THE CHELATE RINGS

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Received August 5, 1937

The term "chelate," proposed by Morgan (179) to designate those cyclic structures which arise from the union of metallic atoms with organic and inorganic molecules, is derived from the Greek word *chela,* referring to the great claw of the lobster and other crustaceans, and is applicable to these ring systems because of the caliper-like character of the associating molecule.

The formation of these rings may involve either primary or secondary valence. In subsequent papers Morgan used the expression "chelate rings" to cover all three types, that is, rings formed by two primary valences, by one primary and one secondary valence, or by two secondary valences.

With the discovery of compounds in which the metal atom was linked to the organic molecule through three and even four groups Morgan devised for these compounds the names "tridentate," literally, three-toothed, and "quadridentate," four-toothed.

Because of the little attention which this field has attracted, the simple variation of acidic and coördinating groups in the polydentate molecules has escaped investigation. The following classification is, however, obvious:

A. Unidentate
    1. Either acidic or coördinating (groups held in the coördination sphere)

B. Bidentate
    1. Two acidic groups (SO_4^{--}, $C_2O_4^{--}$, etc.)
    2. One acidic group, one coördinating group (β-diketones, amino acids, dioximes, etc.)
    3. Two coördinating groups (ethylenediamine, dipyridyl, etc.)

C. Tridentate
    1. Three acidic groups
    2. Two acidic groups, one coördinating group

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    3. One acidic group, two coördinating groups
    4. Three coördinating groups
- D. Quadridentate
    1. Four acidic groups
    2. Three acidic groups, one coördinating group
    3. Two acidic groups, two coördinating groups
    4. One acidic group, three coördinating groups
    5. Four coördinating groups

and so on for quinquidentate and sexadentate.

Of class A thousands of members are known; of classes B1, B2, and B3 numerous examples exist; of class C4 a few examples are known; but of classes C1, C2, and C3 the knowledge is very scanty. Among quadridentate compounds members of classes D3 and D5 only are known. No quinquidentate or sexadentate compounds have been recorded knowingly.

CHARACTER OF COMPLEXES FORMED

Among all the classes the valence of the complex radical is equal to the valence of the central metal atom minus the number of primary valence groups[2] held in the coördination sphere. The successive replacement of simple coördinating groups in the coördination sphere by acidic groups leads to series of compounds the complex ions of which have successively changing ionic charges. The metals of coördination number four furnish series of five compounds; those of coördination number six, seven compounds.

The non-electrolyte members of these series are of particular interest. Among the ordinary coördination compounds (unidentate series) the non-electrolytes have practically zero equivalent conductance but are generally soluble in water. The non-electrolytes which are chelate in character (occur in the polydentate series), however, have very unusual properties and were designated by Ley (134) as *inner complex* compounds. They are extremely insoluble in water but usually soluble in non-polar solvents.[3] They usually have very striking colors widely different from the colors of the normal salts of the metals. They generally possess exceptional stability. The term "inner complex" is frequently confused with

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[2] Primary or principal valence here is differentiated from secondary or coördinating valence in that the formation of the valence link in the former case involves the replacement of a hydrogen atom, while in the latter case no such replacement occurs. No implication is intended that a difference in the bonds exists once they are formed. In formulating the complex compounds a primary valence will be indicated by a full line and a secondary valence by a dotted line, but this distinction is only for the purpose of keeping track of the valences.

[3] As exceptions to this rule are the derivatives of the simple α-amino acids, which frequently crystallize with water of crystallization and are somewhat soluble.

the term "chelate" in the older literature. As the unusual properties ascribed to the inner complexes are not characteristic of all chelate compounds but only of those which are at the same time non-electrolytes, the term "inner complex" must be reserved specifically for chelate non-electrolytes.

In addition, the ring formation of various chelating organic molecules is often limited to certain specific metals. This specificity, combined with the properties just mentioned, makes the inner complexes ideal for the purposes of analytical chemistry.

Excluding for the time those mixed compounds which contain both unidentate and bidentate groups associated with the metal atom, the types of compounds derived from metals of various valences with bidentate groups are as follows:

Coördination number six

P.V.* = 2	P.V. = 3	P.V. = 4	P.V. = 5
$[M(B1)_3]^{-4}$	$[M(B1)_3]^{-3}$	$[M(B1)_3]^{-2}$	$[M(B1)_3]^{-1}$
$[M(B2)_3]^{-1}$	$[M(B2)_3]^{0}$	$[M(B2)_3]^{+1}$	$[M(B2)_3]^{+2}$
$[M(B3)_3]^{+2}$	$[M(B3)_3]^{+3}$	$[M(B3)_3]^{+4}$	$[M(B3)_3]^{+5}$

Coördination number four

P.V. = 2	P.V. = 3	P.V. = 4
$[M(B1)_2]^{-2}$	$[M(B1)_2]^{-1}$	$[M(B1)_2]^{0}$
$[M(B2)_2]^{0}$	$[M(B2)_2]^{+1}$	$[M(B2)_2]^{+2}$
$[M(B3)_2]^{+2}$	$[M(B3)_2]^{+3}$	$[M(B3)_2]^{+4}$

(* P.V. = principal valence; B1, B2, and B3 represent one attached mole cule of the respective classes.)

It is apparent that inner complex compounds result from B1 molecules with elements whose principal valence and coördination number are both four, carbon being the only example, and theoretically from elements whose principal valence and coördination number are both six, no examples being known. Chelating molecules of type B2 yield inner complexes with elements whose coördination number is just twice the principal valence, that is, either six-three or four-two combinations. Fortunately for analytical purposes this is the most common case. Theoretically, molecules which chelate by two secondary valences only, class B3, would yield inner complexes only with elements of zero valence.

Similarly tridentate molecules yield the following types of compounds, one unidentate molecule either acidic (X) or coördinating (A) being necessary to fill out the coördination number of four:

Coördination number six

P.V. = 2	P.V. = 3	P.V. = 4	P.V. = 5
$[M(C1)_2]^{-4}$	$[M(C1)_2]^{-3}$	$[M(C1)_2]^{-2}$	$[M(C1)_2]^{-1}$
$[M(C2)_2]^{-2}$	$[M(C2)_2]^{-1}$	$[M(C2)_2]^{0}$	$[M(C2)_2]^{+1}$
$[M(C3)_2]^{0}$	$[M(C3)_2]^{+1}$	$[M(C3)_2]^{+2}$	$[M(C3)_2]^{+3}$
$[M(C4)_2]^{+2}$	$[M(C4)_2]^{+3}$	$[M(C4)_2]^{+4}$	$[M(C4)_2]^{+5}$

Coördination number four

P.V. = 2		P.V. = 3	
$[M(C1)X]^{-2}$	$[M(C1)A]^{-1}$	$[M(C1)X]^{-1}$	$[M(C1)A]^{0}$
$[M(C2)X]^{-1}$	$[M(C2)A]^{0}$	$[M(C2)X]^{0}$	$[M(C2)A]^{+1}$
$[M(C3)X]^{0}$	$[M(C3)A]^{+1}$	$[M(C3)X]^{+1}$	$[M(C3)A]^{+2}$
$[M(C4)X]^{+1}$	$[M(C4)A]^{+2}$	$[M(C4)X]^{+2}$	$[M(C4)A]^{+3}$

Members of only a relatively few of these types of compounds are known.

A similar outline of compounds containing quadridentate groups can be easily made, and the number of possible types of compounds is readily seen to be enormous, but again even fewer examples are known. With our knowledge in its present state a discussion of the possible types of quinquidentate and sexadentate compounds would be of little value, although the synthesis of such compounds is by no means impossible.

The numerous gaps among the more simple compounds, bidentate and tridentate, demand our more immediate attention. While a complete and detailed compilation of the chelate compounds would be most desirable, the suggestion of Pfeiffer (194) that another great division be added to Beilstein consisting of the chelate rings has not yet been considered seriously.

The present Beilstein system is not well adapted to the purposes of the chelate compounds, as the metallic derivatives are listed under the organic materials from which they are derived. The perspective of the smaller field of the chelate rings is thus submerged by the greater mass of organic chemistry, and the finer distinctions among the chelate compounds are too easily missed. A shorter survey is therefore likely to be more useful.

RING STRUCTURE—ACIDIC AND COÖRDINATING GROUPS

While the chelate rings can be classified on the basis of the number of members contained in the ring, such a classification is necessarily arbitrary and more restricted than the broader one proposed above.

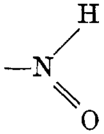
Without a doubt the number of members in the ring plays a fundamental rôle in the formation of the chelate rings, and the ultimate solution of the subtle relations between the specificity of various organic compounds for certain metals and the structure of the molecule will rest on a consideration of the number of ring members and on their dimensions and mode of linkage. The work of Sidgwick (237) and of Pfeiffer (193, 194) has opened up the way in this direction.

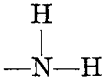
Among the various organic groups which may unite with metals by the replacement of hydrogen, that is, function as acids by primary valence, the more common are the following:

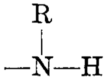
—COOH (carboxyl)

$—SO_3H$ (sulfonic)

—OH (enolic hydroxyl)


(oxime)


$—\overset{\overset{\displaystyle H}{|}}{N}—H$ (primary amino)

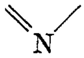

$—\overset{\overset{\displaystyle R}{|}}{N}—H$ (secondary amino)

As secondary valence groups which combine with metals by simple coördination or addition without the replacement of hydrogen are the following groups:

$—NH_2$ (primary amino)

$—\overset{|}{N}H$ (secondary amino)

$—\overset{|}{N}—$ (tertiary amino)


(cyclic tertiary amino)

=NOH (oxime)

—OH (alcoholic hydroxyl)

=O (carbonyl)

—S— (thioether)

These lists could be easily lengthened but to little point, as practically all of the chelate rings known involve combinations of the functional groups given. Some of the groups behave in both ways and occasionally the function involved is difficult to determine precisely.

The various combinations of these groups will be taken up, two at a time (bidentate), considering first the combinations of two primary valences (B1), then one primary and one secondary valence (B2), and so on, as outlined in the fourth paragraph.

Combinations will be made in the order in which the groups are listed, and numbered alphabetically. Where examples are unknown the combination will simply be skipped.

B. THE BIDENTATE COMPOUNDS

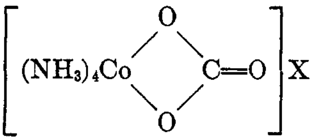
Among the chelate compounds members of the bidentate group are the longest known and the most thoroughly studied. The greater part of all the known chelate rings are of this type.

B1. Two primary valences

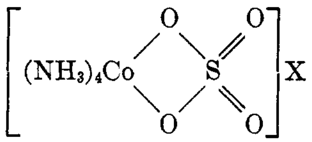
a. Inorganic dibasic acids

Numerous compounds are known in which various dibasic inorganic anions occupy two positions in the coördination sphere surrounding a metal atom. While the carbonato compounds are perhaps the most important of these substances, since they are frequently used as starting materials in the syntheses of other coördination compounds, complexes are known in which the radicals SO_4^{--}, SO_3^{--}, $S_2O_3^{--}$, SeO_4^{--}, SeO_3^{--}, CrO_4^{--}, and MoO_4^{--} occupy two coördination positions.

Four-membered rings are produced when these groups coördinate, and probably for that reason the compounds are less stable than the corresponding compounds of dibasic organic acids (see next section) which yield five- and six-membered rings. For the most part the compounds containing these chelating dibasic acid radicals contain just one such group, as in the compounds



and



although a few are known which contain three such rings, that is, have a coördination number of six completely filled out by bidentate groups alone:

$[Co(SO_3)_3]Na_3$	$[Fe(SO_4)_3]Na_3$	$[Ir(SO_4)_3]K_3$
(ref. 112)	(ref. 277)	(ref. 48)

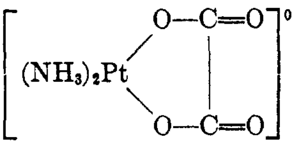
Such compounds are usually not very stable or well defined, and exact proof of their nature is frequently lacking.

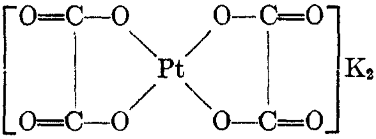
The positions in the coördination sphere occupied by these chelating groups are generally considered to be the adjacent or *cis*-positions, the groups not being large enough to span the axial or *trans*-positions. Assuming no rearrangement to occur, the replacement of these groups by two unidentate groups leads also to *cis*-compounds, and this procedure is frequently used for determining the configuration of coördination compounds.

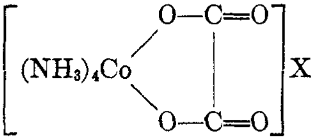
The composition of many minerals can be neatly explained by the use of coördination formulas involving chelate rings of this type. The recent text of Morgan and Burstall contains an excellent treatment of these minerals (178).

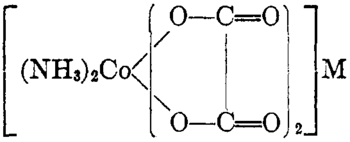
b. Two —COOH groups (organic dibasic acids)

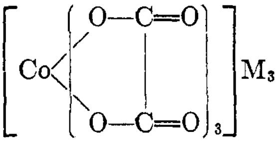
The oxalato compounds, in which the radical of oxalic acid occupies two positions in the coördination sphere forming five-membered rings with metal atoms, are well-defined stable compounds. A great number of oxalato compounds of metals of coördination numbers of four and six are known, the metal being implicated in one, two, or three rings:





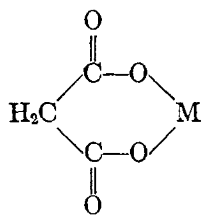






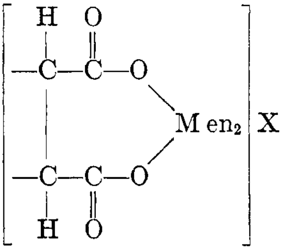
The trioxalato compounds of trivalent metals of coördination number six, —cobalt, chromium, manganese, iron, vanadium, rhodium, iridium, ruthenium, aluminum, antimony, bismuth, yttrium, etc. (110, 117, 118), —have played an important rôle in the coördination theory because of their asymmetric character, which permits resolution into optically active isomers.

Similar compounds are known with malonic acid which yields six-membered rings,



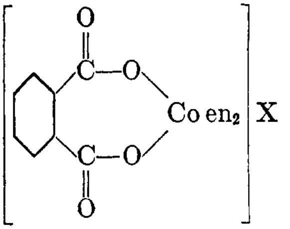
These compounds are known in the various types listed under the oxalato compounds. They are stable and well defined.

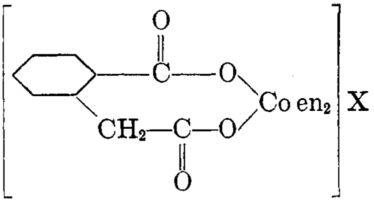
With the higher homologues which would yield rings of seven or more members no compounds are known in which a metal atom is implicated in more than one such ring. Werner (282) was unable to obtain cobalt compounds with succinic, malic, or tartaric acids. Duff later went into this question quite extensively (54). He found that the action of mesotartaric, maleic, dibromosuccinic, itaconic, and citraconic acids on carbonato-diethylenediamino-cobalti bromide yielded crystalline compounds of the type



while *d*-tartaric, malic, mesaconic, and fumaric acids gave only viscid syrups which could not be crystallized. The carboxyl groups of the acids which gave cyclic structures are known to be in the *cis*- or neighboring positions, while in the remaining four acids the carboxyl groups are averted from each other. Succinic acid gave the typical cyclic compound only at elevated temperatures, although succinic anhydride rapidly reacted with water and the carbonato salt to give the desired compound. Succinic acid itself, although able to yield an anhydride, is regarded as having a *trans*- or fumaroid structure (54, 88).

Duff (55) also found that phthalic and homophthalic acids gave crystalline compounds containing seven- and eight-membered rings.

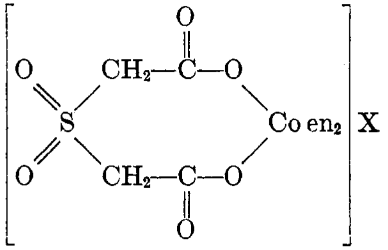




Glutaric acid, which would give an eight-membered ring, does not yield crystalline compounds.

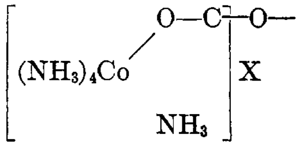
A series of copper complexes with several dicarboxylic acids and various substituted malonic acids was studied potentiometrically by Riley (213, 215). The stability of the compounds was interpreted on an electronic basis.

The first eight-membered chelate ring prepared was the ethylenediamine cobalt complex with sulfonyldiacetic acid,



prepared by Price and Brazier (205).

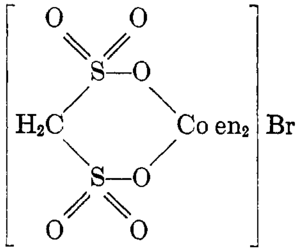
Under certain conditions only one limb of the dibasic acids may occupy a position in the coördination sphere,



Duff (56), who reviewed the methods of preparing this type of compound and extended the work to the organic dibasic acids, found the situation to be quite general, and discovered an interesting type of polynuclear compound in which two metal atoms are joined together through these acids.

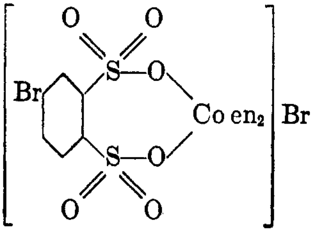
c. Two —SO_3H groups

Methionic acid was first shown to give chelate rings by Price and Duff (206), who prepared



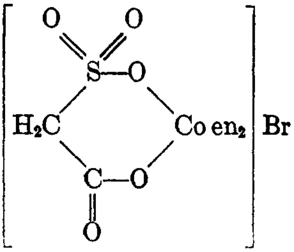
by the action of the acid on the corresponding carbonato compound.

The aromatic *o*-disulfonic acids apparently function similarly, for Duff (55) prepared



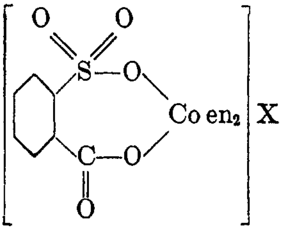
d. One —COOH group and one —SO_3H group

The action of sulfoacetic acid on carbonato-diethylenediamino-cobalti bromide was found by Price and Duff (206) to give the compound



containing a six-membered ring. Corresponding tetrammino compounds were later studied by Dubský and his coworkers (52). As would be expected, benzylsulfoacetic acid, $C_7H_7CH(SO_3H)COOH$, gives a similar compound (55).

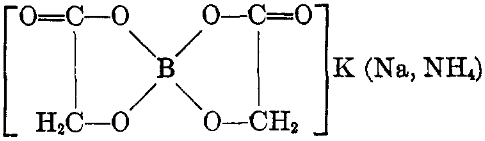
Sulfobenzoic acid also gives a crystalline ethylenediamine cobalt compound (55):



e. One —COOH group and one —OH group (both acidic)

Definite assignment of composition or structure to the metallic complexes of the aliphatic hydroxy acids is often very difficult. The weakly acidic but variable character of the hydroxyl group introduces uncertainty as to whether the hydrogen atom of the hydroxyl group has been replaced by metal or not, and as the complexes themselves frequently do not permit isolation in the solid state their constitution is frequently left in doubt. Much of the information then comes from measurements of various types on aqueous solutions.

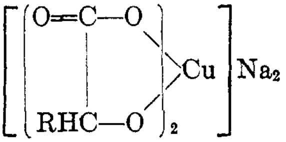
Toward boron, glycolic acid functions dibasically. The alkali metal salts of the complex acid formed,



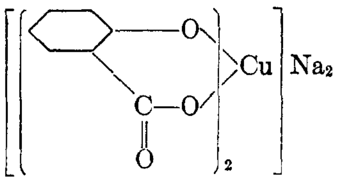
have been obtained in crystalline condition (227), and their solutions have been carefully studied by a variety of methods (29).

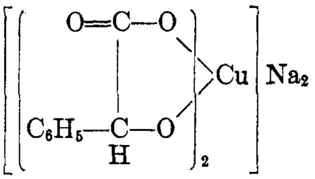
The study of this complex formation between the hydroxy acids and boric acid has proven fruitful in several ways. Böeseken and his students (26), by the resolution of the boron complex with hydroxybutyric acid, have furnished evidence of the tetrahedral character of the boron atom; and they have successfully applied the method to the differentiation of the *cis-* and *trans-*2-hydroxycyclopentanecarboxylic acids and similar compounds (27, 28).

The literature on the metallic derivatives of the hydroxy acids has been carefully reviewed by Wark (270), who concluded that the complexes are more stable the more strongly the alcoholic hydroxyl group functions as an acid. The complex copper compounds of glycolic and lactic acids

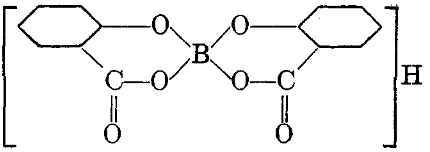


are stable only in the presence of an excess of the sodium salts of the acids; the evidence for the existence of the complexes is based on potentiometric studies. The stronger acids, salicylic and mandelic, give stable crystalline complexes (273) of the same type.





A large number of very stable cyclic metallic derivatives of salicylic acid are known. Noteworthy among them is salicylato-boric acid,

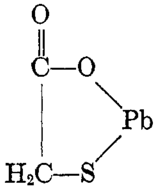


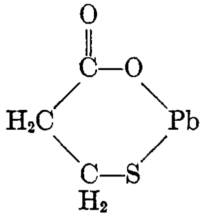
which was resolved into enantiomorphic constituents by Böeseken and Meulenhoff (24), proving that the groups are arranged around the boron atom tetrahedrally. Further studies on the various salts of salicylato-boric acid were made by Rosenheim (227). Two salicylato-ferric acids are known (280), corresponding to coördination numbers four and six.

The hydroxy and dihydroxy dibasic acids, such as malic and tartaric acids, form many very stable complexes,—for example, with copper as in Fehling's solution and with antimony as in tartar emetic. Wark has simplified this field considerably by the isolation of a number of crystalline cupri-tartrates and malates (189, 271, 272, 274), but the structure of these compounds is not yet entirely clear.

f. One —COOH group and one —SH group (both acidic)

A number of metallic derivatives of thioglycolic and various other sulfhydrylcarboxylic acids are known in which the organic acid functions dibasically, for example, the lead salts of α-sulfhydrylpropionic acid (12), β-sulfhydrylpropionic acid (122), and *o*-sulfhydrylpropionic acid (12):





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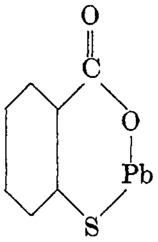


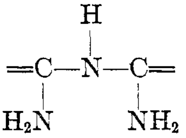
The coördination sphere of the lead atom does not appear to be filled in these cases.

g. Two —CONH₂ groups (both acidic). The Biuret reaction

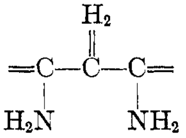
The red color produced by the interaction of biuret, $H_2NCONHCONH_2$, with cupric salts in alkaline solution was first observed by Wiedmann in 1848 (288). The reaction was later shown to be characteristic of proteins and many other substances (220, 221). Schiff, who carried out an extensive series of studies on the reaction (231), isolated the compound

$$K_2[Cu(biuret)_2]$$

He classified the materials which gave the reaction into three classes depending on their similarity to (*1*) biuret, (*2*) malonamide, and (*3*) oxamide. The arrangements of atoms typical of these groups are, respectively,

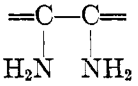


$=\underset{H_2N}{C}-\overset{H}{N}-\underset{NH_2}{C}=$



$=\underset{H_2N}{C}-\overset{H_2}{C}-\underset{NH_2}{C}=$

and



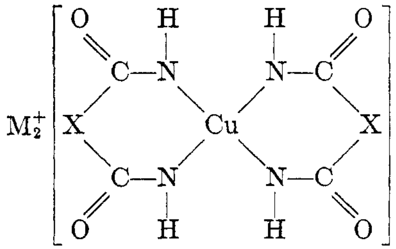
$=\underset{H_2N}{C}-\underset{NH_2}{C}=$

The double bonds may unite the carbon atoms to oxygen or sulfur, the compounds then functioning as dibasic acids. When the double bonds combine imino groups with the carbon atoms (iminobiuret, diiminobiuret) the compounds function monobasically, yielding non-electrolyte compounds (see B2, e). While the structures involved here are obviously cylic, some interesting preliminary clarifying work was carried out on analogous unidentate compounds, namely on succinimide by Tschugaeff (255), phthalimide by Ley and Werner (142, 143), and barbituric acid by Rising and her collaborators (217), all of which yield compounds of the general type

$$M_2^+[Cu(imide)_4]\cdot xH_2O$$

Rising (216, 217) has reviewed the work on the biuret reaction and applied the test to various substituted derivatives in an attempt to find the essential features of the reaction. The imino group of biuret is considered to play no part in the reaction, since malonamide, in which it is replaced by CH_2, and oxamide, in which it is absent, give the reaction. Substitution of one or both of the hydrogen atoms of the methylene group has no effect. In oxamide the substitution of one hydrogen atom of each amino group is permissible, but when both hydrogen atoms of one amino group are replaced the test fails. With malonamide and biuret a single substitution of amino hydrogen has no effect, but symmetrical disubstitution (one hydrogen of each amino group replaced) stops the reaction; this, however, is probably due to the decreased acidity caused by the separation of the acid groups (compare the strengths of oxalic and malonic acids).

Whether the active form of the compounds is the acid amide or the acid imide tautomer cannot be decided with certainty, but the complexes undoubtedly have the structure



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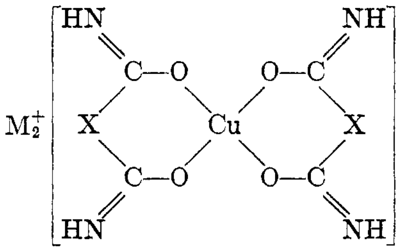
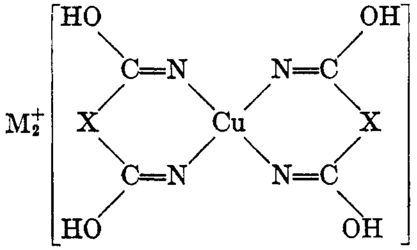


(where X = NH or CH_2, or is absent).

Replacement of the hydrogen of the imino group is also possible.

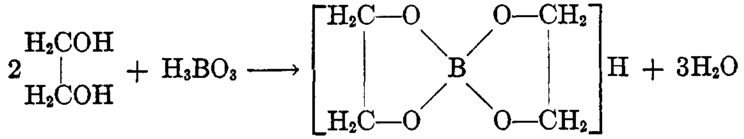


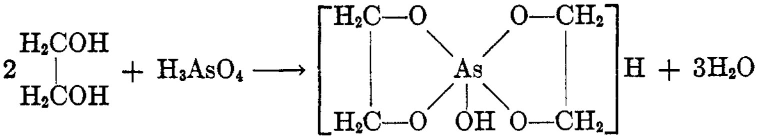
These formulas were originally proposed by Tschugaeff (255), and have been accepted by Ley (143), Kober, and others. Kober (125, 126) has extended this type of formulation to the copper derivatives of the polypeptides, but as these are probably polydentate molecules they will be discussed later. For other views on the structure of biuret compounds see the work of Traube (251) and of Jesser (116, 146).

h. Two —OH groups (both acidic)

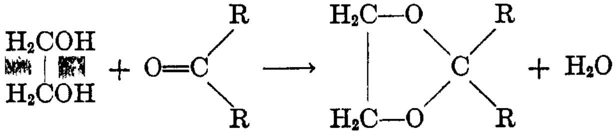
The great difference in the acidic character of the hydroxyl groups of aliphatic and aromatic compounds sharply differentiates the character of their compounds with the metals. While ethylene glycol shows little acidic behavior toward the metals, *o*-dihydroxybenzene acts as a dibasic acid, forming numerous well-defined chelate compounds.

The glycols do act acidic toward the non-metallic elements, especially boron and arsenic, however, although the reaction is more of the nature of esterification than of salt formation.



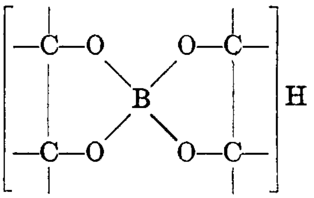


These reactions are similar to the action of the glycols on aldehydes or ketones:

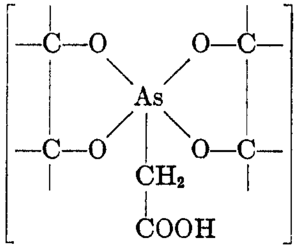


The mutual effects of the interaction of polyhydroxy alcohols and boric acid have been known for a long time. There is an enormous rise in the optical activity of the alcohol if it be active, and the acidity and electrical conductivity of the solutions undergo great increases. In the presence of glycerol or mannitol, boric acid becomes a fairly strong monobasic acid and can be readily titrated with bases. On closer study of this problem Böeseken (21) found that the position of the hydroxyl groups had a great influence on the effect produced; hydroxyl groups on neighboring carbon atoms and in the same plane produced the maximum increase in the conductivities of boric acid solutions. This immediately became very useful in the determination of the configuration of the sugars (2), diols (150, 99, 30), and other polyhydroxy compounds of various types (1, 85, 31).

Although solid compounds of this type have been isolated (90, 99), proof of their structure rests largely on evidence obtained from solutions (29, 23). The composition of the complexes is undoubtedly



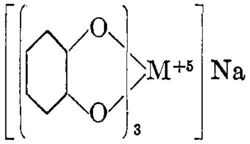
The action of the diols on arsenic acid, while not so clean cut as on boric acid, has a direct bearing on the structure of the glycols. Englund (65) found that various glycols exerted different effects on the solubilities of arsonic acids, particularly arsinoacetic acid, in 99 per cent acetic acid. The 1,2-glycols exert a pronounced effect, 1,3-glycols less; stereoisomers (racemic, active, and meso forms; *cis*- and *trans*-forms of cyclic diols) behave very differently; but variations in substituents exert relatively small effects. A number of hydroxy compounds were studied and the results can be interpreted only on the basis of ring formation of the type

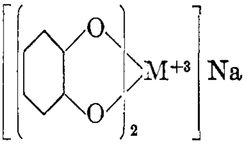


It has been known for some time that the presence of polyhydroxy compounds frequently prevents the precipitation of metallic hydroxides by caustic alkalies. The nature of the complexes formed is little known.

Traube (248, 249, 250) has recently isolated alkaline-earth salts of the iron complexes with mannitol, sorbitol, and a number of other hydroxy compounds. Cryoscopic and conductivity measurements are lacking on these compounds, however, so that it is difficult to assign definite structural formulas. The complexes are probably polydentate in character, the iron being attached to the alcohol through three or more hydroxyl groups.

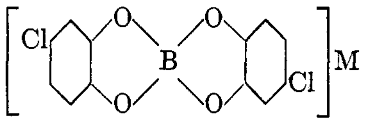
The more acidic character of the aromatic hydroxyl group leads to more definite and stable metallic derivatives. The simplest of the diphenols, pyrocatechol, furnishes a long list of stable, well-defined compounds with metals of coördination numbers both four and six. Weinland (278, 279) obtained compounds of pentavalent arsenic and antimony (coördination number six), and Rosenheim (225) prepared the corresponding compounds of trivalent arsenic, antimony, and bismuth.





Definite proof of the structure of the tripyrocatechol arsenic (+5) complex was given by Rosenheim and Plato (226), who resolved the compound by means of cinchonine. They were able to obtain the active alkali metal salts and even the active free acid.

The substituted pyrocatechol boron complexes



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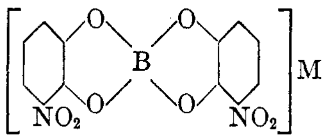
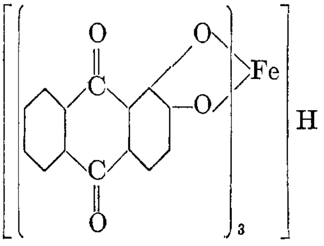


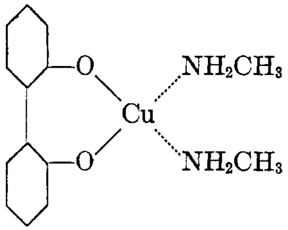
were resolved into their optically active components by Böeseken and Mijs (25, 22), proving the tetrahedral character of the quadricovalent boron atom.

Alizarin similarly forms metallic derivatives. Weinland and Binder (275) prepared various alkali metal salts of the complex acid with ferric iron



and related these to various mordant dyestuffs.

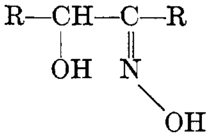
Several chelate cupric compounds of 2,2′-biphenol were obtained by Brady and Hughes (34). In some of these the biphenol apparently acted as a monobasic acid (see B2, g), but at least in di(methylamino)-cupric biphenol



the biphenol behaved as though it were dibasic. The seven-membered ring produced here is probably non-planar, in view of the work on the stereochemistry of the ortho-substituted biphenyls.

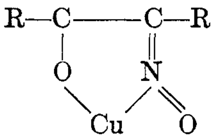
i. One —OH group and one =NOH group (both acidic)

The α-acyloin oximes of the general formula



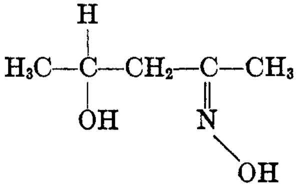
$$\mathrm{R{-}CH(OH){-}C({=}N{-}OH){-}R}$$

behave toward copper as dibasic acids, yielding green, insoluble, cupric salts:



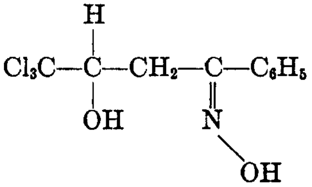
Feigl and his students (77, 73) have investigated a number of these compounds for their utility in the analysis of copper, and have studied the effects of various substituents on the color and solubility of the copper salts. Feigl has designated the α-acyloin oximes as a "copper-specific" group. α-Benzoin oxime is the reagent of the group most widely used. Knowles has found that it precipitates molybdenum (124) quantitatively also. The reagent also precipitates nickel and cobalt, at least under certain conditions (114), but the compounds are of a different type (see B2, 1).

When the two active groups are separated by an intervening carbon atom as in



$$H_3C-\underset{OH}{\overset{H}{C}}-CH_2-\underset{\underset{\diagdown OH}{N}}{\underset{\|}{C}}-CH_3$$

or



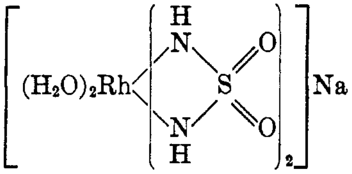
$$Cl_3C-\underset{OH}{\overset{H}{C}}-CH_2-\underset{\underset{\diagdown OH}{N}}{\underset{\|}{C}}-C_6H_5$$

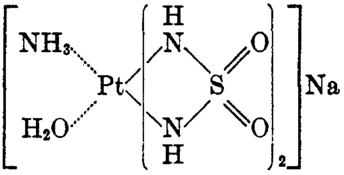
the activity toward copper is lost (75).

β-Benzoin oxime, the stereoisomer having the oxime hydroxyl group directed toward the alcoholic hydroxyl group, forms a gray-brown copper salt, insoluble in water but soluble in ammonia and obviously having a constitution entirely different from that of the α-benzoin oxime copper compound (167).

j. Two $—NH_2$ groups (both acidic)

Rhodium and platinum compounds of sulfamide, $O_2S(NH_2)_2$, were prepared by Mann (157), in which the sulfamide functions as a dibasic acid,





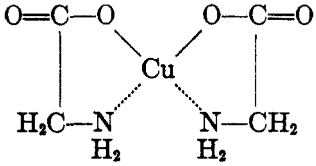
Like cobalt, rhodium and platinum (quadrivalent) have the coördination number six. The metals appear capable of taking up only two molecules of the sulfamide, however, the remaining coördination positions being occupied by unidentate groups. This behavior of sulfamide is very much like that of dimethylglyoxime toward cobalt.

Mann was able to resolve the rhodium compound using phenylethylamine, and in this way proved that the complex ion must have a *cis-* rather than a symmetric *trans*-structure.

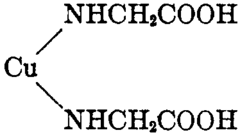
B2. One primary valence and one secondary valence

a. One —COOH group (acidic) and one —NH_2 group (coördinating)

The metal salts of the amino acids were the first of the inner complexes to be recognized as such. The cyclic character of copper glycine was appreciated simultaneously by Bruni and Fornara (39, 38) and by Ley (134). The compound had already been shown to be slightly dissociated and monomolecular by Curtius (44, 45), using the freezing-point method. The electrical conductivity of the compound was found to be practically negligible; for example, at a dilution of 256 liters the equivalent conductance is 0.90. The color of the compound is practically identical with that of the copper ammoniates. The compound is apparently coördinatively saturated, as it takes up very little ammonia giving a barely perceptible color change. These facts can only be explained by assuming both carboxyl and amino groups to be linked to copper as in

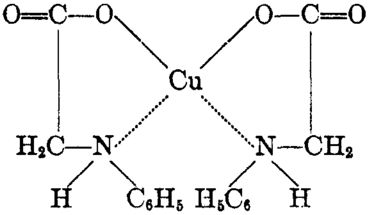


The possibility of linkage of copper to nitrogen by replacement of one amino hydrogen atom



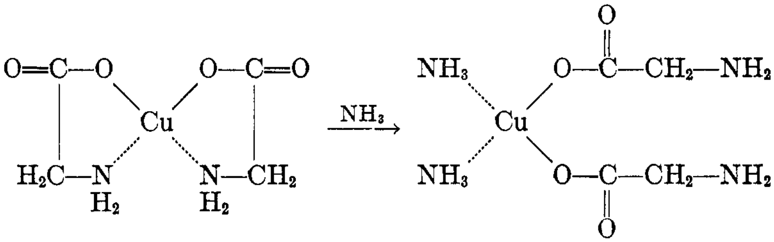
is ruled out for the dialkylated derivative, in which both hydrogens of the amino group have been substituted, forms analogous compounds (134).

The introduction of aliphatic or aryl groups into the methylene group changes the color of the metallic derivatives but slightly. An aryl substitution in the amino group, however, brings about a great change in color. Thus the copper compound of phenylglycine

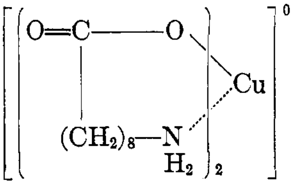


is grass-green in color, although very similar in color to the aniline complex with cupric acetate, $Cu(C_2H_3O_2)_2(C_6H_5NH_2)_2 \cdot 2H_2O$ (134). The light absorption of these and numerous similar compounds was extensively studied by Ley (135, 133, 144, 138).

While the dissociation of these compounds is very slight and nearly all the reactions of the metals fail on their solutions, it is nevertheless definite. Boiling alkalies gradually deposit cupric oxide, and ammonia slowly causes ring opening (133):

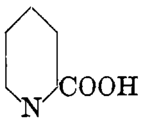


The β-amino acids similarly form cyclic compounds with metals, a six-membered ring then being present. When the amino group is farther removed, however, as in the γ-, δ-, or ε-amino acids chelation does not occur, the seven-, eight-, or nine-membered rings which would be produced apparently being impossible (266). In view of the more recent work on the higher membered rings it might be expected that polymembered chelate rings might exist. This was tested by Pfeiffer and Lübbe (199) with ω-aminopelargonic acid, which would form the twelve-membered ring:



They found no tendency for such ring formation to occur.

The acids with adjacent cyclic nitrogen atoms similarly form rings with the metals. Among these, α-picolinic and quinaldinic acids



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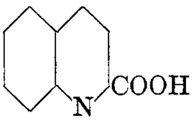


are characteristic. Several other acids of this type have been studied (140), and their unique reactions with ferrous iron observed.

A number of interesting applications to the stereochemistry of the metals have been made with the members of this group. In a planar arrangement of four covalences *cis–trans* isomerism should be observed. This has not been found with nickel or copper, but has been observed with platinum (94, 203) and palladium (203).

The cobalt and chromium compounds with the amino acids are known in two isomeric modifications (144, 145, 136) corresponding to *cis–cis* and *cis–trans* configurations about the octahedrally arranged sexacovalent metals. The determination of the configuration of these isomers has been handicapped by their completely saturated character. The introduction of optically active acids into the complexes has thrown some light on the subject and has given rise to some very interesting cases of optical activity involving partial asymmetric syntheses (137, 141, 164, 4).

A potentiometric study of the effects of alkyl substitution on the tendency of aminoacetates to coördinate with copper was made by Riley and Gallafent (214).

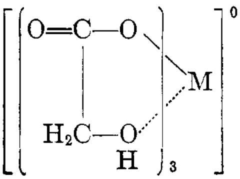
b. One —COOH group (acidic) and one —OH group (coördinating)

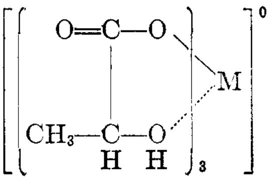
As pointed out in section B1, e, the precise differentiation of the metallic derivatives of the aliphatic hydroxy acids into these groups is difficult because of the variable character of the hydroxyl group, which may function in ring formation either as an acid or simply by coördination. Analytical data on crystalline compounds indicate that in the boron compound of glycolic acid the hydrogen atoms of both groups are replaced, but in the rare-earth glycolic acid compounds only one hydrogen atom is replaced.

The rare-earth salts of glycolic and lactic acids were prepared by Jantsch (113, 111). The equivalent conductance of these compounds is markedly lower than that of the corresponding acetates or phenylacetates, e.g.,

	V	
$La(C_2H_3O_2)_3$ (acetate)	1024	89.5
$La(C_2H_2(C_6H_5)O_2)_3$ (phenylacetate)	1200	91.2
$La(C_2H_3O_3)_3$ (glycolate)	1200	70.3
$La(C_3H_5O_3)_3$ (lactate)	1024	54.1

While the conductivities in the last two cases are far greater than that of a typical inner complex compound such as copper glycine, the values are much lower than those of the first two strictly normal salts, indicating that there occurs at least partial chelation of the type





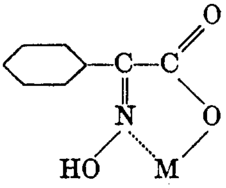
Replacement of the hydrogen atom of the hydroxyl group by methyl or phenyl does not change the properties of the compounds. As would be expected, aqueous solutions of these salts give the normal reactions of the metals.

Similar views on the constitution of the metallic salts of the hydroxy acids had been put forward earlier by Ley (135, 139) on the basis of conductivity measurements of Calame (40).

Further evidence along these lines has been recently reported by Riley and his students (78).

c. One —COOH group (acidic) and one =NOH group (coördinating)

Metallic compounds of the oxime of phenylglyoxylic acid have been reported by Hieber and Leutert (102). Of the two forms of the compound the less stable α-form yields complexes with metallic salts very slowly, being converted at the same time to the β-form. The β-modification reacts instantly, yielding complexes which are formulated:

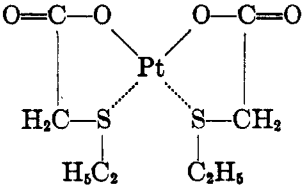


The β-form of the chelating molecule undoubtedly has the *syn*-phenyl configuration.

For a further discussion of the members of this group, with particular reference to hydrogen bonding, the reader is referred to the monograph of Meisenheimer and Theilacker (169).

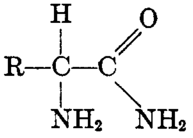
d. One —COOH group (acidic) and one —S— group (coördinating)

A platinum compound of ethylthioglycolic acid was prepared by Ramberg (207) and shown to have a cyclic structure of the type



e. One $—CONH_2$ group (acidic) and one $—NH_2$ group (coördinating)

During a series of studies on the biuret reaction, Rising (219, 291) found that amino acid amides

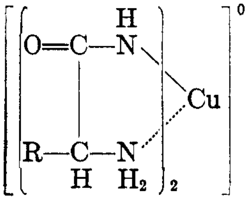


$$R—CH(NH_2)—C(=O)NH_2$$

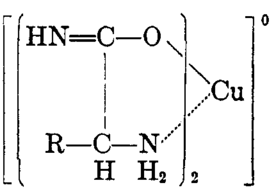
formed copper compounds, with or without the aid of alkali, the products having the composition

$$[Cu(\text{amino acid amide})_2]^0$$

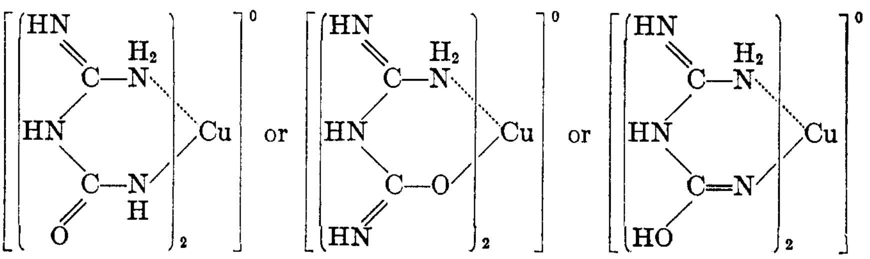
The compounds were isolated as red amorphous powders, definite in composition and stable toward water. Their solutions are non-conducting, proving their non-electrolyte inner complex character. Whether hydrogen has been replaced from the amide group or from the hydroxyl group of the tautomeric imide form has not been established, but undoubtedly the compounds correspond to one of the following structures:



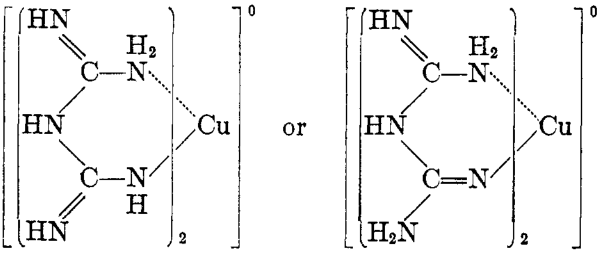
or



Monoiminobiuret, $H_2NCONHC(:NH)NH_2$ (guanylurea or dicyanodiamidine), and diiminobiuret, $H_2NC(:NH)NHC(:NH)NH_2$ (biguanidine), yield the same sort of copper compounds (89, 6), where at least in the case of diiminobiuret the metal must be linked to nitrogen. While



Copper monoiminobiuret

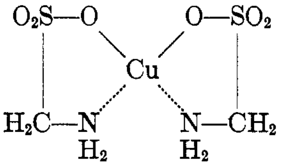


Copper diiminobiuret[4]

these compounds may possibly be regarded as biuret compounds, they are non-electrolytes and different in character from the typical biuret compounds (B1, g).

f. One —SO_3H group (acidic) and one —NH_2 group (coördinating)

The copper salt of aminomethylenesulfonic acid is deep blue in color like copper glycine and is assigned the chelate structure



The salt is far more extensively dissociated than the copper salt of glycine, however (171). The copper salt of aminosulfonic acid, H_2NSO_3H, has a normal composition.

The compounds of corresponding aromatic acids were studied by Pfeiffer (192).

g. Two —OH groups (one acidic and one coördinating)

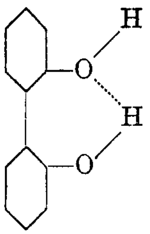
Considerable evidence points to the fact that 2,2′-biphenol (I) is itself coördinated (34). The univalent thallium (II) and diethyl-thallium (III) derivatives are also apparently coördinated compounds,

---

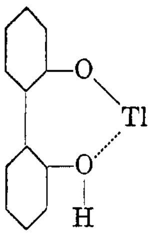
[4] Diiminobiuret tends to form the compound

$$[Cu\ (diiminobiuret)_2]SO_4$$

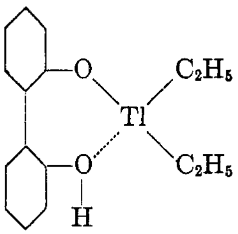
where chelation occurs by two secondary valences (209,100) and gives the above compound only when treated with alkali; the compound separates free of alkali metals, however.



I



II



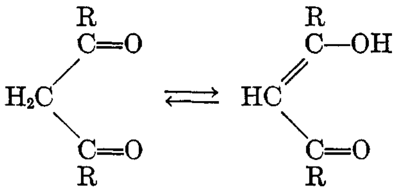
III

although the thoroughly saturated character of the inner complexes (non-electrolytes) here is not so completely borne out. Biphenol also acts as a bidentate chelating group in classes B1 and B3.

h. One —OH group (acidic) and one =O group (coördinating)

In this group of compounds fall the metallic derivatives of the 1,3-diketones, the aromatic *o*-hydroxyaldehydes, and the *o*-hydroxyphenones.

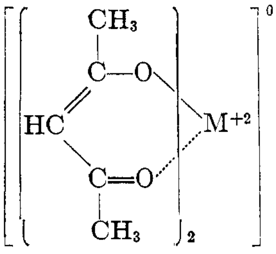
The 1,3-diketones form metallic compounds by virtue of their ability to enolize:



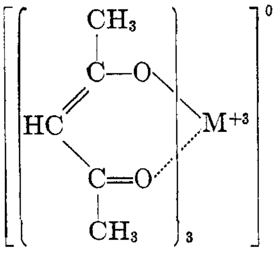
Keto form Enol form

Although numerous metal derivatives of the simplest member, acetylacetone (both R = CH_3), had long been known, their cyclic character was first pointed out by Werner in 1901 (283).

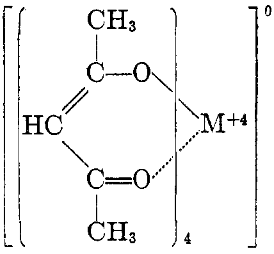
The acetylacetonates of practically all of the metals have been prepared (183). Most are of the non-electrolyte type



Be, Cu, Ni, etc.

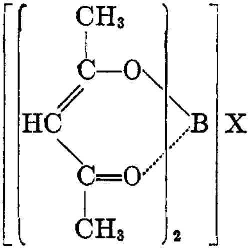


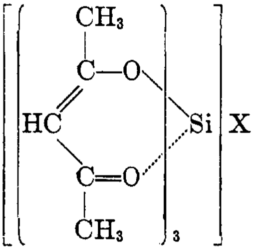
Al, Se, Cr, etc.

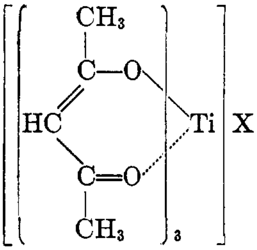


Th, Zr, Ce, U

and are insoluble in water, soluble in non-polar solvents, etc. Their stability is exceptional; many can be distilled without decomposition at temperatures ranging to over 300°C., which has led Morgan to remark (181) that acetylacetone has given wings to the metals. Among the metals whose principal valence does not happen to be just half of the coördination number, the acetylacetonates of boron, silicon, and titanium prepared by Dilthey (49, 50) should be mentioned.



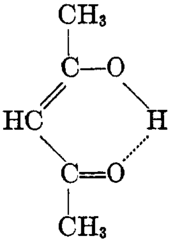




Acetoacetic ester and its analogues are members of this group, and their copper derivatives, used by Hieber (101) in determining the extent of enolization of these compounds, are inner complexes.

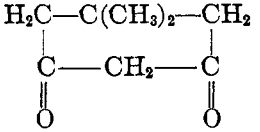
The relative stability of the copper compounds has been found to parallel the percentage of enol form in the pure compounds (174).

Sidgwick (238) concluded from chemical and physical properties that the enol form of the 1,3-diketone is mainly if not wholly a cyclic structure in which hydrogen is coördinated to the carbonyl oxygen.



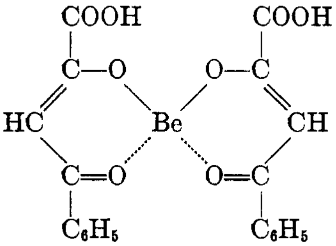
Characteristic —OH absorption in the infra-red is lacking in these compounds (107), and this is further evidence for such chelation or hydrogen bonding.

The cyclic diketone 5,5-dimethylcyclohexanedione-1,3



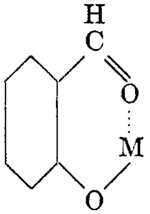
does not yield metallic derivatives of the type just discussed (286), nor are the physical properties of the pure diketone like those of the aliphatic, readily enolizable diketones.

Among the interesting applications of the 1,3-diketones to the stereochemistry of the metals may be mentioned the benzoylpyruvic acid derivative of beryllium.



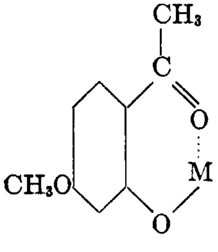
The brucine salt of this complex was found by Mills and Gotts (172) to exhibit definite mutarotation, which is considered to be definite proof of the tetrahedral character of the beryllium atom.

Numerous metal compounds of salicylaldehyde are known of the following type:



In general they are formed in organic solvents and do not appear to be very stable toward water.

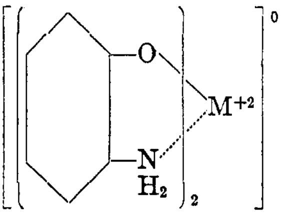
The *o*-hydroxyacetophenones are also capable of yielding complexes with the metals, for Pfeiffer (197) has prepared the cobalt, copper, and nickel derivatives of *p*-methoxy-*o*-hydroxyacetophenone (päonol), which are typical inner complex compounds.



i. One —OH group (acidic) and one —NH_2 group (coördinating)

Hieber and Levy (103) have recorded divalent cobalt compounds of monoethanolamine in which part of the attached ethanolamine molecules in the complex chelate by replacement of the hydroxyl hydrogen atom. The compounds are formed only in alcohol, and the situation is further complicated by the formation of polynuclear compounds. The nickel, copper, and zinc compounds were also studied (104); the greater tendency seems to be for the ethanolamine to chelate by two secondary valences, however.

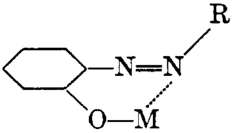
As would be expected, the aromatic compounds, in which the hydroxyl group is much more acidic, furnish more definite, stable compounds (106). The *o*-aminophenol derivatives of copper, nickel, zinc, and cadmium



are typical inner complex compounds.

j. One —OH group (acidic) and one —N═N— group (coördinating)

In the course of a study of the chelate rings formed in mordant dyeing, Morgan (185) showed that in the azo dyestuffs containing an *o*-hydroxyl group, mordanting took place with the formation of chelate rings, the metal being attached by secondary valence to the azo group



Such ring formation cannot occur when the hydroxyl group is in the meta- or para-positions, and this is in accord with the long-established rule that such compounds are never dyestuffs.

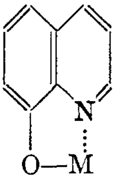
More recently Elkins and Hunter (58) have found that the formation of cupric, nickel, and cobaltic compounds is characteristic of all *o*-monohydroxyazo compounds and that such formation occurs readily by the action of the metallic acetates on the azo compound. The salts correspond to the formulas R_2Cu, R_2Ni, and R_3Co, R being the molecule of the *o*-hydroxyazo compound minus one hydrogen atom. The salts are typical inner complexes (non-electrolytes); they are insoluble in water and polar solvents, but readily soluble in non-polar solvents. They are very stable, melting in the neighborhood of 200°C. without decomposition to form deeply colored liquids.

The existence of these compounds is interpreted as evidence that the geometrical arrangement of the groups attached to the azo group is *trans* (58). Absorption spectra data also indicate that the hydroxyl hydrogen atom of these *o*-hydroxyazo compounds is coördinated to the azo group.

The blue magnesium lake with *p*-nitrobenzeneazoresorcinol which is used as a qualitative test for magnesium (244, 228, 64) is undoubtedly due to chelation of this sort.

k. One —OH group (acidic) and one $\diagdown N \diagup$ group (coördinating)

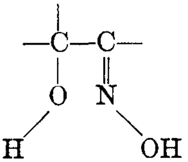
Numerous metallic derivatives of 8-hydroxyquinoline are known of the general chelate type



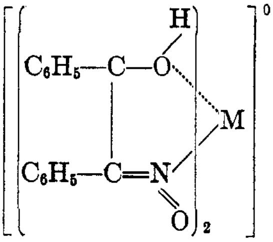
These salts were suggested for analytical purposes by Hahn (95) and Berg (15) in 1926; since then they have undergone very rapid development and are now extensively used. Berg (16) has contributed a monograph dealing exclusively with the applications of 8-hydroxyquinoline to analytical chemistry.

l. One —OH group (acidic) and one =NOH group (coördinating)

Two types of compounds, both containing as functional groups a hydroxyl group and an oxime group, have been found to yield insoluble compounds with copper. In the acyloin oximes, investigated by Feigl (69, 77, 72), the characteristic atomic grouping is

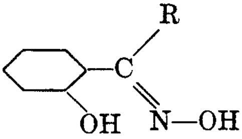


Toward copper these compounds act as dibasic acids, both hydrogens being replaced by the metal, and therefore they were discussed under class B1. Jennings, Sharratt, and Wardlaw (114) found, however, that α-benzoin oxime functions toward nickel, palladium, and divalent platinum as a monobasic acid, giving typical inner complex compounds of the formula:



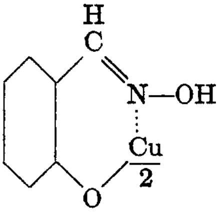
These compounds exist in two mutually interconvertible forms, but the nature of this isomerism has not yet been explained. Still another nickel derivative of α-benzoin oxime was obtained in which the oxime formed the chelate rings by coördinating valences alone (see B3, e). α-Benzoin oxime thus functions as a bidentate molecule in all three classes.

The other copper-specific group is that of the aryl aldoximes and aryl ketoximes containing an *o*-hydroxyl group

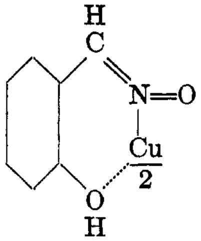


Salicylaldoxime, the simplest member of the class, was first employed as an analytical reagent for copper by Ephriam (66). A further investigation by Ephriam (67) showed that this ability to precipitate copper from acetic acid solutions was not destroyed by the introduction of substituents into the phenyl group or in place of the aldehyde hydrogen atom.

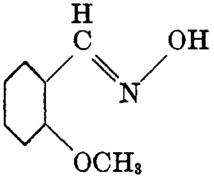
Ephriam preferred to formulate the copper compound as

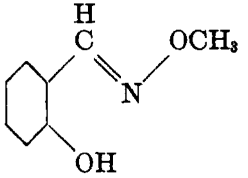


the hydrogen of the —OH group being replaced by the metal. Feigl (75), after pointing out that the principal valence linkage might equally well be to the oxime group,



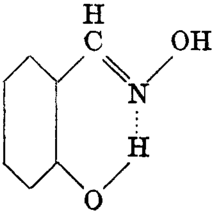
prepared the two methyl ethers of salicylaldoxime



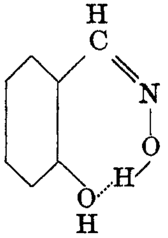


and found that only the compound with the free —OH group (the oxime ether) gave a copper compound. Feigl interprets this as support for the Ephriam formulation in which the hydroxyl hydrogen is replaced by the metal atom.

The *anti*-phenyl form of salicylaldoxime has been assumed to be present in all of these complex formation reactions and, indeed, in view of the great amount of evidence accumulated in the field of the oximes of the α-diketones (see B2, o and p) this is undoubtedly correct. Brady (33) has also brought forward several arguments in favor of hydrogen-bond formation through the hydroxyl hydrogen atom

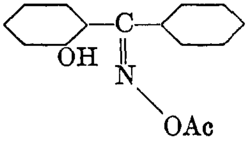


rather than through the hydrogen of the oxime group

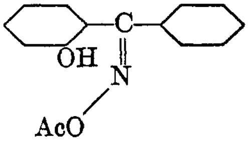


in salicylaldoxime itself.

This has been more recently confirmed by infra-red absorption measurements (98). Again, of the two acetates (19, 127) of 2-hydroxybenzophenone oxime



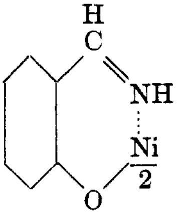
and



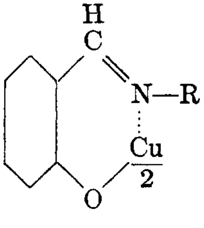
only the isomer in which the —OAc group is toward (*cis* to) the phenolic —OH gives characteristic —OH absorption (98). Hydrogen bonding is evidently present in the *trans*-isomer. Meisenheimer (168) has also shown that of the two forms only the *trans*-form yields complex salts with nickel.

m. One —OH group (acidic) and one =N—R group (coördinating)

The action of nickel salts on *o*-hydroxyaldehydes in aqueous ammonia solutions leads, surprisingly enough, to the nickel salt of hydroxyaldimines



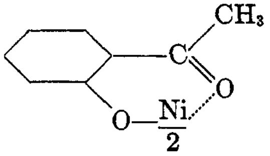
in which the aldehyde oxygen atom has been replaced by =NH. Pfeiffer (196) and his coworkers, who stumbled onto this, found on surveying the literature that such a reaction had been observed as far back as 1840 by Ettling (68). Later Schiff (230) and Delépine (47) reported similar copper compounds:



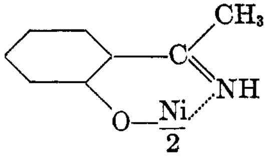
$R = CH_3, C_6H_5, CH_2C_6H_5$

Pfeiffer found that copper, nickel, and zinc caused this same replacement, but that calcium and magnesium salts led to normal salts with no formation of imine.

With *o*-hydroxyacetophenone the replacement of the oxygen atom by the imino group did not proceed in dilute ammoniacal solution, but went rapidly and completely on warming a solution of the nickel salt of *o*-hydroxyacetophenone in concentrated ammonia:



(greenish-yellow)

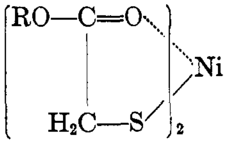


(dark red)

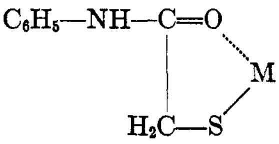
n. One —SH group (acidic) and one =O group (coördinating)

The acidity of the —SH group of thioglycolic acid, $HSCH_2COOH$, overshadows the acidic behavior of the carboxyl group. There is some indication that thioglycolic acid forms chelate rings by replacement of hydrogen atoms from both the —COOH and the —SH groups. More definite compounds are obtained when the acidic function of the carboxyl group is voided by ester or amide formation and the carbonyl oxygen atom can then enter into chelate ring formation by simple coördination.

The nickel derivatives of the methyl and ethyl esters of thioglycolic acid (51) are typical.



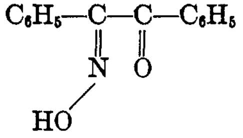
The metal derivatives of thioglycolic acid anilide are also chelate compounds



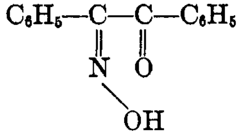
The analytical utility of these compounds has been pointed out by Berg and Roebling (17), who advocate the use of thioglycolic-β-aminonaphthalide (Thionalid) as a reagent for the detection and determination of various heavy metals.

o. One =NOH group (acidic) and one =O group (coördinating)

That the stereochemical configuration of the monoximes of the α-diketones governed their reactions with the metals was first recorded by Whiteley (287), who found that of the two isomeric benzil monoximes



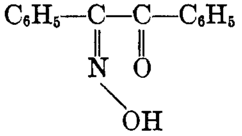
α-form



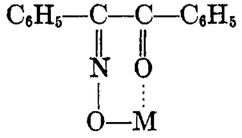
β-form

the α-form yielded a deep blue ferrous compound, while the β-form did not. Tschugaeff extended this work to cobalt, nickel, and platinum (263). These compounds are highly stable, being unattacked by mineral acids or cyanides, and possess very striking and anomalous colors.

On the basis of the coördination theory these were immediately seen to be cyclic compounds. The configuration originally assigned to the α-benzil monoxime on the basis of the Beckmann rearrangement was the *syn*-form



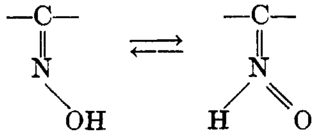
and Werner (285) assigned to its metallic derivative the structural formula



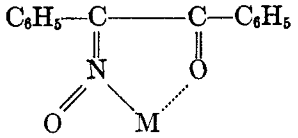
rejecting the five-membered ring earlier proposed by Tschugaeff (263, 254). This six-membered ring structure was widely accepted and appeared in the literature for some time.

The work of Meisenheimer on the oximes, however, has led to a complete reversal of the interpretation of the Beckmann rearrangement, namely, that the assumption that the rearranging groups were *cis* to each other was erroneous (166, 18). There can be no doubt now that the *trans* shift is correct and that α-benzil monoxime must actually be the *trans*-isomer. The difficulty with the above formula for the metallic derivatives immediately becomes obvious.

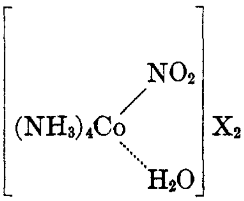
Pfeiffer and Richarz (201) resolved this problem by assuming that the tautomeric nitrone form of the oximes



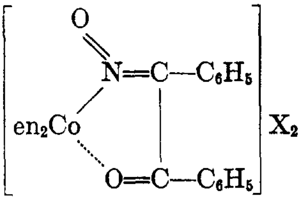
was responsible for formation of metallic compounds. (Brady and Mehta (35) have isolated oxygen and nitrogen ethers corresponding to each of these forms.) The hydrogen atom is replaced by metal, giving a direct metal-to-nitrogen linkage. This results in the formation of five-membered rings:



The metal–nitrogen linkage is well known among the coördination compounds, for example, the nitro cobalt ammines, $[Co(NH_3)_5NO_2]X_2$ and $[Co(NH_3)_4(NO_2)_2]X$, both of which are yellow in contrast to the nitrito compounds, for example, $[(NH_3)_5Co—ONO]X$, which is pink in color and unstable, passing slowly into the corresponding nitro compound. Pfeiffer found that the colors of the very similar compounds



and

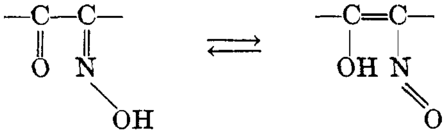


were practically identical (195).

The monoximes of the α-diketones give characteristic color reactions with ferrous salts. Feigl and his coworkers have investigated a series of these compounds from the standpoint of the so-called "iron blue reaction." The work has been summarized in his book (74).

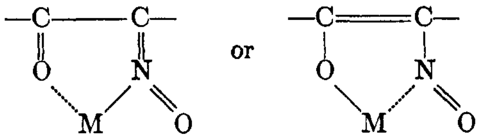
The copper complex of β-benzil monoxime has been used to follow the interconversion of the α- and β-forms of benzil monoxime in various solvents (245).

The nitrosophenol group is tautomeric with the diketone monoxime group



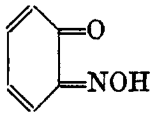
Oximinoketone form Nitrosophenol form

It is difficult to know which of these forms is responsible for salt formation; whether to write the formula of the metallic derivatives as

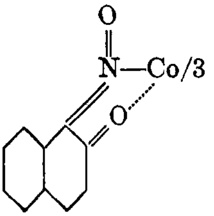


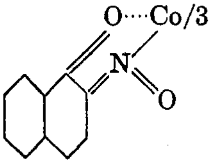
Perhaps this is a question of resonance, both forms being present.

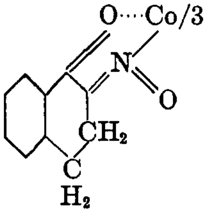
Besides simple *o*-nitrosophenol



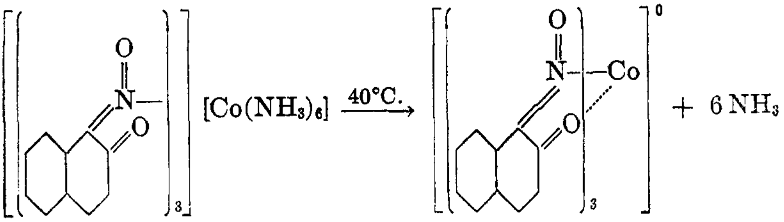
the metallic compounds of which were investigated by Baudisch (9, 11), there also fall in this class the analytically useful cobalt reagents α-nitroso-β-naphthol (108, 163), β-nitroso-α-naphthol (13), and 2-isonitroso-1-ketotetralin (242). Formulated on the ketoxime form their cobalt derivatives may be considered to be





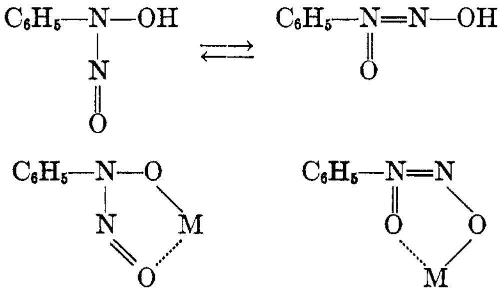


The great tendency for chelation to occur in these compounds is illustrated by a reaction carried out by Morgan and J. D. Main Smith (184), who found that the normal hexamminocobalti (luteo) salt of α-nitroso-β-naphthol on slight warming in aqueous solution rapidly expelled ammonia:



The authors further showed that the numerous derivatives of α-nitroso-β-naphthol, so extensively used as dyestuffs, owe their mordanting properties to just such ring formation as this, and that other attached groups, —SO_3H, etc., are inactive.

The analytical reagent cupferron, the ammonium salt of nitrosophenylhydroxylamine (8, 10, 5), also falls in this class. The reagent and metallic derivatives may again be written in tautomeric or resonance forms.



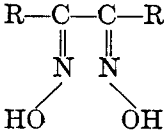
$$C_6H_5-N(OH)-N=O \rightleftarrows C_6H_5-N(=O)=N-OH$$

p. One =NOH group (acidic) and one =NOH group (coördinating)

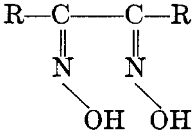
The metallic compounds of the dioximes of the α,β-diketones (substituted glyoximes) were discovered by Tschugaeff (264). In a series of investigations he studied the behavior of a number of differently substituted glyoximes against various metals. The nickel and palladium salts were always insoluble in alkaline or neutral solutions, and had the general formula $(HD)_2M$, where H_2D represents the dioxime molecule and M the metal (256, 257). Cobalt formed soluble compounds and appeared capable of combining with only two molecules of the dioxime. Numerous cobalt compounds with the dioximes were isolated in which the remaining two coördination positions are occupied by various coördinating or acidic groups,

$[Co(HD)_2(NH_3)_2]X$, $[Co(HD)_2(NH_3)X]$, and $[Co(HD)_2X_2]M$ (252, 259)

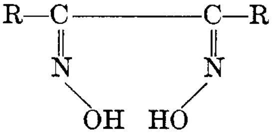
Complex formation of the dioximes, again, is dependent on the stereochemical configuration of the oxime. Three stereoisomeric forms of the symmetrically substituted dioximes exist, corresponding to the configurations



anti-

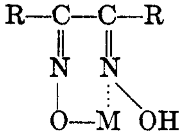


amphi-

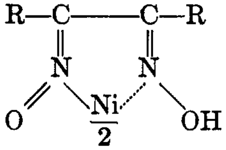


syn-

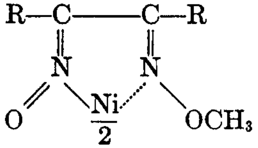
Of these the α-modification yields typical, brilliant red nickel salts. The older configuration determinations assigned the *syn*-form to the α-modification, and the metallic complexes were written as six-membered ring structures.



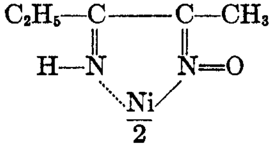
The inadequacy of this formulation on the basis of the newer configuration determinations which assign the *anti*-configuration to the α-form is readily seen. Applying reasoning similar to that adapted to the monoximes, the structure of the dioximes may be represented as

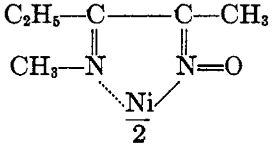


involving the tautomeric nitrone form of the oxime and a five-membered ring, one oxime group being bound to the metal through primary valence, nitrogen to nickel, and the other by secondary valence (102, 195). That the hydroxyl group of the second oxime plays no part and the metal is not linked to oxygen is shown by the ready formation of exactly similar complexes by the mono-*O*-ethers (246, 36, 191):



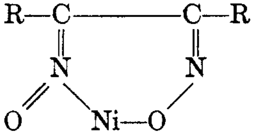
Pfeiffer has also found (191) that, when one of the oxime groups is replaced by an imino or methylimino group, complex formation occurs in identical fashion.





As mentioned, the *anti*-dioximes form stable, brilliant red compounds with nickel. Indeed, the tendency for such formation to occur is so great that hot aqueous or alcoholic-aqueous solutions of the dioxime will dissolve metallic nickel, copper, cobalt, or iron, liberating hydrogen (204, 170).

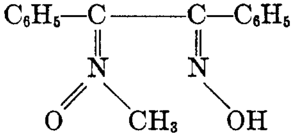
The *amphi*-dioximes (γ-form) give yellow or green-yellow compounds with nickel in which one molecule of dioxime is attached to one atom of nickel, the hydrogens of both oxime groups being replaced by the metal (3, 165, 102). The metal is apparently attached to one group through nitrogen and to the other through oxygen, corresponding to



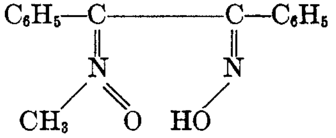
The compounds are usually amorphous, poorly defined, and difficult to purify. They are stable toward alkalies, but in contact with acids they pass rapidly into the red, stable, isomeric compound of the α-dioxime.

The *syn*-dioximes (β-form) are completely incapable of forming compounds with the metals.

These steric factors clearly indicate that the nitrogen atom must be free on the side toward which the metal is to add. This is again borne out by the fact that neither of the mono-*N*-ethers of α- or β-benzil dioxime



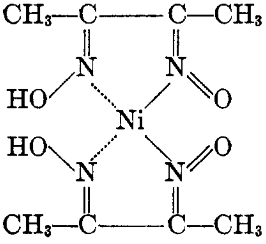
α-form

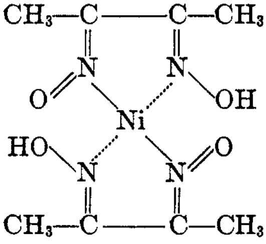


β-form

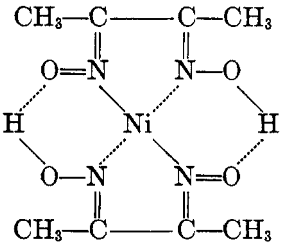
yields compounds with nickel (36).

A closer inspection of the structural formulas assigned the dioxime-metal compounds, e.g., nickel dimethylglyoxime, will show that if the organic molecules are disposed about the nickel in a plane, *cis-trans* isomerism may be expected depending on which of the oxime groups are united to the nickel by principal and which by secondary valence:



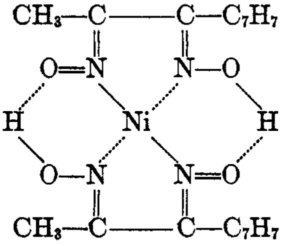


That no such isomerism has ever been observed may be explained by a tautomeric shift of the hydrogen atom (243), or, better, by assuming hydrogen bonding to occur between the neighboring oxygen atoms. Brady (36) writes the formula thus:

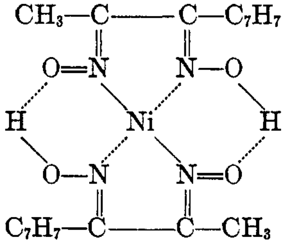


This formula also explains the lack of reactivity of the hydroxyl group in these compounds. Tschugaeff (204) found that nickel dimethylglyoxime would not react with phenyl isocyanate, and Barker (7) states that acetic anhydride has no effect on it. With methyl iodide nickel dimethylglyoxime yields an addition product from which water regenerates the original red nickel compound. Brady and Muers (36) report that nickel dimethylglyoxime gives no methane with methylmagnesium iodide in amyl ether.

The dioximes have been very useful in proving the planar structure of the quadricovalent nickel atom. Sugden (243, 41) has prepared two isomeric nickel derivatives of unsymmetrically substituted glyoximes corresponding to *cis*- and *trans*-configurations



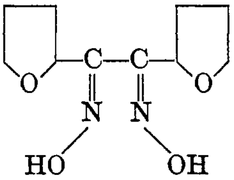
cis



trans

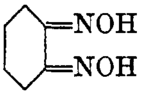
Palladium shows the same type of isomerism (57).

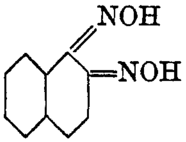
The practically specific action of the α,β-dioximes in forming insoluble nickel compounds has led to their widespread use in the qualitative and quantitative analysis of nickel. The insolubility of the usual reagent, dimethylglyoxime, in water, however, is a great disadvantage. Soule (241) has found that α-furil dioxime



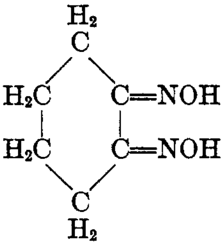
is soluble to about 10 per cent in water and, besides being more sensitive as a qualitative test, has a lower metal content. This reagent warrants more widespread use.

The specific activity of the dioxime group for nickel is lost in the unsaturated cyclic *o*-diquinone dioximes





which act as dibasic acids and form precipitates with numerous metals (70). Cyclohexanedione dioxime,

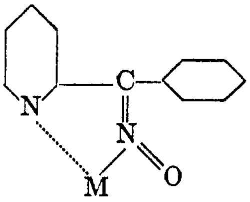


on the other hand, is again specific for nickel and more sensitive than dimethylglyoxime (269). The reagent is water-soluble and is frequently cited in papers dealing with organic analytical reagents as being the ideal organic reagent. It has not been widely adopted, however.

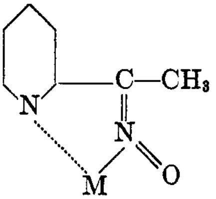
The dioximes of α,γ- and α,δ-diketones do not form chelate rings with metals (261).

q. One $=$NOH group (acidic) and one $\diagdown N \diagup$ group (coördinating)

The complex metallic derivatives of this class were first found by Tschugaeff (254, 261), who prepared the platinum and palladium derivatives of phenyl-α-pyridyl oxime and formulated them as chelate compounds. The metallic compounds of methyl-α-pyridyl ketoxime have also been studied (60). These compounds are formulated after the Pfeiffer method (195) as

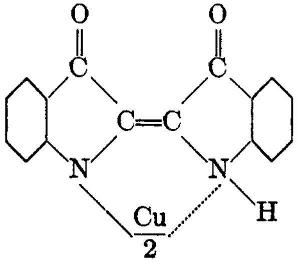


and

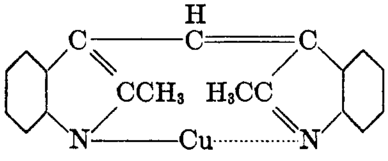


r. Two $-\overset{|}{\text{N}}\text{H}$ groups (one acidic and one coördinating)

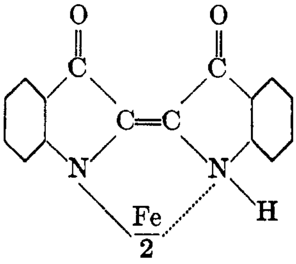
In a series of papers Kunz (129, 130, 132, 131) investigated the metallic derivatives of indigo and similar compounds, with particular reference to the bearing the compounds had on the metal–porphyrin problem. While Kunz assumed that the metals in his compounds were linked to the nitrogen atoms by secondary valences alone, careful reviews of the compounds by Kuhn (128) and by Schmitz-Dumont (233) lead to the conclusion that this assumption was wrong and that the metals unite with the dyestuff with the replacement of hydrogen. The copper derivative of indigo is then



From stereochemical considerations and other reasoning, Kuhn concluded that the metal in these compounds is attached to the carbonyl oxygen rather than to the imino nitrogen atom. Kuhn's formula is given in the next section. The compound bis-(α-methyl-β-indyl)methene, in which the oxygen atoms of the indigo molecule have been removed, still yields metallic derivatives, for example, a monovalent copper compound (132, 233) in which one atom of copper is united to one molecule of the organic compound

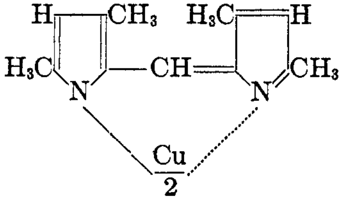


The extremely interesting iron compound of indigo was shown by Kunz and Kress (131) to exhibit a most astonishing similarity to hemoglobin. On heating iron carbonyl with indigo in pyridine, carbon monoxide is evolved and a yellowish-red compound is obtained.



A pyridine solution of this compound rapidly absorbs oxygen, the color shifting at the same time from red to green. One molecule of oxygen is added for each atom of iron. The oxygen is only loosely held, for it is released by the application of a vacuum, the color changing back to the original red. Carbon monoxide destroys this ability to take on oxygen. Chilling a solution of the green compound yields a solid which does not give up its oxygen in a vacuum and which on heating gives oxidation products of indigo. These properties are just those of hemoglobin, and the iron–indigo compound is thus a unique breathing model.

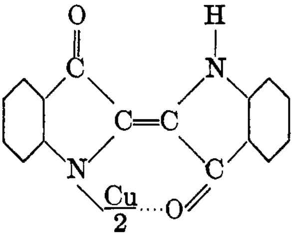
Bearing even more directly on the hemoglobin problem are the copper compounds of the dipyrrylmethenes, for example, of tetramethyldipyrrylmethene:



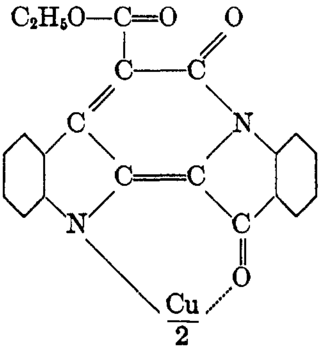
synthesized by Fischer and Schubert (84).

s. One $\overset{|}{\text{—N}}\text{H}$ group (acidic) and one =O group (coördinating)

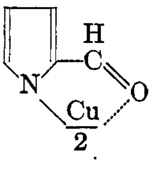
As mentioned in the preceding section, Kuhn (128) considered the secondary valence of the metals in their complexes with indigo to be directed toward the carbonyl oxygen rather than toward the imino nitrogen atom. This is in agreement with the modern views that indigo has a fumaroid (*trans*) structure. Chelation on a *trans* structure could then only occur from nitrogen to oxygen:



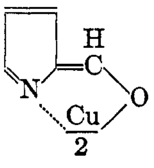
Kunz found that indigo-malonic ester also readily gave copper and cobalt compounds in which necessarily the metal is linked to nitrogen and oxygen:



An inner complex copper compound of α-pyrrolealdehyde was prepared by Emmert (61) by the action of the aldehyde on copper oxide in xylene. The compound is sensitive to water and is probably best formulated as a derivative of the aldehyde rather than its tautomeric enolic form, that is,



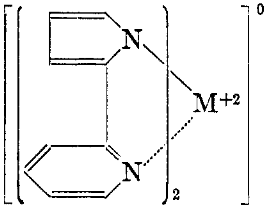
rather than

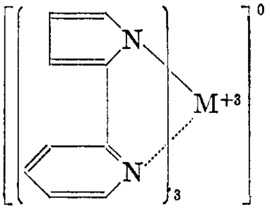


inasmuch as the copper derivatives of numerous enolic compounds are perfectly stable toward water. In physical properties pyrrolealdehyde itself is differentiated sharply from other aldehydes, such as benzaldehyde and furfuraldehyde.

t. One $-\overset{|}{N}H$ group (acidic) and one $\overset{\diagdown\ \diagup}{N}$ group (coördinating)

Several metallic complexes of α-(α'-pyridyl)pyrrole were prepared by Emmert and his coworkers (59, 61). The pyrrole groups act acidic in these compounds and the copper, zinc, cadmium, nickelous, ferric, and cobaltic compounds are typical inner complexes (non-electrolytes) having the following structures:

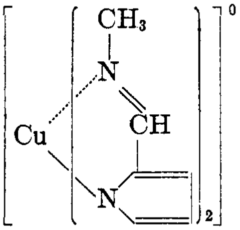


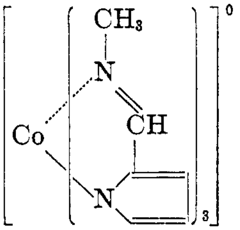


They possess anomalous colors, and are insoluble in water but soluble in organic solvents. The zinc and aluminum compounds exhibit extremely beautiful fluorescence.

u. One $-\overset{|}{N}H$ group (acidic) and one $=N-$ group (coördinating)

Inner complex compounds of α-pyrrolealdmethylimine



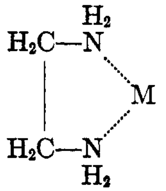


were prepared by Emmert and his students (61).

B3. Two coördinating valences

a. Two $-NH_2$ groups (both coördinating)

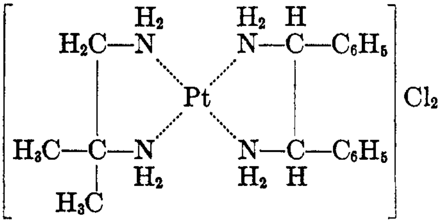
The first of the compounds which we now consider to be cyclic were the ethylenediamine complexes of platinum and cobalt discovered by Jörgensen in 1889 (119). The ethylenediamine complexes fitted beautifully into the coördination theory of Werner if the assumption was made that each of the amino groups occupied a position in the coördination sphere of the metal giving rise to a ring structure:



It was further assumed that the two groups of the coördinating molecule must occupy *cis*- or neighboring positions, the molecule simply not being large enough to span the *trans*- or axial positions. Assuming also that no rearrangement occurs on replacing the ethylenediamine molecule by two other groups, this furnishes a powerful method for determining the configuration of isomeric coördination compounds, and this procedure has indeed been extensively employed.

Ethylenediamine compounds with a great number of metals have been made; with cobalt alone the number of *cis–trans* isomeric pairs which have been studied approaches thirty.

The ethylenediamine derivatives played another important rôle in furnishing asymmetric complex molecules which could be resolved into optically active constituents. Indeed it was only with the optical resolution of the complexes that the coördination theory received unreserved acceptance. This field has been rather widely studied and the literature has been adequately reviewed by Jaeger (109) and by Bailar (4). A substituted ethylenediamine platinum derivative was employed by Mills and Quibell (173) in their extremely neat proof of the planar configuration of the quadricovalent platinum atom. They were able to resolve isobutylenediamino-meso-stilbenediamino-platinous chloride,

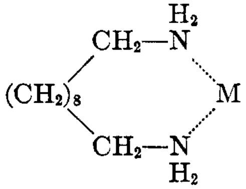


a compound which is completely asymmetric if the platinum atom has a planar configuration, but which possesses a plane of symmetry if the coördinating groups are tetrahedrally disposed.

The enormous increase in stability resulting from ring formation may be seen from a comparison of the compounds $[Ni(NH_3)_6]X_2$ and $[Ni\,en_3]X_2$. The former is rapidly hydrolyzed in water, as shown by its conductivity and cryoscopic behavior, its aqueous solution has a distinct odor of ammonia, and at a dilution of 100 liters it yields a precipitate of nickel hydroxide; the aqueous solutions of the latter, however, are entirely normal and stable even at a dilution of 1000 liters (262).

Trimethylenediamine behaves analogously to ethylenediamine in its action toward the metals, six-membered rings being formed.

Several studies have indicated, however, that higher membered rings of this type cannot form or are extremely unstable. Tetramethylenediamine (putrescine) and pentamethylenediamine (cadaverine) do not form cyclic compounds with nickel, cobalt, or copper (198, 253, 262, 284, 199). Pfeiffer has more recently found (199) that decamethylenediamine, $H_2N(CH_2)_{10}NH_2$, and octadecamethylenediamine, $H_2N(CH_2)_{18}NH_2$, are incapable of forming ring structures with copper or nickel corresponding to



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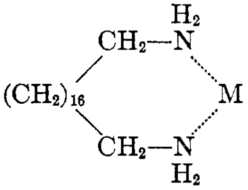
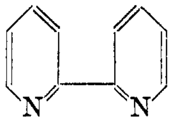


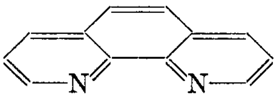
which would contain thirteen and twenty-one members, respectively.

The metallic complexes of *o*-phenylenediamine, $C_6H_4(NH_2)_2$, are not as stable as those of the aliphatic amines (105).

b. Two $\diagdown N \diagup$ groups (both coördinating)

The very interesting metallic compounds with α,α'-dipyridyl and with *o*-phenanthroline

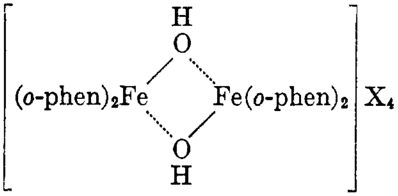




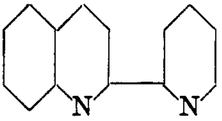
were discovered by Blau (20) in 1898. Among the numerous metallic derivatives of these compounds are the striking blood-red ferrous salts in which three molecules of the base are attached to one atom of iron, $[Fe(dipy)_3]X_2$ and $[Fe(o\text{-phen})_3]X_2$. The complex radicals are readily formed and very stable. They furnish an extremely sensitive test for ferrous iron (76, 229). On oxidation these red ferrous compounds are converted to blue ferric compounds, the shift in color being reversible. The *o*-phenanthroline complex was employed by Walden, Hammett, and Chapman (268) as an oxidation–reduction indicator and its utility has been rapidly extended (37). The shift

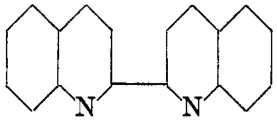
$$\underset{\text{red}}{[(o\text{-phen})_3\text{Fe}]X_2} \underset{[H]}{\overset{[O]}{\rightleftarrows}} \underset{\text{blue}}{[(o\text{-phen})_3\text{Fe}]X_3}$$

occurs at the high potential of 1.14 volts and is ideal for use in dichromate or ceric sulfate oxidation. While the *o*-phenanthroline ferric complex is readily produced by the oxidation of the ferrous complex as indicated above, the action of *o*-phenanthroline on ferric salts yields an amorphous brown powder (20), which has recently been shown by Gaines, Hammett, and Walden (86) to be a binuclear compound of the composition

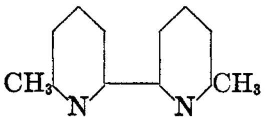


The similarity in structure of α,α'-dipyridyl and *o*-phenanthroline immediately suggests that the condition for complex formation is simply that the cyclic nitrogen atoms be attached to adjacent carbon atoms. The isomeric phenanthrolines and α,β'-, β,β'-, and γ,γ'-dipyridyl fail to give any reaction with ferrous iron. Much more surprising, however, was the discovery by Smirnoff (239) that α-pyridyl-α'-quinoline and α,α'-diquinolyl

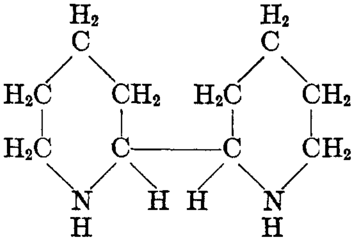




fail to give the ferrous reaction. Smirnoff attributed this to a saturation of the residual affinity of the nitrogen atoms by the neighboring "aliphatic-like" conjugated double bond system of the benzenoid ring of quinoline. Willink and Wibaut (290) have found, however, that the test also fails with 6,6′-dimethyl-2,2′-dipyridyl.



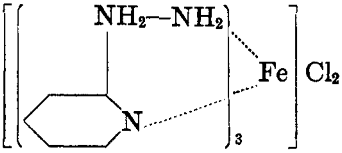
Apparently the α,α'-linkage is a necessary but not the sole condition for chelation of these compounds. Smirnoff predicted that the isomeric diisoquinolines joined by carbon atoms neighboring the nitrogen atoms will give the iron reaction, but this point has apparently not yet been tested. α,α'-Dipiperidyl



also yields a red ferrous complex (20).

c. One $\diagdown N \diagup$ group and one —NH_2 group (both coördinating)

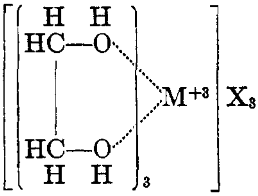
Somewhat similar to the ferrous dipyridyl compound is the ferrous complex with α-pyridylhydrazine



described by Emmert and Schneider (62).

d. Two —OH groups (both coördinating)

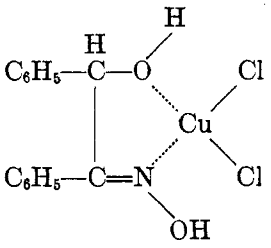
A great number of compounds were prepared by Grün and his coworkers (91, 92) in which ethylene glycol and several other 1,2-glycols, propyleneglycol, pinacol, etc., were coördinated to metals. Three molecules of the glycol but never more entered the compounds, corresponding to ring formation of the type:



Glycerol acts in a similar manner (93), but as three molecules always enter into the complex probably only two hydroxyl groups are coördinated, the third being left free, that is, glycerol functions as a bidentate rather than a tridentate molecule. Well-defined crystalline compounds have been obtained in these cases. Other less definite evidence along this line has also been presented (87).

e. One —OH group and one =NOH group (both coördinating)

As mentioned previously, α-benzoin oxime functions as a bidentate molecule in all three classes: i.e., both groups functioning as acids (B1, i); one as an acid, one by coördination (B2, l); and both by coördination. The latter case was observed by Jennings, Sharratt, and Wardlaw (144), who prepared the copper and nickel compounds



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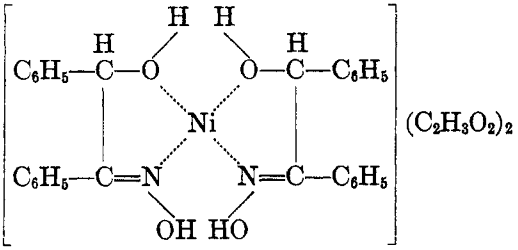
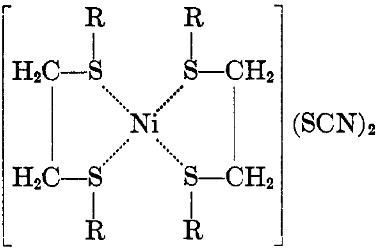


f. Two —S— groups (both coördinating)

The organic monosulfides, R—S—R, form stable coördination compounds with a number of heavy metals, for example, platinum, palladium, and mercury. The copper and nickel compounds with the monosulfides are little stable or non-existent. With those disulfides where ring formation may occur, the stability is enormously increased and the copper and nickel compounds are well defined.

Tschugaeff (258, 265, 260, 267) studied a series of dithioethers of the general formula $RS(CH_2)_nSR$. Variation in the alkyl groups had little effect, although the aryl compound, $C_6H_5S(CH_2)_2SC_6H_5$, would not coördinate with copper or nickel. When n = 2, corresponding to the formation of five-membered rings by chelation, the disulfides gave fine crystalline compounds with nickel and copper of the type of



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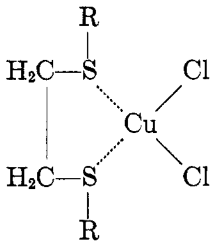
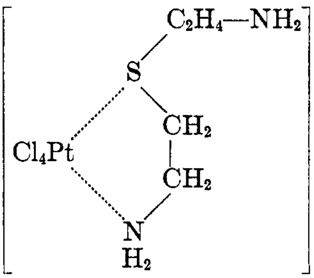


When n = 0, 1, 3, or 5, corresponding to three-, four-, six-, or eight-membered rings, the ability to form metallic compounds was completely absent.

Morgan (182) has reviewed the chelate compounds of the dithioethers; surveying the periodic table systematically he concluded in general that the thioethers chelate with those metals which normally form sulfides. He has also measured the heats of formation of these compounds (180). The metallic derivatives of numerous other disulfides of this same type have been studied (14).

g. One —S— group and one —NH_2 group (both coördinating)

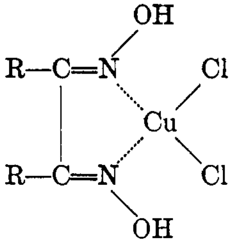
Mann (155) prepared a quadrivalent platinum compound with β,β'-diaminodiethyl sulfide, having the composition



The free amino group of this compound is capable of adding acids. By fractionally crystallizing the *d*-camphorsulfonate of this compound Mann isolated optically active components of the compound. The asymmetry of the molecule resides in the sulfur atom, which through coördination becomes similar in structure to the sulfoxides which had previously been resolved.

h. Two =NOH groups (both coordinating)

In their usual reactions the dioximes of the 1,2-diketones form chelate rings by the replacement of the hydrogen atom of one oxime group, the second oxime group attaching to the metal by secondary valence. The dioximes have also been found to form chelate rings by secondary valences alone (43, 235), giving copper compounds of the type



C. THE TRIDENTATE COMPOUNDS

Of the four possible classes of tridentate compounds corresponding to the combinations of primary and coördinating valence, members of all classes are known, although the evidence in the case of class C1 is rather weak. The total number of tridentate compounds is very small.

C1. Three primary valences

Of the various tribasic acids which might enter into complex formation as tridentate groups, occupying three coördination positions about a metal atom, phosphoric acid is the first which is called to mind.

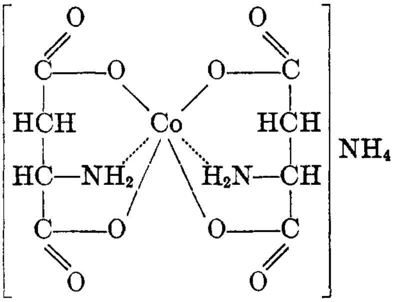
A number of salts of two phosphatoferric acids, $H_3[Fe(PO_4)_2]$ and $H_6[Fe(PO_4)_3]$, were described by Weinland and Ensgraber (276). In the former the phosphate radical apparently occupies three coördination positions. The situation is very complicated, however. Jensen (115) has recently reviewed and extended some of the knowledge of these compounds.

The action of phosphoric and citric acids on aquopentammino-cobalti salts leads to pentammino compounds in which only one limb of the acid occupies a coördination position (56).

C2. Two primary valences

a. Two —COOH groups (acidic) and one —NH_2 group (coördinating)

That aspartic acid, $HOOCCH_2CHNH_2COOH$, and trivalent cobalt form a permanganate-colored lake was briefly noted by Lifschitz (147). Further investigation (289) of this phenomenon has shown that this deep permanganate-colored compound forms by the action of aspartic acid on cobaltic oxide or various cobalt ammines; it is stable toward acids but sensitive to alkalies. The compound is very soluble in water, and evaporation of the solution yields only a glassy resin. Addition of ethyl alcohol or higher alcohols to its aqueous solutions gives only oily emulsions; methyl alcohol, however, precipitates a light lavender powder which is either the free acid $H[Co(C_4H_5O_4N)_2]$ or its ammonium salt, depending on whether the compound was prepared from cobaltic oxide or a cobalt ammine. Although somewhat variable in composition, the ammonium salt was shown by conductivity measurements to be a uni-univalent electrolyte. Migration experiments in agar gel indicate that the colored ion is negatively charged. The structure given the compound (289) is



Pfeiffer (202) has recently examined the copper derivative of aspartic acid and found it to be the cupric salt of copper aspartic acid,

$$[Cu(C_4H_5O_4N)_2]Cu \cdot nH_2O$$

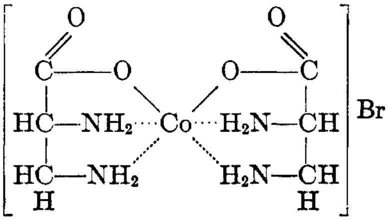
He prepared also the sodium and barium salts of the complex acid. Although Pfeiffer formulates the compound as having the aspartic acid molecules linked to the copper atom through the amino group and only one carboxyl group, leaving the second carboxyl group free, this is probably incorrect, and the complex diaspartato-cupric anion is better formulated like the above cobalt compound, that is, as a tridentate molecule.

Glutamic acid, $HOOCCH_2CH_2CHNH_2COOH$, forms copper compounds similar to those of aspartic acid (202). The lead (12, 122) and cobalt (236) derivatives are probably tridentate compounds of this class.

C3. One primary and two coördinating valences

a. One —COOH group (acidic) and two —NH_2 groups

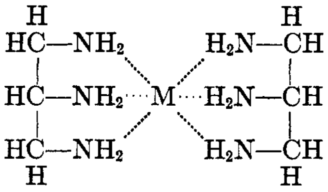
The action of the α,β-diaminopropionic acid hydrobromide on cobaltic oxide or, better, on carbonato-tetrammino-cobalti bromide (289) leads to the complex cobalt compound $[Co(C_3H_7O_2N_2)_2]Br$. The salt crystallizes without water of crystallization, and conductivity measurements indicate that it is a uni-univalent electrolyte. The structure of the compound is undoubtedly



C3. Three coördinating valences

a. Three —NH_2 groups

A series of investigations into the coördination compounds of α,β,γ-triaminopropane by Mann and Pope (162, 161) and later by Mann (151, 152, 153, 154, 156) has yielded unique and interesting results. With the metals of coördination number six, compounds of the general type



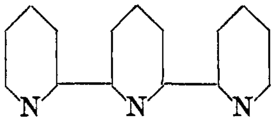
M = Co, Pt, Rh, Ni

are produced in which one molecule of the triamine occupies three coördination positions about the metal atom. The great stability of these compounds is indicated by the fact that nickel and divalent platinum add two molecules of the triamine, forming compounds in which the coördination number is six; this is very unusual, at least in the case of the latter element.

The triamine can also act as a substituted diamine, the resulting complexes being of a very novel type.

b. Three $\diagdown\!\!\diagdown\mathrm{N}\diagup$ groups (coördinating)

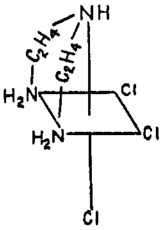
During the preparation of α,α'-dipyridyl by the catalytic dehydrogenation of pyridine, Morgan and Burstall (176) isolated α,α',α''-tripyridyl,

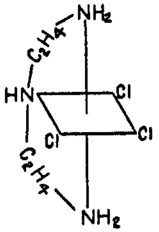


They found that this base gave a deep purple ferrous compound, $[Fe(tripyridyl)_2]Br_2 \cdot 1.5\ H_2O$, in which the base apparently acts as a tridentate group. The platinum, rhenium, and rhodium complexes with the base were subsequently studied (177, 175). A method of determining iron in sea water has been devised (42) based on the reaction of the base with ferrous iron.

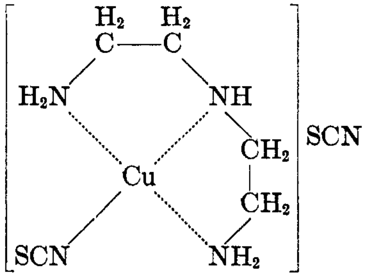
c. Two —NH_2 groups and one $\overset{|}{\text{—N—}}$ group (coördinating)

In an effort to prepare an optically active compound in which the asymmetry of the molecule was due to coördinated nitrogen, Mann (158) studied the coördination compounds of β,β′-diaminodiethylamine, $HN(CH_2CH_2NH_2)_2$. Among other compounds he prepared several salts in which the amine functioned as a tridentate molecule. The platinum compound $[Cl_3Pt\ (\text{diaminoethylamine})]Cl$ may have two configurations:





Only one form of the compound was obtained, however. A cobalt compound of the hexammine type was prepared, $[Co(\text{diaminodiethylamine})_2]I_3$, and two copper compounds:



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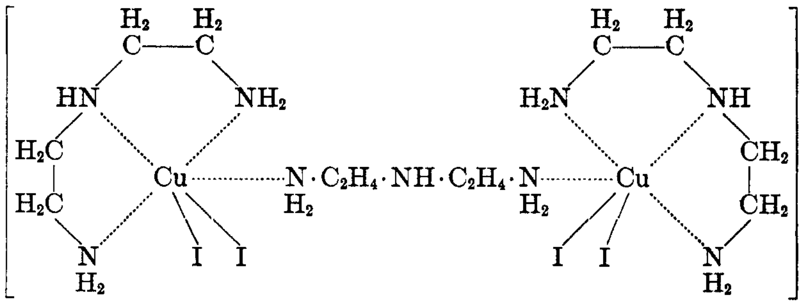
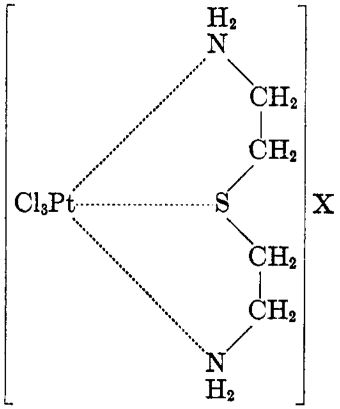


Peacock has also worked on similar compounds (190).

d. Two —NH_2 groups and one —S— group (coördinating)

During a study of the stereochemistry of coördinated sulfur, Mann (155) obtained a tridentate platinum compound containing β,β'-diaminodiethyl sulfide



Two forms of this compound are possible, similar to those suggested above for the platinum salts of β,β'-diaminodiethylamine, but only one form was found.

D. THE QUADRIDENTATE COMPOUNDS

D1. Four primary valences

No examples of this class are known.

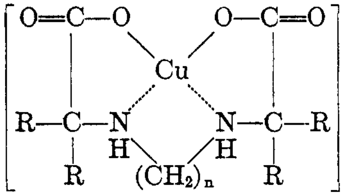
D2. Three primary valences, one secondary valence

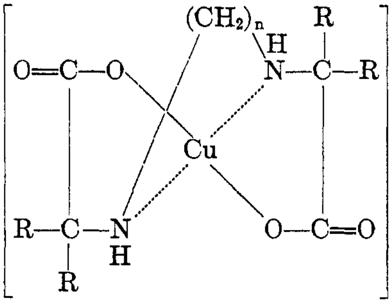
No examples of this class are known.

D3. Two primary valences, two secondary valences

a. Two —COOH groups and two $\overset{|}{\text{—NH}}$ groups

N. Schlesinger (234) investigated the copper salts of a number of polymethylene-bis-(α-imino acids) of the general formula: $(CH_2)_n$-$(NHCRR'COOH)_2$. For values of n of 2 and 3 a single form of the copper salt was found, blue in color; for n = 10, violet-colored salts resulted, but again only one form. For intermediate values of n, 5 and 7, two modifications, blue and violet, were obtained. The compounds were non-electrolytes, as indicated by conductivity measurements, and had normal molecular weights. Schlesinger attributed the existence of two forms of the intermediate members to *cis–trans* isomerism:

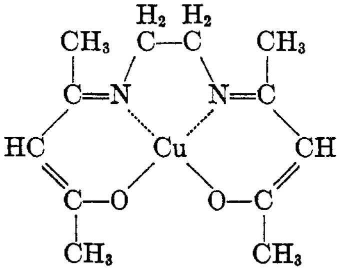




The spanning of the *trans*-positions of the copper atom can occur only with large values of n. Four different amino acids were tried in these compounds, and the results appear to be fairly general. The interpretation of these results has been criticized by Reihlen (210).

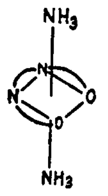
b. Two —OH groups (acidic) and two =N— groups (coördinating)

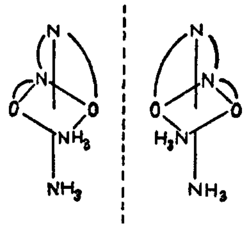
While trying to prepare a copper compound containing both ethylenediamine and acetylacetone, Morgan and J. D. Main Smith (186, 187) obtained a green copper salt of a condensation product of ethylenediamine with two molecules of acetylacetone. The copper compound, which has the following structure

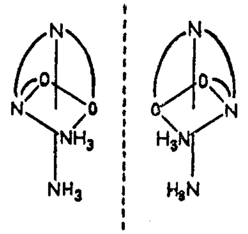


had been obtained earlier by Combes in 1889.

Beside furnishing copper, nickel, and palladium compounds which have all the properties of inner complex compounds (the nickel compound can be boiled without decomposition), the quadridentate behavior of the condensation product, ethylenediamine-bisacetylacetone (abbreviated as "ec"), was convincingly demonstrated by the preparation of the cobaltic compound, $[Co(NH_3)_2ec]X$. This compound exists in five forms,—one inactive form and two enantiomorphic pairs,—all of which were found by Morgan and Main Smith. These forms correspond to the various possible arrangements of the quadridentate molecule about the coördination sphere:

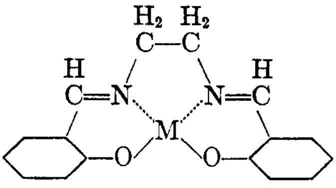




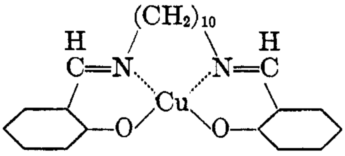


Both of the racemic mixtures were resolved and their optical rotatory powers found to differ considerably. These results are not only an example of excellent experimental work but a brilliant confirmation of the general principles underlying the formation of chelate rings.

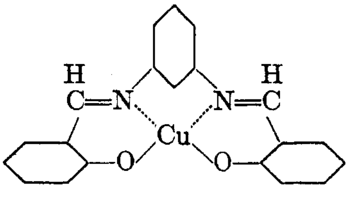
The formation of metal compounds with salicylaldimine (B2, m) led Dubský and Sokol (53) to the metal salts of the condensation product of salicylaldehyde with a diamine. A condensation product of ethylenediamine with two molecules of salicylaldehyde was readily obtained by warming a mixture of their alcoholic solutions. This material gave inner complex nickel and copper compounds having the composition

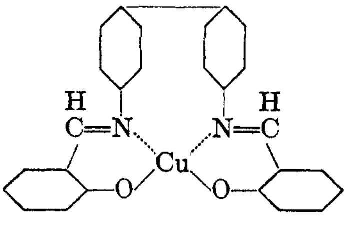


Pfeiffer greatly extended the field (194, 200) by using decamethylenediamine and various aromatic diamines in place of ethylenediamine. Like the derivative from ethylenediamine, the *o*-phenylenediamine compound yields metal compounds involving two six-membered and one five-membered ring. A thirteen-membered ring must be present, however, in

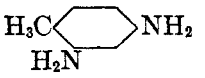


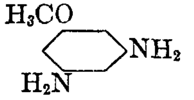
Very surprising is the fact that *m*-phenylenediamine and benzidine yield the same type of compound. On stereochemical grounds it seemed highly unlikely that these compounds would have the structures

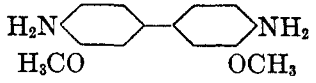




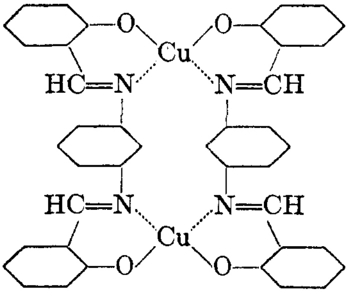
While the molecular weights of the salts of the compounds derived from *o*-phenylenediamine and decamethylenediamine were shown to be normal, such evidence could not be obtained with the *m*-phenylenediamine and benzidine compounds because of their insolubility in all solvents. By using the following substituted diamines







analogous metal salts were obtained which were soluble in chloroform. Their molecular weights are double those of the simple formulas and Pfeiffer considers their structures to be



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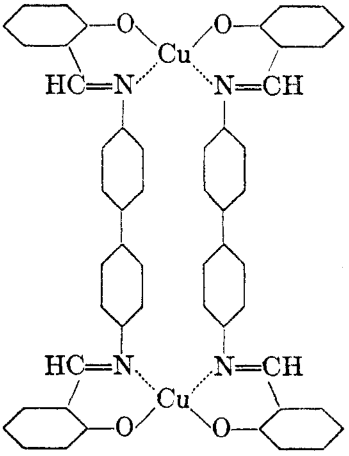
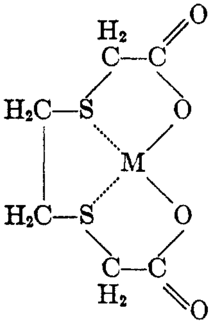


The corresponding *p*-phenylenediamine behaves in the same way, and again the copper derivative is too insoluble for molecular weight determinations; the 1,4-naphthalenediamine compound is bimolecular, however, as well as the 1,5- and 2,7-naphthalenediamine derivatives, and probably the structures of these compounds are the same as those of the *m*-phenylenediamine and the benzidine derivatives.

c. Two —COOH groups (acidic) and two —S— groups (coördinating)

Probably the first synthetic quadridentate compounds recognized as such were the copper and bivalent platinum compounds of ethylenebisthioglycolic acid of Ramberg and Tiberg (208)

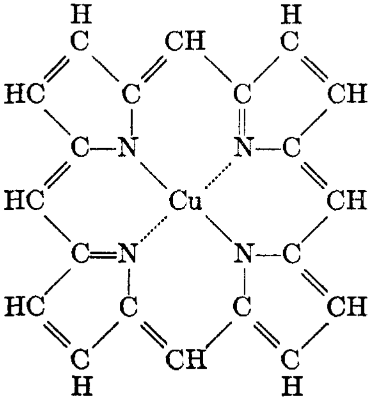


These were immediately known to be inner complex compounds because of their composition, saturated character, and insolubility in water. Similar compounds are prepared from propylenebisthioglycolic acid (212).

d. Two $-\overset{|}{\mathrm{N}}\mathrm{H}$ groups (acidic) and two $\overset{\diagdown\ \diagup}{\mathrm{N}}$ groups (coördinating)

In this group fall the exceedingly important natural pigments, chlorophyll, the green coloring matter of the leaves, containing magnesium, and hemoglobin, the red pigment of the blood, containing iron. The classical work of Willstätter and of H. Fischer has given us an insight into the composition and structure of these materials. In both there is present the great porphyrin ring containing four pyrrole nuclei joined together through their α-positions by methylene groups. The metals appear to be united to the nitrogen atoms of all four pyrrole groups, two by primary and two by secondary valences. In the case of chlorophyll the alcohol phytol, and in the case of hemoglobin the protein globin, is joined to the metal porphyrin molecule.

The parent unsubstituted porphyrin ring has been synthesized by Fischer (82). Its copper compound has the structure

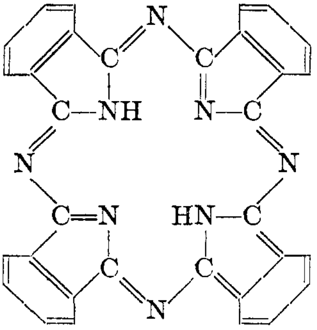


The porphyrins vary from this by substituents on the β-carbon atoms of the pyrrole nuclei.

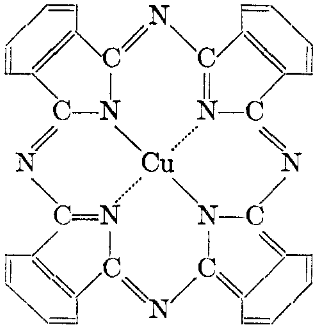
The metal atom undoubtedly plays a significant rôle in the biological processes in which the natural pigments perform such essential functions, that is, the reduction of carbon dioxide by the plant and the transmission of oxygen by the blood, but our knowledge of how this occurs is still in a formative state (96, 224).

It is interesting to note that the oxygen carriers in the blood of various invertebrates contain copper, manganese, or vanadium (all metals of variable valence) instead of iron. The pinion feathers of the turacos, a species of tropical birds, contain a red pigment which is a copper porphyrin of structure similar to that given above (83).

In a very brilliant series of investigations the English chemist Linstead and his students (148) have very thoroughly investigated the blue by-product produced in the commercial manufacture of phthalimide by the action of ammonia gas on fused phthalic anhydride in iron vessels. To this deep blue substance they gave the name "phthalocyanine" because of its origin and color. The by-product material contains iron, but the free organic substance, also deep blue in color, has been isolated and shown to be a large cyclic molecule, markedly resembling the porphyrin rings, but composed of four phthalimide residues fused together through nitrogen atoms, forming a great ring of eight carbon and eight nitrogen atoms.



Phthalocyanine



Copper phthalocyanine

As in the porphyrins, metal atoms can be introduced into the center of the molecule, two hydrogen atoms being simultaneously displaced and the metal also coördinating with the other two central nitrogen atoms. Some twenty metallic derivatives have been prepared, including metals from each group of the periodic table. While these metallic derivatives can be prepared by the action of free phthalocyanine on the metals or their salts, the best way appears to be by the action of the metal on phthalonitrile, condensation and complex formation occurring simultaneously,

$$4C_8H_4N_2 + M \rightarrow C_{32}H_{16}N_2M$$

there being a great tendency for this to occur and the reaction being exothermal. The metallic products are of extraordinary stability, the copper compound, for example, subliming undecomposed at 580°C. In the case of bivalent metals the products have the formula PcM^{+2} (Pc = phthalocyanine minus 2 H); in the case of trivalent elements $PcM^{+3}X$ (X being a univalent negative radical).

Detailed x-ray studies of the free phthalocyanine molecule and its metallic derivatives by Robertson (222, 223) have led to fruitful and very unique results, wholly in agreement with conclusions drawn by Linstead from chemical reasoning. As expected, the molecule is completely planar and the introduction of most metal atoms does not change the cell dimensions appreciably. The stereochemical implications of these compounds have been treated in a joint paper of Linstead and Robertson (149). An investigation into the magnetochemistry of the materials has also been made (123). It has been reported that metallic phthalocyanines are now being manufactured on large-scale production for use as pigments.

Linstead has also extended the study to the corresponding naphthalene compounds (32). Of the ten isomeric dicyanonaphthalenes only the 1,2- and 2,3- compounds undergo reaction with metals. From 1,2-dicyanonaphthalene and magnesium was obtained a mixture of isomeric forms corresponding probably to the four possible arrangements which the extra naphthalene rings may take up around the molecule.

D4. One primary valence and three secondary valences

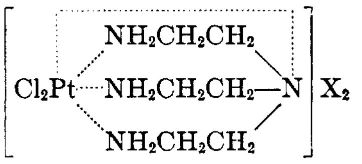
No examples of this group are known.

D5. Four coördinating valences

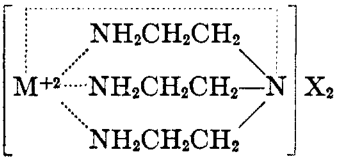
a. Three $-NH_2$ groups and one $-\overset{|}{N}-$ group (all coördinating)

Ordinarily the tertiary nitrogen atom is unable to form stable coördination bonds with metal atoms. In the coördination compounds of β,β',β''-

(triaminotriethyl)amine, studied by Mann and Pope (159), the coördination of the amino groups holds the tertiary nitrogen in the molecule, forcing it to coördinate. These are the first compounds of tetramines to be described, and apparently the first where an aliphatic tertiary nitrogen atom occupies a coördination position. With tetravalent platinum the base yielded the compound



with divalent platinum, nickel, and palladium the following compounds:



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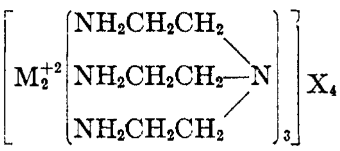


The arrangement of the four nitrogen atoms about a metal of coördination number four is difficult to picture sterically. Molecular weight and conductivity measurements indicate that the compounds are monomolecular. Reihlen (210) interpreted these compounds as proof of the tetrahedral distribution of the valences of the quadricovalent platinum atom,—the only distribution possible under the circumstances. The proof of the planar structure of the quadricovalent elements platinum, palladium, and nickel is now so overwhelming that the tetrahedral configuration is undoubtedly wrong. And yet the difficulty with the structure of these compounds still remains, as it is certainly impossible for the molecule to occupy the four corners of a square around the metal atom.

The corresponding triaminotripropylamine yields an analogous nickel compound, but not a platinum compound (160). Triaminotrimethylamine is apparently incapable of existence (121).

POLYDENTATE MOLECULES OF UNKNOWN CONSTITUTION

The ability of the peptides to dissolve freshly precipitated copper oxide was noted frequently by Emil Fischer (79) during the course of his researches on the amino acids and proteins. Although he remarked on the beauty and finely crystalline character of the copper derivatives, he analyzed relatively few and in no case attempted an explanation of their structure.

Structural formulas were assigned by Kober (126, 125) to the copper derivatives of the polypeptides; the reasoning underlying these formulations is often difficult to follow and the work needs further substantiation. Rising (218) and Wenaas (281) have also worked on these compounds. However, the field cannot yet be considered as settled.

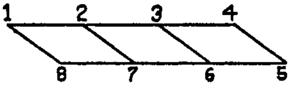
According to Fischer (81) the α- and the β-amino acids are able to form copper salts, but the γ-, δ-, and ε-amino acids are unable to do so. This is in accord with the work of Ley and Tschugaeff, as we have already seen (B2, a). The presence of a hydroxyl group in the molecule does not void this rule, as is shown by serine (α-amino-β-hydroxypropionic acid), isoserine (α-hydroxy-β-aminopropionic acid), δ-amino-α-hydroxyvaleric acid, and ε-amino-α-hydroxycaproic acid. Fischer pointed out, however, that the presence of more than one hydroxyl group might alter the situation.

Traube and W. Fischer (247) found this to be true, as copper hydroxide dissolved in δ-amino-α,γ-dihydroxyvaleric acid, $CH_2(NH_2)CH(OH)CH_2CH(OH)COOH$, giving a complex compound which could be isolated only as a dark blue glass but which had the constant composition $Cu_3(C_5H_8O_4N)_2 \cdot 8H_2O$.

The same curious relation of two atoms of copper to three molecules of hydroxyamino acid exists in the copper salt of hydroxyaspartic acid, $HOOCCH(NH_2)CH(OH)COOH$, prepared by Dakin (46),

$$Cu_3(C_4H_4O_5N)_2 \cdot 8H_2O$$

It will be noted that if the four covalences of the copper atom lie in one plane and the -ol type of polynuclear linkage be present that a trinuclear molecule will afford just the eight coördination positions required by the eight active groups of the two molecules of amino acid.



Considerable work will have to be done before such a configuration can be regarded as established.

Analytical data appear to point toward a tridentate structure for the copper salt of isoserine (80).

The combination of metals with proteins has also been attacked from other angles (240, 188).

The activation of the enzyme arginase by metals has been pointed out by Hellerman (97), who believes that complex formation of some sort occurs between the metal and the enzyme. If so, the product is probably polydentate in character.

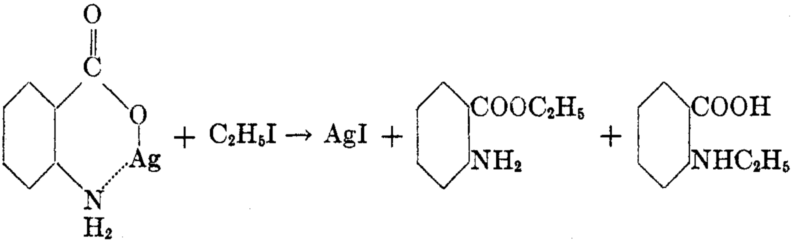
THE EVIDENCE FOR CHELATION

The chelate rings were a natural outgrowth of the coördination theory. Just when a cyclic structure was first proposed for one of these compounds is difficult to determine. The idea of ring structure in the ethylenediamine complexes runs subconsciously through the early papers of Werner without being definitely expressed. In 1901, however, Werner (283) specifically assigned a cyclic structure to platinum acetylacetonate, and other similar structures were soon suggested: for copper glycine by Ley (134), for nickel dimethylglyoxime by Tschugaeff (262), and so on.

A great body of consistent evidence has been built up proving the existence of the chelate rings, and while the principles stated or assumed in the foregoing work can hardly be doubted, the underlying facts should not be forgotten. Briefly they are these:

1. While the coördination number of certain metals is invariably four or six in thousands of cases of unidentate compounds, only two or three molecules of organic compounds bearing two associating units unite with such metals. Providing the compound be monomolecular, attachment of all four or six units with subsequent ring formation must be assumed if the coördination positions are to be all occupied.
2. The failure of analytical tests for the metals on solutions of their complex salts shows the absence of the simple ions of the metal, and conductivity and migration experiments prove the complex ion to be a non-electrolyte, anion or cation, as calculated assuming chelation to occur.
3. The compounds are saturated and incapable of adding further coördinating addenda; for example, copper glycine will not take up ammonia (134).
4. Absorption spectra curves are identical with analogous compounds known not to be cyclic (133, 138).
5. Predictable isomeric phenomena have been realized, as for example with the glycine compounds of cobalt and platinum and the dioximes of nickel and palladium.
6. Compounds rendered asymmetric by chelation have been resolved in numerous cases.
7. Groups involved in chelation are non-reactive, such as the carbonyl group of the acetylacetonates, which will not react with phenylhydrazine (211, 63), the amino group of the amino acid salts, which cannot be acetylated (122), and so on.
8. The formation of the chelate type of compound occurs only with those organic molecules which are stereochemically so arranged as to yield rings of four to seven members and not by those not so arranged, this difference generally being very sharp.
9. Chelating groups enter equally into reactions when a chelate ring is

broken by double decomposition, as shown by Karrer (120) in the reaction of the silver salt of anthranilic acid with ethyl iodide:



Taken together these facts are abundant proof of the cyclic nature of the chelate compounds.

From the foregoing survey it will be readily appreciated that the chelate rings have an unusual application to a variety of otherwise unrelated fields.

The mechanism of the function of the metals in biochemical problems is known to be chelate in nature in the case of chlorophyll and hemoglobin, and undoubtedly the part played by metals in the activity of certain enzymes and in the nutritional requirements of the plants and animals is of the same character.

The great saving of time and the increased accuracy in analytical processes which result from the discovery of specific organic reagents is so obvious as to require little mention. The best reagents which have been proposed so far are of the non-electrolyte chelate *inner complex* type. Feigl, Berg, and other workers have been pursuing this field for some time, and their results are most encouraging.

In furnishing a neat and comprehensive theoretical basis for mordant dyeing Werner and, later, Morgan and his students have made an exceptionally valuable application of the chelate rings.

For settling the questions related to the stereochemistry of the metals the chelate rings have proven a very useful and fruitful tool, and further examples of this are appearing regularly. In the field of organic chemistry the chelate compounds have been employed in deciding questions of structure and in following changes in configuration. Many pharmaceutical preparations are chelate compounds.

In the chelate compounds, therefore, we have a field of widely different and important applications, a field which combines all the attraction of synthetic chemistry and stereochemistry with the possibilities of solving important problems in analytical and biochemistry. It is a field, however, which has many uncharted regions and offers abundant opportunity for exploration.

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