Unit 4

More Catalytic Processes

4.1 Lecture 15: Nitrogen Fixation

5/3:

- General form:

$$N_2 + 6\,H^+ + 6\,e^- \longrightarrow 2\,NH_3$$

  - Alternatively, it could be $N_2 + 3\,H_2 \longrightarrow 2\,NH_3$.
  - A simple reaction on paper, but in practice and mechanistically, very difficult.

- Nitrogen is one of the essential elements for life (CHNOPS), but we can't absorb it from the air in its elemental form as N≡N gas. Indeed, we need it to be **fixed** before we can incorporate it (i.e., through food sources).

- Main pathways:

  - Lightning.

$$N_2 + O_2 \xrightarrow{h\nu} NO, {NO_2}^-, {NO_3}^-$$

    - 4-10 million tons per year.
    - Nitrate can be used by organisms; converted into useful nitrogen.

  - Natural enzymatic fixation.

    - 100-300 million tons per year (probably closer to the 100 side).
    - 40/60 ocean/land ratio.
    - Done by the enzyme nitrogenase, with FeMoCO[1] as a cofactor.

  - Mankind.

    - About 190 million tons per year.
    - Thus, mankind is currently fixing more nitrogen than all natural sources combined by a fair amount right now. This is what allows us to feed the planet at its current population.
    - Accomplished by the **Haber-Bosch process**.

- **Haber-Bosch process**: Humanity's primary method of fixing nitrogen.

$$N_2 + 3\,H_2 \underset{\text{Fe/Mg}}{\overset{\Delta, P}{\rightleftharpoons}} 2\,NH_3$$

  - -92 kcal/mol (thermodynamically favored but kinetically difficult).
  - 200 atm of pressure (pushes the equilibrium to the right via Le Châtelier's principle).

[1] Literally pronounced as its written, i.e., "fih-MOH-koh."

  - 400 °C (required for the rate).
  - Potassium is an activator.

- 2 Nobel prizes for this: Fritz Haber (1918) and Carl Bosch (1931).
  - Controversial at the time because the process facilitated the explosives industry and Haber was a Nazi.
  - World War I and II would not have been sustainable for Germany without this process.

- Mechanism:
  - On the surface of the iron catalyst, the pressure binds H_2 gas as hydrides and N_2 gas as bridging nitrides (between various iron atoms at the surface). It follows in a statistical and thermodynamic manner that amine ligands will be formed on the surface attached to the iron. These can then break off into ammonia gas.
  - A solid state heterogeneous process.
  - Nobel Prize (2007) to Gerhard Ertl for this mechanism.

- This process is highly efficient, but very energy intensive as well.
  - As such, there is a race to find a less energy-intensive catalytic alternative.

- Molecular systems: The nitrogenase enzyme.

$$N_2 + 8\,H^+ + 8\,e^- \xrightarrow{ATP} 2\,NH_3 + H_2$$

  - Other extant cofactors include FeVCO and FeFeCO, but they are less common.
  - Since ATP is used, this is still a very energy-intensive process.
  - N_2 bonds to metal centers in many ways:
    - Linear, bent, side-on, bridging linear, bridging side-on, multi-metal center bridging, etc.
  - N_2 complexes are much less common than CO complexes since N_2 is a terrible ligand.
    - The HOMO in N_2 makes it a σ donor, but CO's negative formal charge on the carbon makes it a better σ donor.
    - Additionally, CO is a much better π acid due to its polarization.

- Allen and Senoff (in 1965) reported the first dinitrogen complex.

$$RuCl_3 \cdot 3\,H_2O + N_2H_4 \cdot H_2O \longrightarrow [Ru^{II}(N_2)(NH_3)_5]^{2+}[Cl_2]^{2-}$$

  - N_2H_4 is hydrazine (rocket fuel), and is much more stable as a hydrate.
  - The product is d^6 with 18 e^- and has $\mu_{N_2} = 2170\text{-}2115\,cm^{-1}$ (the range depends on the anion).
  - For reference, free N_2 has a stretching frequency of $2331\,cm^{-1}$.

- Yamamoto gives the first example of a dinitrogen complex formed from free N_2 ($HCo(PPh_3)_3(N_2)$).

- Joe Chatz, George Leigh, and Dilworth in Sussex (of the British/American camp), and Hidai and Nishibayashi (of the Japanese camp) became interested in nitrogen fixation following Yamamoto's work.
  - Second and third row Group 6 complexes such as molybdenum were the focus.
  - Example: $MoX_4L_2 \xrightarrow[Na/Hg]{N_2,\,L} Mo(N_2)_2L_4$.
    - L is typically a phosphine.
    - With various phosphine ligands, you can get different geometries.

  - Another example: *cis*−$W(N_2)_2(PMe_2Ph)_4$ $\xrightarrow[MeOH]{H_2SO_4}$ $2\,NH_3 + N_2 + W^{VI}$(oxo).
    - Works with molybdenum, too, but tungsten gives a better yield.
    - The overall reaction is $W^0 + 6\,H^+ + N_2 \longrightarrow 2\,NH_3 + W^{VI}$.
    - Some important subreactions/steps are $N_2 + 4\,e^- \longrightarrow N_2H_4$ and $N_2 + 2\,e^- \longrightarrow N_2H_2$.

- Mechanism (by Chatt):

$$\begin{aligned} M{-}N_2 &\xrightarrow{H^+} M{-}N{=}N{-}H \\ &\xrightarrow{H^+} M{\equiv}N{-}NH_2 \\ &\xrightarrow{H^+} M(PR_3)_4(Cl)(\equiv N{-}NH_3) \\ &\xrightarrow[-NH_3]{} M{\equiv}N \\ &\xrightarrow{H^+} M{=}NH \\ &\xrightarrow{H^+} M{-}NH_2 \\ &\xrightarrow[-NH_3]{H^+} M^{6+} \end{aligned}$$

  - Very few compounds in the form of the first intermediate (diazene) are known. These compounds are very susceptible to β-H elimination from water, though.
  - The second intermediate has a hydrazido ligand.
  - The fourth intermediate has a nitride.
  - The fifth intermediate has an imide.
  - The sixth intermediate has an amide ligand.

- Hidai uses silanes: $M(N_2)_2(PR_3)_4 \xrightarrow{TMSI}$ TMS−N=N−$MI(PR_3)_4$ $\xrightarrow[N_2]{Na,\,THF}$ $M(N_2)_2(PR_3)_4 + NH(TMS)_2 + NH_3 + NaNH_2 + NaNH(TMS)$, etc.

- Yandulov and Schrock (2003) creates a well-defined catalyst for nitrogen fixation.

  - The catalyst is molybdenum bound to dinitrogen and a tridentate TREN scaffold anion (with hexaisopropal *tert*-phenyl (HIPT) aryl groups).
  - They add eight equivalents of cobaltocene ($CoCp_2$), seven equivalents of lutidinium (a pyridinium acid), and the bulky, noncoordinating counteranion $[BAr^F{}_4]^-$.
  - They fish out Mo−NH_3 + NH_3. Reducing the former product gives $Mo^{III}(N_2)$ with a weak reductant.
    - If you use a slightly stronger reductant (decamethylchromocene; $CrCp^*_2$) and a slow addition of acid, you get approximately 8 turnovers.
  - This is not a great yield, but the important part is that it exists and they can observe all of the intermediates.
    - Observing said intermediates verified the mechanism proposed by Chatt and Hidai.
  - To reiterate, this is the Chatt/Distal[2] cycle they observed: Mo−N≡N $\xrightarrow{H^+,\,e^-}$ M−N=N−H $\xrightarrow{H^+,\,e^-}$ M≡N−NH_2 $\xrightarrow{H^+,\,e^-}$ M≡N $\xrightarrow{H^+,\,e^-}$ M≡NH $\xrightarrow{H^+,\,e^-}$ M−NH_2 $\xrightarrow[-NH_3]{H^+,\,e\text{-},\,N_2}$ Mo−N≡N.
    - Note that molybdenum starts in the 3+ oxidation state at M−N≡N and goes up to 6+ at Mo≡N before cycling back down.

- Shilov had a number of systems, but they were poorly defined.

[2]Note that Chatt and Distal are interchangeable synonyms.

- Other selected examples.
  - Zirconium can do this catalysis in some cases.
  - Laplaza and Cummins (1995) find that molybdenum trisannelides and dinitrogen can go through a kinked transition state to yield two equivalents of $L_3Mo{\equiv}N$.
- Iron:
  - Present in all enzymatic cofactors that mediate nitrogen fixation.
    - Until 10-15 years ago, they thought it wasn't directly involved though.
  - $(PR_3)_4Fe(N_2) \xrightarrow{XS\ H^+}$ only trace amounts of NH_3.
  - Yuki et al. (2012) finds that simple iron salts and even substituted ferrocenes react with a strong reductant, sodium, and TMSCl to make $N(TMS)_3$ (which is catalytic and can be transformed into ammonia). The yield is about 25 equivalents per iron.
    - This shows that iron can do this chemistry.
  - Dr. Anderson's thesis work with Jonas Peters finds that $Fe(N_2)(B(PR_2Ph)_3) \xrightarrow[XS\ HBAr^F{}_4]{XS\ KC_8} NH_3$[3] (Anderson et al., 2013).
    - Seven equivalents per iron. More recent tinkering has brought it up to nearly 100 equivalents per iron.
    - Mechanism: $L_3FeN_2{}^- \xrightarrow{2\,H^+} L_3Fe{\equiv}N{-}NH_2{}^+ \longrightarrow \longrightarrow \longrightarrow NH_3$.
    - Suggests a Chatt/Distal mechanism.
  - Differing mechanistic proposal: Alternating mechanism.

$$
\begin{aligned}
Fe{-}N_2 &\xrightarrow{H^+,\,e^-} Fe{=}N{=}N{-}H \\
&\xrightarrow{H^+,\,e^-} Fe{-}NH{=}N{-}H \\
&\xrightarrow{H^+,\,e^-} Fe{-}NH{-}NH_2 \\
&\xrightarrow{H^+,\,e^-} Fe{-}NH_2{-}NH_2 \\
&\xrightarrow[-NH_3]{H^+,\,e^-} Fe{-}NH_2 \\
&\xrightarrow[-NH_3]{H^+,\,e\text{-},\,N_2} Fe{-}N_2
\end{aligned}
$$

    - This doesn't require as many oxidation states as the Chatt mechanism (which favors iron, which doesn't easily form oxidation states other than 2+ and 3+).
    - We also don't see a nitride or imide intermediate, but we do see a diazene, hydrazido 1−, and hydrazine adducts.
    - Enzyme data supports this mechanism.

4.2 Office Hours (Anderson)

- How much strain is needed for ROMP to proceed?
  - Norbornene is a common one.
  - 4 membered rings.
  - 7- and 8-membered rings are usually not sufficiently strained.

[3] Note that the reactant is the same compound discussed in problem 3 of Homework 1.

  - Cyclopropene does exist, and it does do ROMP, but it polymerizes so quickly that you can't do much with it.
    - If it's cold and you throw in a metathesis catalyst, it will probably work.
    - Recall that it also participates in Diels-Alder reactions.

- ROMP does *not* release ethylene.
  - Ring strain is the driving force.
  - Part (d) is a typo; ethylene gas is the common byproduct of *most* of these reactions. We should still show ROMP as is.

- How do metal d orbitals enable $2+2$ cycloaddition?
  - Butadiene plus ethylene requires ethylene to have filled π^* orbitals (these have the appropriate symmetry).
    - Diels-Alder $4+2$ cycloaddition is allowed.
  - The symmetry of the metal orbitals (esp. d_{z^2} and d_{xy}) enables $2+2$ cycloaddition.

- η and κ bonding?
  - IUPAC likes κ more now, but η is historical.
  - η indicates a continguous π system while κ simply indicates denticity.
  - Figure 2.23a is κ^2 as well.
  - Bidentate ligands bond in a κ^2 fashion.
  - Numbers on these as well as μ should exclusively be superscripts.
  - A metal bound face-on to a carboxylate would be η^3, but this is very atypical/nontexistent bonding. Side-on bonding (i.e., to both oxygens) would be κ^2.

4.3 Discussion Section

5/4:

- Midterm 2 is 5/25/2021.
- Final paper due 5/26/2021; Sophie has asked Dr. Anderson for more information.
  - Due at noon.
  - Sophie will post an example paper.
  - As the last assignment for this course, you will write a critical review of 1 of 6 availabble papers.
  - Some of these papers include material outside the scope of organometallic chemistry. Try to focus on topics relevant to this course. The reviews should be no longer than 700 words not including citations or fiugre captions, althouggh additional ccitations are not requried if you only use information presented in the paper or the class. The critique should be written with Times New Roman 12 point font and 0.5 inch margins.
  - General outline fofr the critiques:
    - 1 introduction paragraph.
    - 2 experimental summary paragraphs.
    - 3 discussion paragraphs.
    - 4 critique paragraphs.
    - Figures.
  - Sophie is willing to look over assignments (email them to her), but we have to get them to her by the 19th for her to take a look.
  - They should be professional but not excessively formal.

  - A more detailed outline will be published later.
  - A critique isn't necessarily a flaw, but more a suggestion of another experiment they could run or some other conclusion they could have drawn.
- Final is 6/3/2021.
- Midterm 1:
  - Biggest issues:
    - Running out of time.
    - Omitting parts of answers (generally not reading instructions in general). If it says draw orbitals, explain, or predict, you need to do that.
  - She'll talk to John about making it/the next one shorter.
  - Syntheses are only one point?
  - If we would like to know more feedback about our exams, we can reach out with specific questions about questions.
  - 1a: Reduce with Na or Hg metal and then throw in MeI. $\frac{1}{2}\,Mn_2(CO)_{10} \xrightarrow[-2\,NaCl]{Na/Hg} Na[Mn(CO)_5] \xrightarrow[-NaI]{MeI}$.
  - 3a: Like-signed lobes donate (*correct notes?*). You can also show either $d_{x^2-y^2}$ or d_{z^2} for σ donation.
  - 3b: We need charges on the metal in $M{-}C{\equiv}O^+$ resonance structures (-, 0, +).
  - 3c: Also identify the dominant resonance structure.
  - 4c: Cp can ring-slip to stabilize the electron count.
  - 4d: Cone angle starts at metal center and includes specifically the full van der Waals radii of the phosphine R groups at the base fo the cone. Most commonly forgotten: metal center, van der Waals radii.
  - 4f: H_2CrO_4 is Cr^{6+}, d^0, while $Cr(CO)_4{}^{4-}$ is Cr^{4-}, d^{10}. The difference is different than you expect because they are actually very similar.
  - 5: First, backcalcculate out spin-state to determine $S = 1$ and $S = 0$. Second, luckily, they're 4-coordinate, so the simplest solutin is to loook for two geometries that ggive the two spin states. You interconvert the things in solution, giving a mixed magnetic moment. $\mu = 2\sqrt{S(S+1)}$.
  - 6: Cp^- is a π donor. Cyclobutadiene is both (the orbital drawing shows that you have a HOMO π donor and a LUMO π acceptor).
  - 7: No extra sites for a better bridge and only bad bridges present (if you draw them you can tell). Whenever you need to compare two ligands, think:
    1. Chelate? Neither ligand.
    2. Hard/soft affinity? Both hard.
    3. Strong field? Isocyanide much stronger, more likely all low spin.
    4. Trans effect? All the same ligand.

4.4 Lecture 16: Hydrogenation

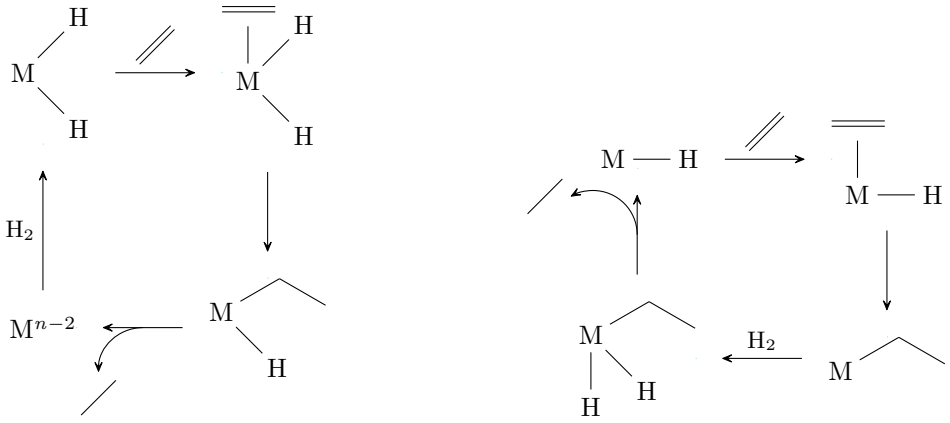
5/5:

- Nobel prize (2001) to Knowles and Noyori, but could have gone to Jack Halpern.
  - A hugely important reaction.
- General form:

$$Y{=}X + H_2 \xrightarrow{cat} H{-}Y{-}X{-}H$$

- Both reagents are activated by the catalyst.

- The chemo, regio, and stereo selectivity has been determined for many of the mechanisms.
- History:
  - Melvin Calvin reports the first hydrogenation reaction in 1938.
    - Iguchi also studied rhodium-amine complexes around the same time.
  - Wilkinson discovers Wilkinson's catalyst ($Rh(PPh_3)_3Cl$) in the 1960s and does other foundational research in this area.
    - Halpern figures out the mechanism by which Wilkinson's catalyst works.
  - Knowles and Noyori: Developed asymmetric hydrogenations.
- Wilkinson's catalyst:
  - Two methods of synthesizing it are given.
- Mechanism (for generic catalyzed hydrogenation):



(a) Dihydride mechanism. (b) Monohydride mechanism.

Figure 4.1: Hydrogenation mechanisms.

- Reactivity trends (for Wilkinson's catalyst):
  - Rates of hydrogenation for olefins: Cyclic > terminal > doubly substituted > *cis* > *trans* > triply substituted.
    - This trend can be utilized for **chemo selectivity**.
  - No reactivity with esters or arenes.
- **Chemo selectivity**: The selective hydrogenation of olefins that more readily hydrogenate in a poly-olefin compound.
  - In other words, chemo selectivity relies on the principle that in a compound with multiple types of double bonds, the ones with higher rates will be selectively hydrogenated first.
- Mechanism (for hydrogenation catalyzed by Wilkinson's catalyst):

$$L_3RhCl \underset{L}{\overset{\text{solvent}}{\rightleftharpoons}} L_2(sol)RhCl \overset{H_2}{\rightleftharpoons} L_2(sol)RhClH_2 \overset{||}{\rightleftharpoons} L_2(||)RhClH_2 \longrightarrow L_2(sol)RhClHEt \xrightarrow[-Et,\,sol]{L} L_3RhCl$$

  - Worked out by Jack Halpern
  - No scrambling of H_2/D_2 (you only observe products with two H's added, and products with two D's added; there are no products with an H *and* a D added).

  - No scrambling with solvent.
  - The above two observations suggest a dihydride mechanism.
  - Note that the solvent is either an alcohol or acetonitrile (MeCN).
  - Note that the step with no new reactants is the turnover limiting step (it is drawn with a monodirectional arrow because it is virtually irreversible).
- Catalyst optimization:
  - Cationic Rh complexes react much faster (e.g., $[RhL_2H_2(sol)_2]^+$).
    - In effect, removing the chloride generates a noncoordinating countercation, which is much more reactive.
  - If you use iridium instead, it's Crabtree's catalyst: $[Ir(COD)(PCCh_3)(py)]^+[PF_6]^-$.
- Compares rates of derivatives of Crabtree's and Wilkinson's catalyst at various temperatures in noncoordinating solvents.
  - We use noncoordinating solvents such as arenes because solvent-binding is a step in some mechanisms, and thus affects the rate.
  - Some variations have significantly less reactivity for cyclic olefins than Wilkinson's catalyst.
  - Conclusion: By making slight changes to the ligands and metal center, you can finely tune the activity of these catalysts to do the type of hydrogenation you want (regioselectivity).
- Directed hydrogenation.
  - We can use solvent binding to dictate the selectivity of a certain hydrogenation.
  - If we have a cyclic substrate with a coordinating ligand above one face, the catalyst can coordinate to that ligand and perform the hydrogenation from that face, heavily favoring a certain stereochemistry in the product.
  - Note that other ligands can affect the extent of substrate coordination.
- Other mechanistic details[4].
  1. The species you observe (the resting state of the catalyst) may not be on the active catalytic pathway.
  2. To deduce the mechanism, the rates of the individual steps should be determined (recall kinetic competence).
- Noyori's bifunctional catalysis (heavily related to Figure 4.3).
- σ-bond metathesis:

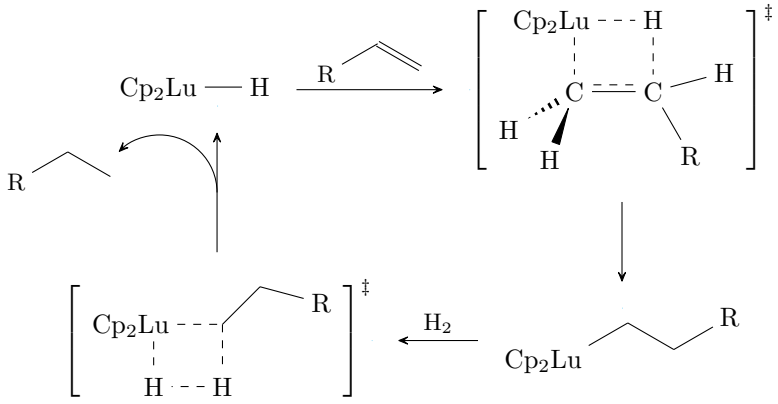


Figure 4.2: Hydrogenation by σ-bond metathesis.

[4]An important process is listed, possibly to be returned to later.

  - This mechanism proceeds through two consecutive σ-bond metatheses.
  - Note the use of an early transition metal (lutetium), 4-membered transition states, and the open coordination site (refer to Lecture 7 for the more on the characteristics of σ-bond metathesis).

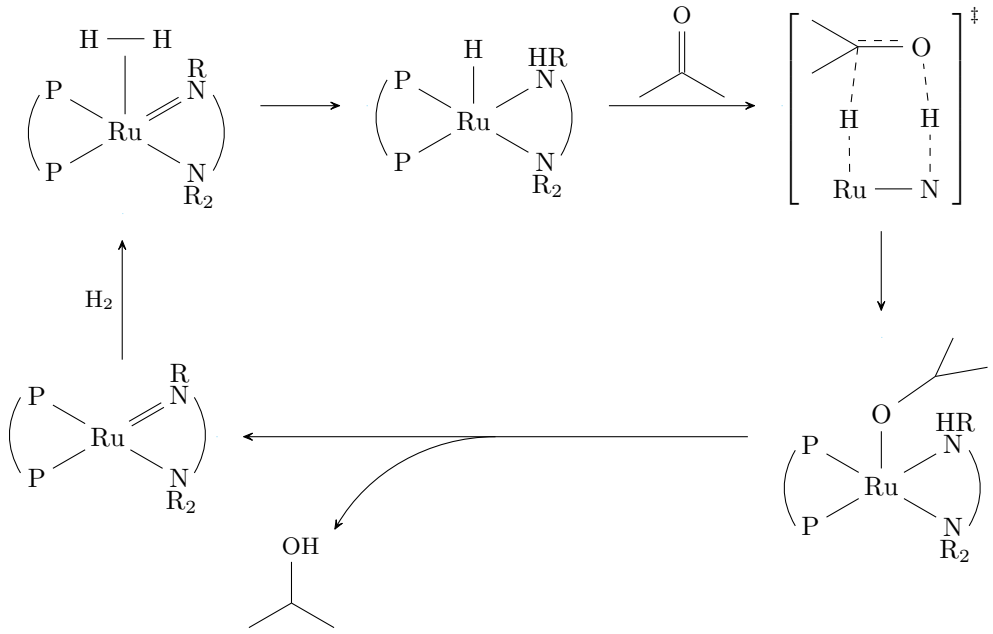
- When catalyzed, the mechanism can be more complicated.
  - There can be nearly innumerably many offshoots.
  - There may only be one on-cycle chain among all of the intermediates. The question is just how to favor this one.

- Radical hydrogenation.

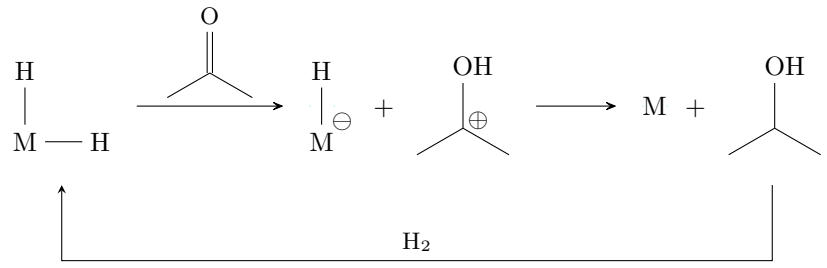
$$L_nM{-}H + Ph{-}{=} \longrightarrow L_nM\cdot + Ph{-}\cdot{=} \longrightarrow L_nM{-}CHMePh \xrightarrow{H_2} \longrightarrow L_nM{-}H + Ph{-}{-}$$

  - This can happen with porphyrins and $HMn(CO)_5$.

- Noyori's catalyst:



(a) Regular.



(b) Ionic.

Figure 4.3: Noyori's catalyst mechanism.

  - Partially reacts via a bifunctional mechanism, but primarily engages in a different mechanistic paradigm called an outer sphere hydrogenation (see Figure 4.3a).

  - In the extreme, we can achieve an ionic pathway (see Figure 4.3b).
    - An example of a substance that does this is $CpW(CO)_2(PPh_3)(OCEt_2)^+$.

- Asymmetric catalysis:
  - At this point in time, hydrogenation is a highly optimized reaction.
    - We can generate catalysts with millions of turnover numbers, very high ee's, etc.
    - Indeed, hydrogenation is one of the most reliable late-stage steps in drug development or natural product synthesis to define chiral centers.
  - Chiral phosphines really shine here.
  - Binap, biphenyl scaffolds with sufficiently large R groups, tri-chicken foot phos, ferrocene derivatives (e.g., chiral dppf derivatives), alkyl backbones (e.g., DIOP), etc.
  - One enantionmer is often bound over the other.

- Transfer hydrogenations:

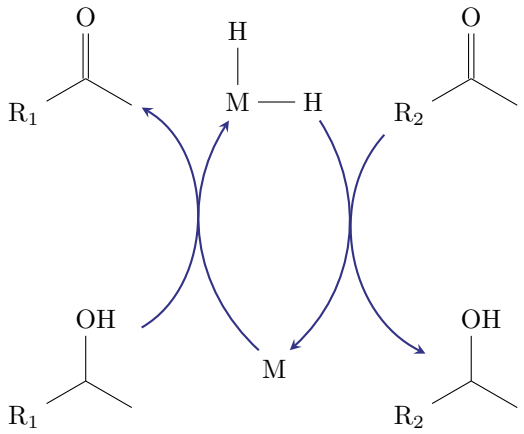


Figure 4.4: Transfer hydrogenation mechanism.

  - Use these if you don't want to use hydrogen gas, e.g., because it's flammable.
  - Basically, we use a transition metal catalyst to transfer two hydrogens (e.g., from an alcohol to a ketone) by means of gaining them to become a dihydride and losing them to return to being just a metal center.
  - As in any hydrogenation reaction, these are all reversible reactions. As such, since we can't use excess hydrogen to push the reaction, we must rely on the electron richness of the alcohol (electron rich alcohols dehydrogenate more easily).
  - The equilibrium can be pushed with Le Châtelier's principle, but we mainly have to consider thermodynamics here (the thermodynamics must be favorable).
    - For example, if $R_2 = Ar$, then we will transform the aryl ketone into an alcohol, but not in reverse (because the aryl is electron deficient and thus its alcohol does not dehydrogenate easily).

- Halpern's contributions to asymmetric catalysis:
  - Reviews some papers.
  - Increasing hydrogen pressure decreases stereoselectivity, which is often kinetically driven.

4.5 Lecture 17: Hydroformylation and Carbonylation

5/7:

- We will now talk about inserting carbonyls.
- Grandfather reaction: Monsanto Acetic Acid Synthesis.
  - Used for many years, but replaced within the last few years.
  - Huge scale: Produces approximately 17 billion pounds of acetic acid per year.
  - About 80% of all acetic acid we use is generated by this process.
  - Several interations historically:
    - BASF (1965) uses cobalt and iodide.
    - Monsanto (1970) uses rhodium and iodide.
    - BP "Cativa" (1996) uses iridium and iodide.
- A big theme in catalysis right now is using first row metals instead of second- and third-row metals because they're cheaper and more abundant.
  - However, it makes sense to use iridium here: 5 million dollars of iridium can run in a reactor for decades.
- General form:

$$CH_3OH + CO \xrightarrow[\text{30-40 atm, 180 °C}]{Rh(CO)_2I_2^-} Me{-}COOH$$

- Mechanism:

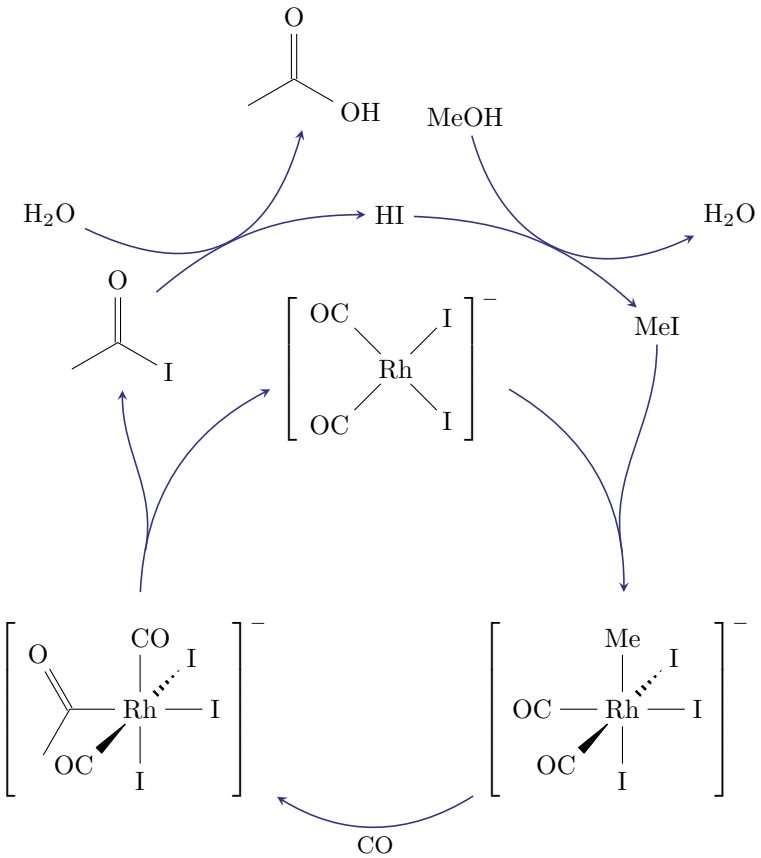


Figure 4.5: Carbonylation mechanism.

  - There are cocatalytic reactions that enable this reactivity.
  - Trace amounts of HI and H_2O facilitate the overall reaction.
    - Inputs are MeOH and CO; output is acetic acid.
    - Everything else is catalytic, or generated in situ.
  - Rate law: Rate = k[Rh][MeI].
  - Side reactions:
    - If the first intermediate is not immediately trapped by CO, it can insert to form a 5-coordinate intermediate that dimerizes in an inactive off-cycle.
    - This side reaction is not *necessarily* deleterious, but it can be.

- This complex has been heavily studied, giving us great insight into each step.
- Oxidative addition.
  - S_N2-type reaction.
  - An attack of the initial catalyst by acetyl iodide can lead to the second intermediate, directly.
  - The 5-coordinate intermediate in the S_N2 process can be attacked by methanol or acetic acid, giving you a methyl ester and acetic anhydride, respectively.
  - Undesirable side reactions:
    - The catalyst can react with HI, forming a RhI_3 precipitate and an $RhI_4(CO)_2^-$ inactive ion; both steps serve to effectively remove rhodium from the catalytic cycle (this is a big problem). However, this can be fixed by adding H_2O (about 10%). This increases the solubility of RhI_3 and turns on the water-gas shift reaction $CO + H_2O \longrightarrow CO_2 + H_2$; the H_2 product of the latter reaction serves as a reductant that transforms $Rh^{III} \longrightarrow Rh^{I}$.
    - Another undesirable side reaction is drawn out and its solution discussed. However...
    - Problem: H_2O is hard to separate from acetic acid (they have similar boiling points and they're miscible). Thus, you would have distill, but that's expensive and time-consuming. Additionally, acetic acid is corrosive. Therefore, this is not a great solution.
    - However, you can add the promotor LiI or LiOAc. It's not clear exactly what the promotor does, but one possible explanation is that you can get to a triiodide dianion that is nucleophilic to the point that it can speed up oxidative addition enough to promote the productive pathway.
    - Another possibility is that iodide binding at other steps can forward the productive pathway.
- You can intercept acetyl intermediates to foster another catalytic process:
- Kovach-Eastman Acetic Anhydride Process.
  - Invented in 1983.
  - Produces 800 million pounds of acetic anhydride annually.
- Mechanism:
  - The only difference between this and the Monsanto acetic acid process (Figure 4.5) is that in the nonorganometallic cycle, we add acetic acid and get acetic anhydride, and then add methyl ester and get acetic acid.
  - Inputs are CO and Me–COOMe.
- Cativa process:
  - Invented by BP.
  - 5 times more active than rhodium-catalysed.

- Uses iridium with a ruthenium promotor.
- Iridium is in the same group as iridium but is faster for oxidative addition.
- The rate law is complicated, depending on [CO], [H_2O], [MeOAc], [MeI] (which you don't actually want in there), [Ru], and [Ir].
  - This process is complex and nonlinear.
- The main species in solution is $Ir(CH_3)(CO)_2I_3^-$.
- The turnover limiting step here is insertion since oxidative addition is so much faster (approximately 150 times faster). However, insertion is 10^5 times slower for iridium.
  - Simplistic explanation: There are even stronger bonds for iridium then for rhodium. This favors bond formation (i.e., in oxidative addition), but not bond breaking (i.e., in insertion).
- However, we can fix the slower insertion rate with promoters, namely $[Ru(CO)_3I_2]_2$.

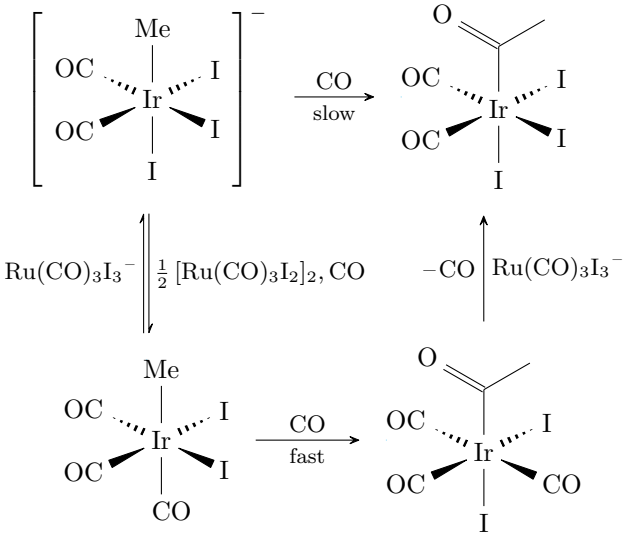


Figure 4.6: Promoting the Cativa process.

- $\frac{k_{fast}}{k_{slow}} \approx 700$, so an almost 3 orders of magnitude gain.

- The overall mechanism for the Cativa process is drawn out.
- Hydroformylation.
- General form.

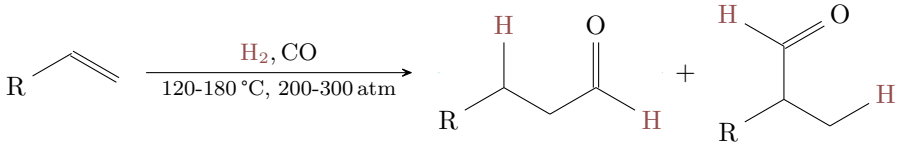


Figure 4.7: The general form of hydroformylation.

- The ratio of the first to the second product is 3-4 : 1.

- Typical catalysts:
  - $HCo(CO)_4$ (synthesized from $Co_2(CO)_8$ as a precatalyst and H_2).
  - $HCo(CO)_3(PR_3)$.

  - $HRh(CO)_2(PR_3)_2$.

- On the gas used in this process (CO and H_2 in a $1:1$ ratio):
  - Called synthesis (or syn) gas.
  - Released when coal is heated.
  - Composed of CO and H_2 in a $1:1$ ratio.
- The rate at which the $HCo(CO)_4$ catalyst acts is given by Rate $= k[H_2][CO]^{-1}$.
  - Thus, we can tweak the rate by adjusting the relative concentrations of the gas.
  - Adding H_2 will increase the rate of reaction, and adding CO will decrease the rate of reaction.
- Mechanism:

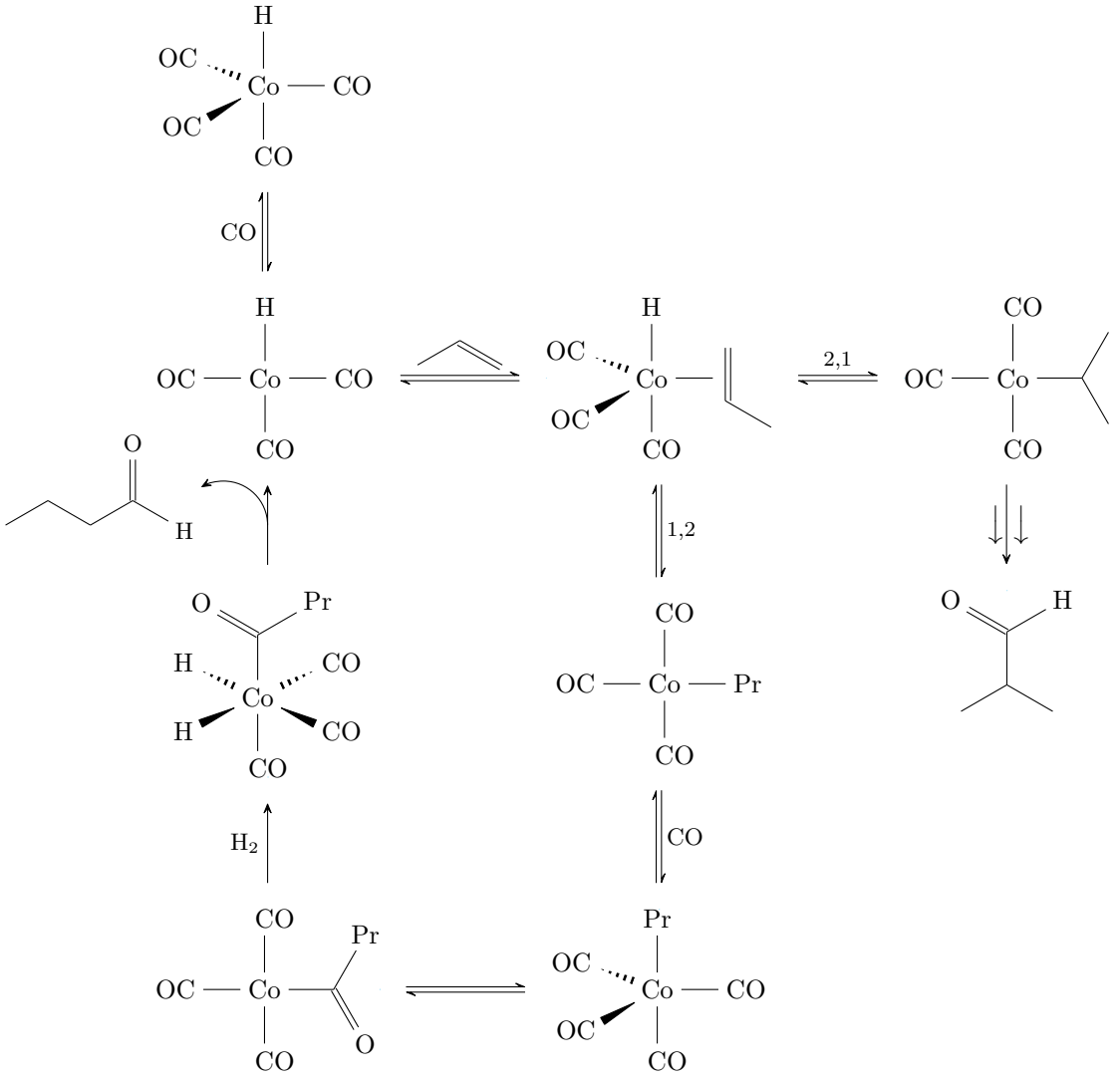


Figure 4.8: Hydroformylation mechanism.

  - The active catalyst is a square planar, d^8, $16\,e^-$ complex.
  - The first intermediate is the key intermediate to determine selectivity because it can insert in a $2,1$ or a $1,2$ fashion.

  - The third intermediate along the $1,2$ branch can be trapped by CO.
    - The off-cycle intermediate can be isolated. Thus, it's a kind of resting state.
  - A similar process (as indicated by the triple arrow) can be used to get from the $2,1$ branch to the final branched product.
  - Control of branching:
    - It's complicated and not entirely clear.
    - However, we are aware of **chain walking**.

- **Chain walking**: The transition from the $1,2$-inserted intermediate and the $2,1$-inserted intermediate and vice versa.
  - An equilibrium process.

- How to control selectivity.
  - Switching $HCo(CO)_3(PR_3)$ increases the rate and selectivity.
  - With a special phosphine, the selectivity of linear to branched is $8:1$.
  - This also enables the hydrogenation of aldehydes to alcohols.
    - An important industrial application of this is transforming (in one step) internal olefins into terminal aldehydes and terminal alcohols.

- First-row metals hydroformylate, but heavier ones do it better.

- Rh-catalyzed hydroformylation:
  - Uses $Rh(CO)_2(PR_3)_2$.
  - Linear-to-branched ratio of $11:1$.
  - Milder conditions (5-10 atm CO / H_2 and 90 °C).
  - The mechanism is similar to that of Co.
  - We make the catalyst water soluble with bulky, heavy phosphines (such as tris(phenyl sulfate)phos) to aid in separation.
  - We are allowed to have two phosphines on rhodium because rhodium has a larger atomic radius. The larger atomic radius of rhodium also enables the use of chelating phosphines, such as...
    - dppe, dppp, dppb, bis(diphenylphosphino)ferrocene (dppf), DPE Phos, Xant phos, and BISBI (the best).
  - Selectivity of chelating phosphines depends on bite angle.
    - $PPh_3 \to 9:1$ ratio.
    - dppe $\to 4:1$ ratio.
    - BISBI $\to 30:1$ ratio.
  - Hypothesis: Larger bite angles will favor PR_3 in the equatorial plane.
    - Favoring 5-coordinate intermediates over 4-coordinate intermediates.