Inorganic Pharmaceutical Chemistry: Atomic and Molecular Structure/Complexation

Part II

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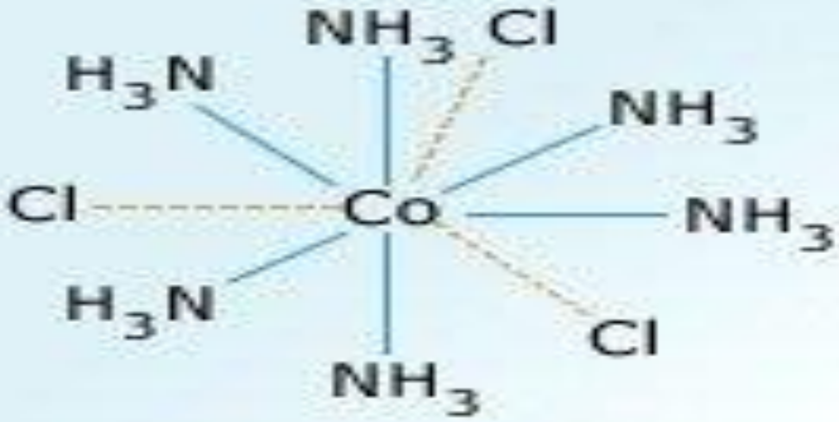
Coordination Compounds and Complexation

- It is largely transition metal chemistry but also involves metals beyond the second period outside the transition series to some extent.
- The metallic cation appears to be able to bond with additional anions or molecules after the normal valence requirements have been satisfied.
- The additional bonding species are usually termed ligands, and appear to bond directly to the metal cation in accordance with the maximum coordination number. **It is the maximum number of ligands that can be accommodated by a metal ion and is a property of the metal and its charge.**
- The ligands occupy space about the metal known as the coordination sphere, and, although they may be displaced by other ligands, they do not normally dissociate (ionize) from the metal. Therefore, the metal and its associated ligands constitute what is known as a complex ion, if charged; the neutral complex or the complex ion with its counter ions is known as a coordination compound.
- **Some complexes are stable in crystalline form and decompose in solution, while others are stable only in solution.**

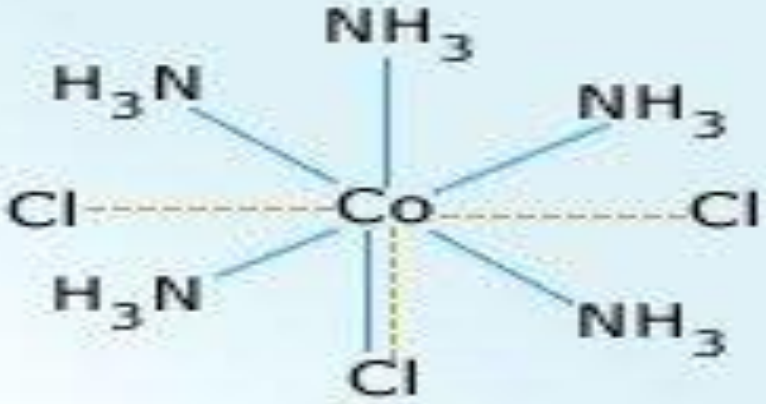
- **Werner's theory** states that the transition metal cation will have two valencies: a primary and a secondary. The primary valence is equal to the oxidation number of the metal cation, is ionizable, and can be satisfied by negative charges. For example, in **$[Pt(NH_3)_6]Cl_4$** primary valency is 4, and the secondary valency is 6.
- **The main points of Werner's theory are:**

1. The central metal atom\ ion in a coordination compound exhibits two types of valencies - primary and secondary
2. Each metal exhibits a specific, maximum number of secondary valences called the coordination number.
3. The primary valences of metal are filled by anions, but the secondary valence (in the coordination sphere) may be satisfied by anions and/or neutral molecules known as ligands. Cationic groups sometimes (but rarely) are present.
4. The ligands are arranged around the metallic ion in certain characteristic geometries. Those compounds having coordination number 2 are either linear or angular, 3 are trigonal-coplanar or trigonal-pyramidal, 4 are usually tetrahedral or square-planer, 5 are square-pyramidal or trigonal-bipyramidal, and 6 are ligands arranged octahedrally.



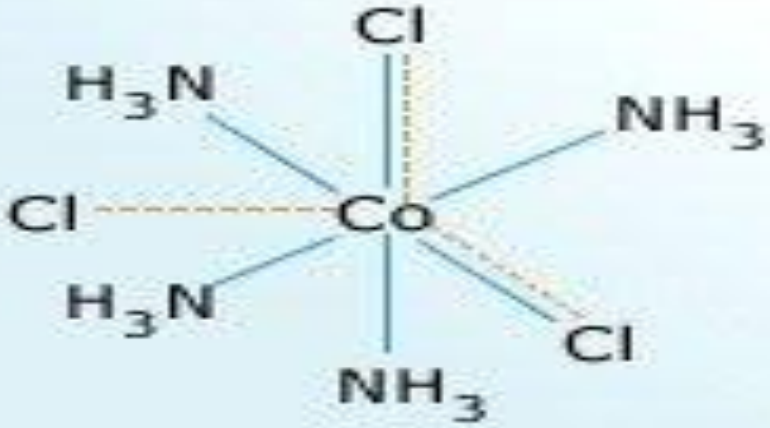
$[Co(NH_3)_6]Cl_3$

I

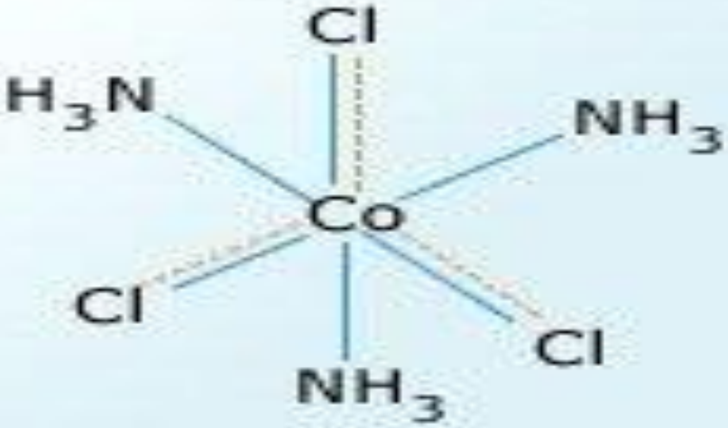


$[Co(NH_3)_5Cl]Cl_2$

II

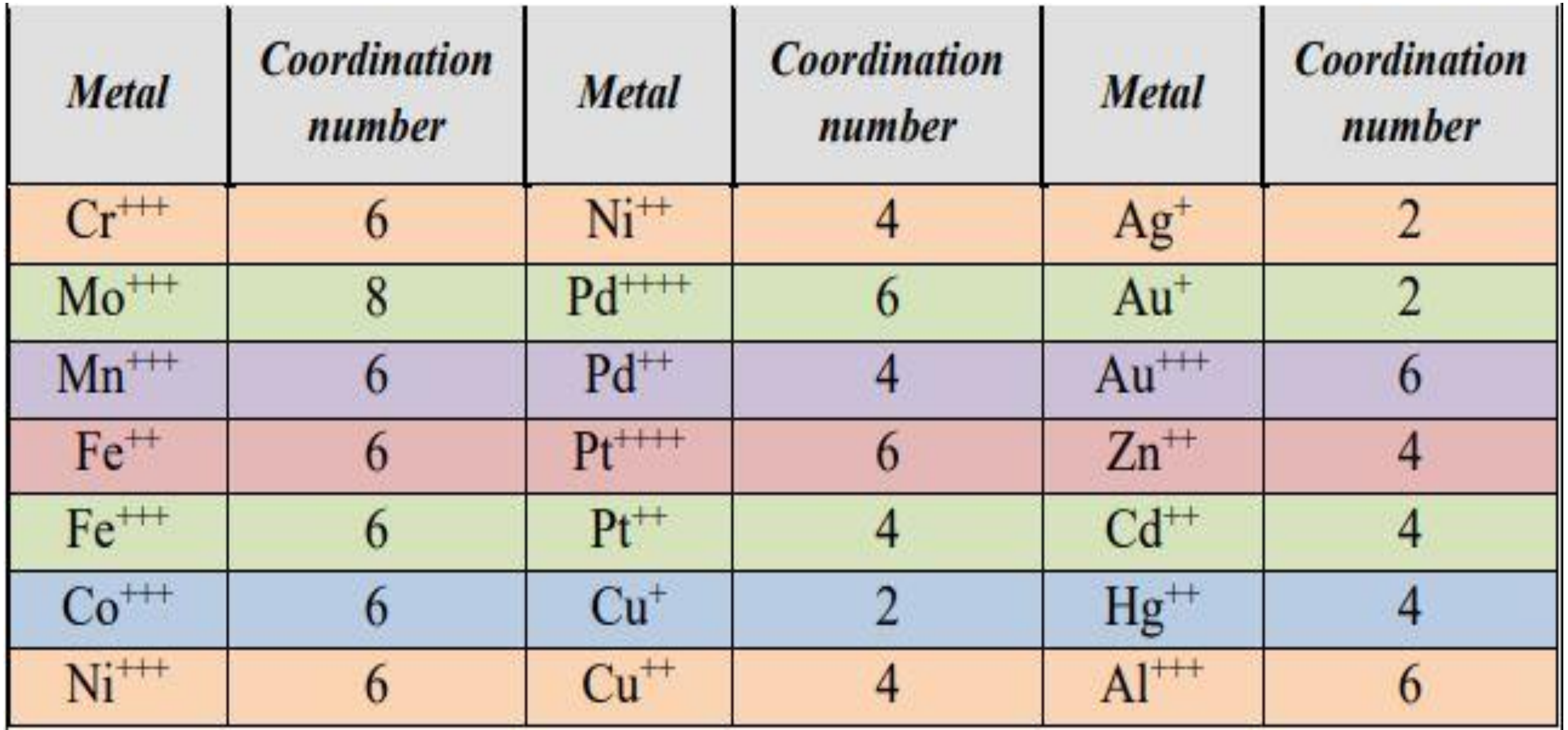


$[Co(NH_3)_4Cl_2]Cl$



$[Co(NH_3)_3Cl_3]$

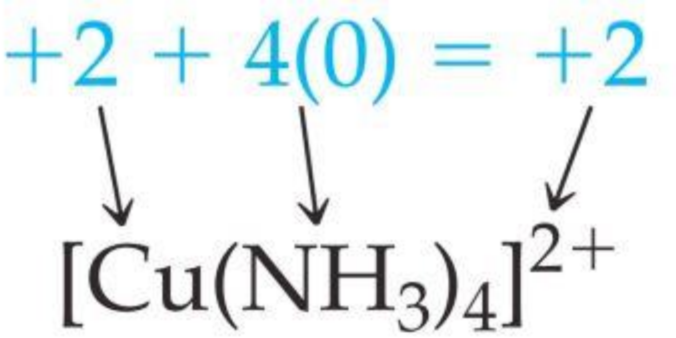
- The most stable complexes are formed by cations of the transition series, particularly the transition element in Group VIIIB. The groups immediately preceding and following in Groups VIB, VIIB, IB, IIB, and IIIB also form stable coordination compounds.
- The major criteria for maximal stability of the metal in a complex involve i) a high positive charge, ii) a small cationic radius, and iii) unoccupied d orbitals.



Metal	*Coordination number*	*Metal*	*Coordination number*	*Metal*	*Coordination number*
Cr^{+++}	6	Ni^{++}	4	Ag^{+}	2
Mo^{+++}	8	Pd^{++++}	6	Au^{+}	2
Mn^{+++}	6	Pd^{++}	4	Au^{+++}	6
Fe^{++}	6	Pt^{++++}	6	Zn^{++}	4
Fe^{+++}	6	Pt^{++}	4	Cd^{++}	4
Co^{+++}	6	Cu^{+}	2	Hg^{++}	4
Ni^{+++}	6	Cu^{++}	4	Al^{+++}	6

Oxidation Numbers
Key issue in metal complexes

- The oxidation state of a metal atom or ion in the complex is the apparent charge carried by it in the complex. It depends upon the atomic number and electronic configuration of the metal atom or ion



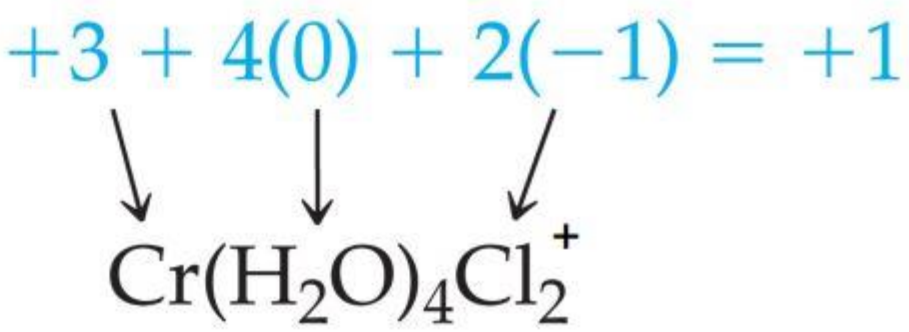
$$+2 + 4(0) = +2$$

$$[Cu(NH_3)_4]^{2+}$$

Easily found using:
Charge of the complex ion
Charge of the metal ion
Charge of each of the ligands.

Or, knowing the oxidation number on the metal and the charges on the ligands, one can calculate the charge on the complex ion.

Example: $Cr(III)(H_2O)_4Cl_2$



$$+3 + 4(0) + 2(-1) = +1$$

$$Cr(H_2O)_4Cl_2^{+}$$

Electron configuration of metals in complexes

- Generally, a transition metal has an electron configuration like this:

[n noble gas] ns^2 $(n-1)d^m$

Example:

V: $[Ar]^{18}$ $4s^2 3d^3$

Pt: $[Xe]^{54}$ $6s^2 4f^{14}$ $5d^8$

- But, when transition metals lose electrons to become cations. They lose the s electrons first:

Example:

V^{2+}: $[Ar]^{18}$ $4s^0$ $3d^3$

Pt^{2+}: $[Xe]^{54}$ $6s^0$ $5d^8$

Pt^{3+}: $[Xe]^{54}$ $6s^0$ $5d^7$

Orbital Hybridization

- In Chemistry, is defined as the concept of mixing two atomic orbitals to give rise to a new type of hybridized orbitals.
- This intermixing usually results in the formation of hybrid orbitals having entirely different energy, shapes, etc.
- The atomic orbitals of the same energy level mainly take part in hybridization.
- However, both fully-filled and half-filled orbitals can also take part in this process, provided they have equal energy.

❑Key Features of Hybridization

✓Atomic orbitals with equal energies undergo hybridization.

✓The number of hybrid orbitals formed is equal to the number of atomic orbitals mixed.

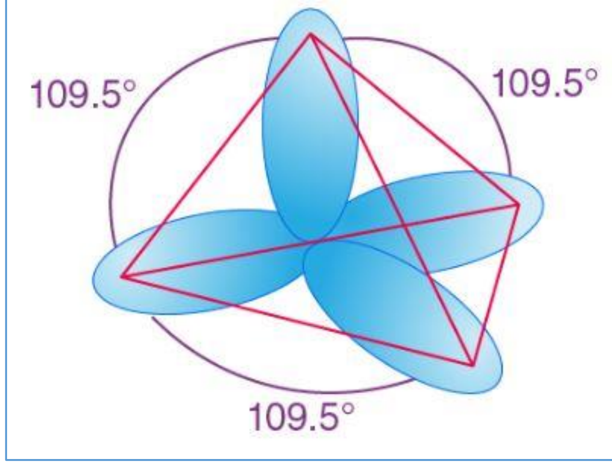
✓It is not necessary that all the half-filled orbitals must participate in hybridization. Even completely filled orbitals with slightly different energies can also participate.

✓Hybridization happens only during the bond formation and not in an isolated gaseous atom.

✓The shape of the molecule can be predicted if the hybridization of the molecule is known.

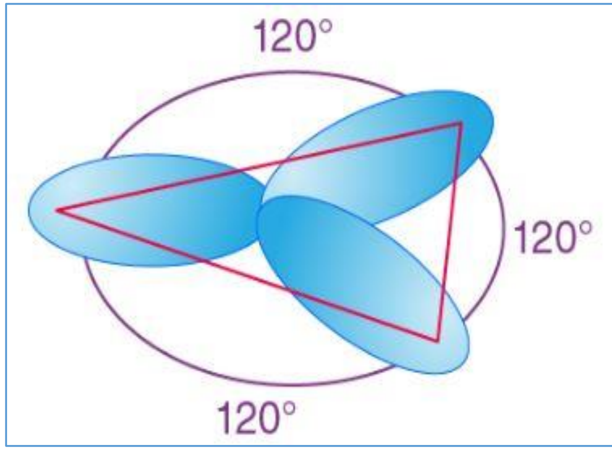
✓The bigger lobe of the hybrid orbital always has a positive sign, while the smaller lobe on the opposite side has a negative sign.

❑*sp*^{3} Hybridization



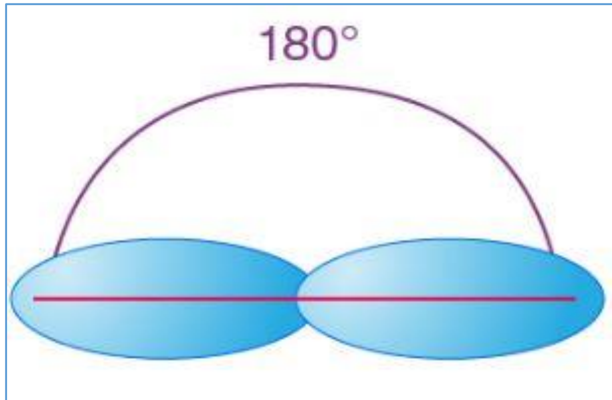
- When one ‘s’ orbital and 3 ‘p’ orbitals belonging to the same shell of an atom mix together to form four new equivalent orbitals, the type of hybridization is called a tetrahedral hybridization or *sp*^{3}. The new orbitals formed are called *sp*^{3} hybrid orbitals.

❑*sp*^{2} Hybridization



- sp2 hybridization is observed when one s and two p orbitals of the same shell of an atom mix to form 3 equivalent orbitals. The new orbitals formed are called *sp*^{2} hybrid orbitals.

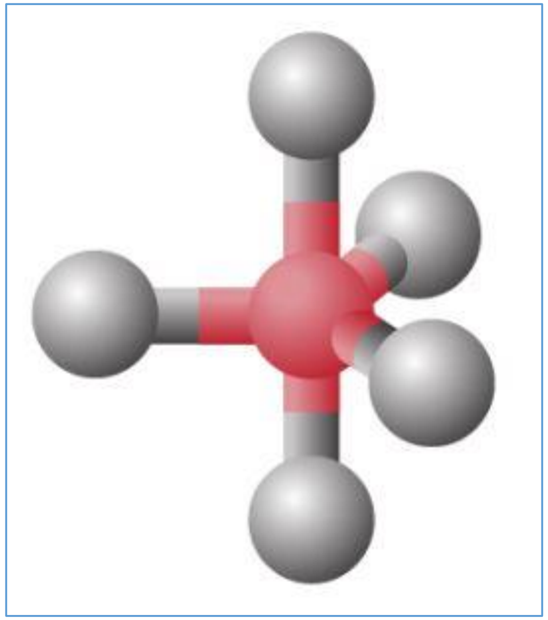
❑*sp* Hybridization



- sp hybridization is observed when one s and one p orbital in the same main shell of an atom mix to form two new equivalent orbitals. The new orbitals formed are called *sp* hybridized orbitals. It forms linear molecules with an angle of 180°.

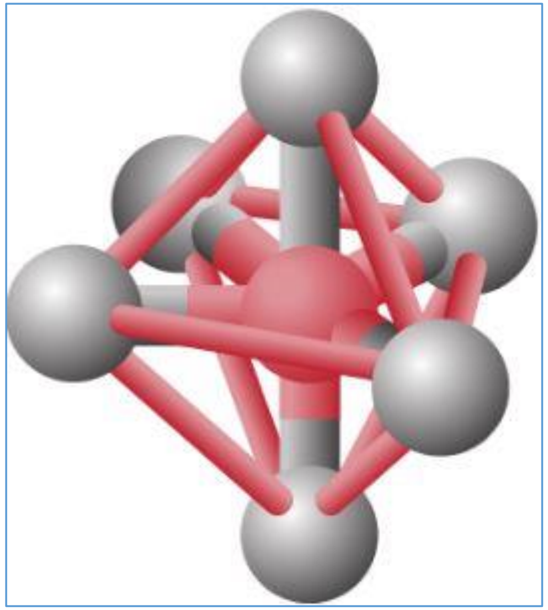
❑sp^3d Hybridization

- sp^3d hybridization involves the mixing of 1s orbital, 3p orbitals and 1d orbital to form 5 *sp3d* hybridized orbitals of equal energy. They have trigonal bipyramidal geometry. Three hybrid orbitals lie in the horizontal plane inclined at an angle of 120° to each other, known as the equatorial orbitals. The remaining two orbitals lie in the vertical plane at 90 degrees plane of the equatorial orbitals, known as axial orbitals.



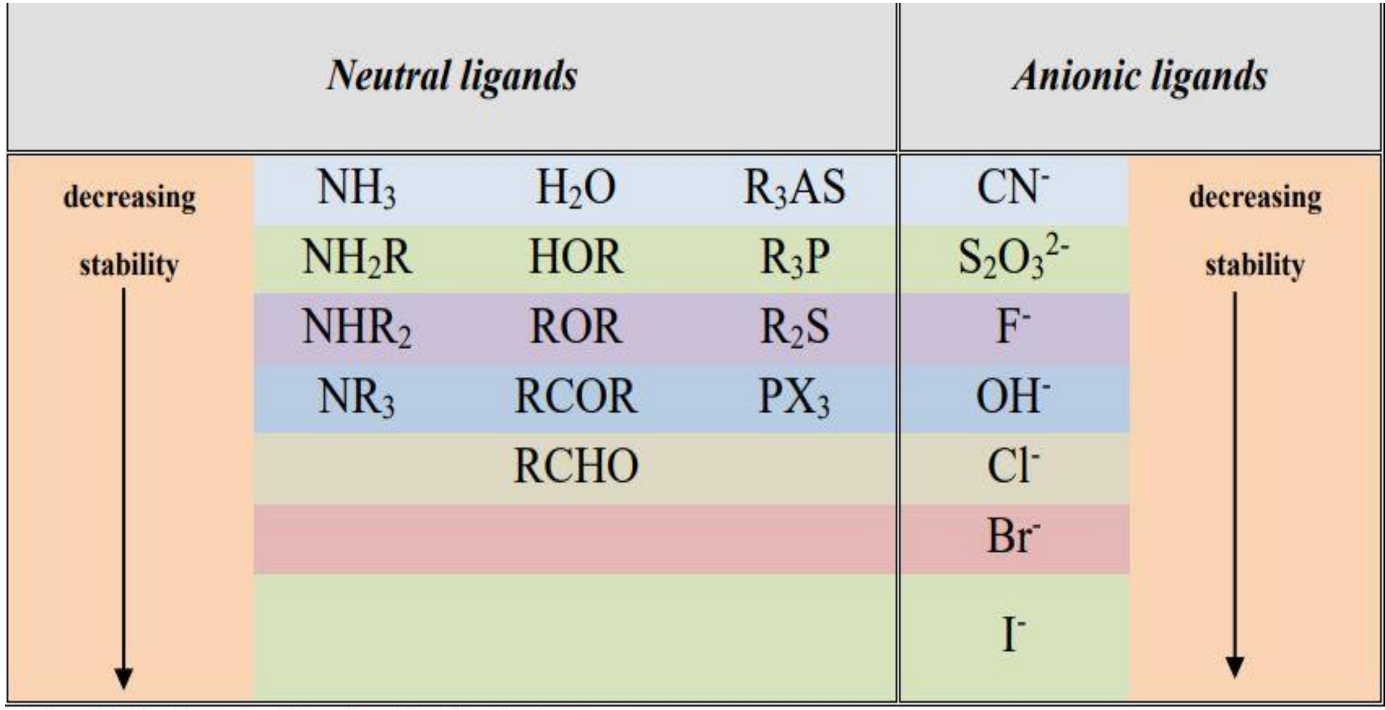
❑sp^3d^2 Hybridization

- **sp^3d^2** hybridization has 1s, 3p and 2d orbitals, that undergo intermixing to form 6 identical **sp^3d^2** hybrid orbitals. These 6 orbitals are directed towards the corners of an octahedron. They are inclined at an angle of 90 degrees to one another.



Properties of Ligands

- The ligand species in complexes are generally anions or neutral molecules.
- Neutral atoms are not usually found as coordinating agents. The one feature that all ligands have in common is the possession of at least **one non-bonded pair of electrons** which is used to form a coordinate covalent bond with the metal ion.
- Coordinate covalent bonding is the major bonding type in complexes, and some complexes do show other types of ligand bonding (e.g., ionic).
- The order of stability of a ligand in a complex follows the order of basicity of the ligand.
- This actually refers to the strength of the electrostatic field emanating from an anion or, in the case of a neutral molecule, the "availability" of the lone pair of electrons.



	Neutral ligands			*Anionic ligands*	
decreasing stability ↓	NH_3	H_2O	R_3AS	CN^-	**decreasing stability** ↓
	NH_2R	HOR	R_3P	$S_2O_3^{2-}$	
	NHR_2	ROR	R_2S	F^-	
	NR_3	RCOR	PX_3	OH^-	
		RCHO		Cl^-	
				Br^-	
				I^-	

R = Alkyl or aryl radical; X = halogen

- Ligand species may then be classified according to the number of positions on the molecule capable of coordinating with a metal.
- Ligands have one nonbonding pair of electrons to donate to the metal ion; they are termed unidentate, indicating that they each form one coordinate covalent bond in a complex.
- Bidentate ligands have two positions arranged so that they both can act simultaneously as donor sites in a complex. Some of these important to pharmacy and medicine are ethylenediamine (en), glycinate (gly), the dianion of oxalic acid (oxalate), and the anion of 8-hydroxyquinoline (oxinate).
- Polydentate ligands are similarly classified as tridentate, tetradentate, pentadetate, and hexadentate.
- When polydentate ligands complex a metal ion a ring structure is produced composed of the metal and the ligand molecule. These ring structures have special significance and are termed chelates from the Greek word chele, meaning claw.
- **In general, the more stable chelates are those where the total number of atoms in the ring including the metal are five, six, or seven. Four- and eight-membered rings are usually unstable.**
- The polydentate ligands used for chelate formation are generally referred to as chelating agents.

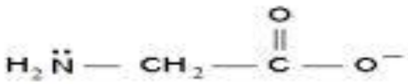
Unidentate $H_2\ddot{O}$: water $:\ddot{F}:^-$ fluoride ion $:C\equiv N:]^-$ cyanide ion $[:\ddot{O}-H]$ hydroxide ion

$:NH_3$ ammonia $:\ddot{Cl}:^-$ chloride ion $[:\ddot{S}=C=\ddot{N}:]^-$ thiocyanate ion └or┘ $[:\ddot{O}-N=\ddot{O}:]$ nitrite ion └or┘

Bidentate Ligand

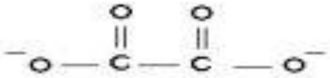
Ethylenediamine (en) $H_2\ddot{N}-CH_2-CH_2-\ddot{N}H_2$

Glycinate (gly)



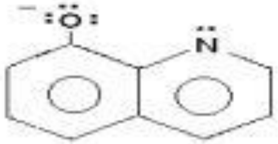
$H_2\ddot{N}-CH_2-\overset{\overset{O}{\|}}{C}-O^-$

Oxalate



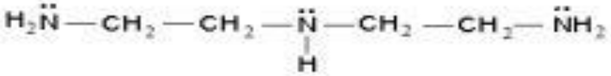
$^-O-\overset{\overset{O}{\|}}{C}-\overset{\overset{O}{\|}}{C}-O^-$

Anion of 8-hydroxyquinoline (oxinate)



Tridentate Ligand

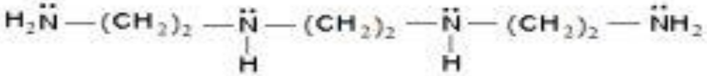
Diethylenetriamine (den)



$H_2\ddot{N}-CH_2-CH_2-\underset{\underset{H}{|}}{\ddot{N}}-CH_2-CH_2-\ddot{N}H_2$

Tetradentate Ligand

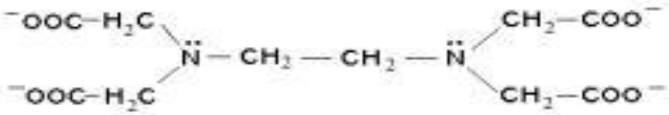
Triethylenetetramine (trien)



$H_2\ddot{N}-(CH_2)_2-\underset{\underset{H}{|}}{\ddot{N}}-(CH_2)_2-\underset{\underset{H}{|}}{\ddot{N}}-(CH_2)_2-\ddot{N}H_2$

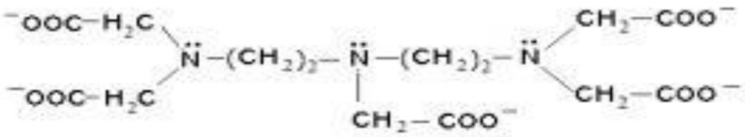
Hexadentate

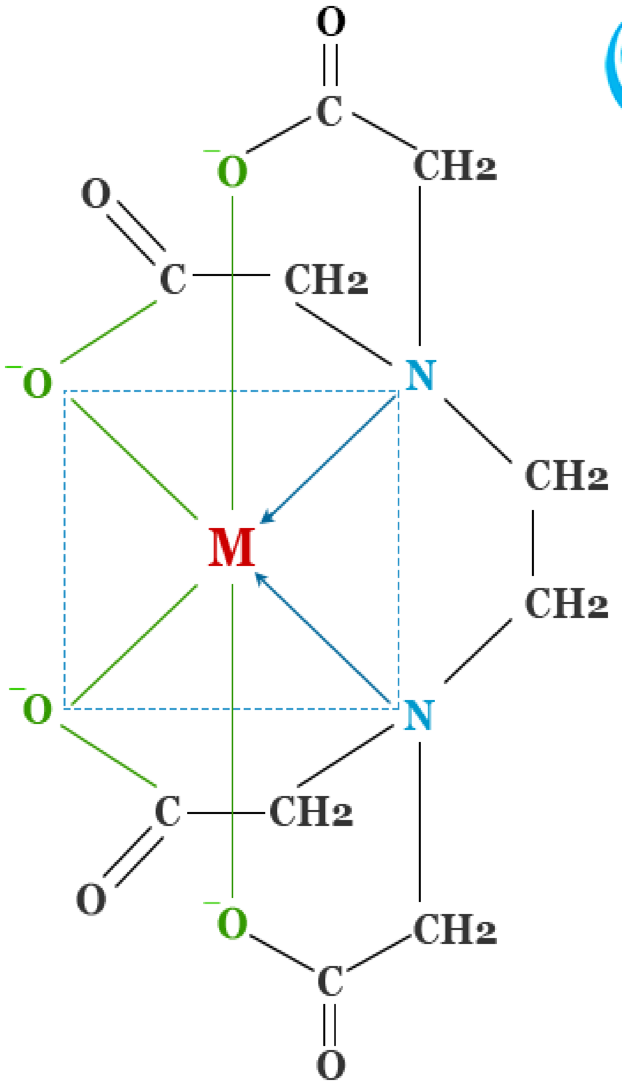
Ethylenediaminetetraacetate (EDTA)



Octadentate Ligand

Diethylenetriaminepentaacetate (DTPA)





M = bivalent metal

Bonding in complexes

- Working on a coordinate covalent bond concept, there are four major theories:

✓ A valence bond theory (VBT) states that the overlap of incompletely filled atomic orbitals leads to the formation of a chemical bond.

✓ Crystal field theory (CFT) describes the breaking of orbital degeneracy in transition metal complexes due to the presence of ligands.

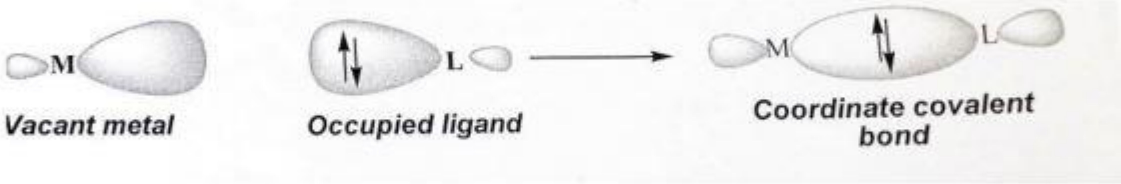
✓ Ligand field theory looks at the effect of donor atoms on the energy of d orbitals in the metal complex.

✓ A molecular orbital theory (MO) is a method for describing the electronic structure of molecules using quantum mechanics.

Valance Bond Theory (VBT)

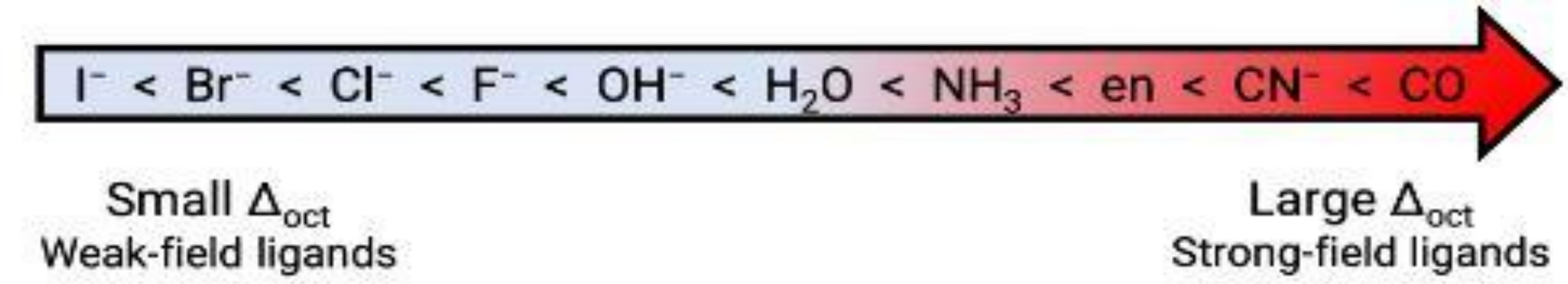
- It uses hybridization ideas. **This theory deals with the electronic structure of the central metal ion in its ground state, the kind of bonding, geometry, and magnetic properties of the complexes**.
- Assumptions of valence bond theory

1. The central metal atom or ion makes available a number of empty s, p, and d atomic orbitals equal to its coordination number. These vacant orbitals hybridize together to form hybrid orbitals which are the same in number as the atomic orbitals hybridizing together. These hybrid orbitals are vacant, equivalent in energy, and have definite geometry.
2. The ligands have at least one -orbital containing a lone pair of electrons.
3. Vacant hybrid orbitals of the metal atom or ion overlap with the filled orbitals of the ligands to form ligand metal bonds.
4. The non-bonding electrons of the metal atom or ion are then rearranged in the metal orbitals (pure d, s, or p orbitals) which do not participate in forming the hybrid orbitals.



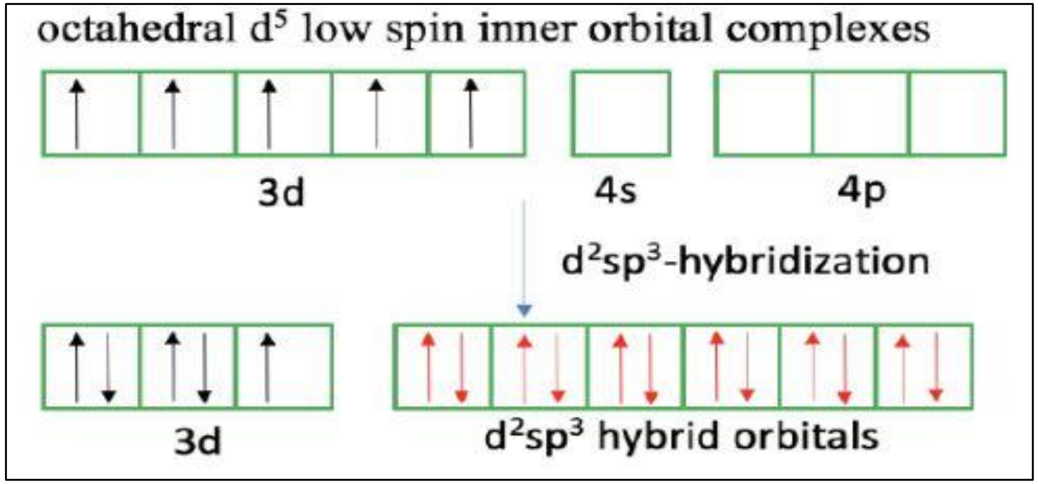
❑Difference Between High Spin and Low Spin Complexes

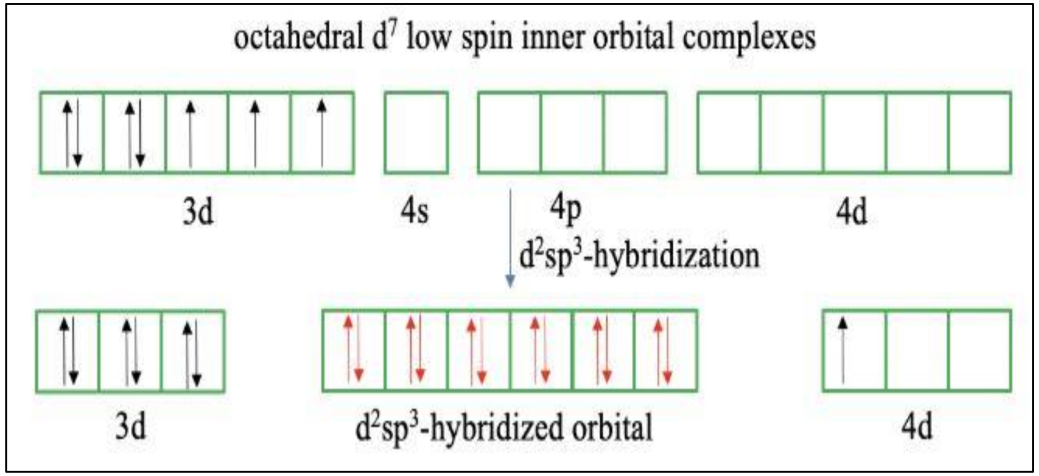
- The key difference between high-spin and low-spin complexes:
- High-spin complexes contain unpaired electrons.
- Low-spin complexes tend to contain paired electrons.
- Furthermore, another significant difference between high-spin and low-spin complexes is that the high-spin complexes are paramagnetic because they have unpaired electrons, but low-spin complexes are diamagnetic because they have all electrons paired.
- Generally, tetrahedral and octahedral compounds are high spin while square planar compounds are low spin.

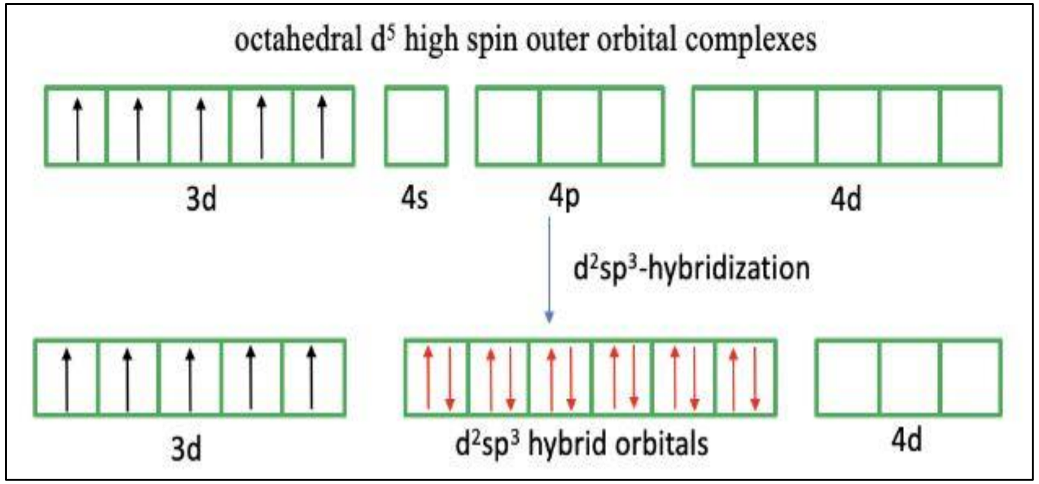


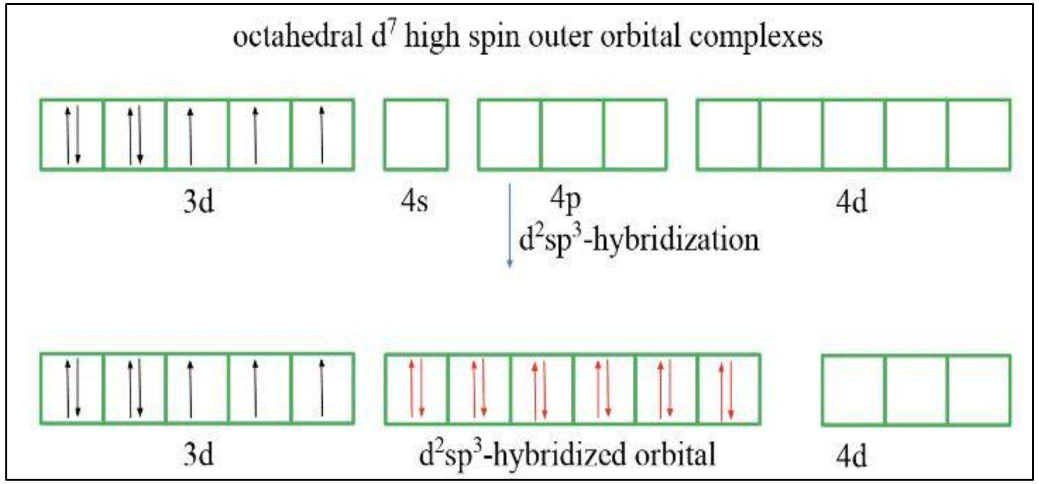
Inner orbital complex and Outer orbital complex

- Inner orbital complexes are composed of metal atoms that use inner shell d orbitals for the hybridization in the central metal atom.
- Outer orbital complexes are composed of metal atoms that use outermost shell d orbitals for the hybridization in the central metal atom.


octahedral d^5 low spin inner orbital complexes


octahedral d^7 low spin inner orbital complexes


octahedral d^5 high spin outer orbital complexes


octahedral d^7 high spin outer orbital complexes

❑Magnetic Moment

- The chemical may be paramagnetic or diamagnetic, depending on the strength of the ligand. The magnetic moment of a system containing unpaired electrons is proportional to the number of unpaired electrons: the stronger the magnetic moment, the more unpaired electrons there are.

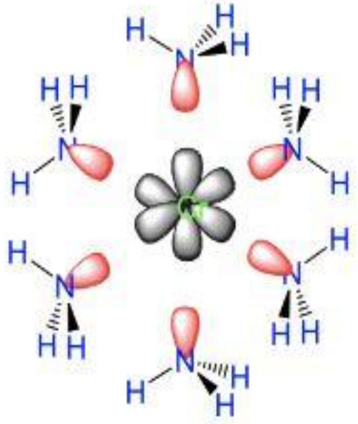
$$\boldsymbol{\mathit{The\ magnetic\ moment}} = \sqrt{\boldsymbol{n(n+2}}$$

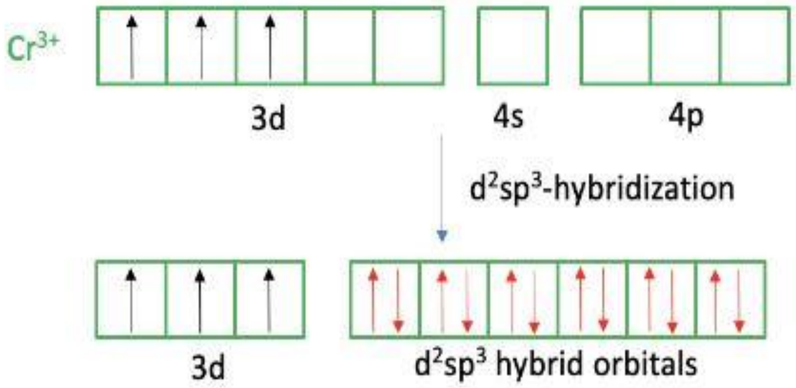
Where, n= number of unpaired electrons

❑Octahedral Complexes

- The hexamine chromium (3+) cation. It has an octahedral shape, with six dative Cr-N bonds.
- In order to explain the six dative Cr-N bonds we would need to overlap six empty chromium valence orbitals with six filled valence orbitals of N. We can see that the six ammine ligands have one electron lone pair each that can serve as the valence orbitals.
- The oxidation state of the chromium is +3 because the ligands are all neutral when the bonds are cleaved heteroleptically, and the complex cation has a 3+ charge.

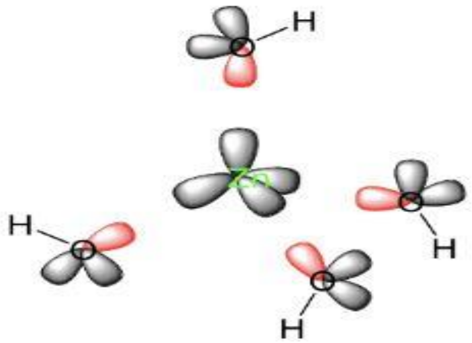
- When a transition metal loses electrons to form a cation, it always loses its two valence electrons first, and then its d electrons.
- The three remaining 3d electrons are expected to be spin up in three different d orbitals according to Hund’s rule.
- These would be two 3d and the 4s orbitals.
- Mix the two empty d-orbitals, the 4s orbital, and the three 4p orbitals to form six so-called ***d^2sp^3*** hybridized orbitals.
- They have the same shape and size, and their lobes point toward the corners of an octahedron.

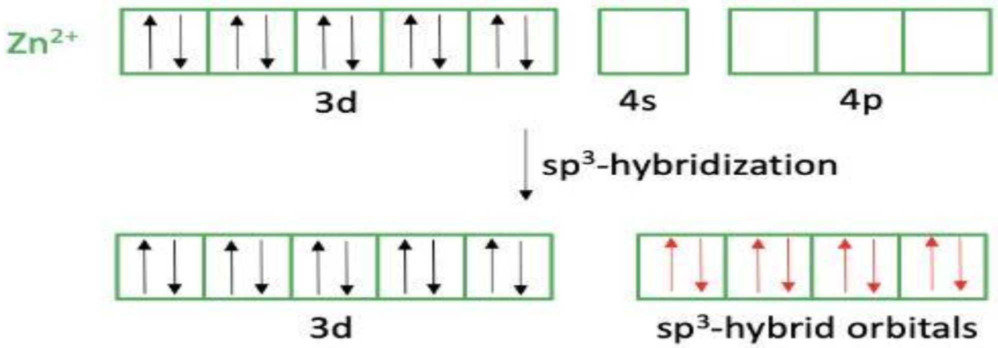




Tetrahedral Complexes

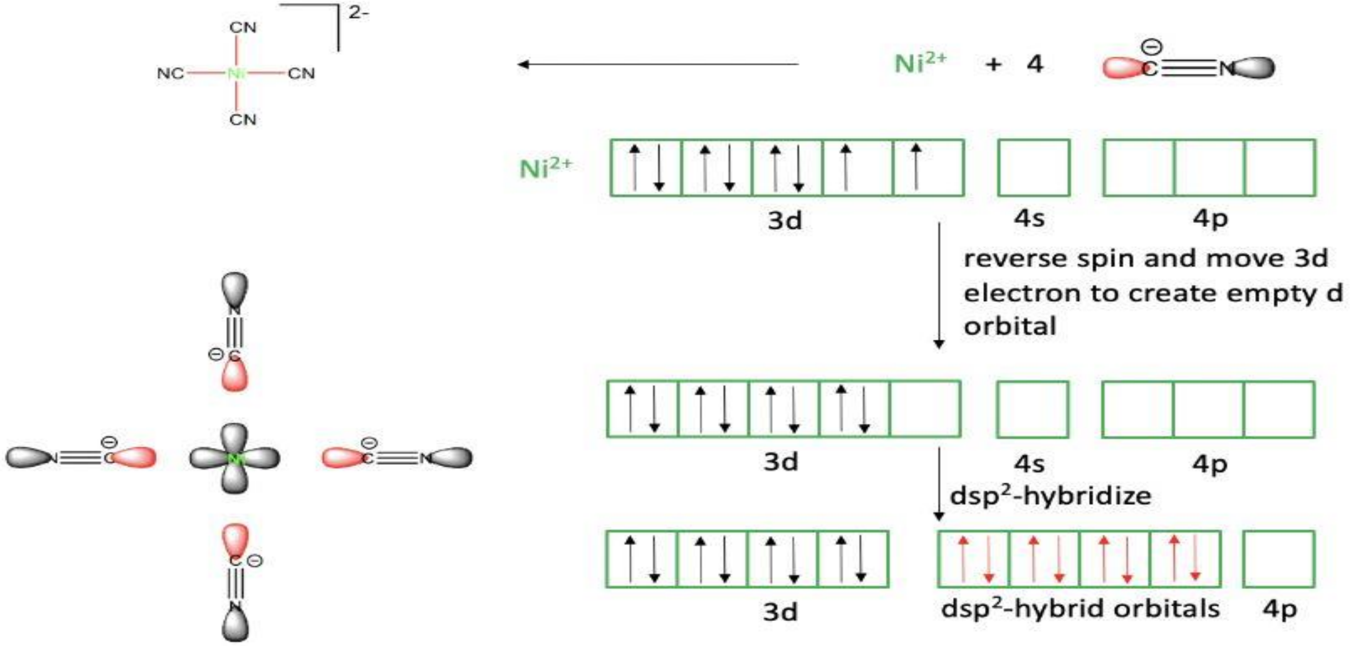
- The tetrahydroxozincate (2-) complex anion
- A neutral zinc atom has the electron configuration $4s^2\ 3d^{10}$. Because we must remove s electrons before we remove d electrons, the Zn^{2+} has the electron configuration $3d^{10}$. Like in the previous example we can justifiably consider the 4p orbitals as additional valence orbitals.
- There is a 90° angle between the p-orbitals which is smaller than the 109.5° tetrahedral bond angle in the molecule. However, we can solve this problem by hybridizing the 4s and the three 4p orbitals to form four ***sp***^{3}-hybridized orbitals.
- These hybrid orbitals have the property that their lobes point toward the corners of a tetrahedron.





Square Planar Complex

- Tetracyanonickelate (2-).
- To explain the four bonds, the Ni^{2+} ion would need to have four empty valence orbitals.
- To create a Ni^{2+} ion we must remove the two 4s electrons, and thus the Ni^{2+} has the electron configuration **$3d^8$**.
- **Do we have four empty orbitals available?** Yes, the 4s and the three 4p orbitals are empty but again they are not equivalent and thus not suitable to explain four equivalent Ni-C bonds.
- **Can we hybridize these orbitals?** Yes, we can, but the resulting four *sp^3* hybridized orbitals would not be suitable to explain the square planar shape, only the tetrahedral shape.
- What valence bond theory suggests in this case is to reverse the spin of one of the unpaired d electrons and move it into the other half-filled d-orbital.
- This produces an empty d-orbital that we can now hybridize with the 4s and two of the 2p orbitals to four ***dsp^2***-hybridized orbitals.



Coordination number of the central metal atom/ion	*Type of hybridisation undergone by the central metal atom/ion*	*Geometry of the complex*	*Examples of complexes*
2	$sp(4s, 4p_x)$	Linear or diagonal	$[CuCl_2]^-$, $[Cu(NH_3)_2]^+$ etc.
3	$sp^2(4s, 4p_x, 4p_y)$	Trigonal planar or equilateral triangular	 $[Cu^+Cl(tu)_2]^0$ (distorted trigonal planar) etc.
4	$dsp^2(3d_{x^2-y^2}, 4s, 4p_x, 4p_y)$	Square planar	$[Ni(CN)_4]^{2-}$, $[PdCl_4]^{2-}$
4	$sp^2d(4s, 4p_x, 4p_y, 4d_{x^2-y^2})$	Square planar	$[Cu(NH_3)_4]^{2+}$ $[Pt(NH_3)_4]^{2+}$ etc.
4	$sp^3(4s, 4p_x, 4p_y, 4p_z)$	Tetrahedral	$[NiCl_4]^{2-}$, $[Cu(CN)_4]^{3-}$, $Ni(CO)_4$ etc.
5	$dsp^3(3d_{z^2}, 4s, 4p_x, 4p_y, 4p_z)$	Trigonal bipyramidal	$Fe(CO)_5$, $[CuCl_5]^{3-}$, $[Ni^{2+}(triars)\ Br_2]^0$
5	$dsp^3(3d_{x^2-y^2}, 4s, 4p_x, 4p_y, 4p_z)$	Square pyramidal	$[Co^{2+}(triars)\ I_2]^0$, $[Ni(CN)_5]^{3-}$ etc.
6	$d^2sp^3(3d_{x^2-y^2}, 3d_{z^2}, 4s, 4p_x, 4p_y, 4p_z)$	Inner-orbital octahedral	$[Ti(H_2O)_6]^{3+}$, $[Fe(CN)_6]^{3-}$ etc.
6	$sp^3d^2(4s, 4p_x, 4p_y, 4p_z, 4d_{x^2-y^2}, 4d_{z^2})$	Outer-orbital octahedral	$[Fe^+(NO^+)(H_2O)_5]^{2+}$, $[CoF_6]^{3-}$ etc.