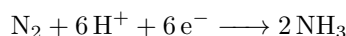


Unit 4

???

4.1 Lecture 15: Nitrogen Fixation

5/3: • General form:



- Alternatively, it could be $\text{N}_2 + 3\text{H}_2 \longrightarrow 2\text{NH}_3$.
- 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 $\text{N}\equiv\text{N}$ gas. Indeed, we need it to be **fixed** before we can incorporate it (i.e., through food sources).

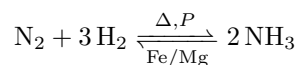
- Main pathways:

- Lightning.



- 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 $\text{FeMoCO}^{[1]}$ 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**.

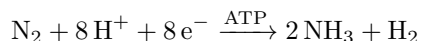
- **Haber-Bosch process:** Humanity's primary method of fixing nitrogen.



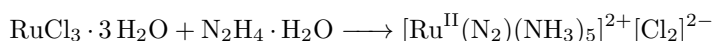
- -92 kcal/mol (thermodynamically favored but kinetically difficult).
- 200 atm of pressure (pushes the equilibrium to the right via Le Châtelier's principle).

¹Literally 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 H₂ gas as hydrides and N₂ 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.

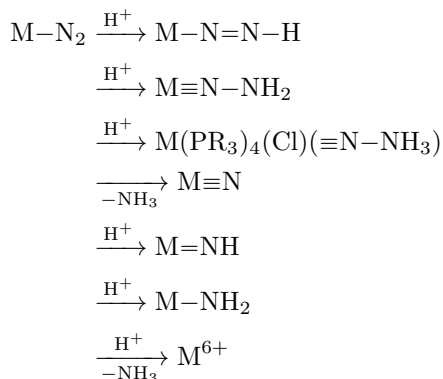


- Other extant cofactors include FeVCO and FeFeCO, but they are less common.
- Since ATP is used, this is still a very energy-intensive process.
- N₂ bonds to metal centers in many ways:
 - Linear, bent, side-on, bridging linear, bridging side-on, multi-metal center bridging, etc.
- N₂ complexes are much less common than CO complexes since N₂ is a terrible ligand.
 - The HOMO in N₂ 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.



- N₂H₄ is hydrazine (rocket fuel), and is much more stable as a hydrate.
- The product is d^6 with 18 e[−] and has $\mu_{\text{N}_2} = 2170\text{--}2115 \text{ cm}^{-1}$ (the range depends on the anion).
- For reference, free N₂ has a stretching frequency of 2331 cm^{−1}.
- Yamamoto gives the first example of a dinitrogen complex formed from free N₂ (HCo(PPh₃)₃(N₂)).
- 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: $\text{MoX}_4\text{L}_2 \xrightarrow[\text{Na/Hg}]{\text{N}_2, \text{L}} \text{Mo}(\text{N}_2)_2\text{L}_4$.
 - L is typically a phosphine.
 - With various phosphine ligands, you can get different geometries.

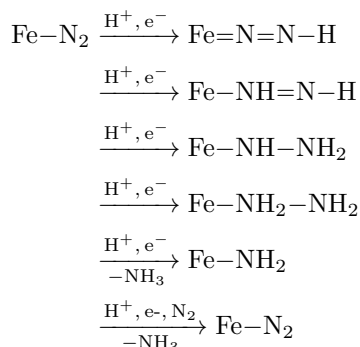
- Another example: $\text{cis-W(N}_2)_2(\text{PMe}_2\text{Ph})_4 \xrightarrow[\text{MeOH}]{\text{H}_2\text{SO}_4} 2\text{NH}_3 + \text{N}_2 + \text{W}^{\text{VI}}(\text{oxo})$.
 - Works with molybdenum, too, but tungsten gives a better yield.
 - The overall reaction is $\text{W}^0 + 6\text{H}^+ + \text{N}_2 \longrightarrow 2\text{NH}_3 + \text{W}^{\text{VI}}$.
 - Some important subreactions/steps are $\text{N}_2 + 4\text{e}^- \longrightarrow \text{N}_2\text{H}_4$ and $\text{N}_2 + 2\text{e}^- \longrightarrow \text{N}_2\text{H}_2$.
- Mechanism (by Chatt):



- 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: $\text{M(N}_2)_2(\text{PR}_3)_4 \xrightarrow{\text{TMSI}} \text{TMS-N=N-MI(PR}_3)_4 \xrightarrow[\text{N}_2]{\text{Na, THF}} \text{M(N}_2)_2(\text{PR}_3)_4 + \text{NH(TMS)}_2 + \text{NH}_3 + \text{NaNH}_2 + \text{NaNH(TMS)}$, 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 hexaisopropyl *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 $[\text{BAr}^{\text{F}}_4]^-$.
 - They fish out $\text{Mo-NH}_3 + \text{NH}_3$. Reducing the former product gives $\text{Mo}^{\text{III}}(\text{N}_2)$ 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: $\text{Mo-N}\equiv\text{N} \xrightarrow{\text{H}^+, \text{e}^-} \text{M-N=N-H} \xrightarrow{\text{H}^+, \text{e}^-} \text{M}\equiv\text{N-NH}_2 \xrightarrow{\text{H}^+, \text{e}^-} \text{M}\equiv\text{N} \xrightarrow{\text{H}^+, \text{e}^-} \text{M}\equiv\text{NH} \xrightarrow{\text{H}^+, \text{e}^-} \text{M-NH}_2 \xrightarrow[-\text{NH}_3]{\text{H}^+, \text{e}^-, \text{N}_2} \text{Mo-N}\equiv\text{N}$.
 - Note that molybdenum starts in the 3+ oxidation state at $\text{M-N}\equiv\text{N}$ and goes up to 6+ at $\text{Mo}\equiv\text{N}$ before cycling back down.
- Shilov had a number of systems, but they were poorly defined.

²Note 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.
 - $(PR_3)_4Fe(N_2) \xrightarrow{XSH^+}$ 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 $Fe(N_2)(B(PR_2Ph)_3) \xrightarrow[XSHBAr^F_4]{XSKC_8} NH_3^{[3]}$ (Anderson et al., 2013).
 - Seven equivalents per iron. More recent tinkering has brought it up to nearly 100 equivalents per iron.
 - Mechanism: $L_3FeN_2^- \xrightarrow{2H^+} L_3Fe\equiv N-NH_2^+ \longrightarrow \longrightarrow \longrightarrow NH_3$.
 - Suggests a Chatt/Distal mechanism.
 - Differing mechanistic proposal: Alternating mechanism.



- 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.

³Note 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 contiguous 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 available 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 figure captions, although additional citations are not required 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 for 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. $\frac{1}{2} \text{Mn}_2(\text{CO})_{10} \xrightarrow[-2 \text{NaCl}]{\text{Na/Hg}} \text{Na}[\text{Mn}(\text{CO})_5] \xrightarrow[-\text{NaI}]{\text{MeI}}$
 - 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 $\text{M}-\text{C}\equiv\text{O}^+$ 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 of the cone. Most commonly forgotten: metal center, van der Waals radii.
 - 4f: H_2CrO_4 is Cr^{6+} , d^0 , while $\text{Cr}(\text{CO})_4^{4-}$ is Cr^{4-} , d^{10} . The difference is different than you expect because they are actually very similar.
 - 5: First, backcalculate out spin-state to determine $S = 1$ and $S = 0$. Second, luckily, they're 4-coordinate, so the simplest solution is to look for two geometries that give 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:

$$\text{Y}=\text{X} + \text{H}_2 \xrightarrow{\text{cat}} \text{H}-\text{Y}-\text{X}-\text{H}$$
 - 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 ($\text{Rh}(\text{PPh}_3)_3\text{Cl}$) 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):

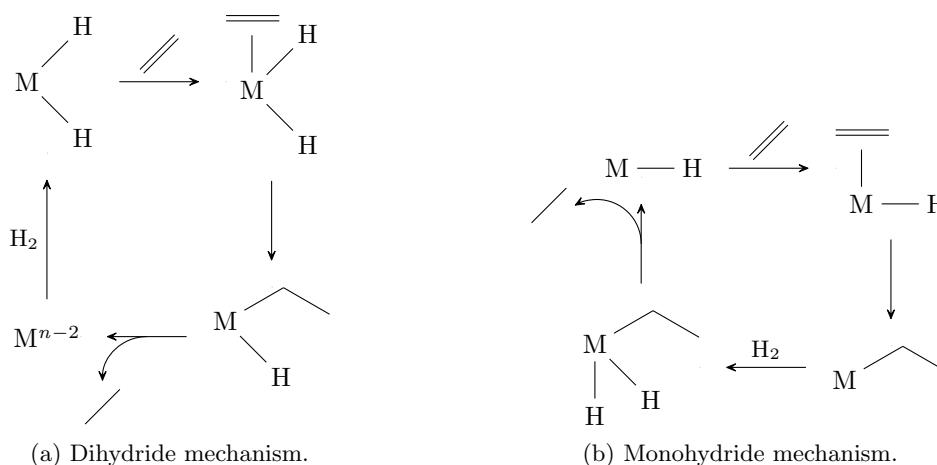
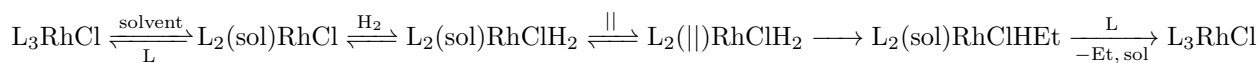


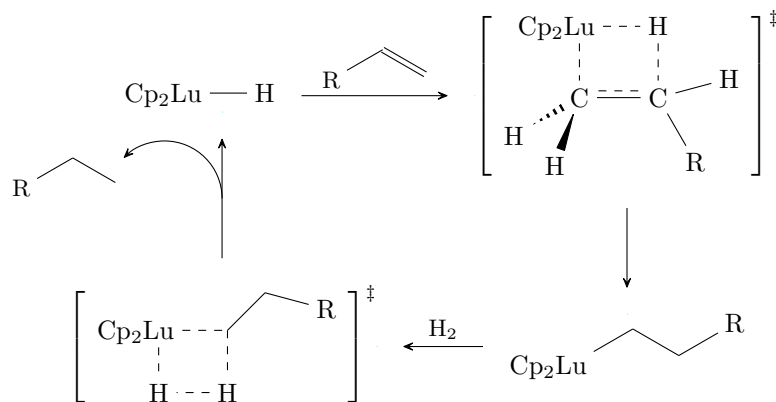
Figure 4.1: Hydrogenation mechanisms.

- 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 polyolefin 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):



- 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., $[\text{RhL}_2\text{H}_2(\text{sol})_2]^+$).
 - In effect, removing the chloride generates a noncoordinating counteranion, which is much more reactive.
 - If you use iridium instead, it's Crabtree's catalyst: $[\text{Ir}(\text{COD})(\text{PCCl}_3)(\text{py})]^+[\text{PF}_6]^-$.
- Compares rates of derivatives of Crabtree's and Wilkinson's catalyst at various temperatures in non-coordinating 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.⁴An 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 innumerable 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:

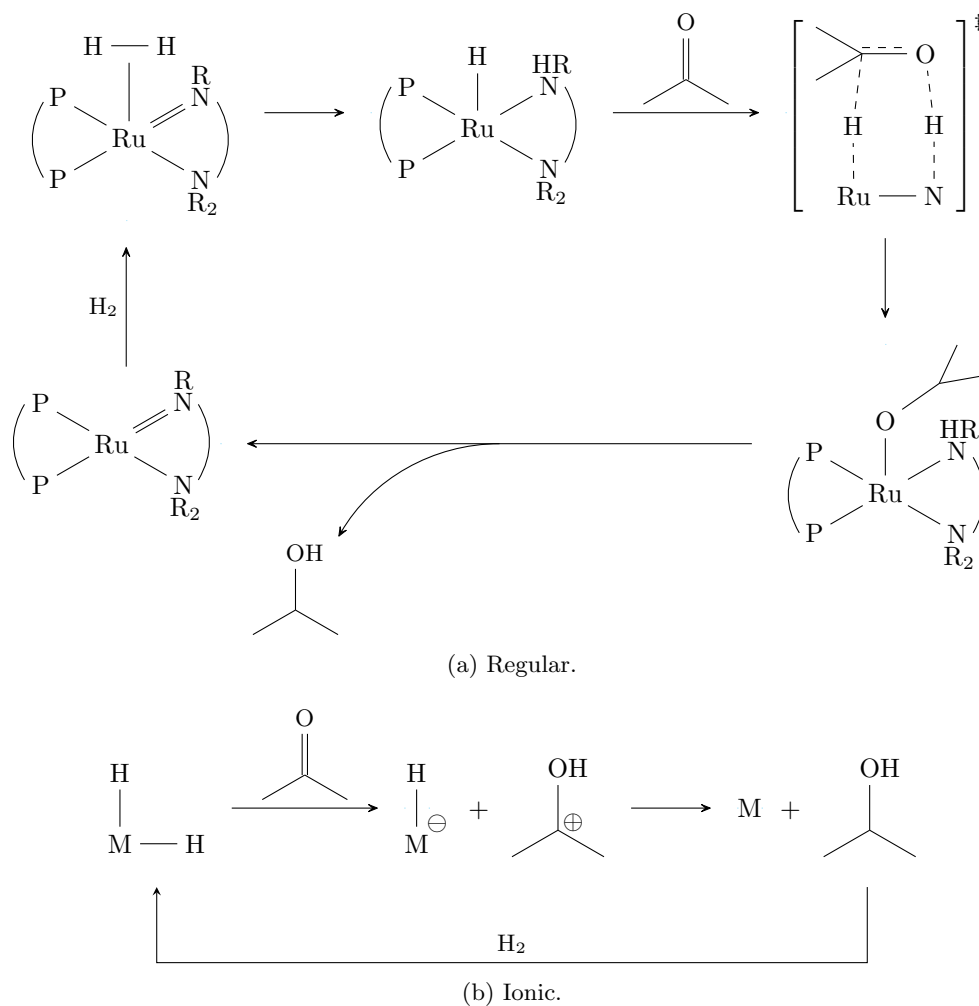


Figure 4.3: Noyori's catalyst mechanism.

- 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 $\text{CpW}(\text{CO})_2(\text{PPh}_3)(\text{OCEt}_2)^+$.
- 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 enantiomer is often bound over the other.
- Transfer hydrogenations:

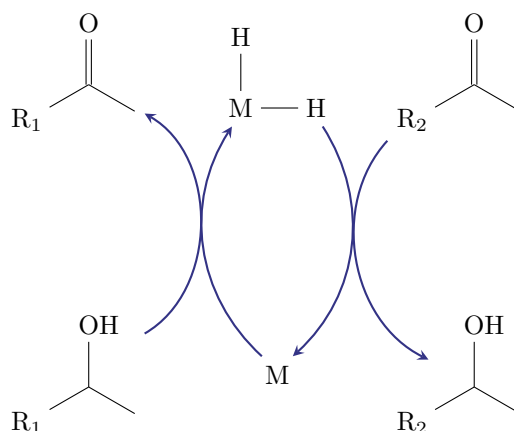


Figure 4.4: Transfer hydrogenation mechanism.

- 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 $R_2 = \text{Ar}$, 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.