WEEK 10 FINAL REVIEW KEY

GOAL: Understand how TLC, melting ranges, and recrystallization play a role in identification of an unknown product. Know how to analyze NMR and IR. Be able to calculate percent yield/recovery. Understand the mechanism of nucleophilic substitution. Know how to prepare and when to use acid-base extraction.

LAB TECHNIQUE TIPS:

a. Melting point/range:
   - Remember that a good melting range is narrow and close to the pure compounds range.
   - Impurities widen and lower the melting range.

b. Recrystallization:
   - Remember that recrystallization involves dissolving and then precipitating a compound into a purer form.
   - One solvent dissolves the product into solution. The other solvent traps impurities behind.
   - Cooling a recrystallization slowly allows for slower precipitation of product. This results in larger, cleaner crystals with fewer impurities. If it is cooled too fast, impurities will recrystallize with the product.

c. TLC:
   - Always label the polar and nonpolar compounds in TLC
   - Like sticks with like: a polar phase will attract polar molecules. A nonpolar phase will attract nonpolar molecules.
   - Know how changing the solvent of a TLC changes the Rf values
   - It's always good to note what you should be seeing, as well as what you should not be seeing, when comparing a sample spot against a standard spot.

d. IR/H NMR spectroscopy:
   - When identifying a compound using either spectra, make sure to look for peaks that may be missing in order to help eliminate certain compounds as possible products. The presence, as well as the absence, of certain peaks are equally as important!
   - Memorize the common $^1$H NMR chemical shifts and IR frequencies provided in lecture!!! Throughout the quarter, you will repeatedly use this method to identify your product. It will make determination of your compound much quicker if you are able to recognize some peaks without having to double check.

CALCULATION TIPS:

a. Percent yield/recovery:
   - Knowing the difference between percent yield and percent recovery will be helpful for your scaffolds. Both can be helpful in describing your results; they will be useful when writing the error analysis portion of your scaffolds.
   - *DON’T JUST MEMORIZE THE EQUATIONS* Understand why you divide actual yield over theoretical yield (percent yield) and recrystallized product over crude product (percent recovery). Doing so will help you understand how you should write about percent yield and percent recovery in your scaffolds.
   - Know how to calculate percent yield given the mass of the impure product.

b. Rf values:
WEEK 10 FINAL REVIEW KEY

- Remember how to calculate Rf values

NUCLEOPHILIC SUBSTITUTION TIPS:
  a. Each compound used in this experiment has a specific purpose. If you know what each compound does, you will be able to piece together nucleophilic substitution mechanism (*will need the mechanism for your post lab appendix*)
  b. Understand when a reaction will favor an SN₁ over SN₂ mechanism
  c. Be able to determine the electrophile and nucleophile in a reaction
  d. Understand the theory behind refluxing and why it is used, not just how it is used.
  e. Remember that nucleophiles can also be bases, so sometimes a compound may act as a base even though the question pertains to nucleophiles. Don’t get tricked.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SN₂ reaction</th>
<th>SN₁ reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkyl halide</td>
<td>methyl &gt; primary &gt; secondary &gt; tertiary</td>
<td>tertiary &gt; secondary &gt; primary &gt; methyl</td>
</tr>
<tr>
<td>Nucleophilic strength</td>
<td>strong nucleophile</td>
<td>poor nucleophile</td>
</tr>
<tr>
<td>Mechanism</td>
<td>1-step</td>
<td>2-step</td>
</tr>
<tr>
<td>Rate limiting step</td>
<td>bimolecular transition state</td>
<td>carbocation formation</td>
</tr>
<tr>
<td>Solvent</td>
<td>polar aprotic</td>
<td>polar protic</td>
</tr>
<tr>
<td>Stereochemistry</td>
<td>inversion</td>
<td>mixed configuration</td>
</tr>
</tbody>
</table>

ACID-BASE SEPARATION TIPS:
  a. Always identify the acid/base and the neutral compound for extraction.
  b. Always identify the aqueous/organic layer.
  c. Use a base to extract an acid into the aqueous layer. To bring the acid back into an organic solution, use a base.
  d. Consider whether a base you’re trying to use can actually deprotonate the compound you’re trying to isolate (HINT: look at pKa’s). If the pKa of the acid is higher than that of the base’s, the base will not deprotonate the acid. A high pKa means low acidity and high basicity. Thus, if the pKa of the acid is higher than the base’s, that means the acid is more basic than the base being used to deprotonate it.

SAFETY:
  1. What do each of the following GHS symbols represent?
**WEEK 10 FINAL REVIEW KEY**

a. Acute/fatal toxicity
b. Irritant & sensitizers
c. Skin, eye, and metal corrosives
d. Carcinogen, mutagen, teratogen

A table of the Global Harmonized System (GHS) is provided at the beginning of your ELN. Make sure to keep a copy of it somewhere accessible! You will utilize the table to characterize chemicals used in future labs. The table provided in your ELN is attached below.
NUCLEOPHILIC SUBSTITUTION:

2. Draw the mechanism for the nucleophilic substitution reaction between benzyl bromide and 4-methoxyphenol, using sodium hydroxide, to produce 1-(benzyloxy)-4-methoxybenzene.

Step 1: NaOH deprotonates the alcohol on 4-methoxyphenol so that it may act as the nucleophile.

Step 2: Deprotonated 4-methoxyphenol (nucleophile) attacks the electrophilic carbon, kicking off the bromine. This creates the product 1-(benzyloxy)-4-methoxybenzene.
**IR/H NMR SPECTROSCOPY:**

3. Although the carbonyl absorption of cyclic ketones generally shifts to higher wavenumber with decreasing ring size, the C=O of cyclopropenone absorbs at lower wavenumber in its IR spectrum than the C=O of cyclohexenone. Explain this observation. (21.82, 3rd ed)

\[
\begin{align*}
\text{cyclopropenone (1640 cm}^{-1} & \quad \text{2-cyclohexenone (1685 cm}^{-1})
\end{align*}
\]

These three resonance structures include an aromatic ring; \(4n + 2 = 2\) \(\pi\) electrons. Although they are charge separated, the stabilized aromatic ring makes these three structures contribute to the hybrid more than usual. Since these three resonance contributors have a C–O single bond, the absorption is shifted to a lower wavenumber.

There are three resonance structures for 2-cyclohexenone, but the charge-separated resonance structures are not aromatic so they contribute less to the resonance hybrid. The C=O absorbs in the usual region for a conjugated carbonyl.

WEEK 10 FINAL REVIEW KEY

A
\[
\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{H}
\]

B
\[
\text{CH}_2=\text{C}
\]

C
\[
\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3
\]

\[
\text{CH}_2\text{CH}_2\text{CH}_3\text{CH}_3
\]

\[
\text{O}
\]

\[
\text{CH}(\text{CH}_3)_2
\]

Spectrum [1]

\[
\text{Wavenumber (cm}^{-1}\text{)}
\]

\[
\% \text{ Transmittance}
\]

Spectrum [2]

\[
\text{Wavenumber (cm}^{-1}\text{)}
\]

\[
\% \text{ Transmittance}
\]

Spectrum [3]

\[
\text{Wavenumber (cm}^{-1}\text{)}
\]

\[
\% \text{ Transmittance}
\]

Spectrum [4]

\[
\text{Wavenumber (cm}^{-1}\text{)}
\]

\[
\% \text{ Transmittance}
\]

Spectrum [5]

\[
\text{Wavenumber (cm}^{-1}\text{)}
\]

\[
\% \text{ Transmittance}
\]

Spectrum [6]

\[
\text{Wavenumber (cm}^{-1}\text{)}
\]

\[
\% \text{ Transmittance}
\]
**WEEK 10 FINAL REVIEW KEY**

**Spectrum [5]:**

CH$_3$CH$_2$CH$_2$CH$_2$COOH (A)
- OH at ~3500–2500 cm$^{-1}$
- C=O at ~1700 cm$^{-1}$

**Spectrum [1]:**

CH$_2$=C(CH$_3$)CH$_2$CH$_2$CH$_3$ (B)
- C=C peak at 1650 cm$^{-1}$
- C$_{sp^2}$–H at ~3150 cm$^{-1}$

**Spectrum [4]:**

\[
\text{C$_{sp^2}$–H at ~3150 cm}^{-1} \\
\text{Phenyl peaks at 1600 and 1500 cm}^{-1}
\]

For these problems, find a functional group to look for on the IR spectrum. For A, the characteristic functional group is a carboxylic acid, telling us that we should see a carbonyl peak and alcohol peak. For B, the only characteristic peaks are a Csp2 and C=C peak, with no other functional groups or heteroatoms. Lastly, for C, there is a phenyl peak and Csp2 peak. Note that all compounds have Csp3 peaks as well, so that cannot be used to differentiate them.

5. Propose a structure consistent with this data (14.60 b, 3rd ed)

C$_9$H$_{12}$: IR absorption at 2850–3150 cm$^{-1}$

Begin by calculating the degrees of unsaturation = 2C + 2 + N - H - X / 2. This gives you 4, telling us that there can be 4 double bonds, 1 double bond and 2 triple bonds, or a mixture of multiple bonds and rings. To get more insight, we can turn to the IR for more data, and we can see that the provided range is for Carbons and Hydrogens, indicating no presence of...
heteroatoms. Thus, there is no C=O bond or C-N triple bond. Next, looking at the NMR, there is a peak at around 7.1 with 5 equivalent hydrogens. It also has a complicated splitting pattern. This likely indicates the presence of a benzene. Next, there is a septet at 3 ppm with 1 H. This tells us that 1 H is split by 6 equivalent neighboring H’s. Thus, there is likely a CH-(CH3)2 structure. Putting this information together, we get the structure below.

6. Rank the indicated carbon atoms in each compound in order of increasing chemical shift. (14.51, 3rd ed)

A fundamental aspect of chemical shift is that the more electronegative atoms present, the more shifted an atom will be. In this case, both groups have oxygen. For the first compound, the closer the carbon is to oxygen, the greater the chemical shift. Thus, Ca will have the highest shift, followed by Cb, then Cc. For the second compound, it will follow a similar pattern where the carbon closest to the oxygen will have a larger chemical shift.
ACID-BASE EXTRACTION:

7. Write out the main steps needed to separate hydrocarbon A and carboxylic acid B by using an extraction procedure. It does not need to be extremely detailed, but should cover the solvent and means of extraction. (19.53, 3rd ed)

1. Dissolve both compounds in CH2Cl2
2. Add NaHCO3 solution. This results in a carboxylate anion of B, causing it to dissolve in the aqueous layer. At the same time, A remains in CH2Cl2
3. Next, separate the layers. Once separated, add HCl to the aqueous layer to protonate the carboxylate, allowing it to come out of solution.

Note that this is not an exhaustive list. It covers what is necessary for an extraction.

8. Which of the following could be used to convert a water insoluble carboxylic acid into a species that would be soluble in the aqueous phase?
   a. MgSO4 pKa = -3
   b. 1.5M HCl strong acid (completely dissociates in aqueous solution)
   c. 1.0M NaCl strong acid (completely dissociates in aqueous solution)
   d. 2.0M Na2SO4 pKa = 1.92
   e. Saturated NaHCO3 pKa = 10.3

As stated in the acid-base extraction tips above, use a base to extract an acid into the aqueous layer. To bring the acid back into an organic solution, use a base. For this example, we are looking for something basic enough to deprotonate a carboxylic acid, so that it can be extracted into the aqueous layer. Each answer choice is labeled with their respective pKa's. The pKa of a carboxylic acid is ~5.

Consider whether a base you're trying to use can actually deprotonate the compound you're trying to isolate (HINT: look at pKa's). If the pKa of the acid is higher than that of the base’s, the base will not deprotonate the acid. A high pKa means low acidity and high basicity. Thus, if the pKa of the acid is higher than the base’s, that means the acid is more basic than the base being used to deprotonate it.
WEEK 10 FINAL REVIEW KEY

The only answer choice with a pKa higher than the carboxylic acid is answer choice E. Saturated NaHCO₃ is the only compound basic enough to deprotonate a carboxylic acid.

MELTING POINT/RANGE:

9. Explain the observed trend in the melting points of the following three isomeric alcohols: \((\text{CH}_3\text{)}_2\text{CHCH}_2\text{OH} \ (-108\ ^\circ \text{C})\), \(\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH} \ (-90\ ^\circ \text{C})\), \((\text{CH}_3\text{)}_3\text{COH} \ (26\ ^\circ \text{C})\). (9.45, 3rd ed)

Melting points depend on intermolecular forces and symmetry. \((\text{CH}_3\text{)}_2\text{CHCH}_2\text{OH}\) has a lower melting point than \(\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}\) because branching decreases surface area and makes \((\text{CH}_3\text{)}_2\text{CHCH}_2\text{OH}\) less symmetrical so it packs less well. Although \((\text{CH}_3\text{)}_3\text{COH}\) has the most branching and least surface area, it is the most symmetrical so it packs best in a crystalline lattice, giving it the highest melting point.

10. The melting point of a pure compound is known to be 95-97°C. What will happen to the melting range if this compound has impurities in it?

When impurities are present in a compound, they tend to change the melting range in two ways: (1) the range becomes lower, so in this case, it would be less than 95°C, and (2) it broadens the range between the low and high values. An example for this could be a range of 82-89°C. The actual change depends on the identity of the compound and impurities as well as their relative amounts. Thus, if you were to get a melting point reading different from the listed value, there is a strong chance that impurities are present in your compound.

TLC:

11. A new student is planning to use thin layer chromatography (TLC) for his research project. After setting up the apparatus the student forgets to place a lid on the TLC jar. He obtains poor results after running the TLC experiment. Which of the following can best explain his bad results?

A. The open system prevents the evaporation of the solvent on the TLC plate
B. The open system evaporates the solvent on the TLC plate
WEEK 10 FINAL REVIEW KEY

C. The open system evaporates the solvent in the solution
D. The open system prevents the evaporation of the solvent in the solution

TLC is a laboratory technique commonly used to separate components of a mixture. Mixtures are placed on the TLC plate (stationary phase), which is then transferred to a jar containing the solvent. The solvent travels through the plate and carries components of the mixture along with it. Based on its properties, each component is dragged to different distances on the plate. The relative distances traveled by each component can be used for separation and identification.

It is important to place a lid on the jar because the solvent will be a volatile substance. An open system will allow for the solvent to evaporate from the TLC plate and reduce the amount of solvent traveling through the plate. The solvent in the solution will evaporate, but it is negligible and inconsequential to the data collected on the TLC plate.

RECRYSTALLIZATION:

12. Compound A is readily soluble in hexane, ligroin, and diethyl ether but insoluble in water, methanol, and acetone. (Ligroin is a mixture of C7 and C8 hydrocarbons.) Which one of the following solvent pairs is not appropriate for crystallization of Compound A?
   a. acetone - ligroin
   b. acetone - diethyl ether
   c. acetone - hexane
   d. acetone - methanol
   e. all of the above

Compound A is soluble in inorganic solvents (i.e. nonpolar solvents), but it is insoluble in organic solvents (i.e. polar solvents). Recrystallization works best with a solvent/antisolvent pair. Thus, pairing an inorganic and organic solvent together will work during the recrystallization of compound A. This is why answer choices A, B, and C are not correct. Answer choice D is correct because it pairs two organic solvents for use in a recrystallization. If these two were used in a real experiment, we can expect to obtain a highly impure product at the end of the recrystallization.

CALCULATIONS:

13. You are given two spots, A and B along with their Rf. The solvent is nonpolar. Determine which compound is more nonpolar.

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>Rf = 0.63</td>
<td>Rf = 0.88</td>
</tr>
<tr>
<td>Solvent Front</td>
<td>5.2 cm</td>
</tr>
</tbody>
</table>
WEEK 10 FINAL REVIEW KEY

Recall that Rf = distance of spot / distance of solvent. We need to solve for the distance of the spot. Additionally, since we have a nonpolar mobile phase, the compound that is more nonpolar will stick to it better than the polar stationary phase. Thus, the compound that is more nonpolar should have a larger distance. Solving for A, we have 0.63 = x / 5.2. Solving for x, we get 3.3 cm. Next, for B, we have 0.88 = y / 5.2. Solving for y, we get 4.6 cm. Thus, compound B traveled the farthest and is the more nonpolar compound.

14. In the substitution reaction between benzyl bromide and 4-methoxyphenol, a student started with .95 mL of benzyl bromide and 20 mL of a 0.35 M 4-methoxyphenol solution in ethanol. They then obtained 326 mg of pure 1-(benzyloxy)-4-methoxybenzene. What is the percent yield of pure 1-(benzyloxy)-4-methoxybenzene?

- a. 47%
- b. 68%
- c. 22%
- d. 75%
- e. 82%

Steps:
- Determine the limiting reagent by converting both reagents into moles and comparing

  0.95mL benzyl bromide x (1.44g benzene bromide / 1 mL) x (1 mol / 171g benzyl bromide)  
  = 0.008mol benzyl bromide

  20mL 4-methoxyphenol x (1L / 1000 mL) x (0.35mol 4-methoxyphenol / 1L) 
  = 0.007mol 4-methoxyphenol => limiting reagent is 4-methoxyphenol because it runs out first

- Use the limiting reagent to calculate theoretical yield of product

  0.007mol 4-methoxyphenol x (1mol 1-(benzyloxy)-4-methoxybenzene / 1mol 4-methoxyphenol) 
  x (214.3g 1-(benzyloxy)-4-methoxybenzene / 1mol) 
  = 1.5001g 1-(benzyloxy)-4-methoxybenzene
WEEK 10 FINAL REVIEW KEY

- Determine actual yield (given in the problem)

  Obtained: 326 mg x (1g / 1000mg) = 0.326 g product

- Use the formula percent yield = (actual yield / theoretical yield) x 100% to calculate percent yield

  Percent yield = (0.326 g product / 1.5001g 1-(benzyloxy)-4-methoxybenzane) x 100%
  Percent yield = 21.73% ≈ 22%