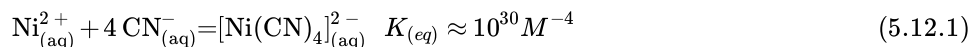


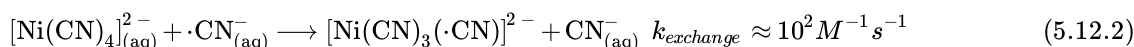
5.12: Ligand Substitution Reactions

Transition metal complexes can exchange one ligand for another, and these reactions are important in their synthesis, stereochemistry, and catalytic chemistry. The mechanisms of chemical reactions are intimately connected to reaction kinetics. As in organic chemistry, the mechanisms of transition metal reactions are typically inferred from experiments that examine the concentration dependence of the incoming and outgoing ligands on the reaction rate, the detection of intermediates, and the stereochemistry of the reactants and products.

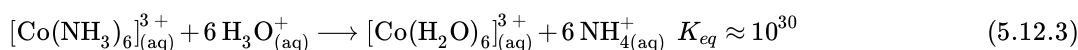
Thermodynamic vs. kinetics. When we think about the reactions of transition metal complexes, it is important to recall the distinction between their *thermodynamics* and *kinetics*. Take for example the formation of the square planar tetracyanonickelate complex:



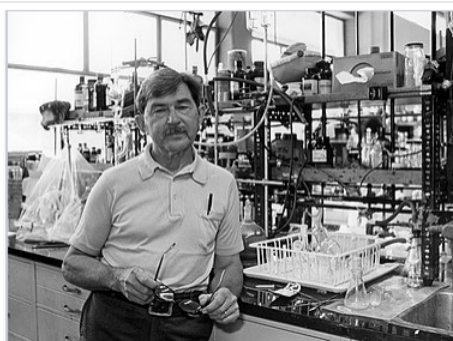
Thermodynamically, $[\text{Ni}(\text{CN})_4]^{2-}$ is very **stable**, meaning that the equilibrium above lies very far to the right. Kinetically, however, the complex is **labile**, meaning that it can exchange its ligands rapidly. For example the exchange between a ^{13}C labeled CN^{-} ion and a bound CN^{-} ligand occurs on the timescale of tens of milliseconds:



Conversely, a compound can be thermodynamically **unstable** but kinetically **inert**, meaning that it takes a relatively long time to react. For example, the $[\text{Co}(\text{NH}_3)_6]^{3+}$ ion is unstable in acid, but its hydrolysis reaction with concentrated HCl takes about one week to go to completion at room temperature:

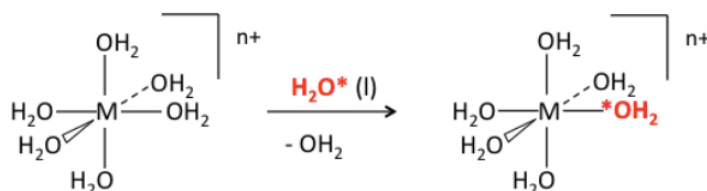


Henry Taube, who studied the mechanisms of ligand exchange reactions in simple test tube experiments, classified transition metal complexes as **labile** if their reaction half-life was one minute or less, and **inert** if they took longer to react. The dynamic range of ligand substitution rates is enormous, spanning at least 15 orders of magnitude. On the timescale of most laboratory experiments, the Taube definition of lability is a useful one for classifying reactions into those that have low and high activation energies. As we will see, the **crystal field stabilization energy (CFSE)** plays a key role in determining the activation energy and therefore the rate of ligand substitution.



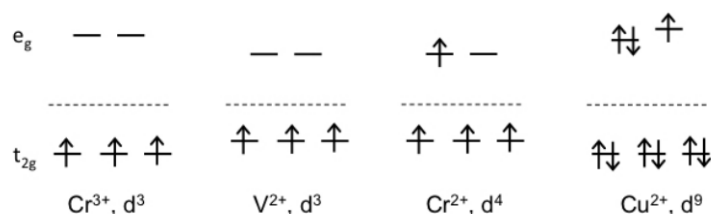
Henry Taube (Stanford University) received the 1983 Nobel Prize for his work on the electron transfer and ligand exchange reactions of transition metal complexes

Crystal field stabilization energy and ligand exchange rates. Let's consider a very common and simple ligand exchange reaction, which is the substitution of one water molecule for another in an octahedral $[\text{M}(\text{H}_2\text{O})_6]^{n+}$ complex. Since the products (except for the label) are the same as the reactants, we know that $\Delta G^\circ = 0$ and $K_{\text{eq}} = 1$ for this reaction. The progress of the reaction can be monitored by NMR by using isotopically labeled water (typically containing ^{17}O or ^{18}O):



The most striking thing about this (otherwise boring) reaction is the vast difference in rate constants - about 14 orders of magnitude - for different metal ions and oxidation states:

M^{n+}	$\log k \text{ (sec}^{-1}\text{)}$
Cr^{3+}	-6
V^{2+}	-2
Cr^{2+}	8
Cu^{2+}	8



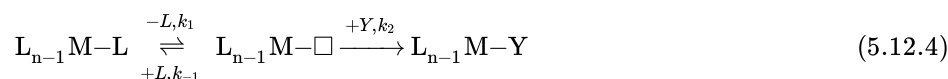
While at first it may seem strange that the same ion in two different oxidation states (Cr^{3+} vs. Cr^{2+}) would be inert or labile, respectively, we can begin to rationalize the difference by drawing d-orbital splitting diagrams for the complexes. What we find is that octahedral complexes that have **high CFSE** (Cr^{3+} , V^{2+}) tend to be **inert**. Conversely, ions with electrons in high energy e_g orbitals (Cr^{2+} , Cu^{2+}) tend to be labile. In the case of Cr^{3+} and V^{2+} , the energy penalty for distorting the complex away from octahedral symmetry - to make, for example, a 5- or 7-coordinate intermediate - is particularly high. This activation energy for ligand substitution is lower for Cr^{2+} and Cu^{2+} , which already have electrons in antibonding e_g orbitals.

Based on the rules we developed for calculating the CFSE of transition metal complexes, we can now predict the trends in ligand substitution rates:

- Octahedral complexes with **d^3 and d^6 (low spin)** configurations, such as Cr^{3+} (d^3), Co^{3+} (d^6), Rh^{3+} (d^6), Ru^{2+} (d^6), and Os^{2+} (d^6) tend to be **substitution-inert** because of their high CFSE.
- Square planar d^8** complexes, especially those in the 4d and 5d series, are also **substitution-inert**. Examples are complexes of Pd^{2+} , Pt^{2+} , and Au^{3+} .
- Intermediate cases are complexes of Fe^{3+} , V^{3+} , V^{2+} , Ni^{2+} , and of main group ions (Be^{2+} , Al^{3+}) that are hard Lewis acids. These complexes make strong metal-oxygen bonds and have water exchange rates in the range of 10^1 - 10^6 s^{-1} .
- Ions with zero CFSE** exchange water molecules on a timescale of nanoseconds ($k \approx 10^8$ - 10^9 s^{-1}). These include ions with d^0 , d^5 (high spin), and d^{10} electron counts, including alkali metal (Li^+ , Na^+ , K^+ , Rb^+ , Cs^+) and alkali earth (Mg^{2+} , Ca^{2+} , Sr^{2+} , Ba^{2+}) cations, Zn^{2+} , Cd^{2+} , Hg^{2+} , and Mn^{2+} . In these cases the CFSE is zero and the energetic cost of breaking octahedral symmetry is relatively low.
- For p-block elements, faster exchange occurs with larger ions (e.g., $Ba^{2+} > Ca^{2+}$ and $Ga^{3+} > Al^{3+}$), because Lewis acid strength decreases with increasing ion size.
- The Cu^{2+} ion (d^9), as a **Jahn-Teller ion**, is already distorted away from octahedral symmetry and is therefore quite **labile**, exchanging water ligands at a rate of about 10^8 s^{-1} .

Ligand Substitution Mechanisms. For an ML_n complex undergoing ligand substitution, there are essentially three different reaction mechanisms:

- In the **dissociative mechanism**, a ML_n complex first **loses a ligand** to form an ML_{n-1} intermediate, and the incoming ligand Y reacts with the ML_{n-1} fragment:



This mechanism is illustrated below for ligand substitution on an octahedral ML_6 complex. The intermediate state in this example involves a trigonal bipyramidal ML_5 fragment as well as free L and Y ligands.

If the rate determining step is the dissociation of L from the complex, then the concentration of Y does not affect the rate of reaction, leading to the first-order rate law:

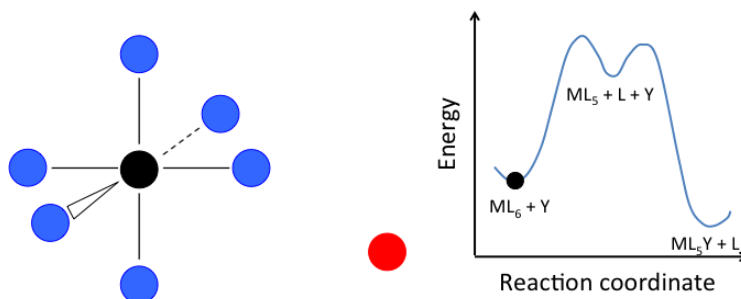


Illustration of the dissociative ligand substitution mechanism for an ML_6 complex. The reaction energy profile is shown at the right.

$$Rate = k_1[ML_n] \quad (5.12.5)$$

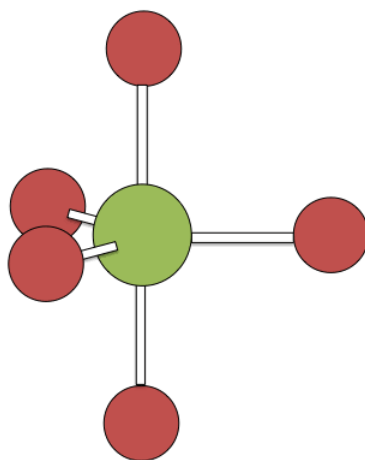
In the case of an octahedral complex, this reaction would be first order in ML_6 and zero order in Y, but only if the highest energy transition state is the one that precedes the formation of the ML_5 intermediate. If the two transition states are close in energy (as in the case of the animation at the right), then the rate law becomes more complicated. In this case, we can simplify the problem by assuming a low steady-state concentration of the ML_n intermediate. The resulting rate law is:

$$Rate = \frac{k_1 k_2 [Y][ML_n]}{k_{-1}[L] + k_2[Y]} \quad (5.12.6)$$

which reduces to the simpler first-order rate law when $k_2[Y] \gg k_{-1}[L]$. Because the formation of the transition state involves dissociation of a ligand, the entropy of activation is always positive in the dissociative mechanism.

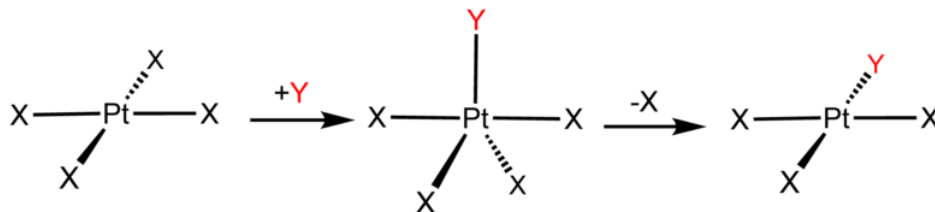
- In the **associative mechanism**, the incoming ligand Y attacks the ML_n complex, transiently forming an ML_nY intermediate, and the intermediate then loses a ligand L forming the $ML_{n-1}Y$ product

Complexes that undergo associative substitution are typically either coordinatively unsaturated or contain a ligand that can change its bonding to the metal, e.g. a change in the hapticity or bending of a nitric oxide ligand (NO). In homogeneous catalysis, the associative pathway is desirable because the binding event, and hence the selectivity of the reaction, depends not only on the nature of the metal catalyst but also on the molecule that is involved in the catalytic cycle.



Berry pseudorotation mechanism

Examples of associative mechanisms are commonly found in the chemistry of d^8 square planar metal complexes, e.g. Vaska's complex ($\text{IrCl}(\text{CO})[\text{P}(\text{C}_6\text{H}_5)_3]_2$) and tetrachloroplatinate(II). These compounds (ML_4) bind the incoming (substituting) ligand Y to form pentacoordinate intermediates ML_4Y , which in a subsequent step dissociate one of their ligands. Although the incoming ligand is initially bound at an equatorial site, the **Berry pseudorotation** provides a low energy pathway for all ligands to sample both the equatorial and axial sites. Ligand dissociation must occur from an equatorial site according to the principle of microscopic reversibility. Dissociation of Y results in no reaction, but dissociation of L results in net substitution, yielding the d^8 complex ML_3Y . The first step is typically rate determining. Thus, the entropy of activation is negative, which indicates an increase in order in the transition state. Associative reactions follow second order kinetics: the rate of the appearance of product depends on the concentration of both ML_4 and Y .



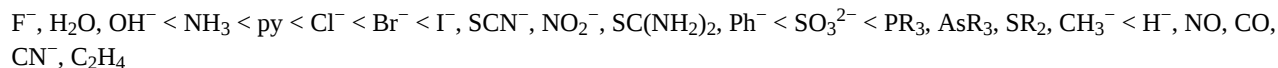
The Trans Effect, which is connected with the associative mechanism, controls the stereochemistry of certain ligand substitution reactions.

The trans effect refers to the labilization (making more reactive) of ligands that are **trans** to certain other ligands, the latter being referred to as **trans-directing ligands**. The labilization of trans ligands is attributed to electronic effects and is most notable in square planar complexes, but it can also be observed with octahedral complexes.^[18] The cis effect is most often observed in octahedral complexes.

In addition to the *kinetic trans effect*, trans ligands also have an influence on the ground state of the molecule, the most notable ones being bond lengths and stability. Some authors prefer the term **trans influence** to distinguish this from the kinetic effect,^[19] while others use more specific terms such as **structural trans effect** or **thermodynamic trans effect**.^[18]

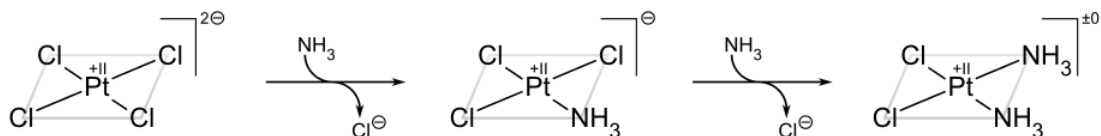
The discovery of the trans effect is attributed to Ilya Ilich Chernyaev,^[20] who recognized it and gave it a name in 1926.^[21]

The intensity of the trans effect (as measured by the increase in the rate of substitution of the trans ligand) follows this sequence:

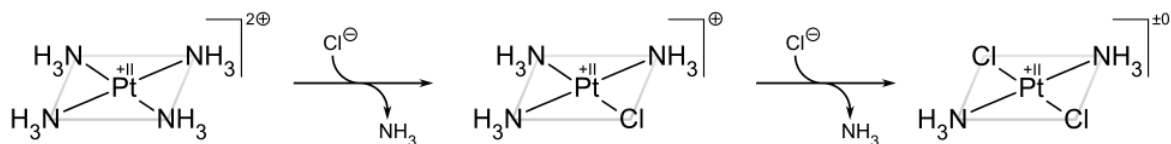


Note that weak field ligands tend to be poor trans-directing ligands, whereas strong field ligands are strongly trans-directing.

The classic example of the trans effect is the synthesis of cisplatin and its trans isomer.^[22] Starting from PtCl_4^{2-} , the first NH_3 ligand is added to any of the four equivalent positions at random. However, since Cl^- has a greater trans effect than NH_3 , the second NH_3 is added trans to a Cl^- and therefore cis to the first NH_3 .



If, on the other hand, one starts from $\text{Pt}(\text{NH}_3)_4^{2+}$, the *trans* product is obtained instead:

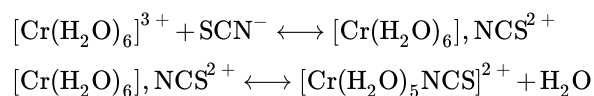


The trans effect in square complexes can be explained in terms of the associative mechanism, described above, which goes through a trigonal bipyramidal intermediate. Ligands with a high kinetic trans effect are in general those with high π acidity (as in the case of phosphines) or low-ligand lone-pair- d_π repulsions (as in the case of hydride), which prefer the more π -basic equatorial sites in the intermediate. The second equatorial position is occupied by the incoming ligand. The third and final equatorial site is occupied by the departing trans ligand, so the net result is that the kinetically favored product is the one in which the ligand trans to the one with the largest trans effect is eliminated.^[19]

- The **interchange mechanism** is similar to the associative and dissociative pathways, except that no distinct ML_nY or ML_{n-1} intermediate is formed. This concerted mechanism can be thought of as analogous to nucleophilic substitution via the $\text{S}_{\text{N}}2$ pathway at a tetrahedral carbon atom in organic chemistry. The interchange mechanism is further classified as associative (I_{a}) or dissociative (I_{d}) depending on the relative importance of M-Y and M-L bonding in the transition state. If the transition state is characterized by the formation of a strong M-Y bond, then the mechanism is I_{a} . Conversely, if weakening of the M-L bond is more important in reaching the transition state, then the mechanism is I_{d} .

An example of the I_{a} mechanism is the interchange of bulk and coordinated water in $[\text{V}(\text{H}_2\text{O})_6]^{2+}$. In contrast, the slightly more compact ion $[\text{Ni}(\text{H}_2\text{O})_6]^{2+}$ ion exchanges water via the I_{d} mechanism.^[23]

Effects of ion pairing. Highly charged cationic complexes tend to form ion pairs with anionic ligands, and these ion pairs often undergo reactions via the I_{a} pathway. The electrostatically held nucleophilic incoming ligand can exchange positions with a ligand in the first coordination sphere, resulting in net substitution. An illustrative process is the "anation" (reaction with an anion) of the chromium(III) hexaquo complex:



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