CHELATE COMPLEXES OF 1,10-PHENANTHROLINE AND RELATED COMPOUNDS

WARREN W. BRANDT

Department of Chemistry, Purdue University, Lafayette, Indiana

AND

FRANCIS P. DWYER AND ELEANORA C. GYARFAS

Department of Chemistry, University of Sydney, Sydney, Australia

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I. INTRODUCTION

The chemistry of coördination compounds has become a highly specialized branch of the science. Several review articles and books have dealt with various broad phases of the problem (12, 26, 27, 158, 192, 196, 220, 242, 276), but there has been no correlated consideration of one family of reagents other than Bjerrum's excellent monograph on the ammine complexes (26).

The extent of the recent studies in the chemistry of the chelate-forming molecules containing the aromatic =N—C—C—N= grouping has made a review of this work both desirable and necessary. The present work is an effort to present the chemistry of a related series of organic reagents in their reactions with metal ions. It is hoped that this critical evaluation will prompt correlations of other systems and further investigation of the one described. Although investigations now known to be in the process of completion or publication will make some of these considerations out of date, they should provide present and future investigators with a coördinated and critical background for interpretation.

The discussion includes the information published prior to January 1, 1954. In sections dealing with observed reactions and stabilities the coverage is intended to be essentially complete. The applications cited are merely representative of the types of analysis possible. No attempt has been made to include the extensive literature in this section.

The terms 1,10-phenanthroline, 2,2′-bipyridine, and 2,2′,2″-terpyridine are the nomenclature recommended by *Chemical Abstracts* and the International Union of Pure and Applied Chemistry. The prefix numbers will be omitted in the text. The abbreviations "phen," "bipy," and "trpy" seem consistent with the nomenclature and should not conflict with common abbreviations for other organic reagents. The letter "B" will be used in the writing of equations to represent the general type of molecule being discussed. The trivial names "ferroin" and "ferriin" are utilized to denote the tris-1,10-phenanthroline ferrous and ferric complexes, respectively.

II. COÖRDINATION COMPOUNDS WITH METAL IONS

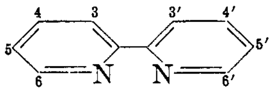
The reaction between iron(II) salts and 2,2′-bipyridine with the formation of intensely red substances was first observed by Blau (29, 32), who isolated a series of salts of the formula $Fe(bipy)_3X_2$ and demonstrated that the color resided in the common cation. The analogously constituted 1,10-phenanthroline, named α-phenanthroline by Blau, who first synthesized the substance, was shown to form similarly colored salts of the same type. When the red iron(II) compounds were treated with chlorine or potassium permanganate in acid solution the color changed to blue; from the amount of reagent consumed it was concluded that the blue substances contained tervalent iron. This was confirmed by the isolation of the chloroplatinates $[Fe(bipy)_3]_2[PtCl_6]_3 \cdot 5.5H_2O$ and $[Fe(phen)_3]_2[PtCl_6]_3 \cdot 18H_2O$. These substances could not be prepared directly from iron(III) salts and the parent bases, a reaction which it was felt should give the true "ferri-salts"; hence they were designated as "ψ ferri-salts." By ingenious, if somewhat subjective, arguments, it was concluded that the red ferro- and the blue ψ ferri-salts could be assigned to the "luteo" or hexammine class in Werner's new classification. According to the Werner theory (292) the formation of the compounds and their reactions were simple and natural, but by the then current Blomstrand–Jorgenson structural theory they were inexplicable. A number of complex compounds were prepared from copper(II), nickel(II), and cobalt(II) salts, and the bases were stated to react also with zinc, cadmium, and chromium(III) salts, but not with manganese, lead, or aluminum salts (32).

The resolution of the tris-2,2′-bipyridine iron(II) cation into the optically active forms was achieved by Werner (293) in 1912, and interest in these chelate molecules then lapsed for nearly twenty years. It was revived by the discovery of Hammett, Walden, and Chapman (129) that the iron(II) compounds could be used as valuable redox indicators and by the preparative researches of Morgan and Burstall, Barbieri, Pfeiffer, and Jaeger.

It is now recognized that the bipyridine type of chelate molecule rivals in versatility the well-known ethylenediamine, not only in the stability of many of the metal derivatives and in their frequently intense colors, but also in the number of metals that can be chelated.

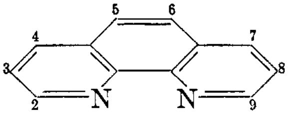
With the exception of the rare earths, numerous examples are known from each periodic group, including the alkali and alkaline earth elements. In the field of biology, bipyridine and phenanthroline have been shown to be useful anthelmintics (7) and to have some, but not pronounced, bacteriocidal value (2).

Bipyridine (I) and phenanthroline (II) function as typical bidentate chelate molecules through the nitrogen atoms with the formation of five-membered rings.



I

2,2′-Bipyridine



II

1,10-Phenanthroline

Attachment of the isomeric bipyridines such as 2,3′-, 2,4′-, or 4,4′-bipyridine to metal atoms would involve many-membered rings and these have been shown (30, 298) not to form stable iron complexes, though they may well attach to other metal atoms as monodentate ligands like pyridine itself. In the same way the structurally isomeric 1,7- and 4,7-phenanthrolines[1] do not act as chelate molecules (268).

When crystallized from water, phenanthroline and most of its substituted derivatives form well-defined monohydrates with characteristic melting points and low solubility in benzene. This property is of value in purification, since the addition of a few drops of water to solutions of the anhydrous substances in benzene precipitates the monohydrate. The molecule of water is hydrogen-bonded to the nitrogen atoms (118).

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[1] Smith and Richter (268) have referred to confusion in the early literature on the nomenclature of these substances.

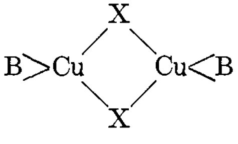
A hydrate of bipyridine has not been described; this is in accordance with crystal structure (46) and dipole moment studies (115, 123), which show that the rings are coplanar but in the *trans* position. However, it is certain that in the metal complexes the pyridine rings are in the *cis* position, and as in phenanthroline, which necessarily has the *cis* structure, coördination occurs in such a way that the chelate ring containing the metal atom is coplanar with the rest of the molecule.

Both chelate molecules have been attached to metal carbonyls and nitrosyls, but in such adducts the properties remain substantially those of carbonyls or nitrosyls. Therefore these compounds will not be discussed in this review.

A. GROUP 1 METALS

Coördination compounds of the alkali metals are relatively rare, as can be anticipated from their large ionic sizes and small electronegativities. Usually the attachment is to oxygen and non-electrolytes result, as when the alkali metal salt of a diketone is treated with one molecule more of the diketone (38, 64, 252). Monophenanthroline lithium perchlorate and bisphenanthroline sodium perchlorate are reported to be preparable in methanol solution. The colorless needles are soluble in hot water, nitrobenzene, and dioxane (228). Similarly, solutions of sodium iodide in acetone yield crystalline precipitates on the addition of phenanthroline or bipyridine (132). No evidence has yet been advanced to show that the base is actually chelated.

The colored copper(I) chelates were first reported by Tartarini (275), who reduced mixtures of phenanthroline or bipyridine and various copper(II) salts in ammoniacal solution with hydrazine, sodium bisulfite, or hydroxylamine. In some instances they were prepared directly from the copper(I) salt and the base. The following were reported: CuSCN·phen, CuI·2phen, CuSCN·bipy, and CuI·bipy. Subsequently, the red color developed by the reduction of copper(II) salts in the presence of phenanthroline was recommended for the microcolorimetric estimation of copper (213). Since 2-covalent copper(I) has a linear configuration, it is likely that these substances are all 4-covalent. This view is supported by the isolation of red-brown salts (132) of the form $[Cu(phen)_2]ClO_4$ and $[Cu(bipy)_2]ClO_4$. These are conductors in nitrobenzene solution, as are [CuX·B] ($X = I^-$ or SCN^-; B = phen or bipy). In this solvent spectrophotometric measurements showed the presence of the common ion CuB_2^+; hence they should be formulated as $[CuB_2][CuX_2]$. There was, however, some evidence for a small amount of the bridged dimer (III) in equilibrium:



III

This proposal had been previously advanced (189) for CuI·bipy. Copper(II) complex salts containing one, two, or three molecules of either chelate have been described. Most are hydrated and of a blue or violet-blue color (32, 153, 155, 235). Apart from the isolation of a large number of trischelate metal salts, the existence of the ions $Cu(phen)_3^{++}$ and $Cu(bipy)_3^{++}$ has been demonstrated polarographically (223). Attempts at the resolution of these octahedral complexes have not succeeded, but the phenomenon of "induced asymmetry" has been observed (64).

Bisphenanthroline silver(I) nitrate monohydrate has been obtained as pale yellow needles (201, 228), and there is also a yellow perchlorate, $[Ag(phen)_3]ClO_4$ (235). It is unlikely that the metal is 6-covalent in this substance. The large flat molecule of chelated phenanthroline may have the capacity to hold additional unchelated molecules by van der Waals forces in the solid lattice. It is not inconceivable that this could occur also to some extent in solution. In a calcium compound to which reference is made later no less than six molecules of phenanthroline are present in the solid phase. It is perhaps significant that these anomalously high coördination numbers have not been obtained with bipyridine. Complexes with the silver halides do not appear to have been described.

Very pronounced stabilization of bivalent silver has been achieved with both chelate molecules (9, 136, 201). Usually the silver(I) salt is simply treated with the base and then oxidized anodically or with ammonium peroxydisulfate. The bivalent complexes range in color from orange to red-brown. They are usually sparingly soluble (57) bis derivatives. Trisbipyridine silver(II) nitrate has been described, and presumably here the metal is octahedrally coördinated (201). The usual condition of non-oxidizability of the anion applies, and peroxydisulfates, nitrates, bisulfates, chlorates, and perchlorates have been prepared. The potential of the system AgB_2^+/AgB_2^{++} has not been determined, and would be difficult in any event, owing to the low solubility of the oxidant.

Oxidation to the tervalent state has not been reported, though lead dioxide, ozone, bismuth dioxide, and cerium(IV) salts have been tried as oxidizing agents (185).

Univalent gold can be expected to behave similarly to copper(I), but no complexes with either base have been reported. In the course of their work on organogold compounds, Foss and Gibson (117) prepared $[AuBr_2 \cdot bipy][AuBr_4]$ incidentally; more recently Block and Bailar (33) prepared a series of compounds with both chelate molecules. The Au(III) cation contained two covalently bonded halogens and one molecule of the chelate, the salts being of the form $[Au(B)X_2]X$ and $[Au(B)X_2][AuX_4]$ (X = Cl, Br). Compounds containing more than one molecule of base per gold atom were not obtained.

It appears from conductometric and spectrophotometric studies that the substances $[Au(B)X_2]X$ rearrange in nitrobenzene solution (132).

$$2[Au(B)X_2]X \rightleftarrows [Au(B)X_2]^+ + [AuX_4]^- + B$$

B. GROUP 2 METALS

By the reaction between phenanthroline and the alkaline earth perchlorates in methanol solution, Pfeiffer (228, 235) obtained colorless crystalline solids $[M(phen)_3](ClO_4)_2$ (M = Be, Mg) and $[M(phen)_4](ClO_4)_2$ (M = Ca, Sr, Ba). A crystalline substance of the formula $[Ca(phen)_6](ClO_4)_2$ was also isolated, but this was thought to be an inclusion compound, because it decomposed in 5 per cent methanol in ether to the tetrakis compound. The molecular weight of the tetrakis calcium compound in nitrobenzene was found to be 435 compared with the theoretical value of 959. Though Pfeiffer cited the ammines $MCl_2 \cdot 6(\text{or } 8)NH_3$ as evidence, high coördination numbers of six for beryllium and eight for calcium, strontium, and barium are most improbable. As pointed out earlier, additional molecules of unchelated base may well be attached by van der Waals forces. No bipyridine compounds have been described.

The colorless zinc and cadmium complexes with both bases have been investigated by a number of workers (38, 153, 173, 231, 232, 235, 252) and appear to be 4- or 6-covalent, containing one, two, or three molecules of the base. In aqueous solution the zinc ion may attach one, two, or three molecules of phenanthroline (168), and polarographic studies have demonstrated that in the presence of at least one hundred fold excess of the base, the ions $Cd(bipy)_3^{++}$ and $Cd(phen)_3^{++}$ exist (68).

The mercury complexes appear to have been little investigated. There is a report of a sparingly soluble $HgI_2 \cdot bipy$ that can be used for the analysis of bipyridine (201), and trisphenanthroline mercuric perchlorate has been prepared (228, 235). The latter substance may be only 4-covalent.

C. GROUP 3 METALS

Aluminum compounds with these chelates have not been described, although it is probable that they could be prepared under anhydrous conditions. Rare earth complexes are not known.

In aqueous solution indium salts yield the sparingly soluble colorless complexes $[In(bipy)_3]X_3$ and $[In(phen)_3]X_3$ ($X = Cl, Br, I, SCN$). These substances do not appear to hydrolyze very easily, but they have not been resolved into the enantiomeric forms (72, 272). Preliminary investigations show that gallium can coördinate three molecules of either chelate, but the complex cations are hydrolyzed to some extent in aqueous solution with the separation of gallium hydroxide (73).

A bisbipyridine thallium(I) nitrate has been prepared (228), and a bisphenanthroline thallium(I) iodide has been obtained by pyrolysis of the tervalent complex (273).

In aqueous or dilute alcoholic solution thallium(III) is coördinated by both bases to yield sparingly soluble complexes of the form $[Tl(B)]X_3$ ($X = Cl, Br, SCN$) (273). The evidence available does not allow one to decide whether these involve dimeric bridged structures or should be formulated as $[Tl(B)X_2]X$.

The orange-red iodides, $Tl(B)_2I_3$, do not react with starch–potassium iodide in dilute acetone solution and the existence of the I_3^- ion thus seems to be precluded, so that these substances may well be $[Tl(B)_2I_2]I$. Consequently, they provide an interesting addition to the list of valence-stabilized compounds, since the simple iodide TlI_3 does not exist. A similar chelate structure has been proposed for the bisethylenediamine thallium(III) iodide (137).

D. GROUP 4 METALS

Phenanthroline chelates with tin(II) and lead(II). $[Sn(phen)_3](ClO_4)_2$ and $[Pb(phen)_4](ClO_4)_2$ have been described (235). Although the lead compound has been quoted (192) as an example of 8-covalency, the evidence available is purely analytical and this substance may contain free phenanthroline. Tetrachlorobipyridinetin(IV) has been obtained by reaction of stannic chloride and the base in alcohol. The corresponding bromide, $Sn(bipy)Br_4$, has been isolated as unstable, highly insoluble, brown needles (3).

E. GROUP 5 METALS

Recent work (210) shows that vanadium coördinates with phenanthroline in the oxidation states of +2, +3, and +4, giving deeply colored complex salts.

Vanadium(II) solutions react to give the intensely blue-violet $V(phen)_3^{++}$. Most salts of this cation are extremely soluble in water, but the iodide can be obtained as unstable blue-black crystals. The solutions are oxidized rapidly even in the absence of air to give the tervalent complex cation. It appears that little stabilization of the bivalent state is achieved by coördination.

Aqueous solutions of vanadium(III) salts react to give deep violet-purple colors, due to the ion $[V(OH)(phen)_2]^{++}$. This is similar to the brown iron(III) complex cation and is also presumably dimeric. The sulfate and perchlorate are sparingly soluble and stable in air, but the solutions are slowly oxidized to a tetravalent vanadium complex cation. In non-aqueous solvents or by fusion with phenanthroline, the purple crystalline $[V(phen)_2Cl_2]Cl$ can be obtained, but it is easily hydrolyzed.

From solutions of vanadyl salts the greenish-yellow $[VO(phen)_2]SO_4 \cdot 5H_2O$ and $[VO(phen)_2](ClO_4)_2 \cdot 4H_2O$ can be obtained. The structures of these salts are unknown. However, from solutions of vanadium(IV) chloride in carbon tetrachloride $V(phen)_2Cl_4$ can be isolated as a brown precipitate, which can be formulated as $[V(phen)_2Cl_2]Cl_2$.

The only other Group 5 element which coördinates is bismuth. It forms the salt $[Bi(phen)_3](ClO_4)_2$ (235), which is not necessarily 6-covalent.

F. GROUP 6 METALS

The chelation of bipyridine with chromium(II) salts was first reported by Barbieri and Tettamanzi (10), who isolated the black bromide, $Cr(bipy)_3Br_2 \cdot 6H_2O$. The dark brown solution rapidly lightens in color in the air with the formation of the Cr(III) complex, but the solid appears to be stable in dry air (8, 44). The extent of the stabilization achieved by coördination can only be speculated upon, since data as to the redox potential are unavailable, although it is believed (8) to be appreciable. However, it might be mentioned that the sparingly soluble chromium(II) salt addenda with hydrazine are also quite stable in the solid state. This can be ascribed to either their insolubility or the reducing power of the hydrazine molecule (163, 278). The magnetic moment of the bromide (3.27 B.M.) indicated $3d^24s4p^3$ bonds, and it is suggested that the strong bonds and electron pairing are due to pronounced double bonding here as with iron(II) (44). An attempted resolution through the tartrate was not successful (72), owing to rapid oxidation to the Cr(III) complex cation. If the latter were optically labile, as anticipated, then rapid electron transfer would also cause racemization of the Cr(II) compound (85).

When solutions of $[Cr(bipy)_3]Cl_2$ are treated with magnesium, reduction to the Cr(I) complex has been claimed to occur and a blue perchlorate isolated. The magnetic moment (2.1 B.M.) is slightly high for the required one unpaired electron with $3d^2 4s4p^3$ bonding. In solutions of $Cr(bipy)_3^{++}$ the following equilibrium has been proposed (135):

$$2Cr(bipy)_3^{++} \rightleftarrows Cr(bipy)_3^{+} + Cr(bipy)_3^{+++}$$

Since one might expect Cr(I) to be 4-covalent, confirmation of this work is desirable.

Hammett, Walden, and Edmonds (130) have reported the preparation of $Cr(phen)_3^{++}$ and the determination of the potential of the reaction:

$$Cr(phen)_3^{++} \rightleftarrows Cr(phen)_3^{+++} + e^-$$

However, it now seems possible that Cr(II)–phenanthroline complexes may not exist. Instead, during the course of the preparation the phenanthroline is reduced to an orange substance of unknown composition. This is the substance that is reversibly oxidized (100).

With tervalent chromium, the yellow $[Cr(bipy)_3](ClO_4)_3$ is made from the bivalent complex (10) and $[Cr(bipy)_2Cl_2]Cl$ from anhydrous chromium(III) chloride in methanol solution in the presence of a trace of zinc dust (44). The phenanthroline analog of the latter substance has been prepared by fusion of anhydrous chromium chloride and the base (236), and the tris compound $[Cr(phen)_3]$ $[Cr(SCN)_6]$ from potassium hexathiocyanatochromate(III) and the base in boiling alcoholic solution.

It has been observed that solutions of reduced molybdenum give a red color with bipyridine, but no definite compound has been isolated (169).

No definite compound results from the interaction of uranium(IV) chloride and bipyridine in alcoholic solution, but on the addition of potassium thiocyanate, a small amount of yellow $[U(bipy)_3](SCN)_6$ is precipitated. This is probably the result of oxidation (3).

G. GROUP 7 METALS

With 2,2′-bipyridine and Mn(II) salts the yellow trisbipyridine compounds $Mn(bipy)_3X_2$ result (204), but one molecule of the chelate is easily lost in aqueous solution and the diaquo salts result. Pfeiffer (235) has prepared $[Mn(phen)_4](ClO_4)_2$ and by distillation of this substance obtained the bis derivative. There is evidence, however, that trisphenanthroline complexes exist in aqueous solution (230). For reasons advanced previously, the tetrakis derivative is almost certainly not 8-covalent. The Mn(II) compounds apparently are not capable of being oxidized to the tervalent compounds, but by operating with ammonium peroxydisulfate it is possible to obtain the octahedrally coördinated

$[MnO_2(bipy)_2]S_2O_8$ (221). The magnetic moment of $[Mn(bipy)_3]Br_2$ indicates five unpaired electrons; hence electron pairing or significant double bonding does not occur (44).

With the exception of the simple salts of bipyridine with perrhenate, hexachlororhenate(IV), and tetracyanodioxorhenate(V), no rhenium derivatives of either base have been described (209).

H. GROUP 8 METALS

The elements of the iron triad, iron, ruthenium, and osmium, form complex cations of great stability in the bi- and tervalent states. The red iron(II) trischelates are so well known that they need no further comment, but the evidence for the existence of bis and mono derivatives is of special interest in order to locate the point at which the paramagnetic hydrated ferrous ion changes to the diamagnetic cation with strong covalent bonds. Spectrophotometric evidence for the existence of the ion $Fe(bipy)^{++}$ has been obtained by Krumholz (170) and Baxendale and George (19). This is in disagreement with the findings of Ferrari (113) and Gould and Vosburgh (125). Jaeger (155) has claimed to have obtained $FeSO_4 \cdot bipy$ as a crystalline solid, but when mixed with barium chloride, only the tris compound $[Fe(bipy)_3]Cl_2$ resulted. The existence of the pale yellow $Fe(phen)^{++}$ has been demonstrated in sulfuric acid solutions of the base in the presence of a large excess of ferrous salt (167). There does not appear to be any reliable evidence, however, for the existence of either $Fe(bipy)_2^{++}$ or $Fe(phen)_2^{++}$ in aqueous solution. In the orange solutions of 2-methylphenanthroline and iron(II) salts, there appears to be an equilibrium between mono-, bis-, and trischelated cations. Negligible amounts of the tris compound are present, very much of the bis compound, and a small amount of the mono compound. The lability of the system is demonstrated by the complete precipitation of the tris complex as the perchlorate (145, 147).

Recent work (12a) has shown that $[Fe(bipy)Cl_2]$, $[Fe(bipy)_2Cl_2]$, and $[Fe(phen)_2Cl_2]$ can be obtained by the same method used to prepare $[Ni(bipy)_2Cl_2]$ (234). When trisbipyridine iron(II) chloride hexahydrate is heated *in vacuo* at 100°C. loss of water and one molecule of bipyridine results, with the formation of violet $[Fe(bipy)_2Cl_2]$. This substance is paramagnetic (5.1 B.M.) and can be considered to have four unpaired electrons, the excess moment being due to Fe(III) impurity or insufficient diamagnetic correction. With small amounts of water the substance becomes red, and in alcoholic solution spectrophotometric studies show only the presence of the usual tris compound. At 150°C. the violet substance, with further loss of bipyridine, changes to the red $[Fe(bipy)Cl_2]$. Preliminary studies show that this is paramagnetic (1.8 B.M.). Whether the paramagnetism is due to impurity or the structure is a planar dimer, with metal–metal interaction, remains to be determined.

At 150°C. the trisphenanthroline compound changes to the blue paramagnetic (5.2 B.M.) $[Fe(phen)_2Cl_2]$, which does not undergo further change at 200°C. (12a). The dark red dibromo and diiodo bisphenanthroline compounds have been reported (163a) as being obtained from the tris compounds *in vacuo* at

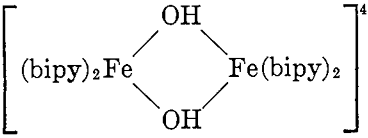
100°C. and as being slightly paramagnetic and diamagnetic, respectively. However, the tris compounds are merely dehydrated at this temperature (12a), but at 255°C. the blue dibromo bis compound, which is paramagnetic (4.9 B.M.), results. Loss of phenanthroline from the iodide does not occur even at this temperature. Though the situation is not identical, it can be reasonably inferred that the diaquo ion $[Fe(phen)_2(H_2O)_2]^{++}$ is also paramagnetic, as required by the hypothesis of orbital stabilization.

The orange-red trisbipyridine ruthenium(II) chloride was first prepared by heating a mixture of ruthenium(III) chloride with bipyridine at 250°C. Tetrapyridine is formed in the reaction (41). The trisbipyridine and trisphenanthroline complexes are more conveniently prepared by refluxing an aqueous alcoholic mixture of potassium pentachlorohydroxyruthenate(IV), the organic base, and sodium hypophosphite (71, 95). The cations $Ru(bipy)_3^{++}$ and $Ru(phen)_3^{++}$ are remarkably stable and are unattacked by boiling concentrated hydrochloric acid or caustic alkalis. The free bases can be obtained as crystalline solids and are stable, unlike $[Fe(bipy)_3](OH)_2$ (32).

The intensely dark-green $Os(bipy)_3^{++}$ is obtained by heating mixtures of potassium hexachloroösmate(IV), osmium metal, and bipyridine at 250°C. The use of ammonium hexabromoösmate(IV) obviates the necessity for the presence of free osmium (43). The dark greenish-brown $Os(phen)_3^{++}$ is best prepared from the base and ammonium bromoösmate at 200°C. in glycerol solution (84). Both of these complex cations are comparable in stability with the ruthenium analogs, and the free bases can be isolated (43, 84).

The oxidation of $Fe(bipy)_3Cl_2$ and $Fe(phen)_3Cl_2$ was first reported by Blau (32), who isolated the green chloroplatinates. The blue perchlorates are also easily isolated (44, 97). The magnetic moment of $[Fe(bipy)_3](ClO_4)_3$ (2.1–2.4 B.M.) shows that strong $3d^24s4p^3$ bonds are present (44). In the light these blue substances become red, presumably as a result of reduction, but the reaction has not been studied.

Addition of the bases to solutions of iron(III) salts does not yield the foregoing trischelated compounds (32); instead, brown binuclear salts, $[Fe(B)_2 \cdot OH]_2X_4$, result (119). All attempts to prepare the blue compounds directly have failed, and in ether or acetone solution, for example, brown water-soluble substances, $[FeCl_3 \cdot bipy]$ and $[FeCl_3 \cdot phen]$, result (253, 254). The binuclear substance, IV, has a moment of 1.4 B.M., much smaller than the theoretical value calculated for spin only and the partial neutralization of the moment has been advanced in support of the binuclear structure (119). Michaelis and Granick (199) in a reëxamination of the compound found the values of 2.1 B.M. for the almost saturated solution and 2.4 B.M. for the solid and concluded that there is no appreciable metal–metal interaction.



IV

Irving (146) has compared the structure of this substance with the diol-*N*,*N'*-diethylethylenediamine copper(II) salts and proposed that the diol-bridged structure is adopted to relieve steric strain, in this case due to the three large molecules attached to the iron(III) ion. It should be pointed out, however, that there is no significant difference in the octahedral covalent radius of iron(III) compared with iron(II) (225) to suggest that iron(III) salts should behave differently from iron(II) salts. It is known that when phenanthroline is added to very weakly acid solutions of iron(III) salts, a basic salt is precipitated (268), and further, that at the pH at which the binuclear complex is formed the iron(III) ion is already hydrolyzed, i.e., has at least one OH^- group already attached. In the same way, the very stable potassium ferricyanide cannot be made directly from iron(III) salts and potassium cyanide. The blue tris ruthenium(III) compounds also cannot be prepared directly from ruthenium(III) salts and the bases in either neutral or acid solution (90).

Oxidation of the cation $Ru(B)_3^{++}$ is easily effected anodically or with cerium(IV) in nitric acid solution, but pure crystalline salts of the blue cation $Ru(B)_3^{+++}$ have not been isolated, as they rapidly undergo reduction. Some results are available on the reaction between phenanthroline and potassium pentachloroaquoruthenate(III). In neutral or weakly acid solutions, green or brown complex cations, $[Ru(phen)_2X_2]^+$ ($X = Cl, OH$), are conveniently isolated as the perchlorates. With hydrochloric acid replacement of the hydroxyl groups occurs, and this reaction is reversed with sodium hydroxide. Oxidation with ceric nitrate leads to deep blue ruthenium(IV) compounds, and reduction to orange or brown ruthenium(II) compounds with some disproportionation to the tris complex. There is some evidence that *cis* and *trans* forms may exist, but no evidence has been obtained for diol-bridged structures as with iron(III) (90).

After oxidation with chlorine, salts of the red cation $Os(B)_3^{+++}$ are easily isolated (86). Dichloro-bisbipyridine osmium(III) chloride has been reported among the products of pyrolysis of mixtures of potassium hexachloroösmate(IV) and bipyridine (43).

The tervalent cations $M(B)_3^{+++}$ ($M = Fe, Ru, Os$) undergo a remarkable reaction when the solutions are made alkaline. Reduction occurs instantly; if acid is added at once, reoxidation can be effected. The reaction was first reported by Blau (32), who observed the odor of ozone following the addition of alkali. Hydrogen peroxide can also be detected (86). In weakly acid solutions of the iron and ruthenium compounds the reduction also occurs slowly (95, 97).

The following reaction is said to occur (283):

$$Fe(C_{12}H_8N_2)_3^{+++} + OH^- \rightarrow Fe(C_{12}H_8N_2)_3^{++} + OH$$

The ozone and hydrogen peroxide doubtless arise from reactions of the hydroxyl radical. It is noteworthy that oxidation of the bivalent complexes is not effected by ozone or dilute hydrogen peroxide at room temperature.

In the cobalt triad, compounds of cobalt(II), cobalt(III), and rhodium(III) have been described, but no iridium compounds.

Brown tris cobalt(II) salts with a wide variety of anions are readily prepared in the absence of oxygen by direct addition of three molecules of the base to the simple cobalt(II) salt. Mono and bis compounds are also known in which the metal can be either 4- or 6-covalent, with water molecules occupying some of the coördination positions (32, 44, 154, 235, 236). The moment of the perchlorate $Co(bipy)_3(ClO_4)_2$ (4.85 B.M.) indicates ionic bonds (44).

Oxidation of the cobalt(II) complexes can be effected with oxygen, hydrogen peroxide, or chlorine. The yellow tris compounds are diamagnetic like most cobalt(III) compounds (44). One molecule of the base is easily disengaged and replaced by aquo groups. Though it has been stated (236) that $Co(phen)_3Cl_3$ yields a red color with ferrous sulfate only on long heating of the solution, this is at variance with the method of preparation of *cis*-dichloro-bisphenanthroline cobalt(III) chloride by removing one molecule of the base simply by refluxing in chloroform solution. Green *trans*-dichloro-bisphenanthroline cobalt(III) chloride, though it dissolves in nitrobenzene to a green solution, yields a rose-colored solution in water because of rapid aquation. This is confirmed by the isolation of $[Co(phen)_2(H_2O)_2][Cr(NH_3)_2(SCN)_4]$ from the aqueous solution (235, 301).

Rhodium(III) salts can attach one, two, or three molecules of bipyridine, but only the brown compound $Rh(bipy)_3Cl_3$ has been obtained pure (152). The substance $[Rh(bipy)_2Cl_2]Cl$ has been isolated, and the substance $Rh(bipy)Cl_3 \cdot 4H_2O$ with varying amounts of ionizable chlorine. The lability of these substances and also of cobalt(III) complexes contrasts with those containing ethylenediamine. In many experiments a sparingly soluble pink substance, $Rh_2(bipy)_3Cl_6$, was obtained. This can be formulated in various ways in which rhodium is in both the cation and anion, such as $[Rh(bipy)_3][RhCl_6]$. Compounds containing rhodium and phenanthroline have not been described.

When mixtures of rhodium(III) chloride and bipyridine are treated in methanol solution with zinc amalgam, intensely colored violet solutions result. These rapidly change to yellow in the air and presumably contain chelated derivatives of rhodium(II) or rhodium(I) (72).

All of the metals of the nickel triad can be coördinated with either base, but nickel(II) alone attaches three molecules. The bright pink tris compounds are of the same order of stability as the iron(II) compounds, and the phenanthroline complex is the more resistant to acids. This can be heated in 10 *N* sulfuric acid for a short time without decomposition (82). Their magnetic moments, the nature of the bonds, and the failure to oxidize them to nickel(III) complexes are discussed subsequently (page 977). Salts of the cation $Ni(B)_3^{++}$ with a wide variety of anions are known (32, 202, 229, 234).

The bright green $Ni(bipy)_2Cl_2$ can be prepared by heating the tris compound *in vacuo* at 140°C. for 2 hr. (234). The substance very rapidly disproportionates when added to water, to yield the pink tris cation; but when it is added to a solution of potassium iodide, the blue $[Ni(bipy)_2(H_2O)_2]I_2$ immediately separates (12a). It is of interest to mention that when *d*-$Ni(bipy)_3Cl_2$ is subjected to pyrolysis, the optical activity is lost (13). This does not indicate, however, whether the bis compound has the *cis* or the *trans* octahedral structure.

The bisphenanthroline compounds are much more stable, though they also undergo disproportionation. When phenanthroline is added to nickel salt solutions, the formation of the bis compound is evidenced by the resulting blue color, but even when the ratio of nickel salt to base is less than 1:2, the addition of sodium perchlorate instantly precipitates a substantial portion of the metal as the pink trischelated salt. On standing for a short time, only the pale green color of the hydrated nickel ion remains (82). The blue and blue-violet $[Ni(phen)_2(H_2O)_2]Cl_2 \cdot 3H_2O$ and $[Ni(phen)_2(H_2O)_2](ClO_4)_2$ have been obtained, however, in crystalline form (229, 234).

Jaeger and van Dijk (151a) claim to have obtained the mono derivative $[Ni(bipy)(H_2O)_2]SO_4$ in two crystalline forms, blue and also indigo needles, by the reaction between the tris compound and excess nickel sulfate solution. The same substance could be obtained by direct synthesis in alcoholic solution. The substance $[Ni(phen)(H_2O)_4](ClO_4)_2$ has been described as being formed when nickel perchlorate and phenanthroline in the ratio of 5:1 are heated in 30 per cent methanol (229). The bis- and monochelated compounds in the resulting mixture were then separated by crystallization. The mono compound gave dark blue solutions in methanol. The evidence for the isolation of these mono complexes does not appear entirely satisfactory. The stabilities favor the trischelates so strongly, and the rates of dissociation are so high (13) for the monochelates, that in a solution where equilibrium is rapidly attained, they must be present in very low concentration. Spectrophotometric evidence, however, does suggest that the nickel ion can form mono complexes (284) in aqueous solution.

Bivalent palladium is almost invariably 4-covalent and attaches usually one molecule of either base to form the sparingly soluble $[Pd(B) \cdot X_2]$ ($X = Cl, Br, I, SCN, NO_2$). These substances are more soluble in the presence of excess of the base, and the existence of the ions $Pd(B)_2^{++}$ in such solutions is evidenced by the isolation of the perchlorate, $[Pd(phen)_2](ClO_4)_2$, and the 2-naphthol-6-sulfonate. Mixed tetramines containing ethylenediamine and pyridine can be isolated and dichloro-phenanthroline palladium(II) can be oxidized to the easily reducible tetrachloro-phenanthroline palladium(IV) (181, 182, 247).

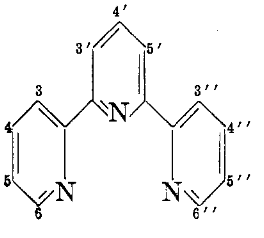
Platinum(II) behaves in a similar manner to palladium, one molecule of bipyridine coördinating firmly and the second weakly. The substance $[Pt(bipy)Cl_2]$ exists in yellow and red dimorphous forms. The bis chloride cannot be isolated, but $[Pt(bipy)_2][PtCl_4]$ and $[Pt(bipy)_2]I_2 \cdot 2H_2O$ exist. The latter has red and black forms in the solid state. Mixed tetramines containing ammonia, pyridine, and ethylenediamine can be prepared and also triamines, $[Pt(bipy)(NH_3)X]X$. Treatment of the tetramines and also the triamines with acids causes loss of the ammonia, ethylenediamine, etc. and leaves the monobipyridine compound.

Oxidation to platinum(IV) complexes can be effected with chlorine. The substances $[Pt(bipy)_2Cl_2][PtCl_6]$, $[Pt(bipy)Cl_4]$, and $[Pt(bipy)(Py)Cl_3]Cl$ result (205).

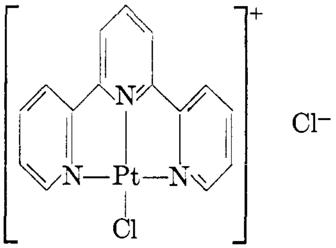
III. THE POLYPYRIDINES AND THEIR METAL COMPLEXES

A. 2,2′,2″-TERPYRIDINE [2,6-DI(2-PYRIDYL)PYRIDINE]

This substance (V) was isolated (203) among the products of the dehydrogenation of pyridine with anhydrous ferric chloride in an autoclave at 500°C. A substance described originally as 2,2′,X″-terpyridine, which also gave an intense color with iron(II) salt solutions, was subsequently shown to be a dimorphous form of 2,2′,2″-terpyridine (207). Terpyridine (V) acts as a tridentate planar chelate molecule, and the formation of the platinum derivative [Pt(trpy)Cl]Cl (VI) has been advanced as evidence for the planar distribution of the bonds about bivalent platinum (206).



V



VI

Vapor-phase bromination gives a mixture of the 6-bromo and 6,6″-dibromo derivatives (42), the former of which produces a weak magenta color with iron(II) salts, while the latter is insoluble in acids and no color reaction occurs.

The chelate complexes derived from Cu(II), Ag(I), Ag(II), Zn(II), Cd(II), Hg(II), Pd(II), Pt(II), and Ir(III) contain one molecule of the base, while those from Fe(II), Co(II), Co(III), Ni(II), Ru(II), Os(II), Cr(III), and In(III) contain two. Since the bonds from the nitrogen atoms to the metal must lie in the plane of the pyridine ring and resonance requires coplanarity of the three rings, it follows that all the bonds from the chelate must be planar. Though the molecule can encompass three positions in a plane in the planar or octahedral coördinations, it is apparent that there is some strain involved, the bonds from the nitrogen atoms being at a little less than 90°. This would suggest, as actually is the case, that the metal complexes would be somewhat less stable than would be anticipated for a tridentate chelate molecule. From models it can also be seen that even if the stabilizing resonance in the system is sacrificed and the pyridine rings are moved out of coplanarity, it is not possible for the molecule to span three positions in tetrahedral coördination. It has been suggested, therefore, that the zinc, cadmium, and mercury complexes have the planar configuration (207). If this is so, these complex compounds are further examples of forced bond deformation analogous to some metal derivatives of phthalocyanine (180). The steric conditions and the bond strengths do not seem, however, to be so favorable here. The zinc and cadmium complexes formulated as [M(trpy)Cl]Cl could well be of the form $[M(trpy)Cl_2]$, with one of the donor nitrogens remaining unattached. The formulation of the mercury derivative $Hg(trpy)(NO_3)_2$ is difficult in the solid state, though in solution the complex ion could be $[Hg(trpy)(H_2O)_2]^{++}$. Difficulties also arise in the formulation of the colorless silver(I) compounds $Ag(trpy)NO_3$ and $Ag(trpy)ClO_4$. It is possible that the silver could be linear 2-covalent when either the center nitrogen atom is not attached or is attached by a weak bond, or the substance is polymeric, utilizing single nitrogen–metal bonds.

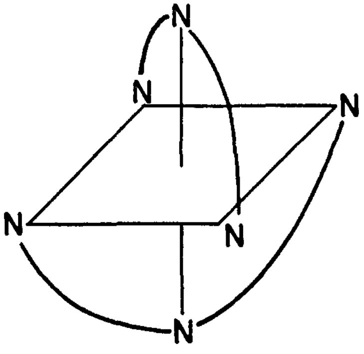
If the metal is tetrahedral 4-covalent, like monovalent copper, the same difficulties arise as with zinc and cadmium.

The silver(I) compound can be oxidized anodically to the brown terpyridine silver(II) nitrate, formulated as $[Ag(trpy)NO_3]NO_3$, and a chlorate and perchlorate of the same type have been isolated. It is noteworthy that a second molecule of the chelate could not be attached. According to the results of Cox, Webster, and Wardlaw (62), bispicolinic acid silver(II) is planar.

With copper(II) chloride, the green substance $[Cu(trpy)Cl]Cl \cdot 2H_2O$ is formed, and from the increase in solubility in the presence of excess base, there is some evidence for the existence of the octahedral ion, $Cu(trpy)_2^{++}$, in solution. The pale yellow palladium compound $[Pd(trpy)Cl]Cl$ is obviously similar to the red platinum(II) compound (VI).

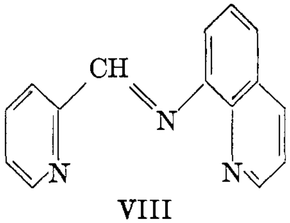
The stable bivalent platinum compounds $[Pt(trpy)X]X$ ($X = Cl, Br, OH$) can be oxidized with chlorine to trichloro-terpyridine platinum(IV) chloride, analogous to the iridium compound $[Ir(trpy)Cl_3]Cl$.

With octahedral coördination, Morgan and Burstall considered three arrangements of the two chelate molecules. Only one of these possible arrangements satisfies the condition of coplanarity of the pyridine rings, that in which the molecules of the base are arranged in two equatorial planes at right angles (VII).



VII

This has a plane of symmetry, and attempts to resolve the stable ruthenium(II) and nickel compounds, $[M(trpy)_2]^{++}$, were not successful. It might be mentioned that a substituent in one of the outside pyridine rings can confer asymmetry. A substance of such a type is the planar tridentate molecule 8-(2-pyridylmethyleneamino)quinoline(VIII), the iron(II) compound of which has been obtained in enantiomeric forms (77).



VIII

Bisterpyridine iron(II) salts are characterized by an intense purple color, so intense that a definite color reaction for iron(II) is observed at concentrations of one part in two million. As an analytical reagent, it has been used for the determination of iron in sea water and in marine plankton (61). Oxidizing agents, such as chlorine and cerium(IV) salts, change the color to green (or sometimes yellow), but though the ion $Fe(trpy)_2^{+++}$ undoubtedly exists in these oxidized solutions, attempts to isolate crystalline salts have failed. This appears to be due not only to its tendency to undergo reduction to the iron(II) compound, but also to loss of one of the tridentate ligands (89).

The red ruthenium(II) and dark brown osmium(II) complex compounds have been prepared (207) by pyrolysis of mixtures of the base with ruthenium(III) chloride and ruthenium metal, and with potassium hexachloroösmate(IV) and osmium, respectively. These substances show a stability towards acids comparable to that of the analogous bipyridine and phenanthroline derivatives. Oxidizing agents convert them to the green tervalent derivatives. Bisterpyridine ruthenium(III) salts have been obtained only in solution, but bisterpyridine osmium(III) perchlorate can be isolated as a crystalline solid (207). The redox potentials of the complexes of the iron triad are discussed subsequently.

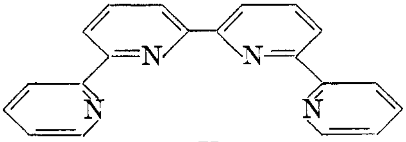
Cobalt(II) salts react with the organic base in aqueous solution with the formation of the deep brown ion $[Co(trpy)_2]^{++}$, which can be isolated as the almost black bromide $[Co(trpy)_2]Br_2 \cdot 3.5H_2O$. The formation of this ion has been used as a colorimetric method for the estimation of cobalt (213).

Oxidation of a mixture of cobalt(II) chloride and terpyridine with chlorine yields the yellow substance $[Co(trpy)_2]Cl_3 \cdot 7H_2O$, analogous to the chromium (III) complex $[Cr(trpy)_2]Cl_3 \cdot 2H_2O$. The latter is obtained from anhydrous chromium(III) chloride and the base in alcoholic solution in the presence of a trace of zinc dust. The bischelate nickel compounds are light brown and are stated to be comparable in stability to the trisbipyridine compounds (207).

The indium complex salts separate as precipitates on mixing an alcoholic solution of the base with the halides in aqueous solution. They can be crystallized from acetone, but are decomposed by dilute acid or alkali (273).

B. 2,2′,2″,2‴-TETRAPYRIDINE [6,6′-DI(2-PYRIDYL)-2,2′-BIPYRIDINE]

2,2′,2″,2‴-Tetrapyridine (IX) has been obtained by heating bipyridine with either ferric chloride or ruthenium(III) chloride, or by the Ullmann synthesis from 2-bromopyridine and 6,6′-dibromo-2,2′-bipyridine (42).



IX

The coördination compounds have been described by Morgan and Burstall (208), who consider that the molecule acts as a planar quadridentate base. From a model, however, this does not appear at all likely, since the fourth nitrogen atom is quite far from the required position for square coördination. At best it could only function as a tridentate molecule, and even here steric difficulties may arise from the fourth pyridine ring. From superficial inspection this molecule might be considered analogous to the porphyrin or phthalocyanine molecules, but the latter form a closed system with pyrrole rings which form six-membered chelate rings, whereas with tetrapyridine they would all be five-membered.

All of the metal chelates contain one molecule of the substance and do not appear to be notably stable. The silver(I) compound, Ag(tetrpy)NO_3, obtained as yellow needles, significantly is not oxidized by peroxydisulfate ion to the Ag(II) complex. The latter is usually 4-covalent and probably planar, and this suggests strongly that the base is not functioning as a quadridentate. Similar difficulties of formulation of the Ag(I) complex arise as with Ag(trpy)NO_3.

With iron(II) salts, a greenish-yellow color reaction of relatively low intensity occurs. The sparingly soluble reddish-brown Fe(tetrpy)$SO_4 \cdot 4H_2O$ and the greenish-brown bromide and iodide have been isolated. Examination of the published properties of these substances suggests that they have not the robustness of the bipyridine complexes

Hydrated salts [M(tetrpy)]X_2 (M = Co (pink), Ni and Cu (green), Zn and Cd (pale yellow)) also have been prepared. It has been suggested that in all of these substances the complex cation is planar, but it seems more probable that in all of them molecules of water are included in the coördination sphere of the metal and the usual stereochemistry applies. The formulation of the cobalt(III) compound as [Co(tetrpy)Cl_2]Cl·$3H_2O$ implies quadridentate chelate function, but there is not good evidence that the third chlorine is ionized or, alternatively, that some of the water molecules are not really coōrdinated aquo groups.

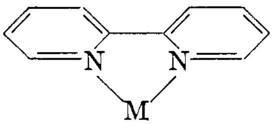
C. HIGHER POLYPYRIDINES: 2,2′,2″,2‴,2⁗-PENTAPYRIDINE [2,6-BIS(2,2′-BIPYRIDYL-6-YL)PYRIDINE] AND 2,2′,2″,2‴,2⁗,2′⁗-HEXAPYRIDINE [6,6′-BIS(2,2′-BIPYRIDYL-6-YL)-2,2′-BIPYRIDINE]

These compounds have also been prepared (42) by the Ullmann reaction. No metal chelates from the pentapyridine have been reported. Hexapyridine has been stated (42) to form a tetrachloride and to yield a series of complex cations with the transition metals in which one mole of the base is united with one atomic proportion of the metal ion. From the stereochemistry of the substance it does not seem possible that it could act as a sexadentate molecule even if the coördination of the metal atom involved a group of planar hexagonal orbitals.

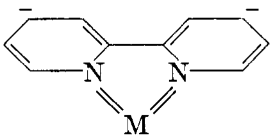
IV. THE NATURE OF THE BONDS

Bipyridine and phenanthroline are both relatively weak bases, yet they chelate with such a wide variety of metal ions and the resulting complexes are generally of such a high order of stability that it is evident that much more is involved than the simple functional grouping —C=N—C—C—N=C—. A comparison with ethylenediamine, a much stronger base with the same atomic grouping, is instructive. Trisethylenediamine ferrous chloride, like the hexammine, is a weakly colored substance, easily hydrolyzed in water. It is paramagnetic, with ionic or $4d^2 4s 4p^3$ bonds (134, 159). The deeply colored bipyridine and phenanthroline compounds, on the other hand, are decomposed slowly by acids, and their diamagnetism (44, 49, 50) indicates strong covalent $3d^2 4s 4p^3$ bonds. The trisethylenediamine ruthenium(II) and osmium(II) salts have not yet been prepared; it can be inferred that they will be very easily oxidized in the air, but will probably be more stable than $Fe(en)_3Cl_2$. The diamagnetic (116) ruthenium(II) and osmium(II) compounds with bipyridine and phenanthroline resist boiling concentrated acids and alkalis and like the iron(II) compounds are easily obtained in the enantiomeric forms. In the same way the stability and the existence of optical forms of the nickel compounds contrast sharply with the trisethylenediamine nickel salts.

As far as the iron triad of Group 8 is concerned, there is also the remarkable stabilization of the bivalent state evidenced by the redox potentials. In the bivalent iron, ruthenium, and osmium compounds, all of the available *d*, *s*, and *p* orbitals are filled and this in itself favors strongly the bivalent state because oxidation would involve the removal of one electron. Nyholm (44, 219), following the original suggestion of Pauling (161, 225), has proposed that the major factor responsible for electron pairing and strong covalent binding in many of these compounds is the formation of double bonds, and suggested that structures X and XI contribute to the resonance hydrid.

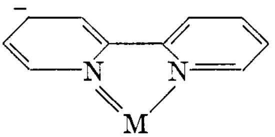


X

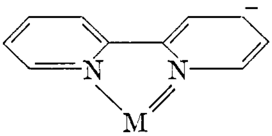


XI

Similar structures can be written for the phenanthroline compounds. Since for octahedral coördination a maximum of only three double bonds is permissible, structures such as XII and XIII would be preferable.



XII



XIII

Similar structures have been proposed for copper phthalocyanine in order to account for the extraordinarily high stability considered in relation to the low proton affinity of the parent quadridentate molecule (192).

All of these double-bond structures involve the placing of a negative charge on the para carbon atom of the pyridine ring, and it has been suggested (219) that electron-attracting substituents in this position should permit further charge delocalization from the nitrogen atom and enhance the amount of double bonding. It should be remembered that such substituents lower the base strength and hence for this reason tend to lower the stability of the metal complex.

No quantitative data are available on substituted bipyridines of this kind, but the stabilities of the iron compounds with 5-nitro- and 5-chlorophenanthrolines do not show any departure from the usual relationship between strength of the base and stability of the metal complex (34).

The values of the force constants of the carbon–oxygen bonds in tetracarbonyl nickel, bipyridinedicarbonyl nickel, and *o*-phenylenebis(dimethylarsine)dicarbonyl nickel have been compared; the weakening of the carbon–oxygen bond has been ascribed to double bonding by the chelate molecule (222). It is inferred that the nickel–bipyridine bond has some double-bond character. Evidence of this kind is not entirely conclusive. If one compares the infrared spectra of $Ni(CO)_4$ with that of $Fe(CO)_5$ and $Cr(CO)_6$, it is readily apparent that the metal–carbon stretching frequency increases in the order nickel, iron, chromium, and that the carbon–oxygen frequency decreases in the order nickel, iron, chromium (38, 63, 255). If one assumes that the available *d* electrons are used in double-bond formation, it would be expected that the double bondedness should decrease in the order nickel, iron, chromium. This is inconsistent with the observed trends of stretching frequencies for metal–carbon and carbon–oxygen.

Though some double-bond character might be expected to be present in the pyridine–metal link, the experimental evidence is unfavorable. The placing of electron-attracting substituents in the appropriate positions in pyridine and the comparing of the first dissociation constants of the silver ion adducts with $Ag(py)_2^+$ suggests no double bonding (215). Similarly, comparison of the dissociation constants of bispyridine silver ion and of bispiperidine silver ion leads to the same conclusion (27).

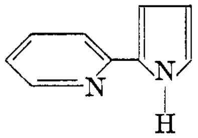
It thus appears that though double bonding is indicated to account for the stabilities of some phenanthroline and bipyridine metal complexes, there is as yet no reliable evidence to suggest that it does occur.

Some interest has been shown in the fact that the trischelate nickel salts cannot be oxidized to the tervalent or quadrivalent states. Though this has been discussed in a recent review (220), some of the implications are worth clarifying. The nickel compounds are paramagnetic, with "ionic" or upper-orbital binding, and the unpaired electrons are thus considered to be in the lower 3*d* orbital. It is proposed that the extent of the double bonding is insufficient for strong covalent (lower-orbital) binding and hence that the electron promotion favorable for oxidation has not occurred. This is consistent with the magnetic data on the assumption that the promoted electrons would be paired in the 5*s* orbital. Oxidation, however, would form a complex cation carrying three or four positive charges. The situation with dichloro-bis-*o*-phenylene(bisdimethylarsine) nickel(III) chloride and dichloro-bis-*o*-phenylene(bisdimethylarsine) nickel(IV) perchlorate (220) is much more favorable, involving complex cations with one and two positive charges.

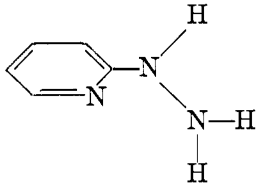
One can agree with the view (44) that in metal complex compounds where electron promotion could conceivably occur, it is far less common than generally supposed, and add that far too little attention seems to be paid to the large energy requirement for promotion. It cannot be accepted as a corollary that where promotion has not occurred, the lower valence states should be preferred, and hence ignore the more favorable orbital hybridization that could well exist in an oxidized state. A few examples which also illustrate the effect of the ligand and of the ionic charge of the complex are pertinent. Trisethylenediamine cobalt(II) chloride is paramagnetic (197) with ionic or $4d^24s4p^3$ bonds having the unpaired electrons presumably in the $3d$ orbital. Promotion of an electron, as may occur in the hexacyanocobaltate(II) or the hexanitrocobaltate(II) ions (225), has not occurred, yet the substance is oxidized very rapidly in the air. The cobalt(II) and nickel(II) compounds of the sexadentate molecule 1,8-bis-(salicylideneamino)-3,6-dithiaoctane are both paramagnetic with ionic bonds (96). The cobalt compound is oxidized spontaneously even in the solid state to the diamagnetic Co(III) compound, but the nickel compound cannot be oxidized. On the other hand, if pyridine-2-aldehyde is substituted for salicylaldehyde in the above sexadentate, the resulting cobalt(II) bivalent cation is not oxidized by dilute hydrogen peroxide in boiling solution (78). It is evident that, in general, valence stabilization by coördination involves a great many factors, and as yet much of our knowledge is incomplete and empirical.

V. Chelate Molecules Similar to Bipyridine

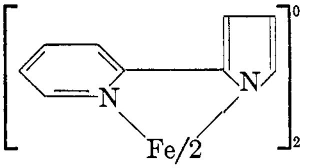
A number of chelate molecules which contain the functional grouping —C=N—C—C—N=C— have been tested for the iron(II) color reaction. As criteria of similarity, we shall consider the intensity of color, the stability towards acids, and the preferred stabilization of the bivalent state. It will be apparent from the subsequent discussion that other chelates which can be included in the bipyridine category also permit the writing of double-bonded formulas. Emmert (103, 104, 105) showed that 2-(2-pyridyl)pyrrole (XIV) and 2-pyridylhydrazine (XV) formed the red iron(II) compounds, XVI and XVII.



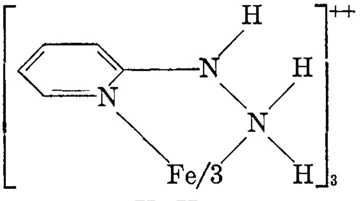
XIV



XV



XVI

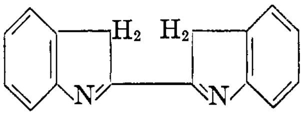


XVII

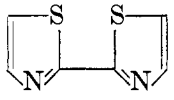
Although the pyridine nitrogens in XIV and XV permit double-bonded formulas, as with bipyridine, the iron compounds were quite unstable and in air were rapidly oxidized to the iron(III) compounds.

2,2′-Dipiperidyl was prepared by Blau (31) and the purity of the substance has been confirmed by Smith (257). It gave a violet color with iron(II) salts, and though no information is available on the composition of the iron compound, it is presumably a trischelate derivative. This compound is of particular interest because double-bond structures are not possible; hence stability and magnetic data would be of great value.

2,2′-Diindoyl (XVIII) has been reported to give a red color reaction with iron(II) (268). One would, however, expect this substance to behave like the sterically hindered 2,2′-biquinoyl (see Section VII).



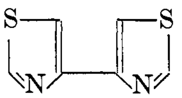
XVIII



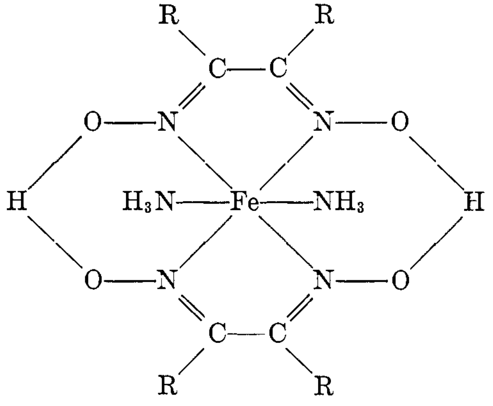
XIX

2,2′-Dithiazole (XIX) was found to yield a red solution with iron(II) salts on heating, and a coral-red bis-2,2′-dithiazole ferrous bromide dihydrate could be isolated. The corresponding substance from 4,4′-dithiazole (XX) was colorless. Erlenmeyer and Ueberwasser (106) concluded that these substances were not analogous to bipyridine and ascribed the difference to the bond angles in the =N—C—C—N= systems. These bond angles are all 120° for bipyridine, but are 110°, 125°, 125°, and 110° in XIX and 125°, 110°, 110° and 125° in XX.

There is some similarity between the dioximes and bipyridine, and double-bond structures can also be written for these metal complexes. The intense purplish-red iron(II) compound with dimethylglyoxime is easily prepared in the presence of bases (ammonia or pyridine), but only two molecules of the oxime are coördinated. The remaining positions are filled by molecules of the added base. The complex compound formed (XXI) is easily decomposed by acids, and ferric hydroxide separates from the solutions on standing (279, 280).



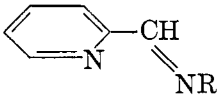
XX



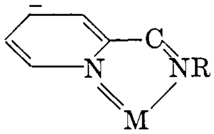
XXI

A number of substances, such as 2-(2-pyridine)quinoline, which do not give iron(II) color reactions are discussed in Section VII.

Recently (77, 78) the Schiff bases (XXII) from pyridine-2-aldehyde and primary aliphatic and aromatic amines have been found to form very intensely colored iron(II) complex salts very similar to those formed with bipyridine.



XXII

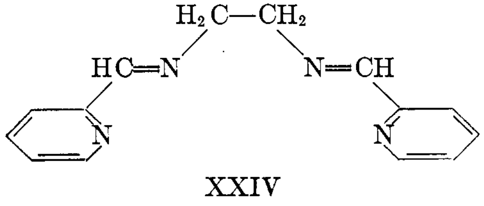


XXIII

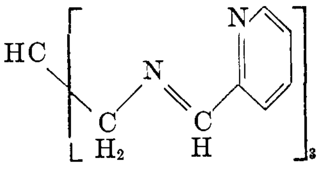
Considerable resonance is possible in these chelate molecules and a double-bonded structure (XXIII) can be written. 2-Pyridylmethyleneaminomethane (XXII: R = CH_3) yields a tris iron(II) compound which is much more intensely colored and qualitatively is more stable than the trisbipyridine compound. Reversible oxidation to the blue Fe(III) compound is possible. Substitution of the more weakly basic aromatic amines, as can be anticipated, lowered the stability of the Fe(II) compound. 2-Pyridylmethyleneaminobenzene (XXII: R = C_6H_5), for instance, gave an iron(II) compound which was sensitive to acids, and which was decolorized on boiling in dilute aqueous solution. The color returned on cooling.

Reference has been made already to 8-(α-pyridylmethyleneamino)quinoline, which is analogous to terpyridine. The Schiff bases from ethylenediamine (XXIV) and trimethylenediamine behave as typical quadridentates toward palladium(II), nickel(II), and copper(II). Unlike 2,2′,2″,2‴-tetrapyridine, these form such intensely permanganate-violet iron(II) derivatives that less than one part of iron in five million parts of water can be detected by the color reactions. The iron compounds can be reversibly oxidized, but are sensitive to acids and have not been obtained analytically pure. The two vacant coördination positions appear to be associated with the relatively low stability.

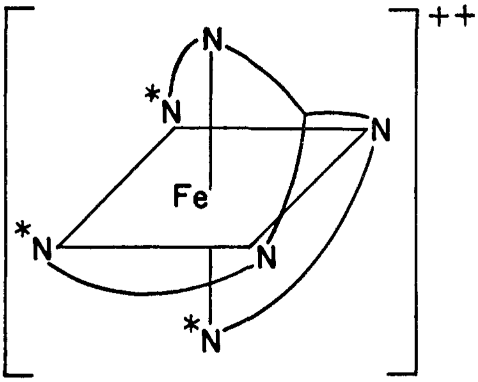
Especially noteworthy is the tris Schiff base (XXV) from pyridine-2-aldehyde and 2-aminomethyl-1,3-diaminopropane. This acts as a sexadentate molecule and can be considered as three linked-molecules of bipyridine. The permanganate-colored iron(II) compound is stable to acid and is not oxidized by cerium(IV) ion in nitric acid solution. A structure (XXVI) involving three double bonds at right angles (nitrogen atoms with asterisk in XXVI) can be written; furthermore, very considerable resonance stabilization is probable.



XXIV



XXV



XXVI

VI. Stability of Metal Chelate Complexes

The past few years have witnessed an increasing interest in the stability of metal chelate complexes. As an important property of such compounds, it has been hoped that this type of data will lead to an increased understanding of their formation and behavior. The stabilities of the metal complexes of a particular reagent are also important to the analytical chemist, as they affect the application of organic reagents to a multitude of problems in separation and measurement.

The determination of the stabilities of the phenanthroline complexes of metal ions has been part of the overall program. The experimental approaches employed have varied considerably. The familiar technique developed by Bjerrum (26), which has provided the bulk of this type of information in other complex systems (192), has been little used. Instead, the more standard approaches of equilibrium and kinetic measurements have been the main methods of attack. These techniques undoubtedly have been made applicable by the intense color of the ferrous complexes. This has provided a convenient method for the determination of small concentrations. The polarographic method for the study of complex stability has been used, but not extensively. The polarographic behavior of the organic molecules concerned is very complex and has not yet been clarified. Potentiometric measurements have been used with some success also. The basicity of the organic molecules has generally been determined by the usual pH or conductometric titration or some modification thereof.

A. THE IRON–PHENANTHROLINE SYSTEM

In order to provide a means of calculating the ferrous-ion concentration in biological fluids containing phenanthroline, Dwyer and Nyholm first determined an instability constant for the system in 1946 (99). Earlier work had established the existence of the trisphenanthroline ferrous ion as the intense red species which had been used analytically. No evidence had been reported for other species involving ferrous iron and phenanthroline. Assuming no interaction between ferric ion and phenanthroline they attributed the change in potential, caused by the addition of phenanthroline to a ferric–ferrous system, to the formation of the trisphenanthroline ferrous ion. The assumption appeared reasonable in the light of the well-known fact that the blue trisphenanthroline ferric ion could not be formed by direct mixing, but had to be prepared by oxidation of the corresponding ferrous complex. Assuming constant ferric-ion concentration, the Nernst expressions for the system prior to and following the addition of phenanthroline were combined. In the resulting equation the instability constant (K_I) for the reaction

$$[\mathrm{Fe(phen)_3}]^{++} \rightleftarrows \mathrm{Fe}^{++} + 3\ \mathrm{phen} \tag{1}$$

is given by

$$K_I = 10^{-\Delta E/0.059} \cdot C_B^3 \tag{2}$$

where ΔE is the change in potential of the system due to the reduction of the ferrous-ion concentration resulting from the addition of the phenanthroline, and C_B is the concentration of the free phenanthroline base. The experiments were carried out around pH 2, necessitating the determination of the acid dissociation constant, K_a, for the reaction

$$\mathrm{phenH}^+ \rightleftarrows \mathrm{phen} + \mathrm{H}^+ \tag{3}$$

as given by

$$K_a = \frac{a_{\mathrm{phen}} \cdot a_{\mathrm{H}^+}}{a_{\mathrm{phenH}^+}} \tag{4}$$

Potentiometric titration established the fact that the phenanthroline molecule reacts with only one hydrogen ion. Measurement of the pH of mixtures of phenanthroline and hydrochloric acid gave a value for pK_a of 5.2 at 25°C. Concentrations were substituted for activities. This value is comparable to a value of 4.8 previously obtained by Albert and Goldacre (1). Neglecting activities in the calculation of the instability constant an average value of pK_I = 17.1 ± 0.8 was obtained.

Lee, Kolthoff, and Leussing later conducted a thorough investigation of the iron–phenanthroline system (166, 178, 179). They used both the equilibrium and the kinetic approaches to the problem. Potentiometric titration confirmed the 1:1 ratio of phenanthroline to hydrogen ion. The two nitrogen atoms are apparently too close together (approximately 2.5 Å.) to permit the presence of two hydrogen ions in solutions of moderate acidity. The decomposition pressures of phenanthroline hydrate give a ΔH for each hydrogen bond to a nitrogen of 7.15 kcal. (118). No evidence has been presented concerning the possibility of another proton being added in strongly acidic solution. The extrapolation to infinite dilution of a plot of pa_{H^+} (in a 1:1 mixture of phenanthroline and phenanthrolium ion) *versus* the square root of ionic strength gave a value of 4.77 for pK_a at 25°C. From this value the activity coefficients of the phenanthrolium ion were obtained at various ionic strengths. The calculation of the degree of hydrolysis of the phenanthrolium ion by conductometric titration with hydrochloric acid gave an independent check of pK_a = 4.96. This value was used in subsequent calculations.

In solutions more acidic than pH 3, the phenanthroline is essentially present as phenanthrolium ion, and the equilibrium

$$[\mathrm{Fe(phen)_3}]^{++} + 3\mathrm{H}^+ \rightleftarrows \mathrm{Fe}^{++} + 3\mathrm{phenH}^+ \tag{5}$$

can be followed by using known amounts of iron, acid, and phenanthroline and measuring the color of the $[\mathrm{Fe(phen)_3}]^{++}$. The activity constant

$$K^1 = \frac{a_{\mathrm{Fe}^{++}} \cdot a^3_{\mathrm{phenH}^+}}{a_{\mathrm{Fe(phen)_3}^{++}} \cdot a^3_{\mathrm{H}^+}} \tag{6}$$

may then be evaluated, using known and estimated activity coefficients and the assumption that $a_{\mathrm{Fe}^{++}} = a_{\mathrm{Fe(phen)_3}^{++}}$. Wide variations of the concentrations of the three starting materials gave a series of constants averaging 4×10^{-7} at 25°C. Calculation of K_I for reaction 1 is given by

$$K_I = \frac{a_{\mathrm{Fe}^{++}} \cdot a^3_{\mathrm{phen}}}{a_{\mathrm{Fe(phen)_3}^{++}}} = K^1(K_a)^3 \tag{7}$$

Using the average value of K^1, a value of $\mathrm{p}K_I = 21.3$ at 25°C. was obtained (178).

This constant was confirmed by an entirely independent method involving the determination of rate constants for the formation and dissociation of ferroin (179). The addition of ferroin to acid solutions 0.01 N and stronger results in dissociation of the complex. The rate of dissociation can be followed by the decrease in color intensity, and a plot made of log c_0/c *versus* t, where c_0 is the initial concentration and c is the concentration at a given time, t. The results from 0.05 and 0.5 M sulfuric acid solutions give the same straight line, demonstrating a first-order reaction independent of hydrogen-ion concentration. The use of 0.005 M sulfuric acid gives the same straight line during the first portion of the decomposition. However, the appreciable formation of ferroin at this acidity causes the plot to deviate markedly as equilibrium is approached. The acid-independent rate constant of dissociation is 0.0045 $\mathrm{min.}^{-1}$, which agrees with the value calculated from the published exchange data (246).

The formation of ferroin is quite slow in solutions more acidic than pH 3. By proper choice of conditions its formation is readily followed by measurement of the ferroin color. By utilizing concentrations of iron, phenanthroline, and hydrogen ion which are large relative to the amount of ferroin formed, it is possible to obtain a forced zero-order reaction. The kinetics may then be treated as a zero-order formation followed by a first-order dissociation. The integrated rate equation for this type of situation is

$$c = A\,\frac{(1 - e^{-k_{\mathrm{diss.}}t})}{k_{\mathrm{diss.}}} \tag{8}$$

where A is a constant, c is the concentration of ferroin, and t is the time. The data obtained by following the formation spectrophotometrically gave a series of straight lines when c was plotted *versus* $(1 - e^{-k_{\mathrm{diss.}}t})/k_{\mathrm{diss.}}$. The slope, A, of the lines was found to be proportional to $[\mathrm{Fe}^{++}]$ and $[\mathrm{phen}]^3$. This relationship is most readily interpretable on the basis of the assumption of three equations,

$$\mathrm{Fe^{++} + phen \rightleftarrows Fe(phen)^{++}} \quad (9)$$

$$\mathrm{Fe(phen)^{++} + phen \rightleftarrows Fe(phen)_2^{++}} \quad (10)$$

$$\mathrm{Fe(phen)_2^{++} + phen \rightarrow Fe(phen)_3^{++}} \quad (11)$$

in which equations 9 and 10 represent rapidly established equilibria, and equation 11 is the rate-determining step. The equation representing the rate of formation then becomes

$$A = k'[\mathrm{Fe(phen)_2^{++}}][\mathrm{phen}] \quad (12)$$

Having assumed that equations 9 and 10 reach equilibrium rapidly, the equilibrium constant for the formation of $\mathrm{Fe(phen)_2^{++}}$ from $\mathrm{Fe^{++}}$ and phen can be expressed by

$$\mathrm{Fe(phen)_2^{++}} = K_{\mathrm{eq.}}[\mathrm{Fe^{++}}][\mathrm{phen}]^2 \quad (13)$$

Combining equations 12 and 13 yields

$$A = k_{\mathrm{form.}}[\mathrm{Fe}][\mathrm{phen}]^3 \quad (14)$$

from which $k_{\mathrm{form.}} = 1.3 \times 10^{19}$ min.$^{-1}$ at 25°C. Activity coefficients were used only in the calculation of the concentration of free phenanthroline from the acid dissociation constant. Calculation of pK_I from the mass action law

$$K_I = \frac{k_{\mathrm{diss.}}}{k_{\mathrm{form.}}} \quad (15)$$

where $k_{\mathrm{diss.}}$ and $k_{\mathrm{form.}}$ are the rate constants of dissociation and formation, gave a value of 21.5 (179), which compares very favorably with the value of 21.3 calculated from equilibrium data (178). Both values contain a factor of K_a^3. These results differ considerably from previous work (298), but the data have been confirmed (34).

The stepwise equations (9, 10, 11) for the formation of ferroin indicate two additional iron–phenanthroline species: namely, $\mathrm{Fe(phen)^{++}}$ and $\mathrm{Fe(phen)_2^{++}}$. The existence of such intermediate complexes would certainly be expected in the light of the work of Bjerrum on stepwise formation of ammine complexes. Early colorimetric investigation of the ferrous–phenanthroline reaction had indicated only $\mathrm{Fe(phen)_3^{++}}$ in solution under the usual analytical conditions. This is essentially true; however, the existence of $\mathrm{Fe(phen)^{++}}$ under special conditions was observed (178, 179) and its characteristics carefully evaluated (167). The ion $\mathrm{Fe(phen)_2^{++}}$ apparently does not exist in appreciable concentration in solution.

In the study of the pseudo zero-order formation of ferroin (179), the straight-line plots of c *versus* $(1 - e^{-k_{\mathrm{diss.}}t})/k_{\mathrm{diss.}}$ did not pass through the origin, indicating the existence of some colored species formed immediately upon mixing the reactants. The color is yellow upon observation. By working in solutions in which the acidity and the ferrous-ion concentration are high relative to phenanthroline, the 1:1 complex can be prepared and is stable for several hours. The absorption spectrum has a broad maximum between 400 and 450 mμ, with a possible peak at 440 mμ (167, 179). The molar absorbance index is approximately 370 (167). Variations of absorbance with changing concentration of the reactants confirmed the existence of the mono complex.

In solutions of pH 4.5–5.5 it can be demonstrated that if excess ferrous ion is present, the theoretical amount of ferroin for the amount of phenanthroline present is not completely formed. Assuming that the incomplete ferroin formation is due to the presence of $[\mathrm{Fe(phen)}]^{++}$, the instability constant of the latter, K_{I_1}, of reaction 9

$$K_{I_1} = \frac{(\mathrm{Fe}^{++})(\mathrm{phen})}{[\mathrm{Fe(phen)}^{++}]} \tag{16}$$

can be determined using the known instability constant K_I for the tris complex. The combination of equations 7 and 16 gives

$$\frac{\mathrm{Fe(phen)}^{++}}{\mathrm{Fe(phen)_3}^{++}} = \frac{K_I^{1/3}}{K_{I_1}}\left[\frac{(\mathrm{Fe}^{++})}{[\mathrm{Fe(phen)_3}^{++}]}\right]^{2/3} \tag{17}$$

Substitution of experimental values in equation 17 gave $\mathrm{p}K_{I_1} = 5.9$ (167). Utilization of the instability constants for the mono- and trischelates permits a calculation of the relative amounts of the different species involved in the ferrous–phenanthroline system (167). The graphical data indicate the absence of any appreciable quantities of $[\mathrm{Fe(phen)_2}]^{++}$. This makes the ferrous–phenanthroline system quite different from the corresponding ammine and ethylenediamine complex systems (26). In the latter two, a stepwise formation is observed in which each intermediate is the predominant species at some point during the course of adding increasing amounts of the complexing agent to the solution. The $\mathrm{Fe(phen)}^{++}$ is never very predominant (not over 3 mole per cent) and the $\mathrm{Fe(phen)_2}^{++}$ has yet to be characterized. The difference between these systems cannot be attributed to a stability due to chelation, yet some property of the arrangement of three phenanthrolines around the ferrous ion gives an abnormally enhanced stability of the 3:1 species over the 2:1 and 1:1.

The ferric–phenanthroline system is somewhat more difficult to study. The reaction products resulting from direct mixing of the reagents have thus far been somewhat incompletely characterized (119, 133, 199, 289). The trisphenanthroline ferric ion is formed only by oxidation of the corresponding ferrous complex. Knowing the instability constant for ferroin and the oxidation–reduction potentials of the ferrous–ferric and ferroin–ferriin systems, it is possible to calculate values for the instability constant of ferriin. Another approach involves the measurement by potentiometric means of the equilibrium represented by

$$\mathrm{Fe}^{++} + [\mathrm{Fe(phen)_3}^{+++}] \rightleftarrows \mathrm{Fe}^{+++} + [\mathrm{Fe(phen)_3}]^{++} \tag{18}$$

These data may then be utilized in the equation

$$K_{I_{\mathrm{ferriin}}} = \frac{a_{\mathrm{Fe}^{+3}} \cdot a_{\mathrm{phen}}^{3}}{a_{\mathrm{Fe(phen)_3}^{+++}}} = \frac{a_{\mathrm{Fe}^{+3}} \cdot a_{\mathrm{Fe(phen)_3}^{++}}}{a_{\mathrm{Fe}^{++}} \cdot a_{\mathrm{Fe(phen)_3}^{+++}}} \cdot K_{I_{\mathrm{ferroin}}} \tag{19}$$

The calculation gave values of the instability constant of ferriin which decrease with increasing hydrogen-ion concentration (178).

$pK_{I_{\text{ferriin}}}$	H_2SO_4	$pK_{I_{\text{ferriin}}}$	H_2SO_4
	M		*M*
14.1	0.05	15.5	2.0
14.6	0.5	20.9	8.0
15.0	1.0		

The hydrogen-ion dependence is evidenced also in the determination of the rate of dissociation of ferriin (179). The rate was followed potentiometrically in a cell containing Fe^{++}, Fe^{+++}, $Fe(phen)_3^{++}$, and $Fe(phen)_3^{+++}$. The specific rate constant for the first-order dissociation varied from 0.0137 min.^{-1} in 0.05 *M* sulfuric acid to less than 0.002 min.^{-1} in 2 *M* sulfuric acid. The direction of the hydrogen-ion dependence of the instability constant is opposite to that which would be predicted if a ferric sulfate complex were forming or if the activity coefficient of ferriin were larger than that of ferroin. The data can be explained by assuming a stabilization of ferriin by the reaction

$$[Fe(phen)_3]^{+++} + H^+ \rightleftarrows [FeH(phen)_3]^{++++} \qquad (20)$$

However, this species has not been demonstrated conclusively, and, owing to lack of information concerning the mechanics of the formation of such an ion and the driving force for it, the possibility of the existence of another explanation must be allowed.

A yellow species formed by the decomposition of the blue $Fe(phen)_3^{+++}$ ion has been identified as having the empirical ratio of $Fe_2(phen)_3$. The structure has not been explained (133). The possibility of a phenanthroline bridge would seem quite unreasonable.

The trisphenanthroline ferrous ion undergoes exchange with ferrous ion slowly, although the complex is diamagnetic and such behavior would not be predicted (246).

B. THE IRON–BIPYRIDINE SYSTEM

The iron–bipyridine system is, in general, quite similar to that of iron–phenanthroline. It has been studied by the same techniques: namely, equilibrium and kinetics. However, the results of different investigators do not agree in several details. The system also possesses a remarkable difference in hydrogen-ion dependence compared to phenanthroline. The validity of the difference seems well established; however, the lack of explanation of the observed phenomenon in either case prevents a sound judgment of the credibility of the difference.

The instability constant for $Fe(bipy)_3^{++}$ was first determined by Dwyer and McKenzie (98), using the previously described potentiometric method (equation 2), to be $K_I = 16.4 \pm 0.4$. This value agrees reasonably well with later values. The equilibrium reaction analogous to equation 5 can be measured and the instability constant $K_{I_{Fe(bipy)_3^{++}}}$ may be calculated from

$$K_I = \frac{(\text{Fe}^{++})(\text{bipy})^3}{\text{Fe(bipy)}_3{}^{++}} \tag{21}$$

by utilization of the acid dissociation constant for the conjugate acid of the base. The calculated value of $\text{p}K_{I_{\text{Fe(bipy)}_3{}^{++}}}$ is 17.1, using $\text{p}K_a = 4.33$ at 25°C. ($\mu = 0.025$) (19). The heat of formation is calculated to be -24.3 ± 1.3 kcal. Other closely agreeing values of these constants have been reported (17, 18, 170, 171, 172).

The kinetic aspects of the iron–bipyridine system resemble the iron–phenanthroline system in that the formation is rapid above pH 5, but in more acidic solution (pH 2–3) the rate is slower and permits easy measurement. In the presence of large excesses of bipyridine the reaction is first order with respect to ferrous ion, and the formation constants are proportional to $(\text{bipy})^3$ or to $1/[\text{H}^+]^3$ (17). This confirms the fact that the free base is reacting and not its conjugate acid. By using comparable concentrations of ferrous ion and bipyridine the rate of formation may be measured at pH 2–6. The data fit a fourth-order reaction expression

$$\frac{d[\text{Fe(bipy)}_3{}^{++}]}{dt} = k_0[\text{Fe}^{++}][\text{bipy}]^3 \tag{22}$$

where k_0 is the observed velocity constant (pH dependent). The fourth-order kinetics fit a stepwise formation

$$\text{Fe}^{++} + \text{bipy} \overset{K_1}{\rightleftarrows} \text{Fe(bipy)}^{++} \tag{23}$$

$$\text{Fe(bipy)}^{++} + \text{bipy} \overset{K_2}{\rightleftarrows} \text{Fe(bipy)}_2{}^{++} \tag{24}$$

$$\text{Fe(bipy)}_2{}^{++} + \text{bipy} \underset{k_b}{\overset{k_f}{\rightleftarrows}} \text{Fe(bipy)}_3{}^{++} \tag{25}$$

where equations 23 and 24 are rapidly established equilibria with constants K_1 and K_2, while equation 25 is the slow reaction having rate constants k_f and k_b for the forward and back reactions. The rate of formation is apparently independent of temperature.

In solutions more alkaline than pH 1.3, the fourth-order rate equation for the formation of $\text{Fe(bipy)}_3{}^{++}$ involves an acid-dependent term and an acid-independent term. The rate-determining steps are assumed to be the reaction of $\text{Fe(bipy)}_2{}^{++}$ with bipyH^+ and bipy, respectively (171, 172). The rate of formation goes through a maximum with increasing concentration of ferrous ion. If it is assumed that this inversion is due to a rapid formation of a species such as Fe(bipy)^{++}, which effectively lowers the ferrous-ion concentration, it is possible to get satisfactory representation of the kinetics. Attempted explanation of the data by the formation of $\text{Fe(bipy)}_2{}^{++}$ gives unsatisfactory agreement.

The dissociation of $\text{Fe(bipy)}_3{}^{++}$ is first order and is dependent upon the hydrogen-ion concentration. It also varies with the type of acid used (17), being different in perchloric acid than in sulfuric or hydrochloric acid. For the consideration of the dissociation reaction, Krumholz (171) developed an equation which involves the hydrogen-ion dependence in solutions of $[H^+] = 5 \times 10^{-2}\ M$.

$$-\frac{d[Fe(bipy)_3^{++}]}{dt} = [k_{d_0} + k_{d_1}[H^+]][Fe(bipy)_3^{++}] \tag{26}$$

This indicates the presence of an acid-dependent dissociation combined with the usual acid-independent mechanism. Since k_{d_1} decreases with increasing $[H^+]$, it is assumed that the rate-determining step becomes a monomolecular decomposition of some intermediate species, such as $FeH(bipy)_3^{+++}$, rather than a bimolecular reaction between H^+ and $Fe(bipy)_3^{++}$. Equation 26 may be expressed as

$$-\frac{d[Fe(bipy)_3^{++}]}{dt} = k_{d_0}[Fe(bipy)_3^{++}] + k_{d_2}[FeH(bipy)_3^{+++}] \tag{27}$$

From this equation the instability constant for the protonated ion, $FeH(bipy)_3^{+++}$, going to $Fe(bipy)_3^{++}$ is $K_I = 0.6$. This reaction is apparently independent of temperature, while the activation energies of the acid-dependent and acid-independent reactions are 26 and 29.5 kcal., respectively.

The rate constants for the formation and dissociation give a value of $pK_I = 17.5$ ($\mu = 0.33$) for the instability constant of $Fe(bipy)_3^{++}$ (171). Values from equilibrium measurement agree well.

The intermediate species required for satisfactory explanation of the kinetics has been investigated separately. Thus, this yellow species has been shown to be $Fe(bipy)^{++}$, and it has been spectrophotometrically characterized ($\lambda_{max.} = 440$ mμ) (19). The instability constant has been determined by equilibrium measurements and by detailed interpretation of the kinetics of formation of $Fe(bipy)_3^{++}$. The values obtained for the pK_I of $Fe(bipy)^{++}$ are 4.2 (18, 19) and 4.4 (170, 171, 172). The value, $K_{I_{Fe(bipy)_2^{++}}} \ngtr 10^{-5}$, listed for the instability constant of $Fe(bipy)_2^{++}$, was obtained by approximation and represents a minimum value attainable (18).

The instability constant for the $Fe(bipy)_3^{+++}$ ion, calculated from oxidation–reduction data, is approximately $pK_I = 12$ (19). The rate of dissociation of the complex appears to be acid-dependent.

From the foregoing discussion it is apparent that a protonated complex, $FeH(bipy)_3^{+++}$, quantitatively fits the available experimental data. However, the explanation does not fit the observed rate constants in high acidities (1.0 N hydrochloric acid) nor does it offer an explanation of the dependence of the rate constants of dissociation on the type of acid (18). It may be unreasonable to expect it to explain the latter fact.

The trisbipyridine ferrous ion undergoes slow exchange with Fe^{++} in a similar manner to the phenanthroline complex.

C. THE IRON–TERPYRIDINE SYSTEM

The instability constant of the bisterpyridine ferrous ion determined by equilibrium measurements is $pK_I = 18$ (36). The terpyridine molecule reacts with two hydrogen ions with an acid dissociation constant for the reaction

$$\mathrm{trpyH_2^{++}} \rightleftarrows \mathrm{trpy} + 2\mathrm{H^+}$$

of 7.1. The stepwise constants for the dissociation have not been determined. An estimation of the constant for $\mathrm{Fe(trpy)_2^{+++}}$ from the oxidation–reduction potential of 1.10 in 0.1 *F* sulfuric acid gives $\mathrm{p}K_I = 11$.

D. A COMPARISON OF THE IRON SYSTEMS

The ferrous–phenanthroline, bipyridine, and terpyridine complexes exhibit a number of similarities. More important, they have points of non-similarity which demonstrate the need for considerable careful investigation directed toward an explanation of some of these observed phenomena. The terpyridine system has not received an amount of study comparable to the other two reagents. This fact, coupled with the different type of coördinating system involved, removes it from much of the discussion.

The bipyridine and phenanthroline systems are very similar in the stepwise formation of metal complexes. In each case, for example, a yellow 1:1 complex has been found and studied under very similar conditions. However, in both cases the 2:1 complex is apparently unstable with respect to the other two and never exists in appreciable concentration in solution. By comparison, a 1:1 species has not been reported in the terpyridine system.

The explanation of the effect of hydrogen ion on the phenanthroline and bipyridine systems seems to present the greatest challenge. It appears to be involved in the dissociation of the ferric complexes of both, but only with the ferrous complexes of bipyridine. The complete explanation of this phenomenon should prove valuable. The existence of species such as $\mathrm{FeH(phen)_3^{++++}}$ introduces many questions concerning the position and means of attachment of the proton and its effect upon the properties of the molecule. Isolation of salts of both the protonated and non-protonated complex should be possible. The extent to which this type of behavior is typical of metal–phenanthroline and metal–amine complexes in general should be explored.

One point which is apparent from the compilation of data is the discrepancy of the instability constant of ferroin based on potentiometric measurements. This presumably is due to an uncorrected interaction between ferric ion and phenanthroline. However, the corresponding value for the bipyridine complex agrees quite well with the results obtained by other methods. Thus the need for further study of the reaction of ferric ion with these molecules is indicated. The state of knowledge of the ferric complexes in general leaves considerable to be desired. The products of direct mixing and the explanation of the failure of completely complexed ions such as $\mathrm{Fe(bipy)_3^{+++}}$ to form directly will require further study. The nature of the compounds formed upon dissociation of the trisferric complexes should prove interesting. Such information might well fit into the problem of the photochemical reduction and x-radiation of the ferric complexes (240). Two differently colored species of the ferric–terpyridine complex have been demonstrated in different acidity (36) and point out the desirability of knowing the influence of hydrogen ion on these species. Only as these factors become known will it be possible to draw sound and thorough conclusions regarding the significance of these important, but yet quite isolated, pieces of data.

E. OTHER METAL SYSTEMS

The investigation of the stability of complexes other than those of iron has progressed slowly. In the case of other metals, the existence of colored species is often completely lacking; even when available, such colors seldom approach the intensity of that of ferroin. Although complexes of the phenanthroline type of compounds are known to form with a large number of metal ions (see Section II), only a few have received quantitative measurement of their stability.

The system zinc–phenanthroline was investigated by Kolthoff (168). The formation of a zinc complex had been indicated by the interference of zinc in the colorimetric determination of iron, and several salts of complexes had been reported in the literature. Zinc forms three well-defined species. The monophenanthroline zinc(II) ion is the main zinc species formed when zinc ion is added to solutions of ferroin and equilibrium is established. The instability constant calculated using the known values for the iron system gives $\mathrm{p}K_{I_{\mathrm{Zn(phen)}^{++}}} = 6.43$. The corresponding constants for the 2:1 and 3:1 complexes were obtained from measurements of the amount of phenanthroline which could be extracted from solutions of zinc and phenanthroline by chloroform. In this manner the average number of phenanthroline molecules retained per zinc ion is obtained. Using a modified Bjerrum-type calculation the values $\mathrm{p}K_{I_{\mathrm{Zn(phen)}_2^{++}}} = 12.15$ and $\mathrm{p}K_{I_{\mathrm{Zn(phen)}_3^{++}}} = 17.0$ are obtained. Confirmation was obtained for these values by conductometric titration of zinc with phenanthroline (168) and equilibrium determinations using ultraviolet absorption measurements (173).

Polarographic measurements of the cadmium–phenanthroline and cadmium–bipyridine complexes give the following values for $\mathrm{p}K_I$: $\mathrm{Cd(bipy)_3^{++}}$, 10.5; $\mathrm{Cd(bipy)_3^{++}}$ in 28.5 per cent alcohol, 10.0; $\mathrm{Cd(phen)_3^{++}}$, 15.2; $\mathrm{Cd(phen)_2^{++}}$ in 28.5 per cent alcohol, 13.2 (68). The apparent loss of one phenanthroline in 28.5 per cent alcohol may possibly be due to the effect of the ethanol on the availability of the metal ion. The quoted values would require an extreme difference in the attraction of the cadmium for the first two organic molecules as compared to the third. The proportional decrease of stability in alcohol of the $\mathrm{Cd(bipy)_3^{++}}$ system is only slightly less than the change in going from $\mathrm{Cd(phen)_3^{++}}$ in water to $\mathrm{Cd(phen)_2^{++}}$ in 28.5 per cent alcohol.

A Bjerrum-type approach has been reported for the cupric–phenanthroline complex, indicating the existence of the trisphenanthroline cupric ion. The instability constants of the three stepwise additions of phenanthroline to cupric ion are 6.30, 6.15, and 5.50. The overall instability constant $\mathrm{p}K_I = 18.0$ (237). This compares closely with the value of $\mathrm{p}K_I = 17.0$ obtained for the trisbipyridine cupric ion from polarographic measurements (223). The proximity of the bipyridine and phenanthroline values does not correspond to the iron or cadmium system, but since values are not available for the complexes of both compounds with any other metals, the significance of this fact is purely conjecture. The polarographic reduction of the trisbipyridine cupric ion goes first to the bisbipyridine cuprous ion and then to the metal. Both reduction steps are reversible, and the bisbipyridine cuprous ion has a value of $pK_I = 14.2$ (223). Thus the individual stepwise stability would seem to be greater for the cuprous complex in contrast to the cupric. It is unfortunate that the copper(II)–phenanthroline complex is not suitable for similar investigation.

The nickel systems with bipyridine and phenanthroline have received some attention (13, 284). This has been directed mainly toward demonstrating the existence of the 1:1, 2:1, and 3:1 complexes and determining the kinetics of the decomposition and racemization. The instability constant for the trisphenanthroline nickel(II) complex is $pK_I = 18.3 \pm 1.1$ (65).

Exchange reactions have been studied between trisbipyridine nickel(II) and nickel(II) (157) and between trisbipyridine vanadium(II) and vanadium(III) (162). In the case of nickel, exchange is quite slow. With vanadium the reaction goes to the extent of 40 per cent in zero time and then stops.

These entries demonstrate the difference in the phenanthroline type of complexes from other series already investigated, e.g., acetylacetone and ethylenediamine. In such systems the usual order or stability of the metal complexes is $Pd > Cu > Ni > Pb > Co > Zn > Cd > Fe > Mn > Mg$. Although the data are too incomplete to permit conclusive statements, this order is obviously quite different for the phenanthroline-type systems. Iron is greater than copper, nickel, and zinc, and the latter three are about equal. Zinc and cadmium are in proper sequence, although separated more widely than is common. The apparently marked deviation of this system from the regular order makes the determination of other constants in the series of interest. The correlation of the stabilities with physical properties such as the second ionization constant will become quite difficult. The existence of a major deviation from the expected regular behavior will necessitate an expansion of the present theories. As data become available, it will become necessary to determine whether the system will fit into the comparison pattern established by Fernelius (112).

VII. Substitution and Steric Considerations

Substitution in the molecules of the parent bases might well be expected to modify somewhat the stabilities and colors of the iron(II) coördination compounds, and also to shift the redox potentials, by alteration of the relative stabilities of the compounds in the bivalent and tervalent states, but not lead to any profound changes. Much the same kind of modification would be anticipated with other metal derivatives. It is now well established that for a given metal there is a relationship between the proton-binding capacity of a ligand and the stabilities of the complexes (27, 192). For example, substitution of the electrophilic bromo or nitro groups in the 4,4′-positions in bipyridine or the 4,7-positions in phenanthroline should merely lower the base strengths and hence reduce the stabilities of the metal complexes.

In the same way, methyl substituents in these positions should increase the stabilities. This property of several 5-substituted phenanthrolines has been determined. The stability of the corresponding ferrous complexes has also been evaluated and a straight-line relationship between pK_I and pK_a demonstrated.

The stabilities were determined by kinetic and equilibrium measurements (34). The variation of the stability of the hydrogen bond in the hydrates of two substituted derivatives has been determined (118).

These results confirm the direct relationship between basicity and stability in a series of substituted phenanthroline complexes, but it is not possible to include bipyridine and terpyridine complexes in such a direct comparison. In the latter case a different number of molecules and hydrogen ions is involved. In order to include terpyridine in the comparison, a concept of the "average basicity per nitrogen" was introduced (36). This value, obtained by dividing the total pK_a of the molecule by the number of nitrogen atoms, permits a direct comparison.

This comparison indicates the failure of the basicity concept to explain more than the variation of stability with substitution in a given molecule with the information now available. The more fundamental variation, that between similar molecules, is not explained and will require further investigation. The variation of double-bonded character in the chelate ring or geometric strain effects might be logical points of attack.

Following the synthesis of a large number of variously substituted phenanthrolines (51, 52, 53, 54, 55, 56), qualitative investigation of the effect of substitution of methyl groups in the phenanthroline ring upon the stability of the corresponding ferrous (35) and cuprous (194) complexes has been made. In the ferrous system, the pH of precipitation of the hydroxide was used as the criterion of stability. The results indicated that a methyl group in the 4- and 7-positions caused the greatest increase in stability, with the 5,6-positions somewhat less effective. The 3,8-positions caused some apparent decrease in stability. These effects are compatible with the π-electron distribution in the molecule (183, 241). The fact that the 2,9-positions cause effects which are not consistent with an explanation due to basicity will be discussed later.

The cuprous system was studied by comparing the pH at which extraction into isoamyl alcohol first occurred as the acidity of the solution is decreased. Here the 2,9-positions cause extraction at by far the lowest pH (1.0). The 3,8- and 5,6-positions were without much effect (pH 3–4), and the 4,7-substitutions caused marked increase in the pH of extraction (pH 7) (194). Since these results are directly opposite to those obtained with the ferrous system it would appear that the two investigations were not both sensitive to stability. Since the factors causing extraction of a precipitate are not thoroughly understood, it might appear that the extraction phenomena were not based primarily upon stability.

In the main, these general principles have been found to apply (*vide infra*), but substitution in the nitrogen-adjacent positions in either molecule and in the 3,3′-positions in bipyridine apparently makes such profound changes in the chelating abilities of the molecules that, as far as iron is concerned, either no complex is formed or the complex is of very low stability. Loss of function is related to the position of the substituents and their sizes and not to their electrophilic properties. It thus appears that neither the base strength nor the partial double-bond character of the nitrogen–metal bond is involved, though few quantitative data are yet available.

TABLE 1

Effect of substitution on the color intensity of chelate complexes

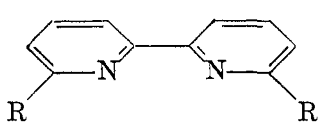
Base	Absorption Maximum	a_M	Base	Absorption Maximum	a_M
	mμ			mμ	
3,3′-Dimethylbipyridine...	526	1770	5,5′-Dimethylbipyridine...	510	8300
4,4′-Dimethylbipyridine...	529	8470	2,2′-Bipyridine...........	522	8650

The orange-colored tris-3,3′-dimethyl-2,2′-bipyridine iron(II) cation is stable in the limited pH range of 4–6 as compared with the pH range of 3–8 for bipyridine itself and various dimethyl-substituted derivatives (48). The effect of substitution on the color intensity is shown in table 1, in which the molar absorptivities, a_M, at the wave length of maximum absorption are compared (48).

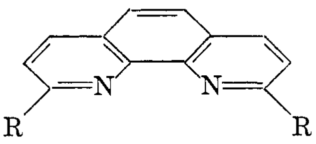
With the larger substituents present in 3,3′-dicarboxy-2,2′-bipyridine, no color reaction occurs and presumably no iron complex is formed (30, 295). It can readily be seen that substituents in these positions, unless quite small, as with the hydrogen atoms in the parent base, interfere sterically with each other and tend to rotate the pyridine rings about the linking single bond in the 2,2′-position. The chelating ability is thereby greatly reduced by the decreased stabilizing resonance in the donor, which requires coplanarity of the rings. More important, probably, is the introduction of strain in the metal–nitrogen bonds, which are forced out of their normal direction in the plane of the pyridine rings (48).

Buckling of the benzenoid ring in 1,10-phenanthroline should occur with hydrogenation in the 5,6-positions and this would move the pyridine rings out of coplanarity. As a result, the iron chelate compound would not be expected to form (45).

A large number of nitrogen-adjacent substituted bipyridines have been prepared (42) and tested for the formation of a red color with iron(II) salts. A single substituent in the 6-position, such as CH_3, Br, CN, NO_2, NH_2, or COOH, appears to lower the color intensity of the reaction considerably. No information is available upon base strengths or the relative stability constants. Disubstitution (formula XXVII) with one exception completely inhibits the color reaction. 6,6′-Dicarboxy-2,2′-bipyridine gives an orange color, but this is undoubtedly due to chelation through the carboxyl group and nitrogen, as occurs in picolinic acid.



XXVII



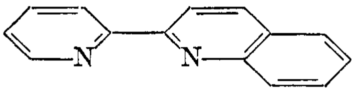
XXVIII

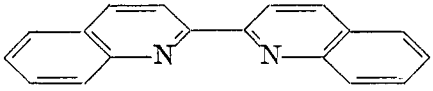
R = CH_3, Br, CN, COOH, NO_2, NH_2.

Since reagents normally attack phenanthroline in the benzenoid ring, 5(or 6)-derivatives are the easiest to obtain and a comparable series of 2- and 2,9-

derivatives (XXVIII) has not yet been tested. However, the tris-2-methylphenanthroline iron(II) salts are of an orange color (147, 227) and recently have been shown to be of low stability. Though 2-methylphenanthroline is a stronger base (pK_a = 5.42) than phenanthroline itself (pK_a = 4.92), it forms much weaker complexes, pK_I = 10.8, as compared with pK_I = 21.4 for $\mathrm{Fe(phen)_3^{++}}$. The presence of the second methyl group in 2,9-dimethyl-1,10-phenanthroline completely inhibits the iron color reaction (52, 147, 194). The only other nitrogen-adjacent substituted derivative prepared, 2-chloro-1,10-phenanthroline, has been found to yield an orange-yellow iron(II) compound, but quantitative stability data are still unavailable (127, 147).

The following substances that can be regarded as nitrogen-adjacent substituted bipyridines have also been reported (139, 256) not to give a color with iron(II) salts: 2-(2-pyridine)quinoline (XXIX); 2-(2-quinoyl)quinoline (2,2′-biquinoline) (XXX); 3-methyl-2,2′-biquinoline (XXXI); 3-methyl-2-(2-pyridine)-quinoline (XXXII); and 1-(2-quinoyl)isoquinoline (XXXIII).


XXIX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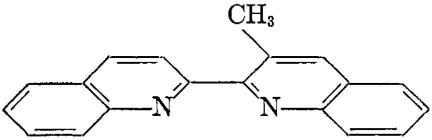
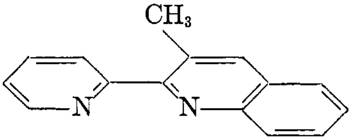
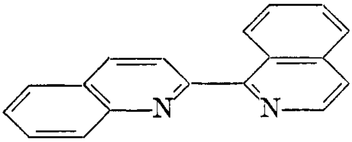

XXXI


XXXII


XXXIII

Smirnoff (256) suggested that in XXIX and XXX the benzene ring with its own system of conjugated double bonds interfered with the donor properties of the nitrogen atoms, and Feigl (109), in support of this view, cited the weaker base strength and the smaller addition capacity of quinoline as compared with pyridine. It was concluded that such considerations were invalid for the 6,6′-disubstituted bipyridines and that here a configuration of the pyridine rings other than in the parent base must be involved.

Since 2,9-disubstitution in the phenanthroline system, in which the pyridine rings are fixed, also apparently inhibits the color reaction, this explanation is untenable.

It is evident that whatever explanation is adduced to explain the inhibition of the iron(II) reaction must apply in some measure to the other metals, and it becomes of interest to examine how general is the lack of reactivity of these substances. The 6,6′-disubstituted bipyridines and also substances XXIX to XXXIII apparently do not lack all coördinating ability. It has been found that biquinoline (XXX) gives the complexes Co(biqn)Cl_2 and Cu(biqn)Cl_2, which have been formulated as typical monomeric 4-covalent compounds (37, 138).

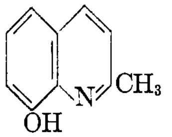
Chelate derivatives containing more than one molecule of the base were not isolated, but when dichloro-biquinoline copper(II) was reduced in the presence of excess of the base, a deep purple solution resulted, which from spectrophotometric studies was concluded to contain the bisbiquinoline copper(I) ion. All of the substances XXVII ($R = CH_3$) and XXIX to XXXIII have also been found to form deeply colored copper(I) derivatives, sometimes stable to dilute acid and considered to contain two molecules of the chelate (139). Qualitative drop tests were applied with XXVII ($R = CH_3$) and with XXIX to XXIII, using most of the metal ions in dilute aqueous solution; no color change was observed. This cannot be taken, however, as good evidence that metals other than copper(I) do not form chelate compounds. Many if formed would be colorless, as with zinc or cadmium, or weakly colored, as with copper(II) or nickel. Ruthenium and osmium, which form the most stable of all of the complex cations with bipyridine and phenanthroline, would not have reacted even with these bases under the experimental conditions used, owing to the slow rate of complex formation.

This lack of precise information necessarily makes much of the discussion that follows somewhat speculative. Hoste was of the opinion that the high position of copper in the sequence of stabilities of metal complexes could account for the apparently unique copper(I) reaction, but it should be pointed out that this series refers to copper(II), and as yet insufficient data are available to fix the position of copper(I).

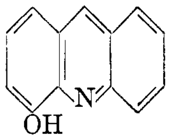
For the bis-2,2′-bipyridine copper(I) ion (223), $pK_I = 14.2$, and for the tris-2,2′-bipyridine copper(II) ion (223), $pK_I = 17.8$. Since K_3 is probably quite small in accordance with the usual weak octahedral coördination of copper(II), it may be inferred that for $Cu(bipy)_2^{++}$ $pK_I = 15$. Comparison of these values with $pK_I = 13$ for the $Fe(bipy)_2^{++}$ ion (19) suggests, if anything, that the chelate molecules that give copper(I) complexes should also react with copper(II) and iron(II).

If it is assumed from the incomplete evidence available that the copper(I) reaction is, in fact, unique, this anomaly can be explained on the basis of the tetrahedral coördination of copper(I) in contrast to the planar or octahedral coördination of the transition elements, and the steric factors introduced by nitrogen-adjacent substitution.

The importance of steric factors in the stabilities of metal complexes has been emphasized (146) and attention drawn to the failure of 2-methyl-8-hydroxyquinoline (XXXIV) to give a precipitate of the aluminum trischelate derivative at pH values below that necessary to precipitate aluminum hydroxide (198). A series of 2-substituted derivatives of 8-hydroxyquinoline and also 1-hydroxyacridine (XXXV) behaved similarly.



XXXIV



XXXV

The similarity in the steric considerations between substances XXVII to XXXIII, and XXXIV and XXXV is obvious. Substitution in 8-hydroxyquinoline adjacent to the hydroxyl group, as might be anticipated, has little effect on the chelating tendency (291).

Even large, strongly basic substituents in the 7-position, such as dimethylaminomethyl, diethylaminomethyl, and piperidylmethyl, while they raise the pH of complex precipitation do not otherwise modify the reaction (238). Substantial support of a more quantitative nature (14, 15) for the effect of substitution comes from studies with di-*N*-substituted ethylenediamines. It will be apparent from table 2 that the addition of even the first ligand to copper or nickel is less readily effected than with ethylenediamine itself and the difficulty increases, as reflected in the smaller values of log K_1, with increasing size of the substituent. Addition of the second and, with nickel, of the third ligand is even more difficult. That these are essentially steric effects is demonstrated by the relatively small effect of substitution on the proton-binding capacity of the molecule (27).

Essentially the same factors are involved in the reactions between pyridine and 2,6-lutidine with the Lewis acids boron trifluoride and trimethylboron. Though the latter base is the stronger, it forms the weaker addition compounds with boron trifluoride and no compound results with trimethylboron (40). It can be inferred that the apparently lowered chelating ability of the nitrogen-adjacent substituted bipyridines and phenanthrolines—and the molecules with quinoline rings can be included in this category—is largely, if not entirely, due to steric hindrance. It can be demonstrated easily with a model or a scale drawing that the attachment of a single chelate molecule would interfere with the

TABLE 2

Chelation of N,N′-dialkylethylenediamines

	en	di-Me-en	di-Et-en	di-*n*-Pr-en
Copper compounds; 25°C.				
pK_1 of base	10.08	10.29	10.46	10.27
log K_1	10.55	10.47	9.30	8.79
log K_2	9.05	7.63	6.32	4.84
Nickel compounds; 25°C.				
log K_1	7.66	7.11	5.62	5.52
log K_2	6.40	4.73	3.3	2.5
log K_3	4.4	1.5		

aquo groups remaining on the metal ion when the coördination is planar or octahedral but not to any significant extent when it is tetrahedral. With the addition of the second and the third ligand, interference would occur between the substituents themselves (14). This is strikingly confirmed by the data on the iron(II) compound of 2-methylphenanthroline, where the successive constants are log $K_1 = 4.2$, log $K_2 = 3.7$, and log $K_3 = 2.9$ following the normal pattern, as against log $K_1 = 5.9$, log $K_2 = 7$, and log $K_3 = 8$ for $Fe(phen)_3^{++}$.

The more open nature of tetrahedral coördination readily permits the addition of two chelate molecules without difficulty. Data on the phenanthroline and bipyridine complexes of zinc (168) and cadmium (68) indicate strong coördination, and it would not be surprising if these metals formed tetrahedral complex cations of appreciable stability with these sterically hindered bipyridines and provided yet another instance of the inversion of the order of stability of metal complexes (148, 186, 187, 188).

VIII. OPTICAL ACTIVITY OF CHELATE COMPLEXES

All of the phenanthroline and bipyridine metal complexes obtained in the enantiomeric forms have been tris derivatives of the Group 8 elements: $M(phen)_3^{++}$ (M = Fe (293), Ru (80), Os (75), Ni (82)); $M(bipy)_3^{++}$ (M = Fe (293), Ru (41), Os (43), Ni (202)). The resolution of bisethylenediaminephenanthroline cobalt(III) chloride has been reported (150).

Resolution of the phenanthroline series is best effected through the antimonyl *d*-tartrates. One of the antipodes forms a very insoluble precipitate on the addition of potassium antimonyl *d*-tartrate, whereas the other diastereoisomer is very soluble. A complete separation is thus achieved in a single precipitation, and the antimonyl tartrate radical is easily eliminated with dilute alkali or sulfuric acid.

Werner (293) resolved $Fe(bipy)_3Cl_2$ by addition of a large amount of ammonium *d*-tartrate to the aqueous solution, and the same method has been used for $Ru(bipy)_3Cl_2$ (41) and $Ni(bipy)_3Cl_2$. Unless both ammonium *d*-tartrate and ammonium *l*-tartrate are employed, only one enantiomer can be prepared in this way. Complete separation can be effected, however, in one operation by the formation of the iodide antimonyl tartrate. When both potassium iodide and potassium antimonyl tartrate are added to solutions of $M(bipy)_3Cl_2$, $[M(bipy)_3]_3I_2 \cdot (SbO\ tart.)_4 \cdot 18H_2O$ is precipitated and contains only one antipode of the complex (81, 83).

Oxidation of the optical forms with retention of configuration can be effected with the iron(II), ruthenium(II), and osmium(II) complexes of both chelates. The crystalline antipodes of $Fe(bipy)_3(ClO_4)_3$, $Os(bipy)_3(ClO_4)_3$, and $Os(phen)_3(ClO_4)_3$ have been isolated (86, 88), and active solutions of $Fe(phen)_3^{+++}$, $Ru(bipy)_3^{+++}$, and $Ru(phen)_3^{+++}$ have been prepared (79, 80, 81, 83). The chemically and optically stable osmium bipyridine compounds have been used to demonstrate the identity of potentials of enantiomeric redox systems (6). In a recent review Basolo (12) has discussed the oxidation of enantiomeric forms and drawn attention to the value of an experimental method for the study of

TABLE 3

Specific rotations of $M(phen)_3(ClO_4)_{2,3}$

Metal	$[\alpha]_D$	$[\alpha]_{5461}$	Metal	$[\alpha]_D$	$[\alpha]_{5461}$
Fe(II)	1432		Os(II)	0	3670*
Ru(II)	1340	2560	Os(III)	0	400
Ru(III)	409	1630	Ni(II)	1460	1740

* $[M]_{5461} = 34{,}800$.

the kinetics of electron transfer based upon the use of optical forms in two oxidation states (85).

Work on the kinetics of racemization of these substances has recently been reviewed critically (12), and though the nickel compounds undergo racemization through a rate-determining dissociation step in aqueous solution, it has now been shown that both dissociation and intramolecular change are involved in aqueous alcoholic solution (16, 67). However, the rates of racemization of the iron(III) compounds, as for the iron(II) compounds, are very much greater than the rates of dissociation; hence intramolecular change seems to be indicated (66). The osmium and ruthenium compounds are optically stable even in boiling aqueous solution (41, 43, 80).

It will be apparent from table 3 that these substances have extremely high specific rotations, especially when it is realized that the molecular weights are usually in excess of 700. Though the complete curves have not been prepared, the rotatory dispersion appears to be anomalous and very large.

The relative generic configurations are of interest. The sign of the rotation in a particular wave length of light is, of course, of no significance. Though the assumption of identity of the least soluble diastereoisomers has been considered dubious (151), the large differences in solubility of the antimonyl *d*-tartrates perhaps makes this simple criterion carry more weight. However, considerable support for the principle comes from the biological experiments, discussed later, in which the stereospecificity was shown to be very pronounced. The mouse intraperitoneal toxicity was found to be greatest for that enantiomer in the phenanthroline series which gave the least soluble antimonyl tartrate. This was (+)-$Ru(phen)_3^{++}$, (+)-$Ni(phen)_3^{++}$, (−)-$Fe(phen)_3^{++}$ in the Na_D line; and $Os(phen)_3^{++}$ with no rotation in the Na_D line but a negative rotation in the Hg_{5461} line. A similar correlation existed between the solubilities of the iodide antimonyl tartrates or the *d*-tartrates in the bipyridine series and the inhibitory action in the enzyme acetylcholinesterase.

Since the biological activity of optically active metal complex compounds has not been studied previously, this is the first instance where biological evidence can be quoted for generic configuration.

Attempts by Pfeiffer and coworkers (230, 231, 233) to resolve the trisphenanthroline and trisbipyridine zinc and cadmium ions were fruitless, but instead provided the first examples of the so-called "first-order" asymmetric transformation among inorganic complex compounds. This term refers to the shift in the $d \rightleftarrows l$ equilibrium of a labile optically active substance to favor one enantiomer, and is brought about by the optical isomer of another optically stable substance. The phenomenon is designated "first order" when it occurs without the separation of a second phase (crystallization of one diastereoisomer), and is to be ascribed to the free-energy difference between the diastereoisomer molecules in solution. This subject, chiefly from the standpoint of organic substances, has been discussed in an excellent review by Turner and Harris (282). With organic compounds the phenomenon seems to be confined to substances in which the labile and the stable optical centers are part of the same molecule, or with salts only in non-dissociating media such as chloroform. The effect is observed with inorganic complex salts in dilute aqueous solution and even where the labile and stable substances are both cations. It has been found that when *dl*-trisacetylacetone cobalt(III)—a neutral complex—is allowed to reach equilibrium in the presence of *d*-trisethylenediamine cobalt(III) chloride one enantiomer is favored, and a partial resolution can be effected in this way (87).

Pfeiffer found that when $Zn(phen)_3SO_4$ was added to a solution of ammonium bromocamphorsulfonate a very large change in rotation occurred (+0.92° → +0.09°). This could not be brought about by addition of zinc sulfate or phenanthroline separately, or by the addition of hexammine zinc ion (which has a plane of symmetry). Other optically active anions or *cations* could be substituted for bromocamphorsulfonate. Similar results have been obtained (64, 230, 231, 233) in the series MB_3^{++} (M = Zn, Cd, Mn, Co, Ni, Cu; B = phen or bipy). Only the nickel compounds have been obtained in the optically active forms and here the movement of the equilibrium to favor one antipode was slow. Recently, the rates of racemization of the *d*- and *l*-forms of $Ni(phen)_3I_2$ have been studied in the presence of bromocamphorsulfonate and cinchoninium ions (66). The rates are different: $K = k_d/k_l = 0.895$ in 2 per cent ammonium bromocamphorsulfonate at 25°C.

The term "configuration activity" (93) has been applied to the general phenomenon of the interaction between optically active species in solution. This involves the assignment of different activity coefficients to the dextro and levo forms of a racemic mixture in the presence of an extraneous optically active substance. Pfeiffer's results may then be accounted for in the following way: In the racemic mixture of $Zn(phen)_3^{++}$, the activities (and concentrations) of the *d*- and *l*-ions are equal, but on the addition of the bromocamphorsulfonate ion the activity coefficients become unequal. Racemization then proceeds until equilibrium is reached, when the activities are equal but the *concentrations* are now unequal; hence the solution shows a rotation due to the excess enantiomer. Precipitation of the iodide, for instance, at this stage must yield an optically inactive salt because the activities of the two enantiomers in solution are the same. The small excess of either optical form will equilibrate if sufficiently labile or will be found in the last fractions of the precipitation. This has been confirmed in the following manner (93). The $Ni(bipy)_3^{++}$ ion is optically labile with a half-life of about 15 min. at 17°C. When the *dl*-chloride was dissolved in the presence of either ammonium bromocamphorsulfonate, quinine bisulfate, or *d*-trisethylenediamine cobalt chloride at 5°C. and immediately precipitated with iodide ion, the first fractions were the *d*-iodide, subsequent fractions were the racemate, and finally the *l*-iodide was obtained. If the mixture was allowed to stand, it underwent mutarotation in the levo direction, and on precipitation, as before, gave first a large amount of racemate and finally a little of the *l*-iodide.

Much still remains to be elucidated, however. The separation of $Ru(bipy)_3I_2$ by the method used for the nickel compound is only just detectable. Though cinchoninium and *N*-methylcinchoninium ions produce a large shift in the $d \rightleftarrows l$ equilibrium of $Zn(phen)_3^{++}$, di-*N*-methylcinchoninium ion is ineffective (233).

The nature of the interaction between optically active ions in solution is a matter for speculation. Most of the ions discussed are rather large and ion-pairs could well exist even in the dilute aqueous solutions by the operation of van der Waals dispersion interaction forces. Such association would be a spatial phenomenon and would be expected to be favored by one antipode more than the other. On the other hand, the differential interaction between multicharged ionic species of the same sign cannot occur in this way. Such an effect must be long range and could be due to van der Waals interaction of charge, if it is postulated that associated with an antipode is an asymmetric distribution of charge. In metal complexes such a charge configuration could be due to the distribution of the central metal ionic charge over the ligands. With the asymmetric carbon atom, the substitution of the concept of four different dipoles for four different groups attached to carbon leads to a similar picture of charge configuration (93). Probably in many systems both mechanisms of interaction are involved.

IX. Redox Reactions

The introduction of the ferroin–ferriin system as an oxidation–reduction indicator of considerable merit (287) was the impetus which brought the chemistry of the metal–phenanthroline chelates into prominence. However, in some respects the endeavor in the oxidation–reduction field has not been as vigorous as in other categories. Nevertheless, several systems have been proposed as indicators (74, 260, 270).

In addition to the interest in indicators, the potentials of many couples have been investigated. The values for iron, ruthenium, and osmium demonstrate dramatically the stabilization of valence states by chelation. The shift in oxidation–reduction potential as a result of complexation is very large with all three metals. It reaches a value of 1.3 v. with ruthenium. However, complete comparison is not possible, owing to the lack of formal potentials for the Os(II) → Os(III) system. It is certain that the shift is considerably greater with ruthenium and osmium than with iron. This would seem to correlate with the observed greater stability of these two (176).

The measurement of the potentials has required different methods, depending upon the relative stability of the system. Ideally, the potential is that measured in a system prepared from an equimolar mixture of the salts of the oxidized and reduced forms (method I). This has been possible in very few cases, but it has been used in the osmium–bipyridine system to study the application of the

Debye–Hückel theory to redox systems (11). More often a potentiometric titration has been carried out and the value determined graphically (method II). With the iron systems, it is common to include excess ferrous ion in the original mixture. This provides a differential titration curve in which the potential of the ferrous–ferric couple also serves as a reference point. In many cases, however, neither of the above approaches is possible, and the usual procedure is to utilize a measured amount of the complex in the lower oxidation state and rapidly add to it sufficient standard oxidizing agent to react with half of the amount present (method III). The maximum value attained after mixing is generally assumed to be the potential of the couple. The values reported are collected in table 4.

The data indicate some points of comparison and differences between the iron,

TABLE 4

Oxidation–reduction potentials

Iron(II)–iron(III)

Acid Normality	Tris Complexes							Bistrpy	Method	Reference
	Bipy	Phen	5-Nitrophen	5-Methylphen	5-Methyl-6-nitrophen	5-Bromophen	5-Chlorophen			
None added	1.096	1.120							I	(97)
0.01	1.084	1.112							I	(97)
0.1	1.071	1.102							I	(97)
		1.10		1.06					II	(35)
								1.076	III	(89)
0.2								1.060	III	(89)
0.5		1.086							I	(97)
								1.054	III	(89)
1.0	0.97		1.26			1.13			III	(267)
		1.073							I	(97)
								0.927	III	(89)
2.0		1.057							III	(97)
		1.06							II	(35)
		1.06							II	(142)
		1.06		1.02					II	(267)
			1.25		1.23		1.11		III	(267)
4.0		1.028							III	(97)
		1.03		1.00					II	(267)
			1.22				1.10		III	(267)
5.0		1.015							III	(97)
6.0		0.996							III	(97)
		1.00		0.96					II	(267)
7.0		0.977							III	(97)
8.0	0.92		1.12				1.04		III	(267)
		0.96		0.93					II	(267)
12.00		0.89		0.86					II	(267)
			1.12				0.97		III	(267)
16.0		0.76		0.70					II	(267)
			1.11						III	(267)

TABLE 4—*Continued*

Ruthenium(II)–ruthenium(III)

Acid Normality	Tris Complexes						Bistrpy	Method	Reference
	Bipy	4,4-Dimethylbipy	5,5-Dimethylbipy	Phen	5-Methylphen	5-Bromophen			
0.002	1.303	1.152	1.240	1.31	1.29	1.41		III	(71)
0.1	1.288	1.115	1.208	1.30	1.28	1.36		III	(71)
				1.27				II	(35)
							1.281	III	(89)
0.2							1.263	III	(89)
0.3	1.279	1.096	1.185	1.29				III	(71)
0.5	1.270	1.087	1.171	1.28				III	(71)
							1.219	III	(89)
1.0	1.257	1.070	1.154	1.26				III	(71)
				1.29				III	(95)
				1.25				II	(35)
							1.202	III	(89)
2.0	1.240			1.24				III	(71)
							1.175	III	(89)
2.1				1.26				III	(95)
3.0	1.222			1.22				III	(71)
4.0				1.21				II	(35)
5.0				1.19				III	(71)
				1.22				III	(71)
				1.22				III	(95)
7.1				1.205				III	(95)
8.0				1.16				II	(35)
10.0				1.16				III	(95)
12.0				1.15				III	(95)
				1.07				II	(35)
13.5				1.105				III	(95)
16.0				0.98				II	(35)

Osmium(II)–osmium(III)

Acid Normality	Complexes			Method	Reference
	Trisbipy	Trisphen	Bistrpy		
None added	0.877			I	(76)
		0.877		III	(76)
0.05	0.863			I	(76)
		0.863		III	(76)
0.1	0.855			I	(76)
		0.859		III	(76)
			0.9512	I	(89)
0.2	0.847			I	(76)
		0.856		III	(76)
			0.944	I	(89)
0.5	0.833			I	(76)
		0.842		III	(76)
			0.9250	I	(89)
1.0	0.819			I	(76)
		0.822		III	(76)
			0.9070	I	(89)
2.0	0.802			I	(76)
			0.8838	I	(89)
3.0	0.775			I	(76)
5.0	0.727			I	(76)

ruthenium, and osmium systems. In all, increasing acid concentration causes lowered potentials. The change is in the direction required by consideration of the effect of ionic strength on the cationic complex. However, the shift in potential is greater than can be explained in this manner. The comparison of the bipyridine, terpyridine, and phenanthroline systems involves both similarities and differences. The bipyridine potentials are generally less negative than those of the phenanthroline systems. However, a definite trend is noticed from iron to osmium. The iron–bipyridine system lies appreciably below that of phenanthroline. With ruthenium and osmium the difference is not significant. The terpyridine potentials in the iron and ruthenium systems are comparable at low acidities to those for the phenanthroline and bipyridine complexes. However, with osmium the terpyridine values are significantly above the other two. Thus for phenanthroline and bipyridine, ruthenium and osmium are alike and different from iron, whereas with terpyridine, iron and ruthenium are similar to each other but different from osmium. It is noteworthy that the potentials of the terpyridine systems are considerably more sensitive to hydrogen-ion concentration.

With all three metals the stability of the reduced form is best with phenanthroline and that of the oxidized form is best with bipyridine (76). The difference in potentials would not seem to be sufficient to explain this property. The oxidation of the phenanthroline molecule in solution has been offered as an explanation (95). However, this has not been definitely demonstrated. In view of the extreme conditions necessary for such oxidation (268), it would seem that another explantation might be sought.

The oxidation–reduction potentials of a large number of methyl-substituted (35) and two hydroxy-substituted (128) phenanthroline complexes with iron(II) have been determined. In the course of the investigation of the methyl derivatives it became apparent that the effects of substitution were regular and could be predicted with reasonable accuracy. Thus a methyl substitution in the 4- or 7-position lowers the potential by 0.11 v., while similar substitution in the 3- or 8-position lowers it by 0.03 v. and in the 5- or 6-position by 0.04 v. The additivity of these values has been demonstrated (35). This is the first system in which properties of analytical interest are so readily predictable. Further advances along the same line should aid in the obtaining of molecules having specifically desired analytical properties with a minimum of synthetic work.

The same predictability was found to hold for the wave length of maximum absorption of both the ferrous and the ferric complexes.

The first correlation of the physical properties of these compounds with substitution was demonstrated by Ewens (107), who found that the potentials of the ferrous–phenanthroline complexes with nitro, methyl, bromo, or chloro substituents in the 5-position gave a straight-line relationship with the pK_a of the correspondingly *p*-substituted benzoic acids. The determination of the pK_a of the substituted phenanthrolines themselves permitted direct correlation (34). Thus the variation in potential can be related directly to the basicity of the nitrogens in the substituted phenanthrolines. From the points available (71) it appears that the same correlation is realized with the ruthenium complexes. These relationships appear reasonable on the basis of the pK_a being a measure of the availability of the electron cloud around the nitrogens and the resultant effect upon the electrons around the central metallic ion. Thus, electrophilic substitution lowers the stability of the complex in both oxidation states, but the stability of the tervalent complex is lowered more than that of the bivalent and E^0 becomes more negative. The converse is true with nucleophilic substituents.

X. Analytical Applications

A. AS OXIDATION–REDUCTION INDICATORS

The proposal by Walden, Hammett, and Edmonds in 1931 (287) that the iron–phenanthroline system might serve as an excellent oxidation–reduction indicator was well received, and ferroin is now a commonly used indicator. Its success has been due to the need for high-potential indicators for titrations with quadrivalent cerium in particular. High precision and accuracy are obtainable. It has been used in titrations with cerium in the determination of iron (130, 175, 268, 286, 287, 288), ferrocyanide (296), niobium (165), thallium (296), uranium (193, 296), antimony (296), chromium and vanadium (297), hydrogen peroxide (296), and arsenic (122).

The 5-nitroferroin complex has also been used in analysis (258, 262, 263, 264, 268), particularly where exceptionally high end-point indication is needed. However, the system is not as stable as ferroin and therefore finds limited usage. The iron–bipyridine complexes suffer from the same limitation (47, 218, 287).

Ferroin has been used in titrations with bromate as an oxidizing agent (274). The interference of free halogen in the titration was obviated by the use of mercuric oxide. It has also been used in reactions utilizing potassium permanganate (165, 297) and potassium dichromate (287). Ferroin is oxidized by dichromate in strongly acid solutions, whereas the reverse reaction can take place in weak acid (174). A more suitable indicator for direct titrations involving potassium dichromate is the 5,6-dimethylferroin (260). The latter indicator provides a more suitable potential for dichromate titrations (see table 4). Exchange studies demonstrated fast electron-transfer reaction between 5,6-dimethylferroin and 5,6-dimethylferriin (101). The oxidation of ferroin has been utilized in the qualitative detection of cerium(IV) (59).

The trisbipyridine ruthenous ion has been proposed as an oxidation–reduction indicator of high stability in hot, concentrated acid solutions and in solutions of high potential (270). The trisphenanthroline osmium(II) complex has also been suggested as having exceptional stability (76). The latter system has a somewhat lower potential (see table 4). The advantages of these systems do not appear to have been utilized yet to any great extent.

B. AS COLORIMETRIC REAGENTS

1. Iron

The intense red color formed by compounds of the phenanthroline type is their primary characteristic. As colorimetric reagents for the determination of iron they have attained international usage. Their application to this determination in all types of materials has produced a large number of incidental references. These are not included in this survey. Phenanthroline has been used in the determination of iron in biological materials (143, 184, 251) and alloys (250), among others (268). In a similar capacity, bipyridine has found application with samples of soil (144), biological materials (102, 160, 164), and miscellaneous materials (268). Terpyridine has been used mostly for the determination of iron in water samples (211).

The wave lengths of maximum absorption of the iron complexes of phenanthroline, bipyridine, and terpyridine are 510, 522, and 552 mμ, respectively (268). Investigation of the series of methyl-substituted phenanthroline derivatives previously described demonstrated the predictability of the change in wave length of maximum absorption with substitution (35). Thus a methyl group in the 4- or 7-position raises the value 1 mμ, in the 5- or 6-position it is raised 5 mμ, and in the 3- or 8-position it is lowered 8 mμ. This sequence is not the same as with the oxidation–reduction potentials, where all substitution lowered the value, with the 4- and 7-positions being the most effective. An attempt was made to find the same numerical predictability with the molar absorptivity. However, no such definite relation was found (35). A very useful concept did develop however. It was shown that the 4- and 7-substituted molecules were the only ones showing significant increases in the intensity of the color. This led to a series of 4,7-substituted phenanthrolines which have since been utilized to more than double the molar absorptivity with iron. This is a dramatic demonstration of the usefulness of generalizations and predictability in the application of organic reagents.

To date the most sensitive reagent described is the 4,7-diphenylphenanthroline (bathophenanthroline), which gives a complex with iron which can be extracted into *n*-hexyl alcohol. The resultant molar absorptivity is 22,400. The determination of iron in water is considerably improved by this increased sensitivity (266). Three compounds with substituted amines in the 3- and 4-positions have been investigated in a similar manner (295). The complexes of these reagents give molar absorptivities of 16,000–19,000 but exhibit peculiar color changes in acid, presumably due to the presence of the amino group (259).

Substitution in general appears to enhance the solubility of the complexes in non-aqueous solvents (101, 140, 190, 266, 295). Rather striking effects are observed with variations in the anion used (101, 190). The separation of iron from vanadium, nickel, and chromium is readily accomplished (190). It also suggests possible applications for the colorimetric determination of anions.

Further application of these generalizations would presumably be possible with substituted bipyridines and terpyridines. The success of this approach might be enhanced by a systematic study of the effect of different substituents. Also, it has never been demonstrated that substitution in the 4- or 7-position always produces the greatest increase in sensitivity, regardless of substituent.

2. Copper

The intense colors formed by compounds of the phenanthroline type with cuprous ion had been reported (275) and analytical application unsuccessfully attempted (213). However, the introduction of a less familiar bipyridine type of reagent, 2,2′-biquinoline, by Breckenridge, Lewis, and Quick (37) called attention to the cuprous reaction. Following a thorough investigation of many similar compounds by Hoste (139) and the establishment of the remarkable selectibity of the reaction, the determination of copper with biquinoline has been applied to several types of materials (60, 121, 126, 141).

The obvious steric factor which seemed to lead to the extreme selectivity of the copper reaction is also present in 2,9-dimethylphenanthroline (265). The increased sensitivity expected for 4,7-substitution was demonstrated with the 2,9-dimethyl-4,7-diphenylphenanthroline complex (269).

3. Other metals

The application of phenanthroline compounds to the colorimetric determination of metals other than iron and copper has been very limited. Terpyridine has been proposed as a reagent for cobalt (212), and phenanthroline for molybdenum (214). An attempt to utilize the strong ultraviolet absorption prompted proposals for the determination of cadmium (285) and zinc (173). These methods have not been utilized to any appreciable extent as yet. The first two systems are relatively unstable, and the last two present formidable experimental difficulties in the form of interferences in the ultraviolet region. Data from spectra for many phenanthroline and bipyridine complexes have been published (300, 301), but no methods proposed.

C. AS AGENTS IN PRECIPITATION

The trisphenanthroline ferrous ion is a good precipitant for many anions. Use of this fact has been made in the precipitation of the fluoride complex of tantalum (120). A good separation from niobium is possible. The qualitative solubilities of many other ions in hydrofluoric acid solution have been determined (120). The insolubility of the ferroin precipitates can be utilized to determine mercury by precipitation of the tribromomercuriate anion (128a) and for the precipitation of the hexaiodostannic(IV) ion (5). The iron–bipyridine complex also is a sensitive precipitant for many anions (111, 239), and can be used in a qualitative test for tannin in wine and leather (110). The bipyridine complex has been utilized in a scheme for microscopic identification of anions (191). The effect of substitution on solubility has been investigated with the 5-nitro and 5-bromo derivatives (268, 277). The solubility of the perchlorate salt of the ferrous complex increases in the order nitro derivative, bromo derivative, parent molecule.

The insoluble complex $Pd(phen)Cl_2$ has been used for the separation and determination of the metal (247, 248, 249). The stability of this complex in concentrated sulfuric acid is utilized in a unique recrystallization which enhances the value of the method (248).

D. MISCELLANEOUS APPLICATIONS

Various properties of complexes of the bipyridine type have been utilized to analytical advantage. Their stability has been used to remove the interference of iron in the determination of other metals. In this manner aluminum can be precipitated as the hydrous oxide while iron is held in solution as the bipyridine complex (261). Similarly the removal of iron interferences facilitates determinations of magnesium, beryllium, and titanium (114). The stability of the nickel and cobalt complexes permits a back-titration to determine the excess bipyridine after its precipitation as the silver complex (58). The oxidation–reduction potential of ferroin permits a colorimetric determination of vanadium (124, 156). High-frequency titrations of many metals can be successfully carried out (131). Phenanthroline complexes have been utilized in the drying of paint (217, 218, 294, 299) to compare the effects of complexed and uncomplexed metals as promoters of the drying of paints and ink (302).

XI. Biological Activity

A wide variety of biological systems are affected by the bases themselves and also by their metal complexes. The effects, however, are usually so distinct that it is evident that entirely different principles are involved in the mode of biological action.

A. EFFECT OF THE ORGANIC REAGENTS

When phenanthroline or bipyridine (or for that matter any substance capable of complex formation) is found to disturb the functioning of a biological system, it is usually assumed that the sequestration of trace metals is involved. These may be present as hydrated ions in the biological fluid medium or attached by some coördinate bonds to protein by sulfur and/or nitrogen linkages. Thus the metal ion may be rendered unavailable to the system if the stability of the complex formed is high. On the other hand, in a situation where the metal ion is bound to a protein surface, for instance, the reagent may attach itself to vacant coördination positions by displacement of aquo groups, thus altering the nature of the enzyme function. Inhibition of enzymes by complex-forming molecules is often used as an indication of a heavy metal constituent. The presence of a particular metal is often accepted when inhibition is caused by its specific analytical reagent, without realizing that true specificity is rare, and that the reaction tendencies may be very different when the metal ion is partly bound to a protein.

The organic molecule itself may be the effective biological agent without the intervention of a metal ion or even the free metal complex. It is unfortunate that all of these possible modes of action are not usually recognized by workers in this field. Generally one explanation is adduced, but the experimental work does not exclude the alternatives. The large amount of relevant work is only briefly surveyed here, and one hesitates to ascribe the biological effects to one particular mode of action.

The following systems were found to be affected by phenanthroline or bipyridine: succinic oxidase (4); triphosphopyridine nucleotide nitrate reductase (216); zymase (303); the reduction of fumarate and malate by molecular hydrogen in the presence of washed suspensions of *Escherichia coli* (176). The latter inhibition could be partially reversed by addition of metal ions. The action of liver and intestine phosphomonoesterases on β-glycerophosphate and of intestine pyrophosphatase on pyrophosphate (69, 70) was considerably accelerated by 5×10^{-4} *M* solutions of the bases.

The endogenous respiration of anabaema (a blue-green alga) (290) and the oxygen uptake (271) of green leaves were inhibited, but that of brain tissue was accelerated (224) by both reagents as well as by their iron(II) complexes. Bacteriostatic action of phenanthroline has been demonstrated on several tubercle bacteria (281), on a number of Gram positive organisms (28, 108), and on rumen bacteria (195). Several of the phenanthrolines inhibited the growth of many fungi (28). *m*- and *p*-Phenanthrolines were less effective than 1,10-phenanthroline, but 2,9-dimethylphenanthroline was the most potent inhibitor. Crude bipyridine oil, obtained from the pyridine sodium reaction, has been reported as toxic to aphides (245), but it has been shown (244) that the most active constituents were α,β-bipyridine and α,β-bipiperidine. A 33 per cent saturated solution of phenanthroline suppressed the chemotactic power of "guinea pig" leucocytes but did not destroy the cells (177). Highly potent anthelmintic action has been observed with both substances (7).

B. EFFECT OF THE METAL COMPLEXES

Metal complexes of phenanthroline, bipyridine, and terpyridine have high biological activity. Toxicity to mice and rats (91) and to frogs and rabbits (20), bacteriostatic and bacteriocidal properties (91), and action on enzymes (91, 92, 200, 224) and on neuromuscular transmission (25, 94) have been demonstrated. The metal complexes used in these investigations were all coördinately saturated and highly stable chemically and had no specific active groups or centers. The redox potentials were out of the biological redox range generally. Whereas chelating molecules themselves can enter into various chemical reactions in a biological system, these stable complexes, in which metal and chelate are held in the firm grip of each other, should be unaffected. The highly stable ruthenium(II) and osmium(II) complexes are ideal for this type of investigation. Beccari (21) has demonstrated that the trisbipyridine iron(II) cation is excreted unchanged through the kidneys of frogs and rabbits. The use of trisphenanthroline ruthenium(II) salts containing radioactive Ru^{106} and a chromatographic technique showed that this compound is not metabolized in rats and mice (91, 92).

Changing the metal in a series of complex cations $\mathrm{M(B)}_{2,3}^{n+}$ (where B = bipy, phen, or trpy, and M = Fe, Ru, Os, Co, Zn, In) left the biological reaction essentially unaffected. But if the ligand is altered—for instance, ethylenediamine is substituted for bipyridine—the biological effect is quite different. These observations indicate that the activity is due to the complex cation as a whole and not to its dissociated fragments. Since no chemical change is involved, the mode of action must be purely physical, such as adsorption. The substances are strongly adsorbed on protein and most likely on negative sites. As a result of the positive charge they may alter the isoelectric point of proteins and may depolarize charged surfaces. Such changes in the zeta potential often lead to changes of dispersity of colloids. By occupying negative sites they may block active spots on enzymes. Whatever the effect, it is caused by virtue of their positive charge or by their mere presence on an active site. The simple mode of action of these complexes offers a unique tool for the investigation of biochemical and physiological processes, and stable metal complexes will probably be used more widely in the future. The desirable features of chemical and biological stability are by no means restricted to complexes of the bipyridine type but apply to many others beyond the scope of this review.

The stereochemical specificity of biological systems towards these substances is noteworthy. In general, this difference is greater between the optical isomers than between complexes of the same configuration but containing different metals. The lethal intraperitoneal dose for a mouse is 5.8 mg./kg. for (+)-$Ni(phen)_3(ClO_4)_2$ but more than 11 mg./kg. for the (−)-form. At a concentration of 10^{-4} *M* the inhibition of the enzyme acetylcholinesterase is 70 per cent by (−)-$Ru(bipy)_3Cl_2$ but only 20 per cent by the (+)-form (91, 92).

The results obtained by the detailed investigations of Beccari (20, 21, 22, 23, 24) with $Fe(bipy)_3^{++}$ on rabbits, and by Dwyer, Rogers, and coworkers (91, 92) with $Ru(phen)_3^{++}$ on rats and mice, using radioactive tracer methods, show a close resemblance. Very small amounts were lethal when introduced intraperitoneally, intravenously, or subcutaneously, but even large oral doses did not cause death. Absorption through the intestine was slow (this has also been observed on humans) (243) and, owing to rapid elimination through the kidney, it was not possible to build up the lethal concentration in the blood. Some indications were obtained of the iron compound being split by intestinal bacteria (20), but no changes were observed with the much more stable ruthenium compound. The (+)-form of the ruthenium–phenanthroline compound is more rapidly absorbed from the intraperitoneal cavity than the (−)-form, and also excreted more rapidly through the kidney. A dose of previously injected (−)-compound suppresses the adsorption of the (+)-compound. Thus an animal which had previously been injected with half the toxic dose of the (−)-compound survived a lethal dose of the (+)-form.

The symptoms caused by the complexes, i.e., torpor, tremor, paralysis of the limbs, clonic convulsions, an unaffected heart, and death due to respiratory failure, indicated an attack on the central nervous system. This has been supported by the finding that these substances are potent inhibitors of acetylcholinesterase (91, 92), and that they have a curare-like action on the neuromuscular transmission (25, 94). Acetylcholinesterase is thought to have two active sites—a negatively charged one, and a so-called esteractic site. The inhibition is competitive and presumably due to adsorption of the positive ions on the anionic sites (92).

Neuromuscular transmission studies have been carried out by Beccari (25) and Dwyer and coworkers (94) on rather similar lines. It is unfortunate that a detailed account of Beccari's work is unavailable. Nervous conduction does not seem to be affected (25), but curare-like effects were obtained on the endplate potentials at synaptic junctions (25). Neuromuscular block was observed at low concentrations with rat diaphragm preparations (94); the response of the frog rectus abdominis preparation to acetylcholine was inhibited (94). Normal activity could be restored by washing out the complexes.

Similar behavior of compounds of such different chemical constitution as curare, decamethonium salts, and the metal complex cations indicates that the common features of low chemical reactivity and the positive charge are the important ones.

It is generally believed that the positive charge associated with a complex cation is not localized on the central metal atom but is fractionally distributed over the complex (226). Since the size of the cations in a series $M(phen)_3^{++}$ is probably very similar, quantitative differences in their biological action should be due to differences in the peripheral charge. These seem to follow a certain order:

Action on rat diaphragm preparation (bipyridine series, *dl*): Fe > Ni > Ru, Os > Zn

Frog rectus abdominis preparation (phenanthroline series, *dl*): Ni > Fe > Ru > Zn

Inhibition of acetylcholinesterase (terpyridyl series): Fe < Ni < Ru < Os. Similarly, $Ni(5\text{-}NO_2\text{-}phen)_3^{++} < Ni(phen)_3^{++} < Ni(5\text{-}Cl\text{-}phen)_3^{++} < Ni(5\text{-}CH_3\text{-}phen)_3^{++}$

The last series of substituted phenanthrolines does not follow the same order as the p*K* of the bases. At the moment it is not possible to predict even qualitatively the order of increasing peripheral charge in such a series of complexes with different metals. Apart from considerations of electronegativities, such factors as amount of double bonding and the use of higher or lower *d*-orbitals could affect the charge distribution.

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