**Assignment #8 (Due May 1, 2023)**

**Chem 436 – Spring 2023**

1. When you subject vinyl bromide or bromobenzene with Sodium Ethoxide, why do you not expect to see an SN2 reaction? [Feel free to show appropriate diagrams of the transition state, hybridization, and/or geometry/steric arguments if necessary]

In an SN2 reaction, of a vinyl halide the carbon undergoing substitution must be rehybridized to sp from sp2. The sp hybridized state has a very high energy and relatively reduces the rate to many orders of magnitude. A second reason is that the nucleophile has to approach the alkene/benzene from the opposite side of the halogen and also in the plane of the alkene/benzene, which results in significant van der waals repulsion of both the LG and the Nuc.

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[In short, both hybridization and van der waals repulsion retard the SN2 reactions to such an extent that they do not occur]

Furthermore, because the carbon at which substitution occurs would have to undergo stereochemical inversion in aryl halides, the reaction would necessarily yield a benzene derivative containing a twisted and highly strained molecule.

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2. Rank the following with respect to their order of reactivities with a nucleophile in a nucleophilic acyl substitution. Justify your order of arrangement. [1=Most Reactive, 4=Least Reactive]



**1, 3, 2, 4**

Consider the stability of the leaving groups in all the cases. CF3CH2O- and CCl3CH2O- are good leaving groups owing to the presence of electron-withdrawing halogens that can stabilize the negative charge. CH3CH2O- is not that stabilized while OH- is a very poor leaving group.

3. Arrange the following in the decreasing order of pKaH [For compounds having more than two Nitrogen, consider the most basic site for this answer]:





4. In the reaction of an α,β-unsaturated carbonyl compound, why do you think Gilman reagent and Grignard reagents behave differently? [Hint: Think along the lines of kinetic and thermodynamic controlled product]

5. Explain why acid-catalyzed ester hydrolysis is reversible but base-catalyzed ester hydrolysis is not.

Acid-catalyzed hydrolysis of ester is reversible and occurs by the SN1 pathway while Base-catalyzed hydrolysis of ester occurs by the SN2 pathway and is irreversible because the end product of base-catalyzed hydrolysis of ester produces alcohol and carboxylate ion (not carboxylic acid), which being resonance stabilized shows very little tendency to react with alcohol, unlike the acid catalysed pathway.

6. You’re performing an experiment and you have got a mixture of benzylamine, benzoic acid, and biphenyl in your final step. How would you separate them using liquid extraction?

Liquid Extraction using basic aq. solution and an immiscible organic solvent (chloroform, ethyl acetate, etc) – Benzoic acid will be dissolved in the basic aq. layer and the organic layer will have benzylamine and biphenyl.

Performing a liquid extraction by treating the organic layer with acidic aq. solution – Benzylamine will be dissolved in the aq. layer, and the organic layer will have biphenyl.

Separately neutralizing the aq. layers to get insoluble precipitates of the amine/acid.

7. Which of the following two amides is more stable and why?





Because of Steric repulsions

8. Which of the following statements are false? Why?

1. Carboxylic acids are weaker acids than HCl
2. The C-O bonds in a formate anion are different [false – due to resonance, both bond lengths are similar]
3. Amides are relatively more reactive than esters [false – amides are less reactive due to partial double bond character of C-N bond]
4. Typically, thiols are more acidic than carboxylic acids [false – thiols typically have pKa ~10-11, unlike carboxylic acids having pKa \_3-5]
5. Acid hydrolysis of nitriles can yield carboxylic acids