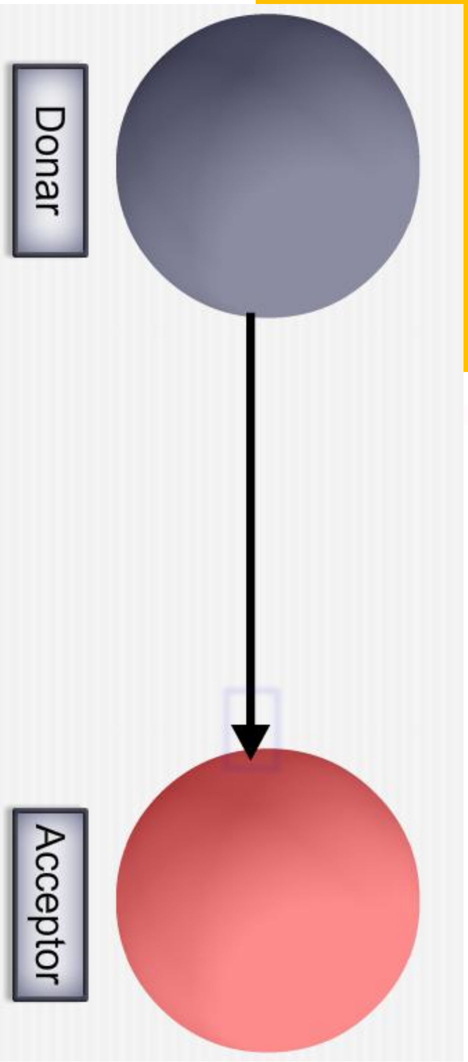
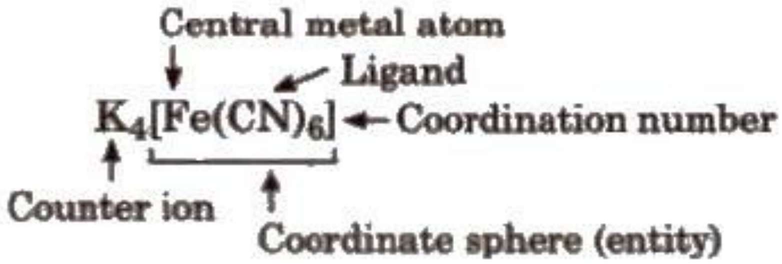
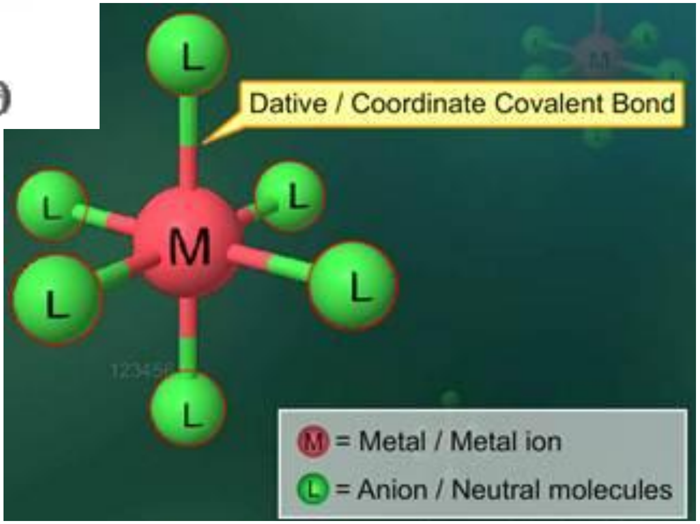
Coordination Chemistry of Radioisotopes

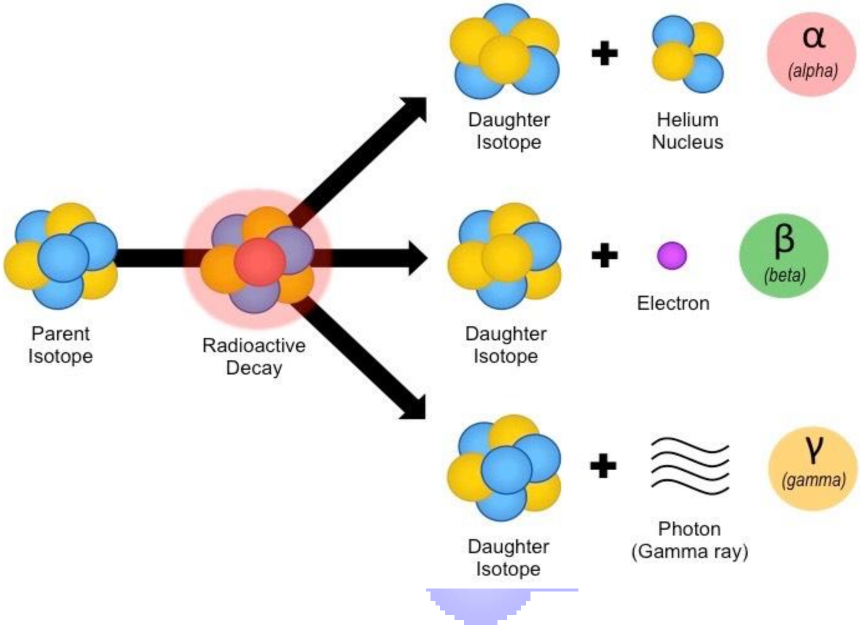


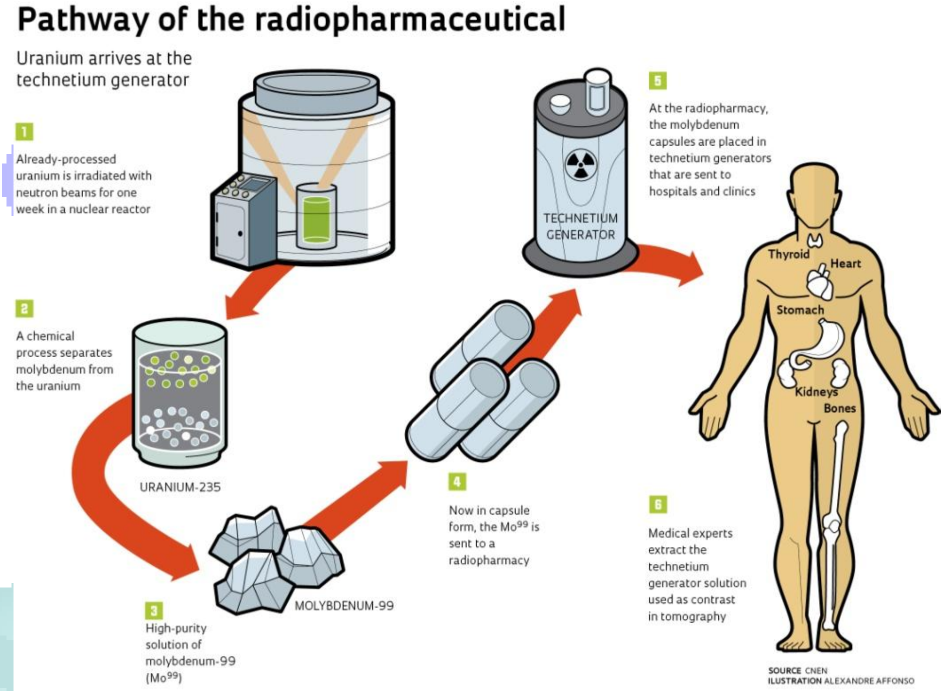
$$K_4[Fe(CN)_6] \xrightleftharpoons{aq} 4K^+ + [Fe(CN)_6]^{4-}$$





Radioisotopes-





Pathway of the radiopharmaceutical

Uranium arrives at the technetium generator

1 Already-processed uranium is irradiated with neutron beams for one week in a nuclear reactor

2 A chemical process separates molybdenum from the uranium

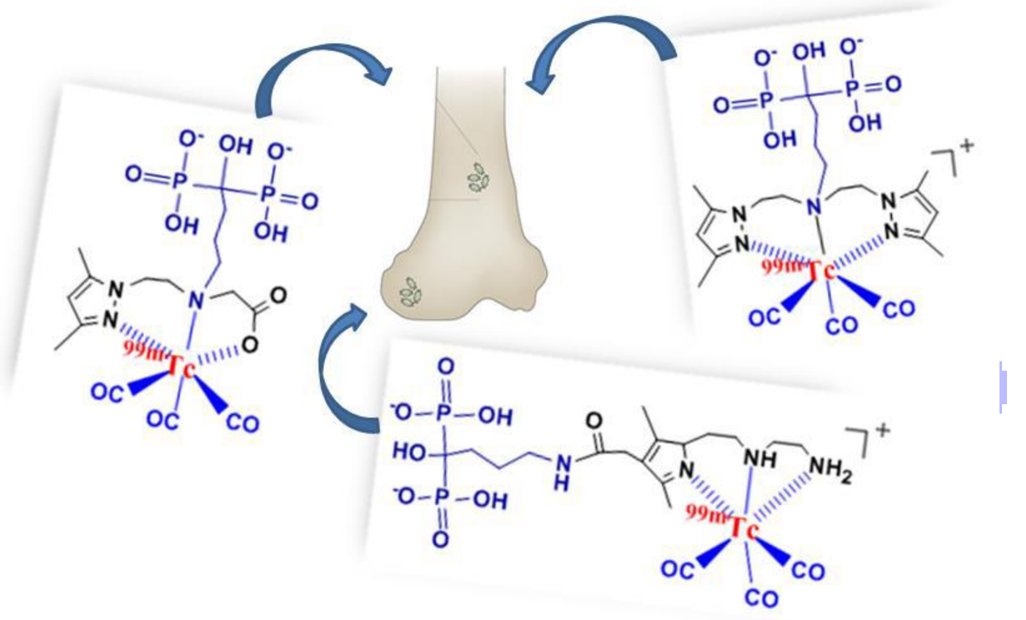
3 High-purity solution of molybdenum-99 (Mo^{99})

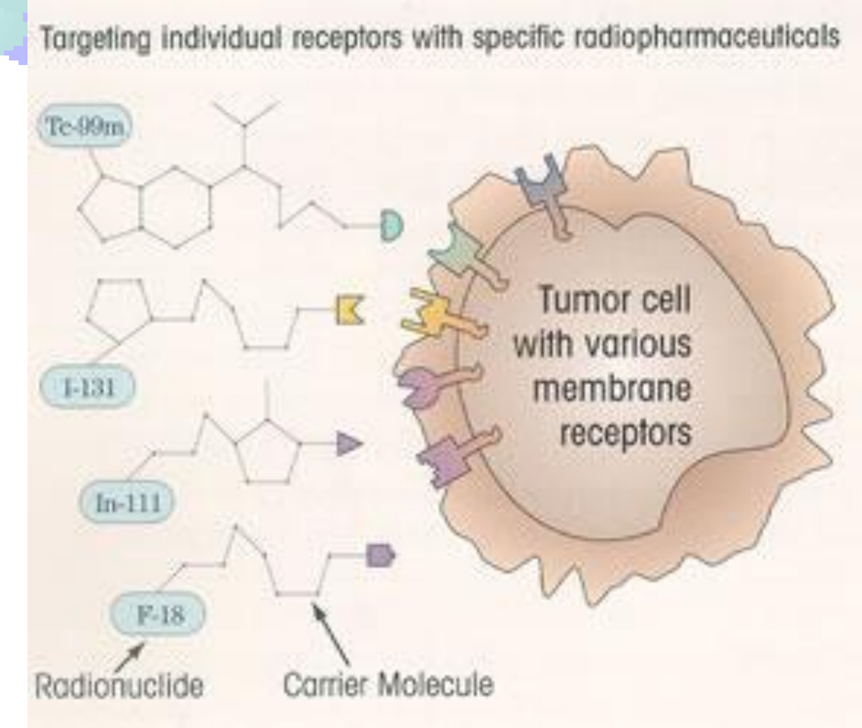
4 Now in capsule form, the Mo^{99} is sent to a radiopharmacy

5 At the radiopharmacy, the molybdenum capsules are placed in technetium generators that are sent to hospitals and clinics

6 Medical experts extract the technetium generator solution used as contrast in tomography

SOURCE CNEN
ILUSTRATION ALEXANDRE AFFONSO



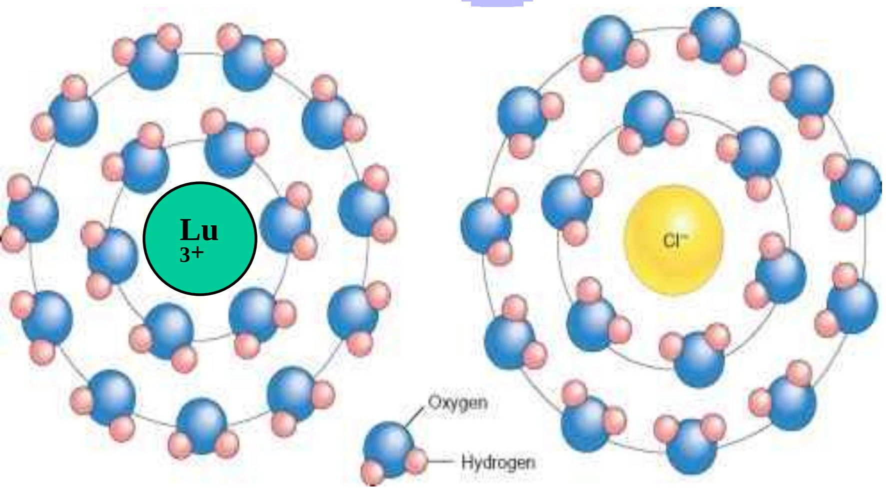


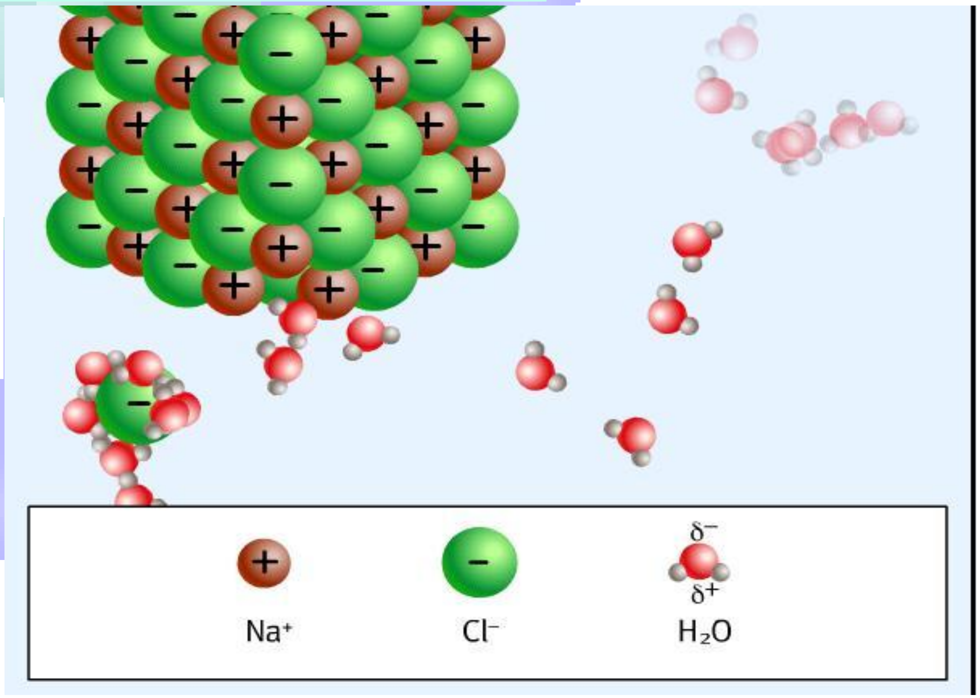
Targeting individual receptors with specific radiopharmaceuticals

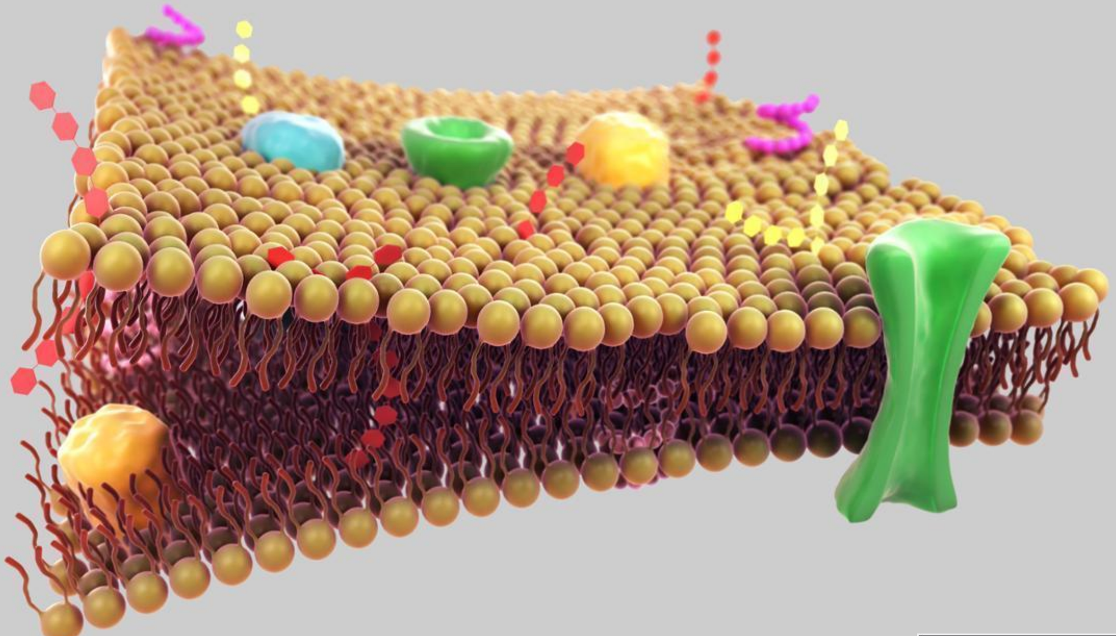
In what kind of molecular or ionic forms are used the radioisotopes in pharmacy and medicine?

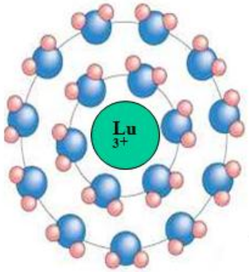
^{111}In, ^{68}Ga, ^{90}Y, ^{177}Lu...

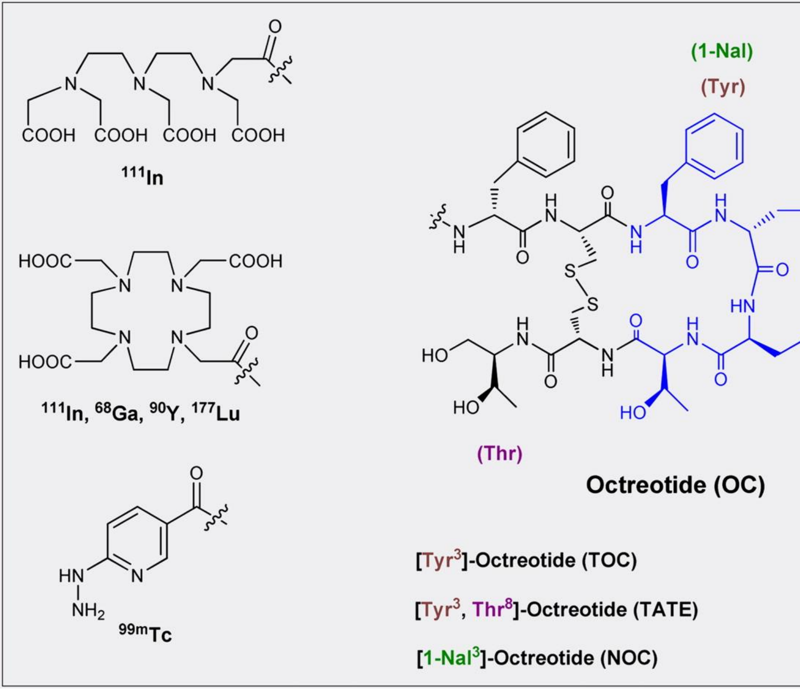
In water solutions these exist as polyvalent
´cations (Lu^{3+}, Y^{3+}...) and they are strongly hydrated
With two or more spheres of water molecules





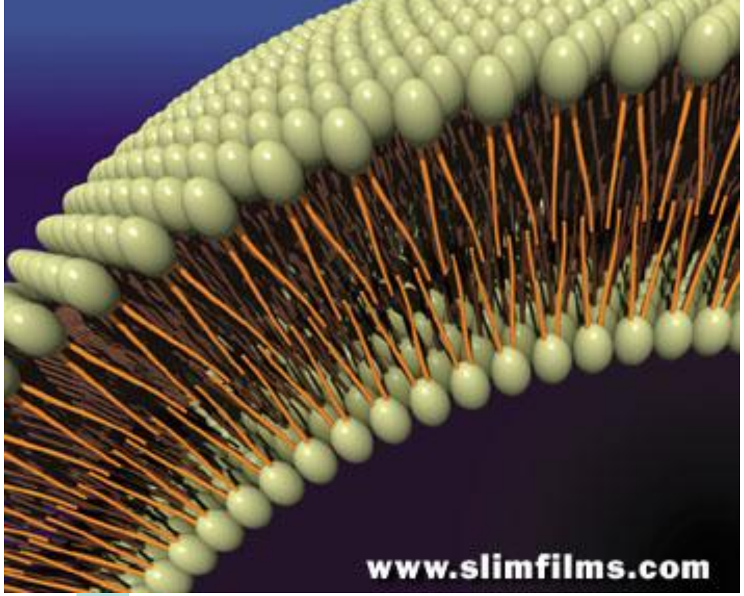


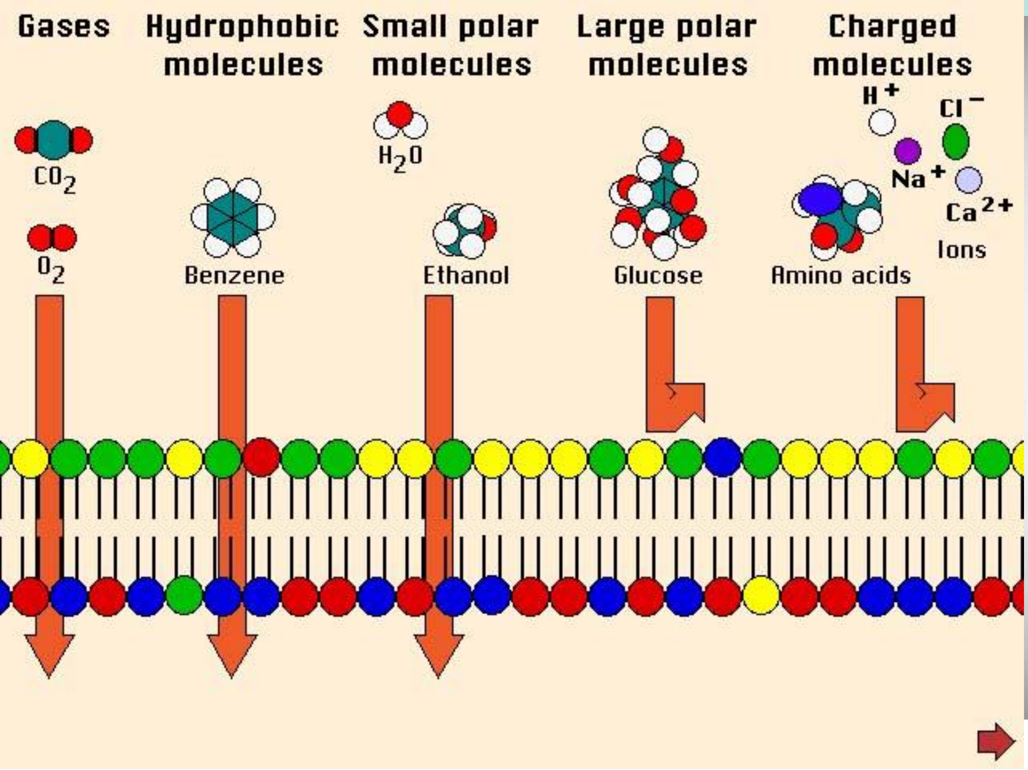

Lu
3+

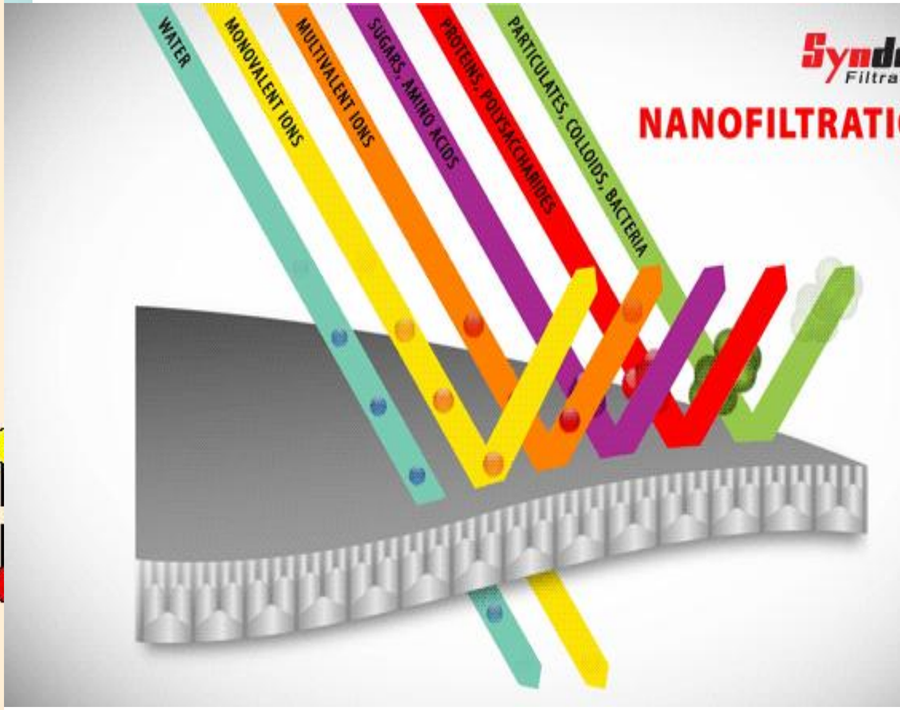

COOH COOH COOH COOH
^{111}In
HOOC COOH
HOOC
^{111}In, ^{68}Ga, ^{90}Y, ^{177}Lu
HN
NH$_2$
^{99m}Tc
(1-Nal)
(Tyr)
(Thr)
Octreotide (OC)
[Tyr^3]-Octreotide (TOC)
[Tyr^3, Thr^8]-Octreotide (TATE)
[1-Nal^3]-Octreotide (NOC)

CELL MEMBRANE

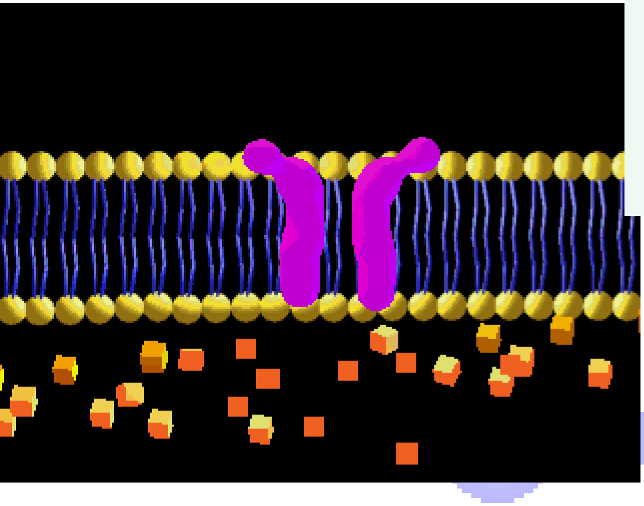
Major barrier For many compounds-crossing it means a good chance for acting on the target



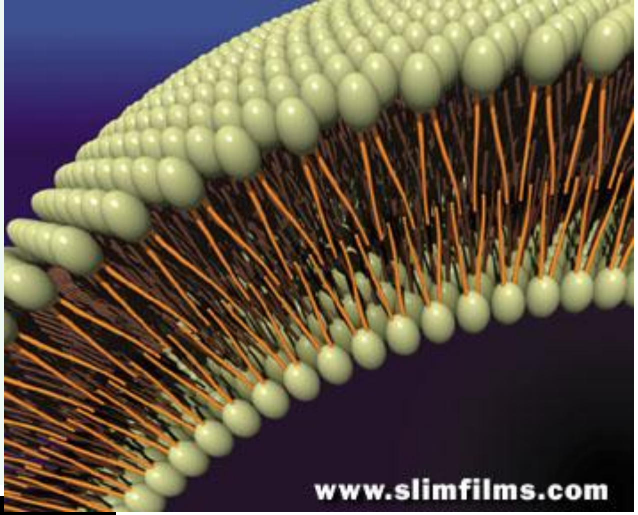


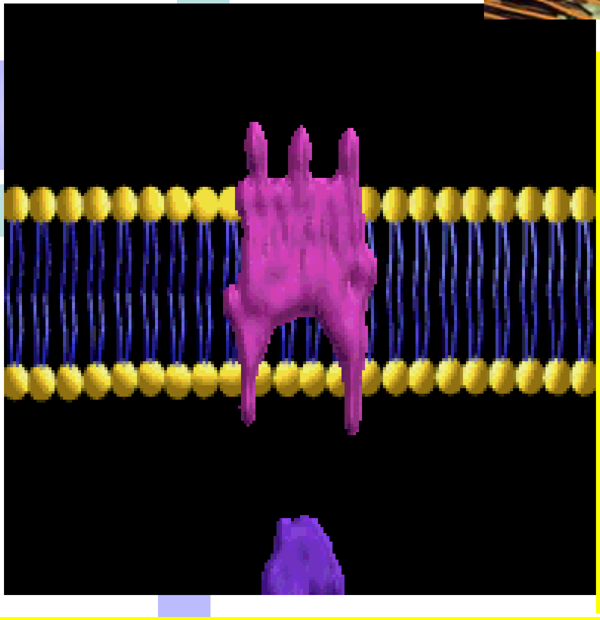


Passive diffusion
-transfer of just some compounds

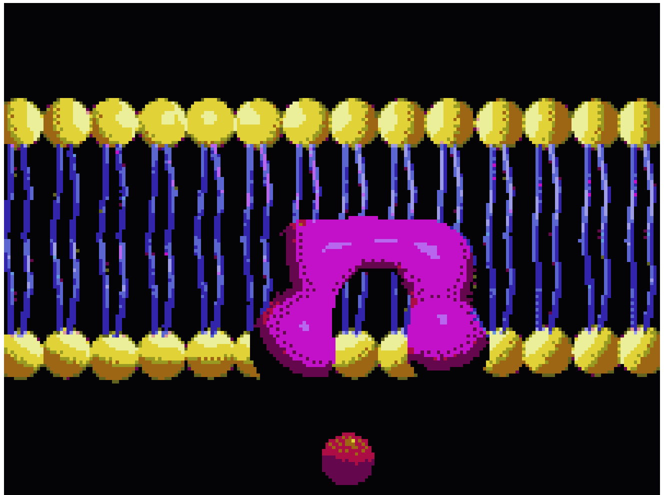


How can some Hydrophilic compound (like metal cations) cross a lipophilic membrane?



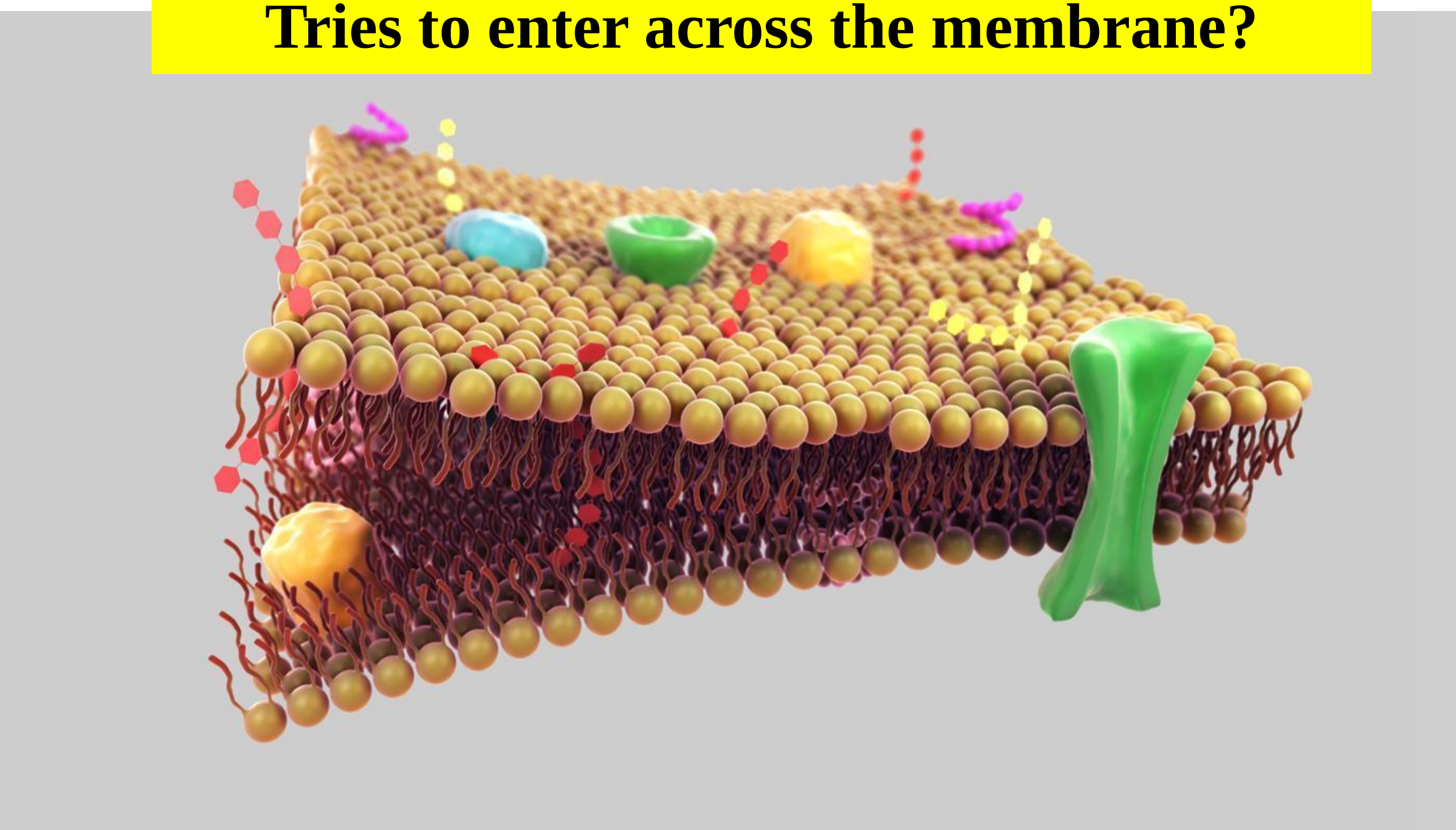


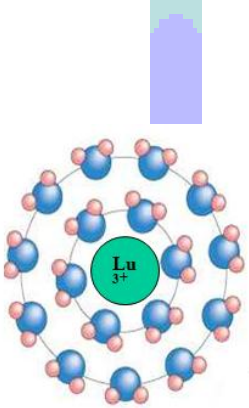
Rejection of the compound off the Lipid membrane
-it happens to Many metal ions



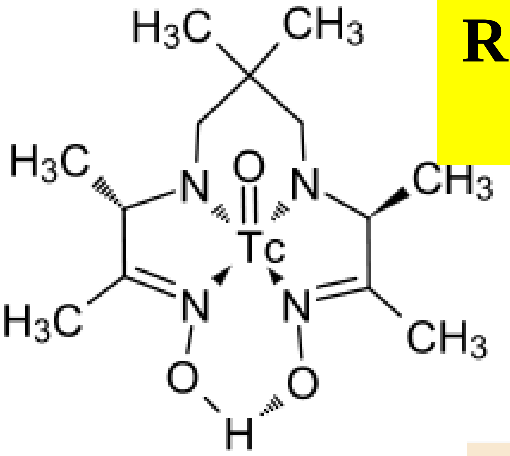
Facilitated transfer
-many metal ions form complexes With ligands and they can cross The membrane in form of complexes

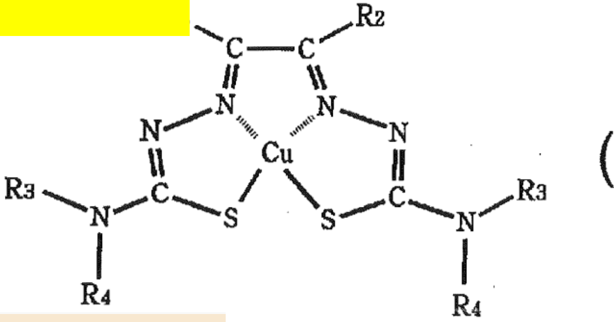
What happens when polycharged bare ion Tries to enter across the membrane?

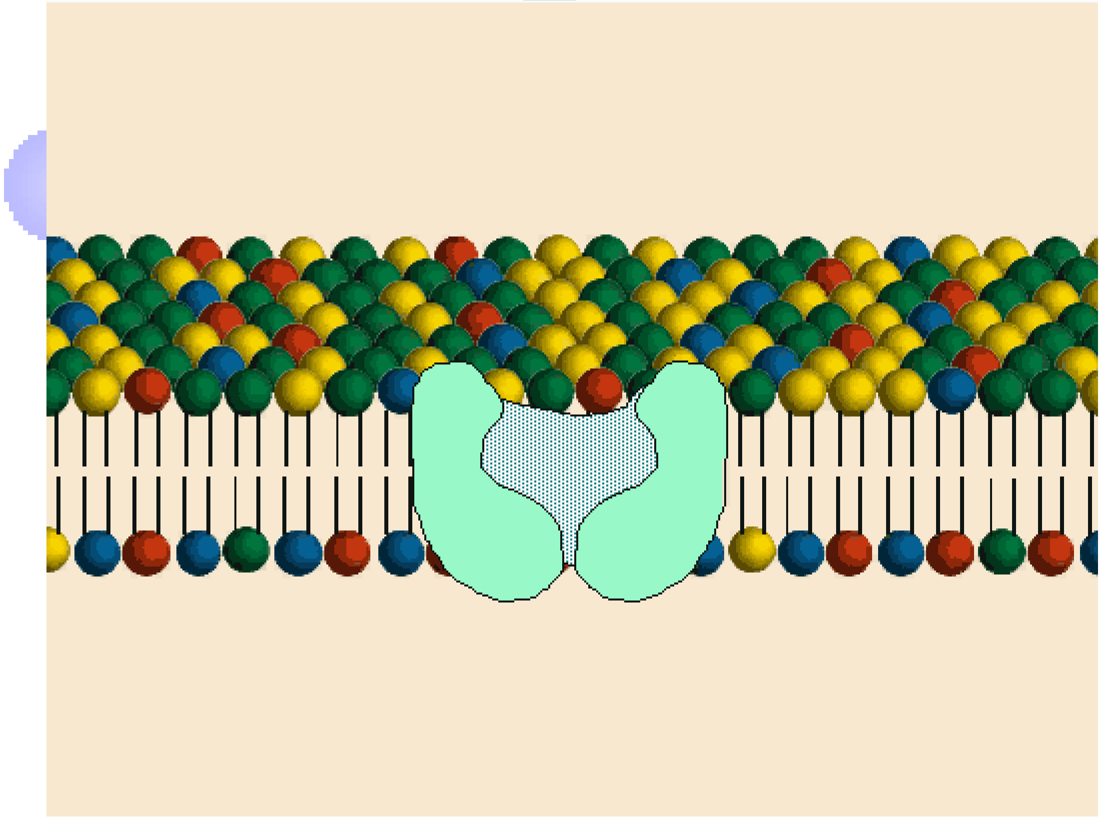




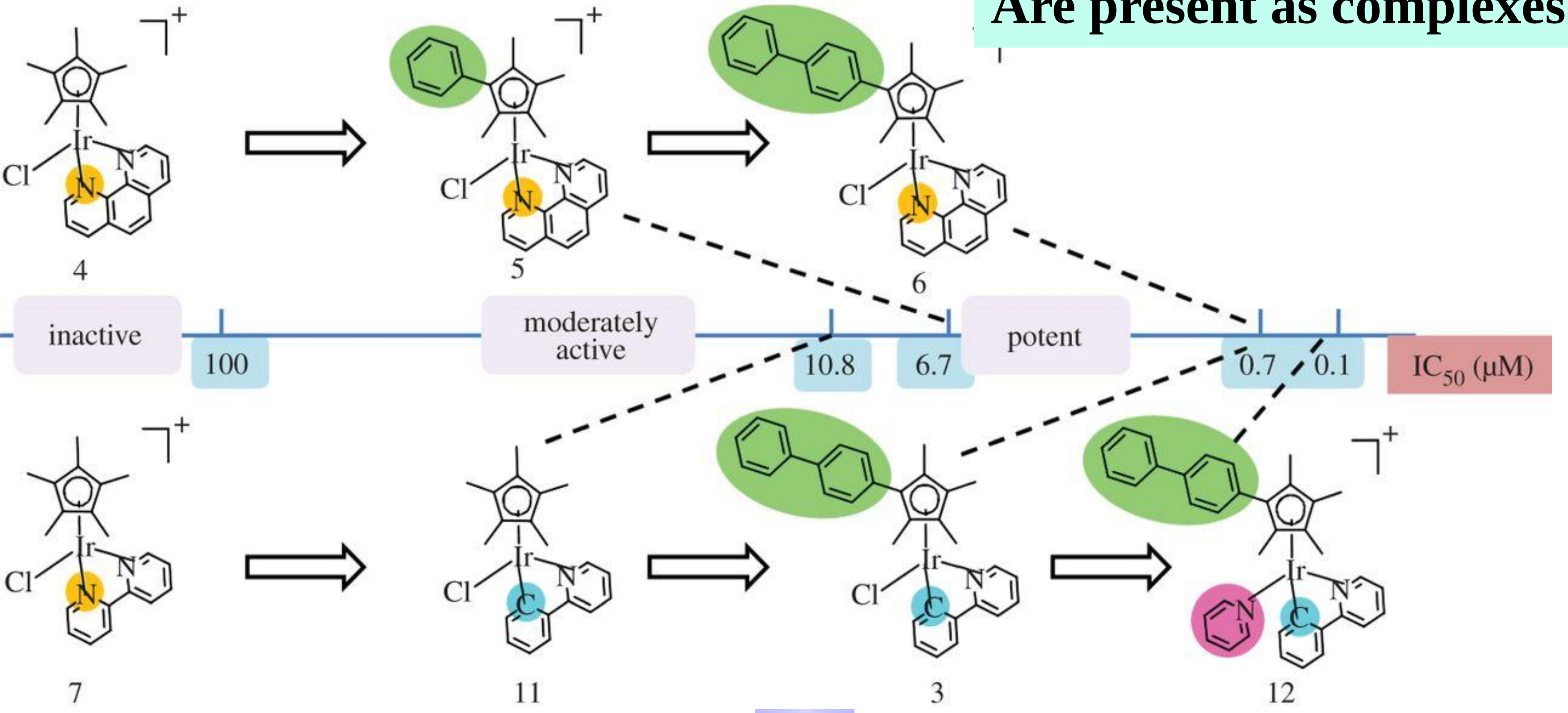
But,...what happens with Radioisotopes when they are present as complexes?





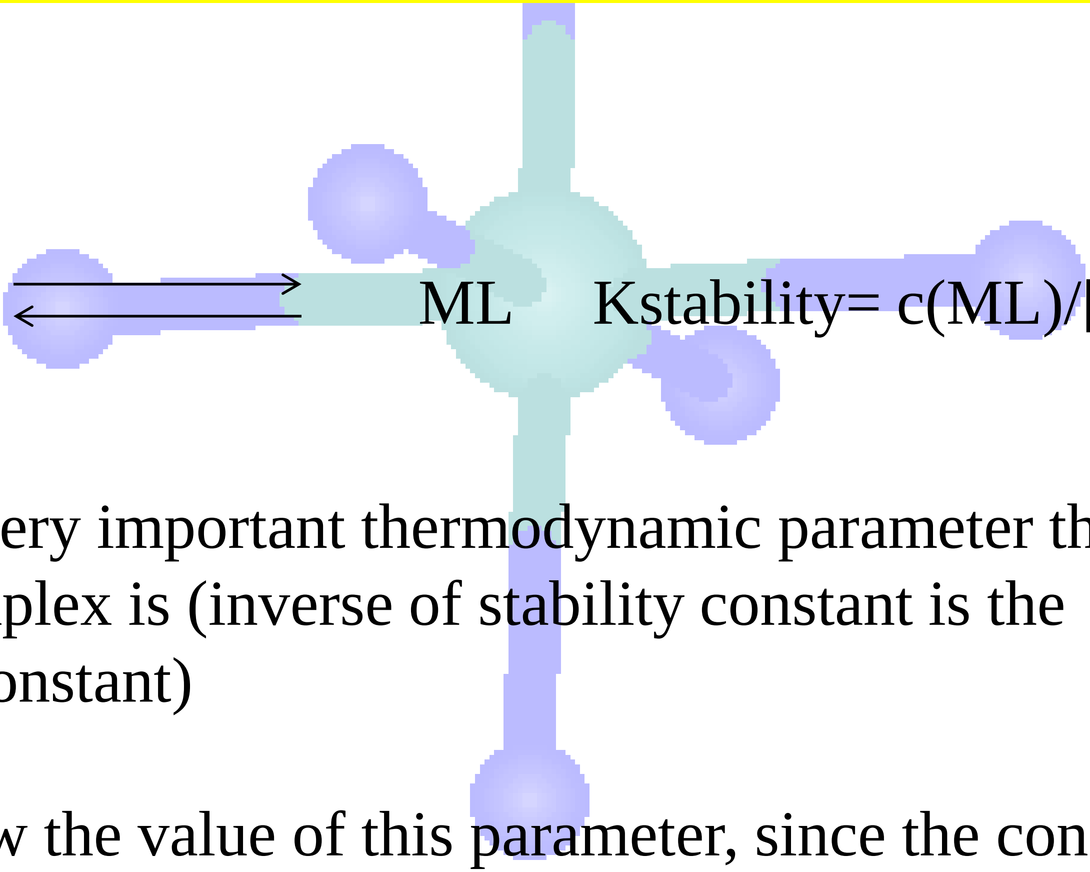


Bioavailability
And effective
Transport is much bigger
If metal ions
Are present as complexes



Complexation Reactions:

-Which parameters are worth to be know, having big Pharmaceutical and physiologival relevance?

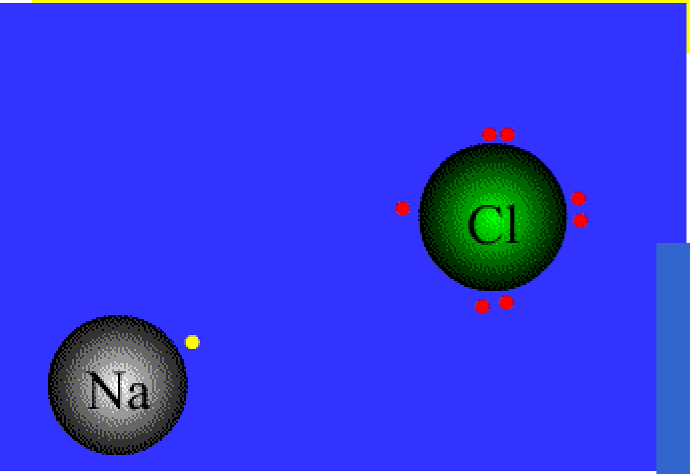


$M + L \rightleftharpoons ML$ $Kstability = c(ML)/[c(M)*c(L)]$

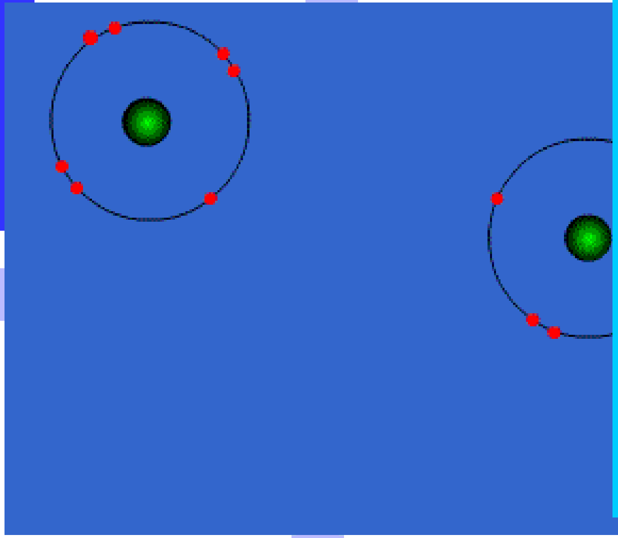
Kstability is very important thermodynamic parameter that shows how Stable the complex is (inverse of stability constant is the Dissociation constant)

One must know the value of this parameter, since the concentration of ***free RADIOISOTOPE*** depends on it!

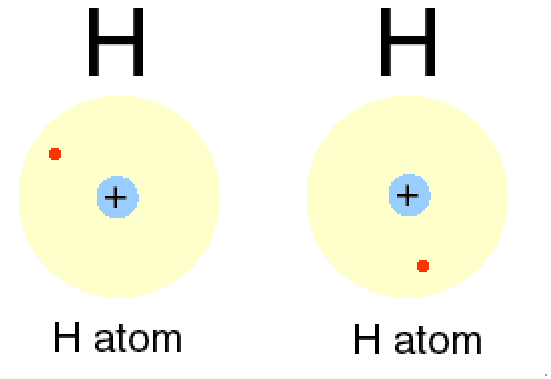
Short history of metal complexes...reminder



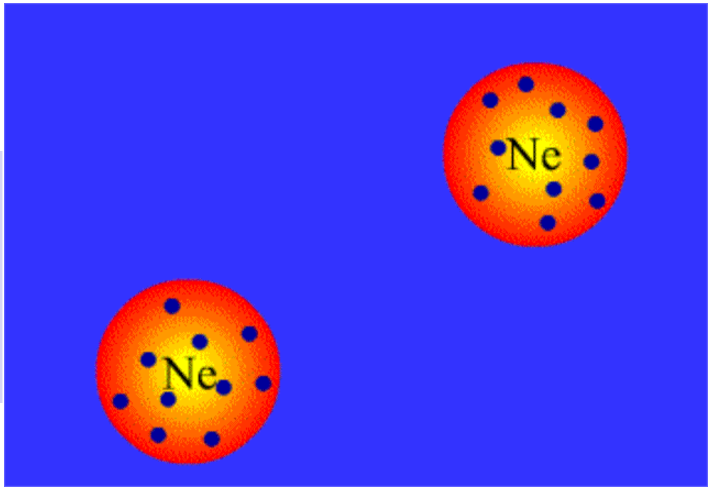
IONIC BOND-Electrostatic „+ -“ interactions
Exchange of electrons



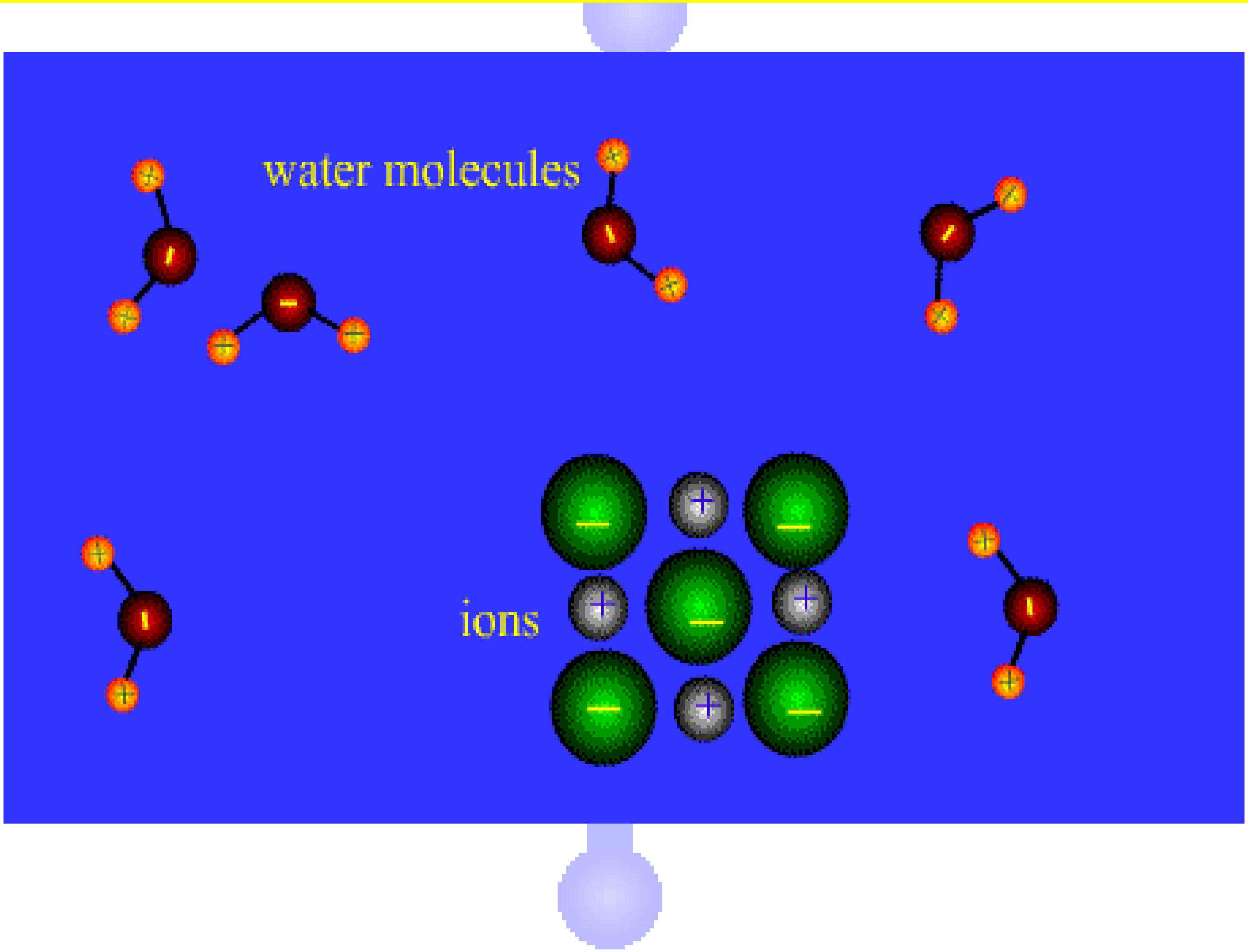
Covalent bonds
„shared electrons
...each atom gives
one electron and
Electron pair is created
that belongs to both
atoms



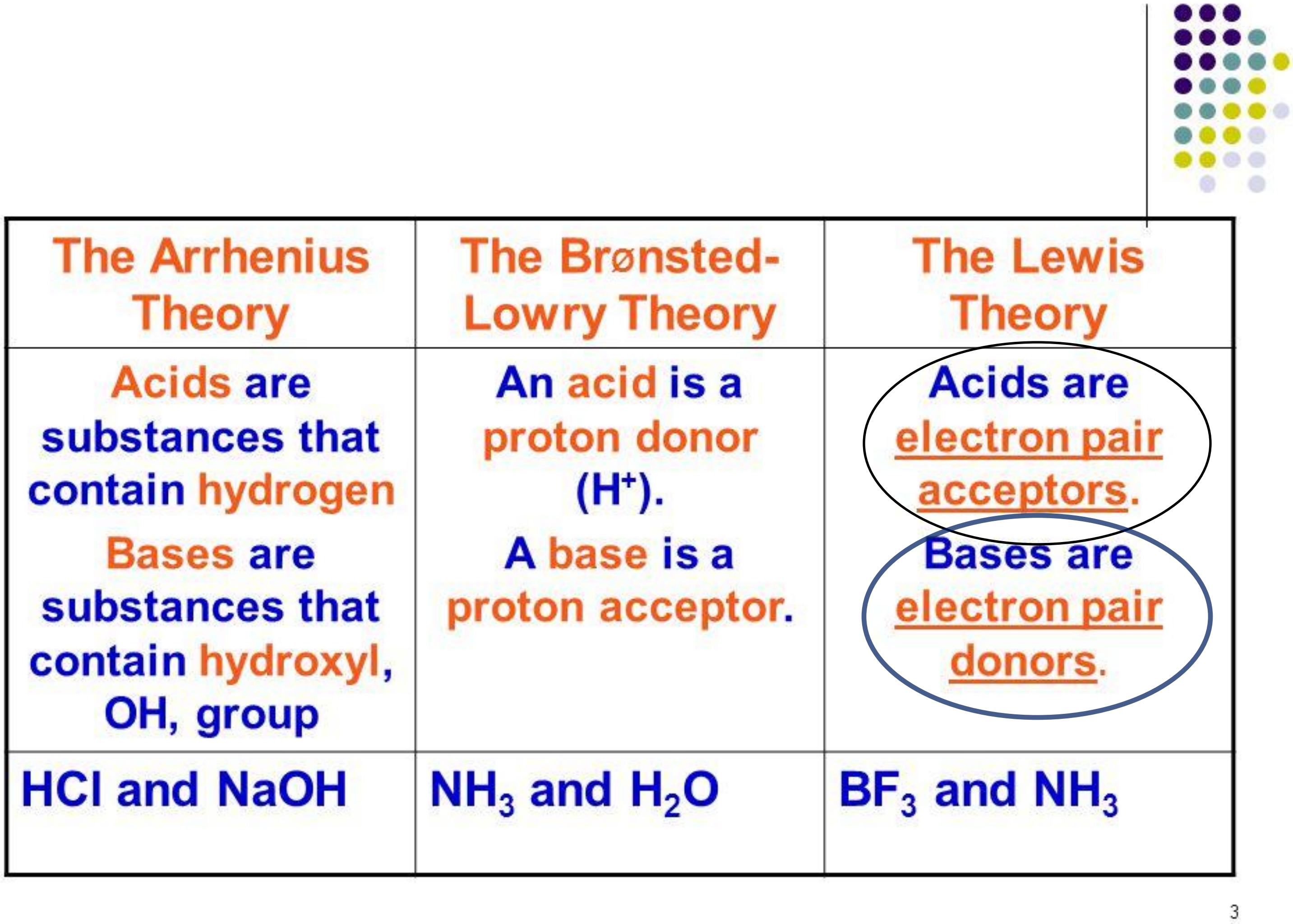
Weak Van der Valls
Induced dipol
interactions



What happens if a crystal compound is placed in water?

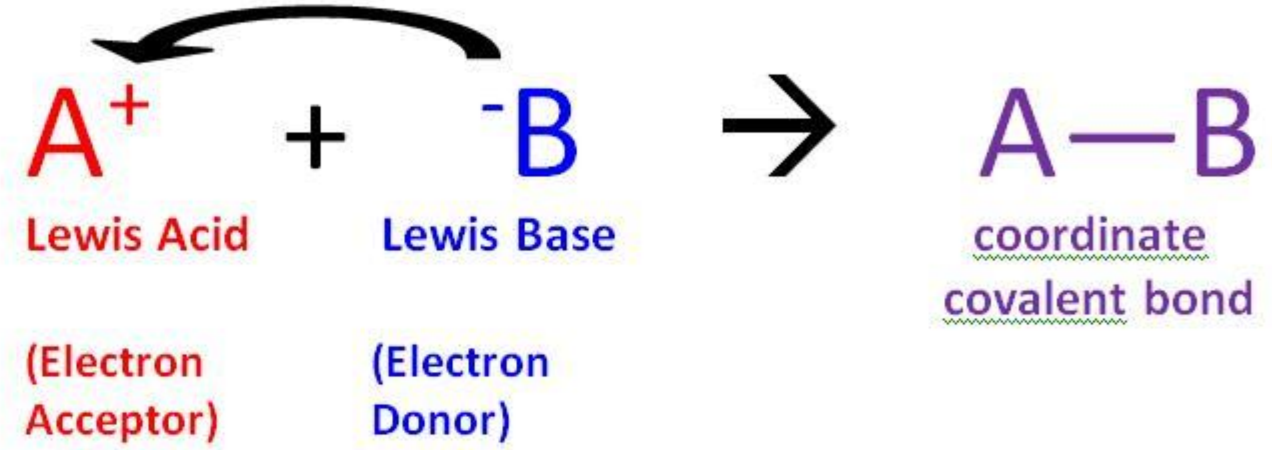


ACIDS AND BASES-Several Definitions and Theories

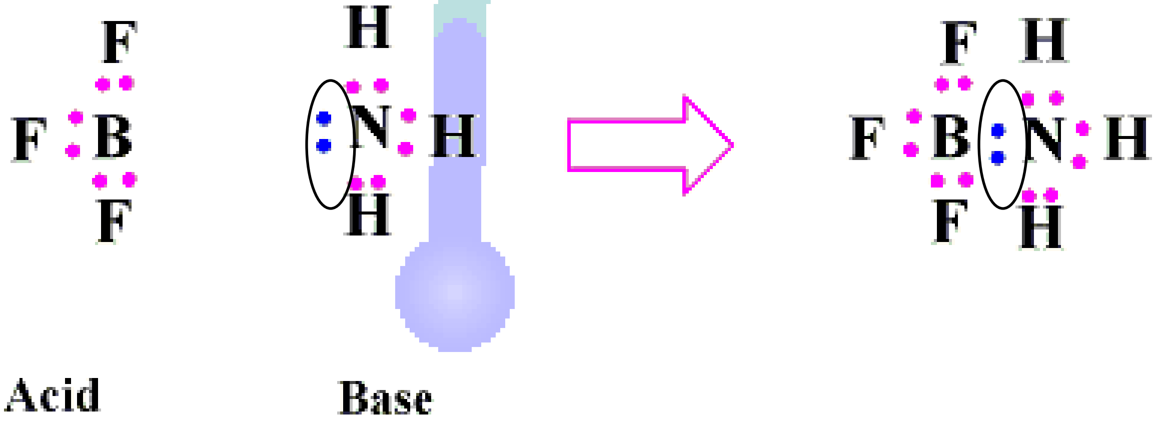


The Arrhenius Theory	The Brønsted-Lowry Theory	The Lewis Theory
Acids are substances that contain hydrogen Bases are substances that contain hydroxyl, OH, group	An acid is a proton donor (H^+). A base is a proton acceptor.	Acids are <u>electron pair acceptors</u>. Bases are <u>electron pair donors</u>.
HCl and NaOH	NH_3 and H_2O	BF_3 and NH_3

Lewis Theory of Acids and Bases



Precondition fos stability of an atom is-8 electron configuration In the last orbital layer!



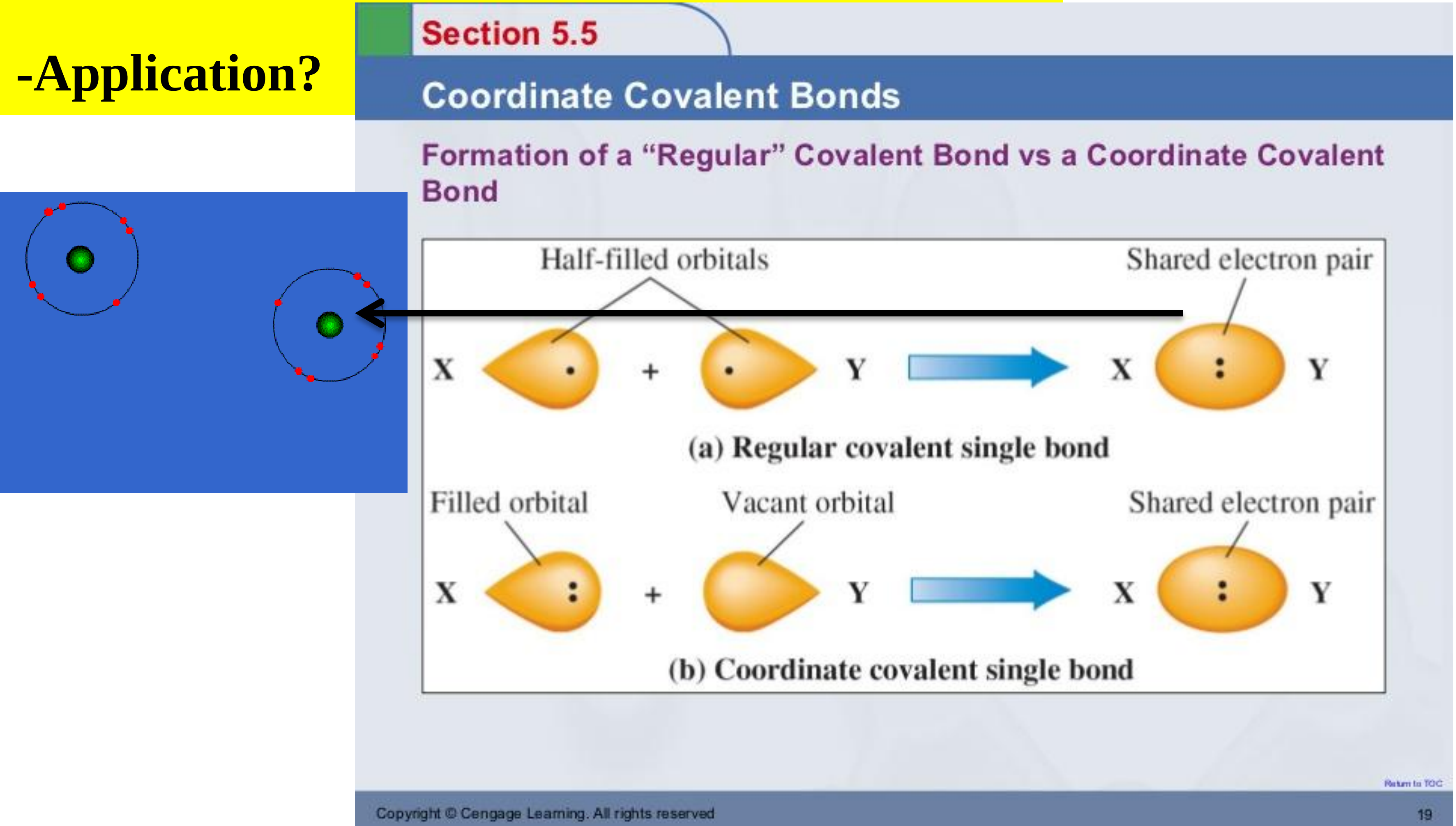
Donor of the electron pair is ONE OF THE ATOMS, not TWO!

COORDINATION CHEMISTRY

-Why it is important?

-How can be interpreted the bond formation?

-Application?



Section 5.5

Coordinate Covalent Bonds

Formation of a "Regular" Covalent Bond vs a Coordinate Covalent Bond

(a) Regular covalent single bond

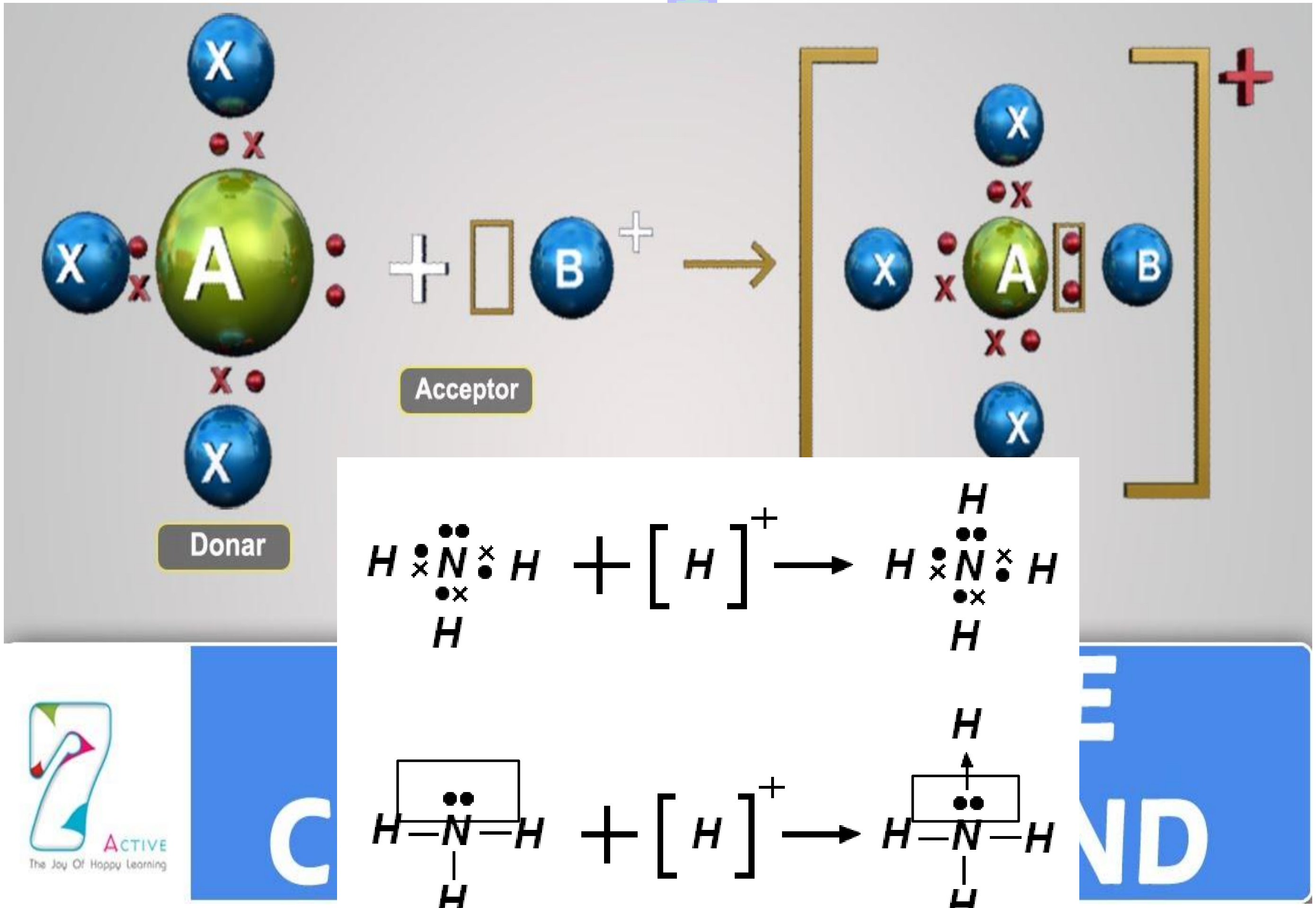
(b) Coordinate covalent single bond

Return to TOC

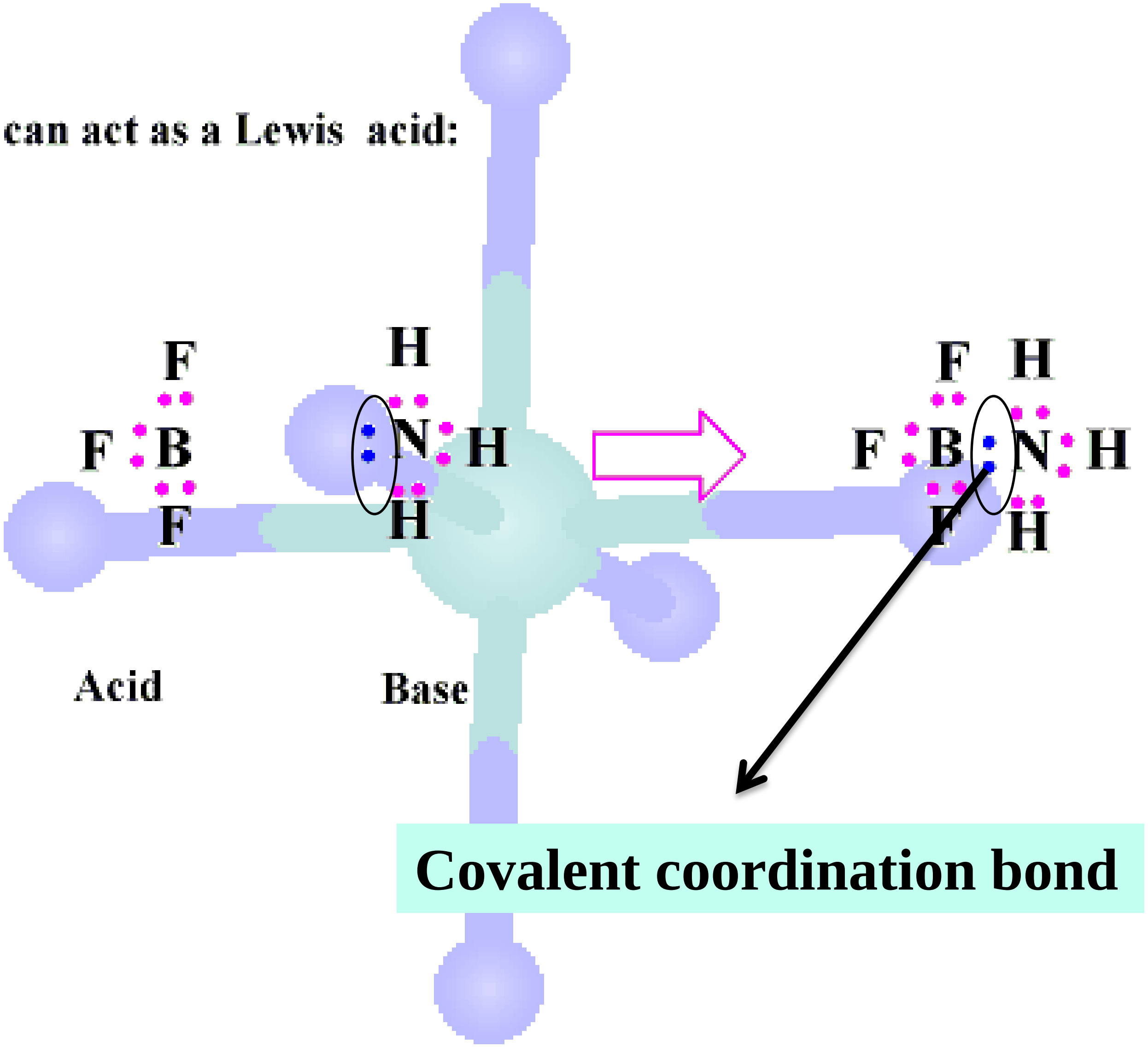
<u>DEFINITION:</u>

<u>COORDINATE COVALENT BOND</u> IS A **CHEMICAL BOND** IN WHICH

A PAIR OF ELECTRONS *<u>OF ONE ATOM</u>* IS SHARED BETWEEN TWO DIFFERENT ATOMS



BF_3 can act as a Lewis acid:



Covalent coordination bond

Coordination Chemistry

- **Transition metal ions** have **non-fully filled orbitals with electrons** and **they act as Lewis acids** i.e. **they can receive an electronic pair from some donor atom**
  - They can form complexes/complex ions

$$Fe^{3+}(aq) + 6CN^{-}(aq) \rightarrow [Fe(CN)_6]^{3-}(aq)$$

Lewis acid Lewis base Complex ion

$$Ni^{2+}(aq) + 6NH_3(aq) \rightarrow [Ni(NH_3)_6]^{2+}(aq)$$

Lewis acid Lewis base Complex ion

Complex with a net charge = complex ion

Complexes have distinct properties

Coordination Chemistry DEFINITIONS

- **Coordination compound**
  - **Compound that contains 1 or more coordination bonds**
  - Example
  - **NH_4^+**
    - $[Co(NH_3)_6]Cl_3$
    - $[Cu(NH_3)_4][PtCl_4]$
    - $[Pt(NH_3)_2Cl_2]$

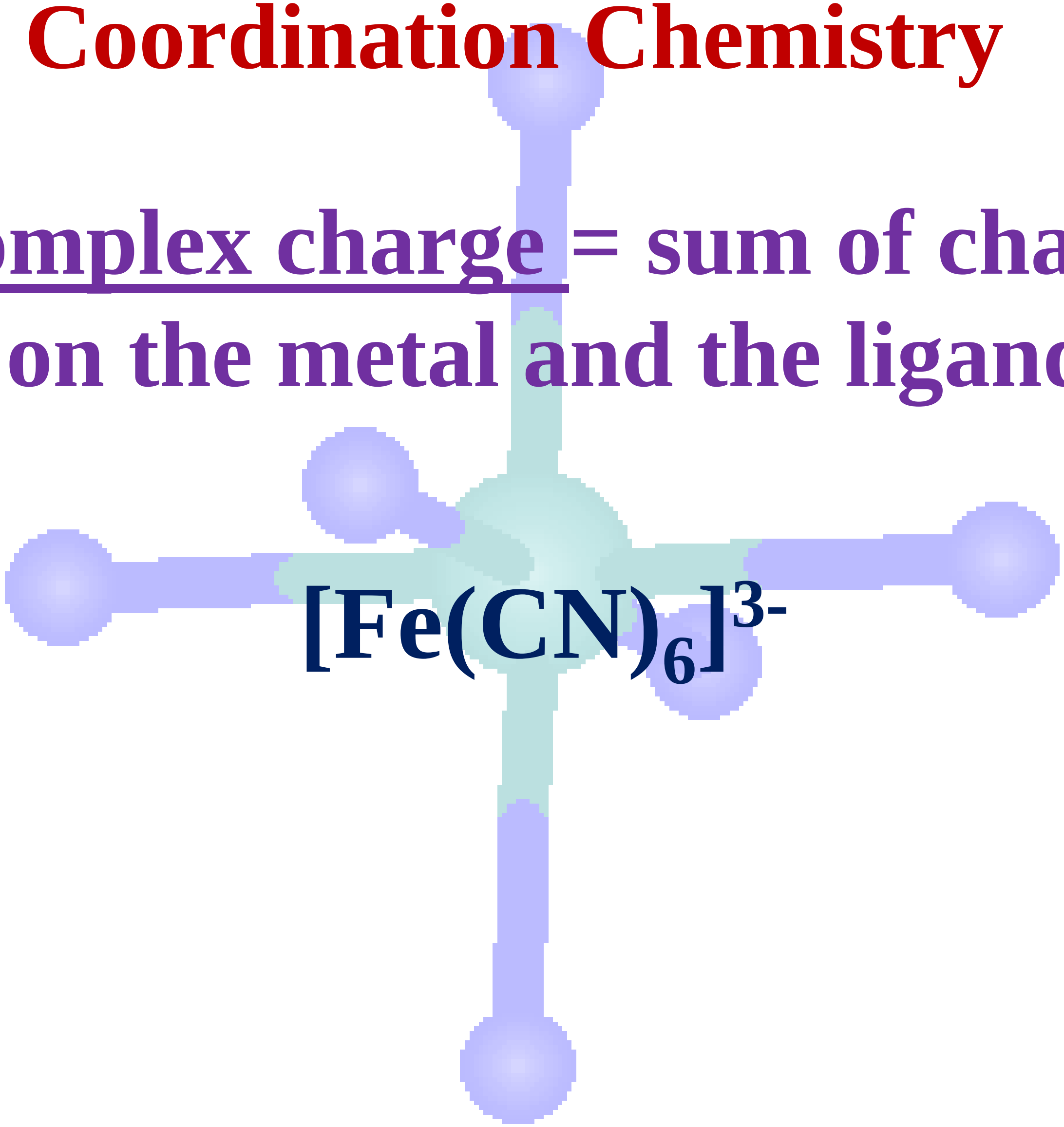
Coordination Chemistry

$[Fe(CN)_6]^3$

- **Coordination sphere**
  - ---**is the system** of **Metal** and **ligands** bound to it
  - --- **LIGANDS ARE ANIONS OR NEUTRAL MOLECULES** THAT ***HAVE AT LEAST ONE ATOM*** that is **DONOR OF ELECTRON PAIR**
- **Coordination number**
  - **number of ligands bonded to the central metal atom or ion** in the complex
    - Most common = 4, 6
    - Determined by ligands
      - **Larger ligands** and those that transfer substantial negative charge to metal favor **lower coordination numbers**

Coordination Chemistry

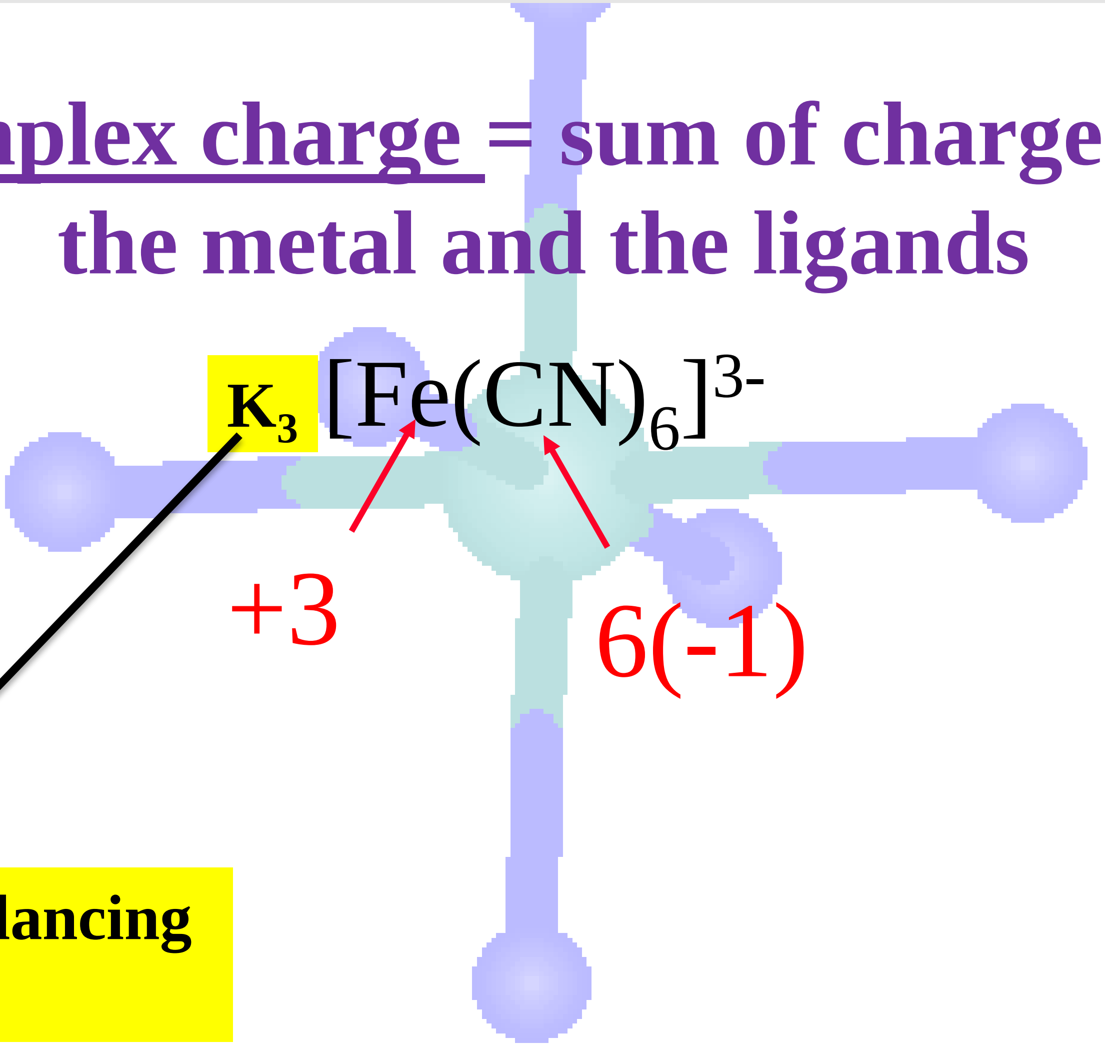
Complex charge = sum of charges on the metal and the ligands



$[Fe(CN)_6]^{3-}$

Coordination Chemistry

Complex charge = sum of charges on the metal and the ligands



$K_3[Fe(CN)_6]^{3-}$

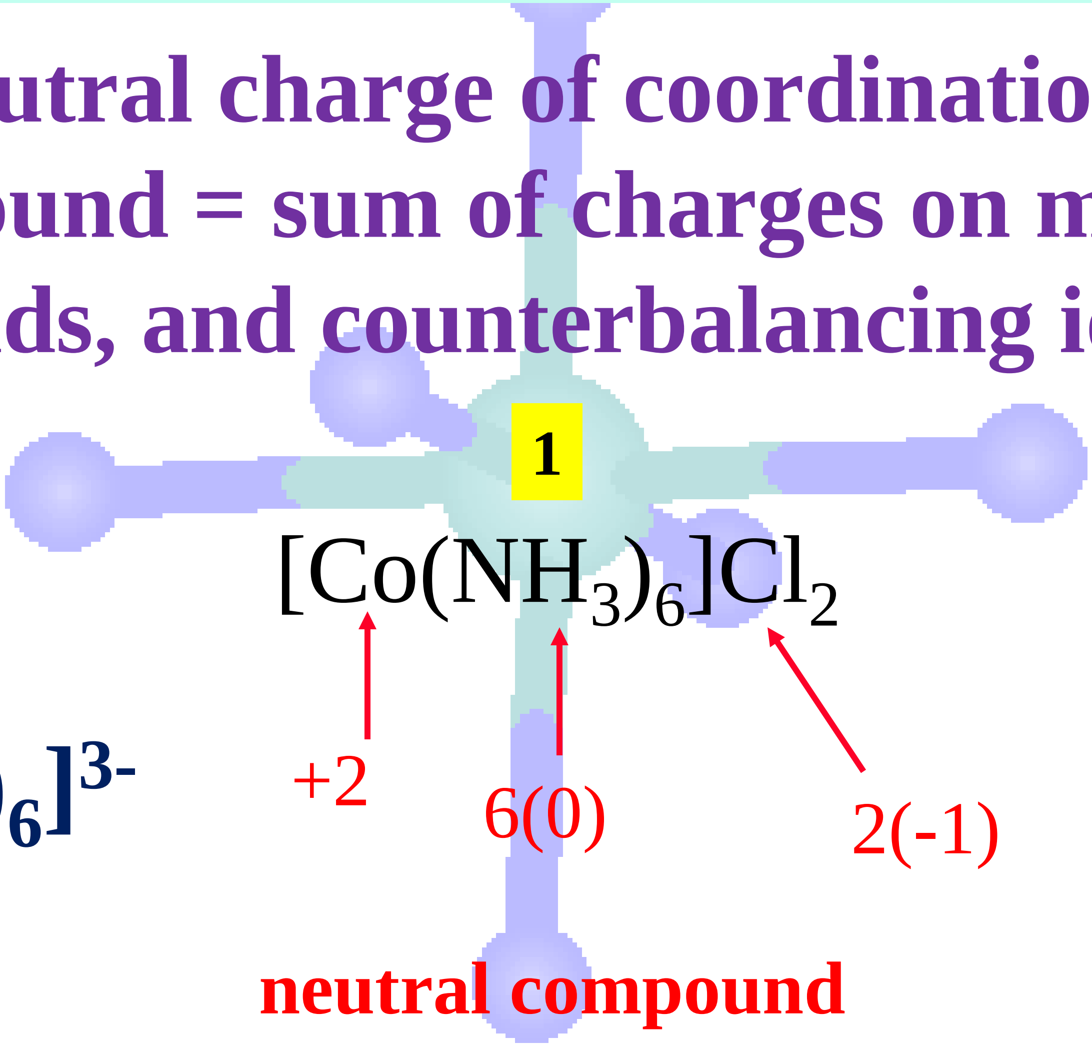
+3

6(-1)

Counter balancing cation

Coordination Chemistry

Neutral charge of coordination compound = sum of charges on metal, ligands, and counterbalancing ions



1

$[Co(NH_3)_6]Cl_2$

+2

6(0)

2(-1)

neutral compound

2

$\mathbf{[Fe(CN)_6]^{3-}}$

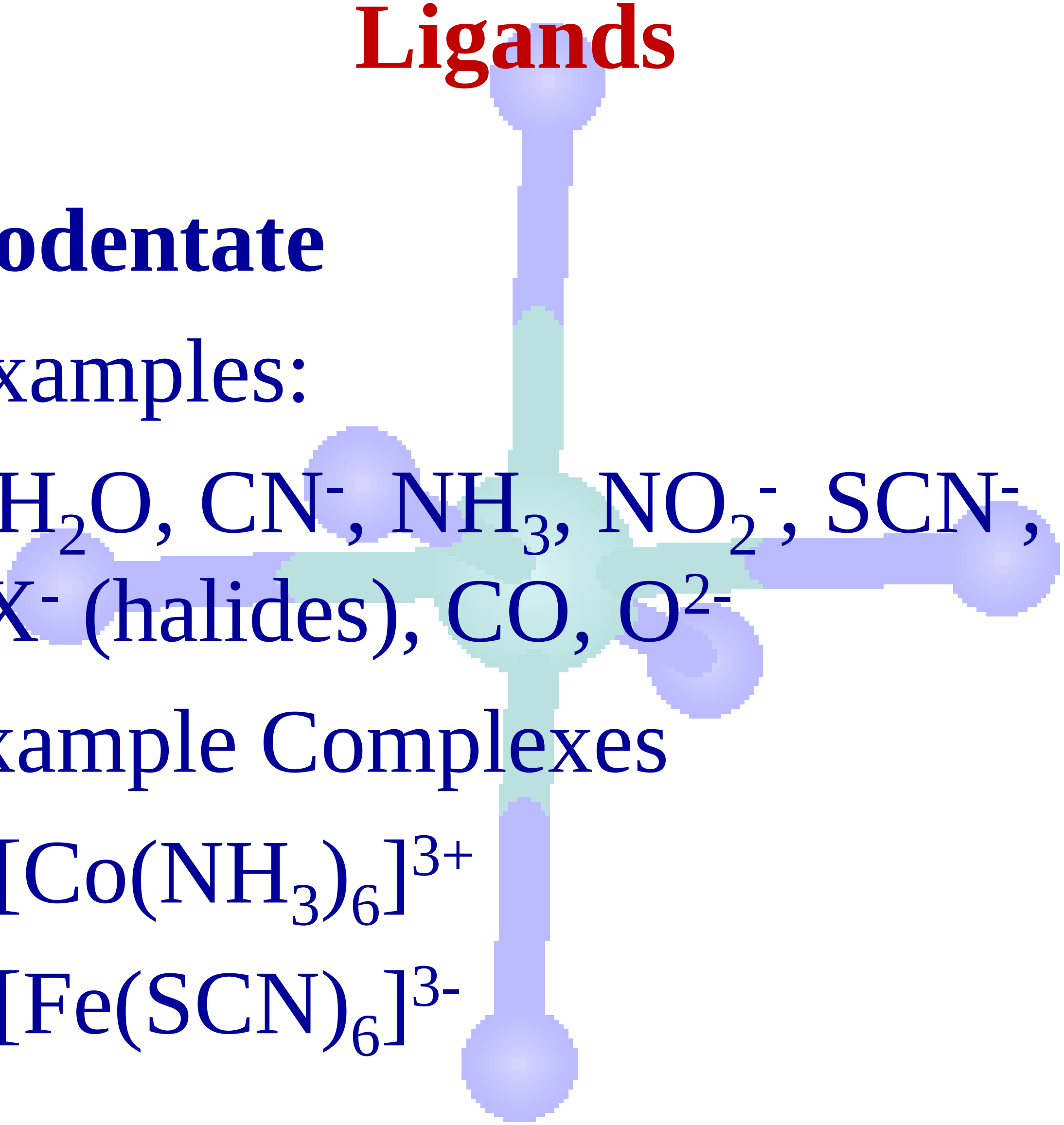
What is the difference between complex „1“ and complex „2“?

Coordination Chemistry

- **Ligands**
  - classified according to the **number of donor atoms present in the ligand structure**
  - Examples
    - monodentate = 1
    - bidentate = 2
    - tetradentate = 4
    - hexadentate = 6
    - **polydentate** = 2 or more donor atoms

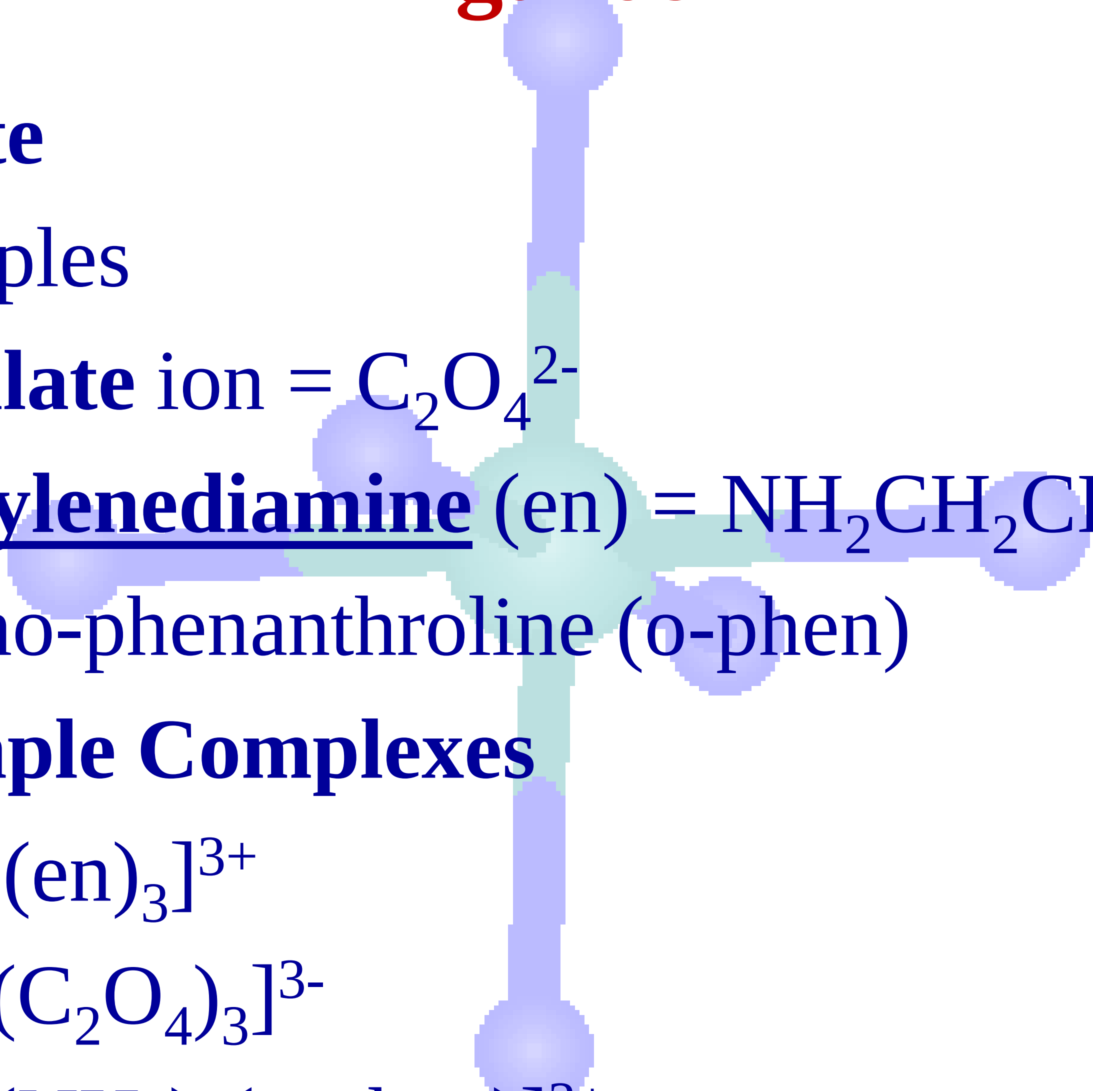
chelating agents

Ligands



- **Monodentate**
  - Examples:
    - H_2O, CN^-, NH_3, NO_2^-, SCN^-, OH^-, X^- (halides), CO, O^{2-}
  - Example Complexes
    - $[Co(NH_3)_6]^{3+}$
    - $[Fe(SCN)_6]^{3-}$

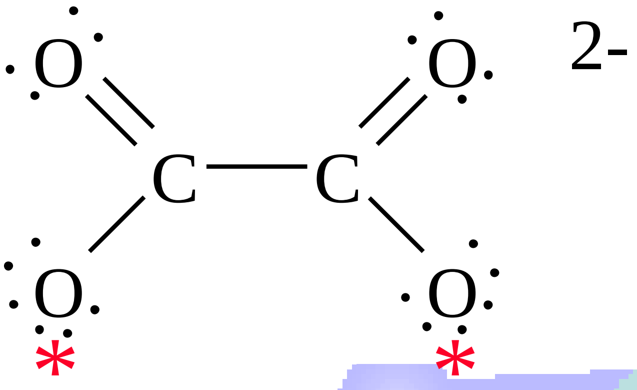
Ligands



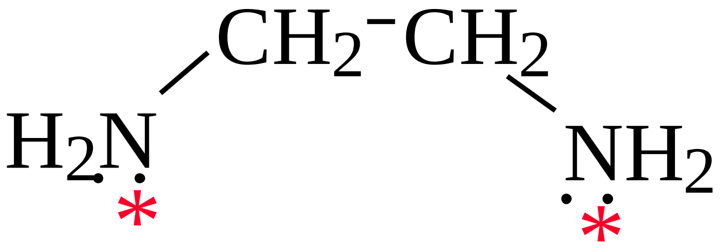
- **Bidentate**
  - Examples
    - **oxalate** ion = $C_2O_4^{2-}$
    - e**thylenediamine** (en) = $NH_2CH_2CH_2NH_2$
    - ortho-phenanthroline (o-phen)
  - **Example Complexes**
    - $[Co(en)_3]^{3+}$
    - $[Cr(C_2O_4)_3]^{3-}$
    - $[Fe(NH_3)_4(o\text{-}phen)]^{3+}$

Ligands

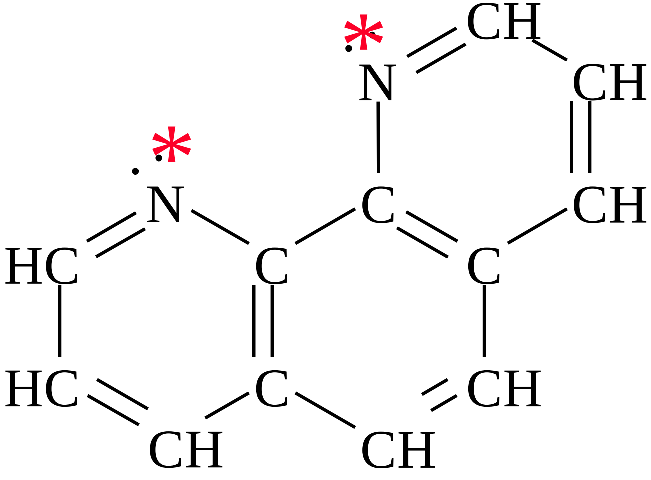
oxalate ion



ethylenediamine



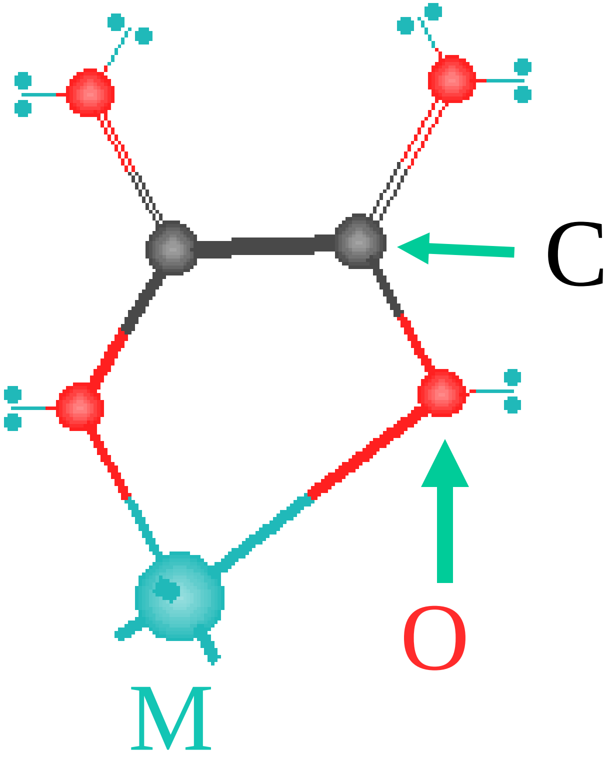
ortho-phenanthroline



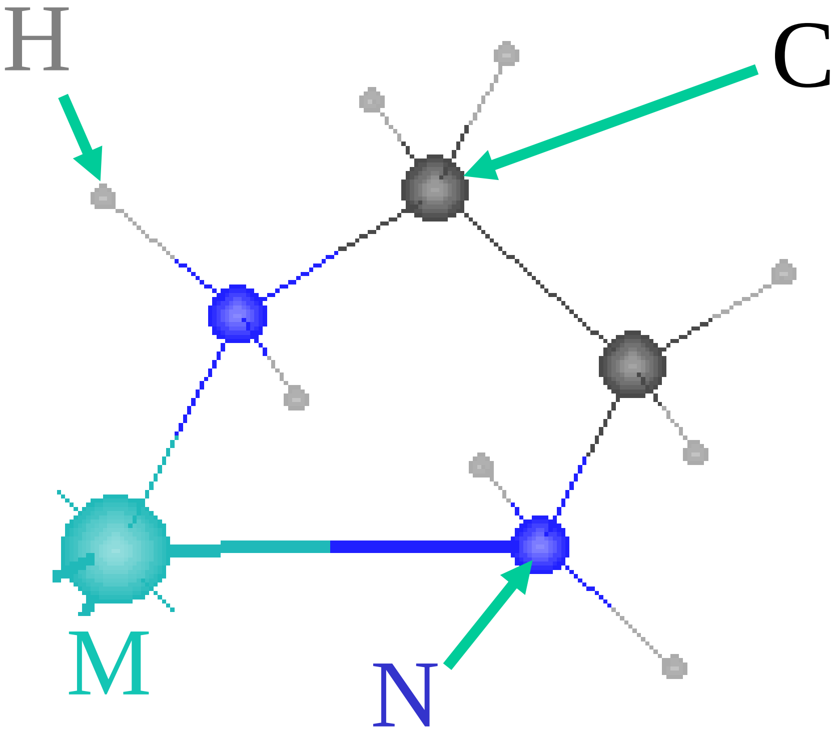
Donor Atoms

Ligands

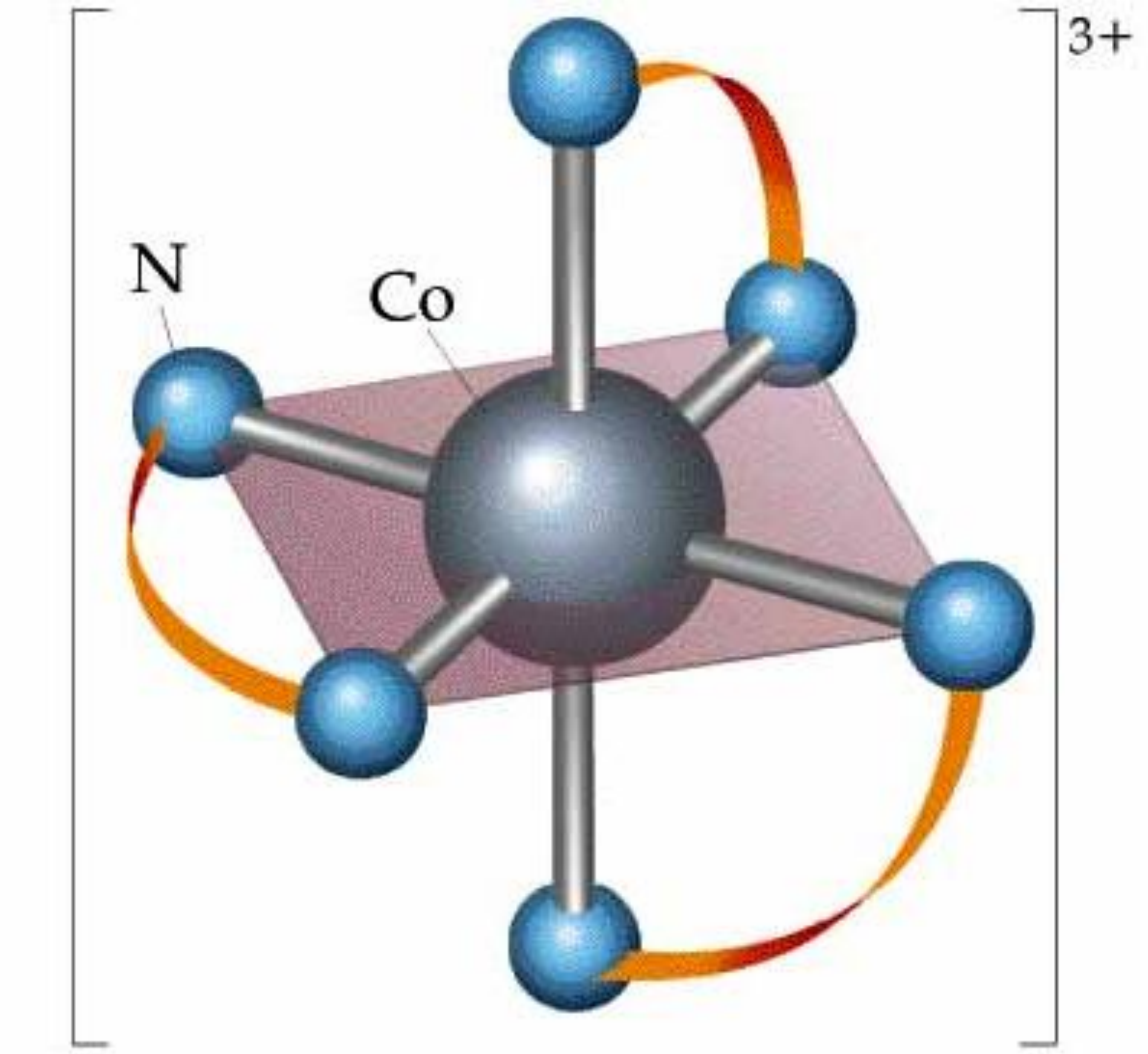
oxalate ion



ethylenediamine

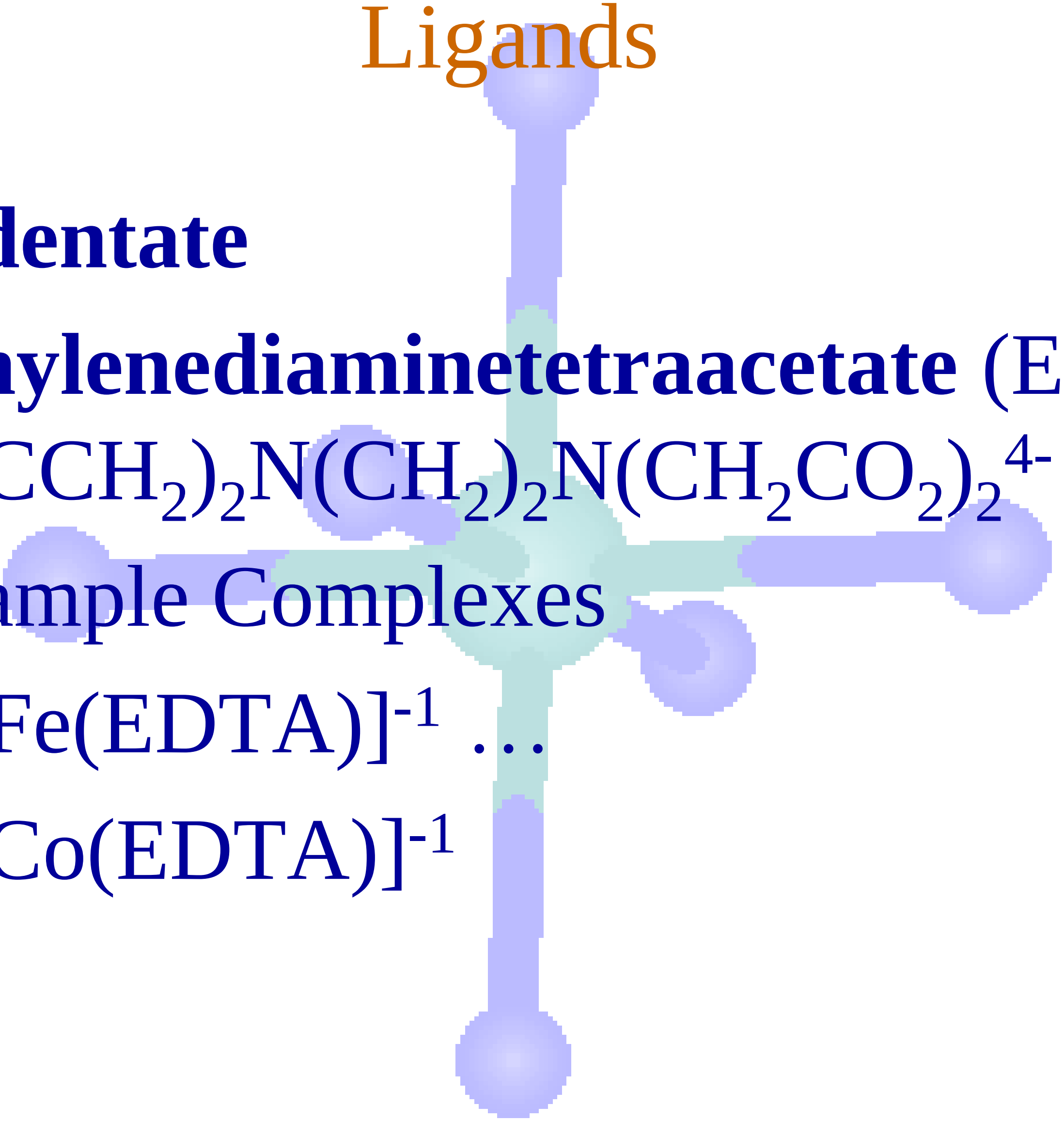


Ligands



$Co(en)_3^{3+}$

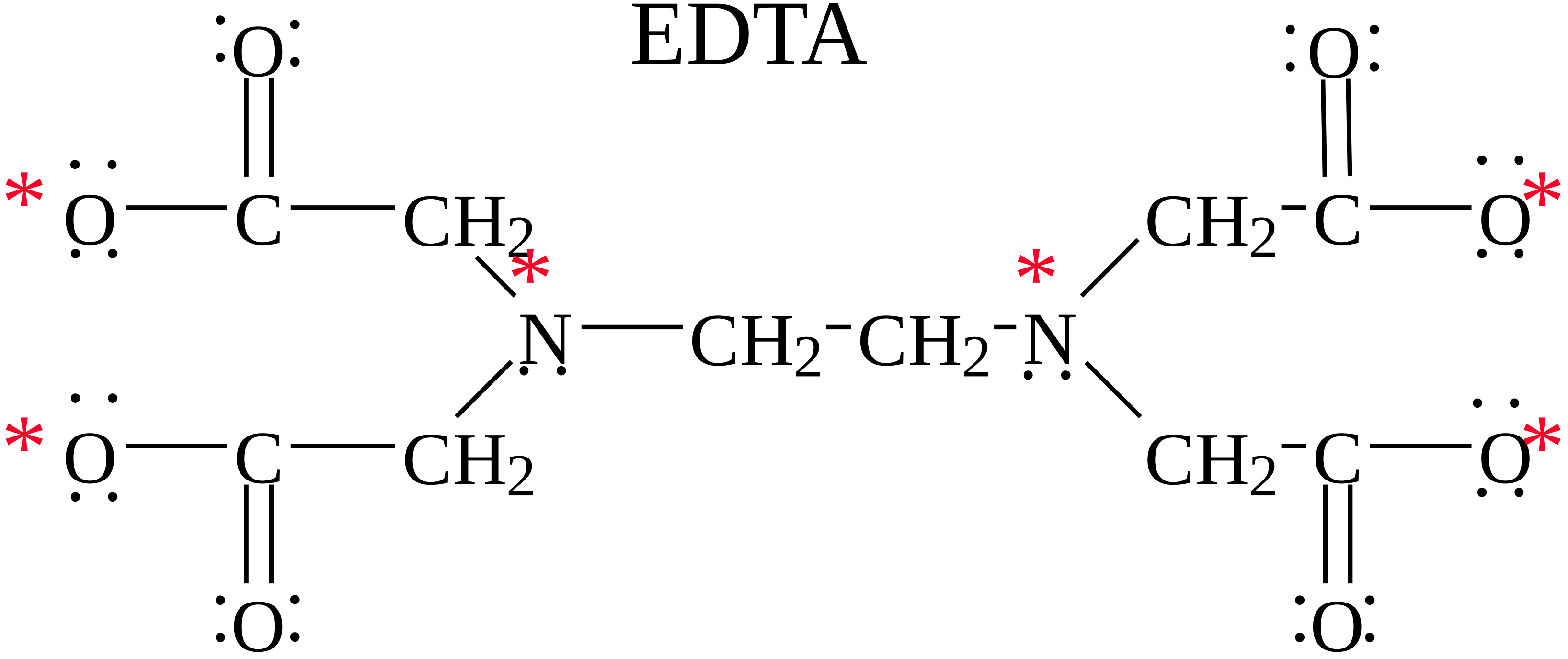
Ligands



- **Hexadentate**
  - **ethylenediaminetetraacetate** (EDTA) = $(O_2CCH_2)_2N(CH_2)_2N(CH_2CO_2)_2^{4-}$
  - Example Complexes
    - $[Fe(EDTA)]^{-1}$ . . .
    - $[Co(EDTA)]^{-1}$

Ligands

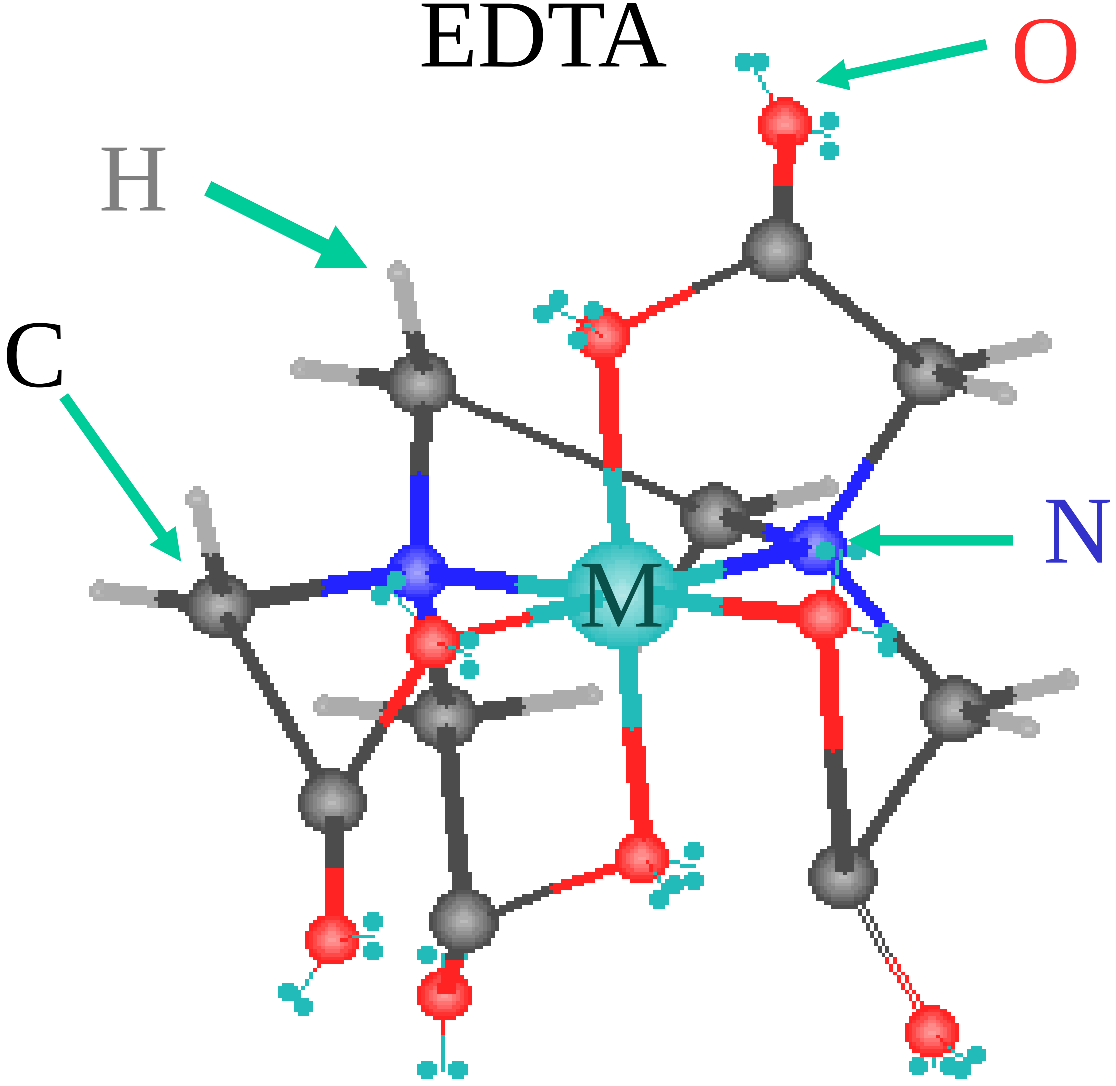
EDTA



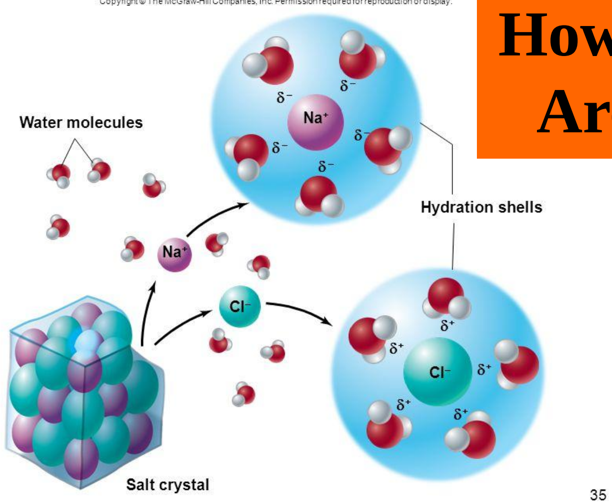
***Donor Atoms**

Ligands

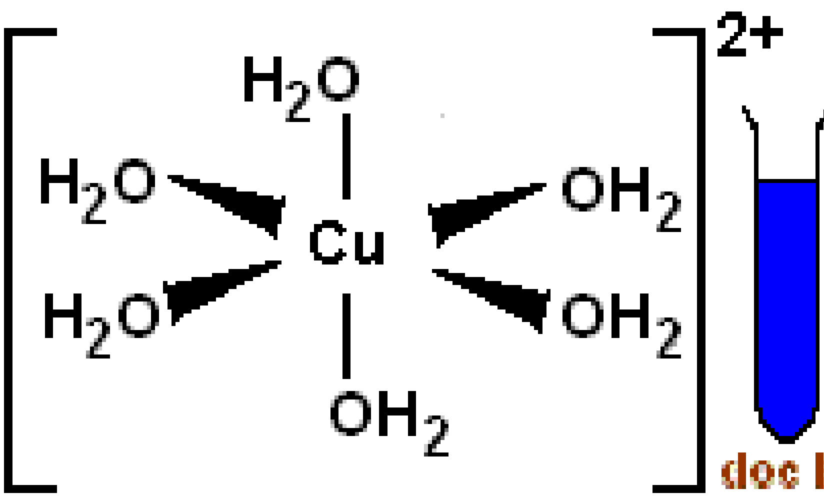
EDTA



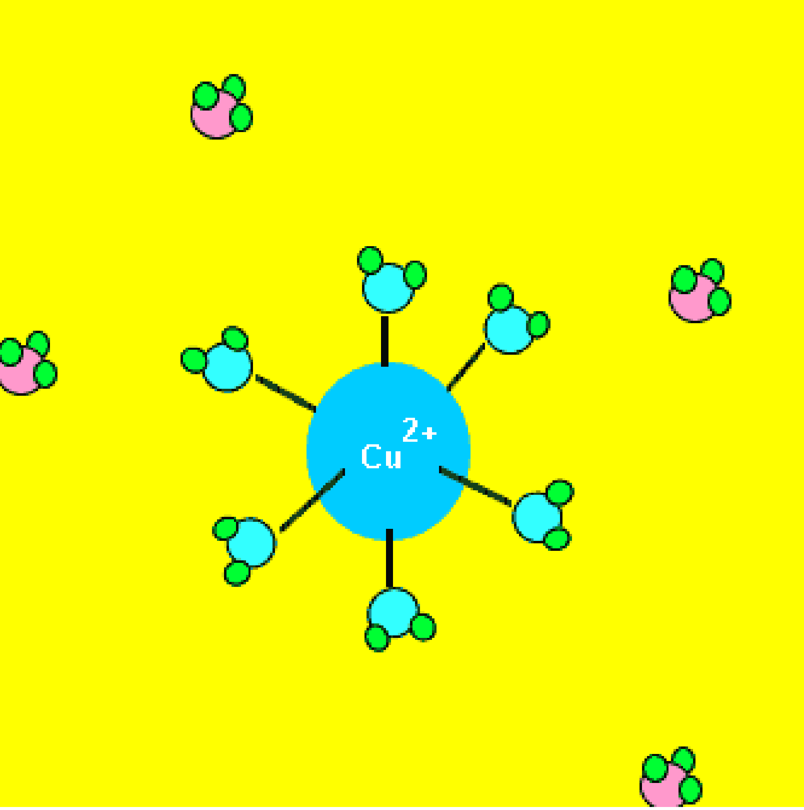
How complexes Are formed?



Ion Hydration in water

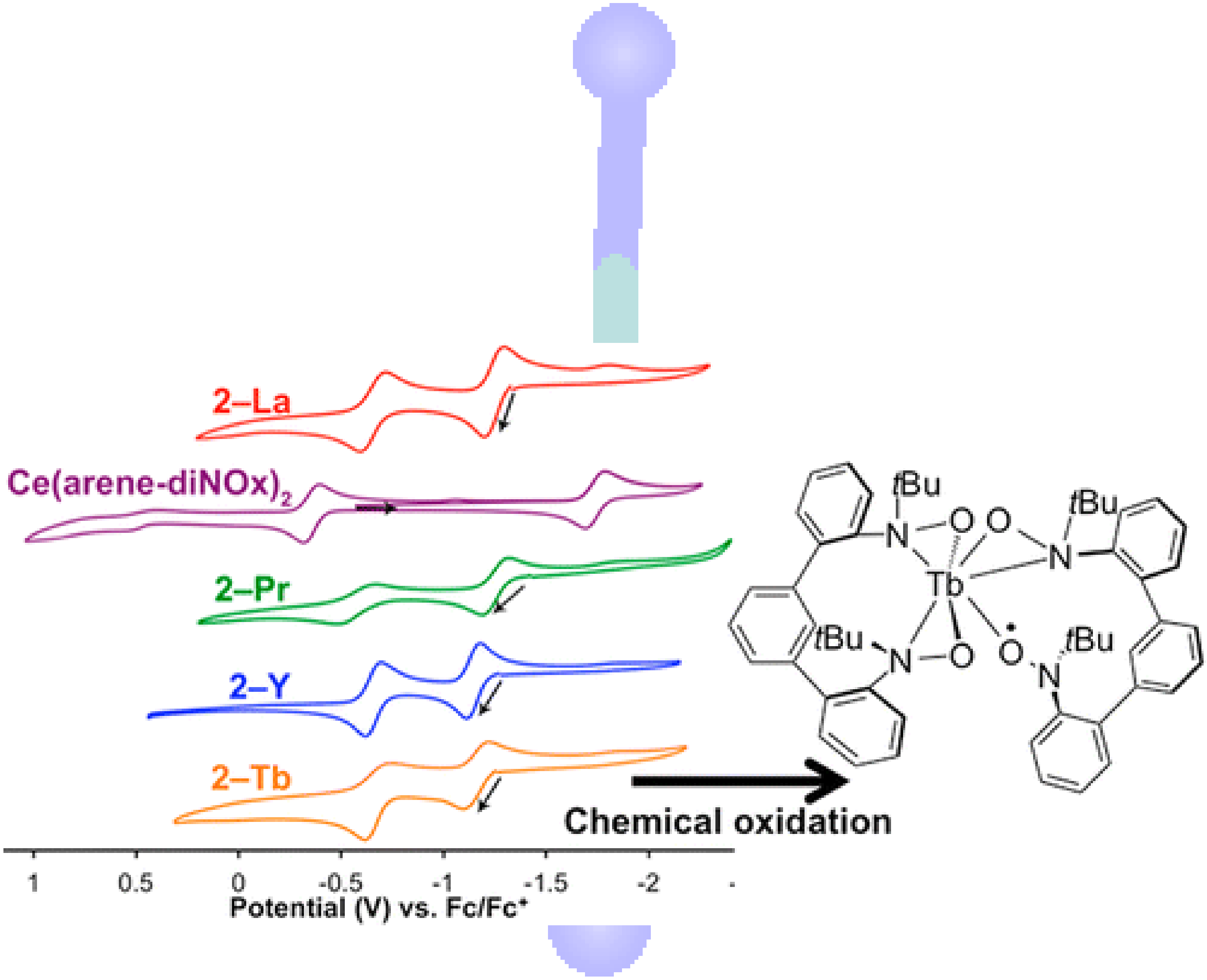


$Cu(H_2O)_6^{2+}{}_{(aq)}$



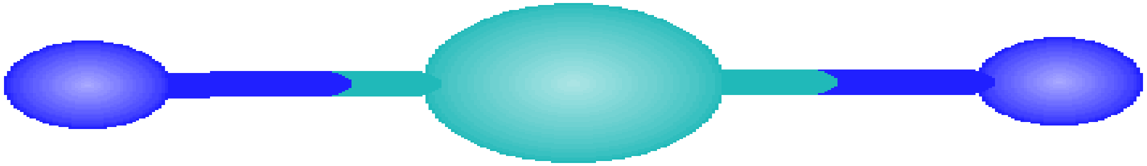
$$Cu^{2+}{}_{(aq)} + 4NH_{3(aq)} \overset{K_{st}}{\Leftrightarrow} Cu(H_2O)_2(NH_3)_4{}^{+2}{}_{(aq)}$$

$$K_{st} = [Cu(H_2O)_2(NH_3)_4{}^{+2}] / ([Cu^{2+}{}_{(aq)}][NH_3]^4) = 10^{12} \text{ at } 25^oC$$


2–La
Ce(arene-diNOx)$_2$
2–Pr
2–Y
2–Tb
1
0.5
0
-0.5
-1
-1.5
-2
Potential (V) vs. Fc/Fc$^+$
Chemical oxidation
tBu
tBu
tBu
tBu
N
N
N
N
O
O
O
O
Tb

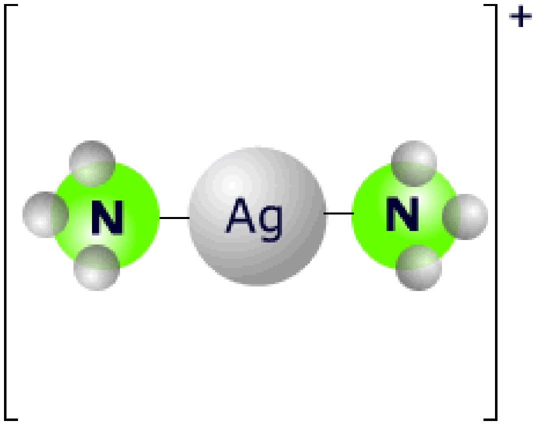
Common Geometries of Complexes

Coordination Number	Geometry
2	Linear



Example: $[Ag(NH_3)_2]^+$

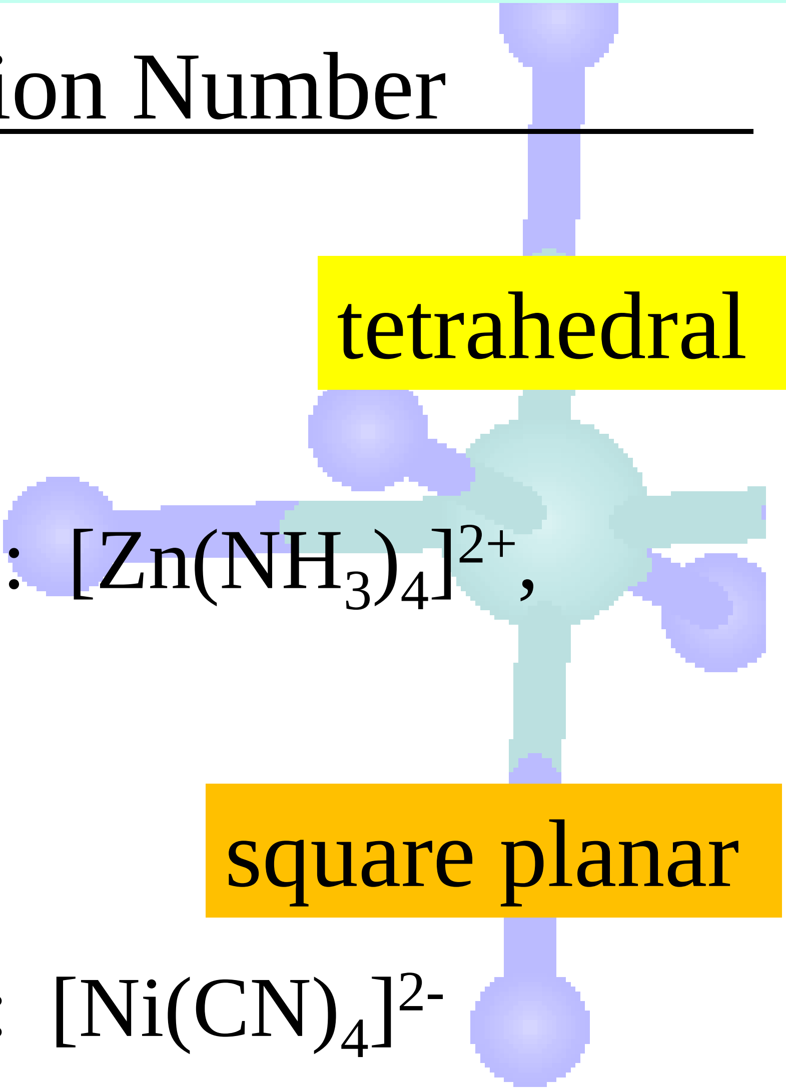
diammine silver (I) ion



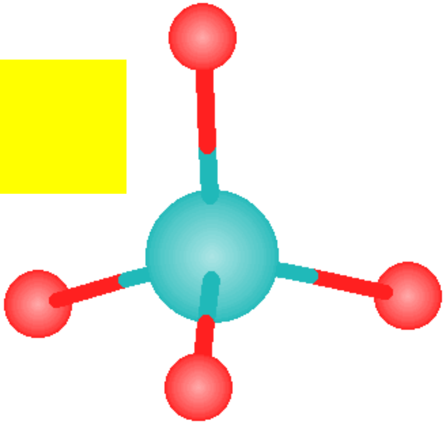
Common Geometries of Complexes

Coordination Number | Geometry

4

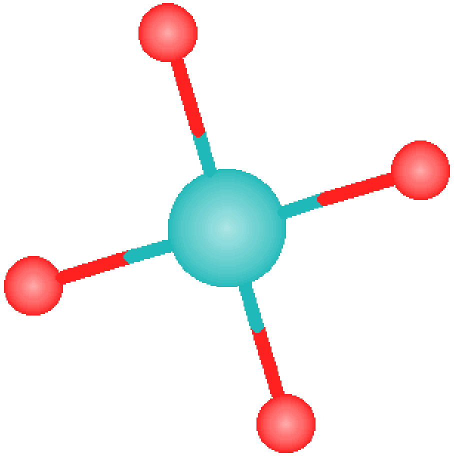


tetrahedral



Examples: $[Zn(NH_3)_4]^{2+}$, $[FeCl_4]^-$

square planar

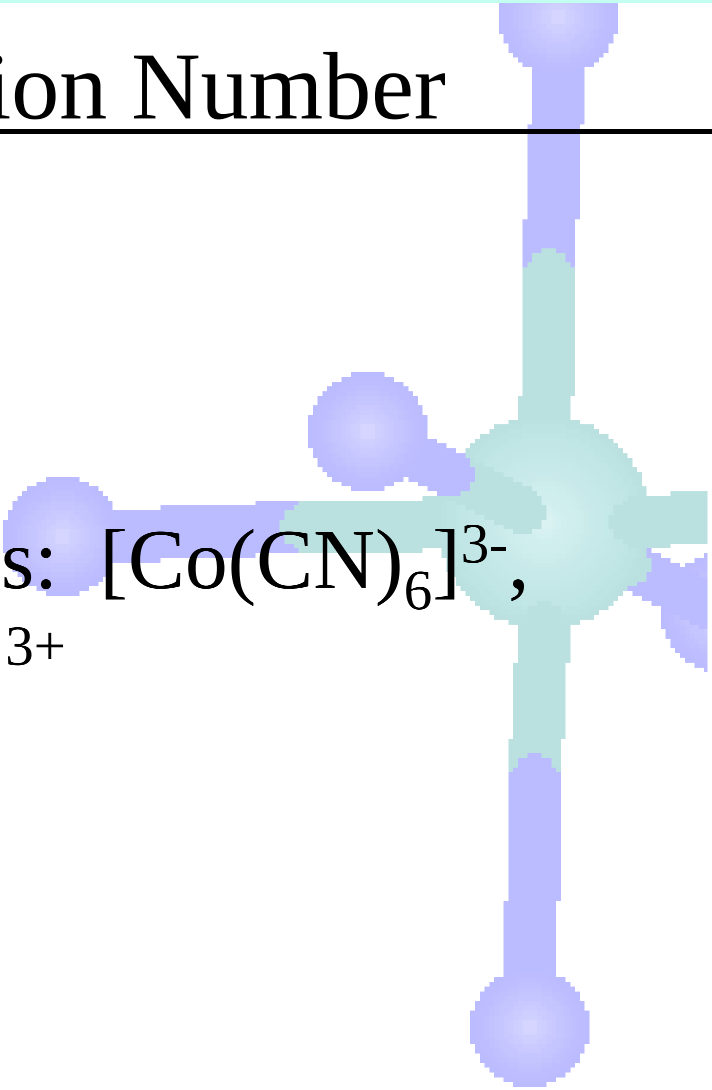


Example: $[Ni(CN)_4]^{2-}$

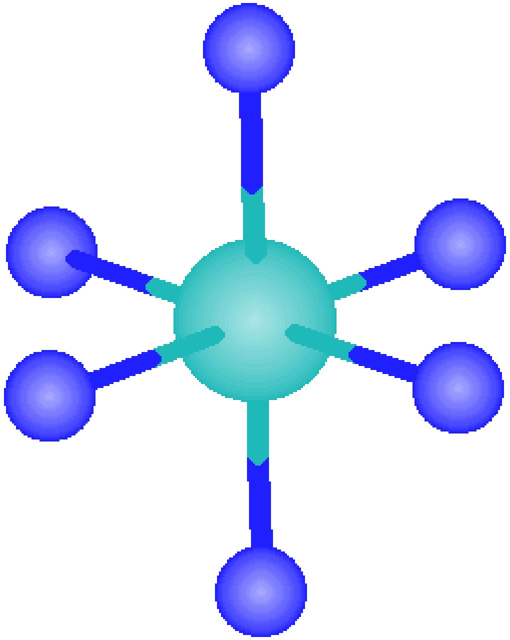
Common Geometries of Complexes

Coordination Number   Geometry

6

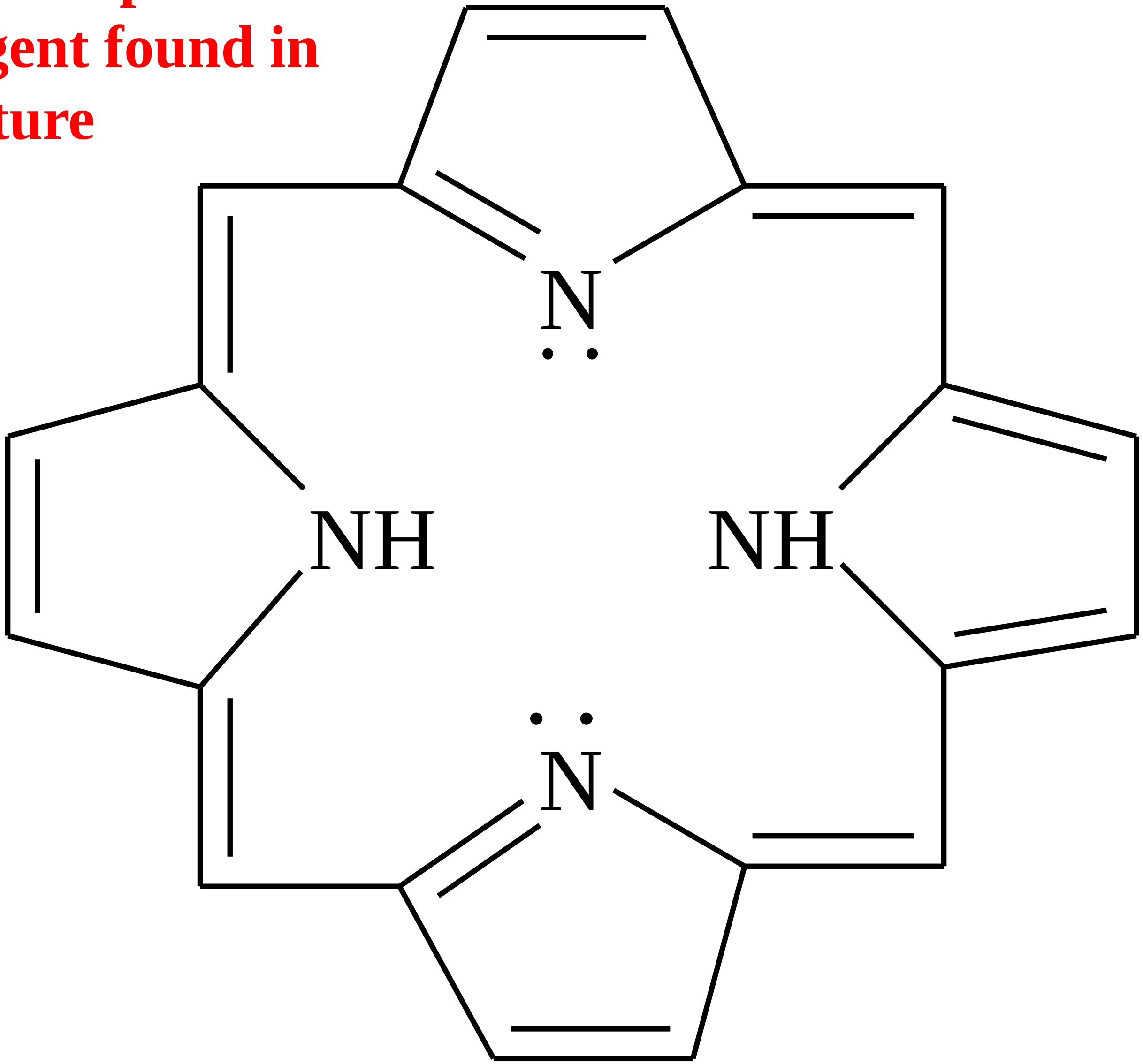


Examples: $[Co(CN)_6]^{3-}$, $[Fe(en)_3]^{3+}$

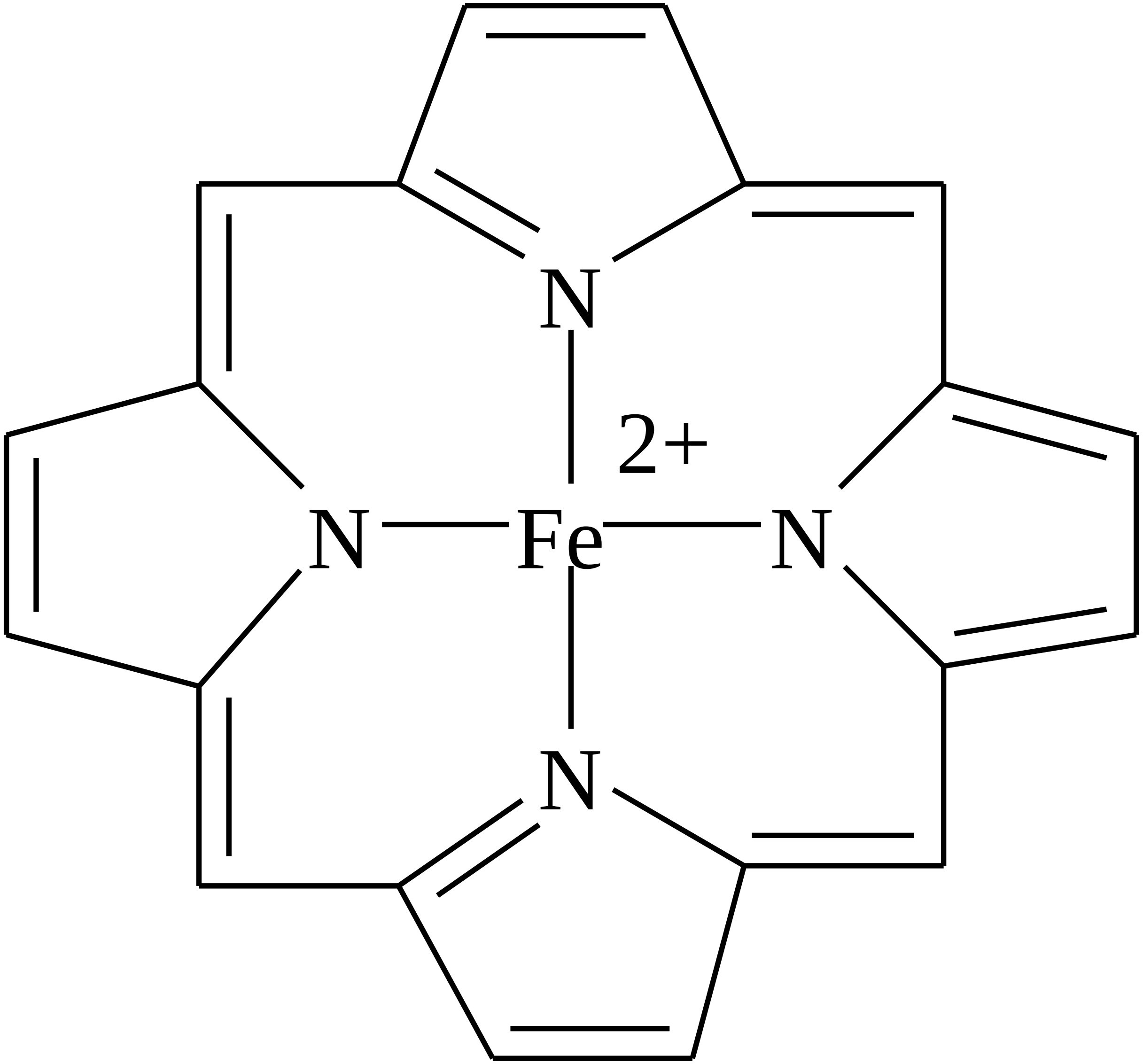


octahedral

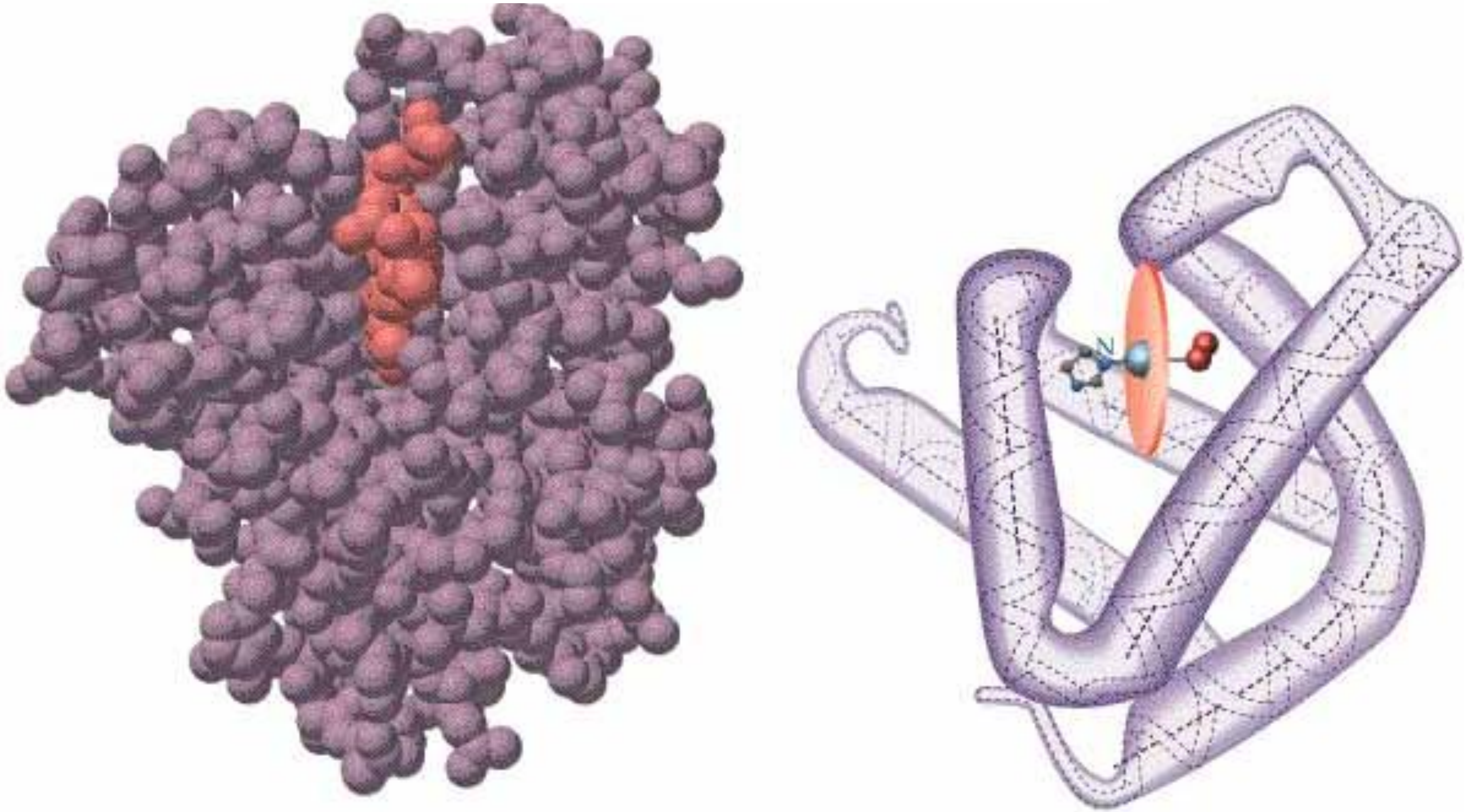
Porphine, an important chelating agent found in nature



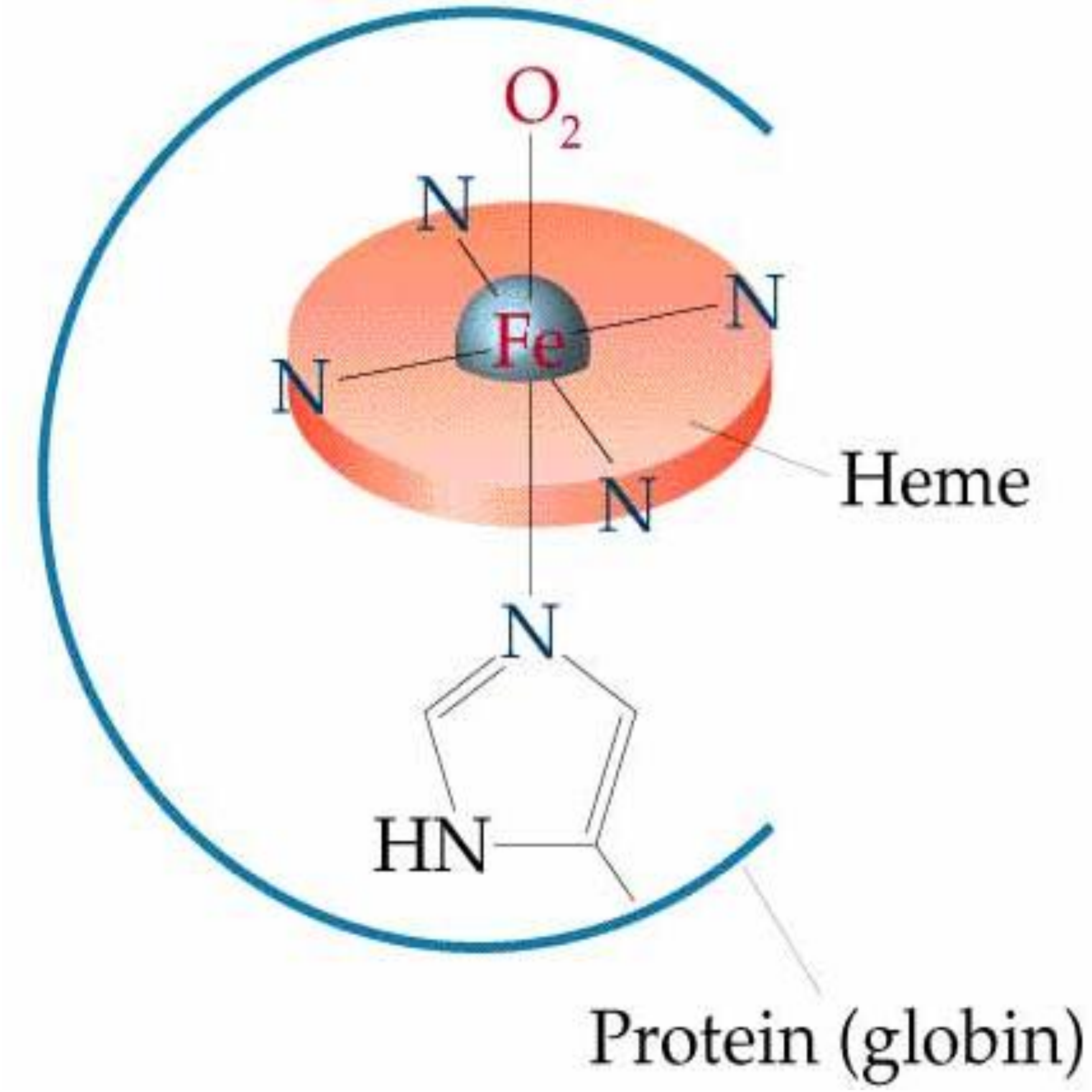
Metalloporphyrin



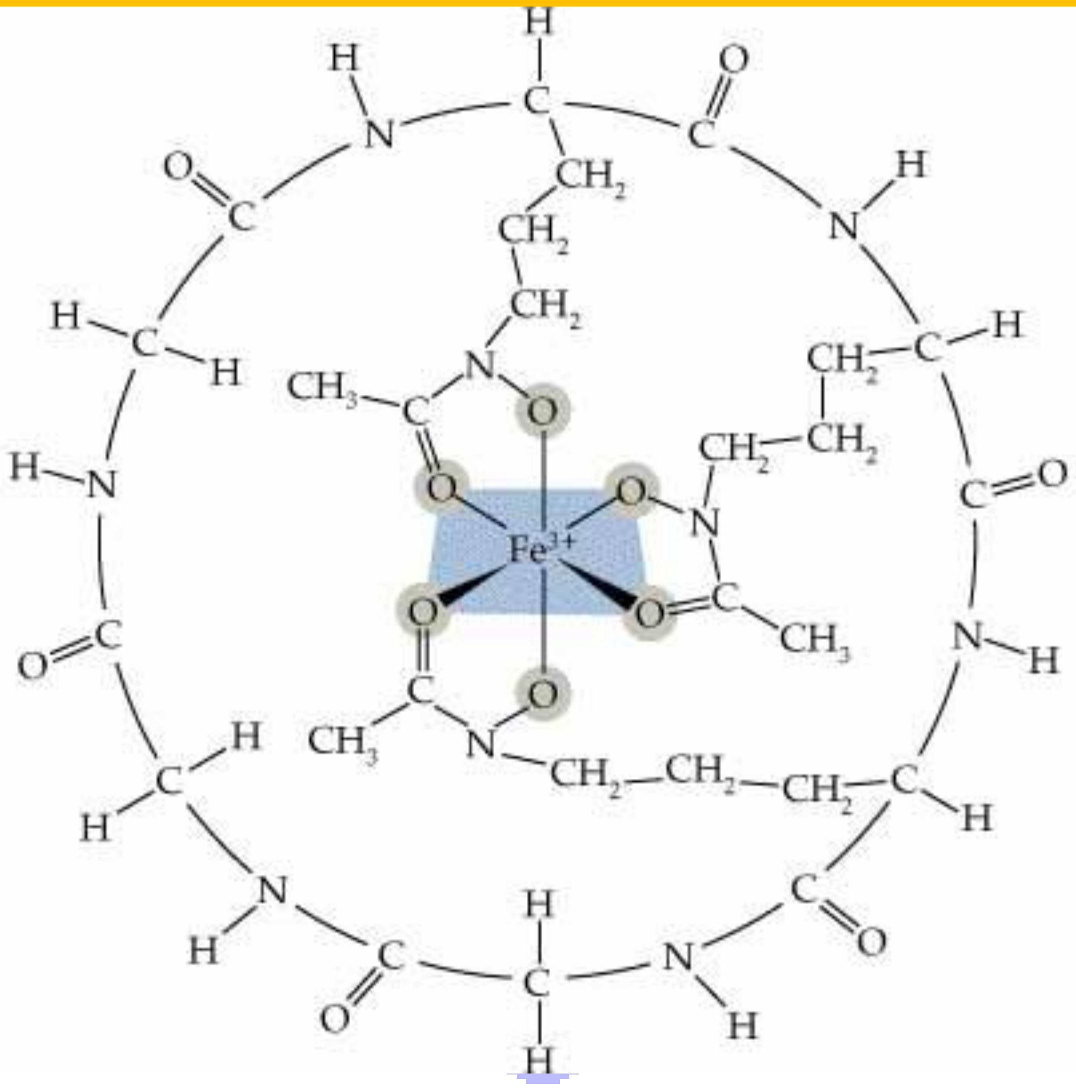
Myoglobin, a protein that stores O_2 in cells

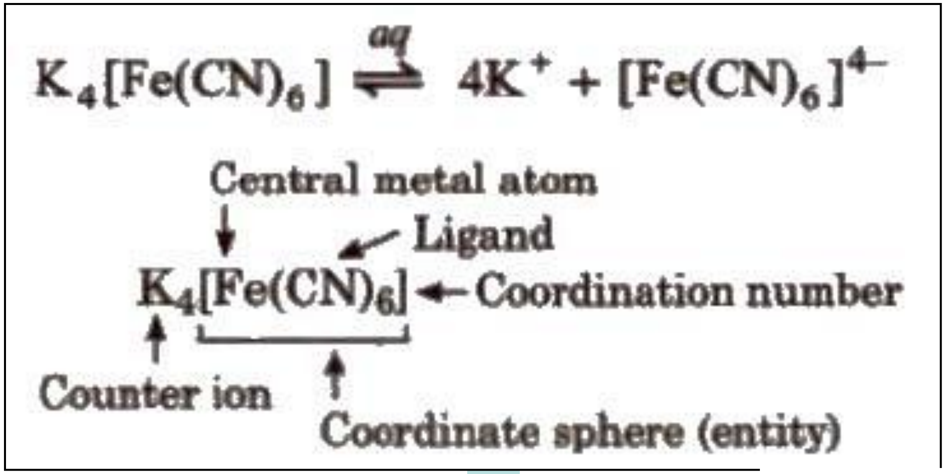


Coordination Environment of Fe^{2+} in Oxymyoglobin and Oxyhemoglobin

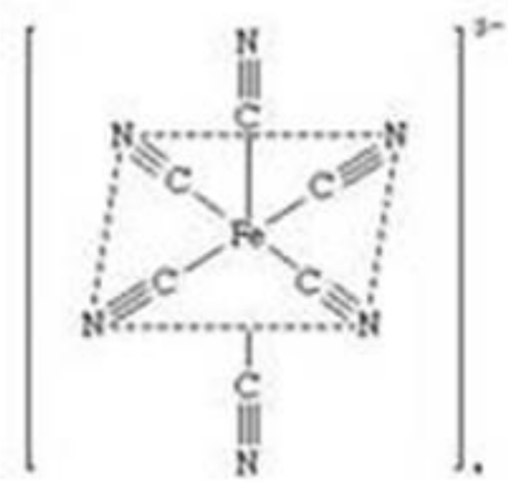


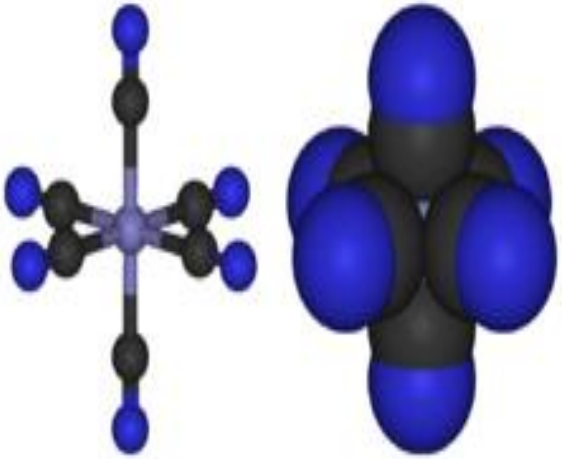
Ferrichrome (Involved in Fe transport in bacteria)



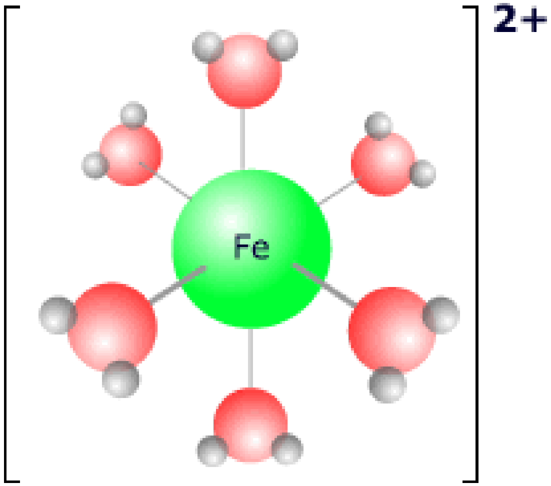


$$K_4[Fe(CN)_6] \xrightleftharpoons{aq} 4K^+ + [Fe(CN)_6]^{4-}$$





hexaaqua iron (II) ion

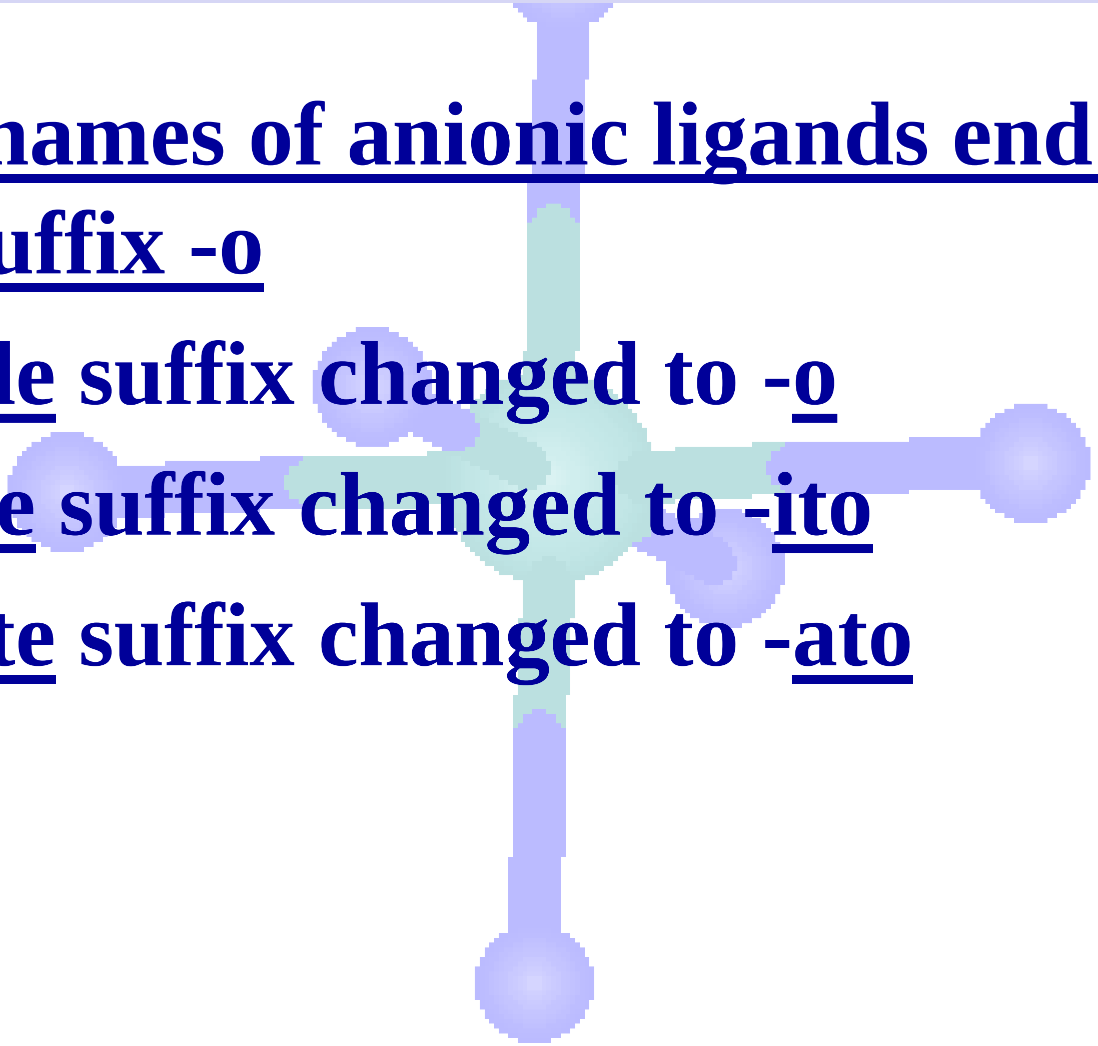


Nomenclature of Coordination Compounds: IUPAC Rules

- **The COUNTER BALANCING CATION** is named before the anion-***IF*** the **COMPLEX HAS A NET OF NEGATIVE CHARGE**
- When naming a complex:
  - **Ligands** are named **first**
    - alphabetical order in case of more ligands
  - **Metal atom/ion** is **named last**
    - oxidation state given in Roman numerals follows in parentheses $\mathbf{K_3[Fe(CN)_6]}$

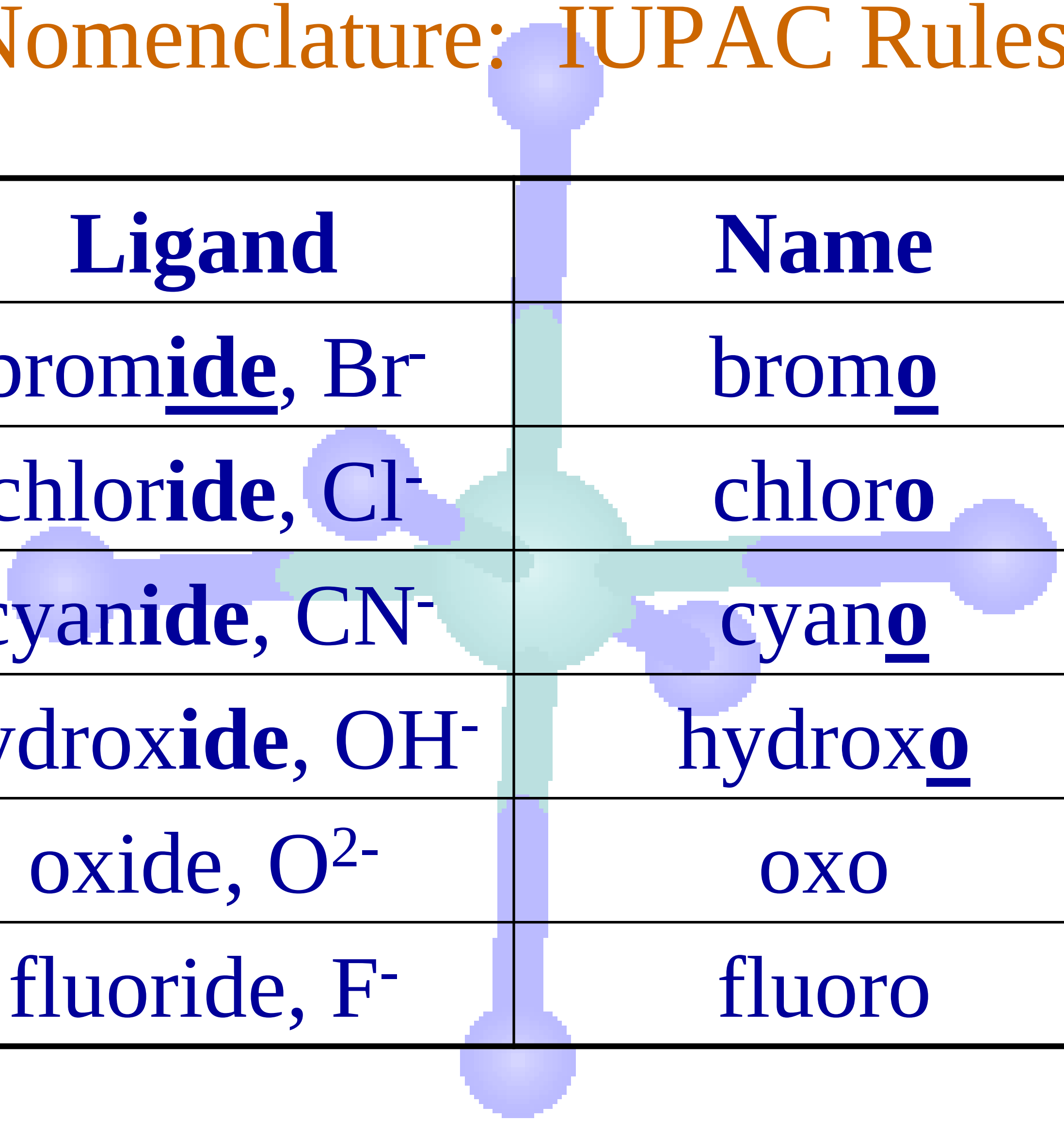
---Potassium hexacyanoferrate III

Nomenclature: IUPAC Rules



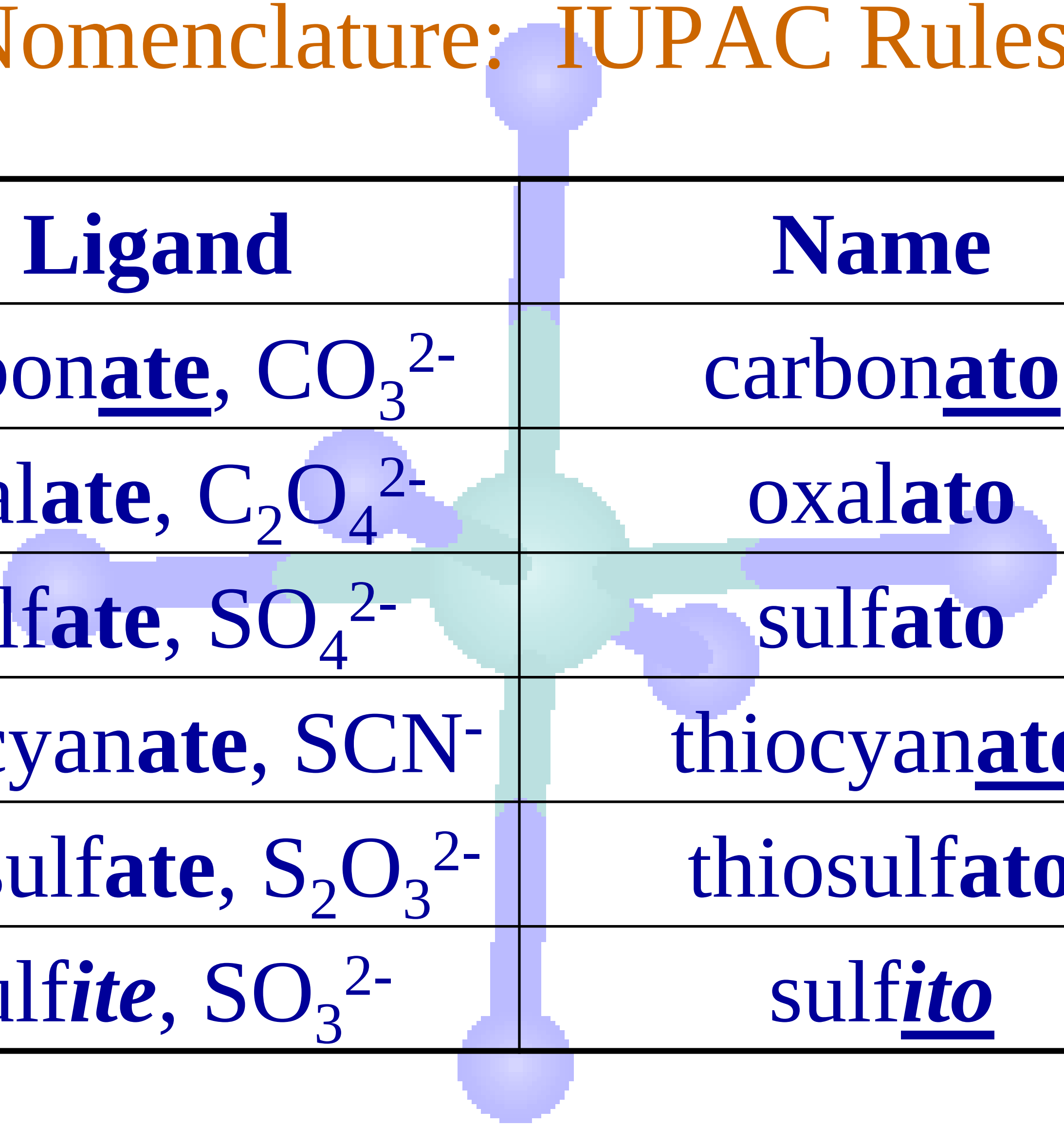
- The names of anionic ligands end with the suffix -o
  - -ide suffix changed to -o
  - -ite suffix changed to -ito
  - -ate suffix changed to -ato

Nomenclature: IUPAC Rules



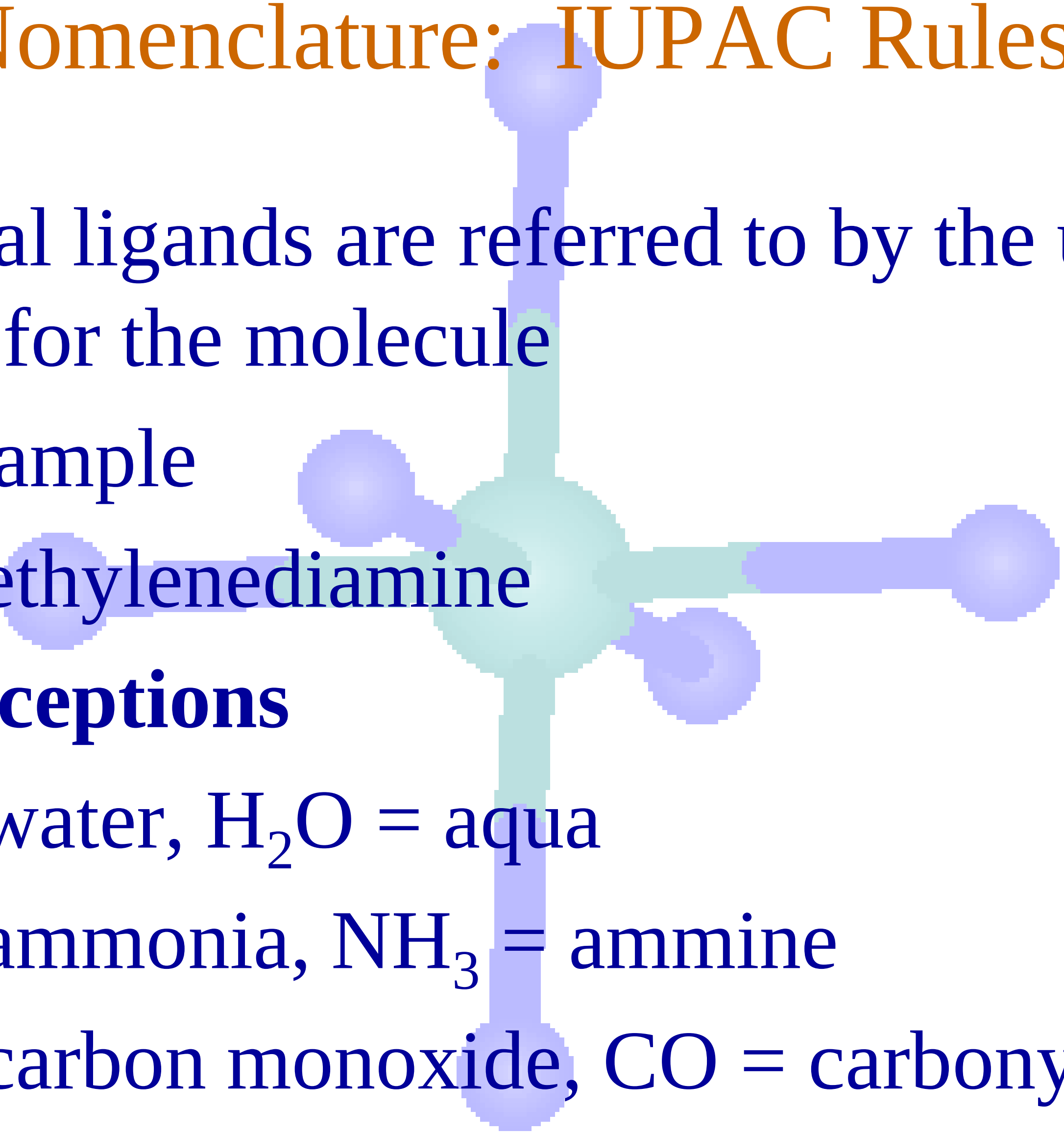
Ligand	**Name**
brom**ide**, Br^-	brom**o**
chlor**ide**, Cl^-	chlor**o**
cyan**ide**, CN^-	cyan**o**
hydrox**ide**, OH^-	hydrox**o**
oxide, O^{2-}	oxo
fluoride, F^-	fluoro

Nomenclature: IUPAC Rules



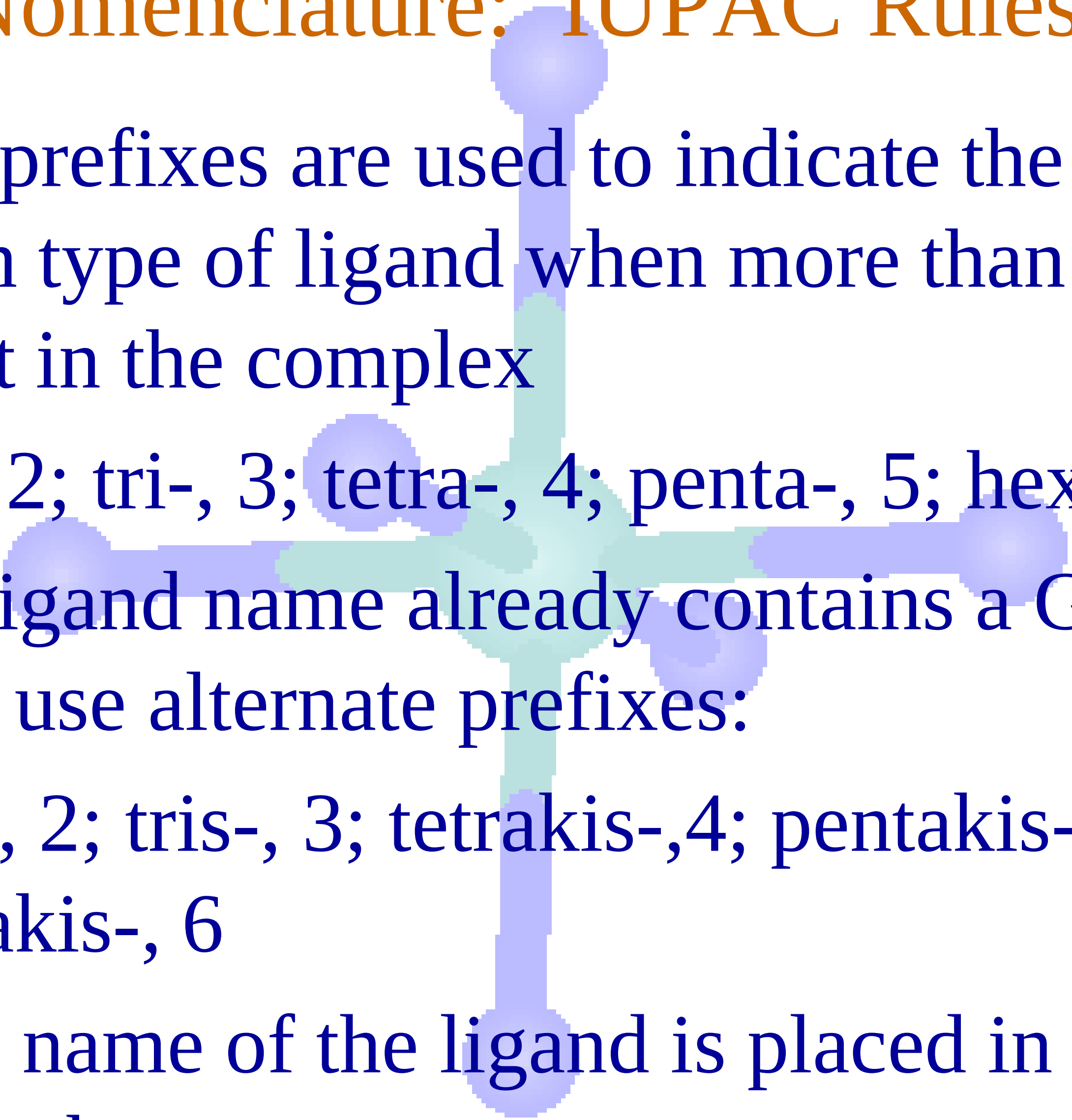
Ligand	**Name**
carbon**ate**, CO_3^{2-}	carbon**ato**
oxal**ate**, $C_2O_4^{2-}$	oxal**ato**
sulf**ate**, SO_4^{2-}	sulf**ato**
thiocyan**ate**, SCN^-	thiocyan**ato**
thiosulf**ate**, $S_2O_3^{2-}$	thiosulf**ato**
Sulf***ite***, SO_3^{2-}	sulf***ito***

Nomenclature: IUPAC Rules



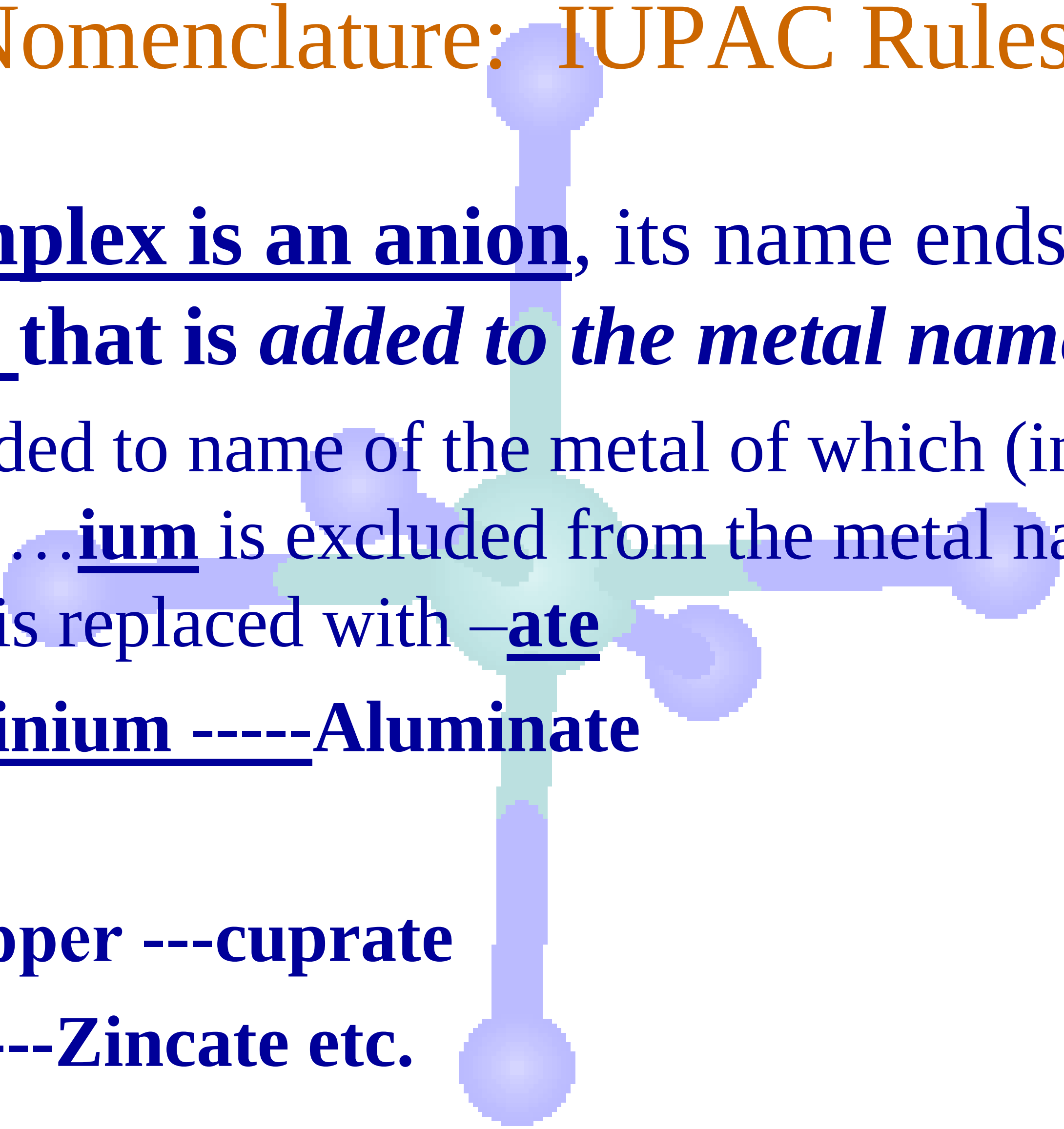
- Neutral ligands are referred to by the usual name for the molecule
  - Example
    - ethylenediamine
  - **Exceptions**
    - water, H_2O = aqua
    - ammonia, NH_3 = ammine
    - carbon monoxide, CO = carbonyl

Nomenclature: IUPAC Rules



- Greek prefixes are used to indicate the number of each type of ligand when more than one is present in the complex
  - di-, 2; tri-, 3; tetra-, 4; penta-, 5; hexa-, 6
- If the ligand name already contains a Greek prefix, use alternate prefixes:
  - bis-, 2; tris-, 3; tetrakis-,4; pentakis-, 5; hexakis-, 6
  - The name of the ligand is placed in parentheses

Nomenclature: IUPAC Rules

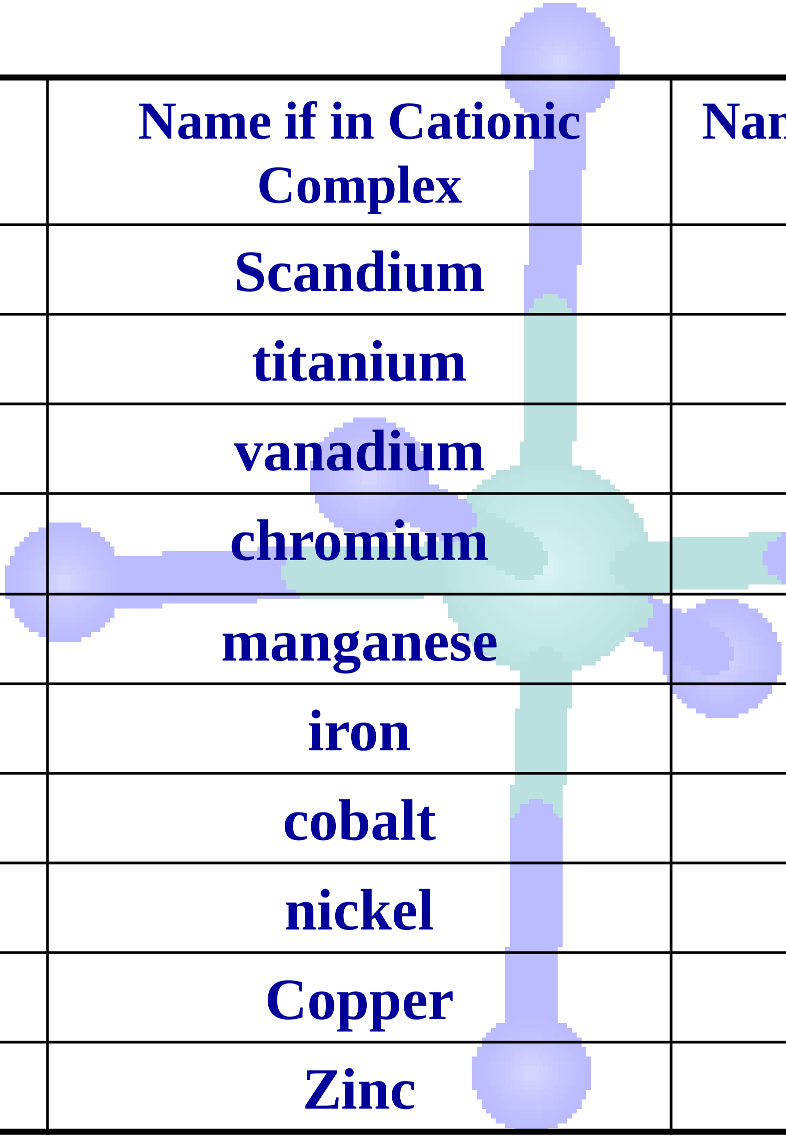


- **If a complex is an anion**, its name ends with the **–ate that is *added to the metal name***
  - appended to name of the metal of which (in many cases) …**ium** is excluded from the metal name and it is replaced with –**ate**
  - **Aluminium -----Aluminate**

…But

  - **…Copper ---cuprate**
  - **Zinc----Zincate etc.**

Nomenclature: IUPAC Rules



Transition Metal	Name if in Cationic Complex	Name if in Anionic Complex
Sc	Scandium	Scandate
Ti	titanium	titanate
V	vanadium	vanadate
Cr	chromium	chromate
Mn	manganese	manganate
Fe	iron	ferrate
Co	cobalt	cobaltate
Ni	nickel	nickelate
Cu	Copper	cuprate
Zn	Zinc	zincate

Examples of complexes:

Name the following coordinative complexes

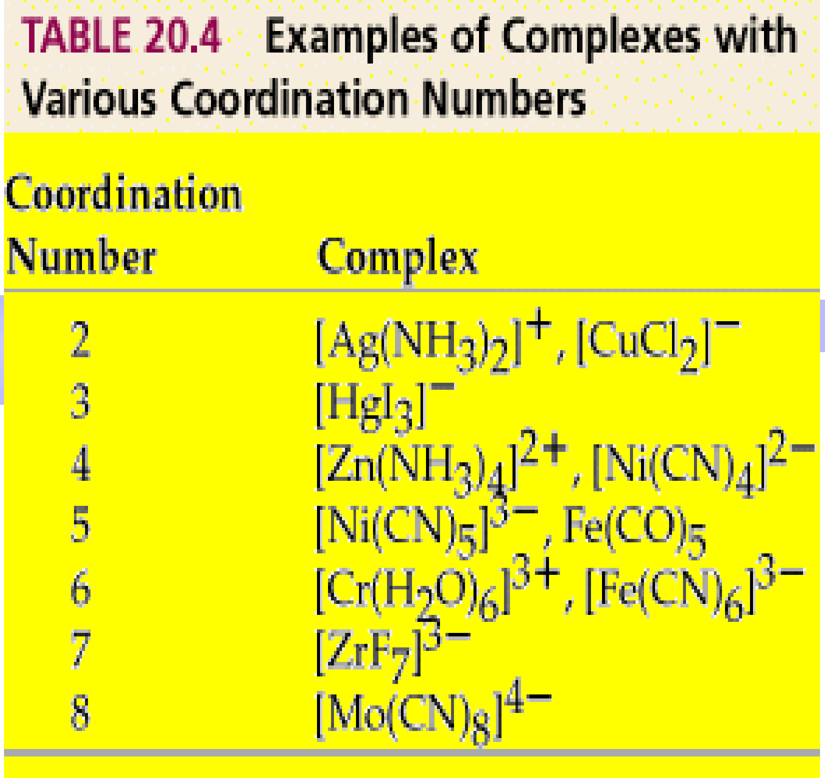


TABLE 20.4 Examples of Complexes with Various Coordination Numbers

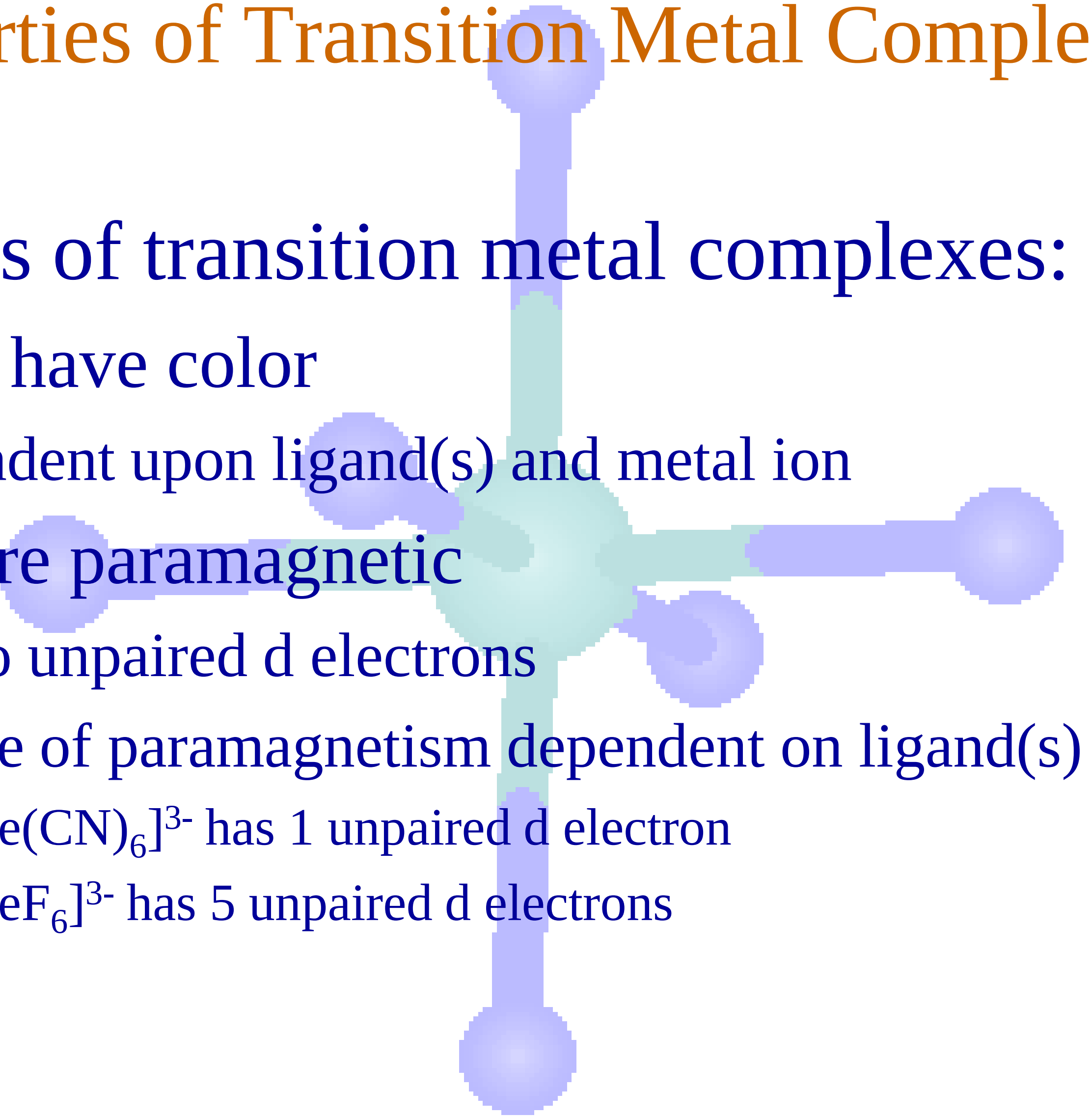
Coordination Number	Complex
2	$[Ag(NH_3)_2]^+$, $[CuCl_2]^-$
3	$[HgI_3]^-$
4	$[Zn(NH_3)_4]^{2+}$, $[Ni(CN)_4]^{2-}$
5	$[Ni(CN)_5]^{3-}$, $Fe(CO)_5$
6	$[Cr(H_2O)_6]^{3+}$, $[Fe(CN)_6]^{3-}$
7	$[ZrF_7]^{3-}$
8	$[Mo(CN)_8]^{4-}$

Examples of complexes:

Name the following coordinative complexes

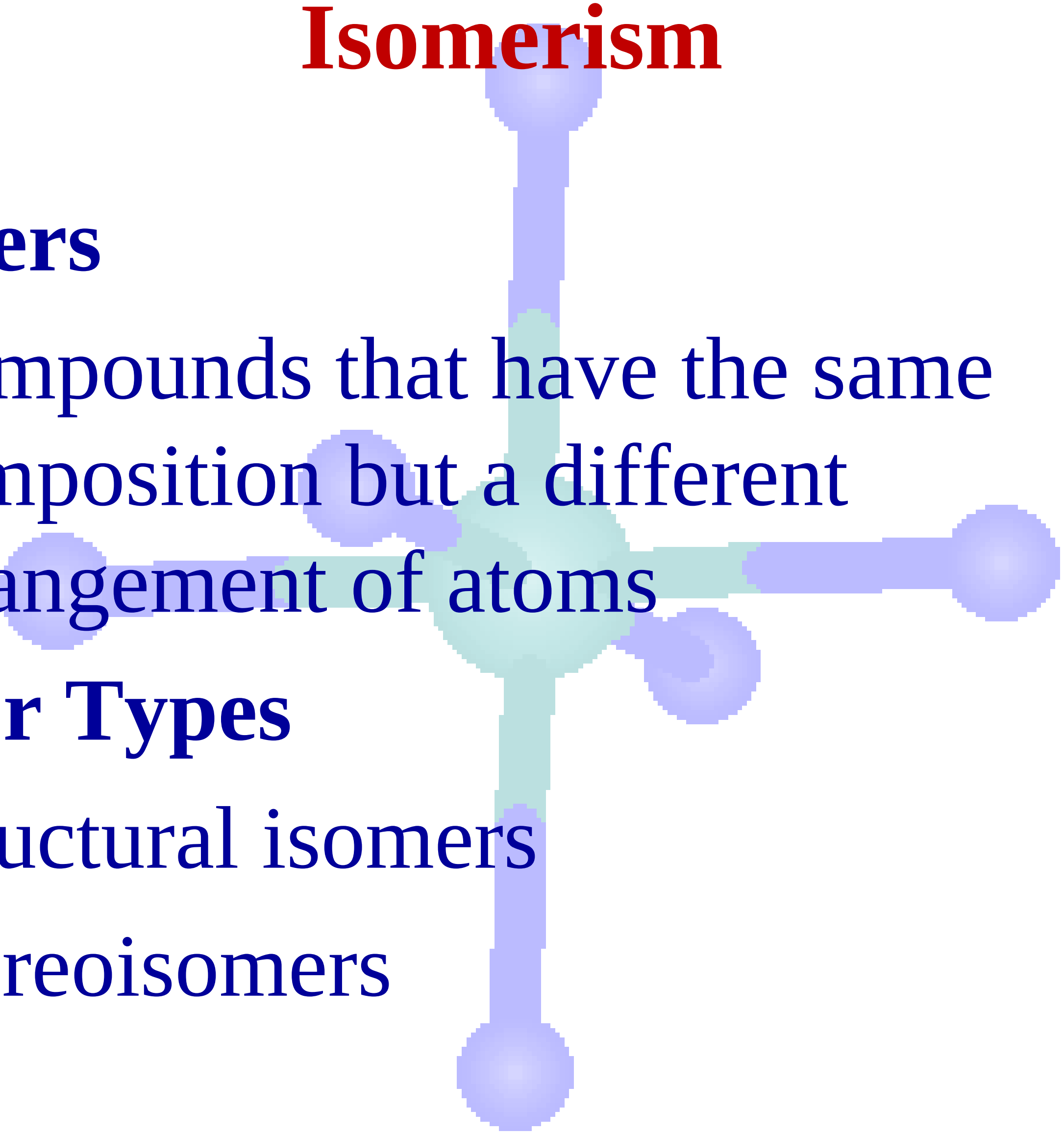
Compound formulae	Complex ion formulae	Showing oxidation state
$[\mathrm{Co(NH_3)_6}]\mathrm{Cl_3}$	$[\mathrm{Co(NH_3)_6}]^{3+}$	$[\mathrm{Co^{III}(NH_3)_6}]^{3+}$
$[\mathrm{CoCl(NH_3)_5}]\mathrm{Cl_2}$	$[\mathrm{CoCl(NH_3)_5}]^{2+}$	$[\mathrm{Co^{III}Cl(NH_3)_5}]^{2+}$
$[\mathrm{CoCl(NO_2)(NH_3)_4}]\mathrm{Cl}$	$[\mathrm{CoCl(NO_2)(NH_3)_4}]^{+}$	$[\mathrm{Co^{III}Cl(NO_2)(NH_3)_4}]^{+}$
$[\mathrm{PtCl(NH_2CH_3)(NH_3)_2}]\mathrm{Cl}$	$[\mathrm{PtCl(NH_2CH_3)(NH_3)_2}]^{+}$	$[\mathrm{Pt^{II}Cl(NH_2CH_3)(NH_3)_2}]^{+}$
$[\mathrm{CuCl_2\{O{=}C(NH_2)_2\}_2}]$		$[\mathrm{Cu^{II}Cl_2\{O{=}C(NH_2)_2\}_2}]$
$\mathrm{K_2}[\mathrm{PdCl_4}]$	$[\mathrm{PdCl_4}]^{2-}$	$[\mathrm{Pd^{II}Cl_4}]^{2-}$
$\mathrm{K_2}[\mathrm{OsCl_5N}]$	$[\mathrm{OsCl_5N}]^{2-}$	$[\mathrm{Os^{VI}Cl_5N}]^{2-}$
$\mathrm{Na}[\mathrm{PtBrCl(NO_2)(NH_3)}]$	$[\mathrm{PtBrCl(NO_2)(NH_3)}]^{-}$	$[\mathrm{Pt^{II}BrCl(NO_2)(NH_3)}]^{-}$
$[\mathrm{Co(en)_3}]\mathrm{Cl_3}$	$[\mathrm{Co(en)_3}]^{3+}$	$[\mathrm{Co^{III}(en)_3}]^{3+}$
$\mathrm{Na_2}[\mathrm{Fe(CO)_4}]$	$[\mathrm{Fe(CO)_4}]^{2-}$	$[\mathrm{Fe^{-II}(CO)_4}]^{2-}$
$[\mathrm{Co}(\eta^5\text{-}\mathrm{C_5H_5})_2]\mathrm{Cl}$	$[\mathrm{Co}(\eta^5\text{-}\mathrm{C_5H_5})_2]^{+}$	$[\mathrm{Co^{II}}(\eta^5\text{-}\mathrm{C_5H_5})_2]^{+}$

Properties of Transition Metal Complexes



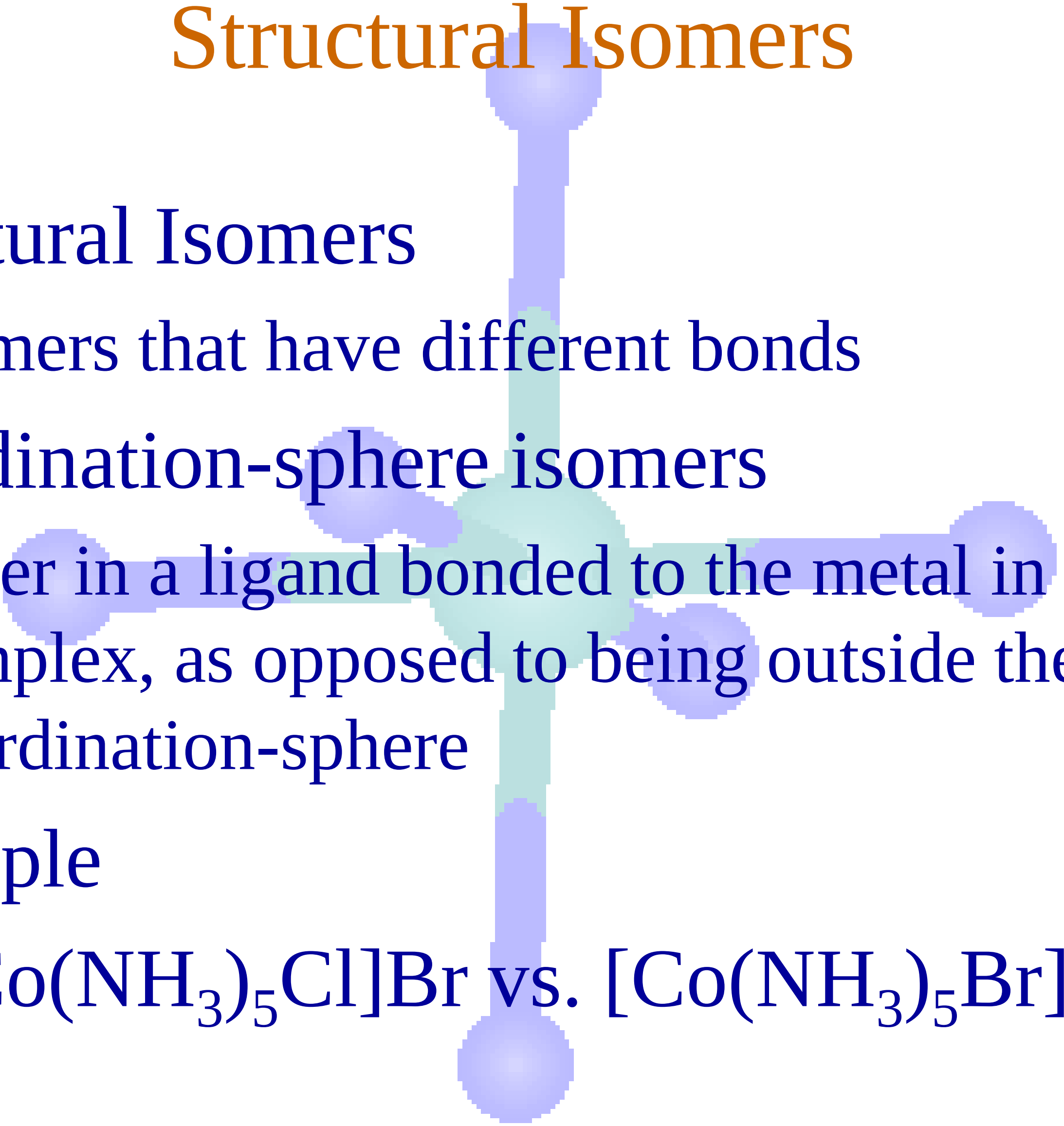
- Properties of transition metal complexes:
  - usually have color
    - dependent upon ligand(s) and metal ion
  - many are paramagnetic
    - due to unpaired d electrons
    - degree of paramagnetism dependent on ligand(s)
      - $[Fe(CN)_6]^{3-}$ has 1 unpaired d electron
      - $[FeF_6]^{3-}$ has 5 unpaired d electrons

Isomerism



- **Isomers**
  - compounds that have the same composition but a different arrangement of atoms
- **Major Types**
  - structural isomers
  - stereoisomers

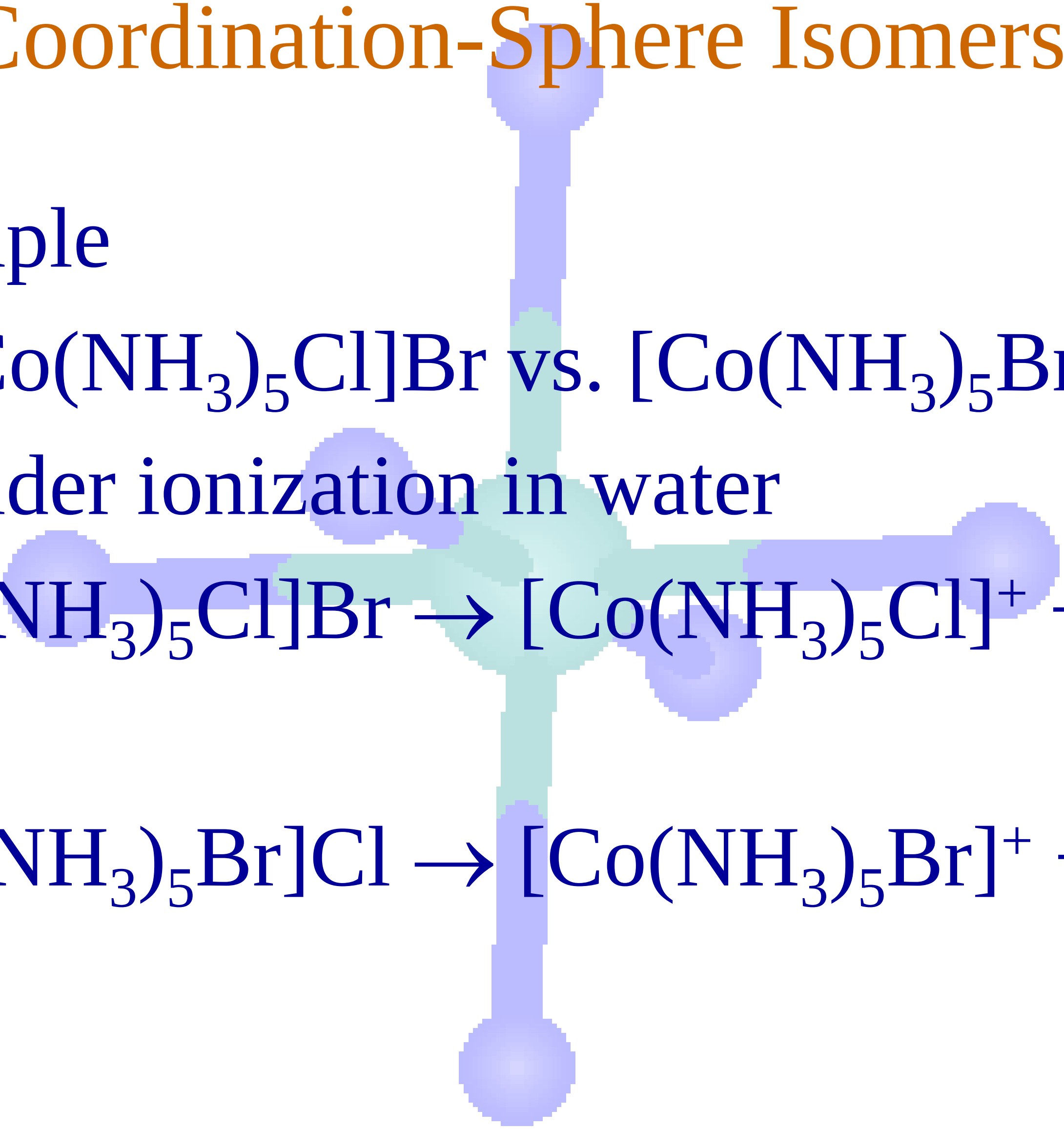
Structural Isomers



- Structural Isomers
  - isomers that have different bonds
- Coordination-sphere isomers
  - differ in a ligand bonded to the metal in the complex, as opposed to being outside the coordination-sphere
- Example

$$[Co(NH_3)_5Cl]Br \text{ vs. } [Co(NH_3)_5Br]Cl$$

Coordination-Sphere Isomers



- Example

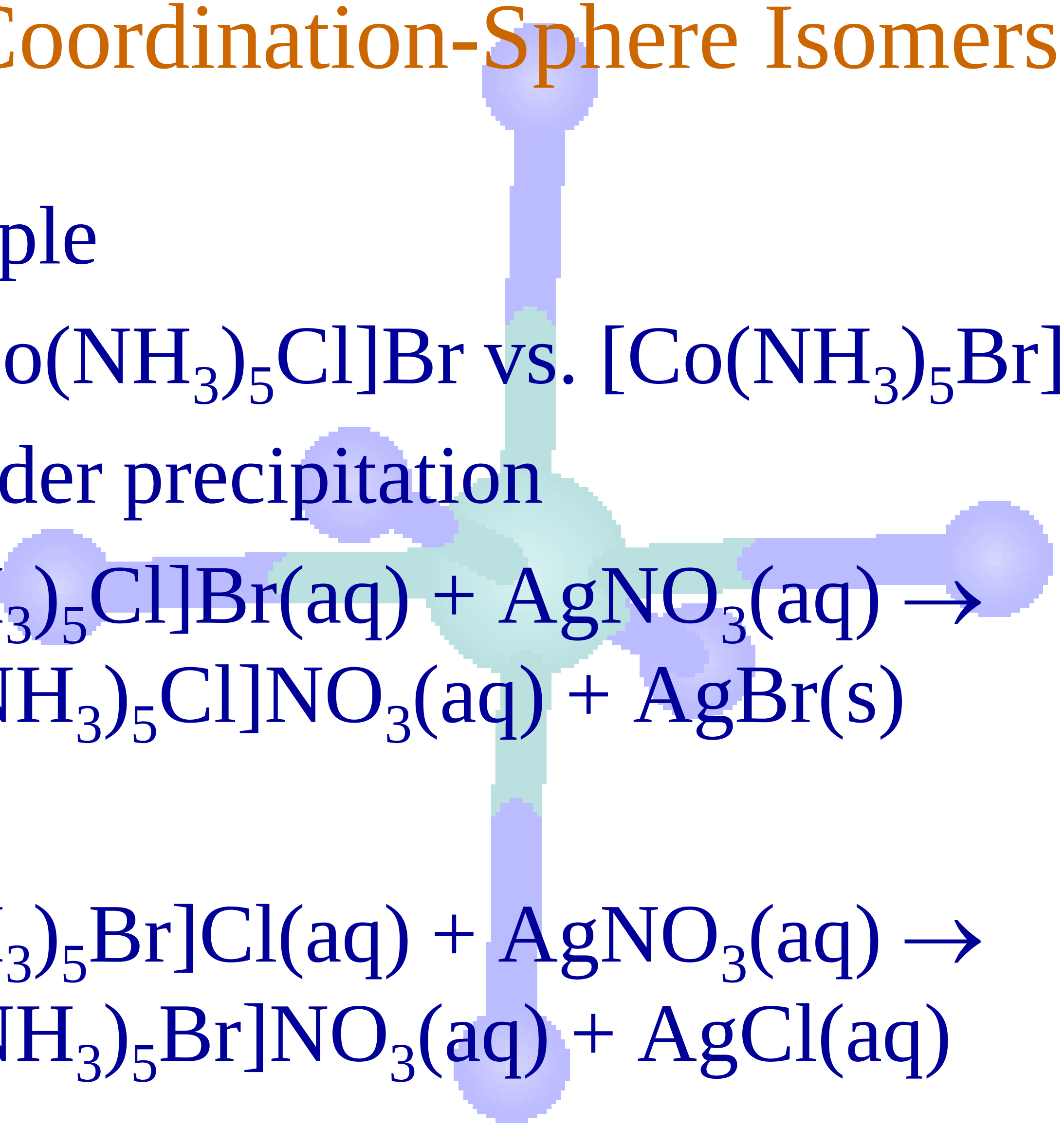
  $[Co(NH_3)_5Cl]Br$ vs. $[Co(NH_3)_5Br]Cl$

- Consider ionization in water

$[Co(NH_3)_5Cl]Br \rightarrow [Co(NH_3)_5Cl]^+ + Br^-$

$[Co(NH_3)_5Br]Cl \rightarrow [Co(NH_3)_5Br]^+ + Cl^-$

Coordination-Sphere Isomers



- Example

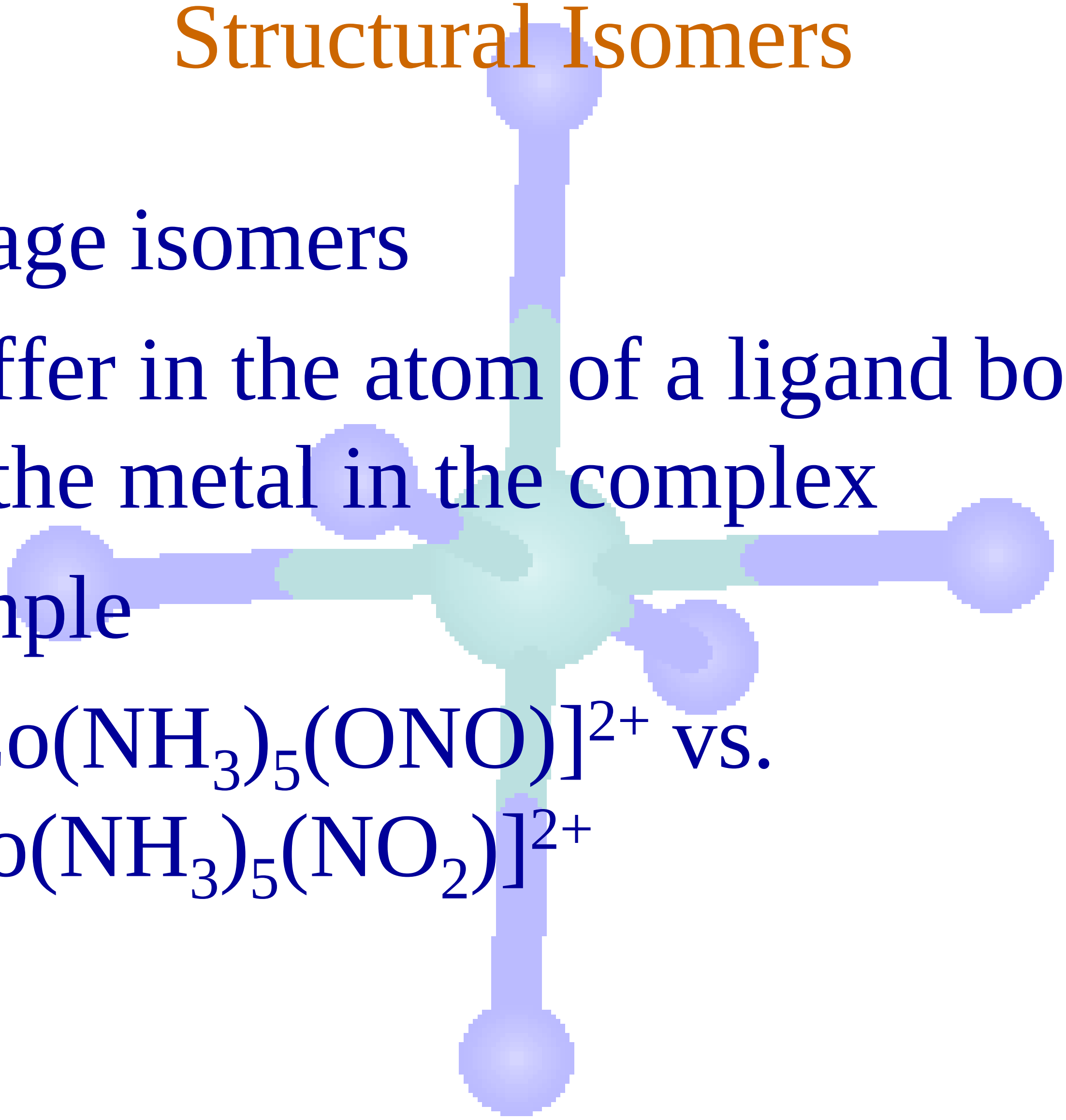
  $[Co(NH_3)_5Cl]Br$ vs. $[Co(NH_3)_5Br]Cl$

- Consider precipitation

$[Co(NH_3)_5Cl]Br(aq) + AgNO_3(aq) \rightarrow$
$[Co(NH_3)_5Cl]NO_3(aq) + AgBr(s)$

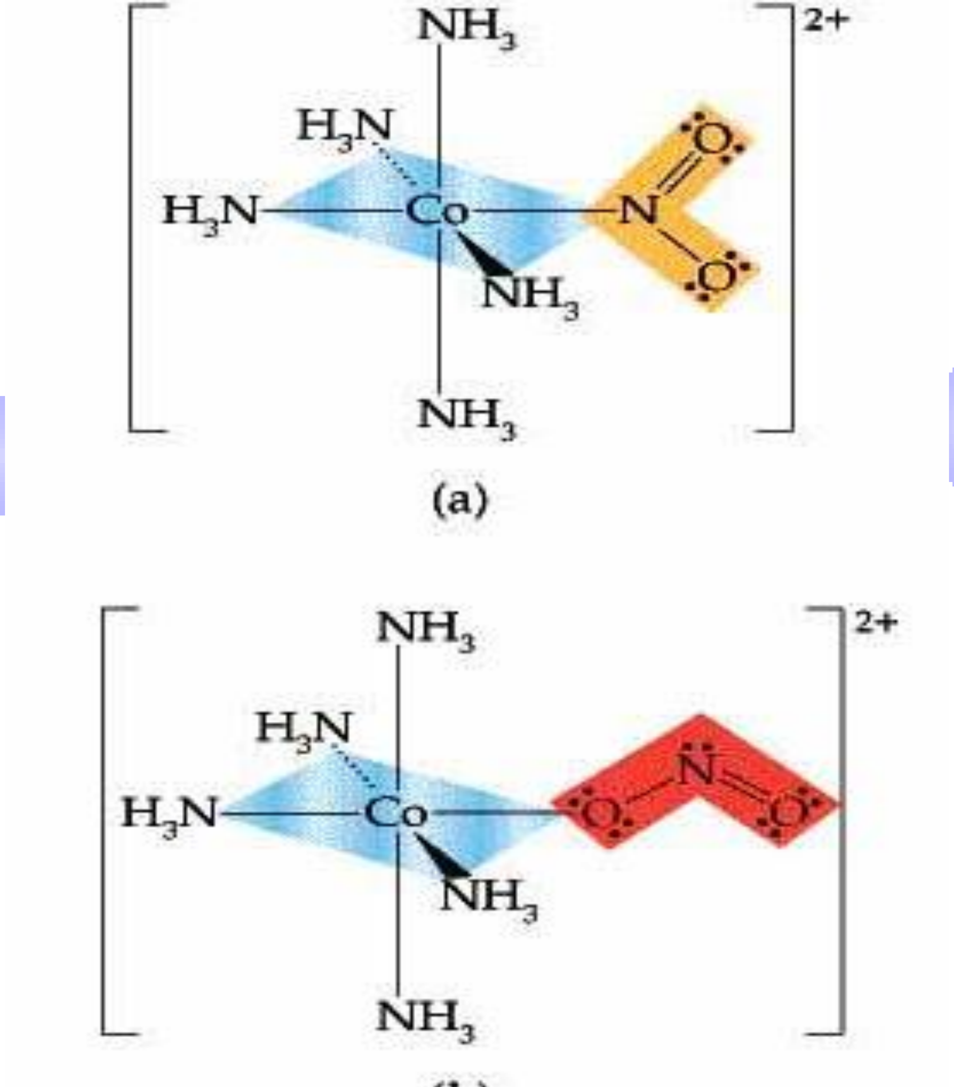
$[Co(NH_3)_5Br]Cl(aq) + AgNO_3(aq) \rightarrow$
$[Co(NH_3)_5Br]NO_3(aq) + AgCl(aq)$

Structural Isomers



- Linkage isomers
  - differ in the atom of a ligand bonded to the metal in the complex
- Example
  - $[Co(NH_3)_5(ONO)]^{2+}$ vs. $[Co(NH_3)_5(NO_2)]^{2+}$

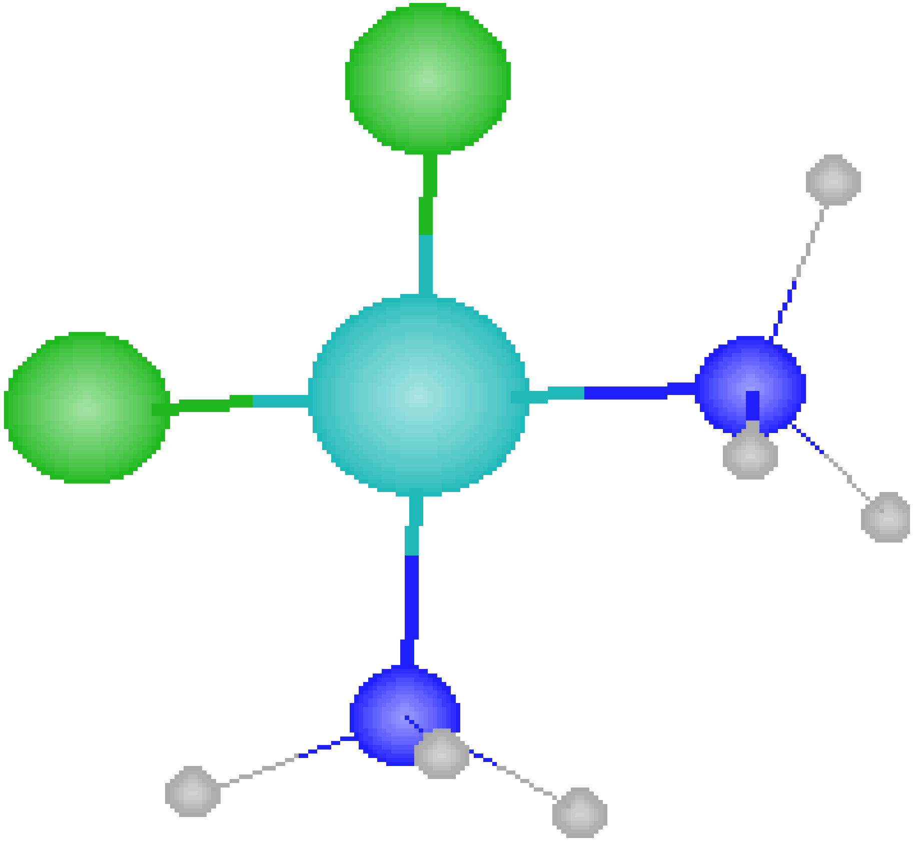
Linkage Isomers



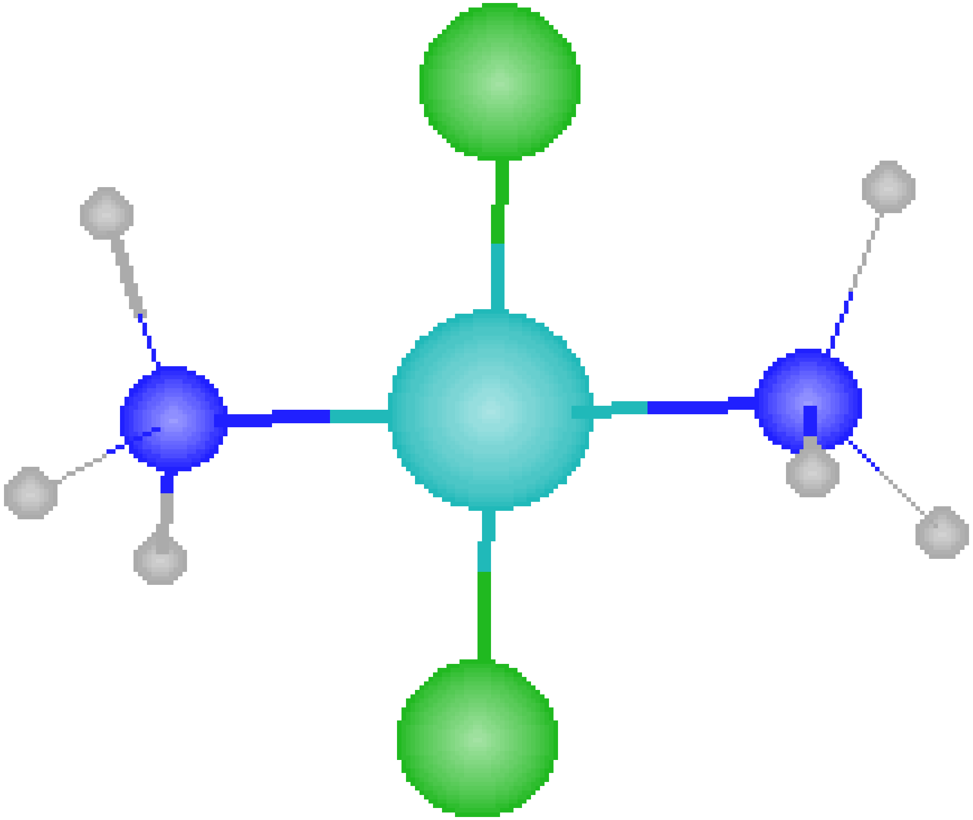
(a)

(b)

Geometric Isomers



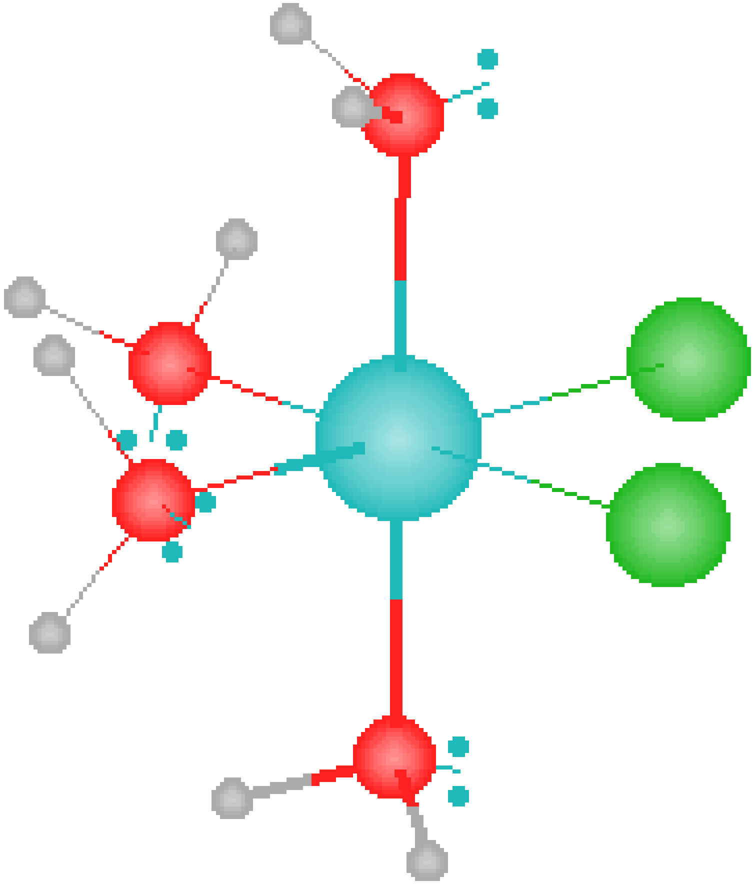
cis isomer



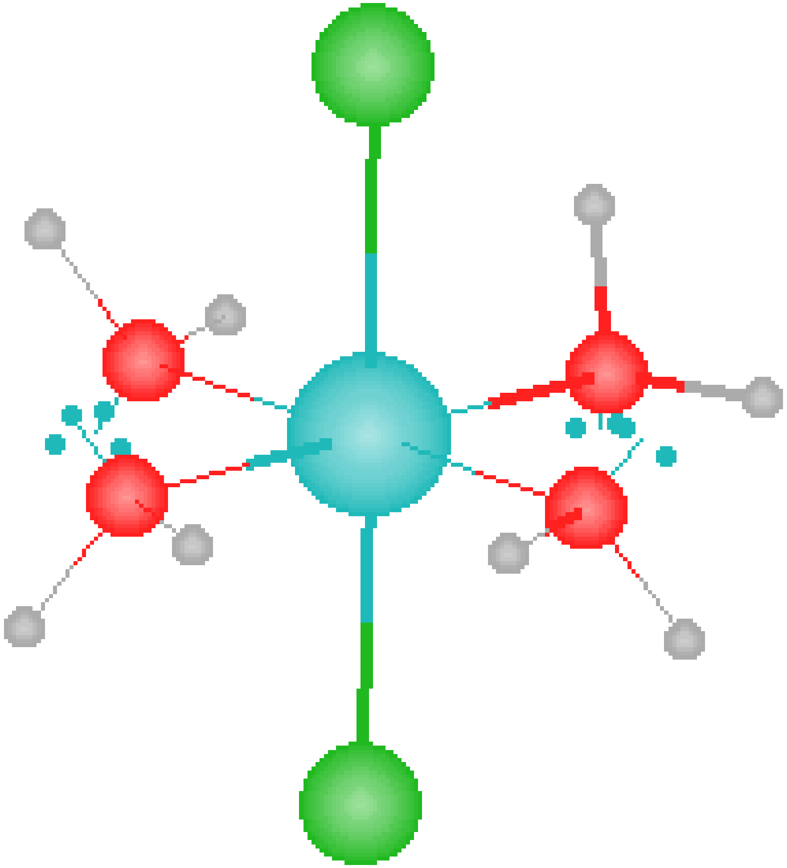
trans isomer

$Pt(NH_3)_2Cl_2$

Geometric Isomers

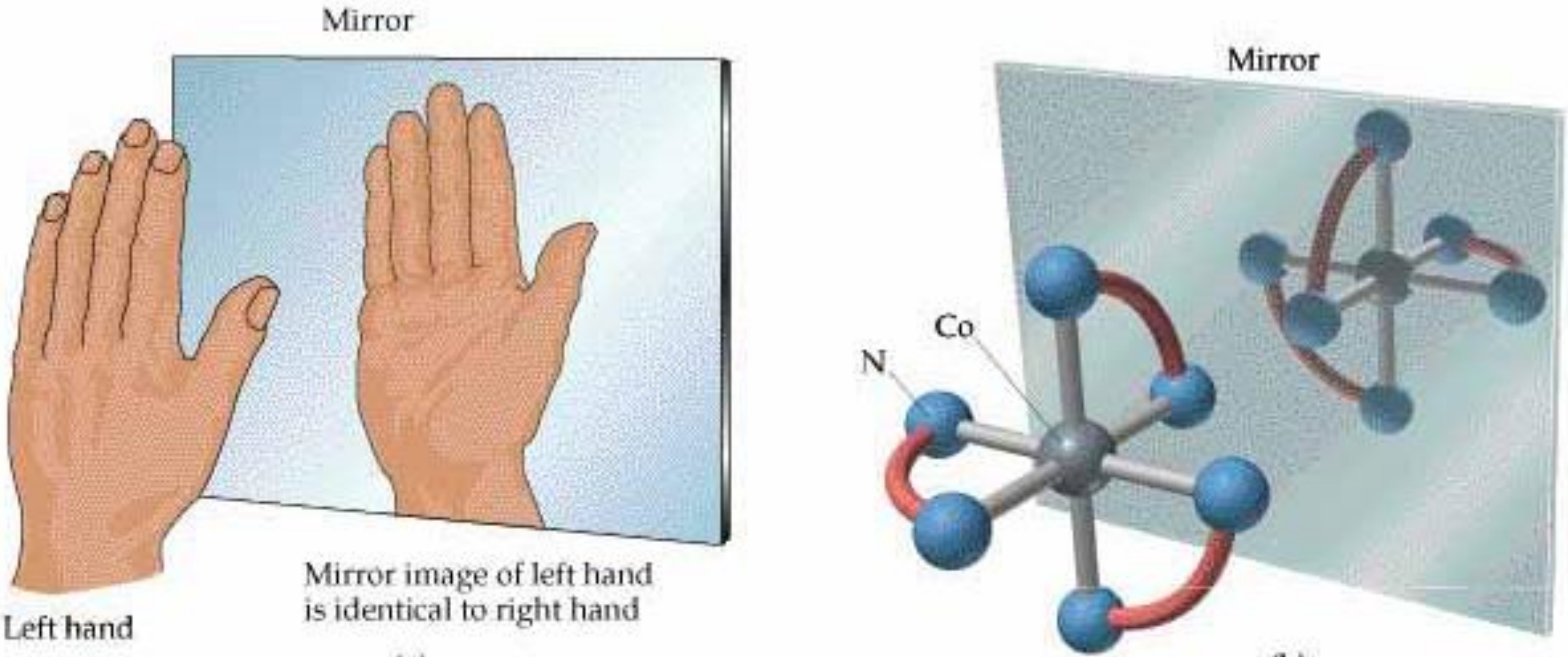


cis isomer



trans isomer

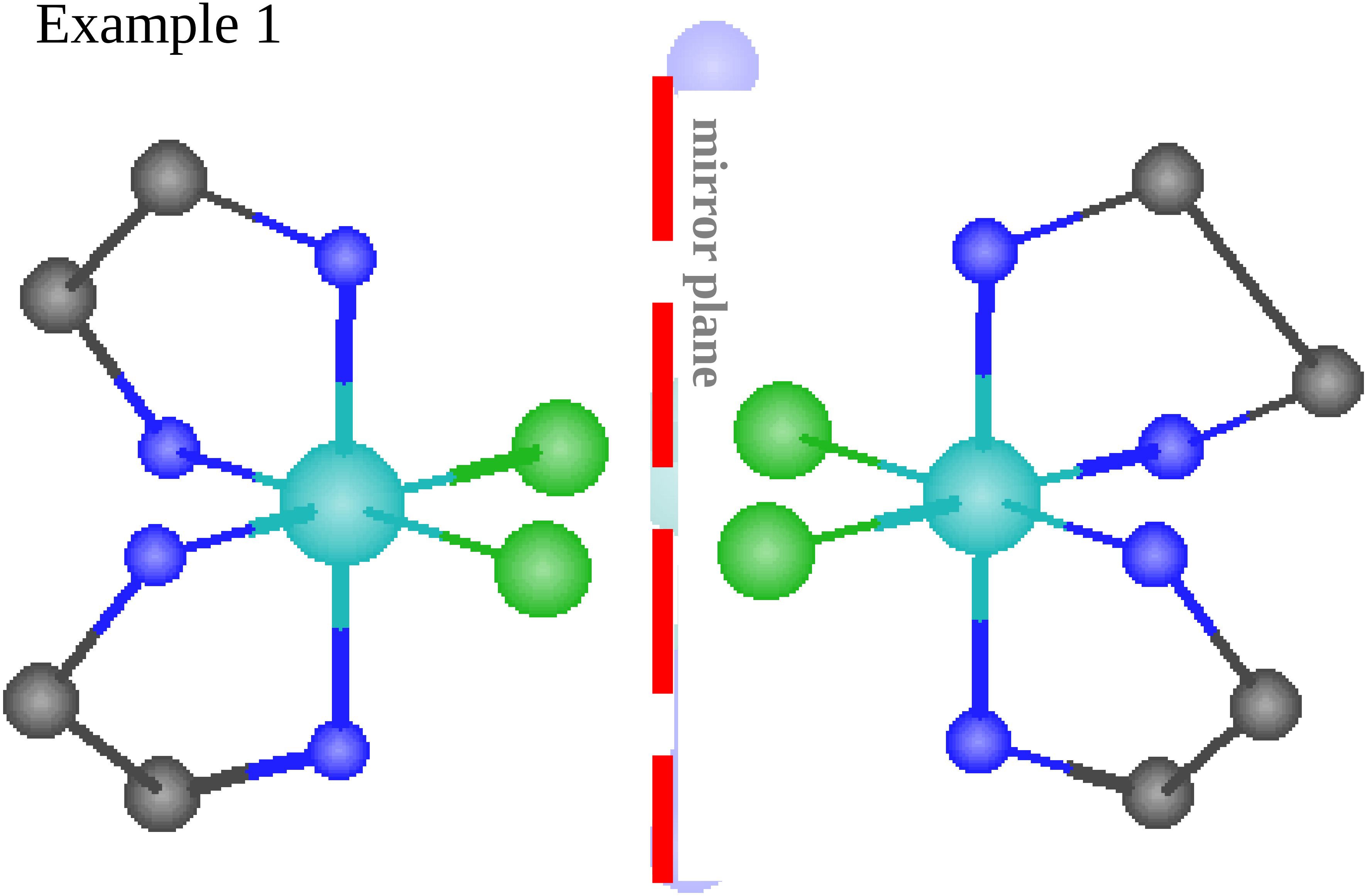
$[Co(H_2O)_4Cl_2]^+$


Mirror
Left hand
Mirror image of left hand is identical to right hand
Mirror
Co
N

(a)

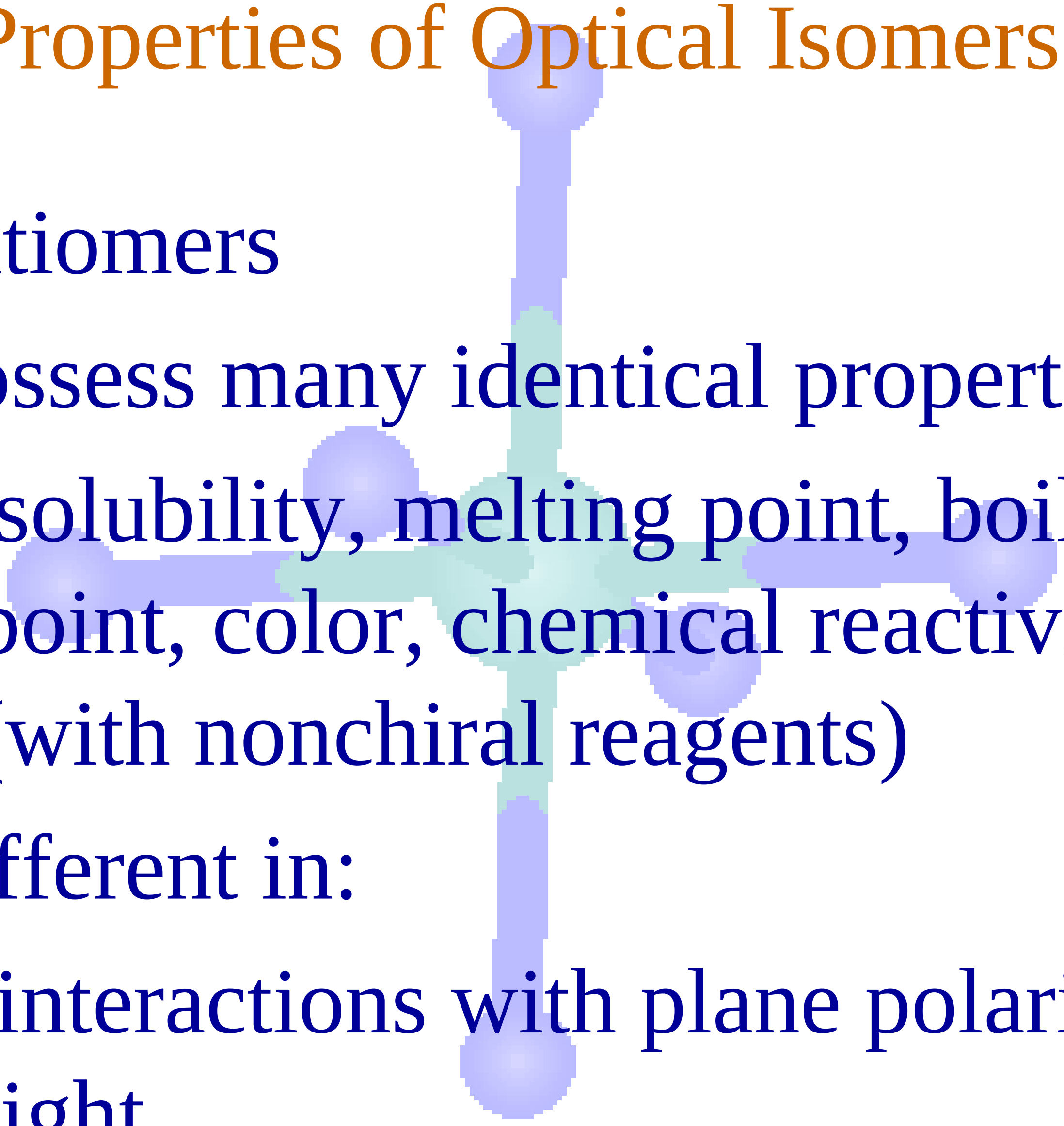
(b)

Example 1



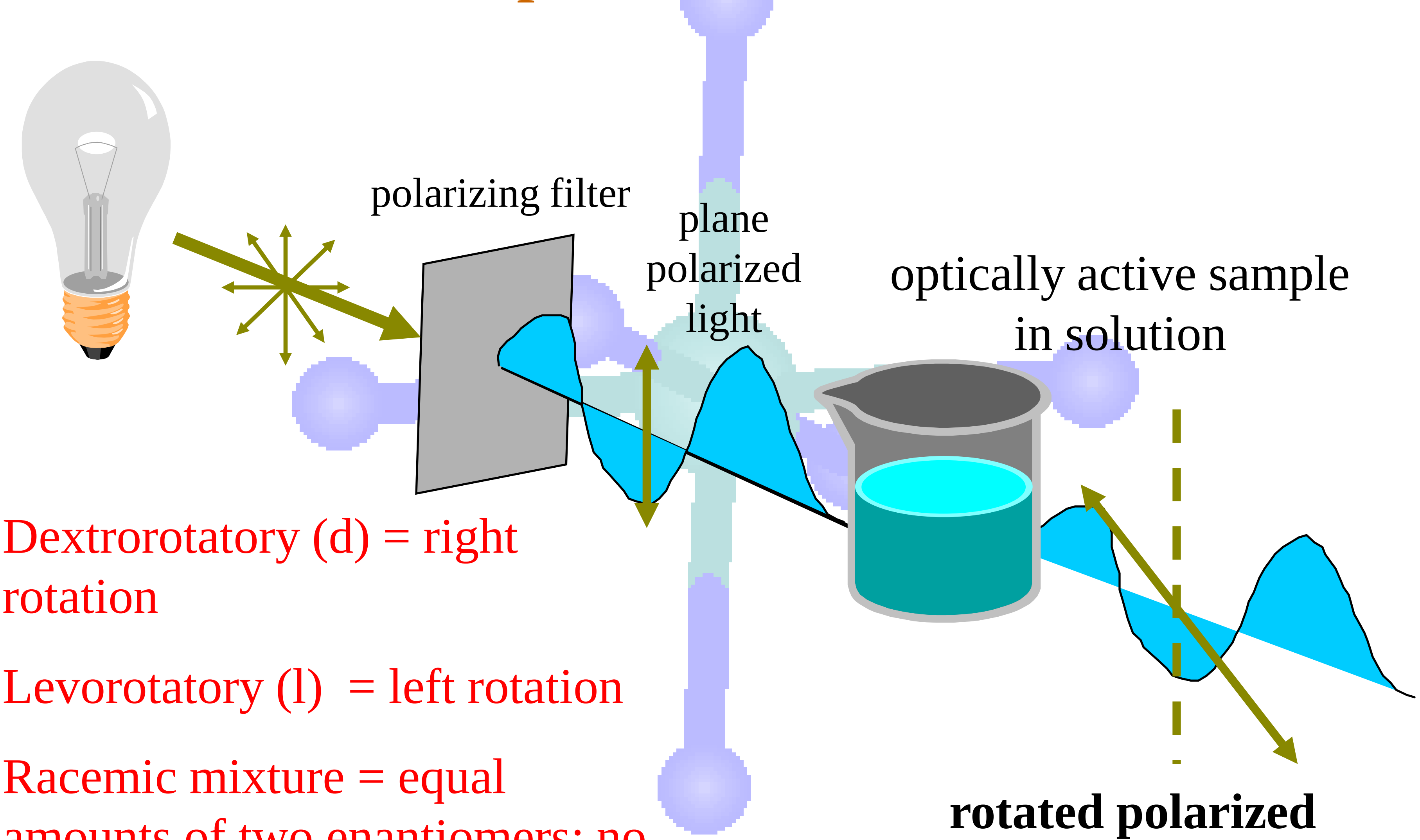
cis-$[Co(en)_2Cl_2]^+$

Properties of Optical Isomers



- Enantiomers
  - possess many identical properties
    - solubility, melting point, boiling point, color, chemical reactivity (with nonchiral reagents)
  - different in:
    - interactions with plane polarized light

Optical Isomers



polarizing filter

plane
polarized
light

optically active sample
in solution

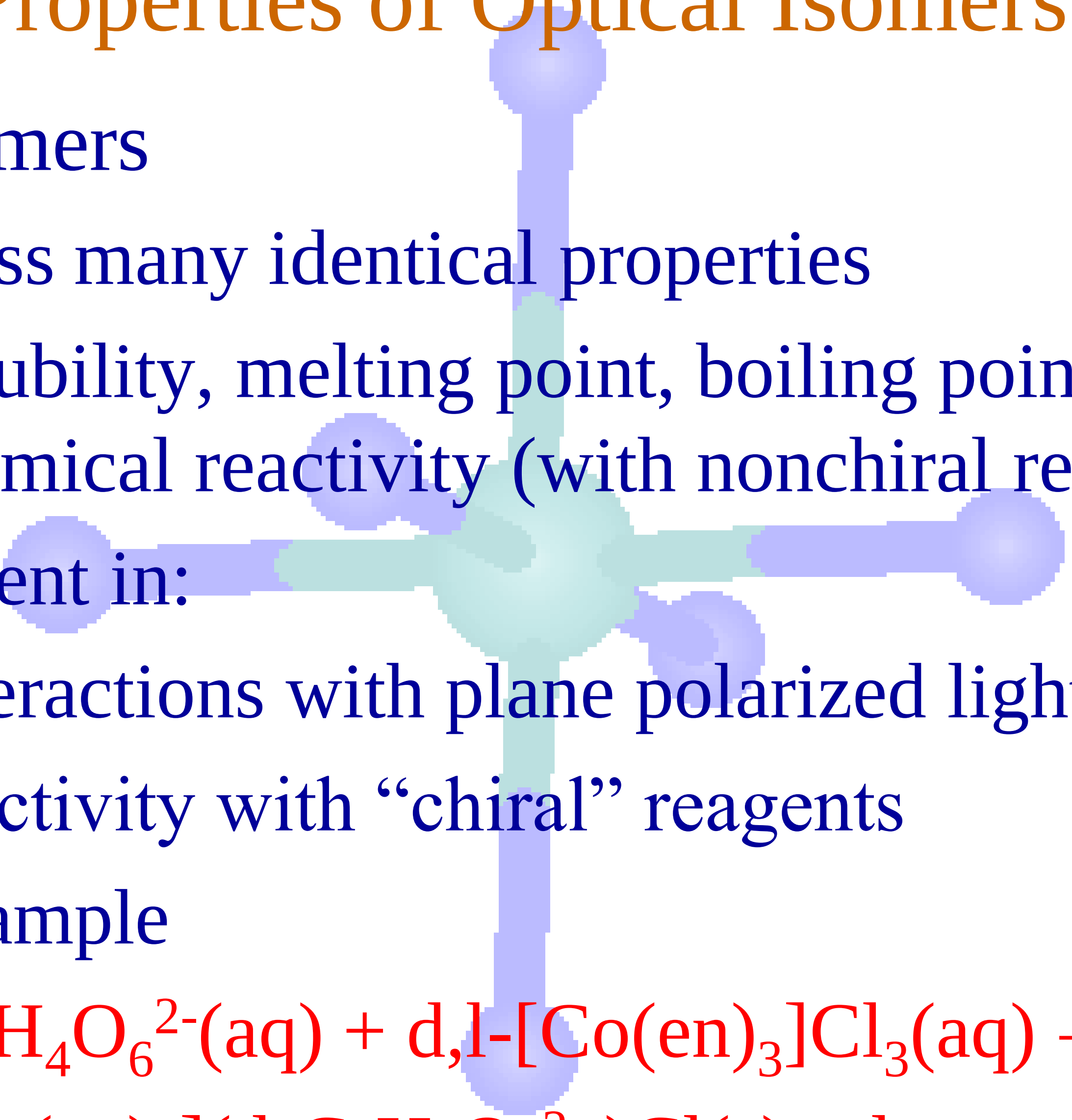
**rotated polarized
light**

Dextrorotatory (d) = right rotation

Levorotatory (l) = left rotation

Racemic mixture = equal amounts of two enantiomers; no net rotation

Properties of Optical Isomers



- Enantiomers
  - possess many identical properties
    - solubility, melting point, boiling point, color, chemical reactivity (with nonchiral reagents)
  - different in:
    - interactions with plane polarized light
    - reactivity with “chiral” reagents

Example

d-$C_4H_4O_6^{2-}$(aq) + d,l-$[Co(en)_3]Cl_3$(aq) →
d-$[Co(en)_3]$(d-$C_4H_4O_6^{2-}$)Cl(s) + l-$[Co(en)_3]Cl_3$(aq) +2Cl^-(aq)

SOME IMPORTANT PARAMETERS BY THE COORDINATION COMPLEXES:

-How **STABLE THE COMPLEX IS**?...***Which thermodynamic Parameter*** can give us hints about stability of a given complex?

---IT IS „**THE STABILITY CONSTANT**“

...

Stability constant can be determined by UV VIS or by Voltammetry

How the **COORDINATION NUMBER OF A GIVEN COMPLEX** Can be determined?

-In SOLID STATE COMPLEXES by RÖNTGEN DIFFRACTION

-byVoltammetry (Electrochemical techniques)

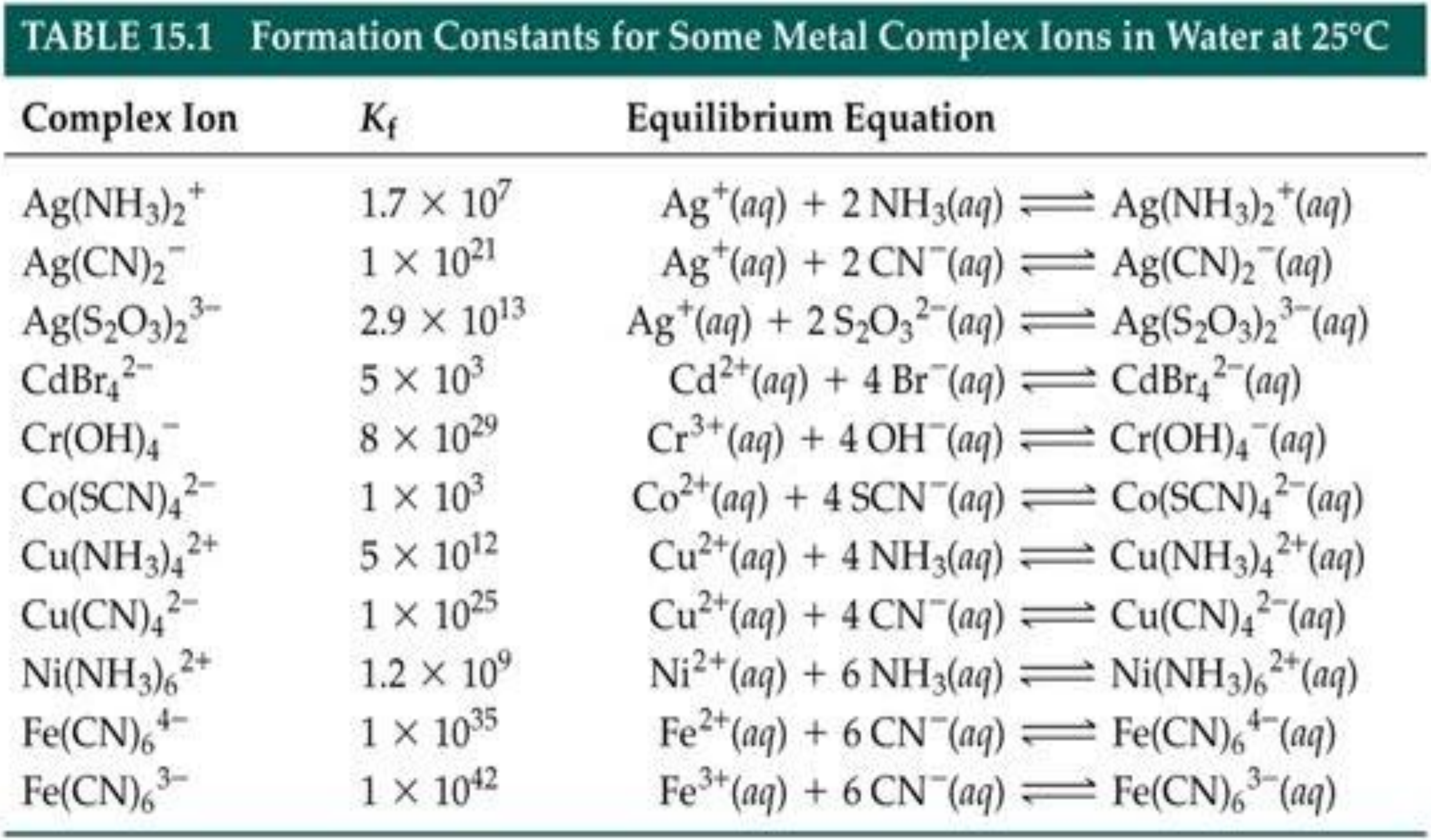
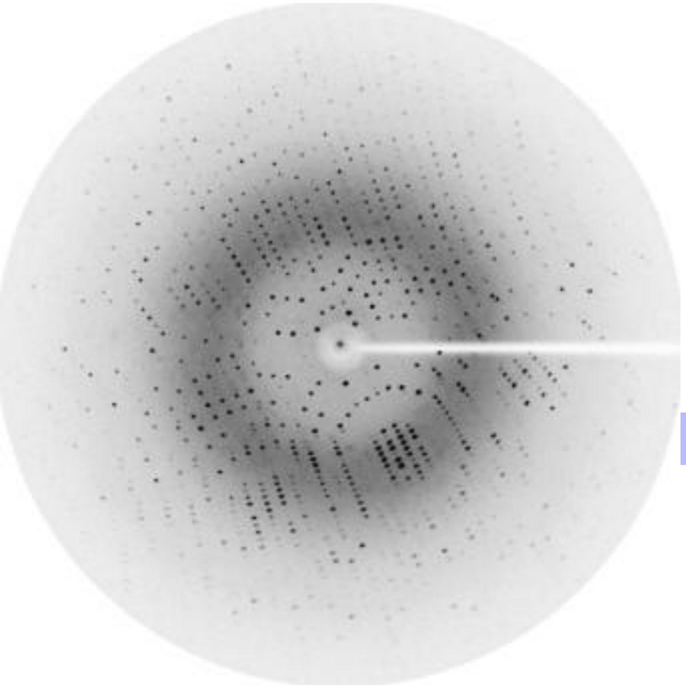
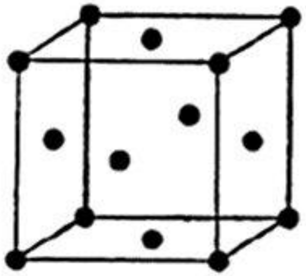


TABLE 15.1 Formation Constants for Some Metal Complex Ions in Water at 25°C

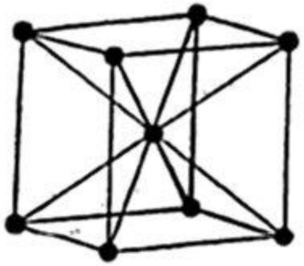
Complex Ion	K_f	Equilibrium Equation
$Ag(NH_3)_2^+$	1.7×10^7	$Ag^+(aq) + 2\,NH_3(aq) \rightleftharpoons Ag(NH_3)_2^+(aq)$
$Ag(CN)_2^-$	1×10^{21}	$Ag^+(aq) + 2\,CN^-(aq) \rightleftharpoons Ag(CN)_2^-(aq)$
$Ag(S_2O_3)_2^{3-}$	2.9×10^{13}	$Ag^+(aq) + 2\,S_2O_3^{2-}(aq) \rightleftharpoons Ag(S_2O_3)_2^{3-}(aq)$
$CdBr_4^{2-}$	5×10^3	$Cd^{2+}(aq) + 4\,Br^-(aq) \rightleftharpoons CdBr_4^{2-}(aq)$
$Cr(OH)_4^-$	8×10^{29}	$Cr^{3+}(aq) + 4\,OH^-(aq) \rightleftharpoons Cr(OH)_4^-(aq)$
$Co(SCN)_4^{2-}$	1×10^3	$Co^{2+}(aq) + 4\,SCN^-(aq) \rightleftharpoons Co(SCN)_4^{2-}(aq)$
$Cu(NH_3)_4^{2+}$	5×10^{12}	$Cu^{2+}(aq) + 4\,NH_3(aq) \rightleftharpoons Cu(NH_3)_4^{2+}(aq)$
$Cu(CN)_4^{2-}$	1×10^{25}	$Cu^{2+}(aq) + 4\,CN^-(aq) \rightleftharpoons Cu(CN)_4^{2-}(aq)$
$Ni(NH_3)_6^{2+}$	1.2×10^9	$Ni^{2+}(aq) + 6\,NH_3(aq) \rightleftharpoons Ni(NH_3)_6^{2+}(aq)$
$Fe(CN)_6^{4-}$	1×10^{35}	$Fe^{2+}(aq) + 6\,CN^-(aq) \rightleftharpoons Fe(CN)_6^{4-}(aq)$
$Fe(CN)_6^{3-}$	1×10^{42}	$Fe^{3+}(aq) + 6\,CN^-(aq) \rightleftharpoons Fe(CN)_6^{3-}(aq)$

Röntgen diffraction

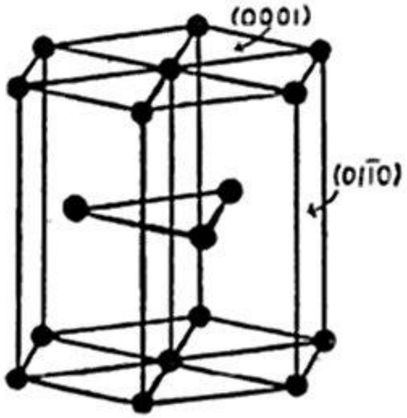




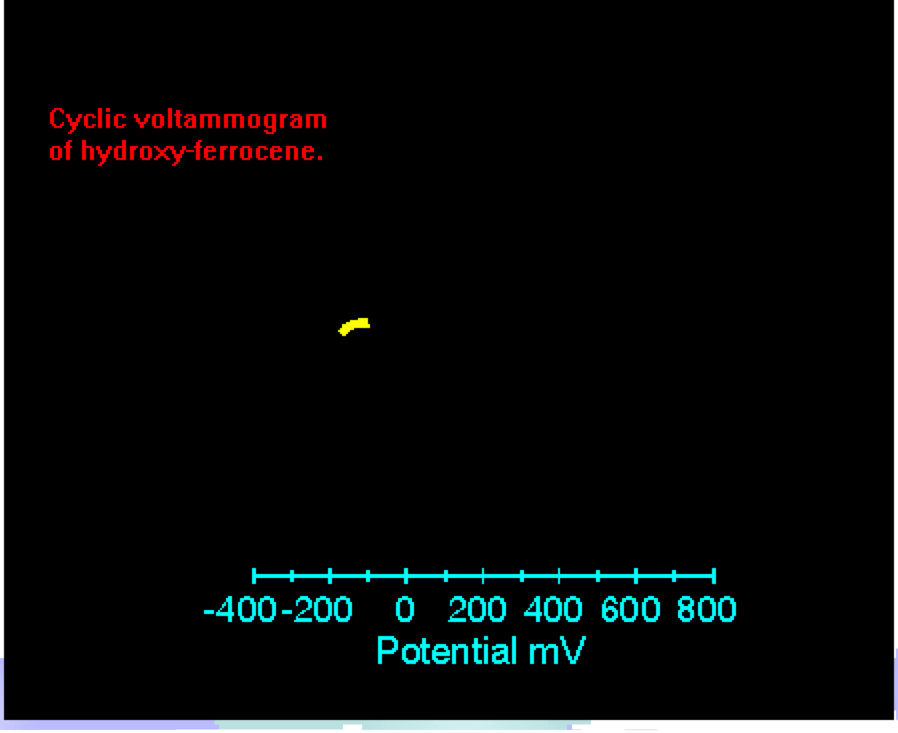
Face-centred cube.



Body-centred cube.



The close-packed hexagonal structure with axial ratio 1.633.



Cyclic voltammogram of hydroxy-ferrocene.