THE GENERAL, SELECTIVE, AND SPECIFIC FORMATION OF COMPLEXES BY METALLIC CATIONS

G. Schwarzenbach

Laboratorium für anorganische Chemie, Eidgenössische Technische
Hochschule, Zurich, Switzerland

I. Introduction

The overwhelming majority of reactions used to detect or determine metallic ions in aqueous solution involve the replacement of water molecules in the hydration shell by other ligands. Reactions of this type include not only complex formation in homogeneous solution but also the formation of precipitates. The solution remains homogeneous if the reagent added as a ligand occupies one or several coordination positions on one and the same individual cation (unidentate ligands, e.g., NH_3, $CH_3CO_2^-$; multidentate chelating ligands, e.g., en, gl^-, $ox^=$).* Precipitation occurs if the ligand links two or several metallic ions together (bridging ligands, e.g., $H_2N—NH_2$, OH^-, $CO_3^=$), so that the infinite network of a coagulate or an ordered crystal lattice results. Transition from the simple metal ion to precipitation naturally proceeds through polynuclear species of low molecular weight, though these intermediate stages are almost always difficult to detect and cannot usually be isolated (*63*) (e.g., $Be_3(OH)_3^{3+}$, $Bi_6(OH)_{12}^{6+}$). An attempt is made in this article to survey the course of such reactions in order to point out some empirical regularities, without, however, giving more than an indication of their theoretical interpretation.

* en = ethylenediamine; gl = glycinate anion; ox = oxalate anion.

II. Stability Constants

It is customary in formulating reactions not to take the solvent into account. This abbreviated way of writing an equation results in the formation of complexes appearing as an association reaction, although, in fact, substitution of water molecules is taking place. In the formation of mononuclear complexes we then obtain reactions of Type 1 (charges are omitted):

$$\mathrm{M} \xrightarrow[K_1]{\mathrm{L}} \mathrm{ML} \xrightarrow[K_2]{\mathrm{L}} \mathrm{ML}_2 \dashrightarrow\!\xrightarrow[K_i]{} \mathrm{ML}_i \dashrightarrow\!\xrightarrow[K_n]{} \mathrm{ML}_n \qquad (1)$$

$$\xleftrightarrow{\quad\beta_2\quad}$$

$$\xleftrightarrow{\qquad\quad\beta_i\qquad\quad}$$

$$\xleftrightarrow{\qquad\qquad\quad\beta_n\qquad\qquad\quad}$$

Apart from a very small number of exceptions, stepwise reactions occur. If the concentration of the ligand L in a solution with a metal ion M is successively increased, a whole series of complexes ML_i with values of i from 0 to a maximum of n is formed one after the other. As a rule the processes come almost immediately to equilibrium, and the elucidation of this equilibrium is consequently the most suitable method for studying such reactions. The results yield information on the nature and concentrations of the species in solution, and what is happening may be described quantitatively by means of the equilibrium constants K_i and β_i. The values of K and β, which are the constants for the formation of individual complexes and for the over-all process respectively, are defined as:

$$K_i = \frac{(\mathrm{ML}_i)}{(\mathrm{ML}_{i-1})(\mathrm{L})} \qquad \beta_i = \frac{(\mathrm{ML}_i)}{(\mathrm{M})(\mathrm{L})_i}$$

Since very many such equilibria have been investigated in the last two decades (*10*), the coordinative behavior of various metal ions and their general reactivity can be assessed with the aid of such equilibrium constants. Thus we can, for example, compare the log K_1 values or the magnitudes of log β_n/n with one another. The former are proportional to the free energy of the addition of the first ligand; the latter give the mean free energy of addition of each of n ligands. The ratio of two successive constants ($q_i = K_i/K_{i-1}$) is also of interest. These quotients give information on the disproportionation reaction:

$$2\mathrm{ML}_{i-1} \rightarrow \mathrm{ML}_i + \mathrm{ML}_{i-2} \qquad (2)$$

Large values of q signify that the complex ML_i is formed in well-defined stages, so that, for a definite concentration (L) in effect only two complexes occur in solution simultaneously. The build-up begins with M and ML and then, when all of M has disappeared, a mixture of ML and ML_2 results, and so on. Large q values are characteristic of the formation of chelate complexes, for which the number of species taking part in the equilibrium is generally less than for complexing by unidentate ligands because a smaller number of ligands suffices to fill the coordination positions. If all values of q_i are zero, which almost never happens, ML_n is formed in one step without intermediate stages, so that the equilibrium mixture contains merely M and ML_n and it is possible to specify only β_n, but not the values of K_i. It has been found by experience that the values of q almost always vary between 0.1 and 10, which indicates that as a rule, more than two complexes are present simultaneously in solution.

Figure 1 indicates the composition of such equilibrium mixtures. The complexes present in the solution for different ligand concentrations (shown on a logarithmic scale on the abscissae) are given as percentages of the total metal concentration and are plotted as ordinates in the sequence M, ML, ML_2 etc. In the uppermost family of curves we are dealing with the system $Cd^{++} + NH_3$, and it can be deduced that complex formation commences at an ammonia concentration of 10^{-4} M; at a ligand concentration of 10^{-2} the solution contains 8% Cd^{++}, 35% CdA^{++}, 44% CdA_2^{++} and 12% CdA_3^{++}. The mean value $\bar{i}$ then rises further as the ammonia concentration increases, but the process is not completed even at log (L) = 0, for this solution contains about 7% CdA_3^{++}, 62% CdA_4^{++}, 30% CdA_5^{++} and 1% CdA_6^{++}. The second set of curves represents the system $Cd^{++} + NH_2 \cdot CH_2 \cdot CO_2^-$ (ligand = gl). The fact that the glycine complexes are more stable than those of ammonia is shown by the shift of the curves in the figure to the left; that is to say, complex formation starts at lower ligand concentrations. In addition, only four regions are present since, in addition to the uncomplexed cation, only three complexes (ML, ML_2 and ML_3) occur, and the stages are more widely separated. The third strip represents the system $Cd^{++} + CH_3 \cdot N(CH_2 \cdot COO^-)_2$, with the doubly negative anion of methyl iminodiacetic acid. A tridentate ligand results from the substitution of a second hydrogen atom of the amine molecule by an acetate group, and this gives complexes of enhanced stability, corresponding with a further displacement of the curves to the left. Since the ligand "min" fills three coordination positions, only two adducts are formed and there are therefore only three regions, corresponding to the existence of the species M, ML, and ML_2. The fourth horizontal column shows the behavior of the nitrilotriacetate ion, $N(CH_2 \cdot COO^-)_3$, which is a quadridentate ligand. After its addition only two unoccupied coordination positions remain on the cadmium ion and the charge falls from +2 to −1. It is therefore likely that a second nitrilotriacetate ion will attach itself only with difficulty. As a result,

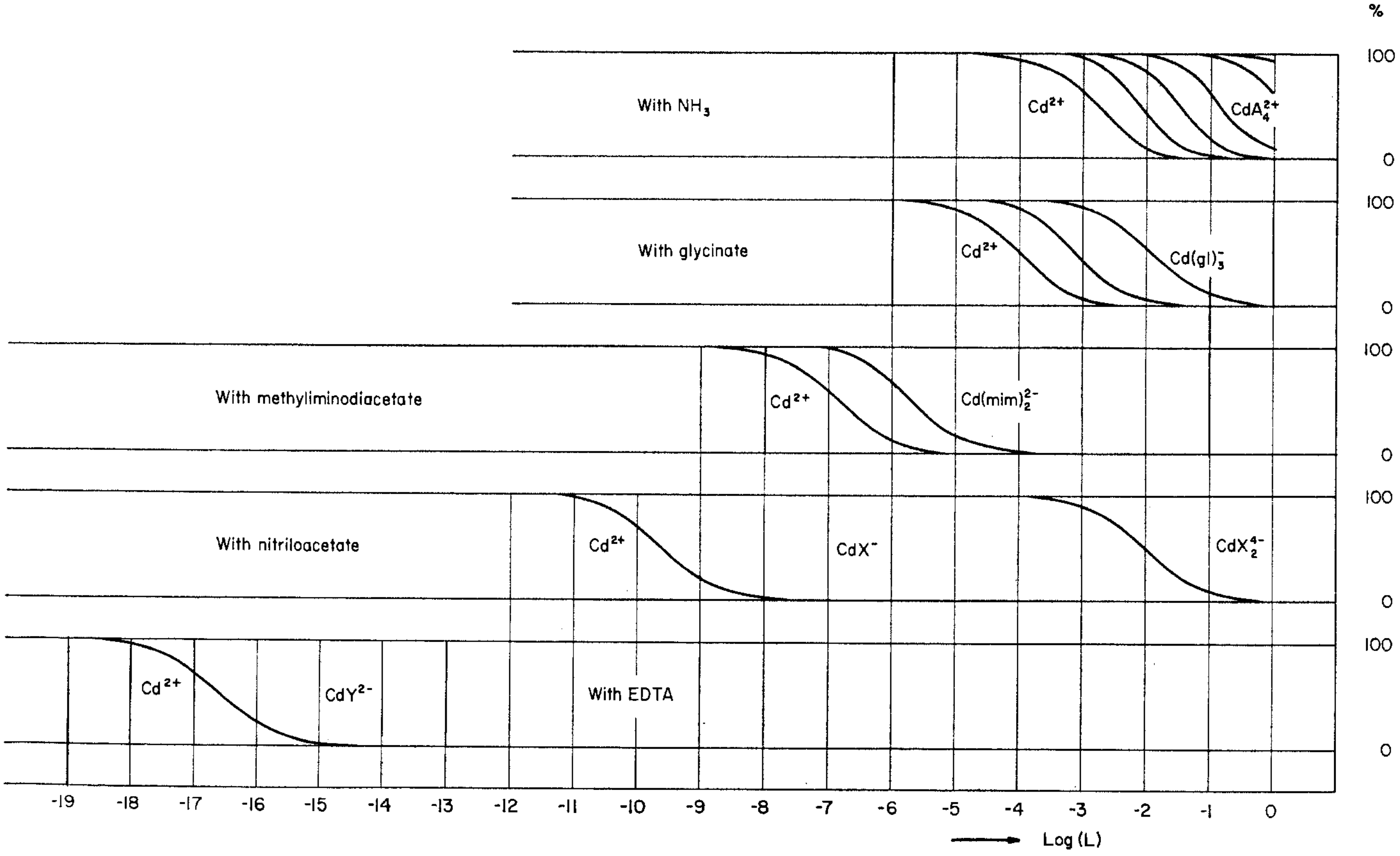


FIG. 1. Complex formation of Cd^{++} with ammonia, glycinate, methyliminodiacetate, nitrilotriacetate, and the anion of EDTA.

formation of ML and ML_2 occurs in widely separated regions of ligand concentration. Complex formation thus occurs in steps that are well separated from one another. The fifth strip in Fig. 1 represents the behavior of the system Cd^{++} + EDTA, the anion of which is able to saturate six coordination positions. As a result only a single complex is formed. Its formation commences at a ligand concentration of 10^{-17}, corresponding to its high stability ($K_1 = 10^{16.5}$).

III. Enthalpy and Free Energy

In comparing equilibrium constants we must bear in mind that it is not the change in free energy, ΔG, but the change in enthalpy, ΔH, in a reaction which has to be taken as a measure of the strength of the chemical bonds which are broken and newly formed. The factual information on ΔH in complex reactions is, however, so scanty that it is impossible to use it to obtain a general picture of the relationships which exist (*46*). On the other hand, formation constants are now known for almost all important complexes (*10*). Moreover, the position of equilibrium is much more important to the chemist than the amount of heat produced in the process. It is for this reason that we will concern ourselves here exclusively with ΔG. Two examples will be given, however, which show that high values of K and β cannot be used without reserve in deducing that there is a high bonding energy between the metal ion and the ligand.

Many complexes are evidently formed simply because of the electrostatic forces between the positive metal ion and an anion or an electrically polar ligand. In this case no new chemical bond results, but only an ion association. Thermodynamically, this means that the change in enthalpy, ΔH, in such reactions is numerically small and may even be positive (endothermic process). In spite of this the formation constant of the complex can be large because the entropy change accompanying the reaction is large and positive, owing to the liberation of many water molecules from the hydration shell accompanying the partial neutralization of charges. The formation of complexes between highly charged metal ions and ligands is always characterized by large positive values of ΔS.

The second example relates to the formation of chelate complexes, the stability of which is always substantially greater than that of the corresponding complex with unidentate ligands (see Fig. 1). Table I gives, by way of example, the formation constants of ammonia and polyamine complexes (*10*) of some metal ions. Let us compare β_2 for the complex with ammonia with the value of K_1 for a diamine (en, tn), β_3 with the K_1 value of the triamine (den), β_4 with the formation constant of the 1:1 complex of an organic tetraamine (trien, tren) and β_6 with the stability of the organic hexamine complex (penten). It is seen at once that a high degree of stabilization results from the formation of chelates. It is, however, clear that the metal-nitrogen bonds made in the formation of a complex by an organic polyamine are not different in character from those in the ammonia complex. In fact it is found that the enthalpy change, ΔH, in the formation of $M(NH_3)_2^{2+}$ is almost the same as that in the formation of $M(en)^{2+}$ or $M(tn)^{2+}$ (*13, 16, 65*), and that $M(NH_3)_3^{2+}$ is formed with almost the same heat evolution as in the case of the chelate complex $M(den)^{2+}$ (*41*). The increase in stability brought about by the formation of the chelate ring, which is referred to as the chelate effect, arises thermodynamically predominantly from the fact that the reactions involved in forming the chelate complex have greater positive entropy changes. Chelate complexes thus have a greater probability of formation than the corresponding complexes with unidentate ligands.

TABLE I

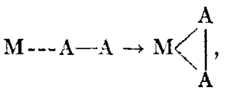
LOGARITHMS OF STABILITY CONSTANTS, K_i, IN ORDER OF INCREASING i

Ligand[a,b]	Ni^{++}						Cu^{++}				Zn^{++}			
NH_3	2.8	2.2	1.7	1.2	0.8	0.03	4.2	3.5	2.9	2.1	2.4	2.4	2.5	2.2
en	7.7		6.4		4.6		10.8		9.3		5.9		5.2	
tn	6.4		4.4		1.2		9.8		7.2					
den			10.7		8.2			16.0		5.4	8.9		5.5	
trien			14.0					20.4			12.1			
tren			14.8					18.8			14.7			
penten				19.3				22.4			16.2			

[a] The data for the NH_3 complexes refer to 30°, $\mu = 1$; those for "en" and "tn" complexes to 25°, $\mu = 1$; all others to 20°, $\mu = 0.1$.

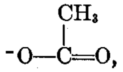
[b] "en" = $NH_2 \cdot CH_2 \cdot CH_2 \cdot NH_2$;
"tn" = $NH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot NH_2$;
"den" = $NH_2 \cdot CH_2 \cdot CH_2 \cdot NH \cdot CH_2 \cdot CH_2 \cdot NH_2$;
"trien" = $NH_2 \cdot CH_2 \cdot CH_2 \cdot NH \cdot CH_2 \cdot CH_2 \cdot NH \cdot CH_2 \cdot CH_2 \cdot NH_2$;
"tren" = $N(CH_2 \cdot CH_2 \cdot NH_2)_3$;
"penten" = $(NH_2 \cdot CH_2 \cdot CH_2)_2N \cdot CH_2 \cdot CH_2 \cdot N(\cdot CH_2 \cdot CH_2 \cdot NH_2)_2$.

This state of affairs may be made clear by a simple model (*17, 49*). Suppose that a bidentate ligand A—A (in which the two ligand atoms are linked by a chain of carbon atoms) is first joined to the cation M by only one of its ligand atoms. The resulting intermediate M---A—A must have the same stability as the 1:1 complex MA with the corresponding unidentate ligand. In the second step the ring will simply close in the case of the chelate ligands:



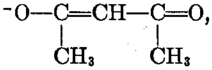
$$M\text{---}A\text{—}A \rightarrow M\left\langle \begin{matrix} A \\ | \\ A \end{matrix} \right.,$$

whereas in forming MA_2 a second freely mobile ligand must be derived from the solution. This process is much less probable than ring closure because, in the intermediate stage of chelate formation, the second ligand is already near the unoccupied coordination position. It is nearer the shorter the chain of atoms between the two ligand atoms in A—A, and as a result the chelate effect will diminish with increase in the number of members in the chelate ring. That this is so is seen in Table I on comparing the stabilities of complexes with ethylenediamine (five-membered ring) and trimethylenediamine (six-membered ring). The increase in stability in forming chelates with seven- and eight-membered rings is insignificant (*50*, *57*). Ring strain clearly arises for rings with less than five members so that, in spite of the greater probability of forming the smaller ring, the stability of the complex decreases because ΔH has become more positive. Four-membered rings have been proved to exist by X-ray crystallographic methods, but there is no case where their formation has led to an increase in stability. The acetate ion,



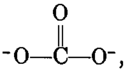
$$^{-}\mathrm{O-\overset{\displaystyle CH_3}{\overset{|}{C}}{=}O},$$

both oxygen atoms of which could attach themselves to a metal atom to give a four-membered ring, just as the acetylacetonate ion



$$^{-}\mathrm{O-\underset{\displaystyle CH_3}{\underset{|}{C}}{=}CH-\underset{\displaystyle CH_3}{\underset{|}{C}}{=}O},$$

adds on to give a six-membered ring, has all the characteristics of a unidentate ligand. The carbonate ion,



$$^{-}\mathrm{O-\overset{\displaystyle O}{\overset{\|}{C}}-O^{-}},$$

is a bridging rather than a chelate ligand. The formation of a three-membered chelate ring is still less likely, and it is therefore easy to understand that hydrazine acts either as a unidentate ligand or as a bridging ligand, in which case it causes precipitation (*59*). Ring strain occurs for Ag^+ and Hg^{++} even with five- and six-membered rings because two ligand atoms are added by these metal ions to give a linear arrangement (*51*, *57*) and a very long chain of atoms is needed to form a strain-free bridge between two coordination positions which are diametrically opposite. It is understandable, therefore, that silver and mercury complexes cannot be stabilized to any extent by the formation of chelates.

All authors agree that the chelate effect is essentially one of entropy. Opinions differ only on the question as to whether stabilization of another sort also occurs in chelate complexes. Measurements have shown that their formation is often somewhat more exothermic than the formation of the corresponding simple complexes and that they absorb at rather shorter wavelengths, corresponding to a somewhat stronger ligand field, which could cause additional stabilization by increasing ΔH (*31, 42*). This question will not be discussed here. For the present discussion the only important point is that, in comparing stabilities of simple complexes with those of chelate complexes in order to assess the tendency to coordination, the chelate effect must be taken into account. In absence of strain log K increases by 2–3 units for each 5-membered chelate ring formed.

IV. Precipitation Reactions

Up to this point it has been assumed that all complex-forming processes take place according to Reaction 1 (Section II). In the introduction it was stated that formation of precipitates can also be taken into consideration in judging the tendency to coordination, since it also involves the formation of complexes, namely polynuclear species. The constants K_i and β_i are also often available for ligands which form precipitates. Mononuclear complexes, the stability of which is given by these constants, are almost always present in the homogeneous solution above the precipitate, where they can be detected by a combination of radiochemical and potentiometric measurements of solubility and activity. In a solution in which AgCl is being precipitated, for example, the complex species AgCl and $AgCl_2^-$ are present, in addition to free uncomplexed Ag^+ cations (*30, 34*). A radiochemical determination with an active silver isotope gives the total concentration of all the species in solution, and the value of (Ag^+) is obtained with a silver electrode. From such determinations with a series of solutions, in which AgCl is precipitated at different alkali chloride concentrations, we can obtain values of K_1 and K_2 for the formation of the simple chloro complexes of silver. Analogous measurements have shown that the species AgSH, $Ag(SH)_2^-$ and AgS^- are present in the precipitation of silver sulfide and how stable these complexes are (*70*).

If no such measurements of the mononuclear species in equilibrium with the precipitate are available, solubility products, K_{sp}, of the slightly soluble precipitates may be compared with one another. The smaller the solubility products the stabler are the bonds between cation (metal) and anion (ligand). Naturally, in making this comparison it is permissible to use only values with the same dimensions. Thus, for example, the solubility product of the 1:1 sulfide of bivalent metals has the dimensions mole^2 liter^{-2}, whereas K_{sp} for the sulfide of a univalent cation has the dimensions mole^3 liter^{-3}.

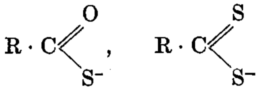
V. Ligands and Ligand Atoms

The nature of the atom which binds the ligand to the metal largely determines the ligand behavior. Only a few ligand atoms will be considered here (the halogens, oxygen, sulfur, nitrogen, and carbon). There is very little quantitative information on complex formation which entails attachment of selenium, tellurium, phosphorus, or arsenic to a metal.

(*a*) The halogens are able to coordinate only as the simplest anions F^-, Cl^-, Br^-, and I^-. The mononuclear fluoro, chloro, bromo, and iodo complexes, or sparingly soluble halides, result.

(*b*) The most important ligand containing oxygen is H_2O, the aquo complexes of which serve as a starting point since water is the solvent normally used. Mononuclear hydroxo complexes are first produced by deprotonation, but the formation of polynuclear species and precipitation almost always follows (*63*); in spite of this, K_1 for OH^- as a ligand is known for most cations. The ion $O_2^{=}$ cannot be studied as a ligand in aqueous solution. Examples of other inorganic oxygen donors are: NO_2^-, NO_3^-, $CO_3^{=}$, PO_4^{3-}, and polyphosphates; $S_2O_3^{=}$, $SO_3^{=}$, $SO_4^{=}$ and ClO_4^-. Organic complexing agents are able to offer the metal ion oxygen in the form of ether R—O—R, and alcohol or phenol, and ketonic or carboxylic oxygen.

(*c*) Sulfur donors are: HS^- and $S^{=}$, $SO_3^{=}$, $S_2O_3^{=}$, SCN^-, thioethers R · S · R, mercaptans and their anions R · SH and R · S^-, thioketones and the mono- and dithiocarboxylate groups



$$R\cdot C\overset{O}{\underset{S^-}{\lessdot}}\ ,\quad R\cdot C\overset{S}{\underset{S^-}{\lessdot}}$$

(*d*) Nitrogen is coordinated by addition of NH_3. Deprotonated ammonia occurs as a ligand for mercury (*35*, *36*, *47*). The ion NO_2^- usually adds on to metal ions through nitrogen and the same is also often the case with SCN^- (*60*, *66*). Organically bound nitrogen coordinates in complex formation with primary, secondary, and tertiary amines, RNH_2, R_2NH, R_3N; Schiff's bases, $>C{=}NR$; carboxylic amides, R · CO · NH_2; nitroso groups R · N=O; oxime groups C=N · OH, and azo groups.

(*e*) The only complex-forming group with carbon as the ligand atom that has been studied in aqueous solution is CN^-.

VI. A- and B-Metal Cations

(*a*) Cations with a rare-gas configuration (d^0 cations), *i.e.*, Be^{++}, Mg^{++}, Ca^{++}, Sr^{++}, Ba^{++}, Al^{3+}, Sc^{3+}, Y^{3+}, lanthanides^{3+}, Ti^{4+}, Zr^{4+}, Hf^{4+}, Th^{4+},

Nb^{5+}, and Ta^{5+}, constitute a related group from the point of view of complex chemistry and will be treated together here as A-metal cations. Their characteristic is that in aqueous solution they are able to form complexes only with F^- and oxygen as donor atoms.

Insoluble fluorides, which are often soluble in an excess of fluoride to form mononuclear complexes, are known to every analyst. It cannot be proved, however, that the chloride ion or any other of the heavy halide anions can be added to the A-metal cations. Possibly loose chloro complexes occur in quite strong hydrochloric acid with the A ions that have a valence greater than three, but they decompose at once on diluting the solution. In contrast to this, the A metals react with all oxygen donors. All of them which are polyvalent naturally form hydroxo complexes which, apart from those of the heavy alkaline earths, go over into sparingly soluble hydroxide precipitates through intermediate polynuclear species.

Difficultly soluble precipitates are likewise formed with $CO_3^=$ and PO_4^{3-}. All the important organic complexing agents for these A cations are also oxygen donors (e.g., tartrates, citrates, the enolates of β-diketones and the anions of aminopolycarboxylic acids, which present several oxygen ligand atoms in addition to one or two nitrogen atoms). Sulfur, on the other hand, is not added to the A cations. Addition of ammonium or alkali sulfide gives slightly soluble hydroxides. In addition, no reaction occurs with sulfur donors such as dithiocarbamates and xanthates, and there is no color reaction with dithizone.

Ammonia also precipitates hydroxides and no ammine complexes result apart from the loose complexes which have been found for alkali earth metals (*10*). Cyanide also precipitates hydroxides because the ligand takes a proton from the solvent and leaves OH^- to react with the metal ion.

The stability of the complex increases rapidly with increase in charge on the metal ion and, with a series of cations of the same valence, those with the smallest radius form the most stable complexes. The validity of this rule can be recognized readily from values of the solubility products of fluorides and hydroxides, as well as from K_1 values for mononuclear fluoro and hydroxo complexes. It is also valid in general for chelate complexes of A cations, such as complex oxalates, tartrates, and citrates. Deviations from the dependence on the cation radius arise if the chelating species possesses more than 3–4 ligand atoms. With EDTA complexes, for example, where the anion has six ligand atoms, the following stability series are obtained:

$$Be^{++} < Mg^{++} < Ca^{++} > Sr^{++} > Ba^{++} \quad \text{and} \quad Al^{3+} < Sc^{3+} > Y^{3+} > La^{3+}.$$

Here the stabilities of complexes of the smallest cations are smaller than those which follow them because the coordination number is often only four (Be^{++}), and the small cation, unlike the larger, cannot, on steric grounds, make use of all six bulky ligand groups in chelation.

Considering the dependence of complex stability on the ligand structure in the case of fluorine- and oxygen-containing ligands, it is at once apparent that anionic ligands give much more stable complexes than uncharged ligands. Oxygen in ethers, ketones, and alcoholic OH groups is able to compete as a ligand with the solvent H_2O, and to attach itself to the metal ions if it forms part of a chelate ligand which also contains more firmly bound anionic oxygen atoms. For a series of anionic ligands the following rule holds: the stability of the complex increases rapidly with the basicity of the ligand oxygen (i.e., its ability to add on a proton), so that we obtain the following stability sequence: $OH^- >$ phenolate $>$ carboxylate $> F^-$. For the series of isoelectric oxo anions the charge decreases simultaneously with the basicity, so that the following stability sequence is explicable: $CO_3^{=} \gg NO_3^-$; $PO_4^{3-} \gg SO_4^{=} \gg ClO_4^-$. This is manifest in the smaller solubility of carbonates compared with nitrates and in that of phosphates compared with sulfates and perchlorates. Some data are available for the K_1 of mononuclear complexes, namely $MgCO_3$, $10^{2.2}$ (*45*); $MgNO_3^+$, $10^{-0.1}$; $CaPO_4^-$, 10^5 (*22*); $CaSO_4$, 10^2. The value for the species $CaClO_4^+$ has not been determined.

(*b*) Cations with an outer shell of 18 electrons (d^{10}) will be referred to as B cations. They are Cu^+, Ag^+, Zn^{++}, Cd^{++}, Hg^{++}, Ga^{3+}, In^{3+}, Tl^{3+} and Sn^{4+}.

Comparing first of all the three univalent ions of the noble metals with the alkali ions, a radically different behavior is found: slightly soluble chlorides, bromides, iodides, and sulfides are in equilibrium with the corresponding mononuclear complexes, all of which are very stable, and very stable ammine and cyano complexes are also formed. It is at once clear that in these cases factors of a different sort from those for the A cations must be operating. That simple coulombic forces are not decisive is seen from the fact that the largest of the three ions gives more stable complexes than the smallest, for the stability sequence is, in general, Cu(I) < Ag(I) < Au(I). It was observed quite early that this sort of complex formation is shown particularly by cations of noble metals and, later, it was found that the first or second ionization potential of the metal from which the cation is derived is a good criterion for assessing its tendency to complex formation (*14, 21, 28, 29, 37*), for this quantity in general parallels the stability of the complex measured by log K_1 or log β_n/n.

As far as the influence of the ligand goes, it is found for the three univalent noble metal cations that there is an increase in the stability of their complexes in the following sequences: $F^- < Cl^- < Br^- < I^-$; $OH^- \ll SH^- \ll S^{=}$; $F^- < OH^- < NH_3 < CN^-$. To establish this sequence one can compare either solubilities or the stability constants of the mononuclear complexes. Table II, for example, shows the values of log K_1 for

TABLE II
STABILITY CONSTANTS OF SILVER COMPLEXES (20–25°)

Complex	AgF	$AgCl$	$AgBr$	AgI	$Ag(OH)$	$Ag(SH)$	AgS^-	$AgNH_3$	$Ag(CN)_2$
log K_1 or $\frac{1}{2}$ log β_2	−0.3 (*10*)	3.0 (*10*)	4.3 (*10*)	8.1 (*10*)	2.0 (*4, 5*)	13.6 (*70*)	20.3 (*70*)	3.1 (*10*)	10.5 (*10*)

mononuclear silver complexes. Most of the ligands are singly charged anions, but the uncharged ammonia molecule is also included. On examining the values, one has the impression that the charge does not play a decisive role in determining stability. Thus the ammonia molecule forms a complex which is appreciably more stable than that from the smaller OH^- and F^- anions. It seems, rather, that the electronegativity of the atom of the ligand element is important, for these values fall in the following sequence:

$$F > O > N > Cl > Br > I \sim C \sim S;$$

this is also the order in which the log K_1 values in Table II increase.

If different ligands having the same donor atom are compared, one again finds an increase in complex stability with increase in basicity. The thioether grouping can be added only to the cations of very noble metals and is greatly inferior to the much more basic mercaptide group. The silver complexes of various amines have been widely studied and it has been found that in general those with the greatest pK form the most stable complexes and that log K_1 even increases linearly with pK (*8*, *11*, *33*). In this case, however, only aliphatic amines, or aromatic and pyridine bases, should be compared with one another.

We will now consider the coordination tendency of the polyvalent B cations by considering a series of isoelectronic ions such as Ag^+, Cd^{++}, In^{3+} and Sn^{4+}. The quite unexpected observation is then made that the stability of the complexes with less electronegative ligand atoms falls with increasing charge instead of increasing, as would be anticipated. The value of log K_1 for the ammonia complexes is 3.1 and 2.7, respectively, for Ag^+ and Cd^{++}, and indium and tin behave toward ammonia similarly to A cations in that the hydroxide precipitates without forming an ammine complex. A fall in stability in passing from Cu^+ to Zn^{++}, Ag^+ to Cd^{++}, or Au^+ to Hg^{++} is also found invariably for anionic ligands of low electronegativity. It is less pronounced in going from II- to III-valent B cations, for the stability often rises somewhat and, in other cases, drops. The following data give log K_1 values for the 1:1 complexes shown (*10*): $AgCl$, 3.0; $CdCl^+$, 1.6;

$InCl^{++}$, 2.4; AgBr, 4.3; $CdBr^{+}$, 2; $InBr^{++}$, 2; AgI, 8.1; CdI, 2.2; InI^{++}, 1.6; AgCN, 10.0; $CdCN^{+}$, 5.4; AuCN, 20; $HgCN^{+}$, 18; $TlCN^{++}$, 10.

On the other hand, with fluoride as a ligand the usual A cation behavior is found, i.e., a rise with increasing charge on the metal ion (AgF, −0.3; CdF^{+}, 0.6; InF^{++}, 4; SnF^{3+}, 5.) This is also the case for mononuclear hydroxo complexes (AgOH, 2; $CdOH^{+}$, 4–5; $InOH^{++}$, 10). The solubility products drop correspondingly in the following sequence, which is also that for A cations with increasing charge:

$$AgOH < Cd(OH)_2 < In(OH)_3 < Sn(OH)_4.$$

The few constants known for complexes with organic oxygen donors (e.g., oxalates) also show a rise in stability with increasing cation charge (*10*).

VII. Electrovalent and Nonelectrovalent Interaction

It is not intended in this article to go into the nature of the forces between the metal ion and ligand. Consideration of the known facts, however, leads us to distinguish between two sorts of associative forces. Coulombic forces are certainly present, and, even if it is impossible to predict quantitatively the free energy of association due to them (*24*), it is nevertheless clear that simple electrostatic forces must operate in such a way that the stability of the complex rises with the valence of the metal ion, and falls with its radius. We find that this relationship holds without exception for the A metal ions, the rare-gas structure of which would, indeed, lead us to expect that their behavior would be particularly simple. The interaction for A cations may therefore perhaps be referred to as "electrovalent," implying that simple electrostatic considerations can be used in discussing the forces between cation and ligand. If this is so, it follows from the observed facts for A cations that for metal ions in aqueous solutions classic coulombic forces allow only fluoride ions and the various oxygen donors to form complexes, with replacement of molecules in the hydration shell. The heavier halogen ions, Cl^-, Br^-, and I^-, the ions HS^- and $S^=$, ammonia, cyanide ion, and the many other organic ligands with N and S are clearly not able, on the basis of coulombic forces, to compete as ligands in aqueous solution with the water molecule, or with OH^-, the product of its deprotonation. For none of the A cations, whatever the radius or charge, is it possible to establish with certainty an association with Cl^-, Br^-, I^-, S, N, or C.

Apart from coulombic forces, there must be other types of interaction which are capable of interpretation only in terms of quantum mechanics. These will be referred to as nonelectrovalent forces and the term will include everything not due to classical electrostatic action, including the possibility of crystal field stabilization (*7*). Nonelectrovalent behavior is encountered in its purest form for noble-metal cations of low charge. In the rough picture of bond formation by the sharing of an electron pair between the central atom and the ligand, it is significant that the stability of the complex is found to increase both with the tendency of the cation to take up electrons (i.e., with increasing ionization potential of the metal involved), and with the tendency of the ligand atom to give up electrons (i.e., with decreasing electronegativity of the nonmetal).

In studying ion association, nonelectrovalent behavior is never encountered in its pure form since coulombic forces must always be operative. For B cations we always have to deal with a superposition of electrovalent and nonelectrovalent interaction. Electrovalent interaction must, however, increase with increasing charge and decreasing radius of the cation and, at the same time, it becomes increasingly difficult for the ligands Cl^-, Br^-, I^-, SH^-, CN^-, NH_3, etc. to compete successfully with H_2O or OH^-. The stability relationships for the complexes of isoelectronic B cations of increasing charge which have been mentioned above are understandable, at least qualitatively, on this basis. The nonelectrovalent interaction with ligands of B cations of low charge changes gradually to electrovalent interaction with increasing charge.

VIII. Transition Metal Cations

These are ions with between 0 and 10 *d*-electrons. Those of the first long period with a valence of two have been particularly fully studied. In the process the Irving-Williams order was discovered (*28*, *29*), according to which the stability of complexes increases in the series

$$Mn^{++} < Fe^{++} < Co^{++} < Ni^{++} < Cu^{++} > Zn^{++}$$

up to copper and then falls in passing to zinc. This rule is valid for almost every ligand. Taking the value of β_i as a criterion, exceptions occur when $i > 4$, for then those cations which usually have a coordination number of only 4 are at a disadvantage compared with those which have a coordination number of 6. There are also polydentate chelate ligands whose structures do not fit sterically into the quasi-square coordination geometry assumed by Cu^{++}, so that octahedral Ni^{++} then forms a more stable complex than Cu^{++}. Finally, Fe^{++} gives complexes of a special sort with CN^-, phenanthroline, and certain other heterocyclic bases, which are characterized by their diamagnetism and deep color. In such cases these cations no longer fit normally into the Irving-Williams series.

The otherwise good validity of the Irving-Williams rule is readily understood in terms of the difference between electrovalent and nonelectrovalent interaction. Radii of transition-metal cations decrease somewhat from Mn^{++} to Cu^{++}, while Zn^{++} has a somewhat greater size. Moreover, ionization potentials of the metals from Mn to Cu increase and fall again with zinc. We would therefore expect that both the electrovalent and the nonelectrovalent behavior of the transition cations would change in accordance with the rule. Since the large changes in ionization potential are much more effective in their action than small changes in ionic radii, nonelectrovalent interaction must undergo a much more marked change than electrovalent interaction. In fact the change in stability for complexes with ligands of low electronegativity is much more marked than for complexes with metal-oxygen bonds. For example log K_1 increases in the case of ethylenediamine complexes from 2.7 for Mn^{++} to 10.8 for Cu^{++} and then sinks again to 5.9 for Zn^{++}, while all oxalate complexes of the series have log K_1 values between 4 and 5. We can say that the electrovalent behavior of the transition ions of like charge remains almost constant, whereas their nonelectrovalent behavior changes markedly. The Mn^{++} ion behaves not very differently from a bivalent A cation, while Cu^{++} shows a markedly more pronounced nonelectrovalent behavior than the d^{10} cation Zn^{2+}.

In recent years it has become customary to explain the Irving-Williams series with the aid of crystal field theory (*9*, *40*). The ions Mn^{++} and Zn^{++} cannot, as d^5 and d^{10} cations, show any crystal field stabilization, while this will increase steadily in the series from d^6 to d^8. This results in the sequence of stability which actually is observed for ligands producing a stronger ligand field than water. The question remains unanswered as to why ligands with N, S, and C produce a particularly strong ligand field when they are quite unable to compete with water in the case of A cations.

Few quantitative measurements are available on the complex-forming behavior of transition cations of the second and third long periods. The nonelectrovalent interaction is, however, certainly the same as for the corresponding cations in the first transition series with the same number of *d* electrons. It increases again in passing to the right and is particularly large for d^7, d^8, and d^9, i.e., for the cations of Rh, Pd, Ir, Pt, as well as for Ag(II) and Au(III). These groups of metals form inert complexes, however, and all reactions occur slowly; this is very useful in preparative studies, but it makes equilibrium measurements difficult or impossible.

IX. General and Selective Complex Formation

It is clear from Sections VI, VII, and VIII that there are both general and selective reagents (*1*, *62*). The fluoride ion and all reagents in which oxygen adds to the metal ion constitute the first group. On the other hand, ligands with N, Cl, Br, I, S, and C are selective, and the selectivity increases with decreasing electronegativity of the element. This is naturally in agreement with familiar analytical experience, in that fluoride, hydroxide, carbonate, and phosphate yield precipitates with almost all polyvalent metal cations, whereas sulfide precipitates only the B cations and transition metal cations. Its selective character has been used since the time of Bergmann and Berzelius in separating metals and is still unsurpassed for this purpose. Reagents with N as the ligand atom and the anions Cl^-, Br^-, I^-, and CN^- function, apart from a very few exceptions (e.g., with Ag^+), as unidentate ligands and not as precipitants; this illustrates clearly the unique character of sulfide for selective separation by precipitation.

We can also differentiate between general and selective reagents in the case of chelate-forming species. Practically all polyvalent metallic ions may be masked by means of the oxygen donors oxalate, tartrate, and citrate, but with polyamines this can be done only with B and transition cations. There are no organic complexing agents in which F, Cl, Br, and I act as donor atoms to the metal ion (organically bonded halogen not being sufficiently nucleophilic) and those which offer carbon as donor, such as the isonitriles, have scarcely been studied from the point of view of the stability of their complexes. There are also rather few organic S donors.

The anions of the aminopolycarboxylic acids are general sequestering agents, and their complexes have greater formation constants than the tartrate and citrate complexes. Data for polyamines, aminocarboxylates, tartrates, and citrates are grouped together in Table III. One can compare, for example, quadridentate "tren" (I) with the anion (X^{3-}) of nitrilotriacetic acid (II) and the sexadentate "penten" (III) with the EDTA anion [Y^{4-} (IV)]. Tartrate (V) and citrate (VI) probably function as tri- and quadridentate ligands respectively.

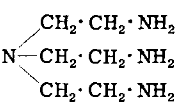
TABLE III

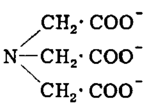
LOGARITHMS OF FORMATION CONSTANTS[a]

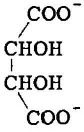
Cation	$M(tren)^{\nu+}$	$MX^{\nu-3}$	$M(penten)^{\nu+}$	$MY^{\nu-4}$	$M(tart.)^{\nu-2}$	$M(citr.)^{\nu-3}$
Ca^{++}	<0	6.4	<0	10.7	1.8	3.2
Ba^{++}	<0	4.8	<0	7.8	1.7	2.8
Al^{3+}	$Al(OH)_3\downarrow$	—	$Al(OH)_3\downarrow$	16.1	—	—
Y^{3+}	$Y(OH)_3\downarrow$	11.4	$Y(OH)_3\downarrow$	18.0	—	—
Th^{4+}	$Th(OH)_4\downarrow$	—	$Th(OH)_4\downarrow$	23.2	—	—
Mn^{++}	5.8	7.4	9.4	13.6	—	3.7
Ni^{++}	14.8	11.3	19.3	18.6	—	5.1[b]
Cu^{++}	18.8	12.7	22.4	18.8	3.2[b]	—
Zn^{++}	14.7	10.5	16.2	16.3	2.7[b]	4.8[b]
Cd^{++}	12.3	9.5	16.8	16.6	—	4.0[b]

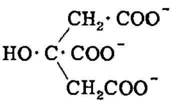
[a] $\mu = 0.1$, 20°C (*10*), but for tartrates and citrates $\mu = 0.15$, 25°C.

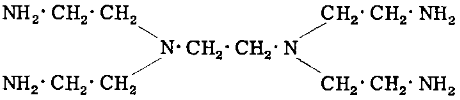
[b] The complexes are more stable in alkaline solution because protons are given up from the alcoholic hydroxyl groups of tartrate and citrate.

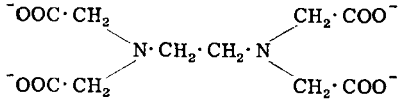

tren
(I)


X^{3-}
(II)


tartrate
(V)


citrate
(VI)

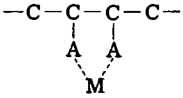

penten
(III)

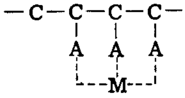

Y^{4-}
(IV)

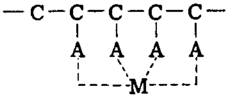
X. Structural Principles of Polydentate Chelating Agents

The general character of tartrate, citrate, nitrilotriacetate, and ethylenediamine tetraacetate as complexing agents, as opposed to the selective character of polyamines, is clearly seen in Table III. It is, however, striking that the strongest general complexing agents contain nitrogen. The explanation of this is to be found in the special structural requirements which must be met when there are more than two donor atoms present, and which can be met only by the incorporation of nitrogen.

For bidentate ligands the two ligand atoms A must be attached to neighboring carbon atoms because of the chelate effect obtained with a five-membered ring [structure (VII)].

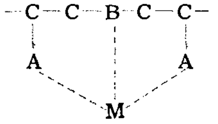

(VII)


(VIII)

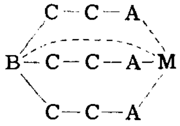

(IX)

If third and fourth ligand atoms are to be introduced it is not satisfactory simply to extend this principle and use molecules of types (VIII) and (IX). If a metal ion had to be added to such molecules using all the ligand atoms A, two or three chelate rings would be formed with several common bonds. Chelate ligands used in this way for coordination would lead to unwieldy and strained structures. Models show that in the molecule VIII only the neighboring corners of a triangular face of a metallic coordination octahedron can be occupied, and even then a certain amount of strain occurs. Occupation of four coordination positions, as in structure (IX), is sterically impossible. A cation cannot use the four available ligand atoms in a chelating agent of such a type.

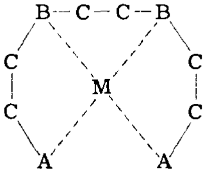
A much more favorable situation is presented by a different type of structure for agents with more than two ligand atoms. This is shown in (X), (XI), and (XII), where it will be seen that some of the ligand atoms, designated as B, are used as members of the chain.



(X)



(XI)



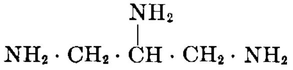
(XII)

Molecules with such a structure can be distributed around an octahedron or tetrahedron with practically no strain. If the coordination sphere of the cation is square, steric difficulties arise with type (XI). That the structural type in (X) is more favorable for tridentate ligands and gives more stable complexes than (VIII) can be seen from the data in Table IV by comparing the two triamines, (XIII) and (XIV), which are represented as "den" and "ptn".

$NH_2 \cdot CH_2 \cdot CH_2 \cdot NH \cdot CH_2 \cdot CH_2 \cdot NH_2$

"den"

(XIII)



$NH_2 \cdot CH_2 \cdot \overset{NH_2}{\overset{|}{C}}H \cdot CH_2 \cdot NH_2$

"ptn"

(XIV)

Comparing the numbers in the first two horizontal lines of Table IV, we see that complexes with "den" are considerably more stable than those with "ptn". The difference is particularly large for copper, the quasi-square

TABLE IV

LOGARITHM OF FORMATION CONSTANTS, K_1[a]

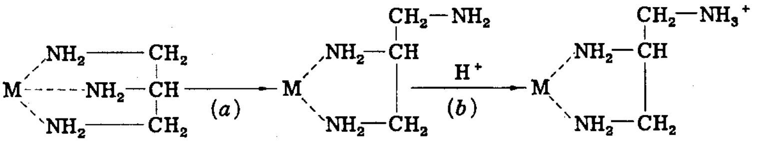
Cation	Co⁺⁺	Ni⁺⁺	Cu⁺⁺	Zn⁺⁺	Cd⁺⁺
"den" complex	8.1	10.7	16.0	8.9	8.5
"ptn" complex	6.8	9.3	11.1	6.8	6.5
"Hptn" complex	4.1	6.0	8.8	4.3	4.7
pK of $[MH\mathit{ptn}]^{3+}$	6.9	6.3	7.3	7.1	7.8
"en" complex	5.9	7.7	10.8	5.9	5.5
"tamm" complex	6.2	9.9	10.8	—	5.4

[a] $\mu = 0.1$, 20° (*10*), for the "en" complexes at $\mu = 1$, 25°.

coordination of which is particularly unsuited to a triamine of the structural type (VIII).

The complex Cu(ptn)$^{++}$ has a stability which is not substantially greater than that of Cu(en)$^{++}$, the complex with ethylenediamine (line 5). For cations with tetrahedral and octahedral coordination the stability difference between M den^{++} and M ptn^{++} is smaller than for Cu^{++}, and M ptn^{++} is still appreciably more stable than M en^{++}.

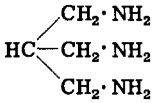
If the ptn complexes are relatively unstable for triamine complexes (because coordination of all three nitrogen atoms leads to a strained structure) we would expect one of the amino groups to break loose from the metal easily. This would be one of the peripheral amino groups because a chelate 5-ring would remain, with a high chelating effect (Reaction 3*a*).



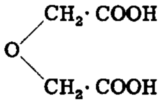
(3)

Such loose amino groups, which are not coordinatively linked, must be detectable by their basic character (Reaction 3*b*). In fact a protonated complex [MH ptn]$^{3+}$ is always found in the equilibrium mixture. Stability constants of such complexes [(MH ptn)/(M)(H ptn)] are given on line 3 of Table IV (*44*). Comparison with the stability constants of the en complexes (line 5) illustrates the interference in the formation of a chelate 5-ring which arises from a positive ionic charge on the complexing species. The p_K values of the hydrogen complexes MH ptn^{3+}, which define the equilibria (Reaction 3*b*), are also readily obtained. The data (line 4) show that M ptn^{2+} complexes are about as strong bases as hydrazine and triethanolamine. No protonated complexes such as M(H den)$^{3+}$ are detectable in the equilibrium mixtures for triamines of the structural type X (*43*).

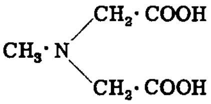
It seems to be impossible to build up a fully effective tridentate chelate-forming species with only peripheral ligand atoms. The triamine XV (trisaminomethylmethane = tamm, last line, Table IV), cannot be considered in relation to the triamine ptn because the unfavorable 6-membered chelated ring would form (*2*).



"tamm"
(XV)



H$_2$digl
(XVI)



H$_2$mim
(XVII)

For a chelating agent with more than two ligand atoms, one or two of the latter must be used in the secondary position, as is the case for the atoms B in (X), (XI), and (XII). If, however, we use oxygen for this purpose, we have an ether oxygen, the coordinating tendency of which is very small. This is shown by the data in Table V by the stability constants of 1:1 complexes with the anion of diglycolic acid (digl). This is a very general complex-forming species, which does not differentiate at all between A-, B- and transition metal cations and, furthermore, forms bonds of almost the same strength to ions of different radii. The complexes, however, are of low stability (*32*).

TABLE V

LOGARITHMS OF FORMATION CONSTANTS, K_1, FOR $\mu = 0.1$, 20°C

Cation	Ca^{++}	Ba^{++}	Cu^{++}	Zn^{++}	Cd^{++}
M digl	3.4	3.3	3.9	3.5	3.4
M glut	1.0	1	3	1.6	—
M min	3.8	2.6	11.1	7.7	6.8

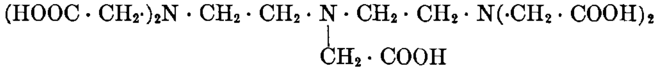
Ether oxygen is such a weakly nucleophilic atom that it has no great effect when it is incorporated in a chelating species. Nevertheless, comparison of diglycolate with glutarate complexes (line 2, Table V) shows that the ether group has a significant stabilizing effect. About the same stabilizing effect can also be obtained—even for the A cations—with nitrogen, which although it is less electronegative than oxygen, is much more basic. This is shown in the third row of data in Table V for the stability constants of the 1:1 complexes of the methyliminodiacetic acid (XVII) anion (min). These complexes with the alkaline earths are about as stable as the diglycollates, though the presence of nitrogen naturally results in greater selectivity, the complexes of B cations are considerably stabilized.

Nitrogen in position B of the structural type X has the great advantage for A cations that it is able to carry a further substituent with a third peripheral oxygen, which leads to a quadridentate complexing agent with the structure XI. With carboxyl oxygen as the peripheral ligand A we get the nitriloacetate ion II, some complexes of which are shown in Table III. Selectivity is again very strongly developed, but A cations are bonded well because three of the four ligand atoms are now oxygen.

A sexadentate ligand potentially capable of coordinating to all metal ions may be built up on the same principles. A second nitrogen atom must be used in its structure so as to be able to attach radicals with further peripheral oxygen atoms. The most favorable conceivable structure is that of the anion of EDTA—all of the chelate rings formed by this anion are five-membered. Any expansion of the ring results in reduced stability of the complex. Trimethylenediaminetetraacetic acid yields complexes with considerably lower formation constants (*53*), and if one or several of the acetate groups in EDTA are replaced by propionate, anions result which again bond less strongly with metal ions (*15*). One or two of the peripheral carboxyl oxygens may be replaced by phenolate groups (*55*), but the products obtained have no advantage over EDTA. It has proved to be disadvantageous to use phosphonate groups in place of acetate (*6*, *68*), for the ethylenediaminetetrakismethyl phosphonic acid,

$$(\mathrm{H_2O_3P\cdot CH_2\cdot})_2\mathrm{N\cdot CH_2\cdot CH_2\cdot N(\cdot CH_2\cdot PO_3H_2)_2}$$

gives somewhat less stable complexes than EDTA. The double negative charge on the peripheral ligand groups clearly has an adverse action, since strong repulsive forces arise between them, which are not compensated by coordination. Trans-1,2-diaminocyclohexanetetraacetic acid (*54*) gives somewhat more stable complexes than EDTA, probably because its anion undergoes a smaller loss in flexibility on coordination, so that the change in entropy associated with the reaction is greater. For highly charged cations and those of greater radii (Th^{4+}, lanthanides), diethylenetriamine pentaacetic acid (*3*, *19*, *67*)



$$(\mathrm{HOOC\cdot CH_2\cdot})_2\mathrm{N\cdot CH_2\cdot CH_2\cdot}\underset{\displaystyle |\atop \mathrm{CH_2\cdot COOH}}{\mathrm{N}}\mathrm{\cdot CH_2\cdot CH_2\cdot N(\cdot CH_2\cdot COOH)_2}$$

is markedly superior, because its anion allows such cations to reach a coordination number of eight, which is their general pattern.

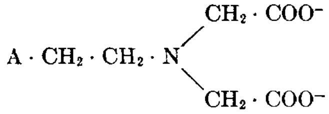
In Section IX we discussed, for the most part, sequestering agents forming complexes which are readily soluble in water. It is possible, however, to differentiate between general and selective reagents in the case of organic precipitating and extracting agents, the complexes of which are mostly soluble in organic solvents though not in water (*52*). The former again have oxygen as the ligand atom and, in certain cases, nitrogen also (e.g., the enolates of β-diketones, cupferron, and 8-hydroxyquinoline).

Reagents with only nitrogen as donor atom and, above all, those with sulfur (e.g., dithiocarbamate, dithiopyrocatechin, and rubeanic acid) are selective for B cations and the transition metals. Finally, there are general and selective reagents among those compounds which form colored complexes that can be used for the spectrophotometric determination of metals, as metal indicators, and to some extent also as metalizable dyes.

XI. Selectivity and Specificity

EDTA and compounds of analogous structure are complexing agents which can hardly be improved upon from the point of view of the stability of the complexes formed. There is, however, still a lack of good selective, and particularly of specific, strong complexing agents. One group of selective sequestering agents is available in the polyamines. Even more marked selectivity could be obtained with S and P as the ligand atoms. Synthesis of such substances is not, however, simple. Moreover mercaptans, phosphines, and arsines oxidize readily and generally have a low solubility in water. There is, neverthelsss, no doubt that they are highly selective.

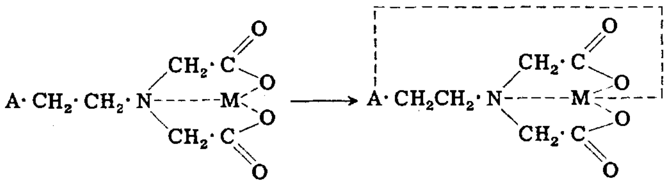
Table VI gives some idea of the improvement in selectivity on replacing oxygen by nitrogen and oxygen. It refers to iminodiacetates of the general formula (XVIII) containing a fourth ligand atom A in the side chain on the nitrogen atom:



$A \cdot CH_2 \cdot CH_2 \cdot N(CH_2 \cdot COO^-)_2$

(XVIII)

As has been explained, the iminodiacetate group adds on to all polyvalent metal ions. If atom A is also able to coordinate, the metal complex increases in stability and log K increases by an amount proportional to the free energy of the ring-closure process shown (4).



(4)

Open complex, *o* Closed complex, *g*

The numbers in Table VI give the difference, log K^g − log K^o, in the stability values for the closed and open species, K^o being calculated from the

TABLE VI

Differences $\Delta = \log K^g - \log K^o$, or Logarithms of Equilibrium Constants for the Ring Closure Process (4)

Substituent A	Ca^{++}	Mn^{++}	Fe^{++}	Co^{++}	Ni^{++}	Cu^{++}	Zn^{++}	Cd^{++}	Pb^{++}
CH_3O—	1.3	0.8	1.0	1.3	1.6	1.9	1.6	1.5	2.3
HO—	1.4	1.0	1.2	1.4	1.6	1.6	1.6	1.7	2.3
H_2N—	0.5	1.5	2.4	3.3	4.0	3.8	3.3	2.8	3.4
CH_3S—	0.1	0.4	1.4	1.8	2.2	2.3	1.4	1.9	2.0
^-S—	0.7	3.1	4.3	6.2	4.0	—	7.4	8.9	8.0

empirically determined dependence of the stability constants of iminodiacetic acid complexes on the basicity of the nitrogen atom (*58*).

The data in Table VI show clearly that even an ether oxygen atom and an alcoholic hydroxyl group as the substituent A in structure (XVIII) result in a significant increase in stability, and that this is of about the same magnitude for all bivalent metallic ions. In contrast to this, the amino group is a much more selective ligand, and the operation of the Irving-Williams series is apparent, apart from the fact that the positions of Ni and Cu are reversed because structure (XVIII) is unfavorable for the quasi-square coordination of Cu(II). The thioether grouping is only weakly nucleophilic, but one can see clearly that Δ becomes more pronounced with increase in the nonelectrovalent behavior of the cation. The deprotonated mercaptide group carrying a negative charge is very selective. It is interesting to see how the d^{10} cations and Pb^{++} move into prominence, with their complexes very strongly stabilized. Data for Cu^{++} are lacking in this series because this ion oxidizes mercaptoiminodiacetic acid to the disulfide (*58*).

The values in the last line of Table VI are clearly related to the solubilities of the sulfides of the metals in question. This is also illustrated in Fig. 2, in which the logarithms of the stability constants of complexes with mercaptoethyliminoacetate [structure (XVIII), A = $^{-}$S—] are plotted against the solubility products of the sulfides. There is a good linear rela-

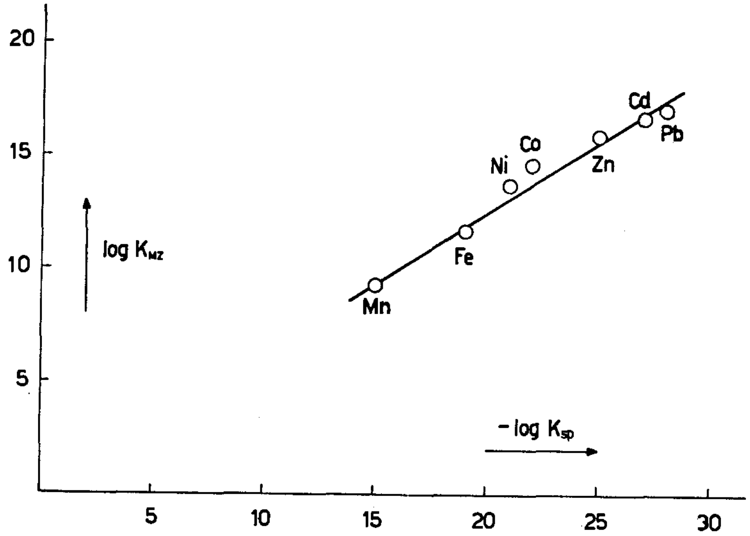
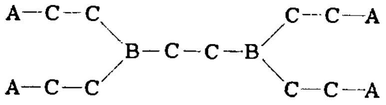


FIG. 2. The stability of the metal complexes of $[S—CH_2—CH_2—N(CH_2—COO)_2]^{3-}$ as a function of the solubility products K_{sp} of the corresponding metal sulfides.

tionship from which only Co and Ni deviate. The solubility products for these two sulfides are, however, uncertain because of dimorphism.

Complexing agents with the structure (XVIII), where A is an element of low electronegativity, carry, in addition to N, only a single ligand atom, which shows preferred addition to d^6 to d^{10} cations. The data in Table VI do, however, make it clear that a chelating agent which is able to provide four to six mercaptide sulfurs as ligand atoms is able to attach itself very selectively to metals. This would be even more the case if the ligand atoms were P and As. Absolute specificity, i.e., a reagent capable of attachment to only one metal cation, cannot be attained because the tendency to coordination is a general property of metal ions which changes only gradually. Certain quite specific reactions are indeed known in analytical chemistry, such as the color reaction of Fe^{++} with *o*-phenanthroline or the precipitation of Ni^{++} with dimethylglyoxime. Investigation shows, however, that *o*-phenanthroline does not in any sense add specifically to Fe(II) *(10)*; what are characteristic of the Fe^{++} reactions are its kinetics *(18)* and the particular absorption spectrum of the 1:3 iron complex *(12)*. The situation is similar for dimethylglyoxime, which is also a quite general complexing agent *(10)*, nickel occupying a special place only because of the low solubility of its derivative.

Increased selectivity, and possibly specificity, may also be produced when the metal ion and chelate ligand are geometrically as compatible as possible. Sexadentate ligands of the general structure (XIX), which experience shows exhibit a maximum chelate effect, form complexes quite generally with considerable strain in the 5 five-membered chelate rings. Ten years ago it was shown *(30, 48)* that EDTA complexes were still able to combine quite generally with a second ligand L:



(XIX)

$$MY^{(\nu-4)+} + L^{\lambda-} \rightarrow MYL^{(\nu-4-\lambda)+} \qquad (5)$$

The mixed complexes $FeYOH^{=}$ and $FeYSCN^{=}$ are formed in this way from FeY^{-}; CrY^{-} gives $CrYOH^{=}$ and $NiY^{=}$ forms the species $NiYNH_3^{=}$ and $NiYSCN^{3-}$. Salts with the following anions have been isolated for Co(III): $CoYCl^{=}$, $CoYBr^{=}$, $CoYOH^{=}$, $CoYNO_2^{=}$. This behavior of EDTA complexes is understandable only if it is assumed that one of the four carboxylate groups is readily cleaved from the metal, leaving a gap in which the hetero-ligand can be added. It has also proved possible to detect the carboxylate group set free, for a proton may be added to it. All EDTA complexes may be protonated at about pH 3:

$$MY^{(\nu-4)+} + H^+ \rightarrow MHY^{(\nu-3)+}. \tag{6}$$

This is a reaction analogous to (3*b*), with which a free amino group was detected in a 1,2,3-triaminopropane complex. Very similar relationships are encountered in the case of the "penten" complexes (structure III), in that these are also able to add protons readily:

$$M(\text{penten})^{\nu+} + H^+ \rightarrow M(\text{H penten})^{(\nu+1)+}. \tag{7}$$

We find here again that one of the amino groups can be split from the metal readily and then protonated (*39*). We have also been able to introduce hetero-ligands in the case of penten complexes, and salts with the following cations have been prepared (*56*): $[Co(penten)OH]^{++}$, $[Co(penten)Cl]^{++}$, $[Co(penten)Br]^{++}$, $[Co(penten)NO_2]^{++}$.

Strains within the complexes manifested by reactions (5), (6), and (7) may also be detected by X-ray methods (*69*). The geometrical relationship in the EDTA complex of tervalent cobalt is shown in Fig. 3. The metal is actually bound to both nitrogen atoms and the oxygens of the four carboxylate groups, but the coordination octahedron is very deformed. Deviations from the normal angle of 90° occur in girdle plane, indicated in Fig. 3 by solid lines linking the atoms; it is particularly large between the valences to the two O atoms on the right (which are not linked by a chain of C atoms), the angle being a full 105°. We can conclude that one of the carboxylate groups in this girdle plane is able to break loose especially easily, leaving a place for a hetero-ligand. The nickel complex $Ni(H_2Y)H_2O$, the geometrical form of which is shown in Fig. 4, actually has a water molecule in the girdle plane (*64*).

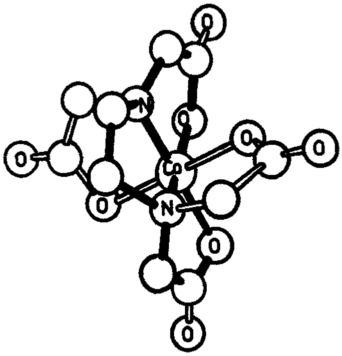


FIG. 3. Geometric structure of the Co(III)-complex of EDTA.

If it were possible to remove this ring strain by slightly enlarging the "mantle" of the metal ion, complexes with chelating agents of the general structure XIX would have a considerably greater stability than has been observed for EDTA and penten complexes. Unfortunately enlargement can be brought about only in definite stages involving the transition from a five to a six ring, which, as has been mentioned, leads to a reduction rather than an increase in stability. It is conceivable, however, that protein structures contain enclaves into which only special metal ions such as Mg^{++} or Mn^{++} can fit, and that specificity in enzyme catalysis by metals arises in this way (*23*, *61*).

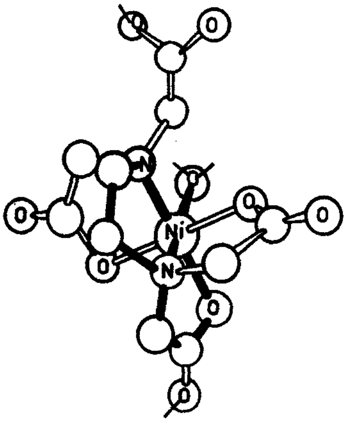
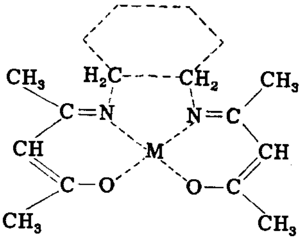


FIG. 4. Geometric structure of NiH_2YH_2O. Molecular units represented by the figure are linked together by hydrogen bridges to form an infinite cristal structure.

Introducing bulky substituents into a chelate ligand usually does not aid complex formation but only hinders it. Specificity can, however, be secured by this method. Introducing a substituent into the 2-position of 8-hydroxyquinoline, for example, will hinder complex formation with Al^{3+} (*26*) and enable us to produce a reagent with which other cations (e.g., Mg^{++}) can be determined in presence of aluminium. An analogous case is provided by 1:10 phenanthrolines, which give general color reactions both with Fe^{++} and Cu^{+}. The reaction with iron may be surpressed by introducing alkyl groups inthe 2- and 9-positions, giving a reagent which still reacts with copper (*27*).

An analogous case arises for the bisacetonylacetonates of 1,2-diamines (*25*). EDAA is the anion of the dienol of ethylenediamine bisacetylacetonate of formula (XX). In each AA section of this anion there is a mesomeric system with a tendency to planarity and the formation of 120° angles. The 5-chelate ring which is formed by coordinating the metal to the nitrogens is forced into the same plane, so that all three chelate rings become coplanar. As a result EDAA is particularly good for occupying the square coordination positions of a metal ion and we consequently obtain selectivity for the d^8 cations Ni^{++}, Pd^{++}, Pt^{++} as well as for the d^9 ion Cu^{++}. In the case of Co(III) complexes two hetero-ligands, such as H_2O, add on in the *trans* positions relative to one another to complete the octahedron (*38*).



(XX)

Complex formation by EDAA may be sterically hindered by the cyclohexane ring shown with a shaded line in formula (XX). Figures 5 and 6 represent atomic models of the complexes of the bisacetylacetones of *cis*- and *trans*-1,2-diaminocyclohexane (DCAA). We find that, for *trans*-DCAA (Fig. 6), in which both amino groups condensed with acetylacetone stand out equatorically from the cyclohexane ring, the latter becomes quasi-coplanar with the chelate rings and hence steric hindrance with the methyl groups of the acetonylacetate residue arises with the hydrogens of the cyclohexane ring. For *cis*-DCAA one of the two amino-nitrogens is situated equatorially and the other axially with respect to the cyclohexane ring. In the complexes the cyclohexane ring is consequently at an angle to the plane of the three coplanar chelate rings (Fig. 5), so that steric hindrance is less.

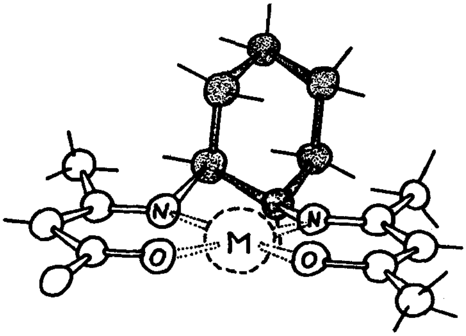


FIG. 5. Drawing of a molecular model of the metal complex of *cis*-diaminocyclohexanebisacetylacetonate.

Models enable us to understand the experimental observation which indicates that, with all metals, the stability of complexes decreases in the following order; M(EDAA) > M(cis-DCAA) > M(trans-DCAA). In addition, the stability of the complex varies with change in the metal in the sequence Pt > Pd > Cu > Ni > Co for all three complexing agents.

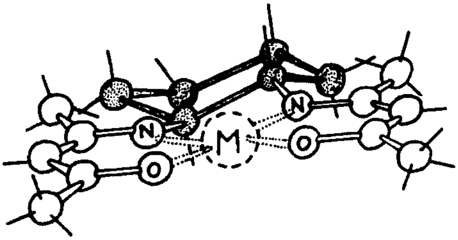


FIG. 6. Drawing of a molecular model of the metal complexes of *trans*-diaminocyclohexanebisacetylacetonate.

Experience shows that only EDAA is able to react with all five metals; *cis*-DCAA is no longer able to form a complex with Co^{++} and *trans*-DCAA adds only to Pt^{++} and Pd^{++}. It has thus become a specific reagent for the two noble metals.

REFERENCES

1. Ahrland, S., Chatt, J., and Davies, N. R., *Quart. Revs.* **12,** 265 (1958).
2. Anderegg, G., unpublished results, Zürich (1960).
3. Anderegg, G., and Schwarzenbach, G., *Helv. Chim. Acta* **42,** 827 (1959).
4. Antikainen, P. J., and Dyrssen, D., *Acta Chem. Scand.* **14,** 86 (1960).
5. Antikainen, P. J., Hectanen, S., and Sillén, L. G., *Acta Chem. Scand.* **14,** 95 (1960).
6. Banks, C. V., and Yerick, R. E., *Anal. Chim. Acta* **20,** 301 (1959).
7. Basolo, F., and Pearson, R. G., "Mechanisms of Inorganic Reactions." Wiley, New York, 1958.
8. Bjerrum, J., *Chem. Revs.* **46,** 381 (1950).
9. Bjerrum, J., *Proc. Intern. Conf. on Coordination Compounds, Amsterdam* p. 116 (1955).
10. Bjerrum, J., Schwarzenbach, G., and Sillén, L. G., "Stability Constants," Chemical Society, London: Vol. I, 1957; Vol. II, 1958.
11. Bruehlman, R. J., and Verhoek, F. H., *J. Am. Chem. Soc.* **70,** 1401 (1948).
12. Busch, D. H., and Bailar, J. C., *J. Am. Chem. Soc.* **78,** 1137 (1956).
13. Calvin, M., and Bailes, R. H., *J. Am. Chem. Soc.* **68,** 949 (1946).
14. Calvin, M., and Melchior, N. C., *J. Am. Chem. Soc.* **70,** 3270 (1948).
15. Chaberek, S., and Martell, A. E., *J. Am. Chem. Soc.* **74,** 6228 (1952).
16. Ciampolini, M., Paoletti, P., and Sacconi, L., *Nature* **186,** 880 (1960).
17. Cotton, F. A., and Harris, F. E., *J. Phys. Chem.* **59,** 1203 (1955).
18. Dickens, J. E., Basolo, F., and Neumann, H. M., *J. Am. Chem. Soc.* **79,** 1286 (1957); **80,** 2354 (1958).
19. Durham, E. J., and Ryskiewick, D. P., *J. Am. Chem. Soc.* **80,** 4814 (1958).
20. Dwyer, F. P., and Carvan, F. L., *J. Am. Chem. Soc.* **8,** 4480 (1958).
21. Fyfe, W. S., *J. Chem. Soc.* pp. 2018, 2023 (1952).
22. Gnepf, H., Dissertation, Zürich (1960).

23. Gurd, F. R. N., "Chemical Specificity in Biological Interactions." Academic Press, New York, 1954.
24. Gurney, R. W., "Ionic Processes in Solution." McGraw-Hill, New York, 1953.
25. Honda, M., and Schwarzenbach, G., *Helv. Chim. Acta* **40,** 27 (1957).
26. Irving, H., Butler, E. J., and Ring, M. F., *J. Chem. Soc.* p. 1489 (1949).
27. Irving, H., Cabell, M. J., and Mellor, D. H., *J. Chem. Soc.* p. 3417 (1953).
28. Irving, H., and Williams, R. J. P., *Nature* **162,** 746 (1948).
29. Irving, H., and Williams, R. J. P., *J. Chem. Soc.* p. 3192 (1953).
30. Jonte, J. H., and Martin, D. S., *J. Am. Chem. Soc.* **74,** 2052 (1952).
31. Jörgensen, C. J., *Acta Chem. Scand.* **10,** 887 (1956).
32. Knöpfel, H., Dissertation, Zürich (1960).
33. Larsson, E., *Z. physik. Chem. (Leipzig)* **169,** 215 (1934).
34. Leden, I., *Svensk. Tidskr.* **64,** 249 (1952); **65,** 88 (1953).
35. Lipscomb, W. N., *Acta Cryst.* **4,** 155, 266 (1951).
36. MacGillavry, C. H., and Bijvoet, J. M., *Z. Krist.* **94,** 240 (1936).
37. Mellor, D. P., and Maley, L., *Nature* **159,** 370 (1947).
38. Morgan, G. T., and Smith, J. D. M., *J. Chem. Soc.* p. 2030 (1925).
39. Moser, P., and Schwarzenbach, G., *Helv. Chim. Acta* **35,** 2359 (1952).
40. Orgel, L. E., Report to Solvay Congress held in Brussels, p. 289 (1956).
41. Paoletti, P., personal communication (1959).
42. Poulson, I., and Bjerrum, J., *Acta Chem. Scand.* **9,** 1407 (1955).
43. Prue, J. E., and Schwarzenbach, G., *Helv. Chim. Acta* **33,** 985 (1950).
44. Prue, J. E., and Schwarzenbach, G., *Helv. Chim. Acta* **33,** 995 (1950).
45. Raaflaub, J., *Helv. Chim. Acta* **43,** 629 (1960).
46. Rossotti, F. J. C., *in* "Modern Coordination Chemistry" (J. Lewis and R. G. Wilkins, eds.), p. 1. Interscience, New York, 1960.
47. Rudorff, W., and Brodersen, K., *Z. anorg. Chem.* **270,** 145 (1952); **274,** 323 (1953).
48. Schwarzenbach, G., *Helv. Chim. Acta* **32,** 839 (1949).
49. Schwarzenbach, G., *Helv. Chim. Acta* **35,** 2344 (1952).
50. Schwarzenbach, G., *Z. anorg. Chem.* **282,** 286 (1955).
51. Schwarzenbach, G., *Helv. Chim. Acta* **35,** 2333, 2337 (1952).
52. Schwarzenbach, G., *Experientia* Suppl. 5, 162 (1956).
53. Schwarzenbach, G., and Ackermann, M., *Helv. Chim. Acta* **31,** 1029 (1948).
54. Schwarzenbach, G., and Ackermann, H., *Helv. Chim. Acta* **32,** 1682 (1949).
55. Schwarzenbach, G., Anderegg, G., and Sallmann, R., *Helv. Chim. Acta* **35,** 1785 (1952).
56. Schwarzenbach, G., and Emmenegger, F. P., unpublished work (1960).
57. Schwarzenbach, G., Senn, H., and Anderegg, G., *Helv. Chim. Acta* **40,** 1886 (1957).
58. Schwarzenbach, G., Senn, H., and Schreider, W., *Helv. Chim. Acta* **38,** 1147 (1955).
59. Schwarzenbach, G., and Zobrist, A., *Helv. Chim. Acta* **35,** 1291 (1952).
60. Scouloudi, H., *Acta Cryst.* **6,** 651 (1953).
61. Seven, M. J., and Johnson, L. A., "Metal Binding in Medicine." Lippincott, Philadelphia, 1960.
62. Sidgwick, N. V., *J. Chem. Soc.* p. 433 (1941).
63. Sillén, L. G., *Quart. Revs.* **13,** 146 (1959).
64. Smith, G. S., and Hoard, J. L., *J. Am. Chem. Soc.* **81,** 556 (1959).
65. Spike, C. G., and Parry, R. W., *J. Am. Chem. Soc.* **75,** 2726, 3770 (1953).
66. Takenchi, Y., and Saito, Y., *Bull. Chem. Soc. Japan* **30,** 319 (1957).
67. Wänninen, E., Dissertation, Abo Akademie Finland (1960).
68. Westerback, S. J., and Martell, A., *Nature* **178,** 321 (1956).
69. Wicklien, H. A., and Hoard, J. L., *J. Am. Chem. Soc.* **81,** 549 (1959).
70. Züst, H., Gübeli, O., and Schwarzenbach, G., *Chimia (Switz.)* **12,** 84 (1958).