Mechanistic Assignment
CHEM 4000A – Medicinal Chemistry
Due at 4:00pm on Friday, October 27th, 2017

You will likely find it easiest to draw your mechanisms by hand (though you can use a program like ChemDraw if you like). The written parts of your answers can either be hand written or typed. As long as I can read them. ☺

Do not take "short cuts" showing protonation or deprotonation steps that can't actually happen because the basic site can't reach the acidic hydrogen. (Be warned that some textbooks, etc. have this very bad habit because it saves them space.)

1. Esters are useful protecting groups for both carboxylic acids and alcohols. Frequently, the simplest possible ester is chosen.

   e.g. A carboxylic acid is protected as the methyl ester.

   e.g. An alcohol is protected by reacting it with either acetyl chloride or acetic anhydride.

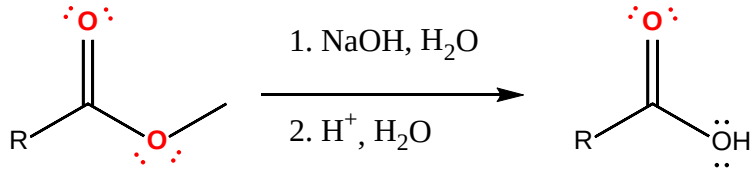
   These sorts of esters can be cleaved by reaction with either aqueous acid or aqueous base. Usually, the acid or base must be quite concentrated and the reaction has to be heated. These sorts of reaction conditions can be too harsh for some molecules though (depending on what other groups they contain).

   Also, sometimes a chemist wants to cleave only one ester in a molecule containing multiple esters. For these reasons, other esters may be chosen as protecting groups.

   e.g. *tert*-Butyl esters can be selectively cleaved under mildly acidic conditions (such as $ZnBr_2$ in CH_2Cl_2 and water at room temperature).

(a) When concentrated aqueous base is used to cleave a methyl ester, the resulting carboxylic acid only contains one of the two oxygen atoms from the original ester:

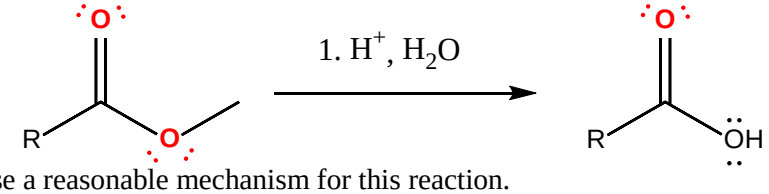
e.g.



Propose a reasonable mechanism for this reaction.

(b) When concentrated aqueous acid is used to cleave a methyl ester, the resulting carboxylic acid only contains one of the two oxygen atoms from the original ester:

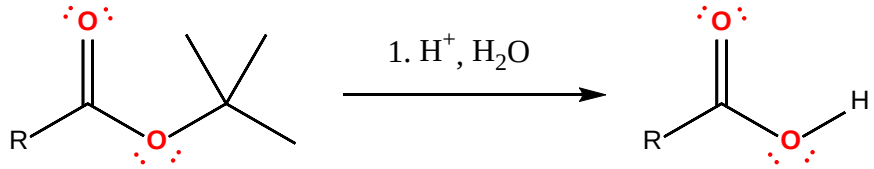
e.g.



Propose a reasonable mechanism for this reaction.

(c) When mild aqueous acid is used to cleave a *tert*-butyl ester, the resulting carboxylic acid contains both oxygen atoms from the original ester:

e.g.



Propose a reasonable mechanism for this reaction.

(d) Explain why the mechanism in part (c) is reasonable for *tert*-butyl esters but not for methyl esters.

2. The thiocyanate ion (SCN^-) has two resonance structures which contribute roughly equally to its structure. Despite this, when thiocyanate reacts with primary or secondary alkyl halides, there is a clear major product. Often, it is the only observed product.

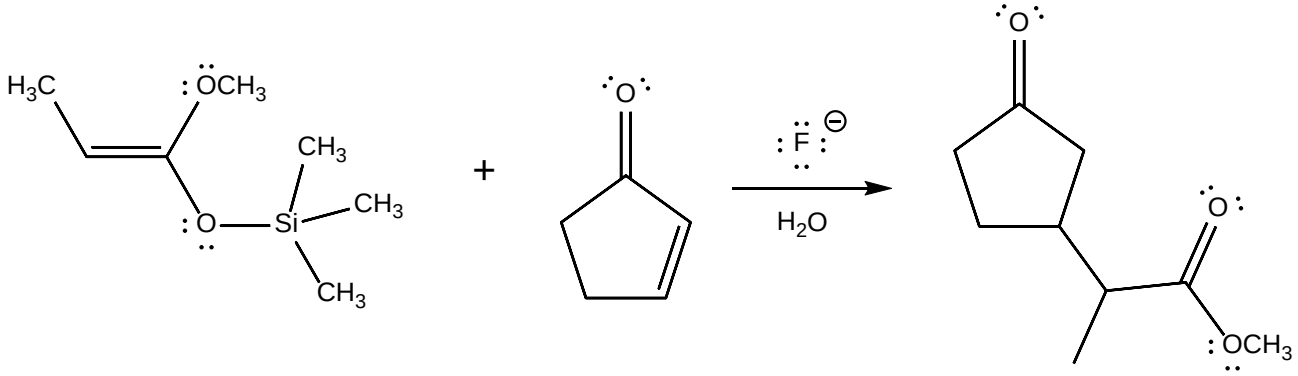
(a) Draw the two resonance structures for SCN^-.

(b) Predict the major organic product of the reaction between bromoethane and $KSCN$.

(c) Propose a reasonable mechanism for the reaction between bromoethane and $KSCN$.

(d) Explain why the reaction gives the product you predicted in part (b) (and not an isomer of that product). *It must be clear which atom from SCN^- became bonded to the carbon chain and why you chose that atom.*

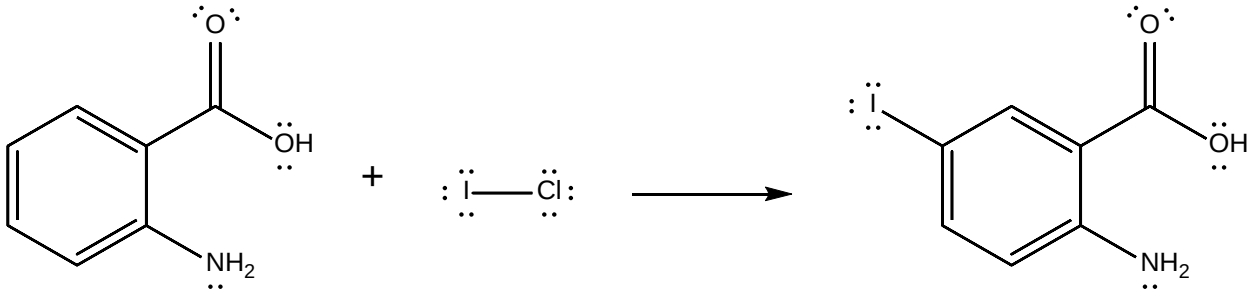
3. Propose a reasonable mechanism for the following reaction:



Hint: Si-F bonds are very strong.

4.

(a) Propose a reasonable mechanism for the following reaction:



(b) Explain the regioselectivity observed for this reaction.