\text{CuIen}}^{\text{CuIen}}$ FROM TITRATION OF CuI_2^- WITH ETHYLENEDIAMINE

Wave length, mμ	[CuIen] × 10^3	[Cu(en)_2^{++}] × 10^4	[CuI_2^-] × 10^4	$K_{\text{CuIen}}^{\text{CuIen}}$ × 10^2
600	4.00	3.50	4.45	0.97
612.4	4.00	3.50	4.45	.97
625.0	3.95	3.73	3.67	1.12
637.5	3.99	3.55	4.49	1.00
			Av.	1.02

$$\log K_{\text{CuIen}}^{\text{CuIen}} = -2.0$$

When the value of $K_{\text{CuIen}}^{\text{CuIen}}$ is 1.02×10^{-2} the fraction of CuIen present at the end-point in the titration of the 1:1:1 mixture would be 0.83. The remainder is CuI_2^- and Cu(en)_2^{++}. If the relative concentrations of CuIen, CuI_2^- and Cu(en)_2^{++} remained the same during the titration of the 1:1:1 mixture the correct values of the constants $K_{\text{CuI}}^{\text{en}}$ and $K_{\text{Cuen}}^{\text{I}}$ are simply the preliminary values multiplied by 0.83. This gives for the correct values

$$\log K_{\text{CuI}}^{\text{en}} = 8.8$$

$$\log K_{\text{Cuen}}^{\text{I}} = 8.2$$

From these values and (8) we obtain

$$\log K_{\text{CuIen}}^{\text{CuIen}} = -2.0$$

This value of $\log K_{\text{CuIen}}^{\text{CuIen}}$ is in agreement, within experimental error of that found by independent measurement.

Discussion

It is of interest to compare the two reactions

$$\text{CuI} + \text{I}^- = \text{CuI}_2^- \quad \log K_{\text{CuI}}^{\text{I}} = 5.49$$

and

$$\text{Cuen}^{++} + \text{I}^- = \text{CuIen} \quad \log K_{\text{Cuen}}^{\text{I}} = 8.2$$

Both represent the addition of I^- as a second ligand but show a large difference. The most obvious difference is that the formation of the mixed complex involves neutralization of charge. Charge neutralization, in general, appears to be a type of reaction which is favored probably because of the favorable entropy change in the de-solvation of the charged species. An additional effect may be that the number of coördination positions filled in CuI is greater than in Cuen^{++}.

A second comparison is

$$\text{Cuen}^{++} + \text{en} = \text{Cu(en)}_2^{++} \quad \log K_{\text{Cuen}}^{\text{en}} = 9.61$$

$$\text{CuI} + \text{en} = \text{CuIen} \quad \log K_{\text{CuI}}^{\text{en}} = 8.8$$

There is no charge neutralization in either of these cases and there is only a relatively small difference in log K. We cannot describe with any confidence why this difference exists although here again there is the difference in numbers of coördination positions filled in Cuen^{++} and in CuI.

The constant for the reaction

$$2\text{CuIen} = \text{Cu(en)}_2^{++} + \text{CuI}_2^- \quad \log K_{\text{CuIen}}^{\text{CuIen}} = -2.0$$

may express again the favoring of charge neutralization. On the basis of statistics alone, the mixed complex is favored and $\log K_{\text{CuIen}}^{\text{CuIen}}$ would be −0.6. DeWitt and Watters[1a] found the following for a similar reaction

$$2\text{Cu(ox)en} = \text{Cu(ox)}_2 + \text{Cu(en)}_2^{++} \quad \log K = -0.95$$

It is evident that many more such reactions must be studied in order to increase our understanding of the factors involved.

IOWA CITY, IOWA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STATE UNIVERSITY OF IOWA]

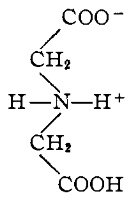
Coördination Compounds of Metal Ions with Derivatives and Analogs of Ammoniadiacetic Acid[1]

BY ROBERT M. TICHANE AND WILLIAM E. BENNETT

RECEIVED SEPTEMBER 6, 1956

To obtain information as to the effect of the structure of a compound on its ability to act as a chelating agent, values for the first and second formation constants of complexes between metal ions and derivatives and analogs of iminodiacetic acid were determined. It was found that definite changes in the chelating ability of ligands could be brought about by structural changes which influence the freedom of motion of the donor groups.

The formation constants of a series of chelates of a given metal ion with ligands of similar structure show a relation with the acid dissociation constants of the ligands. This effect has been noticed in the case of complexes of amines,[2] diketones[3,4] and of compounds related to iminodiacetic acid.[5-9] The general effect observed is that the logarithms of the formation constants of metal complexes of a given type are proportional to the pK values of the complexing agents.



Iminodiacetic acid derivatives are convenient to study since they are generally soluble in water. It was decided that such compounds could be used to study the structural factors which would influence the relationship between the pK of the ligand and its chelating ability. It was of interest to deter-

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(1) From a thesis submitted by Robert M. Tichane to the Graduate College of the State University of Iowa in partial fulfillment of the requirements for the degree of Doctor of Philosophy, 1956.

(2) J. Bjerrum, *Chem. Revs.*, **46**, 381 (1950).

(3) M. Calvin and K. W. Wilson, THIS JOURNAL, **67**, 2003 (1945).

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(5) G. Schwarzenbach, H. Ackermann and P. Ruckstuhl, *Helv. Chim. Acta*, **32**, 1175 (1953).

(6) G. Schwarzenbach, A. Willi and R. O. Bach, *ibid.*, **30**, 1303 (1947).

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mine the effects of three factors: changing of base strength through N-substitution, substitution of oxygen and sulfur for nitrogen in the iminodiacetic acid structure, and the fixing of the spatial configuration of the ligand.

Experimental

Materials.—The free acids hydrazinediacetic[10] (A), nitroiminodiacetic[11] (B), nitrosoiminodiacetic[12] (C), *o*-tolyliminodiacetic[13] (D), phenyliminodiacetic[14] (E), piperidinedicarboxylic[15] (F), pyridinedicarboxylic[16] (G), diglycolic[17] (H) and thiodiglycolic[18] (I) were either prepared according to descriptions given in the literature or were obtained from commercial sources. Some changes were found to be helpful in the methods for the preparation of some of the acids. These are as follows: (1) hydrazinediacetic acid—mix the hydrazine hydrate with potassium carbonate and add potassium chloroacetate, rather than add the hydrazine hydrate to potassium carbonate–potassium chloroacetate mixture. (2) Thiodiglycolic acid—keep the sodium hydroxide and sodium sulfide solutions cool and add slowly to the sodium chloroacetate solution. (3) Nitro- and nitrosoiminodiacetic acid—do not recrystallize from alcohol because of esterification. (4) 2,6-Pyridinedicarboxylic acid—the 2,6-lutidine can be oxidized in 12% permanganate solution by warming slowly and then cooling. (5) 2,6-Piperidinedicarboxylic acid—reduction of the pyridinedicarboxylic acid will take place in aqueous solution. Acetic acid is not necessary.

The metal ion solutions were solutions of the metal chlorides. The Cu^{++}, Ni^{++}, Co^{++} and Zn^{++} solutions were standardized by electrodeposition. The Ca^{++} solution was standardized by the gravimetric oxalate method and the Mg^{++} by the precipitation of the 8-hydroxyquinolinate. Carbonate-free potassium hydroxide solution was prepared by the method of Schwarzenbach and Biedermann.[19]

Apparatus and Procedures.—The experimental method consisted of the titration with carbonate-free potassium hydroxide of solutions containing the chelating agent alone and in the presence of metal ions. The ionic strength was maintained within ±0.002 unit with 0.1 *N* KCl and the temperature was maintained at 30.0°. The *p*H values of the solutions were determined with a Beckman Model G *p*H meter.

Spectrophotometric estimation of formation constants was carried out in the case of some pyridinedicarboxylic acid complexes. The method is outlined by Martell and Calvin.[20] The Cary recording spectrophotometer was used.

Calculations

Values for acid *pK*'s and for formation constants of the complexes were calculated by algebraic methods similar to those used by previous workers.[21] Mixtures of acid and metal ion in a ratio of 1:1 were titrated to obtain data for evaluation of the formation constant of the 1:1 complexes. An acid to metal ion ratio of 1:2 was used for evaluation of the formation constants of the complex $MA_2^{=}$. Following is a summary of the constants determined. (The symbol $A^{=}$ refers to the acid anion.)

$$pK_1 = -\log \frac{[HA^-][H^+]}{[H_2A]}$$

$$pK_2 = -\log \frac{[A^=][H^+]}{[HA^-]}$$

$$K_1 = \frac{[MA]}{[M^{++}][A^=]} \quad K_2 = \frac{[MA_2^=]}{[A^=][MA]}$$

The acid *pK* values determined are in terms of hydrogen ion activity and of concentrations of other species. The metal complex formation constants are in terms of concentration of species.

In the calculation of acid *pK* values and metal formation constants a charge balance relation is used. If the concentration of hydrogen ion is appreciable as compared to other species an error will be introduced unless the concentration, rather than activity, of hydrogen ion is used. The assumption of an activity coefficient of 0.8 gives concentrations of hydrogen ion which are consistent with the data.

In the cases of the 1:1 copper and nickel complexes with pyridinedicarboxylic acid the acid strength of the complexing agent combined with the great stabilities of the complexes made the determination of formation constants by the *p*H method very inaccurate. It was necessary in this case to estimate the formation constants by a spectrophotometric method.[20] Conditions were chosen such that in a solution containing a 1:1 molar ratio of metal ion and acid, the predominant species was the complex MA. By analyzing a solution spectrophotometrically which contained 10^{-2} *M* pyridinedicarboxylic acid, 10^{-2} *M* Ni^{++} and 10^{-2} *M* Zn^{++} and from determined molar absorbancies of Ni^{++}, NiA, Zn^{++} and ZnA, the constant for the reaction

$$NiA + Zn^{++} = ZnA + Ni^{++}$$

could be evaluated. This constant would represent the ratio of the formation constants of the nickel and zinc complexes. From the formation constant of the zinc complex, which had been determined from the *p*H data, the formation constants of the nickel and copper complexes could be estimated.

Results

The results obtained for the acid *pK* values are given in Table I.

TABLE I

ACID *pK* VALUES

	Acids	pK_1	pK_2
A	Hydrazinediacetic	3.02	7.14
B	Nitroiminodiacetic	2.21	3.33
C	Nitrosoiminodiacetic	2.28	3.38
D	*o*-Tolyliminodiacetic	2.58	5.65
E	Phenyliminodiacetic	2.51	5.17
F	2,6-Piperidinedicarboxylic	2.87	9.92
G	2,6-Pyridinedicarboxylic	2.16	4.76
H	Diglycolic	2.90	4.03
I	Thiodiglycolic	3.26	4.29

The logarithms of the formation constants of the 1:1 complexes are listed in Table II. The letters refer to the acids listed in Table I.

Table III lists the results obtained for the values of log K_2. Only in cases where errors are considered to be equal to or less than ±0.1 log unit are values given.

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TABLE II

LOG K_1 VALUES

Acid	Cu	Ni	Co	Zn	Ca	Mg
A	8.1	6.9	6.0	6.0	2.9	1.9
B	2.0	1.7	1.6	1.6	1.6	..
C	1.9	1.4	1.4	1.4	1.3	..
D	5.7	2.4	2.0	2.7	1.2	..
E	5.8	3.8	3.3	3.7	1.5	..
F	10.2	6.8	5.4	6.1	2.2	..
G	10[a]	8[a]	7.0	7.0	4.6	2.4
H	3.9	2.8	2.7	3.6	3.4	1.7
I	4.5	4.1	3.4	3.0	1.4	..
J[b]	10.4	8.2	7.0[c]	7.0[c]	2.7	..

[a] Spectrophotometric values. [b] Iminodiacetic acid. [c] Values found by Chaberek and Martell.[8]

TABLE III

LOG K_2 VALUES

Acid	Cu	Ni	Co	Zn	Ca
A	4.5	5.3	4.9	4.7	..
E	2.1	2.6	2.6	2.3	..
F	5.0	4.8	4.1	5.0	..
G	6.3	6.1	5.5	6.0	2.6
I	2.8	2.6	2.1	..	..
J[a]	5.6[b]	6.4[b]	5.3[b]	5.1[b]	..

[a] Iminodiacetic acid. [b] Values of Chaberek and Martell.[8]

Discussion

There is a general linear relationship between the average pK values for the acids and the log K_1 values for a given element. The best correlation was obtained when the average pK of the acid was used. The ability of the ligand to combine with two hydrogen ions is thus compared with its ability to combine with a single dipositive ion. This relationship is shown in Fig. 1 for all elements. The more electronegative elements show the greatest dependence of log K_1 upon the average pK value which is comparable to the results of Van Uitert, Fernelius and Douglas[4] with β-diketones in water-dioxane mixtures.

To indicate the extent of correlation of average pK values with log K_1, Table IV is given. Expected values are those obtained from the straight lines of Fig. 1.

TABLE IV

(LOG K_1 OBSERVED) − (LOG K_1 EXPECTED)[a]

Acid	Cu	Ni	Co	Zn	Ca
A	...	...	...	...	...
B	...	...	...	...	1.7
C	...	...	...	...	0.6
D	...	−2.0	−2.0	−1.3	−0.6
E	1.0	...	...	...	...
F	−1.8	−2.8	−3.1	−2.4	−1.6
G	6.3	4.7	4.3	4.3	1.4
H	...	...	...	0.9	2.1
I	...	...	...	...	...
J	...	...	...	...	−0.6

[a] Values less than ±0.5 are not listed.

Except for copper the log K_1 values of all other ions with *o*-tolyliminodiacetic acid (D) are lower than expected and, in the case of phenyliminodiacetic acid (E) copper only has an unexpected value. The methyl group appears to cause some type of hindrance to the formation of a chelate and the presence of the phenyl group favors the formation of copper chelates.

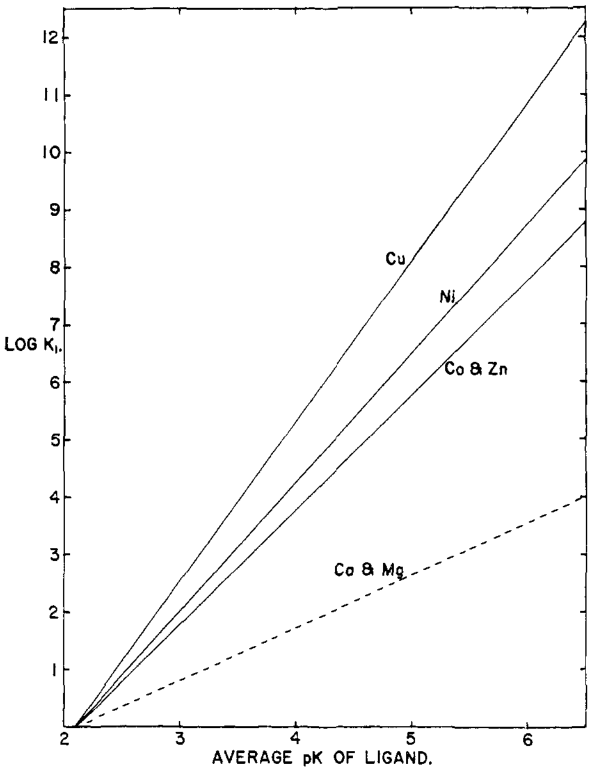
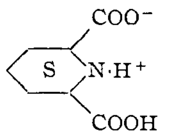


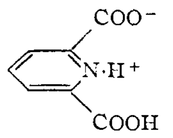
Fig. 1.—Log K values for the formation of 1:1 metal complexes as a function of average pK of the ligand.

The 2,6-piperidinedicarboxylic acid (F) consists of an iminodiacetic acid structure in which the carbons on each side of the nitrogen are joined by a three carbon chain. When a molecular model is constructed for this compound it appears possible that the ring structure may fix the orientation of



(F)

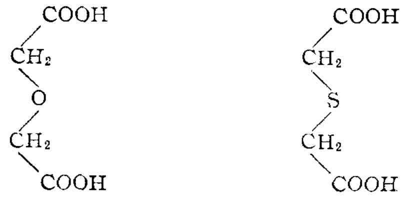
such as to inhibit the movement of the carboxylate groups into positions appropriate to chelation. The opposite effect appears to occur in the case of pyridinedicarboxylic acid (G). The planar configuration



(G)

of the ring fixes the groups in positions favorable to chelation. This configuration would be expected to be especially favorable for copper which forms strong bonds with a square planar configuration.

It is surprising to note that diglycolic acid (H) and thiodiglycolic acid (I) have the expected log K_1 values. It appears that the oxygen and sulfur form coördinate bonds nearly to the same extent as the nitrogen in phenyliminodiacetic acid (E). If only



(I)

the carboxylate ions were bonding, one would expect smaller formation constants.

The log K_2 values increase in about the same order as log K_1. With the more basic ligands log K_1 − log K_2 for copper is greater than for other metals. This is a common type of behavior and is due to the fact that the copper, which normally has a coördination number of four, must, when combining with two ligand molecules, assume six coördination or else must not attach to all possible coördinating groups of the ligands.

IOWA CITY, IOWA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, BUCKNELL UNIVERSITY]

The Stabilities of Metal Complexes of Oxygen-containing Heterocyclic Compounds. Maltol[1]

BY N. JACK CLARK AND B. R. WILLEFORD, JR.

RECEIVED AUGUST 20, 1956

The stability constants of several bivalent metal ions with an oxygen-containing heterocyclic compound, maltol, have been measured in 50% by volume aqueous dioxane at 30° by the Bjerrum potentiometric titration technique. The Irving–Williams stability order of Mn < Co < Ni < Cu > Zn holds for the elements of the first transition series. The usual linear relationships between the logarithms of the stability constants and the acid dissociation constants of the chelating agents and the electronegativity and the second ionization potential of the metal ion are observed.

Among the naturally occurring compounds which are capable of forming metal complexes, there is a group which is characterized by the presence of an oxygen-containing heterocyclic ring. A large number of these are derivatives of the γ-pyrone flavonol and are widely distributed throughout the plant kingdom. These compounds can react with metals by the loss of a proton from the hydroxyl group on the heterocyclic ring. The carbonyl oxygen is then in position to form a five-membered chelate ring with the metal ion. Interest in these metal complexes has taken several forms recently. Quercetin and its glycoside rutin have been used for the treatment of capillary fragility; a number of their metal complexes have been synthesized in an attempt to find forms which are sufficiently soluble to increase the ease of administration.[2] Also, flavonol, quercetin, morin and myricetin have recently found use as analytical reagents.[3] The stabilities of several metal kojates have been measured by Bryant and Fernelius.[4]

It was felt that an investigation of the stabilities of the complexes which various metals form with chelating agents of this type was desirable. There are several complicating structural factors in the flavonols. Accordingly, maltol (3-hydroxy-2-methyl-4-pyrone), a simpler oxygen heterocyclic which is readily available, was chosen as a starting point.

Experimental

The maltol was kindly supplied by the Cliffs Dow Chemical Co. of Marquette, Michigan, and was used as received; m.p. 162–163°, literature[5] 162–164°. Dioxane was refluxed over metallic sodium for 6–8 hr. and then distilled through a four-foot bubble plate column.[6] Water was doubly distilled from alkaline permanganate solution. The tetramethylammonium hydroxide, obtained as a 1 *N* solution from Southwestern Analytical Chemicals, Austin, Texas, was diluted to approximately 0.1 *N* and standardized against primary standard potassium acid phthalate. Metal nitrate solutions were prepared by dissolving weighed quantities of the reagent grade salts in water and analyzing by standard quantitative methods. All other chemicals were reagent grade.

Stability constants were determined by potentiometric titration[7] in a 50% by volume dioxane–water solvent. The solution for titration contained about 0.15 g. of maltol (1.2×10^{-3} mole), 25 ml. of dioxane, 20 ml. of water and 5 ml. of the metal salt solution (0.03 *M*). In several experiments it was necessary to add a known amount of nitric acid to the solution to suppress chelation at the beginning of the experiment. Titrations were carried out at 30.00 ± 0.02° by addition of a standard solution of tetramethylammonium hydroxide from a microburet which could be read with a precision of ±0.002 ml. Titrations of Co(II) and Mn(II) were carried out in an atmosphere of nitrogen. Measurements were made with a Beckman model G *p*H meter with extension type calomel and glass (Beckman 1190–75) electrodes. The instrument was checked before and after each titration with standard buffers which covered the range of meter readings encountered during the titration.

Results and Discussion

The logarithms of the formation constants of the bivalent metal complexes of maltol are listed in Table I.

These are thermodynamic constants obtained by correcting the *p*H meter readings according to the data of Van Uitert,[8] as modified by Irving[9] and

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[1] Abstracted from a thesis submitted by N. Jack Clark in partial fulfillment of the requirements for the degree of Master of Science, Bucknell University, June, 1955. This work was supported by a grant from the Camille and Henry Dreyfus Foundation.

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