Topic IX

Reactions and Mechanisms

IX.1   Module 46: Ligand Substitution in Octahedral Complexes

3/8:
- Suggested reading: Chapter 12.

- Having learned about structure, isomerism, and electronic structure, let's now talk about reactivity.

- What makes transition metals unique is the reactions of the metal center (i.e., the first coordination sphere).

- **Substitution reaction**: A reaction where a ligand in the first coordination sphere is exchanged.

- Factors that affect the rate of substitution:

    - Role of the entering group.
    - Role of the leaving group.
    - Nature of the other ligands in the complex.
    - Effect of the metal center.

- Stable/unstable are thermodynamic terms, and labile/inert are kinetic terms.

    - $[Co(NH_3)_6]^{3+}$ is unstable but inert wrt. aquation (large K_{eq}, but slow to react).
    - $[Ni(CN)_4]^{2-}$ is stable but labile wrt. exchange (small K_{eq}, but equilibrium is established quickly).

- **Potential energy landscape**: A thermodynamic representation of a reaction by a (potentially multidimensional) potential energy surface along its reaction coordinate.

- Thermodynamics and kinetics are two different things, but they can be related.

- Potential energy landscapes with small ΔG and large ΔE_A are slow to react.

    - Increasing ΔG (perhaps by destabilizing the reactant) can speed up the reaction.
    - Increasing ΔG often occurs at the expense of ΔE_A (the activation energy literally decreases as the free energy change increases).

- Consider the reaction $[Co(NH_3)_5X]^{2+} + H_2O \longrightarrow [Co(NH_3)_5(H_2O)]^{3+} + X^-$.

    - The more bulky/less electronegative the X-type ligand, the higher the equilibrium constant and reaction rate.

- But how do we adequately compare different reactions when so many parameters are entangled together?

- One good way to compare kinetics of transition metals is with water exchange rate constants (light/heavy water being exchanged in metal coordination spheres), since this eliminates thermodynamic consternation.

  - There is massive variation among the metals.
  - The fastest (the alkali metals) run up against the **diffusion limit**.
  - Metals with larger atomic radii react more quickly (the alkali and alkaline earth metals follow this pattern nicely, but the transition metals are all over the place).
    - Group 1A: As we go down the group, the cations are getting larger and the charge density decreases, so the M^+-OH_2 bond is getting weaker and more easily broken.
    - Group 2A: The charge density is larger (doubly charged) so the strength of the bond is greater so the rate of exchange is slower.
  - We define such a reaction as having a labile half life if the half life is less than 1 minute; otherwise, it is inert.

- **Diffusion limit**: At most, one molecular collision can result in one successful reaction; thus, reaction rate is bounded above by how many molecular collisions can physically occur in a given period of time at a given temperature.

- You cannot prove mechanisms; you can only disprove other plausible scenarios.

- Possible mechanisms for $ML_5X + Y \longrightarrow ML_5Y + X$ where $X = H_2O$ and $Y =$ anion or vice versa:

- Associative (A): Via a 7-coordinate intermediate.

$$ML_5X + Y \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ML_5XY \tag{slow}$$

$$ML_5XY \xrightarrow{k_2} ML_5Y + X \tag{fast}$$

  - Corresponds to organic S_N2.
  - First step (RDS) is slow since the incoming Y causes steric hindrance.
  - The transition state is either a monocapped octahedron or pentagonal bipyramidal, depending on how the Y attacks.
  - Applying a steady-state approximation for $[ML_5XY]$, we have

$$\frac{d[ML_5XY]}{dt} = 0 = k_1[ML_5X][Y] - k_{-1}[ML_5XY] - k_2[ML_5XY]$$

  - We can solve the above equation for $[ML_5XY]$:

$$[ML_5XY] = \frac{k_1[ML_5X][Y]}{k_{-1} + k_2}$$

  - Substituting the above into the rate constant equation for the fast step will give us the rate law in terms of the reactants (where $k = \frac{k_1 k_2}{k_{-1} + k_2}$):

$$\text{Rate} = k_2[ML_5XY]$$
$$= \frac{k_1 k_2[ML_5X][Y]}{k_{-1} + k_2}$$
$$= k[ML_5X][Y]$$

  - Thus, the S_N2 mechanism is second-order overall, but first-order in both reactants.

- Dissociative (D): Via a 5-coordiinate intermediate.

$$\text{ML}_5\text{X} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{ML}_5 + \text{X} \tag{Slow}$$

$$\text{ML}_5 + \text{Y} \xrightarrow{k_2} \text{ML}_5\text{Y} \tag{Fast}$$

  – Corresponds to organic S_N1.
  – First step (RDS) is slow since its spontaneous elimination of a ligand.
  – The transition state is generally square pyramidal, but if it is sufficiently long-lived, it can reorganize itself into the trigonal bipyramidal state.
  – The dissociative mechanism predicts that the rate of the overall substitution reaction depends on only the concentration of the original complex $[\text{ML}_5\text{X}]$, and is independent of the concentration of the incoming ligand $[\text{Y}]$.
  – Thus, the overall rate law is
    $$\text{Rate} = k_1[\text{ML}_5\text{X}]$$
  – We can also derive this with an analogous kinetic analysis to that used for the A mechanism, the only difference being that we simplify $\frac{k_1 k_2 [\text{ML}_5\text{X}][\text{Y}]}{k_{-1}[\text{X}] + k_2[\text{Y}]}$ to the rate law by noting that $k_2 >> k_{-1}$ or $[\text{Y}] >> [\text{X}]$.

- Interchange (I): As Y begins to bond, X begins to leave, i.e., the bond making to Y and bond breaking to X occur simultaneously.

$$\text{ML}_5\text{X} + \text{Y} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{ML}_5\text{X} \cdot \text{Y} \tag{Slow}$$

$$\text{ML}_5\text{X} \cdot \text{Y} \xrightarrow{k_2} \text{ML}_5\text{Y} + \text{X} \tag{Fast}$$

  – Corresponds to organic SN_2.
  – This is how the majority of ligand substitutions occur.
  – It is too simplistic to assume that a first-order rate law implies D and a second-order rate law implies A. Indeed, most substitution reactions probably involve a mechanism like this, i.e., one that is intermediate between these two extremes.
  – In an interchange mechanism, the intermediate involves an association between the original ML_5X complex and the attacking Y ligand. The Y ligand remains outside the coordination sphere of ML_5X, unlike the S_N2 mechanism, so the intermediate is not seven coordinate. However, it can help weaken the $\text{M}-\text{X}$ bond.
  – Assuming high $[\text{Y}] \approx [\text{Y}]_0$, it can be shown that the rate is given by
    $$\text{Rate} = \frac{k_2 K_1 [\text{M}]_0 [\text{Y}]_0}{1 + K_1 [\text{Y}]_0}$$
    where $[\text{M}]_0 = [\text{ML}_5\text{X}]_0 + [\text{ML}_5\text{X} \cdot \text{Y}]$ and $[\text{Y}]_0$ are initial conditions and $K_1 = \frac{k_1}{k_{-1}}$ is the equilibrium constant for the RDS reaction.
    - At high $[\text{Y}]$ and $K_1[\text{Y}]_0 >> 1$, the rate is first-order in $[\text{M}]_0 \approx [\text{ML}_5\text{X}]$.
    - At lower $[\text{Y}]$, the rate is second order.

- At some point, the kinetic analysis becomes essentially worthless. Indeed, although we speak generally about associative and disassociative reaction mechanisms, the terms A and D are reserved for situations where 7- and 5-coordinate intermediates have actually been isolated and positively identified. If no intermediates have been isolated or identified, the designations I_d and I_a are more appropriate.

  – Two minor variations on the I mechanism are I_d (dissociative interchange) and I_a (associative interchange).

- If breaking the M−X bond is more important, the mechanism is I_d.
- If bond formation between ML_5X and Y is significant, the mechanism is I_a.
- The difference between I_d and I_a is subtle and does not necessarily correspond to whether the observed rate law is first or second order.
- If the rates of a series of comparable substitution reactions are most sensitive to the identity of X, the leaving ligand, then the mechanism is more probably I_d, and vice versa for I_a.
- For example, the rate constants for the anation of $[Cr(NH_3)_5(H_2O)]^{3+}$ by various ligands vary very little. Thus, it is probably I_d. However, the rate constants for the anation of $[Cr(H_2O)_6]^{3+}$ by various ligands vary by three orders of magnitude. Thus, it is probably I_a.

- Solvent (e.g., water) effects in substitution reactions:

  - Many substitution reactions occurring in solvent water may have first-order kinetics regardless of whether their initial steps are primarily D or A.
  - For example, this occurs if aquation is a precursor RDS.
  - If D, Rate $= k[ML_5X]$.
  - If A, Rate $= k[ML_5X][H_2O] = k'[ML_5X]$.
    - ■ The latter equality is valid since water has constant concentration[1].
  - Both mechanisms lead to apparent first-order kinetics.

- Steric factors favoring D or I_d:

  - For most octahedral complexes, steric factors inhibit formation of a CN7 intermediate, which suggests a dissociative mechanism (D or I_d) is more plausible.
    - ■ Even cases showing second-order kinetics may not be A for this reason.
  - For example, aquation of ammine-halides is second order with a first-order dependence on [OH−].
  - If $k_2 >> k_1$, the rate is approximately Rate $= k_2[Co(NH_3)_5X]^{2+}[OH−]$.
  - Calls for an alternate mechanism called S_N1CB, where ligands with lower energy bond as <u>c</u>onjugate <u>b</u>ases and those with higher Δ_0 (hence CB).

- Kinetically analyzes S_N1CB.

IX.2   Module 47: Substitution and Ligand Field Stabilization Energy

3/10:
- Factors that affect the rate of substitution:

  1. Role of the entering group.
  2. Role of the leaving group.
  3. The nature of the other ligands in the complex.
  4. Effect of the metal center.

- Six factors that support a dissociative mechanism:

  1. The rate of reaction only slightly (within a factor of 10) changes on the incoming ligand.
     - Means that the ligand is not significantly involved in the RDS.
  2. Making the charge on complex more positive decreases the rate of substitution.

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[1]Is this what we meant when we said in Labalme (2020) that liquids and solids don't have active mass? In other words, the species should be included in the mass-action expression; they just simply get lumped in with the rate constant generally.

  – Increasing the charge increases the bond strength, making it harder for one ligand to spontaneously break away.

3. Steric crowding increases reaction rate.

4. The volume of activation is positive and reaction rate decreases at high pressure.

  – Especially if the reactant is a gas, for example.

5. Reaction rate correlates with Ligand Field Activation Energy (LFAE) predictions.

6. Stereochemistry can give additional hints.

  – A messy subject unless you use very well crafted multidentate ligands.

- Simple changes in oxidation state can have massive effects on water exchange rate constants[2] (e.g., Cr^{2+} to Cr^{3+} results in a shift of 15 orders of magnitude).

- Variations in complex reactivity:

  – Most first row transition metals are labile[3], but Cr^{3+} (d^3, $S = \frac{3}{2}$) and low-spin Co^{3+} (d^6, $S = 0$) are usually inert.

  – d^7-d^{10}, with filling of e_g^* levels, are labile.

    ■ These configurations tend to have large Jahn-Teller distortions and/or low CFSEs.
    ■ d^7, d^9, and d^{10} cases are more labile than d^8.
    ■ d^8 has a $^3A_{2g}$ ground state, which is immune to Jahn-Teller distortion.
    ■ With strong-field ligands, d^8 may be square planar, often being inert.

  – Inert octahedral complexes tend to be those with high CFSE; viz., d^3 low-spin d^4-d^6.

    ■ ML_6 complexes of both d^3 ($^4A_{2g}$) and low-spin d^6 ($^1A_{1g}$) are immune from Jahn-Teller distortions and therefore can be perfect O_h.
    ■ ML_6 d^3 has CFSE $= -\frac{6}{5}\Delta_o$ and low-spin d^6 has CFSE $= -\frac{12}{5}\Delta_o + 3P$.

- The most inert complexes among the first row transition metals:

  – Co^{3+} is primarily dissociative, but with dependence on the incoming ligand I_d.

  – Cr^{3+} has a dimorphism where it can be I_d or I_a!

    ■ For example, it is I_d in the complex $[Cr(NH_3)_5(H_2O)]^{3+}$ but I_a in the complex $[Cr(H_2O)_6]^{3+}$.

- Water exchange rate constants are greatest for Jahn-Teller distorted species.

  – They are smallest for $d^{3,5,8}$.

- Variations in complex reality: Explained by the potential energy landscape for a substitution reaction $ML_6 \longrightarrow ML_5Y$:

  – O_h to C_{4v} to "O_h."

  – The activated complex is square pyramidal.

  – We can now use the AOM to calculate the LFSE in both the initial O_h state and the transition C_{4v} state.

    ■ The difference between them will be the **ligand field activation energy** or **LFAE**. The LFAE is not particularly useful because it predicts negative activation energies, which are not a thing, but it does allow us to rationalize reactivity trends.
    ■ If LFAE ≤ 0, the reaction is labile; otherwise, it is moderate or slow.

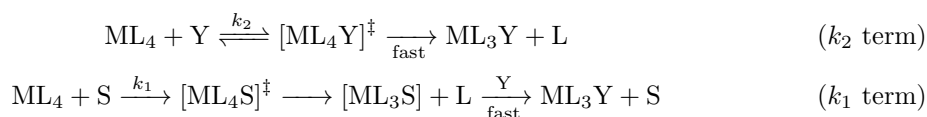[2]We pronounce the units of rate constants, "reciprocal seconds."
[3]Werner was only able to make his conclusions about coordination chemistry because he happened to be working with the relatively inert Co^{3+} complexes.

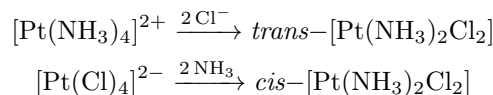# IX.3 Module 48: Ligand Substitution in Square Planar Complexes

- Although steric factors favor D-type mechanisms for octahedral complexes, square planar ML_4 complexes are not so inhibited.

  - For square planar ML_4 complexes, an associative (A) mechanism, in which a coordination number 5 (CN5) intermediate is formed, is plausible.

- The d^8 metals are especially likely to form square planar complexes.

- Substitution of square planar complexes, such as $PtLX_3$, leads to *trans* and *cis* isomers.

- The rate law is
$$\text{Rate} = k_1[PtLX_3] + k_2[PtLX_3][Y^-]$$

  - Suggests two paths, where the first term may be pseudo-first-order due to excess solvent acting as an attacking group.

- If we make L bulkier, we would expect the D pathway to dominate (k_1 increases, k_2 decreases).

- However, both k_1 and k_2 decrease with increasingly bulky ligands, suggesting an associative mechanism:

$$ML_4 + Y \underset{}{\overset{k_2}{\rightleftharpoons}} [ML_4Y]^{\ddagger} \xrightarrow[\text{fast}]{} ML_3Y + L \qquad\qquad (k_2 \text{ term})$$

$$ML_4 + S \xrightarrow{k_1} [ML_4S]^{\ddagger} \longrightarrow [ML_3S] + L \xrightarrow[\text{fast}]{Y} ML_3Y + S \qquad\qquad (k_1 \text{ term})$$

  - S means the solvent.
  - Since $[S] >> [ML_4]$, we see pseudo-first order kinetics in the k_1 term in the rate law.

- In square planar complexes, d-orbital splitting yields a $d_{x^2-y^2}$ LUMO.

  - However, it points exactly toward the ligands, so you cannot fill it without displacing a ligand.
  - Indeed, since ligands cannot attack it, they instead attack the higher-lying metal p_z orbital.

- Note that the stereochemistry stays the same under these reactions.

- An example of the trans effect:

$$[Pt(NH_3)_4]^{2+} \xrightarrow{2\,Cl^-} trans-[Pt(NH_3)_2Cl_2]$$

$$[Pt(Cl)_4]^{2-} \xrightarrow{2\,NH_3} cis-[Pt(NH_3)_2Cl_2]$$

  - The first ligand takes any of the four spots, but the second substitutes opposite the stronger *trans*-directing ligand.
  - In the above example, chloride is a stronger *trans*-directing ligand than amine groups.

- The trans effect:

  - The ratio of *trans* and *cis* isomers is found to vary with the ability of L to acct as a *trans*-directing ligand.
  - The increasing order of *trans*-directing ability is

    $$H_2O < OH^- < py \approx NH_3 < Cl^- < Br^- < I^- < NO_2{}^- < PR_3 \approx SH_2 << CO \approx C_2H_4 \approx CN^-$$
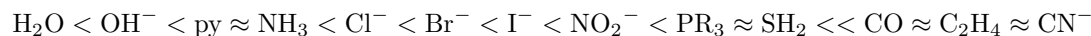
    - This ranking comes from a combination of the following two factors.
  - The effect is kinetic rather than thermodynamic.

- Two factors explain the trans effect (both aim at lowering $\Delta G^{\ddagger}$):

  1. Weakening of the Pt$-$X bond *trans* to the directing ligand (σ-donor effects).
     - Destabilizes the ground state of the reactants.
     - Pt$-$A is influenced by *trans*-Pt$-$T bond because both share Pt p_x and $d_{x^2-y^2}$ orbitals. When the Pt$-$T bond is strong, electron density on those orbitals is shifted away from the Pt$-$A bond.
     - The more polarizable the L ligand, the better *trans*-director it is; e.g., $I^- > Br^- > Cl^-$.
       - ■ The *trans*-directing ligand polarizes the metal ion, inducing a slight repulsion with the negative electron density on the leaving ligand in the *trans*-position.
     - For example, the Pt$-$Cl bond is longer in in *cis*-[Pt(PMe$_3$)$_2$(Cl)$_2$] than in the *trans* form because the stronger σ-donor ability of PMe$_3$ weakens the opposite Pt$-$Cl bond in the *cis* form.

  2. Stabilization of the presumed CN5 intermediate (π-acceptor effects).
     - Stabilizes the activated complex.
     - The strongest *trans*-directors are good π-acceptor ligands.
     - Assuming an A mechanism, substitution involves a trigonal bipyramidal transition state.
     - The *trans* intermediate (activated complex) is more favorable for π-acceptor ligands because it permits π-delocalization in the trigonal plane.
       - ■ When the T-ligand engages in a strong π-backbonding, charge is removed from Pt, making the metal center more electrophilic and stabilizing the TBP intermediate.

- The trans effect has applications to synthesis (synthesizing *cis* versus *trans* square planar compounds).

  - For example, *cis*-[Pt(NH$_3$)$_2$(Cl)$_2$] is cisplatin, the first anti-cancer drug.