Unit 6
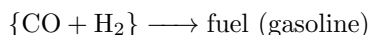
More Catalytic Processes 3

6.1 Lecture 20: Fischer-Tropsch

- Industrial process mainly, but also has applications to renewable energy.

- Mechanism of the industrial catalysis in the first video; more on the molecular chemistry in the second video.

- General form:
$$\{CO + H_2\} \longrightarrow \text{fuel (gasoline)}$$

  - Clearly, the reactants are Syn gas.

- Thermodynamics of $CO + x\,H_2 \longrightarrow$ stuff.

  - As x increases, ΔH and ΔG decrease.
  - Conclusion: The more $C\text{–}H$ bonds you make, the more thermodynamically favorable the process is.
    - A lot of this comes from the thermodynamic reducing power of hydrogen.

- History:
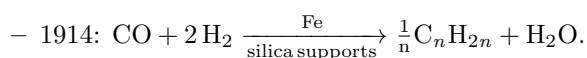
  - 1914: $CO + 2\,H_2 \xrightarrow[\text{silica supports}]{\text{Fe}} \frac{1}{n}C_nH_{2n} + H_2O$.
   - The ratio of the reactants can be tuned.
    - Iron is a solid-state catalyst here. Note that other metals can be used, but iron was the most common.
    - The products are a mixture of medium to long chain alkanes, alkenes, and methane.
    - The challenge and limitation of this process is that it yields a mixture (a Schultz-Flory distribution) of products.
    - This means that there is no real selectivity, although C_7 is most common.
    - This is also why chemists became interested in homogeneous catalysis for this area, because in principle it could give you better selectivity here.

- Industrially:
$$\text{coal} \xrightarrow[\text{reformed}]{\text{steam}} CO + H_2$$
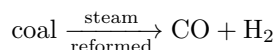
  - This is commonly done in South Africa because they have a lot of coal.
    - CH_4 can also be used as a reactant.
  - The ratio of the product gasses can be tuned by the water-gas shift reaction (see Lecture 17), which is $CO + H_2O \rightleftharpoons H_2 + CO_2$ (in the forward direction).

- ∎ CO_2 can then be removed.
- ∎ One potentially interesting exciting direction that's not been industrially accomplished due to cost is the reverse water-gas shift reaction, which is just the reverse direction.
- ∎ The reverse water-gas shift reaction is interesting because if you could convert CO_2 into $CO +$ H_2O and remove the water, you could feed the CO back into the original process to make gasoline.
  - – Challenges:
    - ∎ Selectivity in the Fischer-Tropsch process.
    - ∎ Source of H_2 (right now we get it from fossil fuels). There is research into how to reduce CO_2 into fuels, but if we can get H_2 from somewhere other than fossil fuels, it's a solved problem.

- Conditions (for the following reaction):

$$\{CO + H_2\} \longrightarrow C_nH_{2n} + n\,H_2O$$
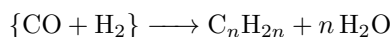
  - – High temperatures (150-300 °C).
    - ∎ Favor faster rates and better conversion yield percentages, but more methane (the least valuable product).
  - – High pressure (1-30 atm).
    - ∎ Favors longer chain alkanes and better conversion since methane is a gas (lower likelihood of eliminating it).
  - – Optimal CO / H_2 concentration.
    - ∎ Cobalt catalysts use $1:2$.
    - ∎ Iron catalysts should have relatively more CO.

- Product (Schultz-Flory) distribution:

$$\frac{W_n}{n} = (1-\alpha)^2 \alpha^{n-1}$$

  - – $\frac{W_n}{n}$ is the average molecular weight?
  - – W_n is the weight fraction of hydrocarbons containing n carbon atoms and α is the chain growth probability (controlled by the catalyst and the conditions).
  - – If $\alpha < 0.5$, then methane dominates.
  - – However, as $\alpha \to 1$, the methane fraction decreases relative to the sum of heavy products.
  - – Sasol (a South African company) mediates this process.
  - – We can use the products for a variety of different things (heptane for fuel, heavier ones for wax [you can buy Sasol wax], etc.).
  - – If we were going to do this globally for fuel, we'd have a lot of wax as a byproduct, which we neither have a place to store nor can afford to do since it's so wasteful. Thus, there is great interest in selectivity for C_6, C_7, C_8, or even butene, from which we could do olefin metathesis to make hexanes.
  - – Two necessary things to use this process for renewable energy:
    1. Find a good source of hydrogen so that we could run the reverse water-gas shift reaction.
       - ∎ The reaction might need to be optimized a bit as well, but in principle that can be done; hydrogen is the real problem.
    2. Improve the selectivity of the Fischer-Tropsch chemistry.

- As with the Haber-Bosch process, this is solid support chemistry.

- Mechanism (initial proposal):

- Solid-state iron binds hydrides and CO on its surface, leading the formation of a formyl species before adding another hydrogen to go to a bound alcohol species, losing H_2O to go to a bound carbene (the carbene is important because it facilitates chain growth), and then proceeding to a bound methyl species. With enough methyl species, you could do other things.
  - Gerhardt Ertl proves this wrong.

- Mechanism (actual):

  - Solid-state iron binds hydrides and carbonyls on its surface. Next, we split CO to make bound carbides and bound oxides. With more H_2, we can mix and scramble the carbides, oxides, and hydrides, kicking out H_2O and making bound carbene species, which can then go on and form the product that we want as described in the initial proposal.
  - Proven with in situ studies performed on the surface of these materials.

- Another key contribution to the proof came from molecular chemistry, which showed that formyl species are generally unstable:
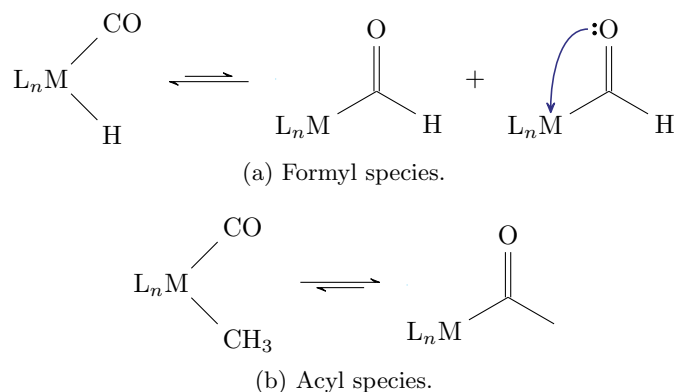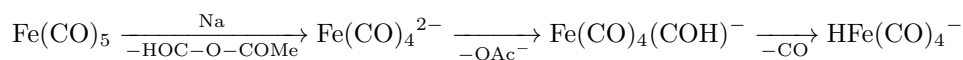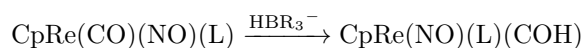

(a) Formyl species.

(b) Acyl species.

Figure 6.1: Stability of metal-carbonyl derivatives.

  - In Figure 6.1a, the reactant is generally favored because it has two bonds instead of one, and metal-hydride bonds are highly thermodynamically favored over metal alkyl bonds.
  - In Figure 6.1b, the product is generally favored.
  - Think about the equilibrium in terms of the nucleophilicity of the X group. Hydrides are not nucleophilic, whereas alkyl species are.

- The synthesis of metal formyl species was pioneered by Jim Collman in 1973.

$$\text{Fe(CO)}_5 \xrightarrow[-\text{HOC}-\text{O}-\text{COMe}]{\text{Na}} \text{Fe(CO)}_4{}^{2-} \xrightarrow[-\text{OAc}^-]{} \text{Fe(CO)}_4(\text{COH})^- \xrightarrow[-\text{CO}]{} \text{HFe(CO)}_4{}^-$$
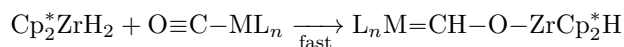
  - The first step is ill defined, and the products of it are a messy mixture of carbon-containing products.
  - The second intermediate (the formyl species) is unstable and will decompose over time to form the final product.

- Chuck Casey and John Gladys found stable formyl species (the product of the following reaction):

$$\text{CpRe(CO)(NO)(L)} \xrightarrow{\text{HBR}_3{}^-} \text{CpRe(NO)(L)(COH)}$$

  - The reactant is a chiral, $18\,\text{e}^-$, d^6 species.

- John Bercaw did more with metal-formyl species:

$$\text{Cp}_2^*\text{ZrH}_2 + \text{O}\equiv\text{C}-\text{ML}_n \xrightarrow[\text{fast}]{} \text{L}_n\text{M}=\text{CH}-\text{O}-\text{ZrCp}_2^*\text{H}$$

  – The first species is an extremely hydridic metal hydride that has very similar properties to LiAlH. It is a $16\,\text{e}^-$, d^0 species.
  – This chemistry is driven by the strength of the zirconium bond ($\approx 130\,\text{kcal/mol}$).
  – Note that although this is technically a formyl species, it's in practice more of a Fischer carbene structure.
    ▪ The bonding is very different and the Lewis acid activation of that strong Zr^{IV} Lewis acid makes this more of a carbene structure.
    ▪ This is useful in C–C coupling reactions.
  – One example of ML_n is Cp_2W.

  – Another one is $\text{Cp}_2\text{Nb}(\text{H})(\text{CO}) + \text{Cp}_2^*\text{ZrH}_2 \longrightarrow \text{Cp}_2\text{Nb}(\text{H})(\text{CH}-\text{O}-\text{ZrCp}_2^*\text{H}) \xrightleftharpoons{\text{fast}}$
  $\text{Cp}_2\text{Nb}(\text{H})(\text{CH}_2-\text{O}-\text{ZrCp}_2^*) \xrightarrow{\text{H}_2} \text{Cp}_2\text{NbH}_3 + \text{Cp}_2^*\text{Zr}(\text{H})(\text{OCH}_3) \xrightarrow[\text{no rxn}]{}$.

    ▪ Nb is niobium.
    ▪ A major problem is once we form that extremely strong metal-oxygen bond, it will not break, so it's very hard to get H_2O off of these species.

- How we think about the molecular systems that form C–C bonds.

  – This is ultimately what happens on solid support surfaces in industrial catalysis.
  – The challenge is that those industrial systems don't have selectivity; molecular systems could in principle provide this (this is an area of active research).

- To recap, we just talked about the potential of early metal hydrides to activate CO (Bercaw's niobium system took it all the way to a methanol equivalent).
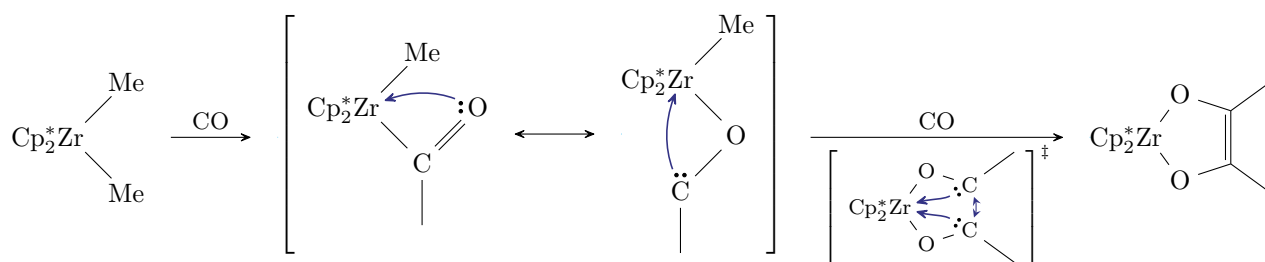
- Bercaw (a titan of organometallic chemistry):

Figure 6.2: Bercaw's first C–C coupling.

  – The first ever C–C coupling that was observed in a well-defined and pretty clean way from CO.
    ▪ Using methyl groups makes it imperfect.
    ▪ The mechanism isn't entirely clear.
  – The second step proceeds from the second resonance structure.
  – Additionally, Bercaw studied reactions with $\text{Cp}_2^*\text{ZrH}_2\text{CO}$, a compound with virtually no π back-bonding:
    ▪ $\text{Cp}_2^*\text{ZrH}_2\text{CO} \xrightarrow{\text{H}_2} \text{Cp}_2^*\text{Zr}(\text{H})(\text{OCH}_3)$, where $-\text{OCH}_3$ is a methanol equivalent.
    ▪ $\text{Cp}_2^*\text{ZrH}_2\text{CO} \xrightarrow{\text{CO}} \text{Cp}_2^*\text{Zr}(\text{H})-\text{O}-=-\text{O}-\text{Zr}(\text{H})(\text{Cp}_2^*)$. Here, we actually see C–C coupling.

- ■ $Cp_2^*ZrH_2CO \xrightarrow{CO, H_2} Cp_2^*Zr(H)-O---O-Zr(H)(Cp_2^*)$. This is even closer to ethylene glycol, but the Zr$-$O bonds are still an issue.
- ■ $Cp_2^*ZrH_2 + Cp_2^*Zr(CO)_2 \longrightarrow Cp_2^*Zr(H)-O-=-O-Zr(H)(Cp_2^*)$

- Similarly, Tobin Marks looked at $Cp_2^*Th(OR)(H)$ (thorium hydride alkoxides), where R $= CH(t\text{-}Bu)_2$ is a pretty bulky super-isopropal ligand abbreviated $i\text{-}Pr^*$:
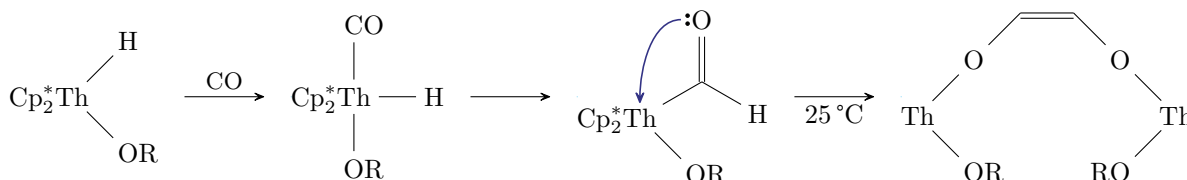

Figure 6.3: Marks' C$-$C coupling.

  - The theme with early metals: If you can get to the Fischer carbene type structure, you can get coupling.

- Pete Wolczanski worked with tantalum silox complexes.

  - $Ta(OSi(t\text{-}Bu)_3)_3 + 2\,CO \longrightarrow 2\,(silox)_3TaO + (silox)_3Ta=C=C=Ta(silox)_3$.
  - This is C$-$C coupling *and* complete deoxygenation.

- Challenge with all of this chemistry: early-metal oxygen bonds are an extreme thermodynamic sink.

  - Unfortunately, the transition from metal-carbon bonds to metal-oxygen bonds is also the driving force of this reactivity.
  - We can get around this issue by trapping the oxygen with other electrophiles.

- Kit Cummins: $MoL_3 \xrightarrow{CO} L_3MoCO \xrightarrow{1\,Na} Na[L_3MoCO] \xrightarrow[-NaCl]{Bu^t-COCl} L_3Mo\equiv C-O-COBu^t \xrightarrow[-CO_2, H_2C=CMe_2]{\Delta}$
  $L_3Mo\equiv C-H \xrightarrow{KBn} [L_3Mo\equiv C]^-$.

  - L $= N(t\text{-}Bu)(xylyl)$.
  - The third step is more explained in organic chemistry, where an electrophile like the one added (pivaloyl chloride) should create an ester speies and lose NaCl.
  - Note that KBn is benzyl potassium.
  - There are very few examples of terminal carbides, but note that this is similar to what happens on the surface of the solid state iron catalyst.
  - This isn't perfect because we're releasing CO_2, but it is a step where the oxygen isn't trapped on the metal center.

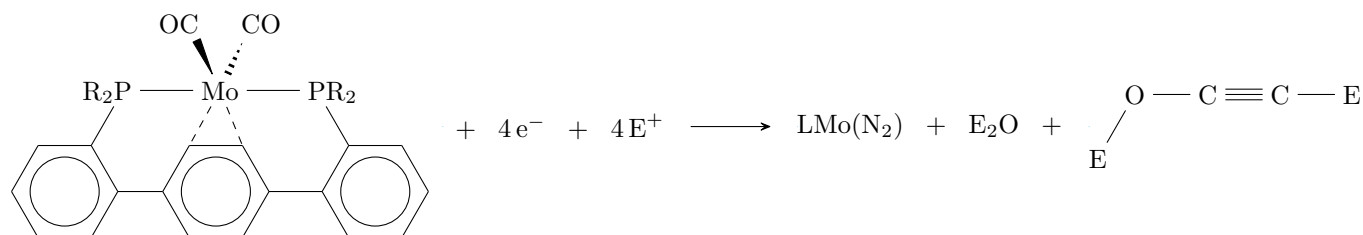- Theodor Agapie (with his graduate student Joshua Buss):

Figure 6.4: Agapie's C$-$C coupling.

- KC$_8$ yields the $4\,e^-$.
  - The electrophile E$^+$ is something like TMSCl, a silane, or another silyl electrophile.
  - This also proceeds through carbides.

- Jonas Peters (on iron): $Fe\equiv C-O + TMSCl \longrightarrow Fe\equiv C-OTMS$.

  - We are trapping the oxygen with an oxygen-silion bond, which thermodynamially are quite strong.
  - Problem: While a silyl electrophile is substantially better than trapping the metal center (which entirely precludes catalysis), the silyl electrophiles generate stoichiometric waste. We need to trap the oxygen with water, not a silyl ether.
  - Thus, what you ultimately want to do is use later metals (like iron), but use hydrogen instead.

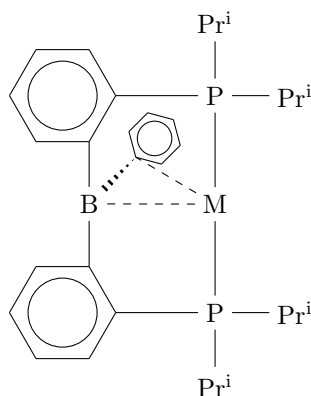- Dan Suess (graduate student of Jonas Peters):

Figure 6.5: The DPB ligand.

- Investigates various reactions of DPB-bound irons.
  - $DPBFe-N\equiv N-FeDPBB \xrightarrow{4\,CO} DPBFe(CO)_2 \xrightarrow{XS\,CO} FeP_2B(CO)_3$.
    - The product here is formally Fe^0, but actually slightly higher than that.
  - $DPBFe-N\equiv N-FeDPBB \xrightarrow{4\,CO} DPBFe(CO)_2 \xrightarrow{H_2} FeP_2(\kappa^2\text{-}BH)H(CO)_2$.
  - $DPBFe-N\equiv N-FeDPBB \xrightarrow{4\,CO} DPBFe(CO)_2 \xrightarrow{1\,K^0} [FeP_2(\kappa^2\text{-}PhB)(CO)_2]^- \xrightarrow{XS\,K^0} [FeP_2B(CO)_2]^{2-} \xrightarrow{2\,TMSOTf}$ a very weird product.
    - The third intermediate is highly activated and somewhat analogous to Fe(CO)$_5{}^{2-}$.
    - The product has a $-C-OTMS$ substituent, as well as a tridentate derivative of the DPB ligand that still bonds through the two phosphines, but instead of partially bonding through the boron and the ipso-carbon of the phenyl ring, the boron binds to an additional C$-$OTMS ligand through the carbon, which in turn binds back to the iron center.
    - This product has many resonance structures; one with particular merit is Fe($\equiv C-OTMS)_2$ with one of the triple bonds bonding datively to the boron, although it implies an Fe^{VI} oxidation state that is likely an overestimation, even though the iron is certainly high-valent here.
    - Note that if the product is treated with hydrogen, we selectively create (Z)-TMSO$-=-$OTMS.
    - This is not catalytic, but it is one of the few examples where we don't generate an intractable metal-oxide, and we do generate a C$-$C coupled product.

- Conclusion: There's a lot of interesting organometallic chemistry surrounding C$-$O activation and getting that prepped for functionalization, specifically via C$-$C bond formation.

- This is not a solved problems.

    - While molecular chemistry offers the promise of selectivity, there are real challenges with activating it and getting H_2O out instead of trapping the oxygen with silyl electrophiles.
    - Part of the issue is the stability of the molecular complexes (they're not as stable as a solid iron surface) and you need a lot of energy to split $C\equiv O$ bonds. On the other hand, if you apply that energy thermally, it will hurt your selectivity.

- There's some extra molecular chemistry in the notes.

6.2   Lecture 21: C−H Activation

5/21:
- A really active area within the last ten years, and a really powerful synthetic technique for functionalizing molecules.

    - The major problem with selectivity is not yet solved though.

- General form:
$$R-H + A \xrightarrow{\text{cat}} R-FG + B$$
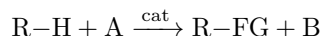
    - A is a functionalizing reagent, FG is a functional group, and B is a byproduct that usually accepts the proton.

- Examples from organic chemistry:

    - $C_4H_{10} \xrightarrow{Br_2} C_4H_9Br$.
    - $C_4H_{10} \xrightarrow[\Delta]{O_2} CO_2 + H_2O$.

- The real challenge from an organometallic perspective is selectivity:

    1. Internal C−H bonds are typically more reactive.
    2. The product is typically more reactive than the starting material.
        - We need to prevent over-oxidation.

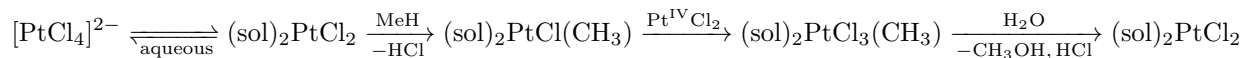- Another challenge is the thermodynamics of this process.

- For example:

    - $C_6H_6 + CO \longrightarrow C_6H_5(COH)$ has $\Delta H = 1.7\,\text{kcal/mol}$.
    - $R-H + H-X \longrightarrow R-X + H_2$ has $\Delta H = 22\,\text{kcal/mol}$ when X = OH.
    - $R-- \longrightarrow R-= + H_2$ has $\Delta H = 30\,\text{kcal/mol}$.
    - You will get some entropic favorability, but you need to put in a lot of driving force — and whenever you do this, selectivity and over-oxidation become problems.

- Classic studies (Shilov's catalyst):

    - $K_2PtCl_6 + CH_3CO_2D + D_2O$ can be mixed with alkanes to incorporate deuterium into said alkanes.
        - ■ Note that K_2PtCl_6 is an oxidant.
    - Data listed.
    - Conclusion: Higher degrees of substitution at less substituted carbons.
    - Basically, you can do this: $R-H \xrightarrow[\text{DClO}_4,\,\text{CH}_3\text{CO}_2\text{D},\,\text{D}_2\text{O}]{K_2PtCl_4\,(12\,\%)} R-D$.
    - Also: $C_5H_{12} + H_2PtCl_6 \xrightarrow[\text{H}_2\text{O}]{\text{NaPtCl}_4} C_5H_{11}Cl$ on both the 1- and 2-carbons.

- Mechanism (monooxidation to form alcohols [very useful]):

$$[PtCl_4]^{2-} \underset{\text{aqueous}}{\rightleftharpoons} (sol)_2PtCl_2 \xrightarrow[-HCl]{MeH} (sol)_2PtCl(CH_3) \xrightarrow{Pt^{IV}Cl_2} (sol)_2PtCl_3(CH_3) \xrightarrow[-CH_3OH, HCl]{H_2O} (sol)_2PtCl_2$$

  – The fact that this process activates methane (MeH) is very good because we have a lot of it and the only thing it's good for is burning.

  ◾ It's not economically viable to capture all the extra methane on oil fields and transport it (instead, they flair it off because that's better for the environment than just releasing it).

  ◾ However, if they could functionalize it immediately and turn it into methanol liquid, which can be transported, that would be a huge boon to industry and the environment.

  – In the last step, water attacks the methyl group on the platinum catalyst, releasing methanol and then reductively eliminating HCl.

  – However, the challenge with this is the second step (with $Pt^{IV}Cl$)

  ◾ For whatever reason, the only oxidant that kinetically works is Pt^{VI}. But we need a lower oxidation state oxidant to solve this problem. Yet we haven't despite decades of research.

- The closest we've come to a solution is work by Periana: $CH_4 + H_2SO_4 \xrightarrow{cat} CH_3SO_4H + 2\,H_2O + SO_2$.

  – CH_3SO_4H is methyl sulfuric acid.

  – The catalyst is a dichloride platinum species with a bidentate chelating dipyrmidine species.

  – $TOF = 1 \times 10^{-2}\,s^{-1}$.

  – $TON \approx 7500$.

  – The TOF and TON are not viable for a large scale industrial process with platinum, but are pretty good.

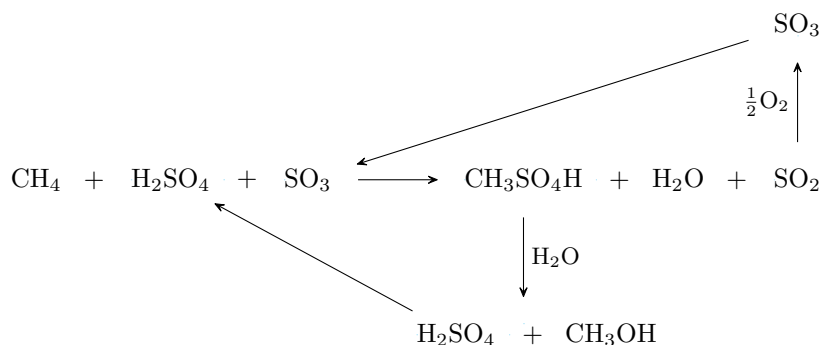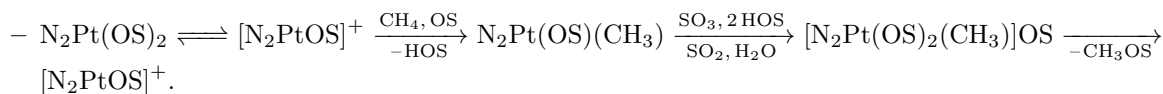- Thus, in principle, we could do this industrially with the following.

Figure 6.6: An industrial version of Shilov's monooxidation to form alcohols.

  – This is pretty powerful, but there are problems:

  – H_2SO_4 is corrosive, which means that this process is hard to scale up.

  – Separation of CH_3OH from H_2SO_4 is also hard (adds cost).

  – The platinum catalyst is also expensive, so you would need a much higher turnover number to make it viable.

  ◾ This is more of a solvable issue; the others, not so much.

- Mechanism:

- $N_2Pt(OS)_2 \rightleftharpoons [N_2PtOS]^+ \xrightarrow[-HOS]{CH_4, OS} N_2Pt(OS)(CH_3) \xrightarrow[SO_2, H_2O]{SO_3, 2\,HOS} [N_2Pt(OS)_2(CH_3)]OS \xrightarrow[-CH_3OS]{}$
  $[N_2PtOS]^+$.
    - ■ Sulfate and related species are abbreviated to OS.
- This is the closest we've gotten to a catalytic process for converting methane into methanol so far.
- Mechanistic notes:
    1. σ adducts.
        - ■ A key step is binding methane, but methane is a terrible ligand.
        - ■ $M(H|CH_3) \longrightarrow M(H)(CH_3)$.
        - ■ There exist other platinum systems where we can study this process in some detail, such as: $(\kappa^2\text{-}Ph_2B(CH_2PR_2)_2)Pt(THF)(CH_3) \xrightarrow[-CH_4]{C_6H_6,\,50\,°C} Pt(THF)(C_6H_5)$.
            - · This presumably proceeds through benzene as a σ adduct.
    2. Oxidation.
        - ■ In the Shilov system, if you use labels, quenching $^{195}PtCl_6{}^{2-}$, you get no $^{195}PtMe$ complexes.
        - ■ Indeed, it appears that $PtCl_6{}^{2-}$ is acting purely as a Cl_2 source.
    3. Reductive elimination.
        - ■ An external nucleophilic attack, as generally supported by mechanistic studies.
        - ■ $(\kappa^2\text{-}PR_2CH_2CH_2PR_2)Pt(CH_3)_3OR \rightleftharpoons [(\kappa^2\text{-}PR_2CH_2CH_2PR_2)Pt(CH_3)_3]OR \xrightarrow{OR'}$
          $(\kappa^2\text{-}PR_2CH_2CH_2PR_2)Pt(CH_3)_2 + CH_3OR + CH_3OR'$.
        - ■ $[PtCl_5(CH_3)]^{2-} \xrightarrow[-Cl^-]{} [PtCl_4Me]^- Cl^- \xrightarrow{H_2O} PtCl_4{}^{2-} + MeOH + H^+$.
        - ■ $[PtCl_5(CH_3)]^{2-} \xrightarrow[-Cl^-]{} [PtCl_4Me]^- Cl^- \xrightarrow{Cl} PtCl_4{}^{2-} + CH_3Cl$.
        - ■ Labeling studies also support the inversion of stereochemistry.

- While methane activation may not yet be feasible industrially, it is in the pharmaceutical industry.

- Directed C−H activation.

- Examples:

    - Early: $(i\text{-}Pr)(H_2N)(H)C\text{-}COOH \xrightarrow{cat\,/\,ox} H_2 +$ the cyclized product.
        - ■ Catalyst is K_2PtCl_4.
        - ■ Using $PtCl_6{}^{2-}$ (10%) as an oxidant gives a 21% yield.
        - ■ Using $CoCl_2$ (10%) as an oxidant and a lower catalyst loading gives a 67% yield.
        - ■ Using $CoCl_2$ (5%) as an oxidant and a dramatically lower catalyst loading gives a 20% yield.
        - ■ Because this is giving a higher yield than catalytically, something else is probably going on.
    - Palladium has started to dominate over platinum.
    - Sanford: $(Me)(CH_3N)C\text{-}CMe_3 \xrightarrow{Pd(OAc)_2} [(Me)(CH_3N)C\text{-}CMe_2CH_2Pd(\mu\text{-}OAc)]_2 \xrightarrow{PhI(OAc)_2}$
      $(Me)(CH_3N)C\text{-}C(CH_2X)(CH_2Y)(MeOAc)$ where X and Y are functional groups.
        - ■ This gives a picture of where palladium can directly activate a C−H bond.
    - Further examples from Jin-Quan Yu and Guangbin Dong (UChicago).
    - The key in all of these examples is a directing nitrogen, to which the palladium catalyst bonds, bringing it close to the hydrogen that we want to activate.
        - ■ This is nicely demonstrated by Guangbin Dong's example, as seen in Figure 6.7.
        - ■ By placing the palladium and hydrogen close together, we can facilitate the oxidative addition even if it is unfavorable or has a high barrier. The chelate effect really helps here.
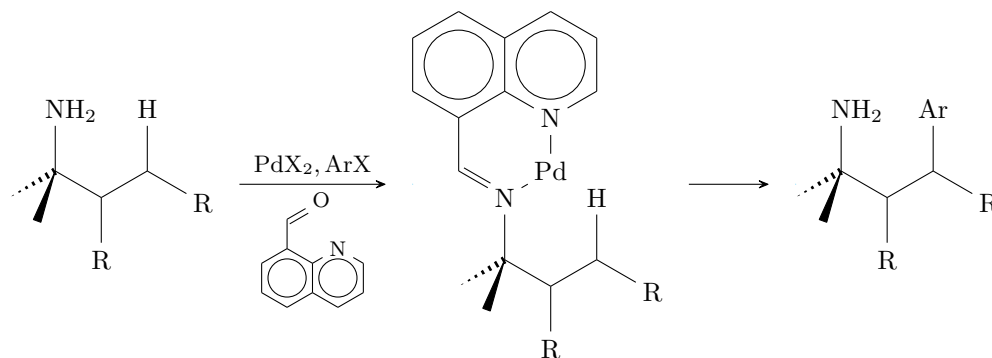
Figure 6.7: Dong's directed C−H activation.

- One of the key features of C−H activation is C−H's are terrible ligands, so tricks like this are essential to get a high effective concentration to drive the forward reaction.

- You can also intercept C−H activations to do carbonylations.

- Examples:

  - $C_6H_6 + CO \xrightarrow[K_2S_2O_8 \ / \ TFA]{Pd(OAc)_2 \ (10\%)} C_6H_5CO_2H \ (100\%)^{[1]}$.

    - Persulfate is our oxidant here.
    - Run at room temperature for 20 hours.

  - $C_6H_{12} + CO \xrightarrow{RT \ (10\%)} C_6H_{11}CO_2H \ (4\%)$.

  - $CH_4 + CO \xrightarrow[K_2S_2O_8 \ / \ TFA]{VO(acac)_2, \ 80\,°C} HC_2H_3O_2 \ (93\%)^{[2]}$.

    - Run at 80 °C for 20 hours.
    - TON = 18.
    - We can also do this without persulfate:

  - $CH_4 + CO + \frac{1}{2}O_2 \xrightarrow[H_2O]{RhCl_3} HC_2H_3O_2$.

    - Run at 100 °C.

  - $2\,CH_4 + H_2SO_4 \xrightarrow{Pd^{II}} CH_3CO_2H + 4\,SO_2 + 6\,H_2O$.

    - Work by Periana.
    - C−C coupling reactivity (related to Fischer-Tropsch).
    - Can pretty easily be pushed to make methane: Reverse water-gas shift to syn gas, Fischer-Tropsch to methane, couple methane to an acetic acid product, to make a chain, to make higher order C−C-coupled products, to feed into other industrial processes.
    - Mechanism shown (not a ton is known, but there are a lot of proposed possible interconversions).

- The key equilibrium that one needs to control for C−H activation: $M + H-CR_3 \rightleftharpoons M(H|CR_3) \rightleftharpoons M(H)(CR_3)$.

  - Typically, the first step is the hard step because C−H ligands are very poor ligands.
    - Even if the C−H activation is thermodynamically stable, you're stuck without the adduct.
  - How to control these equilibria:

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[1]Note that TFA is trifluoro acetic acid.
[2]VO(acac)$_2$ is vanadyl acetylacetanate.

1. Ligands that are good σ-donors (i.e., electron-rich metal centers) favor the products.
2. M^{n+2} d^6 is common, e.g., $Ir^{I/III}$, $Pt^{II/IV}$, $Pd^{II/IV}$.
3. Most common for $4d$ and $5d$ metals because higher oxidation states are more stable as you go down a column and there are stronger bonds that will push the equilibrium toward the right.
4. Small(ish) R's help.
5. Less sterically hindered metals.
6. Electronically unsaturated metals ($\leq 16\,e^-$) help.

– Thermodynamics of activating C−H bonds.

  ■ Data listed.
  ■ Conclusion 1: Thermodynamically, it's more favorable to activate secondary and tertiary C−H's, but sterically, it's more favorable to activate primary ones.
  ■ Conclusion 2: Thermodynamically, it's more favorable to activate H_3C-H > Ph−H > RC≡C−H. It's easier to activate Ph−H bonds over H_3C-H bonds despite the inverse difference in bond strengths because metals can form π adducts with arenes. This bypasses the hard step, allowing the oxidative addition to HMPh to proceed relatively easily.

- Thinking more about σ adducts and oxidative addition:

- Bob Bergman: $Cp^*IrH_2(PMe_3) \xrightarrow[-H_2]{h\nu} [Cp^*Ir(PMe_3)] \xrightarrow{C_6H_{12}} Cp^*Ir(PMe_3)(\kappa^2\text{-}C_6H_{12}) \xrightarrow[\text{chromatography}]{h\nu}$
  $Cp^*Ir(PMe_3)(Cy)(H) \xrightarrow[-C_6H_{12}]{C_5H_{12}} Cp^*Ir(PMe_3)(H)(C_5H_{11})^{[3]}$.

  – There could also be σ-bond metathesis pathways, but it's likely a reductive elimination type process.

- Isotope effects:

  – Kinetic isotope effects (KIEs) are common mechanistic probes.

  – Data listed.

  – In a primary KIE, you would expect protons to react faster than deuterium because they're lighter, they tunnel faster, etc.

    ■ Symbolically, you would expect $\frac{k_H}{k_D} > 1$.

  – However, tungsten and iridium have an inverse KIE (deuterium is faster than hydrogen).

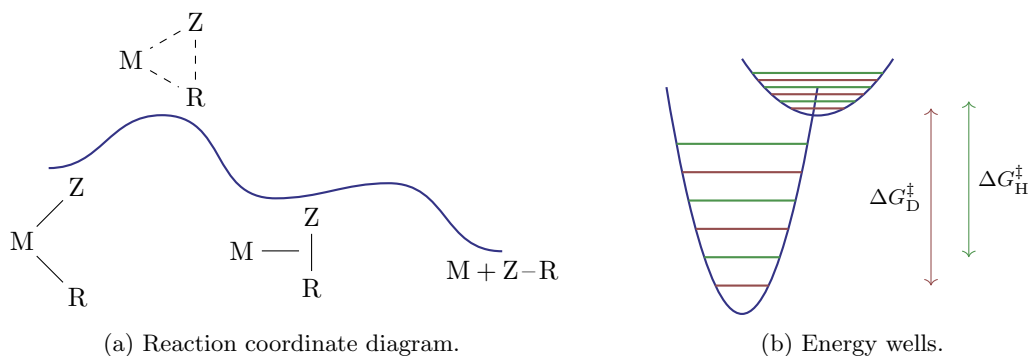 – Explaining KIEs (in terms of vibrational energy).

  – Normal KIEs:

(a) Reaction coordinate diagram. (b) Energy wells.

Figure 6.8: Normal KIE.

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[3] Note that Cy is an abbreviation for cyclohexyl.

- In Figure 6.8a, Z is either a proton or deuterium.
- Notice that this is a downhill reaction.
- The key transition state is the first one.
- Because we're eliminating a strong bond (a C–H bond), we have a transition state with a weaker bond.
- Recall that $E = h\nu$ and $\nu \propto \sqrt{1/\nu}$, where μ is the effective mass of the oscillators and the transition state. Thus, energy decreases as effective mass increases.
- Now think of vibrational wells for the reactant and the transition state (see Figure 6.8b). A proton and deuterium will have identical vibrational spacing, but the levels for deuterium will be lower because deuterium has lower energy. Note also that the spacing is closer together in the wider well because it is wider.
- Thus, we have here that $\Delta G_H^\ddagger < \Delta G_D^\ddagger$ due to zero-point energy effects.
- Essentially, if the transition state has weaker bonds than the starting material, a normal KIE is expected.

- Inverse KIE:

(a) Reaction coordinate diagram.
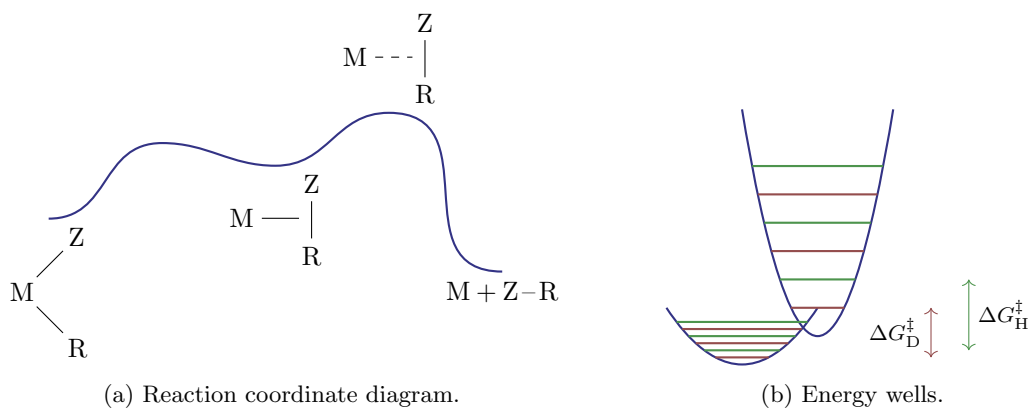
(b) Energy wells.

Figure 6.9: Inverse KIE.

- Notice that this is an uphill reaction.
- The key transition state is the second one.
- Here, we have a transition state with a stronger bond.
- Thus, we have here that $\Delta G_D^\ddagger < \Delta G_h^\ddagger$.
- Essentially, an inverse KIE originates from a transition state having stronger bonds than the starting material, i.e., "later" transition states.
- This can also arise from equilibrium isotope effects.

- Bernskoetter et al. (2009): Observed σ adducts with CH_4.

  - Took rhodium bound to a pincer ligand and a methyl group.
  - Treated it with an acid ($[HBAr^F] \cdot 2\,Et_2O$ [an etherate]) and a funky solvent (CD_2Cl_2F) at a very cold temperature ($-110\,°C$) to make a rhodium κ^2 methane complex.
  - With NMR spectroscopy, they can tell that the methane is rapidly spinning around, so all hydrides are bonding now and then (equilibrating).
  - Comparing the C–H coupling constants for the adduct vs. free methane reveals a slight weakening of the C–H bond, but more importantly, the Rh–H coupling constant is quite a bit weaker than you would expect for a full hydride.

- Primary take away: Directed C–H activation is a very powerful technique because you can put these C–H bonds in close proximity, but one of the biggest challenges is forming σ adducts; in doing this, we can observe the weird inverse KIEs of Figures 6.8 and 6.9.

6.3   Midterm 2 Review

5/22:
- Midterm 2: 5/25 from 6:00-8:00 PM (proctored by Sophie).

- No discussion on the 25th — this is replacing that. Office hours are still on.

- If we follow her comments on the papers, we're almost guaranteed to get a good grade.

  – She's taking time — if she gets our drafts back late, she'll give us an extension.

- Midterm 2 content (top things to focus on in order):

  1. N_2 reduction (the question on dinitrogen reduction from one of your homeworks; really know this).
     – The Schrock paper is really helpful for this!
     – Be able to understand σ donation and π acceptance.
     – Be able to draw orbitals.
     – Know Chatt and Hoffmann mechanisms.
     – First row vs. late row metal preferences.
     – We can show adding a proton and electron together (we don't need to do this separately).
     – Show oxidation states for every intermediate!
  2. Polymerization (chain walking and transfer, how to get the different tacticities).
     – Know the example from your homework.
     – Know the Wacker oxidation.
  3. Hydrogenation/dehydrogenation.
  4. Metathesis (last question on HW 3).
  5. Hydroformylation, hydrocyanation.
  6. Fundamentals of organometallic reactions: Coordination preferences, insertion/elimination preferences, dihydrogen vs. dihydride, just practice going through and drawing mechanisms.
  7. Strong foundation in ligand donor properties — seriously study homeworks and past tests.
     – Relate to "is this exam cumulative?" question.
     – Know CO, ligand binding properties, high spin/low spin, etc.

- The best way to get better at time is to just practice drawing these mechanisms.

  – Go through it when you first get it, do the questions you know quickly, and then proceed to the harder ones.

- See example questions posted!

- Explain how a C_i catalyst gives a hemi-isotactic polypropylene avter activation with MAO to give a Zr alkyl and draw the mechanism of chain growth.

  – Activation step: $L_n MCl_2 \xrightarrow{\text{MAO}} L_n MMe^+$.
    ■ MMAO is another catalyst that's even more spicy.
  – Squiggly methyl means methyl bound with either/unknown stereochemistry.

- TEMPO is a well-known radical trap.

6.4 Lecture 22: Allylic Substitution

5/24:
- General form:

$$-=-\text{CHMeX} + \text{NuH} \xrightarrow[\text{base}]{\text{M}} -=-\text{CHMeNu}$$
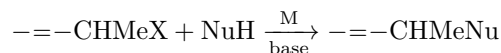
- We feed in an allylic olefin.
- You don't always need a base.
- Seems like a simple S_N2, but there is also other regiochemistry (for instance, the double bond can migrate; see the two products in Figure 6.10).
- Additonally, the mechanism is quite different than that of S_N2, which grants alternative selectivity in terms of both enantiocontrol and regiocontrol.
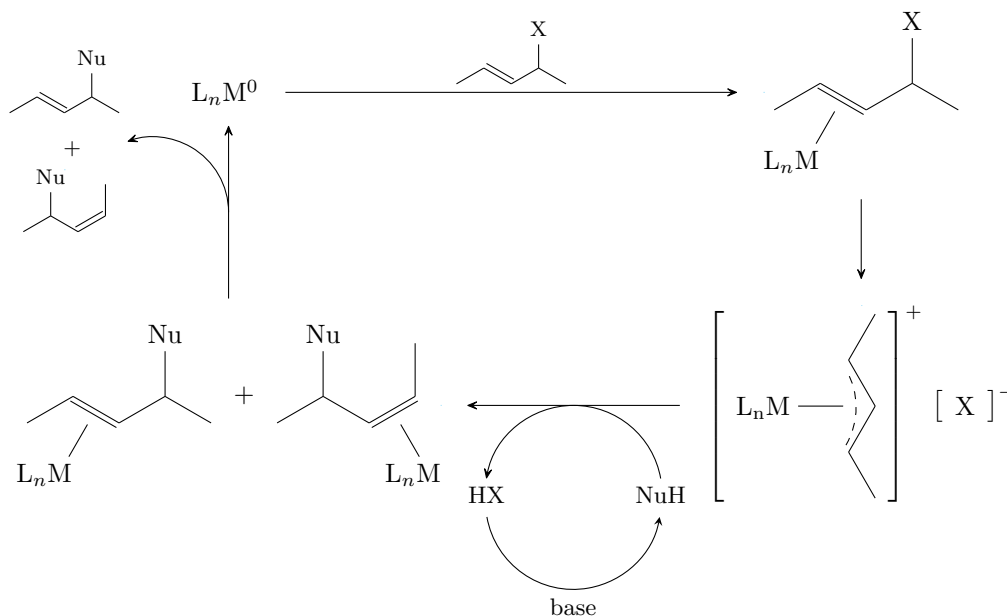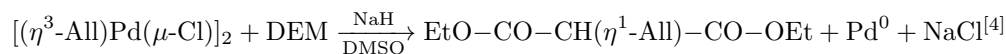
- Mechanism:

Figure 6.10: Allylic substitution mechanism.

- M is frequently palladium.
- X can be an ester, carbonate, phosphonate, hydroxyl, acetate, etc.
- Nu can be an aryl oxide, amine, malonate, etc.
- L_nPd can be Pd(PPh$_3$)$_4$ or Pd(acac)$_2$(PPh$_3$).
- The second step is an oxidative addition to form an allylic species.
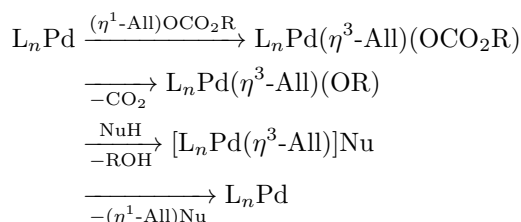- Most cases are an external attack opposite of the metal.

- Tsuji:

$$[(\eta^3\text{-All})\text{Pd}(\mu\text{-Cl})]_2 + \text{DEM} \xrightarrow[\text{DMSO}]{\text{NaH}} \text{EtO}-\text{CO}-\text{CH}(\eta^1\text{-All})-\text{CO}-\text{OEt} + \text{Pd}^0 + \text{NaCl}^{[4]}$$

- One of the earliest stoichiometric examples.
- Taking a process that is not catalytic and making it catalytic.

---

[4]All is an allyl group. DEM is diethyl malonate (see the second reactant in Figure 6.11a).

- Trost pioneers enantioselectivity for this process, which is highly sought after.

  – Achieves 24% ee at first with a chiral ligand at $-40\,°C$.
  – Enantioselectivity is easy because you're erasing any enantioselectivity of the starting material when you planarize into an allyl group and then you can selectively install the enantiochemistry you want in the second step by controlling which face binds to the metal center.

- Nucleophile reactivity: Allyl carbonates > phosphates > acetates.

  – Between an allyl acetate and an allyl carbonate, we might expect the acetate species to be more reactive on the basis of sterics.
    ■ Note that sterics do have some effect: Using bulkier ligands favors allyl acetates.
  – However, the allyl carbonate is more reactive since they make it so that you don't need a base:

$$L_nPd \xrightarrow{(\eta^1\text{-All})OCO_2R} L_nPd(\eta^3\text{-All})(OCO_2R)$$
$$\xrightarrow[-CO_2]{} L_nPd(\eta^3\text{-All})(OR)$$
$$\xrightarrow[-ROH]{NuH} [L_nPd(\eta^3\text{-All})]Nu$$
$$\xrightarrow[-(\eta^1\text{-All})Nu]{} L_nPd$$

   ■ The loss of CO_2 and the subsequent formation of an alkoxide generates base in situ.
   ■ Normally, you would eliminate HX, but here you don't so you don't have to deal with it.

- Epoxides are similar in that they don't need a base.
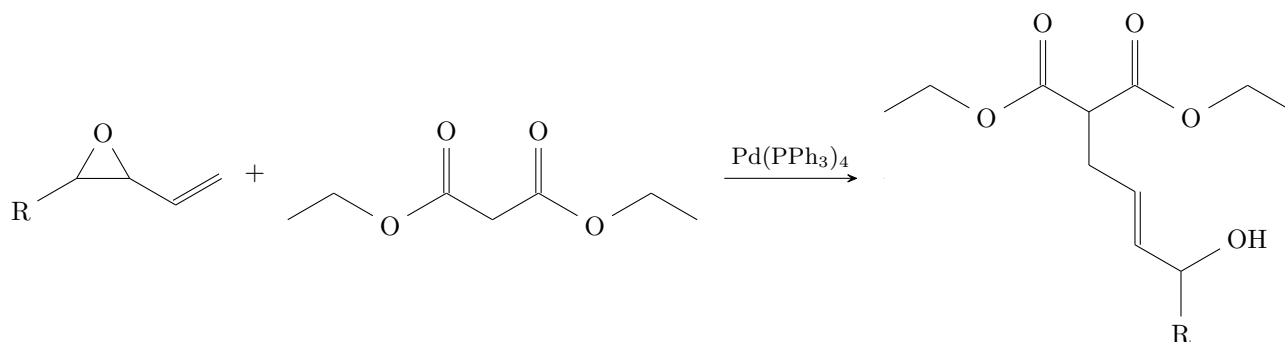
(a) General form.
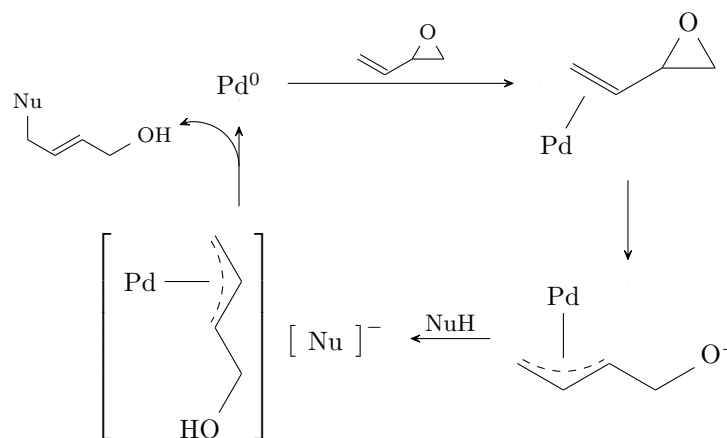
(b) Mechanism.

Figure 6.11: Epoxide allylic substitution.

– The reaction in Figure 6.11a has an 84% yield.

- Nucleophiles:

    – Very broad scope of possible ones.

        ■ Less common with hard, anionic nucleophiles (e.g., amines, amides, imides, aryl oxides).
        ■ Softer nucleophiles are preferred (malonates, enolates, malononitriles).
        ■ These preferences originate from the softness of the palladium center.

    – Thus, very useful.

- One last example (electrophile and nucleophile in the same substrate):
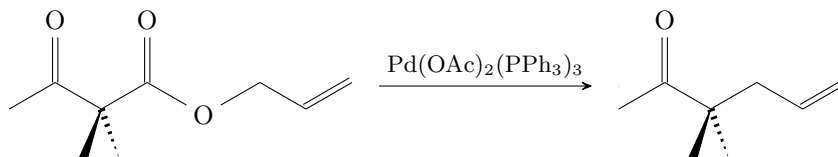

Figure 6.12: Decarbonylization using allylic substitution chemistry.

    – A decarbonylative proccess that proceeds through allylic chemistry.
    – Mechanism shown.