Week 9

Oxidation/Reduction and Organometallics

9.1 Reduction of Carbonyls

3/8:

- In general chemistry, oxidation and reduction referred to the loss and gain of electrons, respectively.
  - In organic chemistry, we think about it differently.
- **Organic oxidation**: Increasing the number of bonds to oxygen or decreasing the number of bonds to hydrogen.
- **Organic reduction**: Decreasing the bonds to oxygen or increasing the bonds to hydrogen.
- Example: Ethene to ethanol is neither an oxidation or reduction since the C−O bond formed is cancelled by the C−H bond formed.
- We now transition to carbonyl chemistry, which will also be really important next quarter.
- **Carbonyl**: Any carbon-oxygen double-bonded system.
  - Important derivatives include aldehydes, ketones, carboxylic acids, esters, and amides.
  - A defining character of carbonyls is their resonance, which we can formalize by representing them as an oxygen anion and a carbocation.
- General reactivity of carbonyls.
  1. Nucleophiles can add to the carbonyl carbon. A slightly acidic aqueous workup from here can form an alcohol.
  2. Oxidation/reduction. Alcohol to carbonyl and vice versa.
- Reduction of aldehydes and ketones.
- General form.

$$\mathrm{RCOR'} \xrightarrow{\text{reagents}} \mathrm{RC(OH)HR'}$$

  - This is a two-step process. We first need a source of H^-, and then an acidic workup.
    - Possible hydride sources are $NaBH_4$ (a weak source) and $LiAlH_4$ (a strong source).
    - The acidic workup reagents are always H_3O^+, H_2O.
- Mechanism.
  - We use the hydride as a nucleophile to attack the carbonyl carbon, and then the acid to protonate the alkoxide intermediate.

- Varying types of carbonyls.
  - Aldehydes and ketones go through the full reaction with both reagents.
  - Esters do not react with $NaBH_4$ (not powerful enough), but do react with $LiAlH_4$. However, they form a primary alcohol in this case.
- Reactivity of carbonyls.

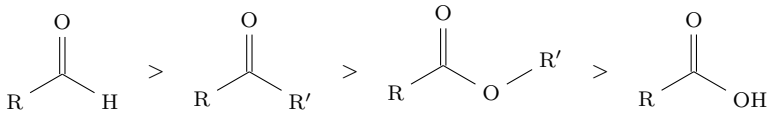
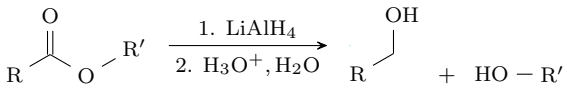


Figure 9.1: Reactivity of carbonyls.

  - $NaBH_4$ stops working after ketones.
- Reduction of esters.
- General form.



- Mechanism.

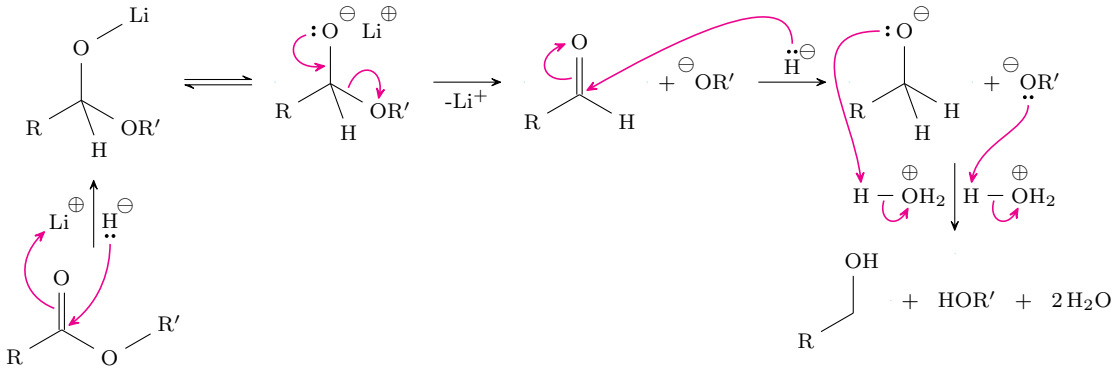
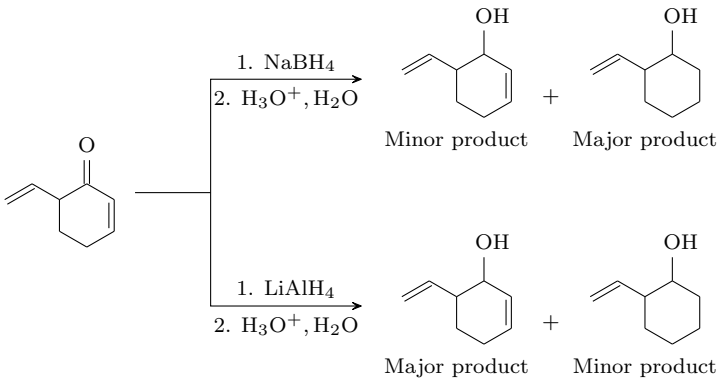


Figure 9.2: Reduction of esters mechanism.

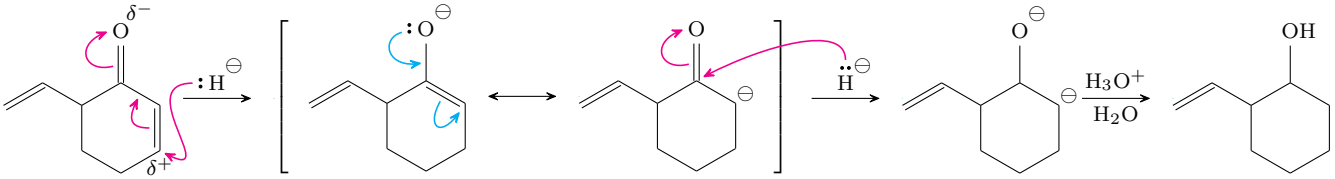
  - Positive lithium ions combine with the oxygen of the carbonyl in the first step. This activates the C=O bond, making the carbon more electrophilic.
    - Thus, by using $LiAlH_4$, we both make the electrophile stronger and introduce a stronger nucleophile.
- **Chemoselective** (reaction): React with one group in the presence of other "related" groups.
  - For example, if we have a ketone and ester in the same molecule, reacting with $NaBH_4$ / H_3O^+, H_2O will yield a chemoselective reduction of the ketone in the presence of an ester. (Reacting with $LiAlH_4$ / H_3O^+, H_2O will alter both groups in a non-chemoselective fashion.)
- Note that we can reduce alkyl halides to hydrocarbons with $LiAlH_4$ / H_3O^+, H_2O.
- Reactivity of an α-β unsaturated compound.

- General form.

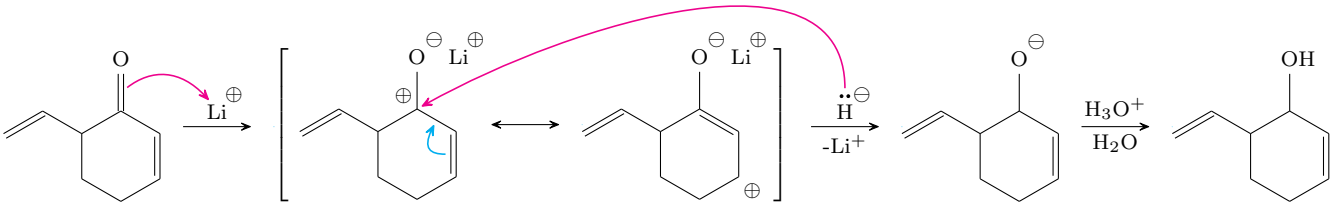


  - With $NaBH_4$, the major product has been reduced both at the ketone and the alkene.
  - With $LiAlH_4$, the major product has been reduced at the ketone only.
  - Note that the alkene that is not conjugated with the carbonyl is untouched.

- Mechanism.



(a) Reduction via $NaBH_4$.



(b) Reduction via $LiAlH_4$

Figure 9.3: Reduction of an α-β unsaturated compound mechanism.

  - On Figure 9.3a.
    - In the leftmost molecule, resonance draws charge toward the electronegative oxygen, making the carbon at the end of the conjugated chain the most electrophilic site in the molecule. Thus, hydride attacks there.
    - The resulting molecule has a ketone as one of its resonance structures, so since ketones are reactive to further hydride attacks, we take this to be the major contributor and react the molecule with hydride again.
    - The 2− product can how be reduced with acid and water.
  - On Figure 9.3b.
    - When Li^+ bonds to the oxygen, it creates a formal carbocation in the ring system that can be delocalized by resonance.
    - However, the carbocation will preferentially exist as a 3° carbocation, so the α carbon is the most electrophilic site in the molecule in this case, making hydride attack there.

- Grignard reagents provide a new way to form C–C bonds.
- **Grignard reagent**: An alkyl magnesium halide compound.
  - Creates carbanions that are both strong bases and strong nucleophiles.
- Forming Grignard reagents.

$$\mathrm{RBr} \xrightarrow[\mathrm{Et_2O}]{\mathrm{Mg^\circ}} \mathrm{RMgBr}$$

  - We need an aprotic solvent such as diethyl ether to stabilize the positive Mg.
    - If there are acidic protons present, the Grignard will just deprotonate them.
- Common Grignard reagents.
  - To add phenyl groups to systems, use phenylmagnesium chloride.
  - To add alkenes to systems, use allylmagnesium bromide.
- Making a Grignard reagent basically inverts the reactivity of the precursor: While the precursor alkyl halide is electrophilic, Grignards are very nucleophilic.
- Grignards can be made out of iodides, bromides, and chlorides.
  - Iodides are more reactive than bromides, are more reactive than chlorides.
  - We commonly find them as bromides, though.
- We can use Grignards as nucleophiles in the reduction of formaldehyde.
  - Creates primary alcohols.
- Using an aldehyde makes a secondary alcohol.
- Using a ketone makes a tertiary alcohol.
- Using an ester adds the Grignard twice and kicks out an alcohol.
- Using a carboxylic acid protonates the alkyl part of the Grignard, releases a magnesium salt, and regenerates the carboxylic acid.
- Since Grignards deprotonate any acids present, we can't use them on molecules that contain alcohols, thiols, carboxylic acids, phenols, amines, and acetylenes.
- Organolithium reagents are conceptually identical to Grignards, but even more ionic/reactive.
- Forming organolithium reagents.

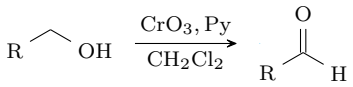
$$\mathrm{RBr} \xrightarrow[\mathrm{Et_2O}]{2\,\mathrm{Li^\circ}} \mathrm{RLi} + \mathrm{LiBr}$$

  - Organolithium reagents are more ionic than Grignards.
    - They are 40% ionic; Grignards are much less.
  - Very reactive (nucleophile and base), but very dangerous, too.

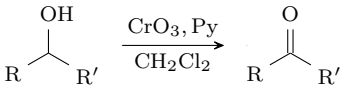
9.2 Oxidation of Alcohols

3/10:

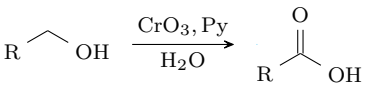
- Alcohol oxidation often occurs with the help of chromium (VI) reagents, of which there are three "flavors."
- **Collins reagent**: The compound CrO_3.
- General form.



(a) Anhydrous oxidation of a primary alcohol.

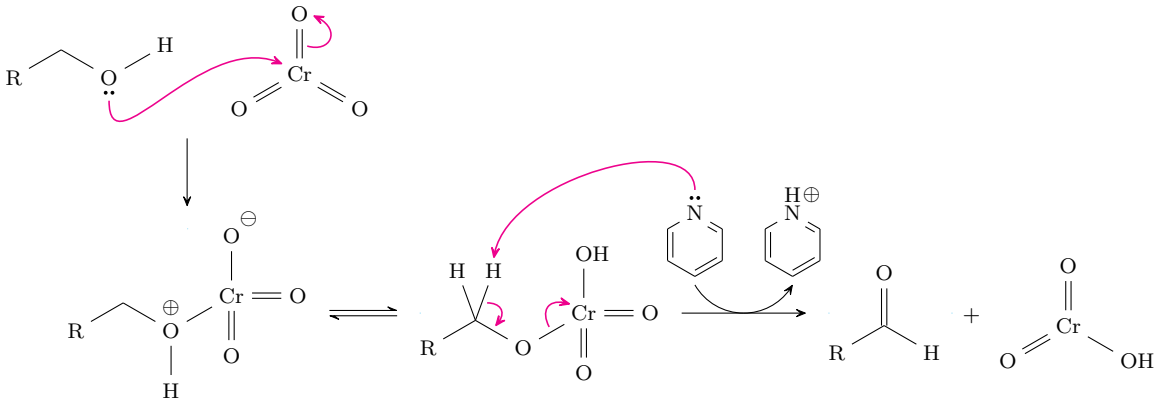


(b) Anhydrous oxidation of a secondary alcohol.

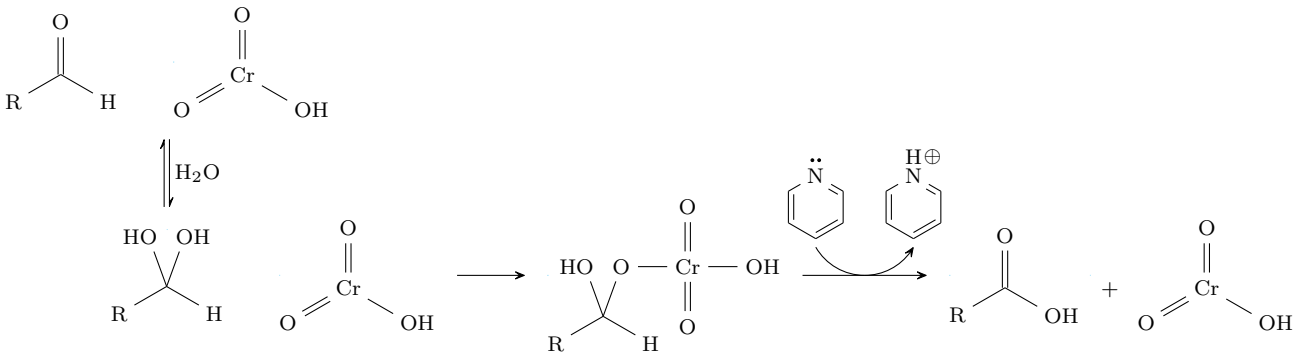


(c) Aqueous oxidation of a primary alcohol.

- Mechanism.



(a) Anhydrous oxidation of a primary alcohol.

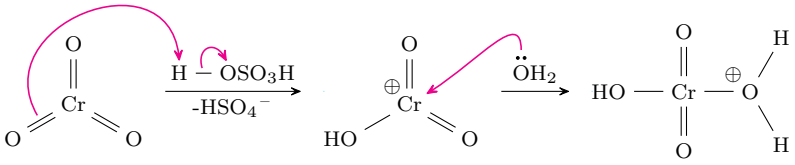


(b) Aqueous oxidation of a primary alcohol.

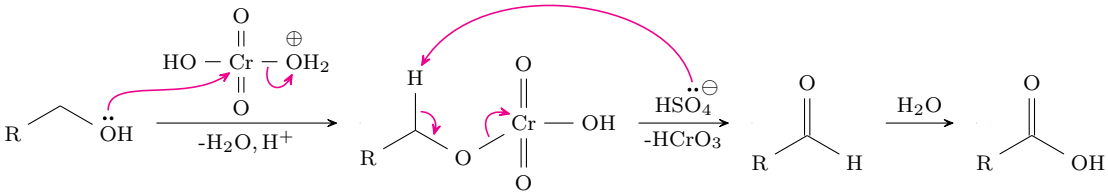
Figure 9.5: Alcohol oxidation via Collins reagent mechanism.

  - On Figure 9.5a.
    - The reversible proton shift may be a 1- or 2-step process.
    - Having a leaving group on the oxygen makes the protons on the α carbon weakly acidic, so pyridine can attack them.
  - On Figure 9.5b.
    - This reaction picks up directly where the other one left off. Essentially, if water is absent, the mechanism will stop after the sequence of steps in Figure 9.5a, and if water is present, the mechanism will continue through the sequence of steps in Figure 9.5a.
    - In the beginning, we note that aldehydes are one of the most electrophilic carbon compounds.
    - Thus, in the presence of water, aldehydes exist in equilibrium with **acetals**.
    - Any acetal that is generated can react with chromium again and another equivalent of pyridine as in the previous mechanism, but this time to generate a carboxylic acid.

- Since water has such an effect on the mechanism, we should be sure specify in the case of oxidation reactions whether the reaction is run under aqueous or anhydrous conditions.
- **Jones reagent**: The mixture $CrO_3 + H_2SO_{4(aq)}$.
- The general form is the same as with Collins reagent, except obviously for the reagents used. In particular...
  - 1° alcohols go to carboxylic acids (water is present).
  - 2° alcohols will go to ketones.
- Mechanism.



(a) Protonated chromic acid formation.



(b) Oxidation of a 1° alcohol.

Figure 9.6: Alcohol oxidation via Jones reagent mechanism.

- **Pyridinium chlorochromate**: The mixture Py, HCl, CrO_3. *Also known as* **PCC**.
  - Mixing these three compounds together yields PyH^+ and CrO_3Cl^-.
    - Note that the chloride is bonded to the chromium center and one of the oxygens adopts the negative charge.
  - We've essentially suped up chromium by adding chloride as a leaving group.
  - Running this in anhydrous conditions allows us to control reactivity (DCM is a good anhydrous solvent here).
- As before, we take 1° alcohols to carboxylic acids and 2° alcohols to ketones.

- **Oxalyl chloride**: The following compound. *Structure*

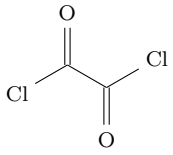
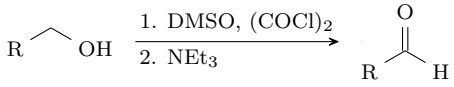
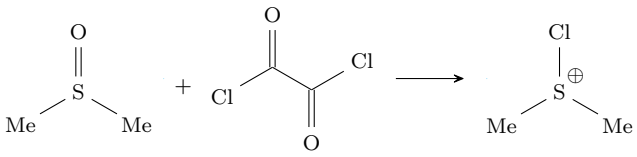


Figure 9.7: Oxalyl chloride.

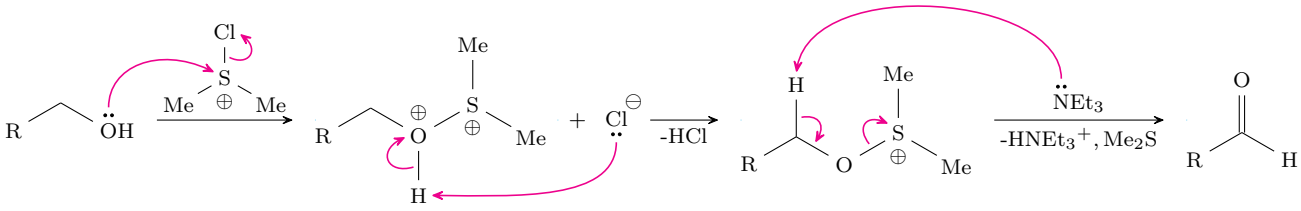
- **Swern oxidation**: An eco-friendly alcohol oxidation mechanism that does away with toxic metal chromium.
- General form.



- Mechanism.



(a) Chlorodimethylsulfonium ion formation.



(b) Oxidation of a 1° alcohol.

Figure 9.8: Swern oxidation mechanism.

  - We won't worry about how the first step proceeds because it's pretty complicated. However, know that it generates an electrophilic sulfur analogous to the chromium.

- A side note on biology.
  - Alcohol dehydrogenase (ADH1), an enzyme in our body, deals with EtOH and other harmful alcohols by transforming them into acetaldehyde.
  - Acetaldehyde is very toxic, though, but in the presence of ADH2 and H_2O, it will form acetic acid (vinegar, which is relatively nontoxic).
  - Being flushed when you drink is a result of having a deficiency of ADH2.
    - Many of the problems associated with drinking come from a buildup of acetaldehyde!
    - You can take ADH1 inhibitors to keep the ethanol around for longer because that's safer than letting acetaldehyde build up.

- Protecting groups.
  - Trimethylsilyl chloride (TMSCl) is a common one.

– Adding it and then a weak base such as NEt_3 with DCM as a solvent leads to the formation of a **silyl-protected alcohol** (see Figure 8.3).

- **Silyl-protected alcohol**: A very stable form of an alcohol which allows the addition of Grignards, etc. to react with the rest of the compound in question. *Given by*

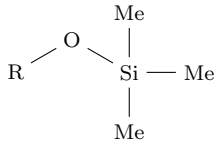
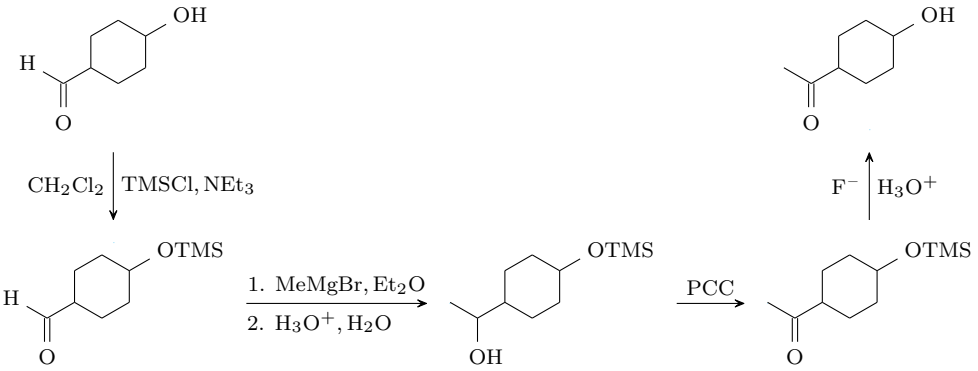


Figure 9.9: Silyl-protected alcohol.

– The silyl protecting group can be removed by acid (H_3O^+, H_2O). This kicks out TMSOH and the alcohol.

– It can also be removed by fluoride (F^-) followed by acid. This kicks out TMSF and RO^- which is protonated to become ROH.

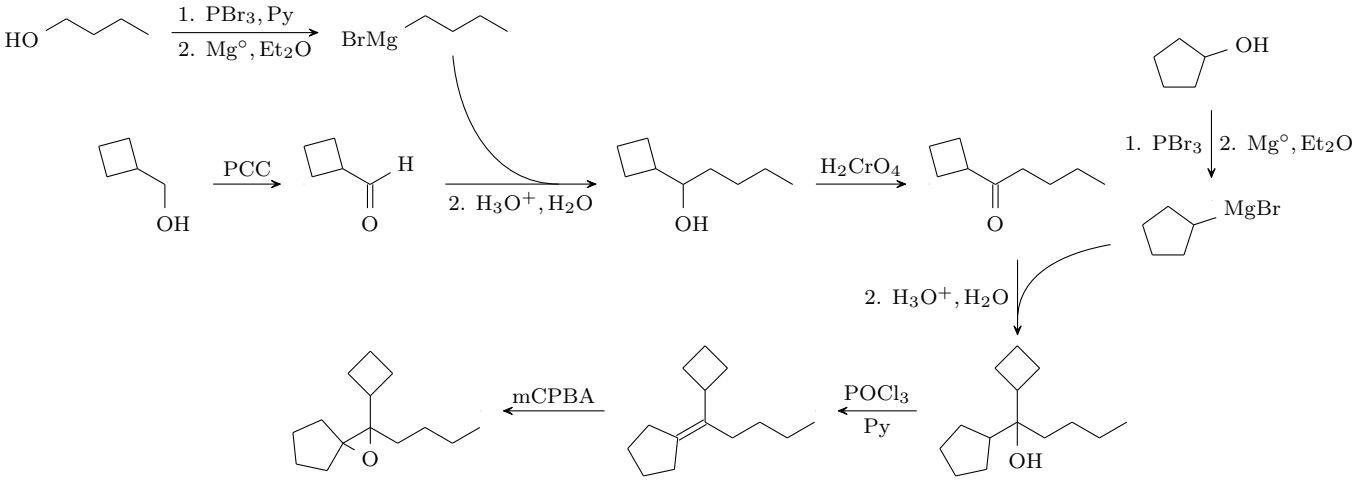
- Example of using protecting groups in a synthesis:



– Remember: Grignards are bases (look out for acidic protons), and make sure there are no other reactive sites on your molecule.

– You can get the products you want, though, via protection and deprotection.

- Practice problem: Synthesize the end product using only carbon atoms from alcohols with 5 or fewer carbons.



- Zaitsev's rule eliminates one alkene and ring strain eliminates the other. Thus, the alkene that's formed is the most stable one.

9.3 Exam 3 Cheat Sheet

3/15:

COMMON ABSORPTIONS	
Aromatic C–C	Two peaks usually in the range of $1500 - 1600\,cm^{-1}$
C=C	$\sim 1650\,cm^{-1}$
C=O	$\sim 1710\,cm^{-1}$ (shifts to $\sim 1735\,cm^{-1}$ for esters)
C≡C	$2100 - 2300\,cm^{-1}$
C≡N	$2100 - 2300\,cm^{-1}$
C–H (aldehyde)	Two peaks at $2170\,cm^{-1}$ and $2810\,cm^{-1}$
sp^3 C–H	Just to the right of $3000\,cm^{-1}$
sp^2 C–H	Just to the left of $3000\,cm^{-1}$
sp C–H	$\sim 3300\,cm^{-1}$
N–H	$\sim 3300\,cm^{-1}$ (one peak for –NH–, two peaks for $-NH_2$)
O–H (alcohol)	$\sim 3400\,cm^{-1}$ (a broad, smooth peak)
O–H (acid)	$\sim 2500 - 3500\,cm^{-1}$ (a very broad, ugly [not smooth] peak)

Common IR spectroscopy absorptions.

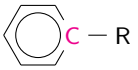
Type of Proton	Chemical Shift (δ, ppm)	Type of Proton	Chemical Shift (δ, ppm)
1° Alkyl, RCH_3	0.8-1.2	Alkyl bromide, RCH_2Br	3.4-3.6
2° Alkyl, RCH_2R	1.2-1.5	Alkyl chloride, RCH_2Cl	3.6-3.8
3° Alkyl, R_3CH	1.4-1.8	Vinylic, $R_2C{=}CH_2$	4.6-5.0
Allylic, $R_2C{=}CR{-}CH_3$	1.6-1.9	Vinylic, $R_2C{=}CRH$	5.2-5.7
Ketone, $RCOCH_3$	2.1-2.6	Aromatic, ArH	6.0-8.5
Benzylic, $ArCH_3$	2.2-2.5	Aldehyde, RCOH	9.5-10.5
Acetylenic, $RC{\equiv}CH$	2.5-3.1	Alcohol hydroxyl, ROH	0.5-6.0*
Alkyl iodide, RCH_2I	3.1-3.3	Amino, $R{-}NH_2$	1.0-5.0*
Ether, $ROCH_2R$	3.3-3.9	Phenolic, ArOH	4.5-7.7*
Alcohol, $HOCH_2R$	3.3-4.0	Carboxylic, RCOOH	10-13*

*The chemical shifts of these protons vary in different solvents and with temperature and concentration.

Approximate proton chemical shifts.

Reminders:

- Alkene reactions to know: hydrogenation ($H_2 + Pd/C$), dihydroxylation (1. OsO_4, 2. $NaHSO_3$), ozonolysis ($O_3 + Me_2S$), hydrobromination (HBr), and bromination (Br_2).
  - Extra possibles: Acid-catalyzed hydration ($H_2SO_4 + H_2O$), oxymercuration/demercuration (1. $Hg(OAc)_2, H_2O$, 2. $NaBH_4$), hydroboration/oxidation (1. BH_3, 2. H_2O_2, NaOH), hydrogenation (H_2 + Lindlar's catalyst for alkynes to *cis*-alkenes, $2\,Na + 2\,NH_3$ for alkynes to *trans*-alkenes), alkyne synthesis (terminal alkyne + 1. $NaNH_2$, 2. RBr).
  - Make ketones/aldehydes with ozonolysis, acid-catalyzed hydration of alkynes, and hydroboration of alkynes (with $(sia)_2BH$ for terminal alkynes to aldehydes).
  - Alkene to diene: 1. Br_2, 2. NaOH.
    - Alkene to alkyne: 1. Br_2, 2. $3\,NaNH_2$.
- Frost method: Point down, MOs at the carbons.

Type of Carbon	**Chemical Shift (δ, ppm)**
1° Alkyl, RCH_3	0-40
2° Alkyl, RCH_2R	10-50
3° Alkyl, $RCHR_2$	15-50
Alkyl halide or amine, R_3CX ($X = Cl, Br, NR'_2$)	10-65
Alcohol or ether, R_3COR'	50-90
Alkyne, $RC{\equiv}R'$	60-90
Alkene, $R_2C{=}R'$	100-170
Aryl, 	100-170
Nitrile, $RC{\equiv}N$	120-130
Amide, $RCONR'_2$	150-180
Carboxylic acid or ester, $RCOOR'$	160-185
Aldehyde or ketone, $RCOR'$	182-215

Approximate carbon-13 chemical shifts.

  - 5-membered rings: 3 bonding / 2 antibonding. 7-membered: 3 bonding / 4 antibonding.

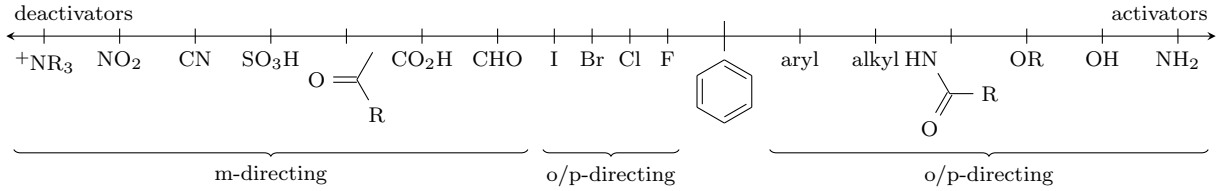
- Aromaticity checklist: Flat, cyclic, conjugated, uninterrupted flow of p-orbitals, $(4n+2)$-rule.
- $(+/-)$ for Diels-Alder reactions!
- F-C reactions happen ONLY IF there is not an EWG on the ring.
- Add stronger EWGs later.
- Nucleophile strengths.

$$^{-}\text{NRH} > \text{RO}^{-} \,/\, \text{HO}^{-} > \text{Br}^{-} > \text{NR}_3 > \text{Cl}^{-} > \text{F}^{-} > \text{H}_2\text{O} \,/\, \text{ROH} > \text{alkene} > \text{benzene}$$

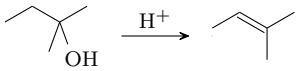
Reactions:

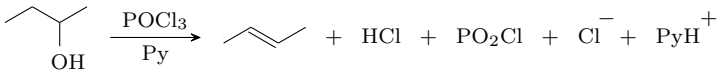
- $=- \xrightarrow[h\nu]{Br_2} =--Br$
  - Chlorination problems: Polychlorination, selectivity.
- $-= \xrightarrow[air]{HBr,\, h\nu} ---Br$
- $C_6H_6 \xrightarrow{D_3O^+} C_6D_6$
- $PhH \xrightarrow[FeBr_3]{Br_2} PhBr$
  - $AlCl_3$, CuI_2.
- $PhH \xrightarrow[H_2SO_4]{HNO_3} PhNO_2$
- $PhH \xrightarrow[H_2SO_4]{SO_3} PhSO_3H$
- $PhH \xrightarrow[AlCl_3]{RCOCl} PhCOR$

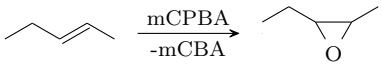
- $\mathrm{PhH} \xrightarrow[\mathrm{AlCl_3}]{\mathrm{RCl}} \mathrm{PhR}$
- benzylic carbonyl $\xrightarrow[\mathrm{HCl}]{\mathrm{Zn(Hg)}}$ reduced carbon
- $\mathrm{PhR} \xrightarrow[\mathrm{H_2O}]{\mathrm{KMnO_4}} \mathrm{PhCOOH}$
  - Needs benzylic hydrogen.
- $\mathrm{PhNO_2} \xrightarrow{\text{reagents}} \mathrm{PhNH_2}$
  - $\mathrm{H_2} + \mathrm{Pd/C}$ or $\mathrm{SnCl_2} + \mathrm{H_2O}$ (selective).
- $\mathrm{PhNH_2} \xrightarrow[\mathrm{HCl}]{\mathrm{NaNO_2}} \mathrm{PhN_2}^+ + \mathrm{X}^-$
  - Mechanism has many equilibrium steps (only first and last are not).
- $\mathrm{PhN_2}^+ \xrightarrow[\mathrm{H_2O}]{\mathrm{Cu_2O}} \mathrm{PhOH}$
  - $\mathrm{PhN_2}^+ \xrightarrow{\mathrm{CuCl}} \mathrm{PhCl}$
  - $\mathrm{PhN_2}^+ \xrightarrow{\mathrm{CuBr}} \mathrm{PhBr}$
  - $\mathrm{PhN_2}^+ \xrightarrow{\mathrm{CuI}} \mathrm{PhI}$
  - $\mathrm{PhN_2}^+ \xrightarrow{\mathrm{CuCN}} \mathrm{PhCN}$
- $\mathrm{PhN_2}^+ \xrightarrow{\mathrm{D_3PO_2}} \mathrm{PhD}$
- $\mathrm{PhBr} \xrightarrow[\mathrm{NH_3}]{\mathrm{NaNH_2}} \mathrm{PhNH_2}$
- $\mathrm{PhCl} \xrightarrow[\mathrm{NuH}]{\mathrm{NaNu}} \mathrm{PhNu}$
- $\mathrm{PhH} \xrightarrow[> 1000\,\mathrm{psi}]{\mathrm{Pd}} \mathrm{CyH}$
- benzene $\xrightarrow[\mathrm{NH_3\,/\,EtOH}]{2\,\mathrm{Li}}$ cyclohexa-1,4-diene $+ 2\,\mathrm{LiOEt}$

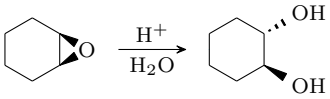


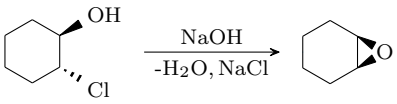
Activators and deactivators.

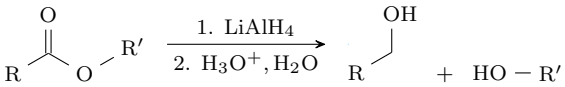
- $\mathrm{ROH} \xrightarrow{\mathrm{HBr}} \mathrm{RBr}$
- $\mathrm{ROH} + \mathrm{SOCl_2} \xrightarrow{\mathrm{Py}} \mathrm{RCl} + \mathrm{SO_2} + \mathrm{Cl}^- + \mathrm{PyH}^+$
  - $\mathrm{PBr_3}$, $\mathrm{PI_3}$.
- $\mathrm{ROH} + \mathrm{Nu} \xrightarrow[\mathrm{NEt_3}]{\mathrm{TsCl}} \mathrm{RNu} + \mathrm{HCl}$
- 

- 

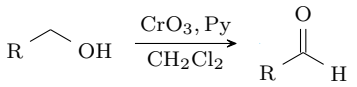
- ROH $\xrightarrow[\text{MeI}]{\text{NaH}}$ ROMe + H_2 + NaI — Williamson Ether Synthesis.
- ROR′ $\xrightarrow{\text{HBr}}$ RBr + R′OH
  - Must use HBr or HI, not HCl.
- 

- 

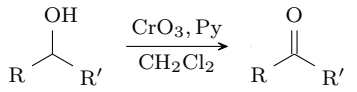
  - Can be trapped by HCl or HBr.
  - Acidic conditions → CC+ stability is important; basic → sterics.
- 

- RCOR′ $\xrightarrow{\text{reagents}}$ RC(OH)HR′
  - $NaBH_4$ or $LiAlH_4$.
- 

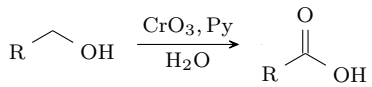
- RBr $\xrightarrow[\text{Et}_2\text{O}]{\text{Mg}^\circ}$ RMgBr
- RBr $\xrightarrow[\text{Et}_2\text{O}]{2\,\text{Li}^\circ}$ RLi + LiBr
- Collins reagent:



(a) Anhydrous oxidation of a primary alcohol.



(b) Anhydrous oxidation of a secondary alcohol.



(c) Aqueous oxidation of a primary alcohol.

  - Jones reagent: $CrO_3 + H_2SO_{4(aq)}$; PCC: Py, HCl, CrO_3; Swern oxidation: 1. DMSO, $(COCl)_2$, 2. NEt_3.

9.4 Chapter 12: Alcohols from Carbonyl Compounds

From Solomons et al. [1].

- Together, reduction of carbonyls and modification by Grignards and organolithium reagents fall under the category of **nucleophilic addition**.
- There exist lowest and highest oxidation states of an organic compound.

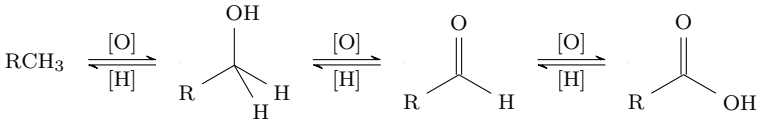


Figure 9.11: Oxidation state spectrum.

  - Note that we use [H] to indicate in a general way that a molecule has been reduced and vice versa for [O].
- "Oxidation of an organic compound may be more broadly defined as a reaction that increases its content of any element more electronegative than carbon" [1, p 537].
- $LiAlH_4$ is also denoted by the acronym LAH.
- Since LAH reacts violently with proton donors to release hydrogen gas, $NaBH_4$ is a much safer (and therefore preferable) reagent for reducing aldehydes and ketones.
  - Importantly, it can be used along with protic solvents.
  - LAH is typically used in Et_2O. After the reaction is complete, EtAc is added cautiously to decompose remaining LAH and then water to decompose the alumina complex, rendering it inert.
- Aldehydes and ketones can also be reduced via $H_2 + Pd/C$ (hydrogen and a metal catalyst) and $Na^\circ +$ ROH (sodium metal in an alcohol solvent).
- Almost all types of alkyl halides can be reduced by $LiAlH_4$ in ether followed by sulfuric acid in water.
  - Note that the proton comes from $LiAlH_4$, so we may use $LiAlD_4$ to replace the halide with deuterium.
- Primary and secondary alcohols can be reduced to carbonyl compounds, but tertiary ones cannot.
  - This is because we need a hydrogen on the α carbon to lose along with the hydrogen from the alcohol group.
- Oxidation of alcohols.

3/11:
  - "Primary alcohols can be oxidized to aldehydes, and aldehydes can be oxidized to carboxylic acids" [1, p 542].
  - "Secondary alcohols can be oxidized to ketones" [1, p 542].
  - "Tertiary alcohols cannot be oxidized to carbonyl compounds" [1, p 542].
- The common mechanistic theme of alcohol oxidation by elimination.
  - We attach a leaving group to the hydroxyl oxygen and deprotonate.
  - Attacking an α hydrogen subsequently causes elimination of that hydrogen and the leaving group; the hydrogen's electrons become the double bond.
- The Swern oxidation is usually carried out at low temperatures.

- Chromic acid (H_2CrO_4) oxidation is discussed, but in a mechanistically different manner to that presented in class.
- Chromic acid is orange-red, but Cr(III) (in the product mixture) is greenish blue. Thus, reagents like Jones reagent can serve as a color-based test for the presence of functional groups including primary and secondary alcohols and aldehydes.
  - This color change was the basis of the original brethalyzer test.
- Since PCC is soluble in solvents other than water (e.g., CH_2Cl_2), it can be used for the necessarily anhydrous monooxidations of alcohols.

3/10:

- **Organometallic compound**: A compound that contains a carbon-metal bond.
- C–M bonds are largely ionic when $M = Na, K$, are largely covalent when $M = Pb, Sn, Hg, Ti$, and are in between when $M = Mg, Li$.
- Reactivity of organometallics increases with increasing ionic character.
  - Alkylsodium an alkylpotassium compounds are among the most powerful of bases, but also react explosively with water and burst into flame when exposed to air.
  - The more stable ones may only be volatile in air, but are still highly poisonous (e.g., Et_4Pb, the infamous antiknock compound formerly used in leaded gasoline).
- Most Grignards exist in equilibrium between an alkylmagnesium halide and a dialkyl magnesium.

$$2\,RMgX \rightleftharpoons R_2Mg + MgX_2$$

- Grignards in their alkylmagnesium halide state also form a complex with their aprotic solvent, attracting electron pairs in two partial bonds to their positive magnesium.
- A Grignard reagent behaves like a strong base and reacts to form a weak conjugate acid (such as its protonated or otherwise alkylated form).
- Grignard reagents can even deprotonate terminal alkynes.
  - This serves as a method of production of alkynylmagnesium halides and alkynyllithiums, though.