

# The Chelate Effect

## I. How to Make a Strong Complex

### A. Factors Effecting M—L Binding Strength = **Molecular Organization**

1) **Complementarity** = sum of size, geometry, and electronic matching between the metal ion and the ligand(s)

- a) The individual components are simple and can be predicted or found experimentally
- b) Example: HSAB Theory predicts  $\text{Fe}^{3+}/\text{O}^{2-}$  is more complementary than  $\text{Fe}^{3+}/\text{S}^{2-}$
- c) Example:  $d^8 \text{Ni}^{2+}$  should have good complementarity with cyclam
- d) Complementarity is only the first step towards complex stability

2) **Constraint** = the number of and flexibility between ligand donor atoms

- a) **Topology** = interconnectedness of donor atoms
- b) **Rigidity** = how fixed in space donor atoms of the ligand are with respect to each other
- c) These constraint factors are more difficult to grasp than complementarity
- d) Maximizing these factors can lead to huge increases in complex stability

## B. Topological Effects

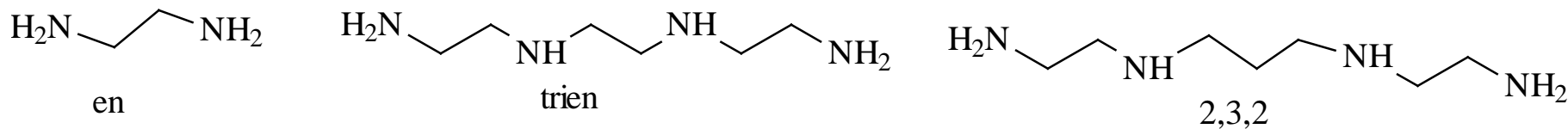
### 1) The Chelate Effect

- Two donor atoms linked together = a chelate (claw)
- Chelate ligands form much more stable metal complexes than monodentate related ligands (up to  $10^5$  times as stable)

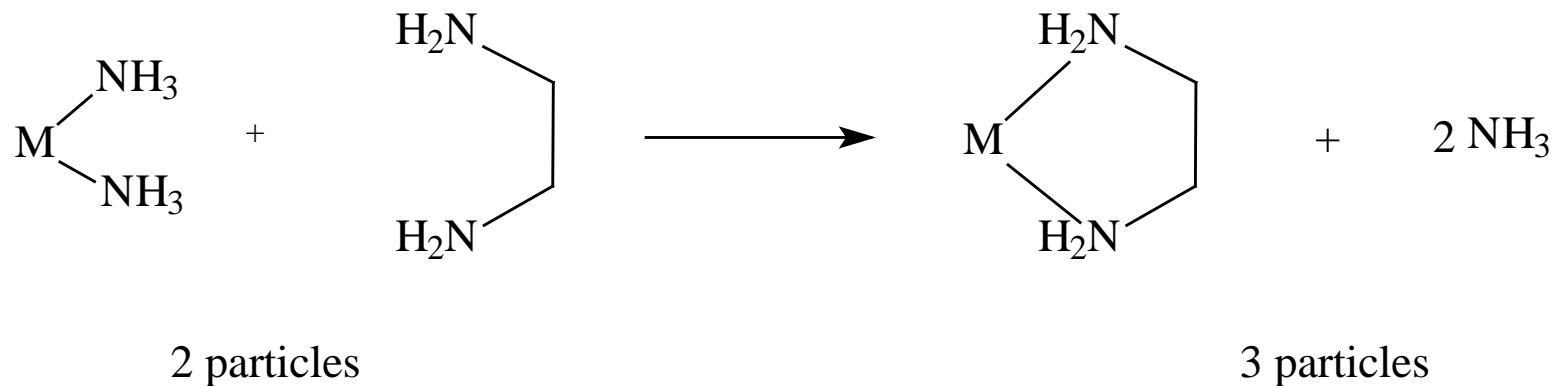
$\text{Ni}^{2+} + \text{L}$  Formation Constants:

L =	$\text{NH}_3$	en	trien	2,3,2
log $\beta$	8.12	13.54	13.8	16.4

better  
complementarity



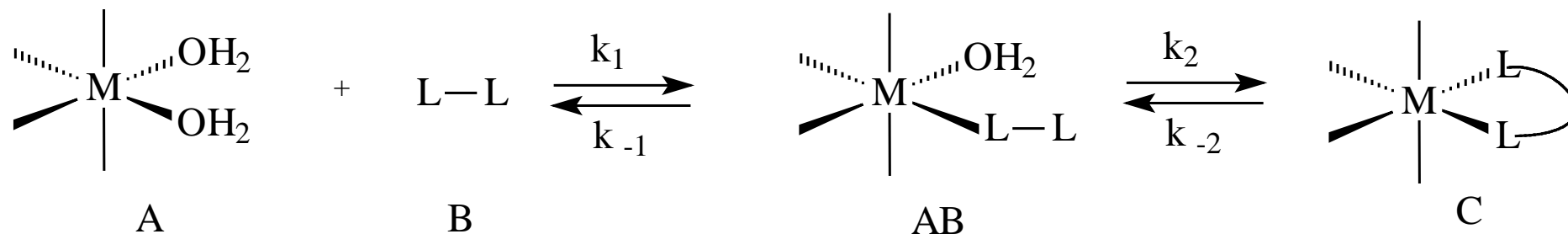
### c) Thermodynamic Reasons for the Chelate Effect = Entropy



	$\Delta G$	$\Delta H$	$\Delta S$	$\Delta(\Delta G)$	$\Delta(\Delta H)$	$\Delta(\Delta S)$
$\text{Ni}(\text{NH}_3)_2^{2+}$	-6.93	-7.8	-3			
$\text{Ni}(\text{NH}_3)_4^{2+}$	-11.08	-15.6	-15			
$\text{Ni}(\text{NH}_3)_6^{2+}$	-12.39	-24	-39			
$\text{Ni}(\text{en})_2^{2+}$	-10.3	-9.8	+4	-3.1	-1.2	+7
$\text{Ni}(\text{en})_2^{2+}$	-18.47	-18.3	+3	-7.4	-2.7	+18
$\text{Ni}(\text{en})_3^{2+}$	-24.16	-28.0	-10	-11.8	-4	+29
					~1.3/ring (small)	Largest Effect

#### d) Kinetics and the Chelate Effect

##### i. Chelate complex formation



ii. The Steady-State Approximation yields:

$$\frac{dC}{dt} = \frac{k_1 k_2 [A][B]}{k_{-1} + k_2} - \frac{k_{-1} k_{-2} [C]}{k_{-1} + k_2}$$

Or rewriting with formation ( $k_f$ ) and dissociation ( $k_d$ ) constants:

$$\frac{dC}{dt} = k_f [A][B] - k_d [C] \quad k_f = \frac{k_1 k_2}{k_{-1} + k_2} \quad \text{and} \quad k_d = \frac{k_{-1} k_{-2}}{k_{-1} + k_2}$$

iii. Assuming a chelate effect,  $k_2 \gg k_{-1}$

$$k_f = \frac{k_1 k_2}{k_{-1} + k_2} = k_1 \quad (\text{the same as for monodentate ligands})$$

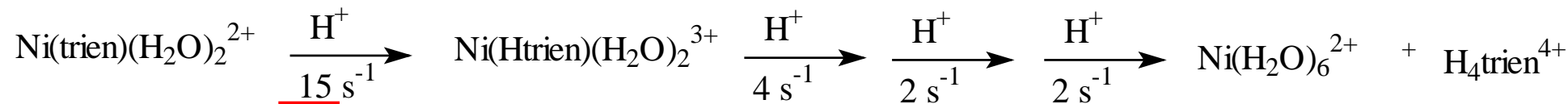
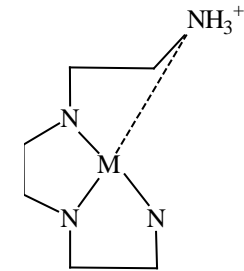
$$k_d = \frac{k_{-1} k_{-2}}{k_{-1} + k_2} = \frac{k_{-1} k_{-2}}{k_2}$$

iv.  $k_f$  is not the source of the chelate effect. It is the same as other ligands

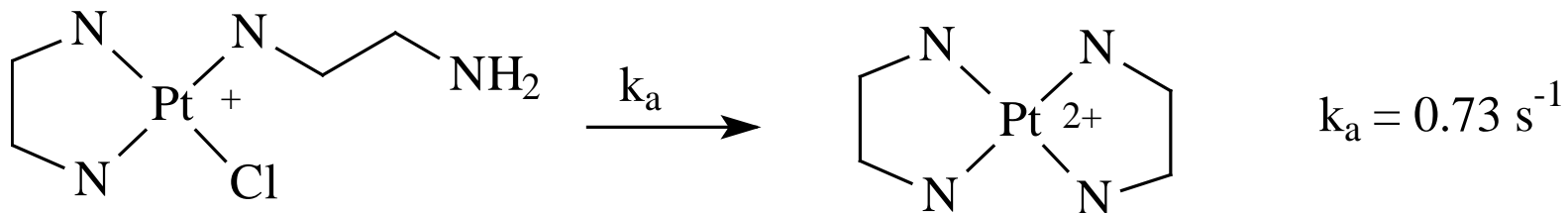
v.  $k_d$  must be the source of the chelate effect (dissociation is slow!)

$k_{-1}$  is the same as for monodentate ligands

$k_{-2}$  (ring opening) is the same as for monodentate ligands:



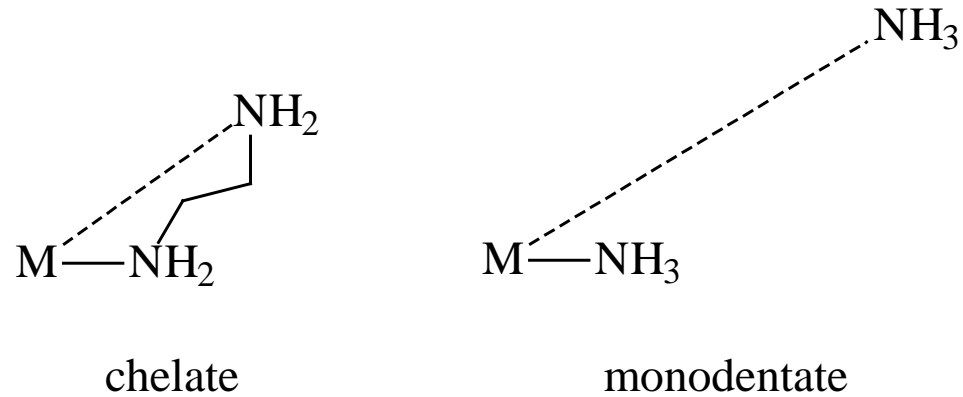
Data for  $k_2$  (ring closing)



$$\frac{k_a}{k_b} = \frac{0.73 \text{ s}^{-1}}{5.4 \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}} = 1.4 \times 10^3 \text{ M} = \text{Effective Concentration}$$

Huge Concentration!

$k_2$ , the formation of the second M—L bond, has been shown to be extremely large compared to a second monodentate ligand binding. This is due to the large “**effective concentration**” of the second donor atom of a chelate



If  $k_2$  is large,  $k_d$  must be small;

**Very fast bond reformation after the first donor dissociates is the kinetic source of the chelate effect**

#### vi. Data

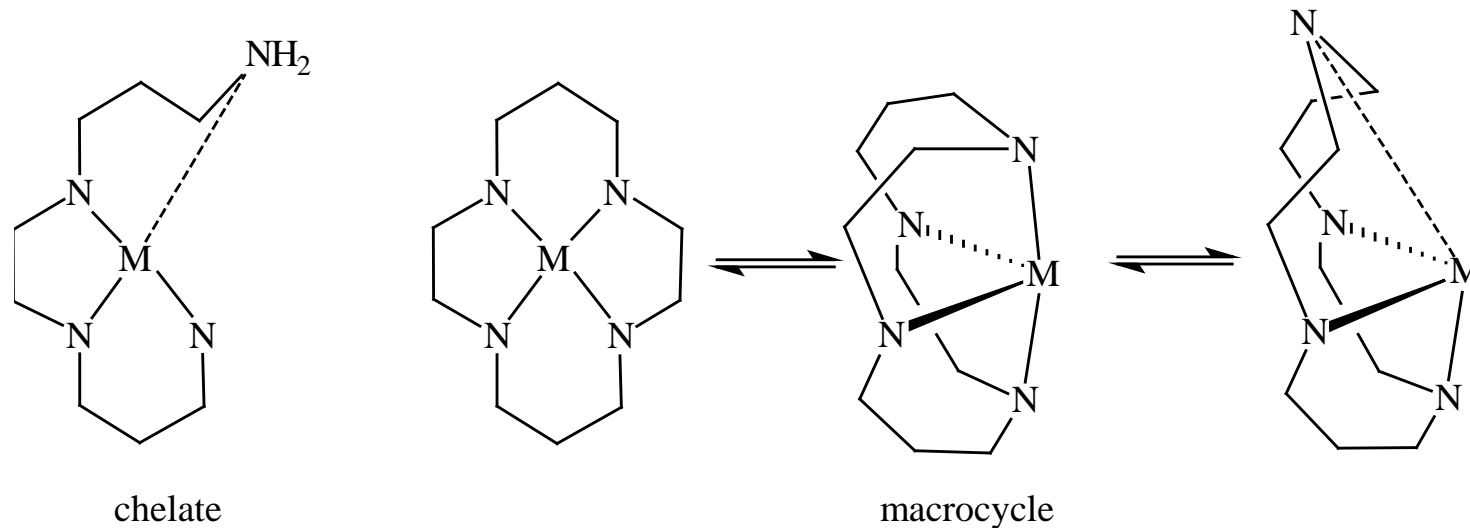
$M^+$	L	$k_f$	$k_d$
$Fe^{2+}$	$HCO_2^-$	$7 \times 10^3$	10
$Fe^{2+}$	$C_2O_4^{2-}$	$2 \times 10^4$	$3 \times 10^{-3}$

## 2) The Macrocyclic Effect

- a) Macrocyclic chelate complexes are up  $10^7$  times more stable than non-cyclic chelates with the same number of donors



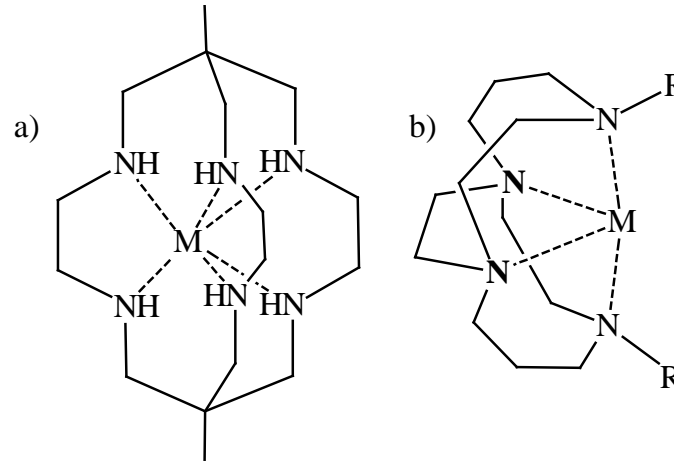
- b) Connecting all of the donors (having no end group) makes  $k_{-2}$  important
- Breaking the first M—L bond requires major ligand deformation
  - The increase in  $E_a$  required greatly slows down  $k_{-2}$



- c) A macrocycle is still a chelate, so it still has the  $k_2$  chelate effect going
- d) The result is a very stable complex as  $k_d$  becomes miniscule

### 3) The Cryptate Effect 土窟

a) Additional connections between donor atoms in a macrocycle further enhance complex stability by making dissociation even more difficult



#### b) Data **bridged-cyclam**

$\text{Cu}(\text{H}_2\text{O})_6^{2+}$  water substitution  $t_{1/2} = 1.4 \times 10^{-9} \text{ s}$

$\text{Cu}(\text{Me}_4\text{Cyclam})$  in 1 M  $\text{H}^+$   $t_{1/2} = 2 \text{ s}$

$\text{Cu}(\text{Bridged-cyclam})\text{Cl}^+$  in 1 M  $\text{H}^+$   $t_{1/2} > 6 \text{ years} = 1.9 \times 10^8 \text{ s}$

#### c) Usefulness of such stable complexes

- i. Oxidation catalysis in harsh aqueous conditions ( $\text{H}^+$  or  $\text{OH}^-$ )
- ii. MRI Contrast agents that must not dissociate toxic  $\text{Gd}^{3+}$



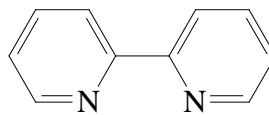
## C. Rigidity Effects

- 1) More rigid ligands (assuming complementarity) make more stable complexes
- 2) Data

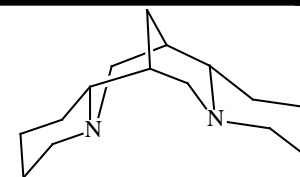
M	L	$t_{1/2}$	difference
$\text{Cu}^{2+}$	en	0.006 s	
$\text{Cu}^{2+}$	bipy	0.025 s	x 3
$\text{Cu}^{2+}$	sparteine	295 min	x $10^6$
$\text{Ni}^{2+}$	dien	0.07 s	
$\text{Ni}^{2+}$	tach	7 min	x ( $6 \times 10^3$ )
$\text{Ni}^{2+}$	TRI	90 days	x $10^8$



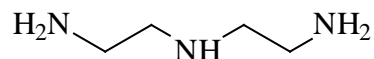
en



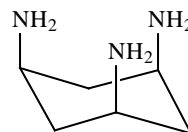
bipy



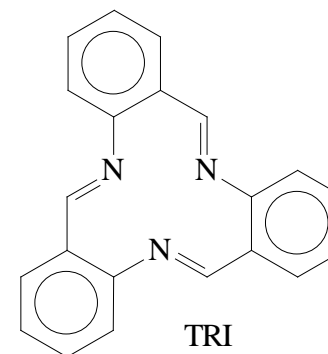
sparteine



dien



tach



TRI

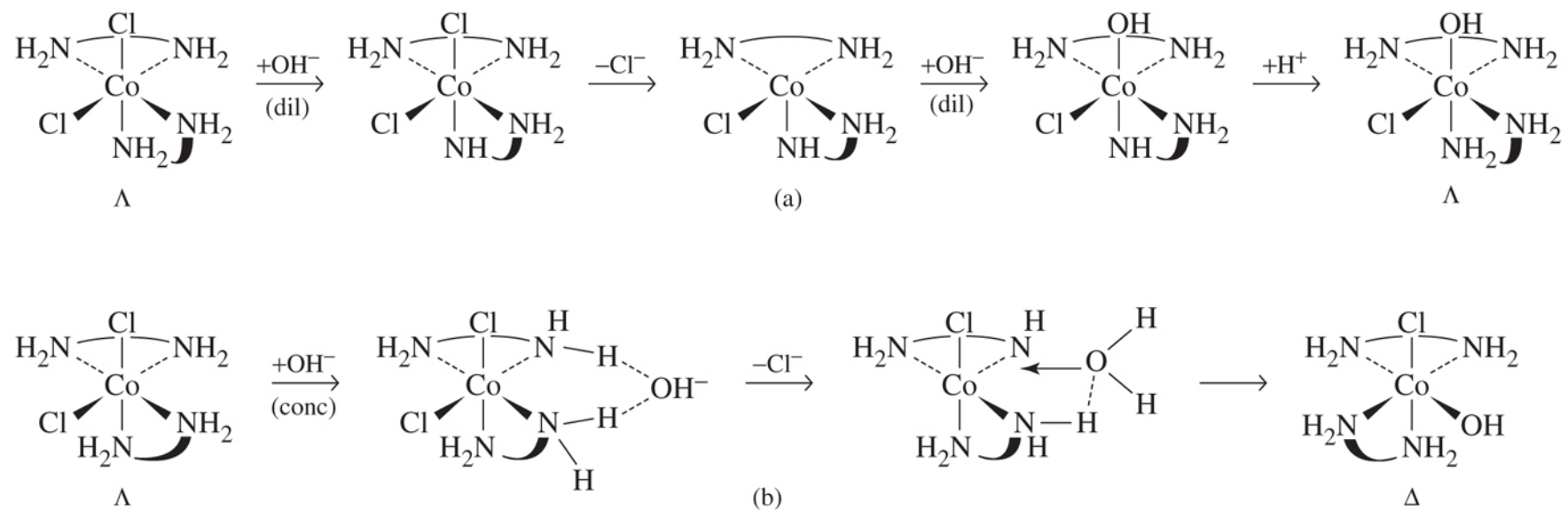
## D. Encompassing Principles

- 1) **Multiple Juxtapositional Fixedness** (Busch, 1970) = lack of end groups and rigidity effects leads to more stable complexes for topologically complex ligands if complementarity is satisfied
- 2) **Pre-Organization** (Cram, 1984): Ligands pre-formed into size and geometry match for the metal ion do not require entropically costly reorganization to bind. This savings in entropy leads to more stable complexes  
Problem: Too much pre-organization can make it hard to get the metal in!

## III. Stereochemistry of Reactions

### A. Retention or Inversion of Stereochemistry is possible during substitution reactions

- 1) Retention is usually favored for  $D$  and  $I_D$  mechanisms
- 2) Inversion is often the result of the  $S_N1CB$  mechanism
- 3) The orientation of the ligand entering the trigonal bipyramidal intermediate determines the outcome

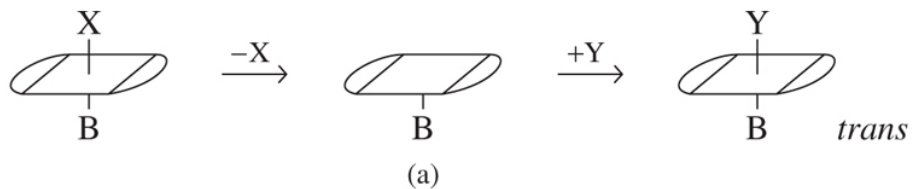


**FIGURE 12-5** Mechanisms of Base Hydrolysis of  $\Lambda$ -*cis*- $[\text{Co}(\text{en})_2\text{Cl}_2]^+$ . (a) Retention of configuration in dilute hydroxide. (b) Inversion of configuration in concentrated hydroxide.

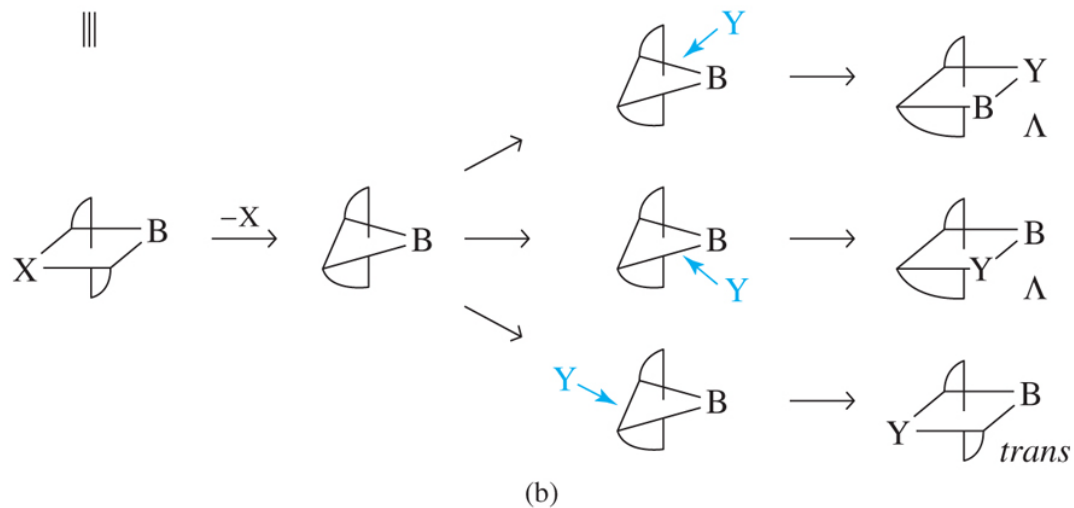
## B. Substitution in *trans* complexes

### 1) 3 possible substitution reactions for $\text{trans-}[\text{M}(\text{LL})_2\text{BX}] + \text{Y}$

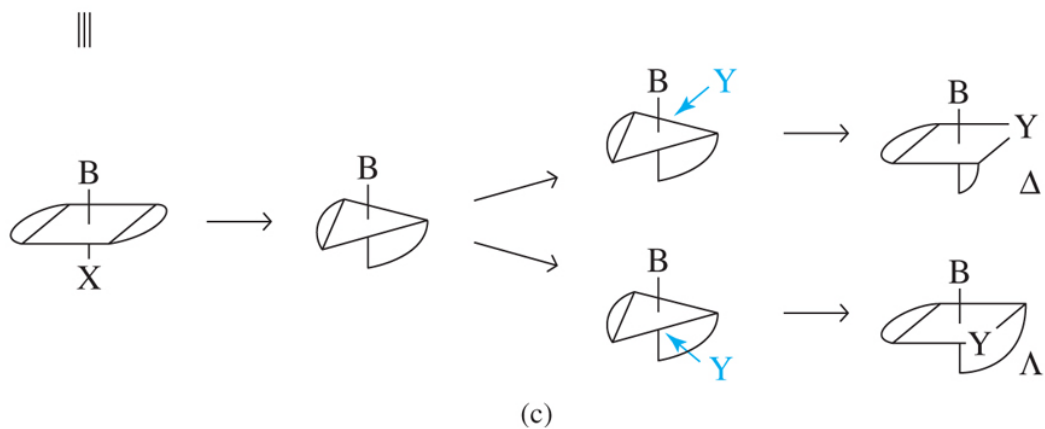
a) Retention of configuration with a square pyramidal intermediate



b) Trigonal bipyramidal intermediate with B in the plane gives a mixture of products



c) Trigonal bipyramidal intermediate with B axial leads to *cis* product



## 2) Experimental Data

- a) Many factors determine the mixture of isomers in the product
- b) Example: Identity of X

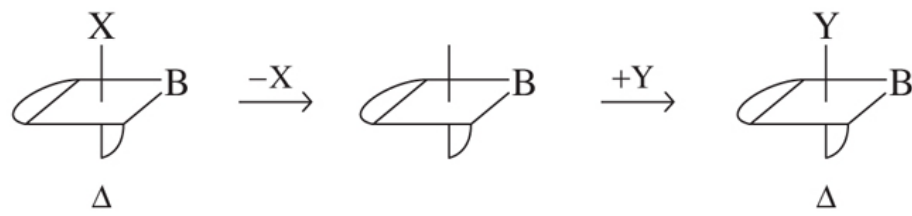
**TABLE 12.10** Rate Constants for Reactions of  $[\text{Co}(\text{en})_2(\text{H}_2\text{O})\text{X}]^{n+}$  at 25 °C,  $k(10^{-5} \text{ s}^{-1})$

X	<i>cis</i> → <i>trans</i>	<i>trans</i> → <i>cis</i>	Racemization	H <sub>2</sub> O Exchange
OH <sup>-</sup>	200	300	—	160
Br <sup>-</sup>	5.4	16.1	—	—
Cl <sup>-</sup>	2.4	7.2	2.4	—
N <sub>3</sub> <sup>-</sup>	2.5	7.4	—	—
NCS <sup>-</sup>	0.0014	0.071	0.022	0.13
H <sub>2</sub> O	0.012	0.68	~ 0.015	1.0
NH <sub>3</sub>	< 0.0001	0.002	0.003	0.10
NO <sub>2</sub> <sup>-</sup>	0.012	0.005	—	—

- c) Prediction is very difficult without experimental data on related complexes

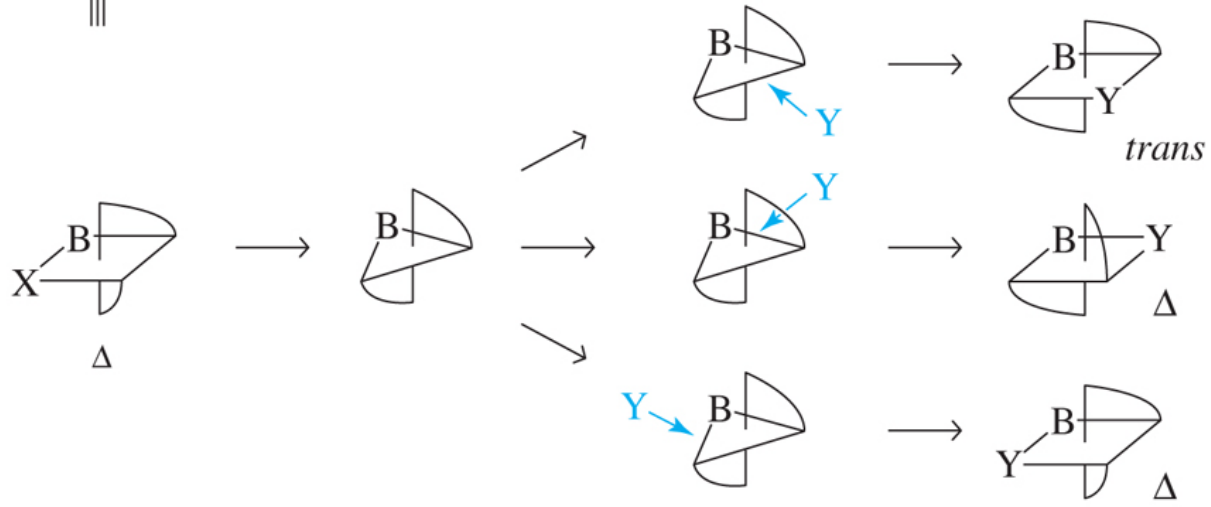
### C. Substitution in *cis* complexes

- 1) The same 3 possibilities exist as for *trans*
- 1) The products are just as hard to predict



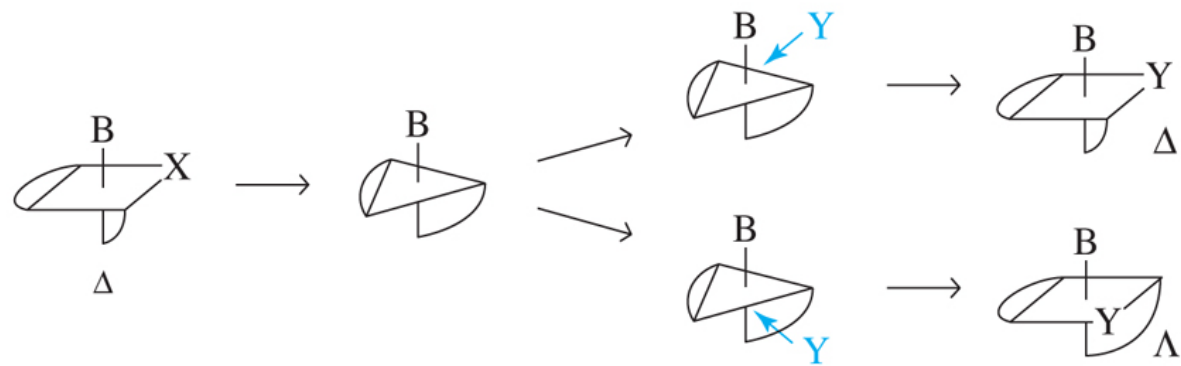
(a)

|||



(b)

|||



(c)

## D. Isomerization of Chelate Complexes

1) One mechanism is simple dissociation and reattachment of one donor of the ligand. This would be identical to any other substitution reaction

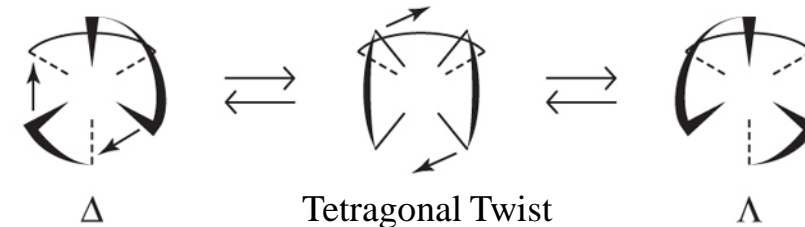
### 2) Pseudorotation

a) “Bailar Twist” = Trigonal twist = all three rings move together through a parallel intermediate

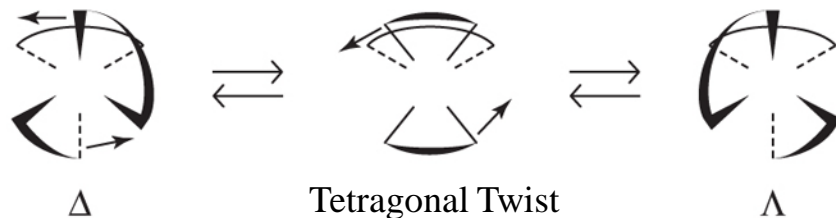
b) Tetragonal Twists = one ring stays the same and the others move



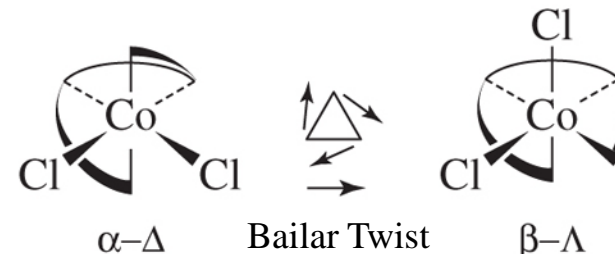
(a)



(b)



(c)



(d)