51C Final Review Key

Carbohydrates

1. Composes of 6% of the major cellular biomolecules
2. Basic units of our foods
   a. Examples: lactose
3. Drawn in chair conformations or sawhorse notation (hexagon)
4. Helps with energy storage like glucose
5. Glucose analogs for imaging tumors
6. They also help make up cell components
   a. Blood type groups: A, B, AB, O
   b. Helps with cell signaling
7. Nomenclature:
   a. Glucose: most common monosaccharide
   b. Stereochemistry: D vs. L
      i. D: resembles R or clockwise
      ii. L: resembles S or counterclockwise
   c. Stereocenter location
      i. Beta configuration: hydroxyl group is on the same face of the farthest stereocenter
      ii. Alpha configuration: hydroxyl group is on the opposite face of the farthest stereocenter
8. Since carbohydrates are hemiacetals and acetals, they can easily react like them
   a. Can convert hemiacetals to acetals
   b. Reactions of the alcohol groups
      i. Acylation
      ii. SN2 attack

Proteins

1. Composes of 60% of cell components
2. Helps run the cell (movers, shakers, scaffolding)
3. Help with therapeutic drugs (EPO and Herceptin)
4. Composed of a chain of amino acids (20 of them)

Electrophilic Aromatic Substitution (EAS)

I. Halogenation - adding a Cl or Br
   A. Reagents
      1. Cl₂, FeCl₃
      2. Br₂, FeCl₃
II. Nitration - adding a nitro group (NO₂)
   A. Reagents: HNO₃, H₂SO₄
III. Sulfonation - adding (-SO3H)
   A. Reagents: SO3, H2SO4
   B. Can be used as a blocking group which can be removed (for synthesis)

IV. Friedel-Crafts alkylation - adding carbon chains
   A. Reagents: any carbon alkyl halide with AlCl3
   B. Susceptible to carbocation rearrangement

V. Friedel-Crafts acylation - adding acyl groups
   A. Reagents: any acyl group with AlCl3

VI. Substituent Effects
   A. Ring Activating - makes it easier to add new substituents
      1. Usually have lone pairs (Nucleophilic sites)
      2. Common groups: -OH, -NR3, -OR
      3. Add future groups in ortho (1,2) and para (1,4)
         a) More resonance structures allows more stability at these positions meaning ortho and para can allow for a stable cationic intermediate
         b) Para will dominant more than ortho due to steric effects
   B. Ring Deactivating - makes it harder to add new substituents
      1. Usually have positive charges
      2. Common groups: -NO2, -NR3(+), -CF3, -SO2H, -CN
      3. Add future groups in meta position (1,3)
         a) Meta position is the least destabilized
         b) There will be (+) charges right next to each other in the ortho and para positions
   C. Special Case: Halogens
      1. Are slightly deactivating BUT ortho and para directing
      2. Deactivating: due to its strong inductive effect
      3. Ortho and para directing: bromine can hold the (+) charge instead of carbons
   D. Other Considerations (Concern for Synthesis)
      1. Methoxy, Hydroxy, and Amine Substituents
         a) Due to its activating nature, it can cause over-halogenation
         b) Can be fixed by changing the solvent to CCl4 with Br2
      2. Amines
         a) Can acylate it to slightly deactivate it
      3. Cannot add Friedel-Crafts to deactivating groups and aniline derivatives (nitrogen on benzenes)
         a) Can add to aniline derivatives by acylating it again
         b) Acyl group can be removed by adding H3O+/H2O

VII. Reagents on Benzene Derivatives
   A. H2, Pd - changes -NO2 to -NH2
   B. Clemmensen Reduction (HCl, Zn/Hg) or Wolff-Kishner Reduction (N2H4, KOH)
      1. Removes ONLY ketones and aldehydes of the (C=O) bond
1.) Provide the appropriate reagents to the following reactions

a)

b)

1.) \( \text{Cl} \)\( \rightarrow \), \( \text{AlCl}_3 \)
2.) \( \text{SO}_3, \text{H}_2\text{SO}_4 \)
3.) \( \text{Cl}_2, \text{FeCl}_3 \) (2 eq.)
4.) \( \text{H}_3\text{O}^+ \)

b)

1.) \( \text{Cl} \)\( \rightarrow \), \( \text{AlCl}_3 \)
2.) \( \text{Br}_2, \text{FeBr}_3 \)
3.) \( \text{Cl}_2, \text{H}_3\text{O}^+ \)
4.) \( \text{NaN}_3 \)

1. PCC
2. NaH
3. \( \text{CH}_3\text{CH}_2\text{Br} \)
4. \( \text{CH}_3\text{MgBr} \)
5. \( \text{H}_2\text{O} \)
2.) Circle the more electrophilic compound in each pair.

a) ![Diagram of more electrophilic compound]

b) ![Diagram of less electrophilic compound]

Look at two things:
1) Inductive effects
2) Resonance effects

The more unstable the resonance structure is, the more reactive the compound will be, and ultimately will be the more electrophilic compound. The below structures are for (a). Follow a similar reasoning for (b).

Inductive effect:

![Inductive effect diagram]

Dipole moments are very similar, so the inductive effect is the same on both compounds. Move on to resonance effects to determine any differences in reactivity.

Resonance effect:

![Resonance effect diagram]

Notice how the dashed blue boxes indicate similar resonance structures. Look at what else is nearby the electrophilic carbon in the carbonyl area. In the right compound (green box), there is a carbonyl with a partial positive charge. A partial positive charge next to a full positive charge is unstable! The left compound does not have this additional partial positive charge, so the anhydride is the more electrophilic of the pair.

3.) Fill in the following boxes with the missing reagent or product.

![Aldol reaction diagram]

Would this require a directed aldol? Yes, or else the product will spontaneously go through aldol condensation due to conjugation.
#1 and #2 can be in either order, but must precede #3 since -Cl is an ortho/para directing group. The substituents are meta to each other.

Reagents for the Clemmensen reduction reduce C=O to C-H (ketone to alkyl). In a similar fashion, it can also reduce N=O bonds to N-H.

Deactivated, meta directing benzene derivatives gives poor yields of Friedel-Crafts products. Therefore, we need to do a Friedel-Crafts acylation followed by Clemmensen’s reduction.

#2’s reagent is the Wolff-Kishner reduction that is used to reduce ketones/aldehydes to alkyl chains. Look at the products to see what the directing powers of each group present is. That will help you in determining the order of the reagents.
4. Provide arrow pushing mechanisms for the following reactions.

A.
B.
C.
Step 1: Make Electrophile

Step 2: Benzene Attacks

Step 3: Regenerate Aromatic Ring