1 Nomenclature

Notation: Recall the following notation (primary, secondary etc.)

- IUPAC naming priority, alcohol > alkene ~ alkyne > halide (more oxidized functional groups have higher priority)
- Alcohols use the suffix "-ol".
- Number to give the -OH the lowest number, and if this is the same numbering from both "ends", then (and only then), number to give the first alkene the lowest number.
- Number to give the first substituent the lowest number only of all else is equal.

Examples

- Numbering is performed to give the alcohol the lowest number, not the substituents.
- For more than one functional group (above right), put the number that refers to the functional group immediately in front of the functional group.

- In this example (b), the -OH group is #4 numbering from either end, therefore it is numbered from the left end to give the alkyne the lowest number, but only because the alcohol is #4 from either end, in all cases number to give the alcohol the lowest number unless there is a special case such as this one.
- Note the use of number directly before the functional group in the examples above, used when we have multiple functional groups.
- When we have multiple functional groups they are included in the name in the order: first -ene (if there is one), then -yne (if there is one) followed by -ol.

In addition to IUPAC names, many organic structures have "common" names, that are often historical, but are still widely used, more than the IUPAC names. Some common alcohols with common names:

- Those with the * symbol you should know.
2 Alcohol Acidity, Return to Substituent Effects

• Alcohols are weak acids, the -OH bonds are similar to those in water.

Example: The simplest alcohol methanol:

\[ \text{pKa} \approx 15.5 \quad \text{H}_2\text{O} \rightleftharpoons \text{CH}_3\text{OH} \rightarrow \text{CH}_3\text{O}^- \quad + \quad \text{H}_3\text{O}^+ \]

- The conjugate base anion of water is the hydroxide anion.
- The conjugate base anion of an alcohol is generically an alkoxide anion, i.e. the conjugate base anion of methanol is the methoxide anion, the conjugate base of ethanol is the ethoxide anion etc.
- In general we will find that the acidity of alcohols is determined by the energy of the electrons in the conjugate base anion, the lower the electron energy in the base, the weaker the base, the stronger acid is the alcohol.
- For Example: Simple Resonance effects significantly influence alcohol Bronsted acidity.

\[ \text{pKa} \approx 19.0 \quad \begin{array}{c} \text{cyclohexanol} \\ \rightleftharpoons \end{array} \quad \begin{array}{c} \text{phenol} \\ \rightleftharpoons \end{array} \quad \begin{array}{c} \text{higher energy electrons, stronger base} \\ \text{lower pKa, stronger acid} \end{array} \]

• The energy of the non-bonding electrons in the conjugate base anion of phenol are lower compared to cyclohexanol due to resonance delocalization/stabilization, phenol is the stronger acid, has the smaller pKa.

2.1 Substituent Effects: An Important New General Concept

• There are three main kinds of substituent effects, inductive effect substituents, alkyl substituent effects and resonance effect substituents.
• Substituent effects primarily influence the energies of the electrons that are involved in Bronsted acidity, and therefore influence this simple chemical reaction in ways that we are already familiar with.
• A complicating factor in Bronsted acidity is that because liberation of a proton generates ions (the proton and the conjugate base anion), we will also sometimes need to take into account ionic solvation effects.

1. Recall the Inductive Substituent Effect:
• Inductive Effect: This is the polarization of electrons in sigma-Bonds due to electronegative elements.
• We previously saw this effect as being responsible for generating bond dipole moments.

• Electron polarization occurs because the electrons are stabilized by proximity to electronegative elements.
• Electronegative elements are electronegative because they have more concentrated positive charges on the nucleus that are not highly shielded by electrons, which lowers the energy (increases the stability) of electrons not only on the electronegative atom but also on adjacent atoms that are connected via \( \sigma \)-bonds.

\[ \text{pKa} \approx 15.5 \quad \text{CH}_3\text{OH} \rightleftharpoons \text{H}_2\text{O} \rightarrow \text{CH}_3\text{O}^- \quad + \quad \text{H}_3\text{O}^+ \]

- The inductive effect normally stabilizes the conjugate base alkoxide anion.
• The inductive effect decreases rapidly with increasing distance between the electronegative element and the electrons of the base anion, here is an example from earlier in the course.

2. Alkyl groups as substituents:
• Alkyl groups stabilize cations by hyperconjugation, and destabilized anions due to electron repulsion.
• Alkyl groups stabilize carbocations by hyperconjugation, a form of resonance, hyperconjugation delocalizes electrons and charge, lowers the total energy of the electrons in the cation:

- Extra methyl groups weakly destabilize the non-bonding electrons in alcohol conjugate base anions.

- The electron donation effect is actually pretty weak in this case, and, probably more important is that the extra methyl groups also decrease solvation of the conjugate base anions, lowering the propensity of the alcohols to ionize in water, decreasing their acidity.

3. Alkyl (electron donating) substituents on a \( \pi \)-System.
• Simple Alkyl substituents weakly donate electron density into the ring as a result of hyperconjugation.
• The conjugate base anion is thus weakly destabilized by the methyl group. Alkyl groups are weakly donating, because hyperconjugation is a much less effective form of electron donation compared to conventional resonance (below), because the donated electrons are already in a strong σ-bond.

4. Stronger Electron Donating substituents on a π-System:
• Minor resonance contributors show how substituents donate electrons into a π-system, e.g. benzene ring:

   ![Diagram showing resonance effects and inductive effects on electron donation and withdrawal in a π-system](image)

   - The -NMe₂ substituents withdraws electron density via the inductive effect, but, the inductive effect is overwhelmed by the resonance donating effect, -NMe₂ is overall electron donating.
   - Electron donating substituents decrease the Bronsted acidity of phenols:

   ![Diagram showing the effect on pKa values](image)

   - The conjugate base π-anion is resonance destabilized by the electron donating -NMe₂ group. The resonance donating effect is stronger than any inductive stabilization by the electronnegative nitrogen.

5. Electron Withdrawing substituents on a π-System.
• Minor resonance contributors show how substituents withdraw electrons from a π-system, e.g. benzene ring:

   ![Diagram showing resonance effects and inductive effects on electron donation and withdrawal in a π-system](image)

   - The -CHO substituent withdraws electron density via the inductive effect, and via the resonance effect illustrated by the minor resonance contributors, -CHO is overall electron withdrawing.
   - Electron withdrawing substituents increase the Bronsted acidity of phenols:

   ![Diagram showing the effect on pKa values](image)

   - The conjugate base π-anion is resonance stabilized by the electron withdrawing -CHO group.
   - The -CHO group is electron withdrawing on a π-system, electron withdrawal occurs by both resonance and inductive effects.

• The pKa of unsubstituted phenol is ca. 9.0.
• Consider 4-nitrophenol:
The conjugate base anion of 4-nitrophenol is directly stabilized by the inductive and resonance effect of the nitro (\(-\text{NO}_2\)) substituent, the formal negative charge is delocalized onto the carbon that the -nitro group is attached, the negative charge is further resonance stabilized by the nitro group, the base anion is stabilized and the acid is thus stronger.

The pKa of unsubstituted phenol is ca. 9.0.

Consider 3-nitrophenol:

The conjugate base anion is not directly stabilized by the nitro (\(-\text{NO}_2\)) substituent because the formal negative charge is not delocalized onto the carbon that the substituent is attached to, there is no resonance stabilization although there is still some inductive stabilization of the conjugate base anion, 3-nitrophenol is more acidic than phenol but less acidic than 4-nitrophenol.

Summary of Electron Withdrawing/Donating Substituents when attached to \(\pi\)-Systems

- **W** increasing electron withdrawing ability

- **D** increasing electron donating ability

*These substituents STABILIZE a negative charge on a benzene ring*

*These substituents DESTABILIZE a negative charge on a benzene ring*

Donating and withdrawing ability is measured relative to hydrogen (H).

Distinguishing the D- and W-groups is easier than it looks (no memorization!).

The donating groups have non-bonding electrons or electrons in \(\pi\)-bonds that can be used to donate to the attached \(\pi\)-system.

Just about every other substituent is withdrawing due to the presence of electronegative elements, W-groups do not have non-bonding electrons on the atoms that is connected to the \(\pi\)-system.

3 Oxidation/Reduction: Definition

- The General Chemistry Definition of oxidation and reduction is the addition and subtraction of electrons.
- Counting electrons in organic structures is difficult because the electrons are mainly shared in covalent bonds.
- There are formal ways of counting electrons in bonds that require learning rules, so we will skip this.
- There is also a slightly less formal way that we will use, that focuses attention on the atoms that are involved in the bonds that are made and are broken for the organic structure in question.
• When a new bond is made (for example) from a carbon atom to a more electronegative atom (usually oxygen), that is oxidation (the more electronegative element “takes” an electron from the carbon).
• When a new bond is made (for example) from carbon atom to a less electronegative atom (usually hydrogen), that is reduction (the more electronegative element “gives” an electron to the carbon).

Oxidation: Making new bonds to more electronegative elements, usually oxygen
Oxidation: Breaking old bonds to (removing or replacing) less electronegative elements, usually hydrogen

Reduction: Making new bonds to less electronegative elements, usually hydrogen
Reduction: Breaking old bonds to (removing or replacing) more electronegative elements, usually oxygen

Attention is focused on the atoms that are involved in the bonds that are made and broken, other atoms are not important.

Examples:

- For the starting organic structure, the new bonds are to both to the less electronegative hydrogen (2 x H added), thus, overall reduction of the organic structure.

- For the starting organic structure, the new bonds are to both to the more electronegative bromine (2 x Br added), thus, overall oxidation of the organic structure.

- For the starting organic structure, bonds are broken to less electronegative H atoms (2 x H are removed), thus, overall oxidation of the organic structure.

- For the starting organic structure, the new bonds are to the more electronegative bromine and to the less electronegative H (1 x Br and 1 x H added), thus, overall neither oxidation or reduction of the organic structure.

- For the starting organic structure, the new bonds are to the more electronegative oxygen and to the less electronegative H (1 x O and 1 x H added), thus, overall neither oxidation or reduction of the organic structure. Note the fact that a H atom is also added to the structure via the -OH group is irrelevant, it is only the atoms that are involved in forming bonds to the organic structure that are important.

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4 Preparation of Alcohols

4.1 Review of Reactions We Have Already Seen

Recall:

4.2 Hydride Reduction of the Carbonyl Group

Catalytic hydrogenation can actually get quite subtle, with different catalysts, one functional group can be reduced in the presence of another, e.g.:

To prepare an alcohol, however, we need to do selective reduction of only the C=O bond, How?

• A Lewis base (e.g. hydride anion) tends not to react with another Lewis base, and so does not react with the alkene, but does react with the carbonyl (C=O) group, which can act as a Lewis acid.

Some (new) reagents:

- electrons not in bond, very reactive
- Al larger, electrons in weaker Al-H bond
- B smaller, electrons in stronger B-H bond
- decreasing electron pair energy

In Principle:
• Both hydride anion and the alkene are nucleophiles (Lewis bases), thus no reaction there.
• A hydride anion (H\(^-\)) and a proton (H\(^+\)) are equivalent to 2 hydrogen atoms (2 H\(^+\)).

**In Practice:**
• NaH is too reactive and too strong a Bronsted base (less selective), NaH will usually deprotonate an aldehyde/ketone rather than add to the C=O bond, LiAlH\(_4\) or NaBH\(_4\) used instead:

![Chemical structure diagram showing reduction of ketone and ester by different reagents.]

• The BH\(_4^-\) anion is less reactive than H\(^-\) because the electrons are in a bond, therefore lower in energy.
• Overall, BH\(_4^-\) supplies H\(^-\), EtOH supplies H\(^+\). Together H\(^-\) and H\(^+\) make H\(_2\).

**Example:** (stereochemistry ignored)

![Chemical structure diagram showing reduction of ketone and ester by different reagents.]

• Why does the NaBH\(_4\) reduce the ketone and not the ester, and the LiAlH\(_4\) reduce both?
• The less reactive NaBH\(_4\) reduces aldehydes and ketones but not esters.
• The more reactive LiAlH\(_4\) also reduces esters (and acids).
• The (H\(_3\)Al-H\(^+\)) bond is weaker than the (H\(_3\)B-H\(^+\)) bond, and so is more reactive.
• Esters and acids are less reactive than aldehydes and ketones due to better resonance stabilization.

![Chemical structure diagram showing resonance structures emphasizing Lewis acid character.]

• Minor resonance structures emphasize the Lewis acid character and partial positive charge on the carbonyl carbon in a ketone, a LB will react faster with an aldehyde and ketone.
• Minor resonance structures show why there is a much smaller partial positive charge on the carbonyl carbon in an ester, a LB will react slower with an ester.

**Alternatively:**

![Chemical structure diagram showing reduction of ketone and ester by different reagents.]

• We can consider that C=O to be a simple \(\pi\)-system (the same way that a benzene ring is a larger \(\pi\)-system), and the ester has a strong donating group attached to the carbon of the C=O, which decreases its reactivity towards a Lewis base/nucleophile, aldehydes/ketones have only weak donating groups attached to the carbon of the C=O group, they are more reactive.
• To reduce the less reactive esters, the more reactive LiAlH\(_4\) is required.
More on LiAlH₄:

- The AlH₄⁻ ion will react violently with water and alcohols, so the proton has to be added in a second acid workup step, hence the notation: 1. LiAlH₄ ... 2. H₃O⁺
- In this second acid workup step, just enough dilute acid is used to "complete" the reaction.
- The protonation is essentially instantaneous, i.e. this is not the same as acid catalyzed addition of water to an alkene (for example), which requires higher concentrations of acid, a lot of time and usually some heat.

\[
\begin{align*}
\text{H₃O⁺} & \text{ LiAlH₄} \\
\text{H₂O} & \text{ LiAlH₄} \\
\text{Li⁺} & \text{AlH₄⁻}
\end{align*}
\]

- This is our first example of an addition/elimination mechanism, we will see this again later.....
- Note complete removal of the –OR group of the ester in the elimination step.
- Elimination occurs because the –OR is a reasonable leaving group (but not great!), and elimination is favored by entropy, and, occurs because the species that is eliminating already has a negative charge on oxygen.
- Note that the –OR leaving group will get protonated in the acid step to form usually a simple alcohol (HOR) that is often not included in the products since it is not part of the main organic structure, it is a by-product.
- A negatively charged oxygen can be a leaving group, but only if the reaction starts with high chemical potential reactants that provide the energy to allow an oxygen anion to leave, for example a strong Lewis base that is an anion, e.g. the aluminum hydride anion (–AlH₄⁻).

Examples: (stereochemistry ignored)

\[
\begin{align*}
\text{MeO} & \text{CH₂} \text{CH₂} \text{CH₂} \text{CH₂} \text{CH₃} \\
\text{NaBH₄} \text{ EtOH} & \text{LiAlH₄} 1. \text{H₃O⁺}
\end{align*}
\]

- NaBH₄ reacts only with the aldehyde, the ester is less reactive and the alkene is also a Lewis base.
- LiAlH₄ reacts with the aldehyde and the carboxylic acid (the acid reaction proceeds via addition/elimination).
- The H₃O⁺ in the LiAlH₄ reaction does not react with the alkene, because in this context, H₃O⁺ means an "acid workup step", which in turn means "add just enough dilute aqueous acid to protonate the negatively charge oxygen atoms". When acid catalyzes water addition to the C=C bond of an alkene the acid concentrations are high, the reaction time is long and the temperature has to be high, the context defines the meaning of H₃O⁺.

5 Oxidation Reactions of Alcohols

Here are a couple of oxidation reactions:

\[
\begin{align*}
\text{R–CH₂–OH} & \xrightarrow{\text{oxidation}} \text{R–C=O} \\
\text{R–CH₂–OH} & \xrightarrow{\text{add 1 oxygen atom}} \text{R–C=O} \\
\text{R–CH₂–OH} & \xrightarrow{\text{further oxidation}} \text{R–C=O}
\end{align*}
\]

- These reactions can be controlled by appropriate choice of reagent/conditions.
A New Cr(VI) Reagent #1:

\[
\text{Na}_2\text{Cr}_2\text{O}_7 + \text{H}_2\text{SO}_4 \xrightarrow{\text{H}_2\text{O}} \text{solvent} \quad \begin{array}{c}
\text{H}_2\text{O} - \text{Cr} - \text{O} \\
\text{H} - \text{Cr} - \text{O} \\
\text{Na}^+ - \text{HSO}_4
\end{array}
\]

- The reagent is sodium dichromate and sulfuric acid dissolved in water, this generates chromic acid "in situ".

**Example with a secondary alcohol:**
- Oxidation to form a ketone:

\[
\begin{align*}
R'\text{C} & \text{O} \text{H} \\
\text{H}_2\text{O} & \text{Cr} \text{O} \\
\text{Na}_2\text{Cr}_2\text{O}_7/\text{H}_2\text{SO}_4/\text{H}_2\text{O} & \rightarrow \text{R} \text{C} = \text{O} \\
\text{oxidation} & \\
\text{don't have to know!!!} & \\
\text{ketone product} &
\end{align*}
\]

- Mechanisms involving oxidation/reduction of metals do not follow the usual patterns of Lewis acid/base Bronsted acid/base reactions, and they tend to be specialized and specific, for this reason you do not have to know this mechanism.

**Example with a primary alcohol:**
- Oxidation to form a carboxylic acid.

The overall process is as follows:

\[
\begin{align*}
\text{R} & \text{C} \text{H} \\
\text{H}_2\text{O} & \text{Cr} \text{O} \\
\text{Na}_2\text{Cr}_2\text{O}_7/\text{H}_2\text{SO}_4/\text{H}_2\text{O} & \rightarrow \text{R} \text{C} = \text{O} \\
\text{oxidation} & \\
\text{aldehyde} & \\
\text{hydrat}e & \\
\text{Na}_2\text{Cr}_2\text{O}_7/\text{H}_2\text{SO}_4/\text{H}_2\text{O} & \rightarrow \text{R} \text{C} = \text{OH} \\
\text{hydrat}e & \\
\text{acid} &
\end{align*}
\]

- Note that formation of the aldehyde from the alcohol is oxidation (removes 2 H atoms).
- Note that formation of the acid from the hydrate is oxidation (removes 2 H atoms).
- Note that formation of the hydrate from the aldehyde is neither oxidation or reduction.

**Details:** First, formation of the aldehyde via the same mechanism as above:
Details: Second, conversion of the aldehyde into the hydrate in the presence of water and an acid catalyst, you do need to know this mechanism. Remember, the reaction conditions involve sulfuric acid in water, the next step is simply acid catalyzed addition of water to the aldehyde:

![Image of aldehyde conversion to hydrate](image)

Final Detail: Third, conversion of the hydrate (a geminal di-alcohol) into a carboxylic acid, via the same mechanism as before, the chromic acid removes 2 hydrogen atoms from the hydrate, which forms the carboxylic acid, the mechanism by which chromic acid does this is the same as formation of the aldehyde from the primary alcohol, you don't need to know this and it is not shown again here:

![Image of hydrate conversion to carboxylic acid](image)

- The hydrate gets oxidized to a carboxylic acid because it is now a (di)alcohol.

Example with a tertiary alcohol:

![Image of tertiary alcohol oxidation](image)

- Tertiary alcohols cannot be oxidized, the necessary hydrogen atom is missing!

- For the same reason, ketones cannot be oxidized, the necessary hydrogen atom is missing.
A New Cr(VI) Reagent #2:

\[
\text{CrO}_3 + \text{HCl} + \text{pyridine} \rightarrow \text{CH}_2\text{Cl}_2 \rightarrow \begin{array}{c}
\text{Cl}^-\text{Cr}=\text{O}^+ \\
\text{H}^+\text{N}^=\text{C} \end{array}
\]

pyridinium chlorochromate (PCC)

- CH\text{Cl}_2 is the **solvent**, therefore there is **no water here**, so any aldehydes that are formed **cannot make a hydrate**, so further oxidation to a carboxylic acid will not occur.

**PCC with a primary alcohol:**

\[
\begin{array}{c}
\text{H} \\
\text{R}^-\text{C}=\text{O} \\
\text{H} \\
\end{array}
\rightarrow
\begin{array}{c}
\text{H} \\
\text{R}^+\text{C}=\text{O} \\
\text{H} \\
\end{array}
\]

don't need to know!!!

**Summary of Oxidation Reactions**

<table>
<thead>
<tr>
<th>R—CH\text{2}.OH</th>
<th>1° alcohol</th>
<th>Carboxylic Acid</th>
<th>Aldehyde</th>
</tr>
</thead>
<tbody>
<tr>
<td>R' R—CH—OH</td>
<td>2° alcohol</td>
<td>Ketone</td>
<td>Ketone</td>
</tr>
<tr>
<td>R' R—C—OH</td>
<td>3° alcohol</td>
<td>no reaction!</td>
<td>no reaction!</td>
</tr>
<tr>
<td>R—C—H</td>
<td>aldehyde</td>
<td>Carboxylic Acid</td>
<td>no reaction!</td>
</tr>
</tbody>
</table>

**Examples:**

- Na\text{2Cr2O7} + H\text{2SO4}/H\text{2O} 
- PCC/CH\text{2Cl}_2 
- no reaction here 
- aldehyde
6 Substitution Reactions of Alcohols (SN1 and SN2) : Water, and other species as Good Leaving Groups

6.1 Recall: SN1 and SN2 Reactions of Alkyl Halides

**Substitution** reactions of alkyl halides (SN1 and SN2)

- **SN2** reaction is a very important substitution mechanism.
- We will try to avoid SN1 if we can since it involves a carbocation intermediate that can rearrange and/or eliminate, although there will be some cases where it will not be possible to avoid SN1.

6.2 Substitution of Alcohols (SN1 and SN2) : Formation of Alkyl Halides

**Consider** the following substitution reaction, is it possible?

- It doesn't work! in fact, this reaction goes in the opposite direction.
- OH is a good nucleophile and will substitute for a halide, which is a good leaving group (think about standard SN2 reactions).

**Reactions with Haloacids**: HCl, HBr, HI, etc.

- This works because water is an excellent leaving group.
- This is a really important principle, if good leaving groups have low energy electrons in the anions, then leaving groups that are neutral, stable small molecules that don’t even have a charge are even better!
- Note the tertiary (3°) alcohol and water being an excellent leaving group, substitution by SN1, SN1 is unavoidable here because the carbon is tertiary.

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• The alcohol is now on a primary carbon, therefore only SN2 is possible (it is not possible to form a carbocation on a primary carbon).
• This reaction goes even though the bromide anion is a poor nucleophile because water is such a good leaving group.
• These previous two mechanisms are important, we will see mechanistic step such as these several times.
• However, the SN1 mechanism still prevails for 2° and 3° alcohols, thus, there is still the usual problem with the cation intermediates such as elimination and rearrangements.
• For 1° alcohols we have the SN2 mechanism, but still, the halide anions are poor nucleophiles, something better is needed.

Compare: Reaction with PBr₃ (phosphorous tribromide).
• An alternate way of converting an –OH group into a good leaving group

- In the first step the leaving group is bromide, in the second step it is the neutral and stable HOPBr₂.
- An SN2 mechanism works well with both 2° and 1° alcohols due to the good leaving group, this is a good reaction.
- The mechanism is not quite as straightforward as standard SN1 and SN2, and it a bit specific for PBr₃, therefore you don’t need to know the details of this mechanism.
- The only problem is 3° halides, which still don’t work well for steric reasons (recall, no Sn2 at 3° centers!).
(Again issue is the stereochemistry of the reaction, if it is SN2 there should be inversion at a chiral center, but the stereochemical outcome of this reaction is less reliable than other SN2 reactions, therefore, we will ignore it!)

Compare: Reaction with SOCl₂ (thionyl chloride):
• Another way of converting an –OH group into a good leaving group:

- Here we have addition/elimination, followed by deprotonation, followed by an SN2 reaction to make an alkyl chloride.
- In the SN2 reaction the leaving groups are Cl⁻ (a good leaving group), and SO²⁻ (a very good leaving group).
- An SN2 mechanism works well with both 2° and 1° alcohols due to the good leaving group, this is a good reaction.
- The mechanism is not quite as straightforward as standard SN1 and SN2, and it a bit specific for SOCl₂, therefore you don’t need to know the details of this mechanism.
- The only problem is 3° halides, which still don’t work well for steric reasons (recall, no Sn2 at 3° centers!).

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(As with PBr₃, another issue is the stereochemistry of the reaction, if it is SN2 there should be inversion at a chiral center, but the stereochemical outcome of this reaction is less reliable than other SN2 reactions, therefore, we will ignore it again!)

### Reaction Summary

<table>
<thead>
<tr>
<th>Preferred Reagents</th>
<th>Chloride</th>
<th>Bromide</th>
</tr>
</thead>
<tbody>
<tr>
<td>1° alcohol</td>
<td>SOCl₂</td>
<td>&quot;SN₂&quot; PBr₃</td>
</tr>
<tr>
<td>2° alcohol</td>
<td>SOCl₂</td>
<td>&quot;SN₂&quot; PBr₃</td>
</tr>
<tr>
<td>1°, 2°, 3° alcohol</td>
<td>HCl</td>
<td>SN₁ &amp; SN₂ HBr</td>
</tr>
</tbody>
</table>

- The mechanisms for PBr₃ and SOCl₂ are a bit complicated, you don’t need to know these, but you do need to know the mechanisms of the HCl and HBr reactions, even when they are not the preferred reagents.

### 6.3 Substitution of Alcohols: Formation of Tosylate Esters (better leaving group)

#### Why are Tosylates Useful?
- They are yet another even more versatile way of converting –OH from a poor leaving group into a good leaving group.
- This is what we have just learned:

  
  \[
  \begin{align*}
  \text{R–OH}_2 & \quad \rightarrow \quad \text{R–Nu} + \text{H}_2\text{O} \\
  \text{Nu} & \quad \text{Good leaving group, works if Nu can tolerate acid.}
  \end{align*}
  \]

- This is OK, except that is rarely useful beyond HCl, HBr, H₂SO₄, etc. because you need to protonate the -OH first, then add the nucleophile (which is a Lewis base and often a reasonable Bronsted base) and hope that the nucleophile doesn't just get protonated, hmmmm, something better is really needed….

- This reaction looks a lot more complicated (but it isn't) and it fixes this problem.

  
  \[
  \begin{align*}
  \text{R–OH}_2 & \quad \rightarrow \quad \text{R–Nu} + \text{tosylate (ester)} \\
  \text{Nu} & \quad \text{tosylate anion, excellent leaving group, works under lots of conditions, this is why tosylates are useful!}
  \end{align*}
  \]

- The tosylate anion is highly resonance stabilized, it is low energy non-bonding electrons, which is why it is such a good leaving group.

#### Where do tosylate (esters) come from?

- You don’t need to know the mechanism, but you do need to know that you need pyridine to remove the proton.

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Some clarification on notation and structure.....

\[
\begin{align*}
\text{"Tosyl" group} & = -\text{Ts} \\
\text{\textit{(para-toluenesulfonate)}} & \\
\text{"Tosylate" group} & = \Theta\text{OTs}
\end{align*}
\]

**Examples:** Useful reactions:

\[
\begin{align*}
\text{weak nucleophile} & \quad \text{Na}^+\text{–}\text{Br} \\
\text{Br} & \quad \text{Na}^+\text{–}\text{CN} \\
\text{N≡C} & \quad \text{Na}^+\text{–}\text{OCH}_3
\end{align*}
\]

6.4 A Different E1 Elimination: The Pinacol Rearrangement Mechanism

**The Pinacol Rearrangement:** (another kind of alcohol dehydration)

- Let's treat this as a mechanism problem, how to solve it and what basic principles can we use to guide us?
- Look carefully at the reagents/conditions (in this case, acid in water).
- Look for differences in start and end structures.
- Need to remove –H and –OH and do an alkyl shift.
- Acid catalyzed, therefore protonate first, no anionic intermediates in presence of acid.

**The Mechanism:**

- Protonate to make a good leaving group (H₂O)
- We have a usual carbocation rearrangement to make a more stable (resonance stabilized) cation intermediate.
- Deprotonation at the end regenerates the acid catalyst.
Example Mechanism Problem: A "Hidden" Pinacol rearrangement

6 Alcohols: Summary of Reactions

- **Vinyl Alcohol**
  - $\text{NaBH}_4$ → $\text{Y/N}$

- **Phenyl Alcohol**
  - 1. Excess $\text{LiAlH}_4$ → $\text{Y/N}$
  - 2. $\text{H}_3\text{O}^+$
    - $\text{NaBH}_4$ does NOT do this reaction

- **1-Octanol**
  - $\text{PCC}$ → $\text{Y/N}$
    - specifying $\text{CH}_2\text{Cl}_2$ solvent is optional

- **2-Octanol**
  - $\text{Na}_2\text{Cr}_2\text{O}_7$, $\text{H}_2\text{SO}_4$ / $\text{H}_2\text{O}$ → $\text{Y/N}$
    - specifying the $\text{H}_2\text{O}$ solvent is optional

- ** Propylene Alcohol**
  - $\text{Na}_2\text{Cr}_2\text{O}_7$ → $\text{Y/N}$
    - $\text{PCC}$ can also be used to do this reaction

- **Cyclopentanol**
  - $\text{SOCl}_2$ → $\text{Y/N}$

- **2-Methylfuran Alcohol**
  - $\text{PBr}_3$ → $\text{Y/N}$

- **2-Chloroethyl Alcohol**
  - $\text{HCl}$ → $\text{Y/N}$
    - $\text{SOCl}_2$ does NOT work for 3° alcohols

- **2-Bromoethyl Alcohol**
  - $\text{HBr}$ → $\text{Y/N}$
    - $\text{PBr}_3$ does NOT work for 3° alcohols

- **2-Iodoethyl Alcohol**
  - $\text{SOCl}_2$, $\text{TsCl}$ → $\text{Y/N}$
    - which is the same as

- **Vinyl Alcohol, tosylate**
  - $\text{Na}^+\text{CN}$ → $\text{Y/N}$
    - and many other SN2 reactions of tosylates

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