**Ligands**:- The term **ligand (ligare [Latin], to bind)** was first used by Alfred Stock in 1916 in relation to silicon chemistry. The first use of the term in a British journal was by H. Irving and R.J.P. Williams in Nature, 1948, 162, 746 in their paper describing what is now called the Irving-Williams series.The atoms, ions or molecules which can donate a pair of electrons to the metal atom or ion to form co ordinate bonds with it, are known as ligands. The common donor atoms are N, O, X, As, P etc.

*Depending upon no. of donor sites present per ligand, ligands are classified into three main categories*





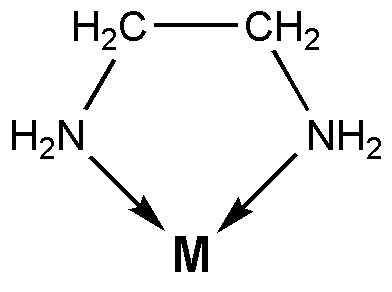
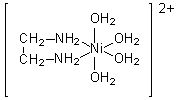
 



Depending upon donor and acceptor properties, ligands are classified in another way. There are some ligands which accept back electrons from filled metal orbitals into their available empty orbitals. This type of classification is—

There are some specially named types of ligands. These are Chelating, ambidentate, macrocyclic and flexidentate ligands.

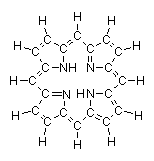
**Chelating ligands:-** The term **chelate** was first applied in 1920 by Sir Gilbert T. Morgan and H.D.K. Drew who stated: "The adjective chelate, derived from the great claw or **chela (chely- Greek)** of the lobster or other crustaceans, is suggested for the caliper like groups which function as two associating units and fasten to the central atom so as to produce heterocyclic rings." These are mainly polydentate ligands. When any two donor atoms of poldentate ligand can form at least a five membered heterocyclic ring with the metal atom, the ligand is called as Chelating ligand.the ring so formed is called Chelate ring and the property is called Chelation. **Chelation** is the formation or presence of two or more separate coordinate bonds between a polydentate (multiple bonded) ligand and a single central atom. Usually these ligands are organic compounds, and are called chelants, chelators, chelating agents, or sequestering agents.As for example—

** **

***A chelating ligand is a polydentate ligand which is attached to a metal by any two of its donor atoms, resulting in the formation of a strain frees at least a five heterocyclic membered ring.***

A chelating ligand must be a poly-dentate ligand, but apoly-dentate ligand may not be a chelating ligand. As for example hydrazine (H2N-NH2) is a bidentate ligand but not a chelating ligand. Thus, every polydentate ligand is not necessarily a chelating ligand.

Porphine is a chelating agent similar to ethylenediamine in that it forms bonds to a metal ion through nitrogen atoms. Each of the four nitrogen atoms in the center of the molecule can form a bond to a metal ion. Porphine is the simplest of a group of chelating agents called porphyrins. Porphyrins have a structure derived from porphine by replacing some of the hydrogen atoms around the outside with other groups of atoms.



One important porphyrin chelate is heme, the central component of hemoglobin, which carries oxygen through the blood from the lungs to the tissues. Heme contains a porphyrin chelating agent bonded to an iron(II) ion. Iron, like nickel, can form six bonds. Four of these bonds tie it to the porphyrin. One of iron's two remaining bonds holds an oxygen molecule as it is transported through the blood. **The chelate effect:-** The chelate effect describes the enhanced affinity of chelating ligands for a metal ion compared to the affinity of a collection of similar nonchelating (monodentate) ligands for the same metal. Let us consider, the two equilibria, in aqueous solution, between the copper(II) ion( Cu2+) and [ethylenediamine](http://en.wikipedia.org/wiki/Ethylenediamine) (en) on the one hand and methylamine, MeNH2 on the other.

Cu2+ + en 🡪 [Cu(en)]2+ ……… (1)

Cu2+ + 2 MeNH2 🡪 [Cu(MeNH2)2]2+ ……….(2)

In (1) the bidentate ligand ethylene diamine forms a chelate complex with the copper ion. Chelation results in the formation of a five–membered ring. In (2) the bidentate ligand is replaced by two [monodentate](http://en.wikipedia.org/wiki/Denticity) methylamine ligands of approximately the same donor power, meaning that the enthalpy of formation of Cu—N bonds is approximately the same in the two reactions. Under conditions of equal copper concentrations and when the concentration of methylamine is twice the concentration of ethylenediamine, the concentration of the complex (1) will be greater than the concentration of the complex (2). The effect increases with the number of chelate rings so the concentration of the [EDTA](http://en.wikipedia.org/wiki/EDTA) complex, which has six chelate rings, is much much higher than a corresponding complex with two monodentate nitrogen donor ligands and four monodentate carboxylate ligands. Thus, the phenomenon of the chelate effect is a firmly established empirical fact. The thermodynamic approach to explaining the chelate effect considers the equilibrium constant for the reaction: the larger the equilibrium constant, the higher the concentration of the complex.

[Cu(en)] =β11[Cu][en]

[Cu(MeNH2)2]= β12[Cu][MeNH2]2

Electrical charges have been omitted for simplicity of notation. The square brackets indicate concentration, and the subscripts to the stability constants, β, indicate the [stoichiometry](http://en.wikipedia.org/wiki/Stoichiometry) of the complex. When the analytical concentration of methylamine is twice that of ethylenediamine and the concentration of copper is the same in both reactions, the concentration [Cu(en)] is much higher than the concentration [Cu(MeNH2)2] because β11 >> β12. An equilibrium constant, *K*, is related to the standard Gibbs free energy, Δ*G* by

Δ[G](http://en.wikipedia.org/wiki/G) = −RT ln *K* = Δ*H* − TΔ*S* where *R* is the gas constant and *T* is the temperature in [kelvins](http://en.wikipedia.org/wiki/Kelvin). Δ*H*is the standard [enthalpy](http://en.wikipedia.org/wiki/Enthalpy) change of the reaction and Δ*S* is the standard entropy change. It has already been posited that the enthalpy term should be approximately the same for the two reactions. Therefore the difference between the two stability constants is due to the entropy term. In equation (1) there are two particles on the left and one on the right, whereas in equation (2) there are three particles on the left and one on the right. This means that less entropy of disorder is lost when the chelate complex is formed than when the complex with monodentate ligands is formed. This is one of the factors contributing to the entropy difference. Other factors include solvation changes and ring formation. Some experimental data to illustrate the effect are shown in the following table.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Equilibrium** | **log β** | **ΔG** | **Δ*H* /kJ mol−1** | **−*T*Δ*S* /kJ mol−1** |
| Cd2+ + 4 MeNH2 🡪Cd(MeNH2)42+ | 6.55 | -37.4 | -57.3 | 19.9 |
| Cd2+ + 2 en 🡪 Cd(en)22+ | 10.62 | -60.67 | -56.48 | -4.19 |

These data show that the standard enthalpy changes are indeed approximately equal for the two reactions and that the main reason why the chelate complex is so much more stable is that the standard entropy term is much less unfavourable, indeed, it is favourable in this instance. In general it is difficult to account precisely for thermodynamic values in terms of changes in solution at the molecular level, but it is clear that the chelate effect is predominantly an effect of entropy.

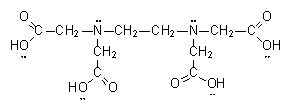
In the case of complex formation of Ni2+ with ammonia or 1,2-diaminoethane, by rewriting the equilibria, the following equations are produced.



Using the equilibrium constant for the reaction (3 above) where the three bidentates replace the six monodentates, we find that at a temperature of 25oC:

ΔG° = -2.303 RT log10 (K)   
 = -2.303 R T (18.28 - 8.61)   
 = -54 kJ mol-1 ]

## Applications of Chelators:- Chelators are used in chemical analysis, as water softeners, and are ingredients in many commercial products such as shampoos and food preservatives. Citric acid is used to soften water, in soaps and laundry detergents. A common synthetic chelator is [EDTA](http://en.wikipedia.org/wiki/EDTA). EDTA is a versatile chelating agent. It can form four or six bonds with a metal ion, and it forms chelates with both transition-metal ions and main-group ions. EDTA is frequently used in soaps and detergents, because it forms complexes with calcium and magnesium ions. These ions are in hard water and interfere with the cleaning action of soaps and detergents. The EDTA binds to them, sequestering them and preventing their interference. In the calcium complex, [Ca(EDTA)]2–, EDTA is a tetradentate ligand, and chelation involves the two nitrogen atoms and two oxygen atoms in separate carboxyl (-COO–) groups. EDTA is also used extensively as a stabilizing agent in the food industry. Food spoilage is often promoted by naturally-occurring enzymes that contain transition-metal ions. These enzymes catalyze the chemical reactions that occur during spoilage. EDTA deactivates these enzymes by removing the metal ions from them and forming stable chelates with them. It promotes color retention in dried bananas, beans, chick peas, canned clams, pecan pie filling, frozen potatoes, and canned shrimp. It improves flavor retention in canned carbonated beverages, salad dressings, mayonnaise, margarine, and sauces. It inhibits rancidity in salad dressings, mayonnaise, sauces, and sandwich spreads. EDTA salts are used in foods at levels ranging from 33 to 800 ppm. In other applications, EDTA dissolves the CaCO3 scale deposited from hard water without the use of corrosive acid. EDTA is used in the separation of the rare earth elements from each other. The rare earth elements have very similar chemical properties, but the stability of their EDTA complexes varies slightly. This slight variation allows EDTA to effectively separate rare-earth ions. EDTA is used as an anticoagulant for stored blood in blood banks; it prevents coagulation by sequestering the calcium ions required for clotting. As an antidote for lead poisoning, calcium disodium EDTA exchanges its chelated calcium for lead, and the resulting lead chelate is rapidly excreted in the urine. The calcium salt of EDTA, administered intravenously, is also used in the treatment of acute cadmium and iron poisoning.



Phosphonates are also well known chelating agents. Chelators are used in water treatment programs and specifically in steam engineering, e.g., boiler water treatment system: *Chelant Water Treatment system.* **Heavy metal detoxification** :-*Chelation therapy --*Chelation therapy is the use of chelating agents to detoxify poisonous metal agents such as mercury, [arsenic](http://en.wikipedia.org/wiki/Arsenic), and lead by converting them to a chemically inert form that can be excreted without further interaction with the body, and was approved by the [U.S. Food and Drug Administration](http://en.wikipedia.org/wiki/U.S._Food_and_Drug_Administration) in 1991. In alternative medicine, chelation is used as a treatment for autism, though this practice is controversial due to the absence of scientific plausibility, lack of FDA approval, and its potentially deadly side-effects. Though they can be beneficial in cases of heavy metal poisoning, chelating agents can also be dangerous. The U.S. CDC reports that use of disodium EDTA instead of calcium EDTA has resulted in fatalities due to hypocalcemia. **Other medical applications**:- Antibiotic drugs of the tetracycline family are chelators of Ca2+ and Mg2+ ions. EDTA is also used in root canal treatment as a way to irrigate the canal. EDTA softens the dentin facilitating access to the entire canal length and to remove the smear layer formed during instrumentation. Chelate complexes of gadolinium are often used as contrast agents in MRI scans. **Chemical analysis**:- Formation of chelated complexes are used in qualitative and quantitative determination of some metal ions. As for example dimethyl glyoxime is mainly used for qualitative determination as well as quantitative determination.





1-nitroso-2-naphtol is used to detect qualitatively or quantitatively the presence of Co(II) ion. It forms a red-brown chelate complex with Co(II) in presence of acetic acid. Chelators are used to separate ions by solvent extraction method.As for example acetyl acetone is used to separate Fe(II) and Cu(II) when present together. This reagent forms a chelate complex with Cu(II),which can be easily extracted by using a suitable organic solvent.



Sodium salt of ethylenediamine tetraacetic acid is used to determine the hardness of water.The chelated complex of edta-2 with Mg(II) is shown as   **Bridging ligand**:-A bridging ligand links two or more metal center. The monodentate ligands which can bind two or more metal atom centers in the formation of complexes are called as bridging ligands. The complexes so formed are known as bridging or polynuclear complexes. The donor atom of a bridging ligand must have at least two lone pair of electrons. Bridging ligands also persist in solution. Polyatomic ligands such as carbonate are ambidentate and thus are found to often bind to two or three metals simultaneously. Atoms that bridge metals are sometimes indicated with the prefix "μ" (mu). Examples of bridging complexes are—



**Bulky ligands**:-Bulky ligands are used to control the steric properties of a metal center. They are used for many reasons, both practical and academic. On the practical side, they influence the selectivity of metal catalysts, e.g. in hydroformylation. Of academic interest, bulky ligands stabilize unusual coordination sites, e.g. reactive co-ligands or low coordination numbers. Often bulky ligands are employed to simulate the steric protection afforded by proteins to metal-containing active sites. Of course excessive steric bulk can prevent the coordination of certain ligands **Ambidentate ligand:-**Monodentateligands having more than one donor atoms and only one of them can attach to a metal atom at a time are known as ambidentate. One example is thiocyanate ion, NCS-, which can bind to the metal center with either the nitrogen or sulphur atoms. Other examples of ambidentate ligands include NO2-/ONO- (O and N), and SO32-/OSO22- (O and S), where the first named atom refers to that which is bonded to the metal center.

 The existence of ambidentate ligands give rise to existence of linkage isomers.The first linkage isomers discovered by S.M. Jorgensen are nitro and nitrito complexes of [Co(NO2)(NH3)5]2+ . [Co(NO2)(NH3)5]2+ exists in a red form and a yellow form. The red form has the NO2- group bound by oxygen, when the ligand is known as the nitrito group, and the yellow form has the NO2- group bound by nitrogen, when the ligand is known as the nitro group. The nitro isomer is more stable than nitrito isomer. The site of an ambidentate ligand which can link to the metal atom is depends on—(1) Position of the metal atom in the periodic table and its oxidation state:- The metal ion with high oxidation state and having available d-electrons can form complexes with ambidentate ligands e.g. Co(III), Rh(III), Pt(IV) etc. (2) The nature of the other ligands:- The complexes containing at least one M-A bond can form complexes with ambidentate ligand containing A as a donor atom e.g. complex containing Co-O bond such as [Co(NH3)5(OH)]2+ can form nitrito complex with nitrosation agent-

[Co(NH3)5(OH)]2+ + NO+ONO- 🡪 [Co(NH3)5(ONO)]2+ This complex on acidification with HCl isomerizes to nitro form. **Macrocyclic Ligand:-**The polydentate ligands in which several donor atoms form a large ring even before complex formation are known as Macrocyclic ligands.Template reaction is used to synthesize macrocyclic ligands.A metal ion such as Ni(II) can be used to assemble a group of ligands which then undergo a condensation reaction to form macrocyclic ligand.The donor atoms in macrocyclic ligands are generally N, O or S. An example is the porphyrin ring, modified forms of which are complexed with Fe at the O2 binding site in haemoglobin, and with Mg in chlorophyll. One class of macrocyclic ligands is Crown ethers.



**Crown ethers:- Crown ethers** are cyclic chemical compounds that consist of a ring containing several ether groups. The most common crown ethers are oligomers of ethylene oxide, the repeating unit being ethyleneoxy, i.e. -CH2CH2O-. Crown ethers are named as x-crown-y where x denotes the total number of atoms in the cyclic backbone and y denotes the number of oxygen atoms. As for example, the name **18-crown-6** indicates that there are 18 atoms in the ring, 6 of which are oxygen. Structures of typical crown ethers are given below:-



Crown ethers strongly bind certain alkali or alkaline earth metal cations, forming complexes. The formation of such complexes depends upon the size of the metal ion and size of the cavity or hole in the crown ethers. The bonding of the metal ion with crown ethers is largely electrostatic. The oxygen atoms are well situated to coordinate with a cation located at the interior of the ring, whereas the exterior of the ring is hydrophobic. The resulting cations often form salts that are soluble in nonpolar solvents, and for this reason crown ethers are useful in phase transfer catalysis. The denticity of the polyether influences the affinity of the crown ether for various cations. For example, 18-crown-6 has high affinity for potassium cation, 15-crown-5 for sodium cation, and 12-crown-4 for lithium cation. The high affinity of 18-crown-6 for potassium ions contributes towards its toxicity. Apart from its high affinity for potassium cations, 18-crown-6 can also bind to protonated amines and form very stable complexes in both solution and the gas phase. Some amino acids, such as lysine, contain a primary amine on their side chains. Those protonated amino groups can bind to the cavity of 18-crown-6 and form stable complexes in the gas phase. Hydrogen-bonds are formed between the three hydrogen atoms of protonated amines and three oxygen atoms of 18-crown-6. These hydrogen-bonds make the complex a stable adduct.