No description of the metal-containing compounds that have found their way into medicine would be useful without first providing basic information on the bonding in metal complexes, their spectral and magnetic properties and, most importantly, the manner in which they react with water and biological targets in the cell. The approach taken in this chapter assumes background knowledge of general and organic chemistry with no previous exposure to inorganic chemistry, as would occur in a junior- or senior-level course at most universities. The concepts presented are for the most part intuitive, requiring basic knowledge of chemistry and physics, but sometimes more abstract issues like quantum mechanics – which explains the spectral properties of metal complexes – will also need to be covered. The overall goal of this chapter is to bring all readers to a common level, providing them with the 'core' of information needed to understand how and why, from the chemical perspective, metal complexes play important roles in medicine.

1.1 Crystal field theory

The bonding that exists in metal complexes, their spectral and magnetic properties and their chemical reactivity are not easily explained using a single theory. However, one approach that is often used in a basic presentation of bonding concepts in transition metal chemistry is crystal field CF theory, which because it is based on simple electrostatic arguments, is relatively easy to understand. In CF theory and MO theory the interactions between the metal ion (M) and the groups attached to it (called ligands and denoted by L) are considered to be electrostatic in nature and the bonding in the compound is described as being salt-like in character. The metal ion, a *cation*, electrostatically interacts with a series of surrounding ligands, which are usually negatively charged or, if they are uncharged, have the negative end of a dipole directed toward the metal ion. Barring any serious steric interactions between the ligands, the arrangements about the metal ion generally have high-symmetry geometries. For example, a 6-coordinte complex – that is, a compound with six ligands attached to the metal ion – has an octahedral arrangement of ligands, while five-coordinate complexes have square or trigonal bipyramidal arrangements, four-coordinate structures are tetrahedral and square planar, and so on. These geometries, along with compounds and intermediates commonly encountered in metal complexes used in medicine, are shown in Figure 1.1.



Figure 1.1 Common geometries of metal complexes and intermediates found in inorganic chemistry

1.1.1 Octahedral crystal field

The first-row transition metal series, which begins with scandium, Sc, fills the 3d level of the atom, while the second- and third-row transition metal series, which begin with yttrium, Y, and lanthanum, La, respectively, fill the 4d (second row) and 5d (third row) orbitals of the atom. The transition metal ions and the electronic configurations of common oxidation states are shown in Figure 1.2. Since ions of these elements have electron occupancies in the *d* level, which is considered the 'valence' level of the ion, CF theory focuses on the change in energy of the *d*-orbitals when charges representing the ligands approach the metal ion and form salt-like bonds.

	3 3B	4 3B	5 5B	6 6B	7 7B	8 8B	9 8B	10 8B	11 1B	12 2B
lons	+2, d ¹ +3, d ⁰	+2, d ² +3, d ¹ +4, d ⁰	$^{+2, d^3}_{+3, d^2}_{+4, d^1}_{+5, d^0}$	+2, d ⁴ +3, d ³ +4, d ² +5, d ¹ +6, d ⁰	$ \begin{array}{c} +1, \ d^{6} \\ +2, \ d^{5} \\ +3, \ d^{4} \\ +4, \ d^{3} \\ +5, \ d^{2} \\ +6, \ d^{1} \\ +7, \ d^{0} \end{array} $	+2, d ⁶ +3, d ⁵ +4, d ⁴	+2, d ⁷ +3, d ⁶ +4, d ⁵	+2, d ⁸ +3, d ⁷ +4, d ⁶	+1, d ¹⁰ +2, d ⁹ +3, d ⁸	+2, d ¹⁰
1 st Row 3ơ ⁿ	²¹ Sc	²² Ti	²³ V	²⁴ Cr	²⁵ Mn	²⁶ Fe	²⁷ Co	²⁸ Ni	²⁹ Cu	³⁰ Zn
2 nd Row 4 <i>d</i> ⁿ	³⁹ Y	⁴⁰ Zr	⁴¹ Nb	⁴² Mo	⁴³ Tc	⁴⁴ Ru	⁴⁵ Rh	⁴⁶ Pd	⁴⁷ Pd	⁴⁸ Cd
3 rd Row 5 <i>d</i> ⁿ	⁵⁷ La	⁷² Hf	⁷³ Ta	⁷⁴ W	⁷⁵ Re	⁷⁶ Os	⁷⁷ lr	⁷⁸ Pt	⁷⁹ Au	⁸⁰ Hg

Figure 1.2 Transition metal ions and their electronic configurations for various oxidation states

The spatial arrangements of the five *d*-orbitals on a Cartesian coordinate system are shown in Figure 1.3. The shapes shown represent the probability of finding an electron in a volume of space about the nucleus of the metal ion. If the metal ion has no bonded ligands – this is referred to as a *free ion* – the energies of all five *d*-orbitals will be the same and are said to be *five-fold degenerate* in energy. This situation is shown on the left side of Figure 1.4. Let's suppose that instead of existing as a free ion, the metal ion is part of a stable complex consisting of six negatively-charged ligands bound to the metal ion in an octahedral array. The way that crystal field theory approaches this situation is to consider what happens to the five *d*-orbitals in the



Figure 1.3 Boundary surfaces of the five d-orbitals

electrostatic field set that is up by the ligands. The first thing that the theory does is to consider a situation in which the total negative charge of the ligands is 'smeared' equally over the surface of a sphere with a radius equal to the metal-ligand bond distance and with the metal ion at its center. Since the d-orbitals have electrons in them and the surface of the sphere is negatively charged, the energies of the *d*-orbitals will be raised; that is, they will become less stable relative to the free ion, due to electrostatic repulsion between the d-electrons and the negatively-charged surface of the sphere. Since the charge on the sphere has no 'directionality' - that is, the negative charges are equally distributed over the entire surface of the sphere - all five d-orbitals must experience the same electrostatic perturbation from the sphere and move as a group to a new energy, E_{0} (see Figure 1.4). The next step is to redistribute the charge on the surface of the sphere and concentrate it at the six points where the axes penetrate the sphere. If the charge at each of the six points is identical, this will produce a perfect octahedral crystal field about the central metal ion and simulate what the d-orbitals experience in an octahedral metal complex. It should be evident that since $d_{x^2-y^2}$ and d_{z^2} are pointed directly at the charges (ligands), they must experience a different perturbation than the three orbitals, d_{xz} , d_{yz} , d_{xy} , that are directed between the charges. While it may not be obvious that both $d_{x^2-y^2}$ and d_{z^2} should experience an identical perturbation from the octahedral field, quantum mechanics shows that d_{z^2} , which has a ring of electron density in the xy plane (Figure 1.3), is actually a composite of two orbitals that are identical to $d_{x^2-y^2}$ except that they lie in the yz and xz planes. Thus, since d_{z^2} is a composite of two orbitals that look like $d_{x^2-y^2}$, it makes sense that the crystal field will affect d_{z^2} and $d_{x^2-y^2}$ identically, as shown in Figure 1.4. It should also be evident that since these orbitals are pointed directly at the ligands, they feel the electrostatic repulsion directly, and thus their energies are *raised* relative to the energy of the spherical field, E_0 . It is possible to show that if the total charge on the sphere is simply rearranged or 'localized' to certain positions on the sphere, the energy of the system cannot change; that is, E_0 for the sphere and the octahedral field must be the same. This is the *center of* gravity rule, which applies to electrostatic models of this type. The consequences of this is that if two orbitals,



Figure 1.4 Generation of the octahedral crystal field from the free ion

 $d_{x^2-y^2}$ and d_{z^2} , are raised by a certain amount, the remaining three, d_{xz} , d_{yz} , d_{xy} , must be *lowered* by a certain amount. Inspection of the shapes and orientations of d_{xz} , d_{yz} , d_{xy} shows that since these orbitals are directed 45° to the axes of the system, and each is related to the others by a simple rotation, all must experience exactly the same perturbation from the charges which are on the axes of the system. This set of orbitals, which are 'triply degenerate', is often referred to as the ' t_{2g} ' set due to its symmetry properties. In a similar fashion, the orbitals, $d_{x^2-y^2}$ and d_{z^2} which are 'doubly degenerate' are referred to as the ' e_g ' set. The labels t_{2g} and e_g are products of the application of *group theory*, a mathematical tool for characterizing the symmetry properties of molecules.

Simple electrostatic arguments show that the spacing between the t_{2g} and e_g levels depends on the distance that the charge is from the origin of the system and the magnitude of the charge. If the distance is decreased or if the magnitude of the negative charge is increased, the splitting between t_{2g} and e_g will increase. As we will see, metal complexes can be made with a wide variety of attached ligands, some of which are negatively charged, for example, Cl^- , CN^- and so on, and some of which are electrically neutral, for example, H_2O , NH_3 and so on. However, one thing that all ligands have in common is that they direct electrons, usually a lone pair, toward the metal ion, and these electrons become the 'point charges' in the crystal field model describing the electronic structure of the complex. Since the ability of different ligands to perturb the *d*-orbitals varies considerably, the spitting between the t_{2g} and e_g sets of orbitals can be quite different for different complexes. In order to address this, crystal field theory denotes the splitting between the t_{2g} and e_g sets as Δ_0 , which is the crystal field splitting parameter. The subscript 'o' in Δ_0 indicates that a crystal field of octahedral symmetry is being addressed. If there are no attached ligands - that is, in the free ion case - there can be no crystal field and Δ_0 is zero. Since the splitting between the levels is different for different metal complexes, Δ_0 , which carries units of energy usually expressed in wavenumbers (cm^{-1}) , varies over a wide range. However, the relative displacement of the t_{2g} and e_g levels in terms of Δ_o from the center of gravity, E_o , is the same for all octahedral complexes with the e_g level at 0.6 Δ_o and the t_{2g} level at $-0.4 \Delta_o$. These values arise because (2 orbitals) \times (0.6 Δ_0 + (3 orbitals) × (-0.4 Δ_0) \equiv 0, which satisfies the center of gravity rule. It should be evident that E_0 is the average crystal field.

1.1.2 Other crystal fields

Numerous anticancer drugs containing Pt^{+2} have a square planar geometry in which four ligands at the corners of a square are bonded to the metal ion (Figure 1.1). The best way to generate the square planar crystal field splitting pattern for the *d*-orbitals is to first consider an intermediate field called the *tetragonal crystal field*. Suppose that the charge on each of the two point charges on the plus and minus z-axis of the octahedral crystal field is slightly reduced in magnitude relative to the other four charges in the plane or, the equivalent situation, wherein the magnitude of the charges on the plus and minus z-axis remain unchanged but the charges are moved to greater distance from the metal ion than the four charges in the plane. In this case, the electrostatic field on the z-axis is *less than* the field seen by the metal ion on the x- and y-axes of the system. As a consequence of this *asymmetry* or non-equivalence in the field, all orbitals with z-components – that is, d_{xz} , d_{yz} and d_{z^2} – will have their energies *lowered*; that is, they will become *more stable* in the applied field (Figure 1.5). Since d_{z^2} is pointed directly at the weaker charges on the z-axis, it must experience greater stabilization – that is, more lowering – than d_{xz} , d_{yz} , which are directed away from the point charges. As a consequence of the center of gravity rule, if some levels go down in energy, others – that is, $d_{x^2-y^2}$ and d_{xy} – must become *less stable* and their energies must be raised.

The limiting case of the tetragonal distortion is the *square planar geometry* in which the two charges on the z-axis have been reduced to zero; that is, there are only four charges in the plane of the system. The removal of the axial charges causes a significant stabilization in d_{z^2} , which moves downward in the energy diagram and passes below (becomes more stable than) the d_{xy} orbital. Since d_{xz} , d_{yz} also have z-components, they are also stabilized by the loss of the axial charges, but to a lesser extent than d_{z^2} . The resulting crystal field splitting diagram, sometime called the *square planar limit*, is shown in Figure 1.5.

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A second very common structure for metal complexes with four groups bonded to the central metal ion is the *tetrahedral* geometry (Figure 1.1). Compared to the previous examples, rationalizing the *d*-orbital splitting pattern for the tetrahedral geometry is less straightforward. Figure 1.6 shows a Cartesian coordinate system in the center of a cube. Placement of charges at opposite corners of opposite faces of the cube and hypothetically connecting them to the metal ion in the center of the cube generates the tetrahedral geometry; that is, all charge–metal–charge angles are 109.5°. It should be evident from the figure that none of the *d*-orbital spoint directly at the charges, and although other relative arrangements of the cube on the *d*-orbital coordinate system are possible, all lead to the conclusion given for the splitting pattern shown in Figure 1.6. The tetrahedral crystal field has a doubly degenerate set of orbitals, the d_{z^2} and $d_{x^2-y^2}$, termed for symmetry reasons the 'e' set, which is *lowest* in energy, and a triply degenerate set, d_{xz} , d_{yz} and d_{xy} , called the 't₂' set, which is *highest* in energy. While this pattern is exactly the opposite of the octahedral case, the labels *e* and t_2 , which also come from group theory, are missing the subscript 'g'. This is because the octahedron has a symmetry element called the *center of inversion* (*i*), which is associated with a mathematical operation in which each point charge of the



CN	Structure	d_{z^2}	$d_{x^2-y^2}$	d_{xy}	d_{xz}	$d_{\rm yz}$
2	Linear ^b	1.028	-0.628	-0.628	0.114	0.114
3	Trigonal ^c	-0.321	0.546	0.546	-0.386	-0.386
4	Tetrahedral	-0.267	-0.267	0.178	0.178	0.178
4	Square Planar ^c	-0.428	1.228	0.228	-0.514	-0.514
5	Trigonal Bipyramid ^d	0.707	-0.082	-0.082	-0.272	-0.272
5	Square Pyramid ^d	0.086	0.914	-0.086	-0.457	-0.457
6	Octahedron	0.600	0.600	-0.400	-0.400	-0.400
7	Pentagonal Bipyramid ^d	0.493	0.282	0.282	-0.528	-0.528
9	Tricapped Trigonal Prism	-0.225	-0.038	-0.038	0.151	0.151

Table 1.1 Relative energies of the d-orbital in various crystal fields^a

^{*a*}Values given are in units of Δ_{o} .

^bLigands or charges are along the z-axis.

^cLigands or charges are in the xy plane.

^d Pyramid base in xy plane. From Table 9.14, p. 412 of Huheey, J.E. (1983) *Inorganic Chemistry: Principles of Structure and Reactivity*, 3rd edn, Harper & Row Publisher, New York.

structure can be passed along a straight line through the central metal ion to reach an identical point charge (Figure 1.5). Since *i* is not present in the tetrahedron, the subscript 'g' is missing from the labels. Although the tetrahedral pattern is the exact opposite of the splitting pattern for the octahedron, the magnitude of the splitting between the *e* and *t*₂ levels for the tetrahedral geometry, denoted as Δ_t , is only 4/9 the value of the splitting between *t*_{2g} and *e*_g of the octahedron; that is, $\Delta_t = 4/9 \Delta_0$ or 0.445 Δ_0 . Thus, for the tetrahedron, the *t*₂ orbital set is at 0.178 Δ_0 and the *e* orbital set is at $-0.267 \Delta_0$.

Table 1.1 gives the energies of the five *d*-orbitals for common geometries in terms of the octahedral crystal field splitting parameter, Δ_0 . The values in the table, which were calculated using a point charge crystal field model, can be used to determine the orbital energy diagrams for geometries other than the octahedral, tetrahedral and square-planar geometries discussed above. The entries in the table assume that if there is more than one electron in the pattern, which is almost always the case, there is no interaction between the electrons, which is never the case. The energies given are the so-called *one electron energies* for the various orbitals in the different crystal fields. If there is more than one electron in the pattern, the electrons can be in the same or different orbitals and will 'see' each other through what are called *configuration interactions*, and the energies of levels given in Table 1.1 will be adjusted to new values. Since determining the new energies of the orbitals is beyond the scope of our work, and changes are in most cases small, the entries in Table 1.1 are reasonable approximations for all multiple-electron systems encountered in this text.

1.1.3 Factors affecting the crystal field splitting parameter, Δ

1.1.3.1 Spectrochemical series

As was earlier pointed out, the point charges used to generate the splitting patterns for various geometries simulate the electrostatic effects of ligands that are bonded to the metal ion. Extensive spectral and magnetic studies on a large number of transition-metal complexes showed that the electronic effect exerted by a specific ligand on the *d*-orbitals of the metal ion is essentially a property of that ligand and independent of the geometry of the complex, the nature of the metal ion or its oxidation state. This characteristic allowed ranking of common ligands in terms of their '*d*-orbital splitting power', to produce a series called the *spectrochemical*

The Ligand ^a	$\begin{array}{l} \textit{Spectrochemical Series, Increasing } \Delta \\ I^- < Br^- < S^{-2} < NC\underline{S}^- < CI^- < NO_3^- < N_3^- < F^- < OH^- < C_2O_4^{-2} \approx H_2O < \underline{N}CS^- \\ < CH_3C\underline{N} < NH_3 < en < bipy < phen < \underline{N}O_2^- < \underline{P}Ph_3 < \underline{CN}^- < \underline{C}O \end{array}$
The Metal Ion	Principal Quantum Number, n First-row transition metal ion, 3 <i>d</i> level, Δ^{3d} Second-row transition metal ion, 4 <i>d</i> level, $\Delta^{4d} \sim 1.5 \ \Delta^{3d}$ Third-row transition metal ion, 5 <i>d</i> level, $\Delta^{5d} \sim 1.75 \ \Delta^{3d}$
The Metal Ion	Oxidation State, Increasing Δ M ⁺ < M ⁺² < M ⁺³ < M ⁺⁴ < M ⁺⁵

Table 1.2 Factors affecting the crystal field splitting parameter, Δ

^aThe underscored atom is the donor atom to the metal ion. *en*, ethylenediamine, 1, 2 diaminoethane; *bipy*, 2, 2' bipyridine; *phen*, 1, 10 phenanthroline.

series (Table 1.2). Ligands on the left of the series, which are referred to as *weak field ligands*, for example I⁻ and Br⁻, cause a small splitting in the *d*-orbitals, while ligands on the right of the series, for example CN⁻ (cyanide), CO (carbon monoxide) – *strong field ligands* – cause a large splitting in the orbitals. While there is little doubt that the order of the ligands in the series is correct (the order is obtained from experiment), the series does not seem to follow our intuitive feeling about which ligands should be high in the series and which should be low. For example, CO, which is uncharged, is highest in the series but iodide, I⁻, which is negatively charged, is lowest in the series. Based on the electrostatic arguments put forth in connection with the crystal field this makes little sense: I⁻ should have a *greater* perturbation on the *d*-orbitals than uncharged CO. Clearly, factors other than simple electrostatic effects must influence Δ_0 . While the crystal field model works well for most of the cases encountered in this text, complexes which have considerable overlap between the orbitals on the metal and ligand – that is, when covalent bonding is present – cause the theory to 'bend' but not completely break down. How basic crystal field theory needs to be modified to accommodate this will be addressed in a later section.

1.1.3.2 Principal quantum number, n

While the spectrochemical series rank orders the experimentally-measured effects of ligands on the splitting of the *d*-orbitals, it is also possible to make some general statements concerning the effects of the metal ion on the magnitude of Δ . If one moves down a given column in the periodic chart, the quantum number n, which is called the *principal quantum number*, increases. For example, the first-row transition metal series elements have electrons in the 3d(n=3) level, the second-row in the 4d(n=4) level and the third-row in the 5d (n = 5) level of the atom. Experimentally, it has been found that the magnitude of the crystal field splitting parameter Δ increases in the order 3d < 4d < 5d, with $\Delta 4d \sim 1.5$ ($\Delta 3d$) and $\Delta 5d \sim (1.75 \Delta 3d)$ (Table 1.2). The effects of this increase with n can easily be seen for the series $[Co(NH_3)_6]^{3+}$, $3d^6$, $[Rh(NH_3)_6]^{3+}$, $4d^6$ and $[Ir(NH_3)_6]^{3+}$, 5d⁶, which have identical geometries (octahedral), ligands (ammonia) and metal ion oxidation states (+3), and belong to the same family (column) of the periodic chart. The values of Δ_0 for these complexes are $\sim 22\,000\,\mathrm{cm}^{-1}$, $\sim 34\,000\,\mathrm{cm}^{-1}$ and $\sim 41\,000\,\mathrm{cm}^{-1}$, respectively, which shows that moving down a given column in the periodic chart does indeed cause the values of the crystal field splitting parameter to *increase* by the approximate amounts given. Since atoms, and ions, become larger with atomic number, M-L bond lengths increase in moving from the first to the second and third rows of the transition metal series. Simple point-charge arguments would predict that if the M-L distance were increased, the magnitude of Δ would *decrease*, not increase as observed. The fact that the opposite is found is further proof that the simple point-charge model cannot be entirely correct and that other factors are important in determining the magnitude of Δ .

1.1.3.3 Metal ion oxidation state

Experimentally, it can be shown that *increasing* the charge on the metal ion – that is, increasing its oxidation state – causes the *d*-*d* absorption bands of the complex to shift toward the UV region of the spectrum, which means that Δ has *increased* (Table 1.2). Since the ionic radius of any ion decreases with an increase in the net positive charge on the ion, the *distance* between the metal ion and its bonded ligands must decrease when oxidation state is increased. Since decreased distance would lead to greater electrostatic repulsions between electrons on the metal ion and the ligands, the observed trends in Δ (with changes in oxidation state on the metal ion) *are* predicted by simple crystal field arguments.

1.1.4 High- and low-spin complexes

When considering the ways in which electrons can occupy energy levels of an atom, ion or molecule, Hund's *rule* states that the electronic configuration with the lowest overall energy is one for which the spins for the electrons are unpaired, even if it means placing electrons in a nearby less-stable orbital (level) in order to do so. For the free ion, the five d-orbitals are degenerate in energy and electrons are added to the orbitals by maximizing the number of unpaired spins. If, for example, there are four electrons in the d-level of a free ion, it is possible to place the electrons in the level in a number of different ways, some of which are shown in Figure 1.7. Experimentally, Figure 1.7a, which has the maximum amount of spin unpairing, is known to be the lowest-energy (most stable) configuration. When describing the electron spin of any system, it is best to use the value of the magnetic spin quantum number, m_s , associated with the spin angular momentum of the electron. Each electron has spin angular momentum of $\pm \frac{1}{2}$ in units of $h/2\pi$. With *n* electrons, the maximum possible value of the total magnetic spin quantum number S is n/2 (all electrons unpaired) and the minimum possible value of S is zero (if n is even) or $\frac{1}{2}$ (if n is odd). For simplicity, the term $h/2\pi$, where h is Planck's constant, is usually dropped. Thus, for the configuration shown in Figure 1.7a, S = (4)(1/2) = 2, while S for Figure 1.7b is (+1/2 - 1/2 + 1/2 + 1/2) = 1 and for Figure 1.7c is (+1/2 - 1/2 + 1/2 - 1/2) = 0. Two factors associated with electronic configurations, coulombic interactions and spin correlations, form the basis for Hund's rule. Since placement of two electrons in the same orbital forces them to occupy the same regions of space, the coulombic repulsion between the electrons will be high, thus destabilizing the system. This obvious electrostatic repulsion makes it easy to see why maximum spin unpairing, maximum S, is desirable. While columbic considerations are important, the ability to exchange one electron with another in a given configuration without changing S is even more important. This aspect of Hund's rule, which is a product of quantum mechanics, in called *spin correlation* or *exchange energy*. Both of these factors – coulombic (electrostatic) and spin correlation (exchange energy) – drive the system to obtain maximum spin unpairing,



Figure 1.7 Some possible electronic configurations for the d^4 free ion and their respective values of S



Figure 1.8 High and low spin possibilities for d⁴ in an octahedral crystal field

and for the free ion case, where all of the *d*-orbitals have the same energy, the configuration with the largest value of S always has the lowest, most negative, energy.

In the presence of an octahedral crystal field the five *d*-orbitals are not degenerate in energy, and a decision needs to be made on how to place the electrons into the *d*-orbital pattern to create the lowest energy configuration. For example, d^4 in an octahedral crystal field can have two possible electronic configurations, which are shown in Figure 1.8. One situation, called the *high-spin* case, has one electron in each of the three t_{2g} orbitals and the fourth electron in one of the d-orbitals of the e_g level, giving S = 2. The energy gained by the system due to the presence of the crystal field is called the crystal field stabilization energy or CFSE, which in this case is $CFSE_{hs} = (3 \text{ electrons})(-0.4 \Delta_0) + (1 \text{ electron})(0.6 \Delta_0) = -0.6 \Delta_0$. This possibility can be written as $t_{2g}^3 e_g^1$. An alternative possibility for arranging the electrons in the levels is also shown in Figure 1.8. In this case all four electrons are in the t_{2g} set of orbitals and since Pauli's principle must be obeyed, two of the electrons in the same orbital must have their spin oppositely aligned. This gives S = 1 for the configuration, which is called the *low-spin* case. The crystal field crystallization energy for this configuration is $CFSE_{ls} =$ $(4 \text{ electrons})(-0.4 \Delta_0) = -1.6 \Delta_0 + P$, where P is the energy required for pairing two of the electrons in one of the orbitals. This possibility can be written as t_{2e}^4 . Since P is the energy lost due to coulombic and exchange effects, its sign is *positive*, meaning that it *destabilizes* the system. Which possibility is found – high-spin or low-spin – clearly depends on which $CFSE - CFSE_{ls}$ or $CFSE_{hs}$ – has the larger *negative* value. This can be found by equating CFSE_{1s} to CFSE_{hs}, which gives $-1.6 \Delta_0 + P = -0.6 \Delta_0$ or $P = \Delta_0$. If the ligands bonded to the metal ion produce a splitting in the *d*-orbitals with $\Delta_0 > P$, the *low-spin* possibility, S = 1, will be more stable. If the ligands produce a splitting with $\Delta_0 < P$, the high-spin situation, S = 2, will be more stable.

The electronic configuration, value of *S* and CFSE for weak and strong octahedral fields are given in Table 1.3. A point to make concerning the entries in Table 1.3 is that the value of CFSE given is the stabilization energy that the system accrues as a result of the presence of the crystal field. This means that the 'reference point' for determining the CFSE is the free-ion case. For example, for the strong-field configuration, t_{2g}^6 , which has S = 0, the value of CFSE in Table 1.3 of $-2.4 \Delta_0 + 2P$ was determined by first writing the electronic configuration for the free-ion case and determining its energy in terms of *P*, the pairing energy. With six *d*-electrons and five orbitals, there must be one paired set of electrons or one unit of *P* for the free ion. Next, the energy of the system due to the presence of the crystal field, in terms of Δ_0 and *P*, was written, which in this case is $-2.4 \Delta_0 + 3P$. There are three pairs of electrons in the t_{2g} set of orbitals, hence 3P, and the extra energy in terms of Δ_0 due to the crystal field is $-2.4 \Delta_0$. Taking the difference between the energy in the presence of the field and the energy of the free ion gives CFSE = $-2.4 \Delta_0 + 3P - P$ or $-2.4 \Delta_0 + 2P$. The remaining entries in Table 1.3 were calculated in a similar fashion. The values of CFSE for crystal fields of other symmetries can easily be obtained using the energies of the orbitals given in Table 1.1. As described above, calculation of *S* and CFSE assumes that there is no configuration interaction; that is, electrons in the pattern operate as independent

Weak Field					Strong Field				
d ⁿ	Config.	S	CFSE	d ⁿ	Config.	S	CFSE		
d^1	$t_{2\alpha}^1$	1/2	$-0.4 \Delta_{ m o}$	d^1	$t_{2\alpha}^1$	1/2	$-0.4 \Delta_{o}$		
d^2	t_{2g}^{2g}	1	$-0.8~\Delta_{ m o}$	d^2	t_{2g}^{2g}	1	$-0.8~\Delta_{ m o}$		
d^3	$t_{2\sigma}^{\overline{3}}$	3/2	$-1.2 \Delta_{\rm o}$	d^3	$t_{2\alpha}^{3}$	3/2	$-1.2 \Delta_{\rm o}$		
d^4	$t_{2s}^{3}e_{s}^{1}$	2	$-0.6 \Delta_{ m o}$	d^4	t_{2g}^{4}	1	$-1.6 \Delta_{\rm o} + P$		
d^5	$t_{2_{0}}^{\bar{3}}e_{0}^{\bar{2}}$	5/2	$0 \Delta_{o}$	d^5	$t_{2\alpha}^{\overline{5}}$	1/2	$-2.0 \Delta_{ m o} + 2P$		
d^6	$t_{2s}^{4}e_{s}^{2}$	2	$-0.4 \Delta_{ m o}$	d^6	t_{2g}^{6}	0	$-2.4 \Delta_{ m o} + 2P$		
d^7	$t_{2_{\sigma}}^{-5}e_{\sigma}^{2}$	3/2	$-0.8~\Delta_{ m o}$	d^7	$t_{2_{\alpha}}^{-5}e_{\alpha}^{1}$	1/2	$-1.8 \Delta_{ m o} + P$		
d^8	$t_{2s}^{-6}e_{s}^{2}$	1	$-1.2 \Delta_{\rm o}$	d^8	$t_{2g}^{6}e_{g}^{2}$	1	$-1.2 \Delta_{\rm o}$		
d^9	$t_{2_{\alpha}}^{6}e_{\alpha}^{3}$	1/2	$-0.6 \Delta_{ m o}$	d^9	$t_{2_{0}}^{6_{0}}e_{0}^{3_{0}}$	1/2	$-0.6 \Delta_{ m o}$		
d^{10}	$t_{2g}^{\bar{6}}e_{g}^{\bar{4}}$	0	$0 \Delta_{ m o}$	d^{10}	$t_{2\alpha}^{\overline{6}}e_{\alpha}^{\overline{4}}$	0	$0 \Delta_{o}$		

Table 1.3 Crystal field effects for weak and strong octahedral fields^a

^a The entries in the table are based on the energies of the levels as if only one electron were present in the system. Placing more than one electron in the levels produces electron–electron interactions, which change the energies of the levels, but this has been neglected in the values given. From Table 9.3, p. 374 of Huheey, J.E. (1983) *Inorganic Chemistry: Principles of Structure and Reactivity*, 3rd edn, Harper & Row Publisher, New York.

non-interacting entities, in which case the one-electron energies in Table 1.1 can be used to estimate the energies of multiple electron cases.

1.2 Molecular orbital theory

The most important theory for discussing bonding in chemistry is molecular orbital (MO) theory. This theory uses the atomic orbitals (AOs) of all of the atoms in a compound to construct molecular orbitals (MOs) the shapes of which depend on the size and shape of, and distance between, atomic orbitals. A critical element of the theory is the wave function, denoted by ψ , which is a mathematical expression that when properly manipulated provides information on a physical system. If the wave function is associated with an atom, it can be used to calculate important properties of the atom, such as the probability of finding an electron in regions of space about the nucleus. If the wave function is associated with a molecule, it can be manipulated to provide information on the energies of bonds, the distribution of electrons in the molecule and other important quantities.

The wave function for an atom contains information on the *principal quantum number* (*n*), for example the '3' in 3*d*, the *orbital angular momentum quantum number* (*l*), for example the number associated with the letter '*d*' in 3*d*, and the *magnetic quantum number* (*m_l*), which distinguishes orbitals of a given *n* and *l*. For a *d*-'subshell', *m_l* has five values, which give rise to the five *d*-orbitals shown in Figure 1.2. For a *p*-subshell, *m_l* has three values, which produce the three *p*-orbitals, *p_x*, *p_y* and *p_z*, often discussed in organic chemistry. The fourth quantum number, called the *magnetic spin quantum number*, *m_s*, is associated with the spin angular momentum of the electron. As we have seen, it has values of +1/2 and -1/2 in units of $h/2\pi$, which refer to the spin moment of the electron relative to an electric or magnetic field. If two electrons occupy the same orbital, the values of *n*, *l* and *m_l* are the same but the spins of the electrons must be oppositely aligned; that is, *m_s* for one electron must be +1/2 and *m_s* for the second must be $-1/2 h/2\pi$.

1.2.1 MO diagram of molecular hydrogen

The best way to describe MO theory at an elementary level is to show what happens when two hydrogen atoms $(H_A \text{ and } H_B)$ come together to form a hydrogen molecule (H_A-H_B) (Figure 1.9). While molecular hydrogen



H₂ Molecular Orbitals

Figure 1.9 Molecular orbital diagram for molecular hydrogen, H_2 . The black dots represent the hydrogen nucleus, a proton

has little relevance to metallo-drugs, qualitatively understanding how MO theory addresses the bonding in this simple molecule paves the way for understanding the bonding in more complicated metal complexes used in medicine.

MO theory starts with writing the complete (many-electron) wave function in terms of wave functions for individual electrons and then each one-electron wave function is written in terms of atomic orbitals. The specific approach for molecular hydrogen is to carry out *linear combinations of atomic orbitals* (LCAO) by taking the sum and difference of the AOs on both hydrogen atoms to find new, *molecular*, wave functions that are associated with the H_2 molecule. For molecular hydrogen, LCAO gives (1.1) and (1.2).

$$\Psi_{\rm b} = [c_1 \psi_{\rm A}(1s) + c_2 \psi_{\rm B}(1s)] \tag{1.1}$$

$$\Psi_{a} = [c_{1}\psi_{A}(1s) - c_{2}\psi_{B}(1s)]$$
(1.2)

In these expressions, Ψ_b is called the *bonding* molecular wave function and Ψ_a the *antibonding* molecular wave function for the hydrogen molecule, while ψ_A and ψ_B are the atomic wave functions for the 1s orbitals on the two hydrogen atoms that were joined together to form the hydrogen molecule. The quantities, c_1 and c_2 , which are positive, are simply weighting coefficients that determine the fraction (amount) of each atomic wave function to be used in making the molecular wave function. Conceptually, the expressions say that there are two ways to combine the 1s orbitals on the two hydrogen atoms, H_A and H_B , when the hydrogen molecule is formed. One gives the bonding MO associated with the bonding wave function, (1.1). This MO gives a spatial volume that allows the electron to be found a significant fraction of the time between the two nuclei (Figure 1.9). The second way to do the combination gives the antibonding MO associated with the antibonding wave function, (1.2). This MO produces a shape that *prohibits* the electron from being found midway between the two nuclei (Figure 1.9). Both of these MOs are referred to as being *sigma type*; that is, they are associated with σ *bonds*, meaning that electron density for these MOs is on the bond axis of the system. In MO language, the bonding MO is labeled $\sigma(1s)$, while the antibonding MO is denoted $\sigma^*(1s)$. For comparison, the other type of MO commonly encountered in chemistry is the *Pi type*, or simply π -*bond*, for which electron density is *not* on the bond axis of the system.

As shown in Figure 1.9, the energies of the 1s AO for both H_A and H_B , E_H , must be identical because both atoms are identical. The energy of $\sigma(1s)$ MO is lowered from $E_{\rm H}$ and it becomes more stable than the $\sigma^{*}(1s)$ MO, which is raised in energy from $E_{\rm H}$. For this situation in which the energies of the two AOs that formed the MOs are identical, the 'makeup' or composition of the $\sigma(1s)$ MO and the $\sigma^*(1s)$ MO must have exactly equal contributions from both $\psi_A(1s)$ and $\psi_B(1s)$; that is, the coefficients c_1 and c_2 in (1.1) and (1.2) are the same and positive. This implies that electrons in this MO spend equal fractions of their time on either hydrogen atom of H₂ Once the molecular orbitals are formed and their approximate energies determined, the last step is to place the appropriate number of electrons into the diagram, filling the levels from bottom up, so that each MO holds two electrons with their spins oppositely aligned (Figure 1.9). Since each hydrogen atom brings one electron to the bonding scheme, the two electrons are placed in the lowest-energy MO, giving the electronic configuration for H₂ of $\sigma(1s)^2$, which is called the ground state of the hydrogen molecule. This stabilizes the hydrogen molecule relative to the two atoms and produces the well-known twoelectron single covalent bond for molecular hydrogen. As is shown in Figure 1.9, the antibonding MO is not occupied by electrons when H_2 is in the ground state. However, it can be occupied by an electron if one of the electrons in the $\sigma(1s)$ MO is moved to the $\sigma^*(1s)$ MO. This event, which would obviously require the addition of energy, is called an *electronic transition*, which could happen if H₂ were to absorb a photon with an energy equal to the energy spacing between $\sigma(1s)$ and $\sigma^*(1s)$. The resulting electronic configuration, which is written as $\sigma(1s)^1 \sigma^*(1s)^1$, is referred to an *excited state* of the hydrogen molecule, which when produced effectively eliminates the bond between the two hydrogen atoms; that is, one electron is in a bonding MO and one is in an antibonding MO. However, since the lifetime of the excited state is short, $\sim 10^{-9}$ s, dissociation of the hydrogen molecule into hydrogen atoms does not appreciably occur under conditions for which the transition can be observed. Located at higher energy (less stable) than the 1s atomic orbital is the 2s atomic orbital of hydrogen. These atomic orbitals interact with one another to produce another set of MOs, $\sigma(2s)$ and $\sigma^*(2s)$, which, if H₂ is in the ground state, are at very high energy and are not occupied.

The basic features of the diagram shown in Figure 1.9 are the same as the features in the diagrams obtained from the application of CF theory. In an octahedral crystal field, a level, e_{g} , is raised in energy relative to some reference point, E_{0} , and a second level, t_{2g} , is lowered relative to E_{0} (Figure 1.4). Placement of electrons in the lower level stabilizes the system, but adding electrons to the upper level destabilizes the system. While there are some similarities between the two theories, they are quite different in the way that they handle the role of the ligands in the bonding model. In crystal field theory the ligands are assumed to be point charges and their presence splits the *d*-orbitals into some pattern. The electrons that were originally on the metal ion before it was involved in complex formation are still 100% on the metal ion and any electronic transitions that are possible can only take place within the split *d*-orbital set. Molecular orbital theory, on the other hand, considers that all atomic orbitals on all atoms can potentially interact to produce new orbitals called molecular orbitals. The extent to which these interactions occur is determined by the shapes of the atomic orbitals and their energies, and the amount of each AO that is 'mixed into' the MO, which is in turn controlled by the weighting coefficients in expressions similar to (1.1) and (1.2). In reality, if all of the orbitals on all of the atoms are addressed in this manner, the mathematics and the subsequent electronic structure become very complicated. Fortunately, inorganic chemists have learned to focus on only those parts of a complete MO diagram that are most relevant to the property of the system being addressed.

1.2.2 MO diagram for $[Co(NH_3)_6]^{3+}$

Consider the *partial* MO diagram for the octahedral complex, $[Co(NH_3)_6]^{3+}$, shown in Figure 1.10. While the complete diagram is more complicated than that given, Figure 1.10 contains enough detail to show how a diagram for a metal complex is created and what information it contains. The MO diagram is divided into three



parts. The left side shows the relative energies of the 3d, 4s and 4p AOs on Co⁺³, the right side gives the orbitals on the six ammonia molecules that interact with the orbitals on the metal ion and the center shows the MOs that form from all of the AOs that are brought to the bonding scheme by the bonded partners. The orbitals on the right side of the diagram are actually the hybrid orbitals, sp^3 , associated with the lone pair of electrons on the ammonia molecule. Since there are six ammonia molecules, there are six lone pairs, each having the same energy. While the fundamental 'units' used in MO theory are the atomic wave functions, 'mixing' some combination of AOs – for example, combining parts of the 2s orbital with the $2p_x$, $2p_y$, and $2p_z$ on nitrogen to form a 'hybrid' orbital – and entering the resulting hybrid orbital into the molecular orbital scheme produces the same mathematical result as using the unhybridized orbitals.

The dotted lines on the diagram show which metal and ligand AOs have been combined to form a particular MO. In order for atomic orbitals on M and L to combine and form a molecular orbital, the AOs on each must have shapes that allow the orbitals to overlap with one another. The labels used on the AOs (upper-case letters) and MOs (lower-case letters) are derived from *group theory*, which is branch of mathematics concerned with the symmetry properties of structures. In addition, the MOs indicate the type of orbital formed; in this case all are σ type. The MOs in the lower portion of the diagram are bonding MOs, while those in the upper part of the diagram, indicated with an asterisk, are antibonding MOs.

The composition of a molecular orbital is determined by the relative energies of the atomic orbitals. If the energies of two interacting AOs are the same, as would occur with a homonuclear diatomic molecule like H₂, the values of c_1 and c_2 in (1.1) and (1.2) are the same. If the energies of the two interacting orbitals are not the same, as would occur when two different atoms are bonded to each other - that is, a heteronuclear diatomic molecule – and the AO on atom 'B' is more stable (at a lower negative energy) than the AO of atom 'A', c_2 is greater than c_1 . For the opposite situation, where the energy of A > B, then c_2 is less than c_1 . For transition metal complexes which contain many atoms there are often more than two AOs contributing to a particular MO, which means that the wave functions are much more complicated than (1.1) and (1.2). While it is not easy to determine how much each wave function contributes to these MOs - that is, the coefficients, c_n , in expanded versions of (1.1) and (1.2) – it is straightforward to determine which centers, metal ions or ligands, make the *major* contribution to the MO – that is, the largest value of c_n . For example, consider the bonding MO, $t_{1u}(\sigma)$, and its antibonding complement, $t_{1u}(\sigma^*)$, shown in Figure 1.10. The fact that energy of $t_{1u}(\sigma)$ lies closer to the energy of the ammonia atomic orbitals than any of the metal atomic orbitals in the diagram means that this MO contains *more* ligand character than metal character; that is, the weighting coefficients, c_n , for the wave functions from L are greater than the coefficients for the wave functions associated with M. Conversely, t_{1u} (σ^*), which is close in energy to AOs on the metal ion – for example 4p – must have contributions that are weighted heavily in favor of the AOs on the metal ion. All of this means that $t_{1u}(\sigma)$ is mostly ligand in character and its complement, $t_{1u}(\sigma^*)$, is mostly metal in character. With one exception, all of the MOs in the diagram are compositions of AOs from both L and M, with $a_{1g}(\sigma)$, $e_{g}(\sigma)$ and $t_{1u}(\sigma)$ being mostly ligand in character and $e_{g}(\sigma^{*}), a_{1g}(\sigma^{*}), t_{1u}(\sigma^{*})$ being mostly metal in character. The t_{2g} set of d-orbitals, which are directed off the axes of the system, have no orbitals with which they can interact on the ammonia side of the diagram. The reason for this is not so easy to explain, but is related to the fact that none of the symmetry properties of the orbitals that are coming from the ligands on the right side of the diagram match the symmetry properties of the t_{2g} set from the metal ion on the left side of the diagram. One of the requirements for the formation of an MO is that the symmetries of the interacting AOs must match and there must be no T_{2g} term on the right side of the diagram. Without any interacting orbital on the ligand side of the diagram, members of the t_{2g} set appear in the diagram as 'pure' d-orbitals and as such are not really molecular orbitals at all. In the MO description of the bonding, they are referred to as *nonbonding* orbitals. For certain ligands, for example CN⁻ and CO, there are antibonding π -type MOs on the *ligand* that can interact with the t_{2g} set on the metal. In this situation, the t_{2g} set *can* form a π -bond between M and the carbon atoms on the ligands, which results in bonding and antibonding π -type MOs in the MO diagram.

It should be evident that determining even the approximate composition of MOs depends critically on the relative energies of the metal and ligand orbitals. The property of the orbital that approximates its relative energy in an MO diagram is its *electronegativity*, and the hybrid orbital of the ammonia molecule is more electronegative (has greater negative energy) than are the 3*d* atomic orbitals of Co^{+3} . If the reverse were true – that is, if the energies of the ligands were raised, less stable, relative to the metal orbitals – the positions of the MOs would be shifted upward in the diagram and compositions of the resulting MOs, in terms of their contributing AOs, would be the reverse of those described above and shown in Figure 1.10.

A final point to make in connection with the MO diagram is the appearance of the molecular orbitals. Consider $a_{1g}(\sigma)$, which is the most stable bonding MO in Figure 1.10. The wave function for this MO would have contributions from the six sp^3 hybrids on the ammonia molecules, with each hybrid being a combination of the 2s and 2p orbitals on nitrogen, and the 4s orbital on the metal ion. When this molecular wave function is used to calculate the boundary surface for the MO, a structure similar to that given in Figure 1.11 results, confirming that electrons in $a_{1g}(\sigma)$ would more likely be found on the ligands than on the metal ion. It should be evident that MOs for multi-atom systems are quite complex, and for the purposes of the brief overview of MO theory given here it is more important to understand the location, electron occupancy and approximate composition of an MO rather than its detailed shape.



Figure 1.11 Approximate shape of the $a_{1g}(\sigma)$ bonding molecular orbital for $[Co(NH_3)_6]^{3+}$

The procedure for placing electrons into the diagram is to fill the diagram, from the bottom to the top, with the total number of electrons that were originally in the orbitals on M and L that created the diagram. In this case there are six electrons from the Co^{+3} ion and 12 electrons from the six lone pairs on the ammonia molecules. Since each individual MO can only hold two electrons with their spins oppositely aligned, the occupancy of the MOs for the ground state of the system is that shown in Figure 1.10. A critical feature of the diagram is that the central portion of the MO field is exactly the splitting pattern predicted by CF theory. There is a triply degenerate set, t_{2g} , which is *nonbonding* in the MO diagram, that is separated from a doubly degenerate set at higher energy, which is the antibonding MO, e_g^* . Calculations show that the distance between these levels is Δ_o , as indicated on the diagram. A photon with the correct energy entering the system could cause one of the electrons in the t_{2g} set to be promoted to a vacant level in the e_{σ}^{*} set, which, aside form the slight change in the labels of the levels, is exactly what is predicted by CF theory. However, unlike CF theory, MO theory provides a much more comprehensive picture of bonding in that transitions outside the *d*-level of the metal ion are possible. For example, since the composition of an MO depends on the amount and types of AOs that created it, an electron in an excitation process could start out from an MO that is mainly ligand in character, for example $t_{1u}(\sigma)$, and end up in an MO which is mainly metal in character. This type of transition, which cannot be accommodated by simple CF theory, is called a *charge transfer transition*, in which charge is transferred from the ligand to the metal ion during the absorption process. Since the direction of the charge transfer is from L to M, the transition carries the acronym LMCT, for ligand-to-metal charge transfer. While the diagram in Figure 1.10 does not have this as a possibility, an electron could also start out in an MO that is mainly metal in composition and terminate in an MO that is mostly ligand in character. Such a transition carries the acronym MLCT, for metal-to-ligand charge transfer.

While there is no doubt that molecular orbital theory is the most comprehensive way to analyze bonding in chemistry, it requires many parameters and even in its qualitative form is quite challenging. Fortunately, crystal field theory along with a basic knowledge of molecular orbital theory will suffice to understand the physical and chemical properties of most of the metal complexes encountered in this text.

1.3 Absorption spectra of metal complexes

One of the most striking characteristics of transition metal complexes is that they are brightly colored. Once it was learned that the absorption bands giving rise to the color were associated with electronic transitions mainly



Figure 1.12 Absorption spectrum of $[Ti(H_2O)_6]^{3+}$ in water. Adapted from Lever, A.B.P., Inorganic Electronic Spectroscopy, 1968, Elsevier

within the *d*-level of the ion, efforts were made to understand the origin of the bands in terms of the electronic structure of the compounds using crystal field theory. Shown in Figure 1.12 is the absorption spectrum of $[Ti(H_2O)_6]^{3+}$, $3d^1$, a metal complex that is purple in color. This complex is an octahedral structure with the single *d*-electron on the Ti⁺³ ion in the lower triply degenerate set of *d*-orbitals; that is, the electronic configuration is, $t_{2g}^1 e_g^0$ (Figure 1.4). Since there is a higher-energy unoccupied level, e_g , it is possible to promote the electron in the lower level to the higher level if the wavelength of light falling on the sample is of the correct energy to bridge the energy gap, Δ_o , between t_{2g} and e_g . Thus, simple CFT predicts that $[Ti(H_2O)_6]^{3+}$ should have a single electronic transition, designated as $t_{2g}^0 e_g^1 \leftarrow t_{2g}^1 e_g^0$, which should be equal to the crystal field splitting parameter, Δ_o . Note that the spectroscopist writes this transition by listing the excited state first and having the transition arrow point to the excited state from the ground state, which is listed last.

Box 1.1 Absorption spectra of metal complexes [1]

A UV-visible spectrophotometer is used to measure the absorption spectrum of a complex in solution. The instrument consists of a light source which emits many different wavelengths of radiation, a grating which systematically selects wavelengths to be passed through the sample and a detector which measures the amount of radiation passing through the sample. If the solute in the solution absorbs light in a certain region of the spectrum, the photons which fall on the sample in this region will be reduced in number relative to the corresponding case in which only solvent is present in the light beam. While the absorbed radiation is quickly reemitted by the solute, the emitted photons are distributed in all possible directions in space, causing the detector to 'see' fewer photons than were directed at the sample.

Each chemical compound has a characteristic absorption spectrum that shows how the compound absorbs light as a function of wavelength. The absorption of radiation by the sample is given by the Beer–Lambert law, $A = \log I_o/I_t = \varepsilon cl$. In this law, the absorbance or optical density, A, is the logarithm of the ratio of the intensity of radiation falling on the sample, I_o , to the intensity of radiation exiting the sample, I_t . The absorbance is also equal to the product of ε , the molar extinction coefficient (molar absorbtivity), c, the concentration of the solute and l, the path length of the beam passing through the sample. If the unit of c is moles/liter (M) and the unit of l is centimeters (cm), the unit of ε is M^{-1} cm⁻¹,

showing that the absorbance, *A*, is a *unitless* quantity. Each absorption band in a chemical compound has a characteristic value of ε , which is in effect a measurement of the 'photon-absorbing power' of that band. Since an absorption band is caused by a transition between states (levels) within the electronic structure of the compound, the magnitude of ε is a measure of the 'allowedness' of the transition between the states. The value of ε , which varies over many orders of magnitude, allows the spectroscopist to assign the transition in terms of a specified set of *selection rules*.

There are a number of ways to display the absorption spectrum of a compound. The x-axis of the plot can be in *wavelength*, λ (usually in nm, 10⁻⁹ m), but the spectroscopist prefers *wavenumber*, \tilde{v} (usually in cm⁻¹), where $\tilde{v} = 1/\lambda$. The latter is used because the distance between states (levels) in the energy-level diagram of a compound is in units of energy and since E = hv and $v = c/\lambda$, energy, E, is proportional to $1/\lambda$, not λ . The y-axis of the plot is usually given in ε (in units of M^{-1} cm⁻¹). Sometimes, if the values of ε span a large range, log ε will be given or the units will be in mM^{-1} cm⁻¹, where mM is M multiplied by 10⁻³ or millimoles. Yet another variation is to multiply the actual value of ε by some factor, for example 10^{-3} , in order to reduce the number of 'zeros' that need to be given on the y-axis of the plot. Thus, if the actual value of ε is 3000 M^{-1} cm⁻¹, the label on the y-axis may be $3.0 M^{-1}$ cm⁻¹, and indicate that the values shown should be multiplied by 10^{3} in order to obtain the actual value of ε . If absorbance, A, is given on the y-axis, one cannot determine the values of ε unless c, the concentration, and l, the path length, are also given. In this case, the values of ε must be calculated using the Beer–Lambert law.

A careful look at the spectrum in Figure 1.12 shows that the spectrum of $[Ti(H_2O)_6]^{3+}$ is a bit more complicated than expected: the absorption band is slightly broadened to its low-energy side. In fact, $[Ti(H_2O)_6]^{3+}$ experiences what is called a *Jahn–Teller distortion*, in which two of the water molecules that are *trans* to each other move slightly closer to the metal ion than the remaining four. This of course slightly changes the symmetry of the crystal field away from 'pure' octahedral to a *tetragonal* distortion of a kind similar to that described in connection with the generation of the square planar crystal field (Figure 1.5). However, in this case the two ligands (charges) on the z-axis move closer to rather than farther away from the metal ion.

The Jahn-Teller effect applies to all chemical systems that have more than one way to indicate an electronic configuration. In this case the single electron could be placed in any one of the three orbitals of the t_{2g} set – that is, d_{xz}^1 , d_{yz} , d_{xy} or d_{xz} , d_{yz}^1 , d_{xy} or d_{xz} , d_{yz} , d_{xy}^1 – and all would yield the same CFSE and total energy. This situation is called a triple orbital degeneracy and the Jahn-Teller theorem states that the system must structurally distort in some way to remove the degeneracy and lower the overall energy of the system. If the two water molecules on the z-axis are slightly 'pushed in' toward the metal ion relative to the remaining four in the plane, the octahedral splitting pattern would distort to the one shown in Figure 1.13, which has the d_{xy} orbital at a lower energy (more stable) than d_{xz} and d_{yz} orbitals. This is called a 'z-in' tetragonal Jahn-Teller distortion because the two ligands on the z-axis of the system have been moved closer to the metal ion than the four in the plane. Of course, any structural change of this type would affect the e_{g} set, causing the $d_{x^2-y^2}$ and d_{z^2} to shift to new positions in the manner shown in Figure 1.13. Since the single electron must occupy the lowest orbital when the system is in the ground state of, for example, d_{xy}^1 , there are now three transitions possible $-d_{xz}, d_{yz} \leftarrow d_{xy}, v_1; d_{x^2-y^2} \leftarrow d_{xy}, v_2; d_{z^2} \leftarrow d_{xy}, v_3$ - where there was only one – $t_{2g}^0 e_g^1 \leftarrow t_{2g}^1 e_g^0$ – in the pure octahedral crystal field. It should now be clear that the hidden band to the low-energy side of the main band at ~17 400 cm⁻¹ in the spectrum of $[\text{Ti}(\text{H}_2\text{O})_6]^{3+}$ is actually v_2 , while the main band at ~20 100 cm⁻¹ is v_3 [2]. The lowest energy transition, v_1 , which is quite small in energy, is in the infrared region of the spectrum and is not easily observed. Since the energy of the $d_{x^2-y^2} \leftarrow d_{xy}$, v_2 , transition is the crystal field splitting parameter, Δ for water bound to Ti⁺³ is ~17400 cm⁻¹ or ~345 kJ mol⁻¹ (Figure 1.12). From the above presentation it is clear that CF theory works well in explaining the absorption spectrum of $[Ti(H_2O)_6]^{3+}$, even accounting for a distortion in the structure of the complex due to the Jahn-Teller effect.



1.3.1 Band intensity/selection rules

Ouantum mechanically, all transitions between electronic states (levels) of chemical compounds are controlled by *selection rules*, which cause some transitions to be strong and others in the compound to be weak. For the kinds of compounds to be discussed in this text, two types of selection rule are important: one that pertains to the orbital motion of the electron, associated with the *orbital angular quantum number*, l, and a second associated with the spin of the electron specified by the magnetic spin quantum number, m_s . For an example of how the selection rule associated with orbital angular momentum works, consider the absorption band associated with the transition, $d_{x^2-y^2} \leftarrow d_{xy}$, v_2 , for $[Ti(H_2O)_6]^{+3}$, which has the electron moving between two different d-orbitals. Since the electron starts out in a d-orbital, d_{xy} , which has l = 2, and it ends up in another *d*-orbital, $d_{x^2-y^2}$, which also has l = 2, the value of *l* does not change in the transition; that is, $\Delta l = 0$. In this case the transition is forbidden by the Laporte selection rule, or to put it another way, the transition is Laporteforbidden. The word 'forbidden' does not imply that the transition is totally absent – it is clearly visible in the spectrum shown in Figure 1.12 - but rather, it simply means that the transition has some restrictions on it that make it weaker (less likely to occur) than other possible types of transition. If the quantum number l changes in a transition – that is, $\Delta l \neq 0$ – the transition is said to be *Laporte-allowed* and the absorption band in this case would be much stronger (more likely to occur) than if $\Delta l = 0$. In discussing the bonding in $[Co(NH_3)_6]^{3+}$ using molecular orbital theory (Figure 1.10), it was pointed out that an electron located in an MO that was mainly p in character (strong ligand contribution) could move to an MO that was mainly d in character (strong metal contribution). An example of such a transition is the LMCT transition, $e_g^* \leftarrow a_{1g}$ (Figure 1.10), in which the electron starts out in an MO that is mainly ligand in character, a_{1g} , and terminates in an MO, e_g^* , that is mainly metal in character. Since $\Delta l \neq 0$ – that is, $d \leftarrow p$ – this transition is Laporte-allowed and its intensity is much greater than a transition with $\Delta l = 0$. While the MO diagram shown in Figure 1.10 does not have MLCT as a possibility (for example, $p \leftarrow d$), such a transition would also have $\Delta l \neq 0$, would be Laporte-allowed and would be strong in intensity.

As will soon be evident, the net spin, *S*, can also change in an electronic transition. This happens when the net spin associated with the starting configuration (ground state) is different than the net spin of the ending

configuration (excited state). The *spin selection rule* address what happens to the spin during a transition; that is, it indicates the difference between the spins of the excited and ground states of the system, referred to as ΔS . If $\Delta S = 0$, the transition is said to be *spin allowed* and the net spin of the system is unchanged during the transition. If $\Delta S \neq 0$, the transition is said to be *spin forbidden* and the net spin of the system must change during the transition. Experimentally, transitions that have $\Delta S = 0$ are much stronger (have a higher probability of occurring) than transitions that have $\Delta S \neq 0$. A simple explanation of why spin-forbidden transitions are weaker than their allowed counterparts is related to the fact that a spin-forbidden transition requires two events to take place: one is the promotion of the electron to a higher energy level and the other is a change in the spin of the electron during the electron to another level without changing its spin.

A final comment on the intensity of absorption bands observed for transition metal complexes pertains to the symmetry of the complex. Mathematicians recognize that all objects in nature have certain symmetry properties called symmetry elements that allow them to be systematically classified into a point group, which specifies a certain set of symmetry elements. Although the details of how this is done will not be given here, one symmetry element called the *center of inversion*, which is given the symbol *i*, is an important determinant of the intensity of a band in the absorption spectrum of a transition metal complex. Consider the structures of the tetrahedral and octahedral complexes shown in Figure 1.1, and note that for the octahedral arrangement of ligands the complex has a special point (the metal ion) through which each of the six ligands can be passed to reach an equivalent point: that is, another identical ligand. Carrying out this symmetry operation on the complex, passing all ligands through the center, will result in a structure which looks identical to the starting complex; that is, it will appear as if nothing was done to the complex. When this condition is met, the object is said to possess the center of inversion, *i*. However, the situation with the tetrahedron is different in that carrying out the same symmetry operation, in this case passing each of the four ligands through the metal ion to an equivalent point on the other side, will result in a structure which, although still a tetrahedron, looks as if the original has been rotated to a new position. In this case the object *does not* possess the center of inversion, *i*. Quantum mechanically, the presence or absence of *i* in a metal complex has a significant effect on the intensity of the d-d transitions for the complex. Consider a d-d transition with $\Delta l = \Delta S = 0$ for two complexes, one of which is an octahedral complex and the other of which has tetrahedral geometry. Experimentally it is found that all of the transitions for the tetrahedral complex, which does not possess the symmetry element *i*, are more intense (they are more allowed) than are the transitions for the octahedral complex, which possesses *i*.

Clearly, the intensities of bands observed in transition metal complexes provide important information on the selection rules operating in the transition, which ultimately paves the way for assigning the bands to specific transitions in the energy-level diagram of the compound. A summary of the type of transition, its expected intensity and an example of the type of complex exhibiting the transition is given in Table 1.4. While the total integrated area under an absorption band is the quantity that is proportional to the probability that the transition will occur, all absorption bands regardless of their origin have approximately the same ratio of the width of the band at half the maximum height of the band to the maximum height of the band; that is, the width at half height. This means that ε_{max} , the molar extinction coefficient at the maximum of the band in units of M^{-1} cm⁻¹, is a good measure of the intensity (probability) of the transition and thus is a useful metric for determining which selection rules apply to a transition.

1.3.2 Spectroscopic and crystal field terms

Analysis of the spectrum of a compound with a d^1 electronic configuration, after accounting for distortions due to the Jahn–Teller effect, proved to be relatively simple and straightforward. However, for complexes with more than one *d*-electron, indeed for most of the known metal complexes, analysis of spectra is more complicated. The problem with multi-electron systems is that once there is more than one electron in a given 'shell' or level of the atom, quantum mechanics dictates that not all spin and orbital angular momentum

Type of Transition	Δl	ΔS	Center of Inversion, i	$\varepsilon_{\rm max}~(\mathcal{M}^{-1}~{\rm cm}^{-1})$	Example Complexes ^b
Laporte-forbidden Spin-forbidden	0	≠0	yes	<1	$[Mn(H_2O)_6]^{2+}$ $O_{1-}S = 5/2 3d^5$
Laporte-forbidden	0	0	yes	1–100	$[Ru(H_2O)_6]^{2+}$
Laporte-forbidden	0	0	no	100–1000	$[NiCl_4]^{2-}, T_d, 3d^8$
Laporte-allowed Spin-allowed	≠0 MLCT LMCT	0	no	1000–50 000	$[MnO_4]^-, T_{d,3}d^0$ $[AuCl(terpy)]^{2+}, s.p., S=0, 5d^8$

Table 1.4 Absorption properties of metal complexes^a

^aThe ranges of molar absorbtivity, ε , given are considered *approximate*. Values outside these ranges have been observed for the various types of transition.

^bAbbreviations: *O*_h, octahedral; *T*_d, tetrahedral; *s.p.*, square planar; *terpy*, 2, 2', 2" terpyridine.

values for the system are possible. For example, suppose that the orbital motion of an electron about the nucleus of an atom is represented by a spinning bicycle tire with an axel or rod about which the tire is spinning. In a nonquantum mechanical world, the tire could spin with any angular velocity, setting up an angular momentum vector, l_i , with any magnitude, perpendicular to the angular velocity; that is, coincident with the axel of the spinning tire. Assume that for a multi-electron case there are many such tires, each with its axel randomly oriented in a different direction in space. The problem with this picture is that quantum mechanics simply does not allow all possible angular velocities or orientations of l_i and specifies that all of the vectors must be of a certain magnitude and must couple in such a way that only certain resultant vectors, L, where L is the vector sum of all l_i , are allowed. This is called *Russell-Saunders* (R-S) coupling and in simple terms it means that only certain angular velocities and orientations of the vectors are allowed. Not only are there restrictions on the orbital motion of the electron about the nucleus but if the electron is considered a particle spinning on its axis, the spinning velocity generates a spin moment, s_i , which is perpendicular to the spinning motion. Quantum mechanics specifies that not all s_i are allowed and that they must couple to give a resultant S which itself is quantized; that is, only certain values of S are allowed. To complicate matters further, L and S, which characterize the orbital and spin motion, can couple with each other to produce a resultant vector, J, which is characterized by the spin-orbit coupling constant, λ (not to be confused with wavelength, which is denoted by the same Greek letter). If the metal atom is relatively light, like the elements of the first-row transition series, coupling between L and S is generally weak, and $|\lambda|$ is in the range 50 to 800 cm^{-1} , which is relatively small. This means that the system can be described by L and S because their coupling together to define J is weak. However, for heavier elements like those in the third-row transition series and the lanthanides and actinides, $|\lambda|$ is greater than 10^3 cm^{-1} . With large $|\lambda|$, *l* and *s*, orbital and spin angular momenta associated with a single electron couple together to give j for a single electron. The coupling of the *j* vectors to produce the resultant J gives rise to a new coupling scheme, called jj*coupling*, for which only J has real physical meaning.

Fortunately, progress on the important issue of how to interpret absorption spectra of metal complexes can be made by embracing the language of the spectroscopist and discussing electronic states or levels of a metal ion in terms of spectroscopic or free-ion *terms* and crystal-field *terms*. The information present in these terms is summarized in Figure 1.14. As with the shapes of multicenter molecular orbitals, it is less important to know the makeup of a 'state' in terms of the different values of S and L that it may contain – called *microstates* – than the fact that the state exists and that it has a specific location in an energy-level diagram of the compound.

For the spectroscopist, analyzing the electronic spectra of transition metal complexes begins by finding the *spectroscopic terms* and their relative energies for the free ion with a specified number of *d*-electrons. These terms are found using a set of rules and while the precise order of states is determined by experiment, the *lowest state is always the state with the highest spin, S, and orbital, L, values.* Next, the spectroscopist applies a



Figure 1.14 Definitions of notations used for free-ion and crystal-field term symbols

crystal field of some symmetry and determines how the *d*-orbitals split in the crystal field. In order to describe what happens to a free-ion term when a crystal field is applied, the spectroscopist uses *group theory* to determine how the free-ion term is *transformed* in the presence of the crystal field. Since the system has been changed from the free-ion case to a situation with a specified crystal field, the *language* used for the free-ion case – that is, free-ion terms – is abandoned and replaced with terminology derived from group theory, which specifies the symmetry properties of the states. These new terms are called crystal-field terms. A list of free-ion terms or spectroscopic terms and their counterpart octahedral crystal-field terms is given in Table 1.5. The crystal-field terms *A*, *E*, and *T* pertain to the number of ways equivalent electronic configurations in the presence of the octahedral field can be written. Since these configurations are related to each other by interchanging electrons in orbitals, *A*, *E*, and *T* indicate the *orbital degeneracy* of the state, while the subscripts on these states, for example 1g, 2g and so on, refer to the symmetry properties (g means that *i* is present) of the state. Like the splitting between the *d*-orbitals, the energies of the crystal-field terms derived from the split *d*-orbitals depend on the crystal field splitting parameter, Δ .

In 1954 two Japanese researchers, Y. Tanabe and S. Sugano, published a classic paper showing in diagram form the ground and excited states for all ions with an unfilled *d*-shell as a function of Δ for octahedral complexes (Figure 1.15). These diagrams, which are referred to as Tanabe–Sugano (T-S) diagrams, have become the mainstay in analyzing the electronic spectra of transition metal complexes. Not only do they allow one to determine the crystal-field terms for the ground and excited states of the ion, but by matching the positions of absorption bands obtained from spectral measurements to the diagram one can find the value of the crystal field splitting parameter, Δ , for the complex.

Spectroscopic Term	Octahedral Crystal-field Term
S	A _{1g}
Р	T_{1g}
D	$E_{\rm g} + T_{\rm 2g}$
F	$\ddot{A}_{2g} + \ddot{T}_{2g} + T_{1g}$
G	$A_{1g} + E_{g} + T_{2g} + T_{1g}$
Н	$E_{\rm g} + 2T_{1\rm g} + T_{2\rm g}$
I	$A_{1g} + A_{2g} + E_{g} + T_{1g} + 2T_{2g}$

Table 1.5Conversion table for free-ion spectroscopic terms into
octahedral crystal-field terms^a

^aNote that 'S', the spectroscopic term, is not in italics. This is different to the spin quantum number, 'S', which *is* given in italics. In the case of the tetrahedron, the subscript 'g' in the crystal-field term is eliminated.

From Table 9.25, p. 443 of Huheey, J.E. (1983) *Inorganic Chemistry: Principles of Structure and Reactivity*, 3rd edn, Harper & Row Publisher, New York.

Box 1.2 Tanabe-Sugano diagrams

Tanabe–Sugano diagrams or T-S diagrams show the relative energies of crystal-field terms for an ion in an octahedral complex. Since these diagrams have been generated using a specific electronic configuration, for example d^3 , they can be used for any metal ion with this configuration, for example $3d^3$, $4d^3$, $5d^3$, with any attached set of ligands, as long as the environment around the metal ion is octahedral (O_h) or nearly so.

An important feature of the T-S diagram is that the x-axis is the lowest energy state (ground state) of the ion and the energies of all other states are plotted relative to it. This axis, which is unitless, gives the value of Δ/B , where Δ is the crystal field splitting parameter in units of cm⁻¹ and *B* is an energy parameter in units of cm⁻¹ associated with how effectively electrons in an orbital repel one another. In a pure crystal field model, the value of *B* for the free ion and the ion in a complex must be the same since the size of the *d*-orbital is the same in both and thus e-e repulsions in the complex and the free ion should be identical. However, this is in fact rarely the case. This is because the bonding between the metal ion and the ligands cannot be described using pure electrostatic concepts, as required by the crystal field model, and some covalent interaction occurs which 'expands' the *d*-orbitals and reduces *B* from its free-ion value when the complex forms.

The fact that the splitting pattern for the d-orbitals in a tetrahedral (T_d) crystal field is the *inverse* of that in an O_h field, $t_{2g}e_g$ vs. et_2 (Table 1.1), means that the T-S diagrams are also applicable to complexes with T_d symmetry. While the order of the free-ion terms is of course independent of the type of crystal field present (when $\Delta = 0$ there is no crystal field), the relative energies of the crystal-field terms which emanate from the free-ion term are *inverted* in changing the geometry of the complex from $O_{\rm h}$ to $T_{\rm d}$. The 'conversion code' for this symmetry change is $d^{\rm n}(O_{\rm h}) = d^{10-{\rm n}}(T_{\rm d})$, where n = the number of d-electrons. Thus, the T-S diagram for $d^4(O_h)$ is also applicable to $d^6(T_d)$. Although the T-S diagrams can be used for both octahedral and tetrahedral complexes, the symmetry properties of both types of complex are not the same in one important respect: while the octahedron possesses the symmetry element, i, the center of inversion, the tetrahedron does not. To indicate this, a crystal-field term associated with an octahedral complex carries the subscript 'g', which denotes the presence of this symmetry element in the complex. For example, the ground-state crystal-field term for the Cr^{+3} ion $(3d^3)$ in the *octahedral* complex, $[CrF_6]^{3-}$, is ${}^{4}A_{2g}$, although the subscript 'g' is not given on the T-S diagram. This same diagram can also be used for the *tetrahedral* complex, $[CoF_4]^{2-}(3d^7)$, in which case the ground-state crystal-field term is ${}^{4}A_{2}$. Because d^{5} has a half-filled *d*-shell, octahedral and tetrahedral complexes use the same d^5 T-S diagram. Diagrams for the d^1 and d^9 cases are simple and are not presented in Figure 1.15. For d^1 , the ground-state spectroscopic term is ²D, which in an octahedral crystal field produces ${}^{2}T_{2g}$ as the ground state and ${}^{2}E_{g}$ as the only excited state. For d^9 , the ground-state spectroscopic term is also ²D, which in an O_h crystal field produces ${}^2E_{\sigma}$ as the ground state and ${}^{2}T_{2g}$ as the only excited state. The tetrahedron–octahedron conversion given above applies to these diagrams as well.

While the origins of the symbols E_g , T_2 and so on which pertain to the symmetry properties of the state are not easy to describe, the superscript on the crystal-field term always denotes the net electron spin of the state, S. Thus, if in a given electronic configuration there are two unpaired electrons, for example V⁺³ (d^2) in an octahedral crystal field, the value of S is 1/2 + 1/2 = 1. The spectroscopist indicates this as a superscript, with the value 2S + 1, on the term, in this case '3', which denotes the *spin multiplicity* of the state. Moreover, this superscript is always the same for the crystal-field terms and the free-ion term from which they are derived; for example, a ³F free-ion term will only produce ³A_{2g}, ³T_{2g} and ³T_{1g} crystal field terms (Table 1.5).

A striking feature of the T-S diagrams for systems with four to seven *d*-electrons is the presence of a vertical line in the diagram. Since the x-axis of the diagram is always the ground state (lowest energy state), a change in the ground state at some value of Δ means that a low-spin state will 'overtake' the high-spin ground state and replace the latter on the x-axis of the diagram. Thus, for example, the ground state for a high-spin octahedral complex of Co⁺³ (3d⁶, $t_{2g}^4 e_g^2, S=2$) is ${}^5T_{2g}$, while the ground state for a *low-spin* complex ($t_{2g}^6 e_g^0, S=0$) with this ion is ${}^1A_{1g}$. Thus the left side of the T-S diagram shows the states that are possible for the high-spin case and the right side of the diagram shows the states possible for the low-spin situation.

As we will see, complexes with symmetries other than O_h and T_d have found their way into medicine. While a detailed description of the electronic structure of these complexes in terms of their crystal field states is beyond the scope of this chapter, the T-S diagrams shown in Figure 1.15 are starting points for analysis of the electronic structures of compounds with lower symmetries.



Figure 1.15 Tanabe–Sugano diagrams. Adapted from Lever, A.B.P., Inorganic Electronic Spectroscopy, 1968, Elsevier

1.3.3 Band assignments and Δ

The basic approach for obtaining the crystal field splitting parameter Δ from absorption spectra of transition metal complexes is to assign the absorption bands appearing in the spectrum of the compound to the crystal states given in the Tanabe–Sugano diagram. Once this is done it is possible to calculate the crystal field splitting parameter, Δ , and other parameters from the positions of the absorption bands of the complex using a fitting procedure. While the fitting process will not be discussed here, assigning the observed



Figure 1.15 (Continued)

bands and estimating the value of Δ_o is a relatively simple procedure, which will be presented in this section.

Figure 1.16 shows the absorption spectrum of $[Co(NH_3)_6]^{3+}$, which contains six ammonia ligands bonded in an octahedral array to Co^{+3} , $3d^6$. This complex exhibits three absorption bands at 769 nm (0.2), 472 nm (56) and 338 nm (46), which are the *lowest-energy d-d* type absorptions for the complex [3]. In listing the bands, the wavelength of the band maximum in nanometers (10^{-9} m) is followed in parenthesis by the molar extinction



Figure 1.16 Absorption spectrum of $[Co(NH_3)_6]^{3+}$ in water. High-energy part adapted from Riordan, A.R. et al., Spectrochemical Series of Cobalt(III). An Experiment for High School Through College, Chem. Educator 2005, 10, 115–119; low-energy part adapted from Lever, A.B.P., Inorganic Electronic Spectroscopy, 1968, Elsevier

coefficient, ε , in units of M^{-1} cm⁻¹. From the d^6 T-S diagram it is evident that two spin states are possible for the ion in an octahedral crystal field, a *high-spin* case, $t_{2g}^4 e_g^2$, with S = 2 and a *low-spin* case, $t_{2g}^6 e_g^0$, with S = 0. As pointed out above, the left side of the T-S diagram gives the crystal field states for the high-spin case (low values of Δ), and the right side of the diagram gives the crystal field states for the low-spin case (high values of Δ). On the basis of the absorption spectrum alone it is often difficult to choose which spin state is associated with the compound, but as will be shown in a later section, this can easily be determined by conducting magnetic measurements on the compound. Since it is known that $[Co(NH_3)_6]^{3+}$ has the low-spin (S = 0) ground state, the right side of the d^6 T-S diagram is used to analyze the absorption spectrum of the complex.

The next step in the process for assigning the *d*-*d* absorption bands of the complex is to determine which selection rules apply to the observed bands. As pointed out above, these rules govern the allowedness of the transition, which is reflected in the value of ε for the absorption maximum of the band. A band with a large value of ε means that the transition is more allowed than in one with a smaller value of ε . As is evident from Table 1.4, the value of ε for the bands at 474 nm and 338 nm indicates that they are most likely Laporte-forbidden spin-allowed transitions; that is, $\Delta l = 0$, $\Delta S = 0$. Since the crystal field ground state of the compound is ${}^{1}A_{1g}$, these bands must be associated with transitions to excited states that have the same spin as the ground state; that is, the superscript on the crystal-field term for the excited state must be '1'. Checking the T-S diagram (Figure 1.15) reveals that the only possibilities which fit the requirements, in order of increasing energy, are ${}^{1}T_{1g} \leftarrow {}^{1}A_{1g}$ and ${}^{1}T_{2g} \leftarrow {}^{1}A_{1g}$, which are derived from the '1' free-ion term of Co⁻³. Thus, the band assignments are ${}^{1}T_{1g} \leftarrow {}^{1}A_{1g}$ at 474 nm (21 200 cm⁻¹) and ${}^{1}T_{2g} \leftarrow {}^{1}A_{1g}$ at 338 nm (29 550 cm⁻¹). The T-S diagram predicts that there should be *two* spin-forbidden transitions ($\Delta S = 0$), which are ${}^{3}T_{1g} \leftarrow {}^{1}A_{1g}$. Because these transitions are spin forbidden they should be much weaker in intensity than the spin-allowed transition. The band at 769 nm (13 000 cm⁻¹) with $\varepsilon = 0.2 M^{-1} cm^{-1}$ has been assigned to the spin-forbidden transition is at higher energy than ${}^{3}T_{1g} \leftarrow {}^{1}A_{1g}$ and overlaps the strong spin-allowed band at 474 nm, this transition appears as a shoulder on the strong band and for this reason is difficult to observe.

Once the band assignments have been made, the next step is to note the energy of the *lowest-energy spin*allowed transition, which in this case is ${}^{1}T_{1g} \leftarrow {}^{1}A_{1g}$. While the theoretical energy of this transition is somewhat complicated, it is approximately equal to the splitting between the t_{2g} and e_g levels of the complex; that is, the crystal field splitting parameter, Δ . In practice, all of the observed bands in the complex are employed in a fitting procedure that uses Δ , B and other interelectronic repulsion parameters as variables. Although the location of the ${}^{1}T_{1g} \leftarrow {}^{1}A_{1g}$ transition suggests that Δ is 21 200 cm⁻¹ (474 nm),

the actual value of this parameter obtained from fitting is $22\,870\,\mathrm{cm}^{-1}$ and the value of *B* is $615\,\mathrm{cm}^{-1}$. The latter value, which is significantly reduced from the free-ion value of $1100\,\mathrm{cm}^{-1}$, shows that while the crystal field model works well for analyzing the spectrum of $[\mathrm{Co}(\mathrm{NH}_3)_6]^{3+}$, complex formation clearly affects repulsions between electrons in orbitals, an observation which cannot be accommodated by a simple electrostatic model.

The general approach given above for estimating the value of Δ can be used for all $d^1 \cdot d^4$ and $d^6 \cdot d^9$ complexes. This means that the location of the absorption band for the *lowest-energy spin-allowed Laporte-forbidden transition approximates the spacing (in energy) between the* t_{2g} and e_g *levels of the octahedral complex*. Since the splitting for the tetrahedral arrangement of ligands is the inverse of the octahedral case, the location of the lowest-energy spin-allowed transition for tetrahedral complexes is also a good measure of the splitting between the e and t_2 levels of the tetrahedral complex, which in this case is Δ_t .

As pointed out above, the T-S diagrams have broad application and can be used for all octahedral and tetrahedral transition metal complexes. While assigning bands for all of the possibilities will not be given here, a few interesting cases are worth noting. Experimentally, solutions of most high-spin complexes of Mn^{+2} ([Ar] $3d^5$) are very pale in color. The absorption spectrum of one of these complexes, $[MnF_6]^{4-}$, which has S = 5/2, is shown in Figure 1.17. Since this complex has the electronic configuration $t_{2g}^3 e_g^2$, transitions are not possible without changing the net spin of the system; that is, all transitions are spin-forbidden transitions. As is evident from the d^5 T-S diagram, the crystal field ground state for the complex is ${}^6A_{1g}$ and all excited states have spin multiplicities that are not spin hextets; that is, excited-state crystal-field terms do not carry the superscript '6'. This condition, where the spin multiplicity of the ground state is different from the spin forbidden, $[MnF_6]^{4-}$ is weakly colored; that is, the absorption bands in the visible region of the spectrum are of low intensity. In this case none of the positions the bands are good estimates of the value of Δ .

If the crystal field around the Mn⁺² ion is increased, for example $[Mn(CN)_6]^{4-}$, the spin state of the metal ion changes from high spin to low spin, $S = \frac{1}{2}$, $t_{2g}^5 e_g^0$. In this case the crystal field ground state is ${}^2T_{2g}$, which allows transitions to higher-energy states with the same doublet spin multiplicity, making these complexes more intensely colored than their high-spin counterparts.

An important message from this analysis is that crystal field theory does a good job of explaining the optical properties of transition metal complexes. With absorption data for the complex, knowledge of basic selection rules and a Tanabe–Sugano diagram, the observed bands in the spectrum of the compound can be assigned and the approximate value of the crystal field splitting parameter Δ determined. Since Δ is a measure of the



Figure 1.17 Absorption spectrum and crystal field band assignments of $[MnF_6]^{4-}$. Adapted from Lever, A.B.P., Inorganic Electronic Spectroscopy, 1968, Elsevier

thermodynamic stability of the complex, it influences the rate at which the compound undergoes a substitution reaction, which in a medical context is often the critical factor determining the efficacy of a compound as a useful drug or diagnostic agent.

A second important message is that the value of B for a complex is often much different to the value of B for the free ion; for example, $B = 615 \text{ cm}^{-1}$ for $[\text{Co}(\text{NH}_3)_6]^{3+}$ vs. 1100 cm⁻¹ for free Co⁺³. Since this parameter is a measure of the interactions between electrons in the orbitals of the metal ion, this means that the interactions in the complex are very different from (they are much less than) the interactions in the free ion. Obviously, the fact that B is different in the complex versus the free ion is inconsistent with a crystal model which assumes that the ligands are simply present to 'perturb' the d-orbitals of the metal ion to a new splitting arrangement. This breakdown of the model prompted a 'patch' for crystal field theory, which ultimately became known as *ligand field theory.* In the latter, the simple electrostatic concepts that lead to the crystal field model are partially abandoned and some form of overlap between the orbitals on the ligands and metal ion – that is, covalent bonding – is allowed. While ligand field theory has proved useful for analyzing the bonding and spectra of complexes where covalent bonding is significant – for example, when the ligands are CN^{-} , CO, phosphine, thiolate and so on – it is ultimately only a patch to the model. The correct method for analyzing the bonding in these compounds is, of course, molecular orbital theory. But since MOT is quite rigorous, and is sometimes cumbersome to use, inorganic chemists have found ways to 'simplify' the bonding analysis of metal complexes. It is remarkable that CFT works as well as it does and it shows that many metal complexes are basically 'salt-like' substances and that simple electrostatic arguments can be used to explain the structure and spectral properties of these interesting materials.

1.4 Magnetic properties of metal complexes

As we have seen, the quantity S is a useful way to indicate the number of unpaired electrons on the metal ion in a complex. If a metal complex has no unpaired electrons on the metal ion, S = 0, and if it is placed near a magnetic field, the applied field will induce circulation of electronic currents, which cause the substance to be repelled by the field. In this case the substance exhibits *diamagnetism* and is said to be *diamagnetic*. However, if the metal ion in the complex has one or more unpaired electron, $S \neq 0$; placing the compound near a magnetic field will set up an electronic current causing it to be *drawn into* the field. This property of being drawn into the field is termed *paramagnetism* and the compound is referred to as being *paramagnetic*. In terms of the strengths of the two forces, the paramagnetic force, on a per atom basis, is the stronger of the two.

The degree to which the material exhibits either effect is called the *effective magnetic susceptibility* of the material, which is denoted by the quantity μ_{eff} and which is given in a unit called the *Bohr magneton* (BM), where $1 \text{ BM} = 9.27 \times 10^{-24} \text{ JT}^{-1}$. While μ_{eff} can vary in a complicated way with temperature, paramagnetic complexes of the first-row transition metal elements have values of μ_{eff} that are relatively independent of T near room temperature. However, for complexes of the second- and third-row transition metal elements, λ , which is the spin-orbit coupling constant, is large and for these complexes μ_{eff} is usually quite sensitive to temperature over all temperature ranges.

The general approach for determining the number of unpaired electrons of a paramagnetic complex is to measure the force with which a sample of the material is pulled into a magnetic field. After making corrections for diamagnetic effects associated with the ligands, the effective magnetic susceptibility, μ_{eff} , associated with the paramagnetic metal ion can be obtained. This value can be compared with the magnetic susceptibility, calculated using a simple formula which assumes that all of the paramagnetism is due only to the spin moments of the unpaired electrons on the metal ion, with no orbital motion. This *spin-only magnetic susceptibility*, μ_{so} , is given in two forms: (1.3), which is in terms of *S*, and (1.4), which is in terms of the number of unpaired electron

on the metal ion, *n*. For example, for a complex with three unpaired electrons, n = 3 and S = 3/2, which gives $\mu_{so} = 3.87$ BM.

$$\mu_{\rm so} = 2\sqrt{S(S+1)}\,\mathrm{BM}\tag{1.3}$$

$$\mu_{\rm so} = \sqrt{n(n+2)} \,\mathrm{BM} \tag{1.4}$$

Experimentally, it is found that metal ions in complexes with an A crystal field ground-state term, for example Co^{+2} in a tetrahedral field with the electronic configuration e^4t^3 and the ground-state crystal 4A_2 , have values of $\mu_{\rm eff}$ that are nearly the same as $\mu_{\rm so}$. This means that the only property contributing to the observed paramagnetism of the compound is the spins associated with the unpaired electrons on the metal ion. However, for metal complexes with E or T ground-state crystal-field terms, for example Fe^{+2} in a tetrahedral field with the electronic configuration e^3t^3 and the ground-state crystal-field term 5E , and Fe⁺³ in a octahedral field with the electronic configuration $t_{2g}^5 e_g^0$ and the ground-state crystal-field term ${}^2T_{2g}$, the value of μ_{eff} is usually *larger* than μ_{so} . This is because there are really two important contributions to the paramagnetism for the sample; one is associated with the spin moment of the electron but the second is associated with the orbital motion of the electron about the nucleus. For example, for T_d , Fe⁺², $e^3 t^3$, which has the 'orbital doublet' ground state E, the electronic configuration which produced the crystal-field term can be written two ways: $d_{x^2-y^2}^2$, $d_{z^2}^1$ $d_{xz}^1, d_{yz}^1, d_{xy}^1$ (a) or $d_{x^2-y^2}^1, d_{zz}^2, d_{xz}^1, d_{yz}^1, d_{xy}^1$ (b), both of which have identical energies. In this case the electronic configuration and the crystal-field term are said to be orbitally doubly degenerate. Inspection of these two electronic configurations reveals that the unpaired electron in the e level of (a) has moved from the d_{z^2} orbital to the $d_{x^2-y^2}$ orbital of (b). While this may seem trivial, it in effect constitutes a motion of the unpaired electron from one orbital to the other; that is, the electron appears to rotate about the nucleus. This rotation produces additional paramagnetism, which increases the magnetic susceptibly above the value calculated from the spinonly formula. A similar argument can also be made for a T ground-state crystal-field term, which is an *orbital* triplet and which was derived from an electronic configuration with three energy equivalent arrangements. These can be seen by simply rearranging the electrons in the t_{2g} (O_h) or t_2 (T_d) levels of the electronic configuration that produced the T crystal-field term. In the end, all complexes which have E or T crystal-field ground states accrue additional magnetic susceptibility from the orbital motion of electrons, so for these cases $\mu_{\rm eff}$ is usually grater than $\mu_{\rm so}$. Fortunately, the contribution made by the orbital motion is not so large as to preclude using the simple spin-only formula to determine the value of S for the complex from μ_{eff} .

The above description of magnetic properties of complexes assumes that the ions with unpaired electron spin are well separated from each other and that there is no interaction between the spins; that is, the systems are said to be *magnetically dilute*. However, for certain substances, such as the iron oxides, in which iron ions are imbedded in an oxide crystal lattice and the separation between ions with unpaired electrons is not large, the individual magnetic moments of ions can couple to produce substances with large net magnetic moments. While the degree of coupling varies in a complicated way with the nature of the paramagnetic ions involved, their separation in the lattice and the physical size of the particle, one case – called *ferromagnetism* – has a large group of spin moments oriented in the same direction, resulting in a large net magnetic moment, which produces a permanent magnetic field for the material. These substances are referred to as *ferromagnetic* materials.

1.5 Reactions of metal complexes

1.5.1 Forward and reverse rates and equilibrium

Most of the metal complexes that have found their way into medicine exert their biological effects by reaction with nucleophiles present in the body. While metal complexes can react through a variety of different



Figure 1.18 Rate curves, concentration vs. time, for the reaction of ML_xX , starting concentration $[ML_xX]_{0}$, with nucleophile Y to form product ML_xY

mechanisms, a substitution reaction, in which a ligand bonded to the metal ion is displaced by an attacking ligand, is the most common. In the hypothetical reaction shown in (1.5), one of the ligands originally attached to the metal ion is replaced by the attacking nucleophile to form a product with the same general structure as the starting material.

$$ML_{x}X + Y \underset{k_{-2}}{\overset{k_{2}}{\rightleftharpoons}} ML_{x}Y + X$$
(1.5)

Suppose that an attacking nucleophile, Y, is added to a solution containing ML_xX . At t = 0, the time of addition, there can be no product ML_xY and the concentration of ML_xX is its initial concentration, $[ML_xX]_0$, with the initial concentration of Y being $[Y]_0$. While activities are required for rate and equilibrium expressions, this work will assume that activities of substances are equal to their concentrations, as would be the case when concentration of starting material, ML_xX , decreases at some rate and the concentration of the product, ML_xY , increases at the same rate. This is depicted in Figure 1.18, which shows how the ratios $[ML_xX]/[ML_xX]_0$ and $[ML_xX]/[ML_xX]_0$ for the reaction change with time. The rate of decrease of ML_xX as a function of time is given by the rate law, (1.6):

$$rate = k_2[ML_xX][Y]$$
(1.6)

In this expression, k_2 is the second-order *forward rate constant*, and [ML_xX] and [Y] are the concentrations of ML_xX and Y, respectively. If there is some mechanism by which starting material can be reformed from the product, the reaction will eventually reach a point where the concentrations of all of the components in the reaction medium will not change with time and the system is said to be at *equilibrium*. In the hypothetical reaction shown in Figure 1.18, equilibrium is reached after ~10 hours. In a similar way to the process in the forward direction, the rate in the reverse direction is given by the *rate law*, (1.7):

$$rate = k_{-2}[ML_xY][X]$$
(1.7)

In this expression k_{-2} is the second-order *reverse rate constant* and [ML_xY] and [X] are the concentrations of ML_xY and X, respectively.

At small intervals of time – that is, just after the nucleophile Y has been added to the medium – the observed rate of disappearance of ML_xX is said to be the *initial rate* of disappearance, which is the *initial slope* of the rate curve for ML_xX . In this region of the rate curve there is very little product and the possibility of making some

starting material through the reaction of X with $ML_xY(1.5)$ is negligible. Since the early part of the rate curve contains no significant 'back reaction', this part of the curve can be used to calculate the true forward *rate constant*, k_2 , for the reaction from the *initial rate* of disappearance of ML_xX , and the initial concentrations, $[ML_xX]_0$ and $[Y]_0$, according to (1.8).

Initial rate =
$$k_2 [ML_x X]_0 [Y]_0$$
 (1.8)

When the system reaches equilibrium, the rates in the forward and reverse directions must be the same to give (1.9) in which the concentrations are the values at equilibrium, indicated by $[ML_xX]_{eq}$, $[ML_xY]_{eq}$, $[X]_{eq}$ and $[Y]_{eq}$. Rearranging this expression gives (1.10), which shows the relationship between the equilibrium concentrations, the equilibrium constant, *K*, and the forward and reverse rate constant for the reaction. Since the free energy, ΔG , is related to the equilibrium constant through (1.11) or its exponential form (1.12), the free energy of the reaction can be calculated from *K* and the temperature. Experimentally, a common way to obtain k_{-2} is to determine k_2 by measuring the initial rate of the reaction, allowing the reaction to reach equilibrium, and determining *K* through the equilibrium concentrations.

$$k_2[\mathrm{ML}_{\mathrm{x}}\mathrm{X}]_{\mathrm{eq}}[\mathrm{Y}]_{\mathrm{eq}} = k_{-2}[\mathrm{ML}_{\mathrm{x}}\mathrm{Y}]_{\mathrm{eq}}[\mathrm{X}]_{\mathrm{eq}}$$
(1.9)

$$\frac{k_2}{k_{-2}} = \frac{[ML_xY]_{eq}[X]_{eq}}{[ML_xX]_{eq}[Y]_{eq}} = K$$
(1.10)

$$\Delta G = -RT \ln K \tag{1.11}$$

$$K = e^{-\frac{\Delta G}{RT}} \tag{1.12}$$

1.5.2 Water exchange rates for metal ions

An important indicator or 'benchmark' of the rate at which a metal ion will be expected to undergo a substitution reaction is the rate at which it exchanges water that is bound to the ion with water that is free in solution. This rate, called the *water exchange rate*, can easily be measured using nuclear magnetic resonance, NMR. The general approach in studying water exchange kinetics using NMR is to employ water that has been labeled (enriched) with ¹⁷O, which is a stable oxygen isotope, is nonradioactive and has high NMR sensitivity. Moreover, since ¹⁷O has a nuclear spin, *I*, of ¹/₂, which is the same as the nuclear spin of a proton, the isotope produces relatively simple, readily interpretable NMR spectra.

One experimental approach for determining water exchange rates using ¹⁷O NMR is to form the *aqua* complex in medium which contains only $H_2^{16}O$, add a known amount of $H_2^{17}O$ and observe the displacement of the bound $H_2^{16}O$ by $H_2^{17}O$ using NMR (1.13).

$$[M(H_2^{16}O)_n]^{z+} + H_2^{17}O \underset{k_{-2}}{\stackrel{k_2}{\longleftrightarrow}} [M(H_2^{16}O_{n-1})(H_2^{17}O)]^{z+} + H_2^{16}O$$
(1.13)

At t = 0, the time of addition of H₂¹⁷O, all of the labeled water in solution will be in its free unbound form. While the observed NMR spectrum depends on the nature of the metal ion and the rate of the exchange process, if the metal ion is diamagnetic and if the water exchange rate is slow compared to the NMR measurement time, two peaks will be observed in the spectrum. If this is the case, the system is said to be in *slow exchange* on the NMR time scale; that is, rate constants for the chemical exchange are $k < \sim 10 \text{ s}^{-1}$. One



Figure 1.19 Simulated ¹⁷O NMR spectrum of a slow exchanging diamagnetic aqua complex, $[M(H_2^{16}O)_n]^{z+}$, in $H_2^{16}O$, a short time after the addition of excess $H_2^{17}O$ to the medium. The intensity of the product peak, $[M(H_2^{16}O)_{n-1}(H_2^{17}O)]^{z+}$, increases with time

NMR peak is due to *free* $H_2^{17}O$ and a second peak, the intensity of which increases with time, is due to *bound* $H_2^{17}O$. A hypothetical ¹⁷O NMR spectrum at some time after the addition of a large excess of $H_2^{17}O$ to a diamagnetic aqua complex is shown in Figure 1.19.

One way to measure the *rate constant* for the reaction to set up the experiment so that the concentration of labeled water, $[H_2^{17}O]$ (the brackets indicate concentration), is much larger than the concentration of the aquated metal ion, $[[M(H_2^{16}O)_n]^{z+}]$. While the exchange is a true second-order reaction and the rate law for the forward reaction is given by (1.14), if $[H_2^{17}O]$ is much larger than $[[M(H_2^{16}O)_n]^{z+}]$, the concentration of $H_2^{17}O$ can be considered constant during the course of the reaction.

$$Rate = k_2[[M(H_2^{16}O)_n]^{z+}][H_2^{17}O]$$
(1.14)

In this case the rate law can be rewritten by incorporating $[H_2^{17}O]$, which is a constant, into k_2 , which is also a constant, to give a new rate expression, (1.15).

$$Rate = k_1 [[M(H_2^{16}O)_n]^{z+}]$$
(1.15)

Since (1.15) shows that the rate of the reaction really only depends on the concentration of one component, $[M(H_2^{16}O)_n]^{z+}$, the equation is the rate expression for a *pseudo first-order* reaction, with k_1 as the *pseudo first-order* rate constant for the reaction. The word '*pseudo*' is used to denote the fact that $[H_2^{17}O] \gg [[M(H_2^{16}O)_n]^{z+}]$, and while the reaction is rigorously second-order (see (1.13)), the observed rate depends only on the concentration of *one* of the components $([M(H_2^{16}O)_n]^{z+})$ and the reaction behaves as a true *first-order* reaction.

Since the NMR observation nucleus is ¹⁷O, which is only present in the product complex and free bulk water, the way in which the concentration of starting material, $[M(H_2^{16}O)_n]^{z+}$, changes with time cannot be directly observed in the experiment. However, this concentration can be obtained using (1.16), which shows that for every molecule of $[M(H_2^{16}O)_{n-1}(H_2^{17}O)]^{z+}$ which forms and is detected by NMR, one molecule of the reactant, $[M(H_2^{16}O)_n]^{z+}$, must have reacted with labeled water. In (1.16), the subscript '0' indicates the concentration at t = 0, while the subscript 't' indicates concentration at some time t after addition of $H_2^{17}O$ to the reaction medium. Substituting (1.16) into (1.15) gives (1.17), which allows determination of k_1 from the starting concentration of $[M(H_2^{16}O)_n]^{z+}$ and the concentration of $[M(H_2^{16}O)_{n-1}(H_2^{17}O)]^{z+}$, measured by NMR, at various times.

$$[[M(H_2^{16}O)_n]^{z+}]_t = [[M(H_2^{16}O)_n]^{z+}]_0 - [[M(H_2^{16}O)_{n-1}(H_2^{17}O)]^{z+}]_t$$
(1.16)

$$Rate = k_1 \{ [[M(H_2^{16}O)_n]^{z+}]_0 - [[M(H_2^{16}O)_{n-1}(H_2^{17}O)]^{z+}]_t \}$$
(1.17)

The relationship between the concentration of unlabeled complex at t = 0, $[[M(H_2^{16}O)_n]^{z+}]_0$, or $[A]_0$, and at some time t, $[[M(H_2^{16}O)_n]^{z+}]_t$, or $[A]_t$, is given by (1.18) and the *half life*, $t_{1/2}$, the length of time required for $[[M(H_2^{16}O)_n]^{z+}]_0$ to decrease to half of its initial value, is given by (1.19).

$$\ln \frac{\left[\left[M(H_2^{16}O)_n\right]^{z+}\right]_t}{\left[\left[M(H_2^{16}O)_n\right]^{z+}\right]_0} = \ln \frac{[A]_t}{[A]_0} = -kt$$
(1.18)

$$t_{1/2} = \frac{0.6931}{k_1} \tag{1.19}$$

When using NMR to study kinetics it is necessary to convert the measured area under an NMR peak, which is proportional to the number of molecules in the solution that produced the peak, to the *concentration* of the substance in the medium. This can be done by having a known concentration of a ¹⁷O-containing substance in solution – that is, an *internal standard* – and determining the relationship between integrated NMR peak area and concentration. Once this is done, $[[M(H_2^{16}O)_{n-1}(H_2^{17}O)]^{z+}]$ can be obtained from NMR peak areas and entered into (1.17) to calculate k_1 .

Clearly, ¹⁷O NMR is a useful way to measure the water exchange rate constant for a metal complex because it shows the build-up product as a function of time. While the hypothetical spectrum shown in Figure 1.19 is for a diamagnetic metal complex with a small water exchange rate constant, some metal ions have very fast water exchange rates and some ions are paramagnetic. For example, the pseudo first-order rate constant, k_1 , for water exchange for K⁺, which is diamagnetic, is ~10⁹ s⁻¹. This means that for this ion a given water molecule bound to the ion is exchanged with one from bulk solvent about 10⁹ times per second! The net effect of the rapid chemical exchange is that the NMR instrument cannot make measurements fast enough to 'see' the bound and unbound water, so it reports the *average* of both. In this case the system is considered to be in *fast chemical exchange* on the NMR time scale, which means that the rate constant for water exchange is $k_1 > \sim 10 \text{ s}^{-1}$. If $[\text{H}_2^{17}\text{O}] \gg [[\text{M}(\text{H}_2^{16}\text{O})_n]^{z^+}]$, only a *broadened* ¹⁷O NMR resonance (no separate peak) is observed. While the analysis is less straightforward than the previously described slow exchanging system, the water exchange rate constant, k_1 , can be determined from the broadened ¹⁷O NMR peak. If the ion is paramagnetic it is still possible to measure water exchange rates with NMR but in this case peaks are generally shifted and broadened and the analysis of the data is more complicated than that presented.

Figure 1.20 shows the water exchange rates for a number of metal ions, measured by ¹⁷O NMR and other techniques [4]. The striking feature about the figure is that the pseudo first-order rate constant, k_1 , for the exchange rate varies by 19 orders of magnitude, ranging from 10^{-10} s^{-1} for Ir^{+3} to 10^9 s^{-1} for Cs^+ . While the latter ion exchanges one of its bound water molecules with bulk water a *billion* times per second, the former exchanges its water molecules once every 300 years! Not surprisingly, a single bonding model cannot be used to explain all of the water exchange rates in Figure 1.20, but as will be evident in the following section, crystal field theory can be used to explain why some rates are very slow, and simple electrostatic arguments can be used to explain why others in Figure 1.20 are very fast.

1.5.3 Transition State Theory, the kinetic rate constant and equilibrium

Observations by Arrhenius and others showed that the kinetic rate constant for any reaction, k, is given by (1.20) and its exponential form, (1.21).



Figure 1.20 Water exchange rate constants and half lives for some metal ions at 25°C. Adapted from Coord. Chem. Rev., 187, L. Helm & A.E. Merbach, Water Exchange on Metal Ions: Experiments and Simulations, 151–181. Copyright 1999, with permission from Elsevier

$$\ln k = -\left(\frac{E_a}{RT}\right) + \ln A \tag{1.20}$$

$$k = Ae^{-\frac{E_a}{RT}} \tag{1.21}$$

In this empirical expression, called the Arrhenius equation, E_a is the activation energy, A is the preexponential factor, R is the gas constant and T is the absolute temperature. The Arrhenius equation shows that while an increase in temperature *increases* the rate constant for the reaction, and thus the rate of the reaction, an increase in E_a decreases the rate constant for the reaction.

In an attempt to more clearly define the factors that influence the rate of a reaction, Eyring and others analyzed the progress of chemical reactions using *transition state theory*. With this theory, a reaction is discussed using a plot with the *reaction coordinate* as the x-axis and the free energy as the y-axis. In order for a reactant to be converted into a product, the reaction must pass through a maximum in the energy, which is denoted as the *transition state* or the *activated complex* (Figure 1.21). Transition state theory considers the energy barrier between the reactants and the products as the *free energy of activation*, which if the reaction is moving in the 'forward' direction is given the designation ΔG^{\dagger}_{f} . Since in Figure 1.21 the reactants are less



Reaction Coordinate Figure 1.21 Reaction coordinate based on transition state theory for a reaction with $-\Delta G_{rxn}$

stable than the products, the free-energy change for the reaction, ΔG_{rxn} , is *negative*, which indicates that the reaction is thermodynamically favored in moving from left to right; that is, from reactants to products. If there is a route for products to return to reactants, the free energy of activation in the reverse, 'back', direction is ΔG_{b}^{\dagger} . Using (1.12), the equilibrium constant, *K*, for such a situation is greater than 1, and if enough time is allowed for the system to reach equilibrium, the concentration of products will be greater than the concentration of reactants.

The relationship between the kinetic rate constant, k, for a reaction and ΔG^{\ddagger} from transition state theory (1.22) is almost the same as with the Arrhenius equation, but the preexponential factor, A, in (1.21) is replaced with the product of a constant, b, and the temperature, T, in (1.22). Like the Arrhenius equation, (1.22) shows that an increase in temperature *increases* the rate constant of the reaction, while an increase in the activation free energy, ΔG^{\ddagger} , *decreases* the rate constant of the reaction. It is also clear that the rate constant k in (1.21) has a slightly different temperature dependence than k in (1.21) but the main temperature dependence for both is in the exponential terms.

$$k = bTe^{-\frac{\Delta G^{i}}{RT}} \tag{1.22}$$

The water exchange reaction for a metal ion can take place through one of two possible mechanisms. One mechanism, called the *associative mechanism* (1.23), involves a water molecule from bulk solvent adding to the metal ion to form a transient high-energy *seven-coordinate* transition state (activated complex), which ultimately decays to the product by losing a water molecule. A second mechanism, called the *dissociative mechanism* (1.24), involves a *five-coordinate* complex in the transition state, which ultimately captures a water molecule to give the product.

$$[M(H_2O)_6]^{z+} + H_2O \to [M(H_2O)_7]^{z+} \to [M(H_2O)_6]^{+z} + H_2O$$
(1.23)

$$[M(H_2O)_6]^{z+} \to [M(H_2O)_5]^{z+} + H_2O \to [M(H_2O)_6]^{z+}$$
(1.24)

For transition metal ions with large crystal field stabilization energy (CFSE), changing the structure of the complex from a six- to either a seven- (associative mechanism) or a five-coordinate (dissociative mechanism) structure is generally energy expensive; that is, it costs energy to do this. Suppose for example the starting six-coordinate complex is d^6 (S = 0), which has CFSE = $-2.4 \Delta_{\circ} + 3P$, and the geometry of the activated complex is a seven-coordinate structure; that is, the associative mechanism. While the exact geometry of the transitions



Figure 1.22 Structures of cisplatin and transplatin

state is not known, a pentagonal bipyramidal structure is a reasonable supposition (Figure 1.1). From the oneelectron energy levels of the *d*-orbitals in Table 1.1, a pentagonal bipyramidal structure with S = 0 would have CFSE of $-1.548 \Delta_0 + 3P$. Thus, for the change in geometry from a six-coordinate octahedral to a sevencoordinate pentagonal bipyramid, the change in the CFSE, or Δ CFSE, given by (1.25), is $-0.852 \Delta_0$.

$$\Delta \text{CFSE} = (-2.4 \,\Delta_0 + 3P) - (-1.548 \,\Delta_0 + 3P) = -0.852 \,\Delta_0 \tag{1.25}$$

The negative sign indicates that from the standpoint of CFSE, the change in the geometry in moving from the six-coordiante octahedral structure to the seven-coordinate pentagonal bipyramidal structure is energetically *unfavorable*; that is, discounting entropy, ΔG^{\ddagger}_{f} in Figure 1.22 is positive. Performing a similar calculation for the structural change from a six-coordinate octahedral to a five-coordinate square pyramidal, a reasonable structure for the transition state gives a $\Delta CFSE$ of $-0.4 \Delta_0$, indicating that from the standpoint of crystal field effects, this *dissociative* process is also energetically unfavorable. Although factors other than simple crystal field effects are important in the rate of substitution of an ion, a useful guide is that when CFSE for the metal complex is large – for example, Ir^{+3} (5d⁶, S=0), Rh^{+3} (4d⁶, S=0), Cr^{+3} (3d³, S=3/2), Ru^{+3} (4d⁵, S= 1/2) – ΔG^{\ddagger}_{f} is generally large and the rate constant for water exchange, indeed any substitution reaction, through (1.21) or (1.22), is small. Similar arguments also apply to complexes with a four-coordinate square planar geometry, for example Pt^{+2} (5 d^8 , S=0). Square planar Pt^{+2} complexes are believed to substitute via an associative process (1.24) involving a five-coordinate transition state, which, if the structure of the intermediate is square pyramidal, has a value of $\Delta CFSE$ for reaching the transition state of $-0.628 \Delta_0$. As is shown in Figure 1.20, these ions have relatively small water exchange rate constants, which is consistent with their large negative values of $\Delta CFSE$. When Δ_0 is small, which happens when the oxidation state of the metal ion is low and if the ion is in the first-row transition metal series, values of CFSE are small. In this case, CFSE of the starting complex and the Δ CFSE required to reach a transition state become less of a predictor of reaction rate and other factors such as the organization of solvent in the solvation sphere of the complex become important in determining the reaction rates of the compound.

For main group cations that have filled outer electronic shells, there is no CFSE. For these ions, simple electrostatic considerations involving the *electrostatic potential* on the surface of the cation that contacts the water molecule can be used to explain exchange rates. For example, if a cation has a large radius and a low net positive charge, the electrostatic potential on the surface of the cation (considered a sphere) that comes into contact with the dipole of the water molecule will be small, leading to a weak electrostatic bond between water and the cation. If the bond is weak, it will be easily broken, which will ultimately translate into rapid exchange of bound water molecules with those in solvent. Consider the series $A1^{+3}$, Ga^{+3} , In^{+3} , the series Be^{+2} , Mg^{+2} , Ca^{+2} , Sr^{+2} , Ba^{+2} and the series Li^+ , Na^+ , K^+ , Rb^+ , Cs^+ , which are given in order of *increasing* ionic diameter or, since the charge on the cation in each series is the same, *decreasing* electrostatic potential on the surface of the cation. Since the smallest member of each series forms the strongest metal ion–water bond, it has the *largest* value of ΔG_{f}^{\ddagger} (Figure 1.21) and the smallest water exchange rate constant, *k*, through (1.21) and (1.22). The water exchange rate data given in Figure 1.20 show that *k* increases with atomic number for each series, which indicates that the simple electrostatic argument given above is probably correct.

	Table 1.6	The trans	effect	series ^a
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^a In this series, CN⁻ is the strongest *trans* directing ligand and water is the weakest. This table is the series stated in text on p. 439 of Miessler, G.L., Tarr, D.A. (2004) *Inorganic Chemistry*, 3rd edn, Pearson Prentice Hall, Upper Saddle River, NJ.

1.5.4 Trans effect and substitution reactions

In even a brief presentation of the substitution properties of metal complexes, it is important to describe the *trans effect* observed for reactions of square planar compounds, especially those of Pt^{+2} , which are potent anticancer drugs. In simple terms, the *trans effect pertains to the ability of a ligand in a complex to direct substitution opposite, or trans, to itself.* This effect was discovered by Chernyaev [5], who after synthesizing many square planar complexes of Pt^{+2} found that the presence of certain ligands attached to the metal ion had the ability to cause the loss of the group that was in the position *trans* to the ligand in a substitution reaction. As might be expected, not all ligands have the same strength in *'trans* directing ability' and ultimately a series, called the *trans effect series* (Table 1.6), was created to rank common ligands by their ability to direct an incoming group (nucleophile) to the coordination site *trans* to themselves. In this series, the ligand with the greatest *trans* directing ability is water, H₂O.

A number of models have been proposed to explain the *trans* effect and why a given ligand is where it is in the series, but in the end none seem to provide an explanation of the ranking of all of the ligands in the series. Early models focused on the structure of the reactants and whether and to what extent groups that were *trans* to strong *trans* directing ligands have their bonds lengthened. These models, which used thermodynamic arguments, assumed that if a bond was slightly longer in the starting complex it would be the bond broken in the substitution reaction. Other models, which were based on transition state theory, and thus provided a kinetic focus, addressed the structure of the transition state or activated complex in the reaction. These models considered how the *electronegativity* of groups and/or their ability to form π -bonds with the metal ion in the transition state affected which groups would be lost when the product was formed. While these models addressed the *trans* effect from the kinetic perspective – that is, they considered the nature of the transition state and discussed what happened in terms of the reaction coordinate – difficulties in estimating the electronegativities of groups and a lack of knowledge of the structure of the transition state made them somewhat difficult to use.

In order to illustrate how the *trans* effect series works, consider the syntheses of the important anticancer drug *cisplatin*, *cis*-diamminedichloroplatinum (II), and its less active isomer, *transplatin*, *trans*-diamminedichloroplatinum (II), Figure 1.22 [6]. Note that when ammonia is incorporated into a metal complex as a ligand, scientific nomenclature requires that the term used in the name of the compound is 'ammine'. In the synthesis of cisplatin, which most often employs the Dhara synthesis [7] (Figure 1.23), a commercially available source of Pt^{+2} , potassium tetrachloroplatinate, $K_2[PtCl_4]$, is reacted with excess potassium iodide, KI, in water [4]. Most of the evidence for reactions of this type shows that the mechanism is *associative*; that is, an iodide ion attacks the platinum ion as one of the bound chloride ligands leaves. This substitution occurs sequentially until all four chloride ligands have been replaced by iodide to form $[PtI_4]^{-2}$. In this reaction, the attacking ligand approaches the platinum ion via the unobstructed z-axis of $[PtCl_4]^{-2}$; that is, it attacks the exposed d_{z^2} orbital of the complex (Figure 1.3) to produce a five-coordinate, most likely trigonal bipyramidal, transition state (Figure 1.1). After $[PtCl_4]^{2-}$ has been converted to $[PtI_4]^{2-}$, the next step in the Dhara synthesis of cisplatin is to add two equivalents of ammonia, NH₃, to the tetra-iodo complex. Note that when addressing a group bound to a metal ion which is an anion, the suffix 'o' is added to the name of the group. The interesting feature of the product of this reaction is that that while two geometric isomers are possible, *cis* and *trans* (Figure 1.23), and the *former* is less *thermodynamically stable* than the *latter*, only the *cis* isomer is formed in the reaction.



Figure 1.23 Synthesis of cisplatin

The key intermediate, which is normally not isolated in this reaction, is $[PtI_3(NH_3)]^-$ (Figure 1.23). The addition of the second equivalent of ammonia to this intermediate can proceed by displacing the iodide ion *trans* to the ammonia, or it can proceed by displacing one of the two iodides that are *cis* to the ammonia. If displacement were purely random, one might expect 67% *cis* (there are two ways to make this isomer) and 33% *trans* (there is one way to make this isomer), but the isolated product *is 100% cis*! This observation is a manifestation of the *trans* effect, which shows that the ability of iodide to direct substitution *trans* to itself is greater than that of ammonia to direct substitution *trans* to itself. Thus, as the reaction proceeds, the iodide ion that is *trans* to the other iodide is lengthening its bond, and it is eventually displaced from the platinum by ammonia to form the *cis* product, *cis*-[PtI₂(NH₃)₂].

The next step in the Dhara synthesis is to replace the two iodides with two water molecules. This is done by adding two equivalents of silver nitrate, AgNO₃, which results in the formation of insoluble AgI. This reaction works because all metal complexes in aqueous solution exist in an equilibrium, which means that some fraction of the ligands bound to the metal ion must be in equilibrium with their unbound counterparts (Figure 1.24). If the complex is thermodynamically very stable, the equilibrium will be largely in favor of the



Figure 1.24 Equilibria involving the iodo complexes in the synthesis of cisplatin

intact complex, but the concentration of *unbound ligand* can never be zero. The equilibrium expressions (Figure 1.24) in the case of *cis*-[PtI₂(NH₃)₂] are written as dissociations (dissociation of I⁻ from platinum) and are described by the dissociation constant, K_d , which is related to the normal (association) equilibrium constant, K, by (1.26).

$$K = 1/K_{\rm d} \tag{1.26}$$

While K_{d1} and K_{d2} (Figure 1.24) for this reaction are likely very small, addition of Ag⁺ ion to the solution as AgNO₃, which is water soluble, causes insoluble AgI to precipitate from solution, which, from Le Chatelier's principle, drives the equilibrium to the right. This phenomenon is called a *phase change*, in which some of the material originally in the solution phase, Ag⁺ and I⁻, moves to a another phase, in this case insoluble AgI. Because nitrate ion, NO₃⁻, is lower in the spectrochemical series (Table 1.2) than water, and the concentration of water is very high, >50 *M*, nitrate ion is simply a 'spectator ion' and is not part of the equilibrium expressions given in Figure 1.24.

The last step in the synthesis is to simply displace the two coordinated water molecules of *cis*-[Pt- $(H_2O)_2(NH_3)_2$]²⁺ by adding an excess of chloride ion as KCl, which forms yellow cisplatin, *cis*-[PtCl₂(NH₃)₂]. Even though Δ_o (H₂O) > Δ_o (Cl⁻), addition of excess chloride ion to the medium drives the equilibrium to the right, and since cisplatin is only sparingly soluble in water, the complex precipitates from solution as its sparingly soluble dichloro form.

The synthesis of *transplatin* (Figure 1.25) also presents examples of the *trans* effect in coordination chemistry. As with cisplatin, the starting material for the synthesis of transplatin is $K_2[PtCl_4]$, which, in this case, reacts with excess ammonia to produce the tetra-ammine complex, $[Pt(NH_3)_4]^{2+}$. The next step is to react this complex with excess chloride ion in hot hydrochloric acid, HCl. In this reaction, the first chloride ion displaces an ammonia molecule from platinum, which, because the solution is very acidic, is immediately protonated to form NH_4^+ . Since the lone pair on NH_4^+ is bound by a proton, the released ammonia molecule is blocked from attacking the platinum ion. The second chloride can either occupy the position *trans* to the first chloride is a better *trans* directing ligand than is ammonia (Table 1.6), the second chloride displaces the ammonia molecule trans to the first chloride to produce transplatin. While the reaction conditions would almost certainly lead to



Figure 1.25 Synthesis of transplatin

further displacement of ammonia from platinum by chloride, transplatin is the least soluble component in the reaction medium and it precipitates from the medium before it has the chance to further react with chloride ion.

1.5.5 Stability of metal complexes

A property of metal complexes that is a measure of their stability in solution is called the *stability constant*, K_f , which is sometimes called the *formation constant*, K_f . In certain cases the stability of a complex may be sensitive to pH, especially in the physiological range, in which case the *conditional stability constant*, at some specified condition, can be indicated. While there are many different ways to determine the stability constant of a metal complex, one is to use absorption spectroscopy to measure spectral changes in solution as ligand is added to the system. For example, consider the equilibrium binding process in (1.27), in which one ligand reacts with a metal ion to produce a 1: 1 complex. The stability constant (equilibrium constant) for this system is given by (1.28), where [ML] is the concentration of complex and [M] and [L] are the concentrations of *free metal ion* and *free ligand*, respectively.

$$\mathbf{M} + \mathbf{L} = \mathbf{M}\mathbf{L} \tag{1.27}$$

$$K = \frac{[\mathrm{ML}]}{[\mathrm{M}][\mathrm{L}]} \tag{1.28}$$

The typical way to determine the stability constant, K, for this system is to first determine the molar extinction coefficient of the complex that forms, ML, by driving the system to the right by adding a large excess of the ligand which complexes all of the metal ion. Once ε_{max} for the complex is determined (Box 1.1), solutions with different concentrations of ligand and a constant concentration of metal ion are prepared and their absorption spectra measured to determine the concentration of complex, ML, in each. By knowing the concentration of ML present in each mixture and the total concentrations of metal ion and ligand in the mixtures, the value of K can be calculated from (1.28).

Most systems are much more complicated than the example given and more than one equilibrium expression is most often involved. For example, consider the reaction of ammonia, NH₃, with the aquated complex $[Cu(H_2O)_6]^{2+}$. Since Cu⁺² has the electronic configuration $3d^9$, it is a Jahn–Teller distorted system with two of the *trans* water molecules on the z-axis of the complex farther away from the metal ion than the other four. Studies using absorption spectroscopy show that in water, ammonia adds to aquated Cu⁺² in a stepwise manner to produce four distinct complexes, a process summarized by (1.29)-(1.32). Unless very unusual circumstances are present, the highest-order complex that forms in the ammonia system is $[Cu(NH_3)_4]^{2+}$, so for simplicity the two weakly-bound water molecules in the axial sites of $[Cu(H_2O)_6]^{2+}$ have been eliminated in the equilibrium reactions.

$$\left[Cu(H_2O)_4\right]^{2+} + NH_3 = \left[Cu(NH_3)(H_2O)_3\right]^{2+} + H_2O$$
(1.29)

$$\left[Cu(NH_3)(H_2O)_3\right]^{2+} + NH_3 = \left[Cu(NH_3)_2(H_2O)_2\right]^{2+} + H_2O$$
(1.30)

$$\left[Cu(NH_3)_2(H_2O)_2\right]^{2+} + NH_3 = \left[Cu(NH_3)_3(H_2O)\right]^{2+} + H_2O$$
(1.31)

$$\left[Cu(NH_3)_3(H_2O)\right]^{2+} + NH_3 = \left[Cu(NH_3)_4\right]^{2+} + H_2O$$
(1.32)

The equilibrium expression for the first step in this sequence is (1.33), which, if the concentration of water is eliminated in the reaction (it is a constant and is incorporated into *K*), gives (1.34).

$$\frac{\left[\left[\operatorname{Cu}(\operatorname{NH}_{3})(\operatorname{H}_{2}\operatorname{O})_{3}\right]^{2+}\right]\left[\operatorname{H}_{2}\operatorname{O}\right]}{\left[\left[\operatorname{Cu}(\operatorname{H}_{2}\operatorname{O})_{4}\right]^{2+}\right]\left[\operatorname{NH}_{3}\right]} = K_{1}'$$
(1.33)

$$\frac{\left[\left[\operatorname{Cu}(\operatorname{NH}_{3})(\operatorname{H}_{2}\operatorname{O})_{3}\right]^{2+}\right]}{\left[\left[\operatorname{Cu}(\operatorname{H}_{2}\operatorname{O})_{4}\right]^{2+}\right]\left[\operatorname{NH}_{3}\right]} = K_{1}$$
(1.34)

The equation which describes the formation of the final complex, called the *overall reaction*, from the free aqua complex and the free ligand is (1.35). By writing the individual equilibrium expressions (1.29)–(1.32) to obtain K_{1-4} , it would be easy to show that the equilibrium constant for the overall reaction (1.35) is the *product* of the individual stepwise equilibrium constants; that is, (1.36). This product is given the designation K_{1-n} or β_n , where n is the number of steps in the overall reaction. Since the values of K_{1-n} and β_n are often very large, the typical way to denote the overall stability constant is log K_{1-n} or log β_n .

$$\left[\mathrm{Cu}(\mathrm{H}_{2}\mathrm{O})_{4}\right]^{2+} + 4\mathrm{NH}_{3} = \left[\mathrm{Cu}(\mathrm{NH}_{3})_{4}\right]^{2+} \tag{1.35}$$

$$\frac{\left[\left[\operatorname{Cu}(\operatorname{NH}_{3})_{4}\right]^{2+}\right]}{\left[\left[\operatorname{Cu}(\operatorname{H}_{2}\operatorname{O})_{4}\right]^{2+}\right]\left[\operatorname{NH}_{3}\right]^{4}} = K_{1}K_{2}K_{3}K_{4} = K_{1-4} = \beta_{4}$$
(1.36)

By systematically increasing the total concentration of ammonia in solution, collecting absorption spectra and fitting the data to a model, the stability constants for the copper–ammonia system at 30 °C were determined to be $K_1 = 1.78 \times 10^4 M^{-1}$, $K_2 = 2.30 \times 10^3 M^{-1}$, $K_3 = 9.77 \times 10^2 M^{-1}$ and $K_4 = 63.1 M^{-1}$, which in this case gives $K_1 \times K_2 \times K_3 \times K_4 = K_{1-4} = \beta_4 = 2.5 \times 10^{12} M^{-4}$, or log K_{1-4} or log $\beta_4 = 12.4$ [8]. Note that while the unit of concentration is indicated in the values of K and β , which is helpful for determining whether the equilibrium expression is written as an *association* or a *dissociation*, it is not possible to take the logarithm of the unit. As pointed out in Section 1.5.1, the concentration of a substance is assumed to be equal to the activity of the substance, which, since the latter is unitless, will not present a problem in obtaining the logarithm of the value.

Similarly to (1.12), the relationship between the stability constant of the overall reaction, K_{1-4} and β_n , and ΔG is given by (1.37), which is related to the change in enthalpy, ΔH , making and breaking bonds, and the entropy, ΔS , the amount of disorder in the reaction, through the well-known equation (1.38).

$$K_{1-4} = \beta_{\rm n} = e^{-\frac{\Delta G}{RT}} \tag{1.37}$$

$$\Delta G = \Delta H - T \Delta S \tag{1.38}$$

1.5.6 Chelate effect

For many years scientists have recognized that ligands which form a ring structure that includes the metal ion, called a *chelate ring*, have exceptional thermodynamic stability. This 'extra' stability, beyond that which would be achieved with a similar system without a chelate ring, is called the *chelate effect* in inorganic chemistry. As with organic chemistry, chelate rings that have a total of five or six atoms in the ring (this includes the metal ion) are more stable than rings with four or seven members. In order to see how the chelate effect works, consider the reaction of two ammonia molecules with aquated Cu^{+2} (1.39) and, for comparison, the reaction of the bidentate ligand, ethylenediamine, $NH_2CH_2CH_2NH_2$, abbreviated 'en', with aquated Cu^{2+} , (1.40).



Figure 1.26 Structure of an octahedral complex with ethylenediaminetetraacetic acid, EDTA, which binds to the metal ion as a tetravalent anion

$$[Cu(H_2O)_6]^{2+} + 2 NH_3 = [Cu(H_2O)_4(NH_3)_2]^{2+} + 2 H_2O$$
(1.39)

$$[Cu(H_2O)_8]^{2^+} + NH_2CH_2CH_2NH_2 \longrightarrow (H_2O)_4Cu + 2H_2O \qquad (1.40)$$

Experimentally, the reaction with ammonia (1.39) has an overall stability constant for the formation of the *bis*-ammonia complex of log $\beta_2 = 7.61$, while the reaction with en (1.40), which results in the formation of a five-membered, en, chelate ring, has log $\beta_1 = 10.73$ at 25 °C [9]. This is an example of the chelate effect in that the presence of the ring increases the stability constant of the Cu²⁺-en complex over that of the Cu⁺² ammonia system by more than three orders of magnitude.

The nomenclature used in referring to the type of chelate ring formed by a ligand is to say the ligand is *bidentate* if it has two points of attachment (two donor atoms) to the metal ion, *tridentate* if it has three points of attachment, *tetradentate* if it four, and so on. While the arrangement of chelate rings, the nature of the donor atoms and their charge, and the size of the rings all affect the stability of the complex, in general ligands which have multiple points of attachment to the metal ion produce the most stable complexes. An example of a common *hexadentate* ligand which forms very stable complexes with a wide variety of metal ions is EDTA, ethylenediaminetetraacetic acid, which is shown in Figure 1.26.

The exceptional stability of metal chelate compounds implies that the binding constant of the ligand toward the metal ion, K, is large, and therefore the change in the free energy, ΔG , through (1.12) is large and negative. Since ΔG is related to ΔH and ΔS through (1.38), it is sometimes possible to determine which thermodynamic quantity makes the most important contribution to the free energy. However, since ΔH and ΔS reflect the *net changes* in these quantities in the reaction, and solvent molecules around the starting materials and products can play an important role, even a qualitative assessment of the relative importance of these quantities is challenging. The fact that there are two 'particles' on the left of reaction (1.40), the aquated complex and the bidentate ligand, and three particles on the right, the bidentate complex and two water molecules – the latter returning to bulk solvent – an increase in *entropy* in moving from left to right (ΔS is positive for the reaction) is often cited as the thermodynamic basis for the chelate effect.

1.5.7 Macrocyclic effect

As might be expected, totally surrounding the metal ion with a ligand that is cyclic and has no 'ends' further enhances the stability of the resulting complex. For example, consider the complexes $[Cu(232 \text{ tet})]^{2+}$ and



Figure 1.27 Structures of $[Cu(232 \text{ tet})]^{2+}$, $[Cu(cyclam)]^{2+}$ and [Cu(TPP)], where TPP is the di-deprotonated porphyrin core of meso-tetra-(p-sulfonatophenyl)porphyrin

[Cu(cyclam)]²⁺, shown in Figure 1.27, which are formed in the reaction of aquated Cu²⁺ with the *acyclic ligand*, 232 tet, or the macrocyclic ligand, cyclam. The stability constant for [Cu(232 tet)]²⁺ at 25 °C is log $\beta_1 = 23.2$, while the stability constant for [Cu(cyclam)]²⁺ is log $\beta_1 = 27.2$ [10]. The observation that the stability constant for a complex containing a macrocyclic ligand is greater than the stability constant for an analogous complex with an acyclic ligand is termed the macrocyclic effect in inorganic chemistry. The values of ΔH for [Cu(232 tet)]²⁺ and [Cu(cyclam)]²⁺ are -110.8 and -135.4 kJ mol⁻¹ respectively, clearly showing that enthalpy contributes to the enhanced stability of the macrocyclic complex. The values of ΔS for the two compounds are 66.9 and 50.2 J mol⁻¹ K⁻¹, respectively, showing that entropy actually favors the formation of the acyclic complex, [Cu(232 tet)]²⁺. Although it is not easy to explain the observed values of ΔH and ΔS from the structures of the complexes alone, or what might be taking place in terms of bond breaking and formation

and what the 'order' (entropy) is like on either side of the reaction, the macrocyclic effect appears to be largely governed by *enthalpic* factors.

The porphyrin ligand, which is present in many biological molecules, is a highly versatile tetraaza (four nitrogen atoms) macrocyclic ligand which forms very stable complexes. In the free form, the porphyrin ligand has two pyrrole hydrogen atoms, which can be lost when the ligand, as a dianion, binds to a metal ion. For example, the reaction of Cu^{2+} with the *tetra* sulfonated porphyrin ligand TPPS produces the complex, Cu-TPPS (Figure 1.27). This complex, which has a stability constant at 25 °C of log $\beta_1 = 38.1$, is considerably more stable than [Cu(cyclam)]²⁺ [11]. Although detailed thermodynamic data for Cu-TPPS are not available, the high stability of the complex is likely due to the fact that the porphyrinato ligand has two negative charges and thus is electrostatically attracted to the metal ion, which is a cation. An additional factor underlying the stability of Cu-TPPS is probably related to the high rigidity of the porphyrin macrocycle. Once a metal ion is bound in the cavity of the ligand, removing the porphyrin requires folding the structure in some manner that would be energetically unfavorable. Thus, highly conjugated, aromatic, porphyrin ligands enhance the macrocyclic effect to an even higher level than other types of macrocyclic structure.

1.5.8 Hard-soft acids-bases

The concept of hard and soft acids and bases, given the acronym HSAB, was introduced by the renowned inorganic chemist Ralph G. Pearson [12]. This concept addresses the rate of formation and thermodynamic stability of metal complexes in terms of the nature of the metal ion and ligand that come together to form a bond. Pearson observed that a metal ion which is a so-called 'hard acid' forms a strong complex with a ligand that is a 'hard base', and a metal ion that is a 'soft acid' also forms a strong complex with a ligand that is a 'soft base'. If the bonding partners are interchanged - that is, soft acid with hard base or hard acid with soft base complexes with lower stabilities result. This early remarkable observation was based on the measured rates and stabilities of complexes and on an assessment of the 'deformability or polarizibility' of the 'electron clouds' on both the metal ion and the ligand. If a metal ion or ligand has a large radius and low net charge, the nucleus has less control over the frontier (outer) electrons and the electron distribution of the ion can be more easily distorted (polarized). A metal ion or ligand donor atom with these properties is considered a *soft acid* (M) or soft base (L). If, on the other hand, an ion has a high charge and a small radius, the electronic shape of the ion cannot be easily polarized or distorted. A metal ion or ligand with these properties is considered a hard acid (M) or a hard base (L). While the observation of which combinations produce the highest stabilities and reaction rates is irrefutable, explaining the effect in terms of the physical properties of atoms and ions is not straightforward and is beyond the scope of the presentation given here. However, one point concerning the connection between the rate of a reaction (a kinetic property) and the stability of the product (a thermodynamic property) is worth noting. From transition state theory, the rate constant for a reaction depends in an inverse exponential way on the activation free energy of the reaction, ΔG^{\ddagger} , through (1.22). On the other hand, the stability constant for the products formed in the reaction, K, is determined from the differences in the free energies of the products and reactants, ΔG_{rxn} , through (1.12). Using the principles of transition state theory, this means that if $\Delta G_{\rm rxn}$ is large and negative, $\Delta G^{\ddagger}_{\rm f}$ is small and positive and the rate constant, k, for reactants moving to products is large (1.22). In the context of the HSAB concept, this means that if all other factors are equal, a soft ligand will react *faster* with a soft metal ion to produce a complex with high stability, while a hard ligand will react with a soft metal ion more *slowly* to produce a complex with low stability. While the exact reasons why hard-hard and soft-soft combinations are better than hard-soft/soft-hard combinations is challenging to explain, simply knowing which combinations lead to products with high stabilities and rates of formation is very useful for assessing whether and to what extent a metal complex introduced into the body will react with nucleophiles found in the biological milieu. A list of the hard-soft acids-bases to be encountered in this text is given in Table 1.7.

Metal Ions (Acids)			Ligands (Bases)			
Soft	Intermediate	Hard	Soft	Intermediate	Hard	
	$\begin{array}{c} Au^{+3} \\ Ru^{+3} \\ Ti^{+2} \\ Fe^{+2} \\ Zn^{+2} \\ Cu^{+2} \\ Tc^{+3} \\ Re^{+3} \end{array}$	Tc ⁺⁵ , Tc ⁺⁷ Gd ⁺³ Ga ⁺³ Ti ⁺⁴ Fe ⁺³ Re ⁺⁵ , Re ⁺⁷ V ⁺⁴ , V ⁺⁵ Rh ⁺³ Mn ⁺²	CN-R CO $R-S^-$ R_2S Cp R_3P dmso CN ⁻	Pyridine Imidazole Br ⁻	H_2O HO^- acac NH_3 RNH_2 R_2NH Cl^- CO_3^{2-} , HCO_3^- $H_2PO_4^-$, HPO_4^{2-} RCO_2^- O^{-2}	
Ligands ((Bases) on DNA/RNA		Ligands (Bases) on Proteins			
Soft	Intermediate	Hard	Soft	Intermediate	Hard	
	Nitrogen sites on, A, G, T, C, U	ROPO ₂ OR	R-S ⁻ , Cys RSCH ₃ , Met	Imidazole RSSR, Disulfide	Lys, RNH ₂ RCO ₂ ⁻ , Asp, Glu	
			RS ⁻ , GSH R-Se ⁻ , Sec		ϕ -O ⁻ , Tyr	

 Table 1.7
 Hard–soft acids–bases

Cp, cyclopentadienyl; dmso, dimethylsulfoxide; acac, acetylacetone; GSH, glutathione.

Problems

- 1. Give the number of *unpaired electrons* in the complexes $[Ni (en)_3]^{2+}$, octahedral, $[NiCl_4]^{2-}$, tetrahedral and $[Ni(CN)_4]^{2-}$, square planar. The abbreviation 'en' is H₂NCH₂CH₂NH₂ or ethylenediamine, which acts as a bidentate ligand with two points of attachment to the Ni^{+2} ion.
- 2. Of the following pairs of complexes, which one has the *larger* crystal field spitting parameter, Δ ? Which complex of the pair has the absorption maxima of its *d*-*d* electronic transitions at *higher* energy? Give reasons for your choice.

 - a. $[CoF_6]^{4-}$ vs. $[CoF_6]^{3-}$ b. $[Fe(CN)_6]^{4-}$ vs. $[Os(CN)_6]^{4-}$ c. $[CoF_6]^{3-}$ vs. $[CoCl_6]^{3-}$ d. $[Co(H_2O)_6]^{2+}$ vs. $[CoCl_4]^{2-}$ e. $[TiF_6]^{3-}$ vs. $[VF_6]^{2-}$.
- 3. Which crystal-field terms (states) are produced from a free-ion 'F' term (state) in octahedral and tetrahedral crystal fields?
- 4. Using an appropriate diagram, give the ground-state crystal-field term, for example ${}^{1}A_{1g}$, for the ions given below. For each possibility, indicate the two lowest-energy excited states that have the same spin multiplicity as the ground state; that is, Laporte-forbidden-spin-allowed transitions.

a. Co^{+2} , tetrahedral

b. Fe^{+3} , octahedral, high spin

c. Fe⁺³, octahedral, low spin

d. Cu^{+2} . tetrahedral.

- 5. Consider that $[Au Cl_4]^-$, $5d^8$, can exist in either of two possible geometries, square planar, S=0 or tetrahedral, S = 1. Using the energies of the *d*-orbitals in Table 1.1, estimate the value of P/Δ_0 at which both geometries, from crystal field considerations, would be equally likely.
- 6. Determine the crystal field stabilization energy, CFSE (in units of Δ_{\circ}), and the electronic configuration, $t_{2g}^3 e_g^1$ and so on, of the following. The quantity S, the total spin quantum number, is the number of unpaired electrons divided by 2.

 - a. $[\text{FeBr}_6]^{4-}$, octahedral, S = 2b. $[\text{Fe}(\text{CN})_6]^{4-}$, octahedral, S = 0
 - c. $[FeCl_4]^{2-}$, tetrahedral, S = 2.
- The complex $[Co(en)_3]^{3+}$ (diamagnetic, S=0) exhibits two absorption bands at 21 550 cm⁻¹ 7. $(\varepsilon, 88 M^{-1} \text{ cm}^{-1})$ and 29600 cm^{-1} ($\varepsilon, 78 M^{-1} \text{ cm}^{-1}$). Using a Tanabe–Sugano diagram and assuming that the symmetry about the cobalt ion is octahedral, assign the two transitions (for example ${}^{3}T_{2g} \leftarrow {}^{4}A_{1g}$) for this complex.
- 8. What is the ground-state *free-ion term symbol* for an ion with the $3d^1$ electronic configuration? What *crystal-field terms* are associated with d^1 in an octahedral crystal field?
- 9. Draw and label the approximate molecular orbital diagrams for an octahedral complex with only σ -bonding between the metal ion and ligands. Indicate which levels in the diagram can be derived using simple crystal field splitting arguments.
- 10. The magnetic moment for a metal complex is 3.92 BM. How many unpaired electrons are there on the metal ion in the complex?
- A complex of a first-row transition metal complex has an octahedral geometry with S = 1 and 11. $\mu_{\rm eff} = 3.42$ BM. Answer the following:
 - a. How many unpaired electrons does the complex have?
 - b. What is the ground-state crystal-field term, including the spin and orbital multiplicity, of the state?
 - c. Briefly explain why μ_{eff} is greater than μ_{so} for this complex.
- The pseudo first-order rate constant for the reaction of the thiol-containing ligand glutathione with a 12. metal complex is 1.2×10^{-2} s⁻¹ at 37 °C. If the concentration of thiol in the reaction medium is 1 mM and the concentration of metal complex is 1 μM , calculate the *second-order rate constant* for the reaction from the data given.
- 13. Carbonic anhydrase (CA) is a zinc-containing enzyme located in the cytoplasm and mitochondria that catalyzes to conversion of carbon dioxide to carbonic acid by reaction with water. If the concentration of carbon dioxide in solution decreases from 220 mM to 55.0 mM in 1.22×10^4 seconds, and the reaction is far from reaching equilibrium, calculate the $t_{1/2}$ (half life) for the first-order reaction.
- The DNA nucleotide adenosine triphosphate, ATP, reacts with the metal complex [ML₃Cl] in aqueous 14. media by loss of the chloride ligand according to the reaction below:

$$[ML_3Cl] + ATP = ML_3 - ATP + Cl^-$$

- a. If the initial rate for this reaction is $3.6 \times 10^{-2} M s^{-1}$ at 37 °C and the initial concentration of both the nucleotide and the metal complex in the reaction medium is 3.0×10^{-3} M, calculate the second-order rate constant, k_2 , for the reaction.
- b. After 24 hours the reaction reaches equilibrium and the equilibrium constant, K, is determined to be, 10^2 . Calculate the free energy, ΔG , for the reaction R = 8.314 J K mol⁻¹.

- c. Calculate the second-order *reverse rate constant*, k_{-2} , to reform starting materials for the reaction.
- 15. Using the *trans* effect series, predict the products of the following reactions. Assume a ratio of starting material to reactant of 1:1.
 - a. $[Pt(CO)Cl_3]^- + NH_3 \rightarrow$ b. $[Pt(NH_3)Br_3]^- + NH_3 \rightarrow$.
- 16. The reaction of a nucleophile with a metal complex produces two products, A and B, which are in equilibrium with each other with $[A]_{eq} = 2[B]_{eq}$ at 37 °C. Calculate the free-energy difference between A and B, $R = 8.314 \text{ J K mol}^{-1}$.
- 17. The equilibrium constants for the addition of the first and second ligand chloride ligand to a metal complex are $K_1 = 3.6 \times 10^4$ and $K_2 = 4.1 \times 10^3$. Calculate log β_2 for this complex.
- 18. The linear two-coordinate Au^+ complex [AuCl(PEt₃)], where PEt₃ is triethylphosphine, is implicated in the reactions of the antiarthritic drug auranofin. When this complex reacts with nucleophiles by losing the chloride ligand, will it form a more stable complex with the ε -amino group (NH₂-R) of the amino acid lysine or the thiol group (HS-R) of the amino acid cysteine? Briefly explain your choice.

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