The classic work on the stereochemistry of metal complexes first gave formulation to the geometric structures of coordination compounds at the turn of the century. The work revolved around the amines of cobalt(III), [Co(NH₃)₆]³⁺, and those of Pt(II), [Pt(NH₃)₂(X)₂]²⁻. These works depended heavily on studies on isomerism, both optical and geometrical, but also reflected the application of what physicochemical tools were available. The subject has been reviewed excellently in a number of sources, of which the outstanding treatments are to be found in the books by Bailar (1) and Grinberg (2). Many recent observations are included in the review by Wilkins and Williams (3). Although early studies were certainly elegant and decidedly thorough in many cases, a number of compelling questions escaped solution or even modest progress until quite recently.

Early techniques were adequate only in dealing with complexes that are kinetically stable. Thus, the importance of Co(III) and Pt(II) to inorganic chemistry during the early decades of this century derives more from the fact that compounds containing these ions are relatively inert in the kinetic sense rather than from any intrinsic significance. The two ions have been of equal importance for each has served to epitomize the inorganic chemistry of an ion such as Co(II), Cu(II), Ni(II), and Cu(II), remained contradiction-ridden and questionable until the development of modern crystal field (or ligand field) theory. To be sure, a few structures were proved early by definitive X-ray studies, and optical isomerism was observed among some six coordination complexes of divalent ions. Indeed, geometric isomerism was known in the case of planar Ni(II). Yet as one viewed the overall chemistry of an ion such as Ni(II) or Co(II), he was confronted with a bewildering array of possibilities with only moderate probability of finding a criterion adequate to settle the structure, short of complete X-ray work.

Applications of Modern Theory

The applications of crystal field theory, and its more sophisticated molecular orbital counterpart, may be illustrated with a very few examples (4-8). The simple idea of a crystal field stabilization energy (CFSE) (9), differing according to atomic number, number of d-electrons, and nature, number, and geometric arrangement of ligands, leads to the prediction that in those cases where the difference in CFSE is a determining factor, ions with 3 or 8 d-electrons would show a marked preference for octahedral coordination as compared to a tetrahedral arrangement of ligands. This is illustrated in Table 1 in the column marked Δ CFSE. The interpretation of the data is that tetrahedral should be rare for d⁴ and d⁸ and most common for d⁷, d⁵, d⁶, d⁴, d⁵, d⁸. A most important consequence of this prediction was the realization that the many nickel(II) complexes long believed to contain tetrahedral coordination spheres were most probably octahedral.

Table 1. CFSE and Relative Stabilities of Tetrahedral and Octahedral Structures

<table>
<thead>
<tr>
<th>Configuration</th>
<th>CFSE(Dq)</th>
<th>Δ CFSE(Dq)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Octahedron</td>
<td>Tetrahedron</td>
</tr>
<tr>
<td>d^4</td>
<td>4</td>
<td>2.67</td>
</tr>
<tr>
<td>d^5</td>
<td>&lt;8</td>
<td>5.34</td>
</tr>
<tr>
<td>d^6</td>
<td>12</td>
<td>3.56</td>
</tr>
<tr>
<td>d^7</td>
<td>6</td>
<td>1.78</td>
</tr>
<tr>
<td>d^8</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>d^9</td>
<td>4</td>
<td>2.67</td>
</tr>
<tr>
<td>d^10</td>
<td>&lt;8</td>
<td>5.34</td>
</tr>
<tr>
<td>d^11</td>
<td>12</td>
<td>3.56</td>
</tr>
<tr>
<td>d^12</td>
<td>6</td>
<td>1.78</td>
</tr>
<tr>
<td>d^13</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

This has been amply demonstrated and it is a by-product of these deductions that it has been intriguing to discover and study true tetrahedral complexes of Ni(II) (10). Perhaps the prime example of such species is NiCl₄²⁻.

In a still more approximate manner, the modern theories clearly agree with the relatively frequent occurrence of square planar structures among ions of...
$d^r$, $d^s$, and $d^p$ configurations, as illustrated (after Pearson (9)) in Table 2.

<table>
<thead>
<tr>
<th>Table 2. CFSE and Relative Stabilities of Octahedral and Square Planar, Strong Field Complexes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Configuration</td>
</tr>
<tr>
<td>$d^r$</td>
</tr>
<tr>
<td>$d^s$</td>
</tr>
<tr>
<td>$d^p$</td>
</tr>
<tr>
<td>$d^{2s}$</td>
</tr>
<tr>
<td>$d^p$</td>
</tr>
<tr>
<td>$d^p$</td>
</tr>
<tr>
<td>$d^p$</td>
</tr>
<tr>
<td>$d^p$</td>
</tr>
<tr>
<td>$d^p$</td>
</tr>
</tbody>
</table>

Concurrent with the emergence of these predictions has been the development of more detailed interpretations of magnetic moments and electronic spectra as useful, if not necessarily definitive, criteria for geometric structure. This is illustrated in Tables 3 and 4, where the usual magnetic and spectral features of planar, tetrahedral, and octahedral nickel(II) complexes are compared. Under favorable conditions, the number, intensity, and positions of the d-d electronic absorption bands provide a distinction between these structures. The “strong field” configurations and experimental ranges of magnetic moments for the three classes of nickel(II) complexes, as given in Table 4, often provides strong corroborate evidence as to stereochemistry. Similar summaries may be assembled from available data on other metal ions.

<table>
<thead>
<tr>
<th>Table 3. Variation of Magnetic Moment of Nickel(II) Complexes with Geometric Structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Octahedral</td>
</tr>
<tr>
<td>$\mu_{\text{eff}}$</td>
</tr>
<tr>
<td>Examples: Ni(H$_2$O)$_6^{2+}$, Ni(NH$_3$)$_4^{2+}$, Ni(dipy)$_2^{2+}$</td>
</tr>
<tr>
<td>Tetrahedral</td>
</tr>
<tr>
<td>$\mu_{\text{eff}}$</td>
</tr>
<tr>
<td>Examples: NiCl$_4^{2-}$, NiBr$_4^{2-}$, NiBr$_4^{2-}$, 2P(C$_4$H$_9$)$_2$</td>
</tr>
<tr>
<td>Square planar</td>
</tr>
<tr>
<td>$\mu_{\text{eff}}$</td>
</tr>
<tr>
<td>Examples: Ni(CN)$_4^{2-}$, Ni(DMG)$_4^{2-}$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 4. Spectral Properties and Stereochemistry of Ni(II)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Octahedral</td>
</tr>
<tr>
<td>$1/\lambda_{\text{max}}$</td>
</tr>
<tr>
<td>8000–13000</td>
</tr>
<tr>
<td>14000–19000</td>
</tr>
<tr>
<td>25000–30000</td>
</tr>
</tbody>
</table>

Although the geometric isomers of the cobalt(III) tetranines have been known for many years, the application of modern measurements and symmetry considerations has provided techniques that may, in some cases, serve to distinguish between the cis and trans forms relatively easily. The trans isomer of Co(NH$_3$)$_4$Cl$_2^{+}$ has $D_{4h}$ symmetry while the cis isomer is only $C_2$, in symmetry. The reduction in symmetry from $D_{4h}$ to either that of the cis or trans isomer results in the splitting of the orbitally degenerate excited states; however, the number of states produced by the splitting is greater in the case of the cis isomer while the separation between individual states produced by the splitting is sometimes greater in the case of the trans isomer. Thus, in the optical spectrum of the cobalt(III) complexes, the bands of the trans isomer are less symmetrical or are sometimes resolved into two components (3). On the other hand the group vibrational frequencies of coordinated amines are commonly split in the case of the cis isomer and not in the trans case. Infrared spectra may be utilized to distinguish the isomeric structure of such carbonyl derivatives as Cr(CO)$_4$B$_2$ (12, 13).

**Optical Activity**

Although the optical activity of metal complexes has received much attention since its discovery by Werner more than half a century ago, a number of very basic issues remain open to investigation. It cannot be claimed that the ultimate source of the rotational power has been interpreted on a broad and detailed theoretical base. A number of investigators have considered the problem, particularly as regards the tris bidentate complexes such as the ethylenediamine complex of cobalt, Co(en)$_3^{3+}$; however, most of these efforts have fallen short of their objectives (14). The most promising theoretical model has not yet been applied to a valid experimental case, but is generally consistent with fact. The earlier efforts were based on the electrostatic model while the latest theoretical treatment involves molecular orbital theory. It appears likely that the rotation cannot simply be ascribed to the perturbations associated simply with the $D_{3d}$ symmetry of the immediate environment of the metal ion. Liehr associates the optical rotation with an angle of cahn, $\alpha$, between the ligand donor orbitals and the metal acceptor orbitals. This implies a strong sensitive dependence of the strength and, perhaps, sign of rotation on ring size and other steric factors (for a given metal ion) as well as on the absolute direction of spiral of the helically disposed bidentate ligands.

**Absolute Configuration**

One of the principal needs of the area relates to the establishing of methods for the determination of the absolute configuration of complexes. Perhaps the most significant experimental result concerning the optical activity of metal complexes during the past decade is the establishing of the absolute configuration of $\textbf{(+)Co(en)}_{3}^{3+}$ ion by a refined X-ray study (15). As shown in structure I, the so-called d-isomer, which has a specific rotation of $+440$ degrees circular
at the mercury green line, has its ligands so arrayed that the structure is similar to that of a left-handed, three-bladed propeller. Thus, the isomer long referred to as dextro actually has a natural screw-form that is left handed according to mechanical conventions. Recognizing the difficulties of nomenclature that so often occur in treating the subject of absolute configuration, Piper (16) has proposed that absolute right-handed helical molecules or ions be called delta (Δ) and the enantiomers be called lambda (λ). The significance of this determination lies in the fact that the availability of a single species for which the absolute configuration is known opens the possibility of the rapid establishment of the absolute configurations of many other related substances through relatively simple techniques for the determination of relative configuration. Such techniques have been considered at length by Basolo (17, 18).

The use of rotatory dispersion measurements has received renewed attention recently in attempts to relate the configurations of complex ions (19, 20). Despite the difficulty of developing detailed theories, the fact remains that the metal ion in an optically active octahedral complex generally constitutes a chromophore congruent with the “center of dissymmetry.” Consequently the absorption bands of the metal ion are optically active. In the case of (+)-Co(en)₃²⁺, absorption bands occur at 470, 340, and 218 μ. Of these only the first and last contribute materially to rotatory power. The rotatory dispersion curves for cobalt(III) complexes have long been suspected of containing sufficient information to relate the configurations of many complexes. Because of the relative ease of measurements, attention has focused on the long wavelength band. The rotatory dispersion curve of (+)-Co(en)₃²⁺ is given in Figure 1. The enantiomer exhibits a rotatory dispersion that is the mirror image of this curve. For very similar complexes, it is not difficult to accept the assignment of relative configuration on the basis of corresponding rotatory dispersion curves. For example, [(+)-Co(en)]⁺⁺, [(+)-Co(-)(pn)l]⁺⁺, [(+)-Co(−)(pn)(en)]⁺⁺, [(+)-Co(−)(en)]⁺⁺, and [(+)-Co(−)(en)]⁺⁺, almost certainly have the same configuration (19).

In all these cases, the spectral band (′A₁₂ → ′T₁₂) occurs at essentially the same position with very little alteration in its shape. Except for the last example, all contain 3 five-membered chelate rings. The similarities in the rotatory dispersion curves of (+)-[Co(en)₃]²⁺, (-)-[Ir(en)₃]²⁺, (−)-[Rh(en)₃]²⁺, and (−)-[Cr(en)₃]²⁺ suggest that the configurations correspond. Certainly, all the ions except Cr(III) are δ in configuration and the transition involved is ′A₁₂ → ′T₁₂.

In the two particular series cited, additional evidence supports the conclusion that the configurations are all congruent. The relative solubilities of diastereoisomeric salts corresponds. (17)-[Co(en)₃]Cl(+)—tartrate = 5H2O (−)-[Rh(en)₃]Cl(−)—tartrate = 4H2O are least soluble, as are the (+)-nitrocamphor salts of (−)-[Cr(en)₃]³⁺, (−)-[Rh(en)₃]³⁺, and (−)-[Ir(en)₃]³⁺. All the ions reputed to be of the same configuration exhibit Cotton effects of the same sign. Finally, a third point of evidence is found in the method of active racemates (18) due to Delepine. In some crystals of racemic materials the enantiomeric sites are distinct and present in stoichiometric ratio. When this is true an isomorphous complex ion of another metal ion may replace one of the enantiomers. Thus, in [(+)-L(-)]Co(en)₃Br₃, the d(+) isomer may be replaced by (−)-[Rh(en)₃]³⁺. This means that (−)-[Co(en)₃]³⁺ and (−)-[Ir(en)₃]³⁺ have the same configuration.

Some similar series may be set up in the case of other ligand types (21); however, it is relatively difficult to connect the various series to one another.

On the basis of similar RD curves, corresponding solubilities, and relative toxicities of enantiomers (21), the following series have been assigned.

(A) (−) [Ni(phen)]⁺⁺, (−)[Ru(phen)]⁺⁺, (−) [Os(phen)]⁺⁺
    (−) [Fe(phen)]⁺⁺ (?)

(B) (−) [Co(C₅O₆)]⁺⁺, (−)[Rh(C₅O₆)]⁺⁺
    (−) [Ir(C₅O₆)]⁺⁺, (−)[Cr(C₅O₆)]⁺⁺

Some of the difficulties and uncertainties of studies in this area become evident even with these relatively ideal, rather selected series. The solubility criteria are based on a complex phenomenon. In some cases (e.g., [Ni(dipy)]₃[tart]-·6H₂O) rapid crystallization with excess anion will bring down one diastereoisomer while slow crystallization from stoichiometric solutions will yield the other.

Many more interesting examples exist among complexes of still lower symmetry, where uncertainties mul-

![Figure 1. The rotatory dispersion of d-(+)-Co(en)₃²⁺.](image)

![Figure 2. Rotatory dispersion curves for (+)-[Co(en)₃]NH₄Cl]⁺⁺, (-)-[Co(en)₃]NH₄Cl]⁺⁺, (-)-[Co(en)₃]NO₃]⁺⁺, and (+)-[Co(en)₃]NO₃]⁺⁺.](image)
tially in the cases of most criteria for configuration. The formation of a cis-tetramine of cobalt(III) leads to a splitting of the optically active \( \Delta \epsilon_1 \rightarrow \gamma \gamma_1 \) transition into three bands, at least two which are optically active. Further the two components of the RD curve may exhibit similar or inverse behaviors. Despite these difficulties, rather convincing correlations have been derived from the combination of RD data and kinetic results (19). This may be illustrated with the series of compounds \((+)-[\text{Co}(en)_2(\text{NH}_3)X]^{3+}\), where \(X = \text{Cl}, \text{H}_2\text{O}, \text{NO}_2, \text{NH}_3\). The RD curves correspond rather closely in shape and exhibit shifts consistent with the spectrochemical series (Fig. 2). Further, the configurations may be related by the reaction sequence

\[
(+)-\text{[Co(en)\textsubscript{2}(NH\textsubscript{3})Cl]\textsuperscript{3+}} + \text{H}^+ \rightarrow (+)-\text{[Co(en)\textsubscript{2}(NH\textsubscript{3})H\textsubscript{2}O]\textsuperscript{3+}} \rightarrow \text{[Co(en)\textsubscript{2}(NH\textsubscript{3})NO\textsubscript{2}]\textsuperscript{3+}}
\]

The first step, aquation of \([\text{Co(en)\textsubscript{2}(NH\textsubscript{3})Cl]}^{3+}\) is reported to proceed with at least 75\% retention of configuration. Conversion of the aquo complex \([\text{Co}(en)\textsubscript{2}(\text{NH}_3)\text{H}_2\text{O}]^{3+}\) into the nitrite derivative proceeds without rupture of the cobalt-oxygen bond, via the nitrito complex. This process occurs with 93\% retention of configuration (23). Clearly the RD and reaction sequence results are in complete accord (19) for the three cases involved. The fourth member of the series \([\text{Co}(en)\textsubscript{2}(\text{NH}_3)\text{Cl}_2]\) may be included with similar assurance as a result of synthetic work in liquid ammonia, whereby Archer and Bailar (24) have shown that the conversion

\[
(+)-\text{[Co(en)\textsubscript{2}(NH\textsubscript{3})Cl]}^{3+} \rightarrow (+)-\text{[Co(en)\textsubscript{2}(NH\textsubscript{3})\text{Cl}_2]}^{3+}
\]

proceeds with better than 80\% retention of configuration. Since the configuration of \((+)-\text{diamino} \text{compound}\) has been related to that of \((+)-[\text{Co(en)}^3]^{3+}\), the absolute configurations of all four ions have been demonstrated. In a similar but perhaps less complete, manner the absolute configurations of a series of ions of the form \([\text{Co(en)}^3XY]\) have been suggested. These include \((+)-[\text{Co(en)}^3(\text{H}_2\text{O})_3]^3+, \text{(+)Co(en)}^3(\text{NO}_2)_3]^3+, \text{and (+)-Co(en)}^3(\text{NH}_3)_3]^3+. Clearly one may conclude that the utilization of the results of rotatory dispersion studies and those of investigations on kinetics and mechanism have led to substantial advances as regards the absolute configurations of a variety of optically active six-coordinate complexes. Further advances in both the experimental and theoretical aspects of configuration are to be anticipated; however, innovation in both experiment and theory will be required to include such novel optically active species or that given in structures II and III (24).

\[
\text{Py} \quad \text{Br} \quad \text{Cl} \quad \text{NO}_2 \quad \text{NH}_3
\]

\[
\text{Pt(IV)} \quad \text{II} \quad \text{Py} \quad \text{Br} \quad \text{Cl} \quad \text{NO}_2 \quad \text{NH}_3
\]

\[
\text{Pt(IV)} \quad \text{III}
\]

**Stereospecificity**

Bidentate ligands that are dissymmetric may, of course, produce isomers. For example all three amino groups may be located at the corners of a triangular face in octahedral tris(glycine)cobalt(III), or, alternatively, the three amino groups may be distributed along an edge.

In the case of optically active ligands, further complications arise, producing many possible isomers. Proplyenediamine, \(\text{NH}_2\text{CH}(\text{CH}_2)\text{CH}_2\text{NH}_2\), is unsymmetric in the same sense as is glycine. In addition it is optically active. Thus, if meso proplyenediamine were used to produce \([\text{Co}(\text{pn})]^3+\), one might immediately expect the following isomers:

- \(\text{f-3}(\text{ddd}), \text{f-3}(\text{ddi}), \text{f-3}(\text{dli}), \text{f-3}(\text{lil}), \text{f-3}(\text{lil}), \text{f-3}(\text{lid})\),
- \(\text{f-3}(\text{ ddl}), \text{f-3}(\text{ddi}), \text{f-3}(\text{ddl})\)

all of which would have the three methyl groups nearest a single face (facial isomers, denoted here by the prefix \(f\)), plus an additional number of isomers in which the methyl groups are nearest a single edge (peripheral isomers), e.g., \(p-b(ddd)\).

Although sixteen isomers are predicted, very marked selectivity occurs during synthesis of the compound. In fact, early studies revealed remarkably few isomers (18). These early conclusions are:

1. The configuration of the ligand is absolute in determining the configuration of the complex.
2. For a given ligand, only one isomer can enter the coordination sphere of a particular metal ion.

Only \(n(\text{iii})\), not \(n(\text{dld})\).

Such conclusions were based on early studies on tris(trans-1,2-cyclopentanediylene)-rhodium(III) and on \([\text{Co}(\text{pn})]^3+\) and \(\text{Pt}(\text{pn})^3+\). The first anomerises arose almost as early. Lifschitz (25) isolated both diastereoisomers of the soluble geometric isomer of tris(alanine)-cobalt(III), \(\text{d}(\text{ddd})\) and \(\text{l}(\text{ddd})\). In 1939, Bailar and McReynolds isolated both optical forms of \([\text{Co}((\text{l}-\text{pn})^3+\text{CO}_3)]^3+\) (26).

Quite recently, the research of Dwyer and co-workers have made clear the thermodynamic aspects of this stereospecificity. The selectivity is relatively small, energetically, but sufficient to influence greatly the relative yields of the isomers found. In the cases of both \([\text{Co}(\text{pn})]^3+\) and \(\text{Pt}(\text{pn})^3+\), two racemates have been isolated and identified (27, 28). In all, the following isomers were observed: \(n(\text{ddd}), n(\text{iii}), n(\text{lil}), n(\text{ddi})\).

In his attempts to produce complexes containing ligands of opposite configurations, Jaeger invariably observed disproportionation (29). For example,

\[
[\text{Co}(\text{+}(\text{pn})\text{Cl})^3+] + (\text{pn}) \rightarrow (1/2)[\text{Co}(\text{+}(\text{pn})\text{Cl})^3+] + (1/2)[\text{Co}(\text{-}(\text{pn})\text{Cl})^3+] + 2\text{Cl}^{-}
\]

Cobalt(III) was a most unfortunate choice for these studies for it is highly likely that the apparent dismutation is the result of the presence of a small amount of cobalt(II) which in the presence of amines will facilitate equilibration via a rapid electron transfer mechanism. Dwyer has shown that the reaction of \([\text{Co}(\text{en})\text{Cl}_2]^+\) with \((\text{-}(\text{pn}) \) yields all possible compounds:

\[
[\text{Co}(\text{en})]^3+, [\text{Co}(\text{en})\text{(}(\text{-}(\text{pn})\text{)}]^3+, [\text{Co}(\text{-}(\text{pn})\text{)}]^3+, [\text{Co}(\text{-}(\text{pn})\text{)}]^3+
\]

Further, it has been shown that the products occur in the statistically predicted abundance (30).

Platinum(IV) has provided a useful vehicle for the
clarification of the question of the ligand-ligand interactions which depends on absolute configuration (31). The reaction of interest is given below.

\[ \text{[Pt}^-(\text{pn})\text{Cl}]+2^+(\text{pn}) \rightarrow \text{d,L- [Pt}^-+(\text{pn})^3++ \]

This and d,L-[Pt(+)(pn)(-)(pn)]^3+ have been resolved into d and L forms. The compounds are extremely stable and unreactive. The isomer yields prepared in this way are essentially kinetically determined since the D:L ratio for Pt(-)(pn)n^3+ prepared in this way is \( \frac{3}{2} \) while the equilibrium ratio is \( \approx 7/1 \).

A classic paper by Bailar and Corey (1959) provides the basis for understanding many of the observations reported on stereospecificity among complexes (32). This represents the first substantial application of conformational analysis to the problem represented by chelate rings.

In Co(en)n^2+, strain-free rings are formed in which the conformation is a staggered or gauche form. However, two such forms are possible and the repulsions between the atoms of the three rings differ according to the form present. The two forms produce different relationships among the skeletal atoms of the structure. For a d-isomer, in the so-called k-rings, the C-C axis is parallel to the major 3-fold axis of the octahedron. The second or k'-ring is slanted or staggered with respect to the major 3-fold axis. This is shown in Figure 3. Further, the k-ring is predicted by calculation to be more stable by about 0.6 kcal/mole than the k'-ring, in a dextro tris-octahedral structure.

Actually, Co(en)n^2+ could be kkk, kkk', k'k'k', or k'k'k'. The analysis shows the kkk form to be favored by about 1.8 kcal/mole or 0.6 kcal per ring on a molar basis. This selectivity occurs because of H-C interactions which appear to account for some 95-99% of repulsion. This conclusion is sustained by the crystal structure of the compound.

These results may be applied immediately to the propylenediamine complexes since the absolute configuration of pn has been determined (33, 34). \( L(+) \) pn has the absolute configuration given in structure IV.

\[
\begin{align*}
\text{CH}_2\text{NH}_2 \\
\text{H}_2\text{N} & \text{C} & \text{H} \\
\text{CH}_3 \\
\text{IV} \\
\end{align*}
\]

In order to minimize repulsions, the methyl group must occur in an equatorial orientation, structure V. Further, for a given isomer of pn, the placing of the CH₃ group in the equatorial position is equivalent to specifying whether the ring is k or k' in configuration. The more stable form of Co(pn)n^2+ should certainly have the k conformation in its rings. These relationships are shown in detail in Figure 3 and structures I, IV, and V. We can now understand clearly why D(+)Co(+)pn^2+ is the more stable isomer and more abundant in synthetic systems at equilibrium.

This has been further demonstrated by studies on the equilibrium mixture of products from systems containing en and (-)pn, and is summarized below (31).

\[
\begin{align*}
\text{Ratio} & \quad \Delta F \\
L-[\text{Co(en)}(\text{-})(\text{pn})^3]^{+}/n-[\text{Co}(\text{en})(\text{-})(\text{pn})^3]^{+} & \quad 2/1 & \quad 0.4 \\
L-[\text{Co(en)(-)}(\text{pn})]^{3+}/(\text{L})-[\text{Co}(\text{-})(\text{pn})]^{3+} & \quad 6/1 & \quad 1.1 \\
L-[\text{Co}(-)(\text{pn})]^{3+}/(\text{L})-[\text{Co}(-)(\text{pn})]^{3+} & \quad 13/1 & \quad 1.5 \\
\end{align*}
\]

As seen, the k'-ring isomer favors the L (or A) octahedral isomer roughly in proportion to its abundance.

The requirement that the bulky group occupy an equatorial position is well supported by equilibrium data on complexes of C-substituted ethylenediamines. For the reaction

\[ \text{Ni}^{2+} + 3\text{AA} \rightarrow \text{Ni(AA)}_3^{2+} \]

the value of log \( K_T \) for en, pn, and d, l-bn (bn = NH₂CH(CH₃)CH(OH)NH₂) is 20.05, 19.77, and 20.39, respectively (55). In these cases, it is possible for all methyl groups to assume equatorial orientations. However, in meso-bn and in \( t \)-bn (NH₂CH(CH₃)₂CH₂NH₂) one of the methyl groups must be axial. In the latter cases, log \( K_T \) is greatly reduced, being 16.74 and 15.98 respectively. In the case of tetramethyl-
ethylenediamine, the repulsions are so great that the tris complex is not formed.

Probably the most dramatic example of stereospecificity in the course of reactions of complexes is that occurring when the cobalt(III) complexes of EDTA and PDTA react with ethylenediamine (36, 37).

\[
(+\text{-}[\text{Co(EDTA)}])^+-3\text{en} \rightarrow (+\text{-}[\text{Co(en)}])^3+ + \text{EDTA}^{-}\]

\[
(-\text{-}[\text{Co(EDTA)}])^3+ + 3\text{en} \rightarrow (+\text{-}[\text{Co(en)}])^3+ + \text{EDTA}^-+X^-\]

For first equation and second, when \( X = \text{Cl, Br} \), the yields of (+) isomer of product is \( \leq 63\% \); when \( X = \text{NO}_2^- \), a racemate is produced.

\[
(+\text{-}[\text{Co(PDTA)}])^3+ + 3\text{en} \rightarrow (+\text{-}[\text{Co(en)}])^3+ + (+\text{-}\text{PDTA})^-\]

Yields of excess isomer is 100%.

As a result of stereochemical studies and detailed investigation of the kinetics of these fascinating processes, mechanisms and complete unequivocal stereochemical paths have been deduced (37). The kinetically derived mechanism is shown below.

\[
\text{Co(EDTA)}^- + \text{en} \xrightleftharpoons[k_{-1}]{h_1} [\text{Co(EDTA)}\text{en}]^- \text{(monodentate en)}
\]

\[
[*\text{[Co(EDTA)en-H]}]^{3-} \xrightarrow[K]{+\text{OH}^-} [+\text{[Co(EDTA)en-H]}]^{3-}
\]

\[
[\text{Co(EDTA)}\text{en-H}]^{3-} + 2\text{en} \xrightarrow{\text{fast}} \text{EDTA}^3+ + \text{Co(en)}^3+\]

When corrections are made for competing hydrolysis reactions, the equation representing this mechanism is obeyed over a range of \([H^+]\) that is 3160 fold and an \([\text{en}]\) range of 575 fold.

The critical kinetic intermediate involves monodentate coordination of the first molecule of en. This species is assumed present in accord with steady state approximations. It is capable of initiating rapid successive substitution steps via an Sx1cb mechanism (9), a proposal in excellent accord with the data. The form of the rate law is such that en must enter the mechanism before \( \text{OH}^- \). Further, though \([\text{OH}^-]\) is in the rate law, that species functions entirely as a catalyst.

Although monodentate complexing of ethylenediamine is required in the critical kinetic intermediate, the manner of chelation of the first molecule of en is critical to the stereospecificity of the reaction. Only readily acceptable assumptions need be made in this regard. (1) The multiply connected ligand will prevent rearrangement. (2) Cis groups, not trans groups, will be replaced. (3) No group is replaced if it is still bound in two chelate rings. Proceeding in this manner, three stereochemical intermediates of similar, or possibly identical, probability may be formed with the first molecule of en. As the additional molecules of en are added, two of the stereochemical intermediates produce racemic \([\text{Co(en)}]^{3+}\). The intermediate showing selectivity involves replacing two equivalent carboxyl groups from the plane of the three fused chelate rings (structure VI). This intermediate produces \([\text{Co(en)}]^{3+}\) of the same absolute configuration as the starting material. Further, the simple conversion

\[
(+\text{-}[\text{Co(EDTA)}])^3+ \rightarrow (-\text{-}[\text{Co(EDTA)}])^- + X^-\]

provides a check on the relationships given. Also, the fact that \([+\text{-}\text{Co(EDTA)}\text{NO}_2^-]\) yields only racemic \([\text{Co(en)}]^{3+}\) is of much significance, for the \(\text{NO}_2^-\) group is held very tightly and most probably occupies one of the positions that must be freed to produce the intermediate that causes stereospecificity. The absolute stereochemical relationships proved in this way are shown in Figure 5.

![Figure 5. Absolute configurations of EDTA complexes (signs refer to rotation at mercury green line).](image)

In the PDTA case, the absolute configuration of the ligand can be deduced from that of pn, while that of the complex follows from \([\text{Co(EDTA)}^-\]). In conformance with expectation, the methyl group in the only known isomer is oriented equatorially. This ligand is perhaps the most extreme in its determination of the geometry of an octahedral complex, the second diastereoisomer does not exist in detectable amounts (38).

It should be recalled that the reaction of \([+\text{-}\text{[Co(PDTA)]}^-\] with en produces \([\text{Co(en)}]^{3+}\) in a totally resolved form and with the opposite configuration to that found in the case of \([+\text{-}[\text{Co(EDTA)}])]^-\) (37). The kinetics of the reactions are essentially the same so that the mechanism must be unaltered except as regards the relative importance of the critical stereochemical intermediates. Since none of the \([\text{Co(en)}]^{3+}\) is of the same configuration as the starting material, the two carboxyl groups coplanar with the \(-\text{C}-\text{C}-\text{N}\) ring of PDTA are not replaced by the same en molecule. The presence of the \(\text{CH}_3\) group has caused the otherwise pairwise identical carboxyl groups to be distinct. In fact, the two groups attached to chelate rings in closest proximity to the \(\text{CH}_3\) group would be expected to be most reactive. Assuming these two groups to be replaced by the first molecule of en and proceeding as before, it is seen that inversion is favored. It is to be expected that the combination of kinetic, structural, and conformational techniques will lead to continued advances in the area of stereospecificity.
Linkage Isomers

The existence of isomeric forms of complexes containing monodentate ligands bound in different ways was first observed in the case of cobalt(III) complexes of nitrite ion in 1893; however, the phenomenon has been extended to include rhodium(III), iridium(III), and platinum(II) complexes only recently (39). The second example of ligand manifesting linkage isomerism was reported by Basolo, Burmeister, and Poe in 1963 (40). The reaction of \(K_2Pd(SCN)_4\) with 2,2'-bipyridine (\(N=\dot{N}\)) in alcohol at \(-78^\circ C\) leads to the formation of the sulfur-bonded complex (structure VII).

When this substance is heated to 150\(^\circ C\), it undergoes rearrangement, forming the nitrogen bonded isomer (structure VIII).

A rather closely related phenomenon of much stereochemical significance, but not involving isomerism has been termed flexidentate chelation. Polyfunctional molecules are often capable of coordinately in a variety of ways, depending on which of their donor groups are bound to a metal ion. The phenomenon is perhaps best illustrated with the simplest amino acid, glycine. In the more familiar complexes, the glycinate anion forms bidentate derivatives as in \([\text{Co(NH}_3\text{CH}_2\text{CO}_2]_2\). However, under certain conditions monodentate coordination occurs, e.g., \([\text{CoCl}_6(\text{NH}_3\text{CH}_2\text{CO}_2\text{H})_2]_2\) (41). Similarly, the anion of EDTA has been found to bind in stable complexes in which it is sexadentate (Fig. 5) (42) pentadentate (Fig. 5) (43), tetradentate (structure IX) (44), and bidentate (structure X) (44).

The significance of this phenomenon may be seen in the fact that a number of naturally occurring amino acids (e.g., cystine, ornithine) undergo such variations in mode of chelation. Further the interaction of metal ions with complex natural substances in biological systems or with polyfunctional medicinals is almost certainly complicated by behaviors of this sort. This is emphasized by X-ray structural results (45) that indicate that in central media, peptide units of glycylglycylglycine bind to copper(II) ion through a terminal amino group and the carbonyl oxygen atom, while in basic systems binding is by means of terminal and ionized amido nitrogen atoms.

Electronic Isomers

For the electronic configuration of free metal ions \(d^4\), \(d^5\), \(d^6\), \(d^7\), and \(d^8\), both high-spin and low-spin complexes have been known for many years. Modern theory suggests that the right balance of structural parameters for a given ion (having such a configuration) might lead to the coexistence of the two spin states. This would represent an isomerism dependent principally on electronic arrangement alone.

It is an interesting fact that relatively detailed theoretical treatments (46) were developed for the case of tetragonal nickel(II), but that the suspected examples have all been shown to involve variations in molecular as well as electronic structure.

Eaton, Phillips, and Caldwell (47) have established that the unusual isomerism of the nickel(II) complexes of aminotropaneimine derives from a conformational equilibrium involving diamagnetic planar and paramagnetic tetrahedral forms of the four-coordinate complexes. A more complex behavior has been observed among the N-substituted salicylaldimines (48, 49). Depending on the nature of the alkyl or aryl group on the imine nitrogen, varying behaviors are observed. A tetrahedral (paramagnetic)-planar (diamagnetic) conformational equilibrium has been found. Also, with lower sterical requirements on the part of the substituents, polymeric, paramagnetic octahedral forms also occur.

In contrast to the behavior of nickel, compounds have been found with iron and cobalt, for which the possibility of electronic isomerism remains, as yet, uncomplicated by indications of variations in coordination number or conformation. George and co-workers (50) are able to account quantitatively for the anomalous magnetic and spectral properties of the hydroxides of iron(III) hemoglobin and myoglobin on the assumption that the substances are composed of isomers of high-spin and low-spin forms. Stouffer, Busch, and Hadley (51) have found that certain six coordinate cobalt(II) complexes mostly with \(\alpha\)-trime structures analogous to 2,2',2''-terpyridine, exhibit anomalous magnetic moments whose temperature dependences suggest the existence of high and low spin forms in equilibrium. For example, the room temperature magnetic moment of bis(2,6-pyridindialdihydrazone)cobalt(II) iodide (ligand structure XI) is 3.04 Bohr magnetons while the usual high-spin and low-spin values are approximately 5 and 1.9 Bohr magnetons, respectively.

Although any structural differences that exist between the electronic isomers of the cobalt(II) complex are almost certainly more subtle than in the nickel(II) case, the probability remains that the bond distance and bond angles differ substantially. Indeed, in view of the nonequivalent electronic distributions, identical atom arrangements seem unlikely for electronic isomers even in those instances where coordination number and symmetry remain unaltered.

Template Reactions

The presence of a metal ion during the course of an organic reaction may have a profound effect on the stereochemistry of the process. The formation of cyclic chelates about metal ions provides the best ex-
amples of such processes. In these cases the metal ion may be considered to serve as a template, effectively organizing the reaction either by stereoselective arrangement of reactants or by favoring the formation of a product ideally suited for chelation.

Perhaps the classic example is that of phthalocyanine formation, essentially from phthalonitrile and the metal ion. However, this complicated reaction is not fully understood and is carried out under conditions not well suited to detailed study.

A number of other fully cyclic chelates have recently been reported. The simplest example is that due to Schrauzer (52) and Thierig and Umland (65). In this case, the proton from the hydrogen bridge in bis(di-methylglyoxime) nickel(II) has been replaced by the function \(BX_2^+\), where \(X = \text{For CeH}_{6}\) (structure XII).

A similar process is found in the reaction of tetra-dentate biacetylbis(mercaptoethylimino)nickel(II) with alkyldihalides (54).

The dissolution of tris(ethylenediamine)nickel(II) perchlorate in acetone leads to a most remarkable reaction, forming a cyclic ligand (55).

The most recent example of a cyclic ligand has been obtained by the self-condensation of \(\beta\)aminobenzaldehyde in the presence of Ni(II) or Cu(II) (56). The product of the condensation has been formulated according to structure (XIII).

These unusual substances (57) exhibit remarkable stabilities, many of them resisting boiling concentrated mineral acids. Further, such reagents as sulfide, dimethyl glyoxime, and, in certain cases, even cyanide fail to remove the metal ion from its encycled coordination site. The fact that the metal ion is instrumental in the synthesis of these cyclic ligands requires special emphasis. In this regard, the planar metal ions, copper(II) and nickel(II), understandably have dominated studies leading to the synthesis of new tetradentate macrocycles. Metal ions tending more generally to favor other stereochemistries might confer different structures on ligands synthesized under their directive influence. As an indication that this is true, Curry and Busch (58) have reported the synthesis of a macrocyclic sexadentate ligand in the presence of iron salts.

Recent advances in the stereochemistry of metal complexes have been made in many ways on many subjects in addition to the several summarized here. Although a number of alternate subjects are of equal or greater importance, the author has chosen to emphasize areas not necessarily so widely reviewed in the context of stereochemistry as others, or those of his own interest.

Acknowledgment

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Literature Cited

(14) These are summarized in a paper soon to appear: Liehr, A. D., J. Phys. Chem., in press.


(21) Dywer, F. P., (deceased) and Sargeson, A. M., private communication.


