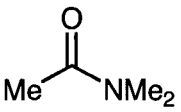
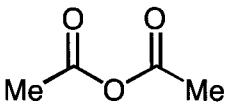
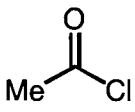
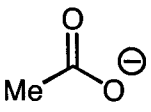
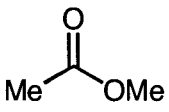
1. Rank the following acyl derivatives based on their reactivity as electrophiles toward hydroxide ion (1 = most reactive, 5 = least reactive).









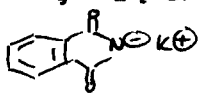


4	2	1	5	3

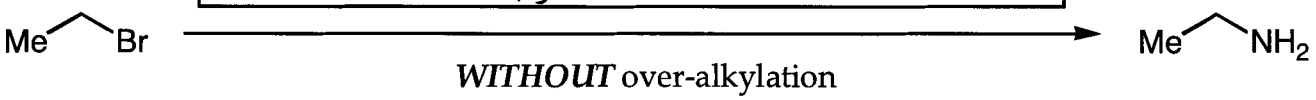
2. In the boxes, please provide the reagents for the illustrated transformations. More than one step may be required.

a) (three correct answers)

#1 – 1. NaN_3 2. $LiAlH_4$ 3. wkup

#2 – 1.  2. H_2NNH_2

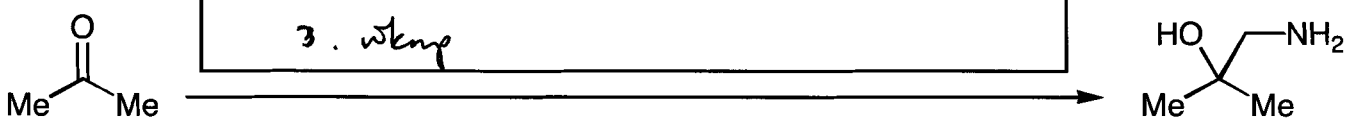
#3 – excess NH_3



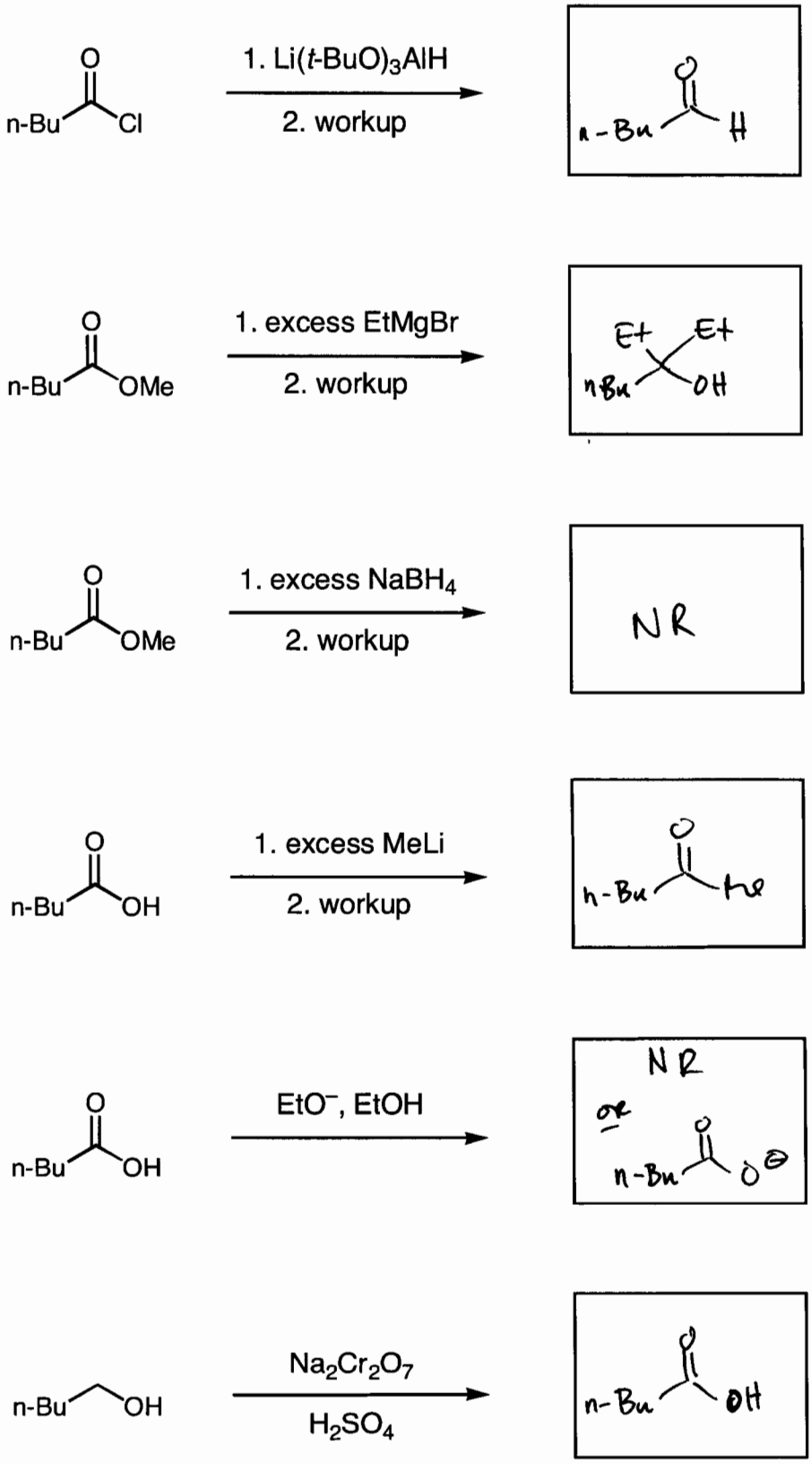
WITHOUT over-alkylation

b)

1. HCN, cat. KCN
2. $LiAlH_4$
3. wkup

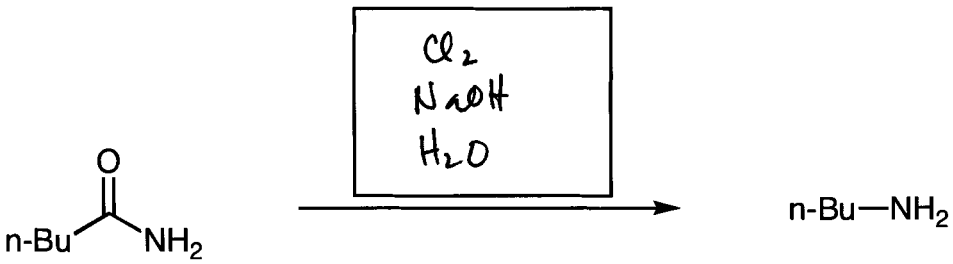


3. Please provide the requested products. If no reaction is expected, write "NR".

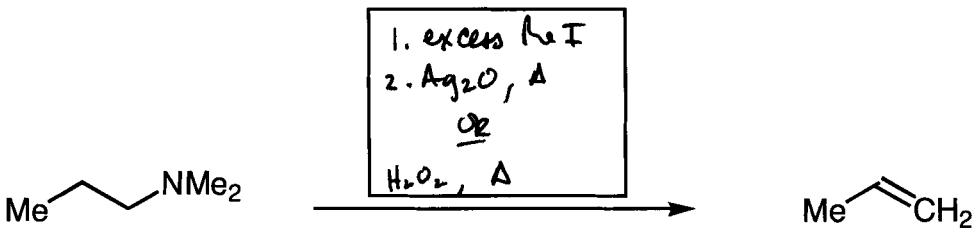


4. Please provide the requested reagents.

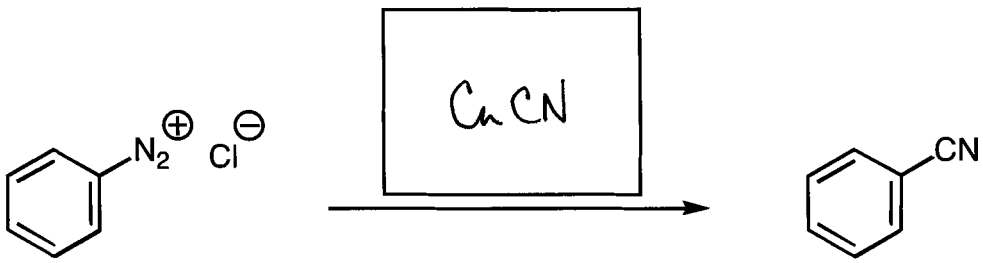
a)



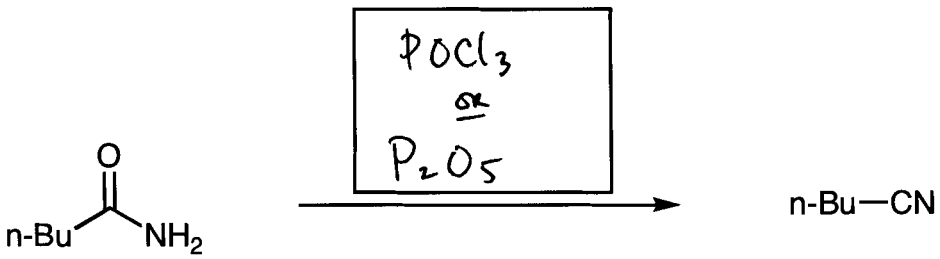
b)



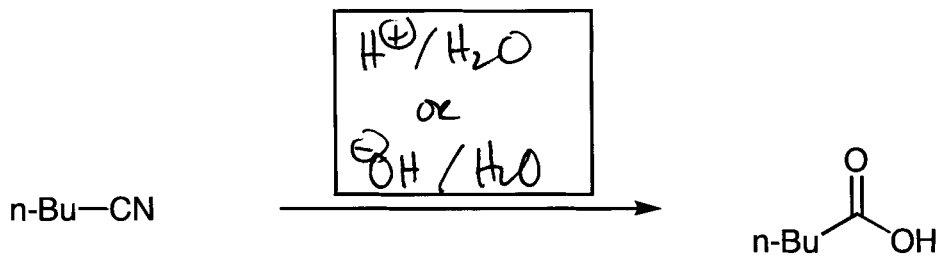
c)



d)



e)

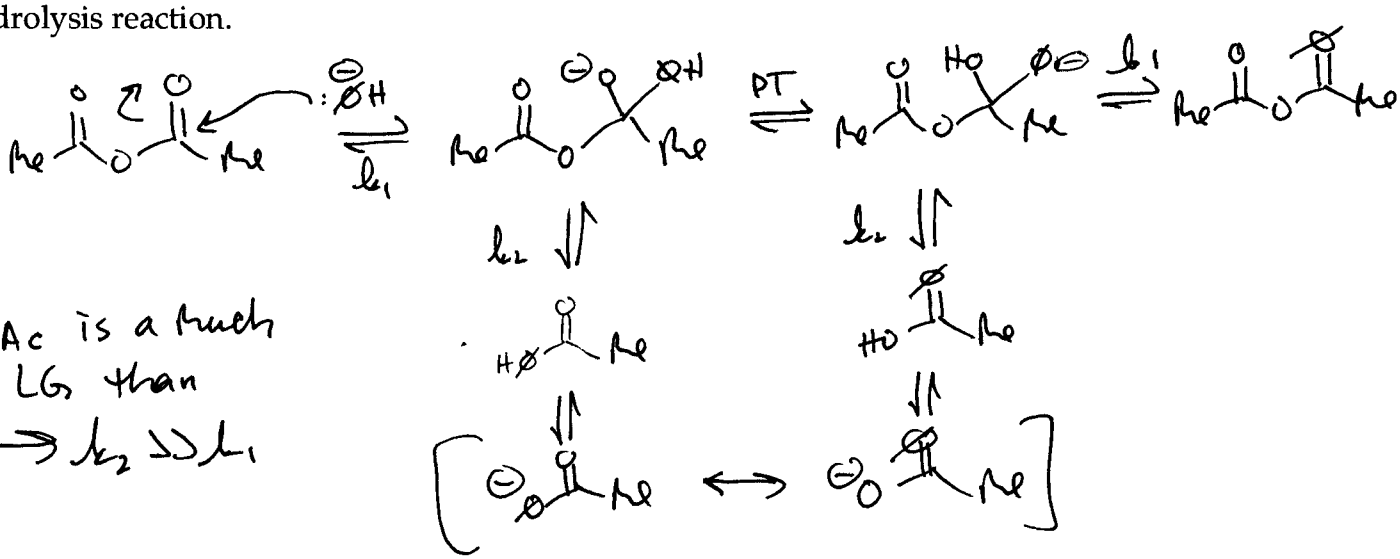


5. Consider the labeling experiment outlined below.:

stop the reaction at 50% conversion and examine the recovered anhydride for incorporation of ∅

∅ = isotopically labeled oxygen

In analogy with the discussion in class regarding the labeling studies of acyl chlorides, esters, and amides, carefully explain what level ("high" or "low") of ∅ incorporation you expect to observe in the recovered anhydride. Your answer should include the mechanism for this hydrolysis reaction.

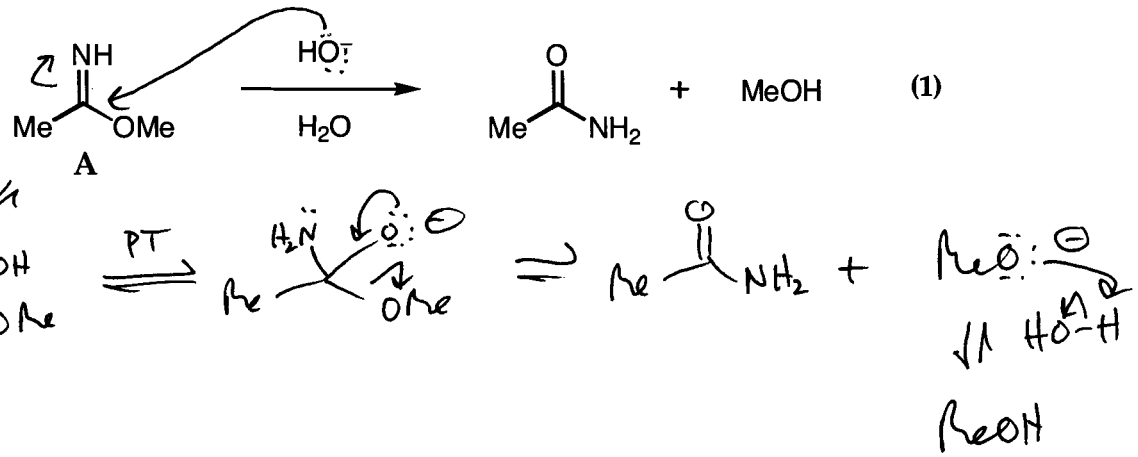


$\ominus OAc$ is a much better LG than $\ominus OH \Rightarrow k_2 \gg k_1$

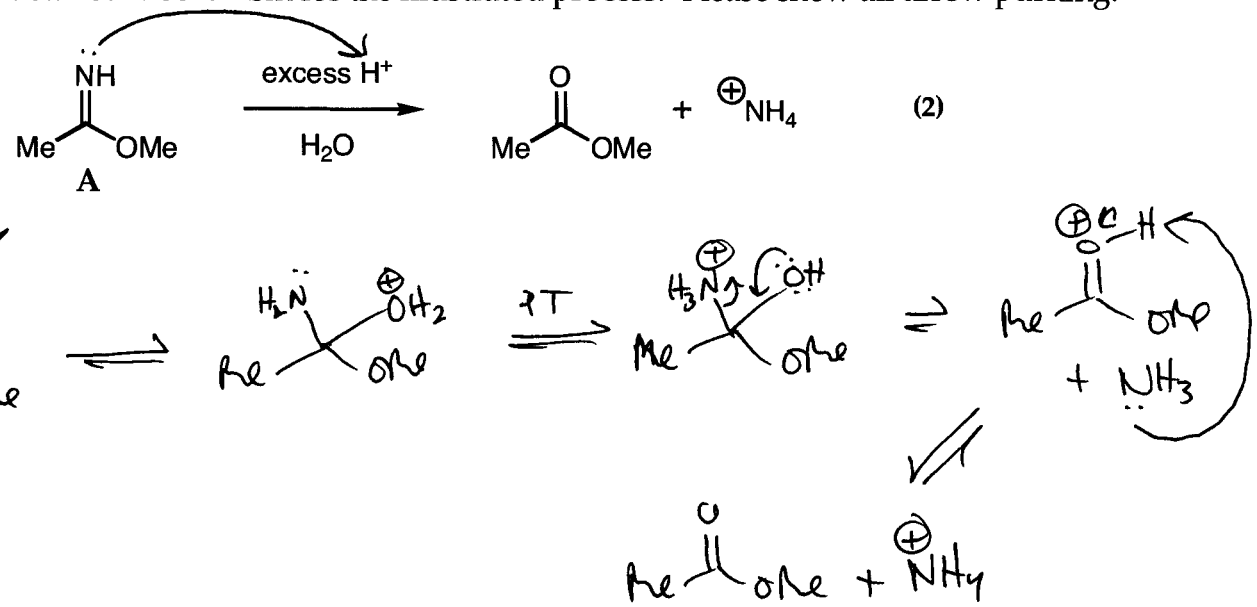
There should be low incorporation of the ∅ label into the recovered anhydride. When the tetrahedral intermediate forms, it can either collapse to reform the anhydride or the acid. Formation of the acid is much faster because $\ominus OAc$ is a much better leaving group than $\ominus OH$. Very little of the intermediate reverts back to anhydride, so incorporation of the label is low.

6. Methyl acetimidate (**A**) is hydrolyzed in aqueous sodium hydroxide to give mainly acetamide and methanol (eq 1). In aqueous acid, **A** hydrolyzes to give primarily methyl acetate and ammonium ion (eq 2).

a) Provide a detailed mechanism for the illustrated process. Please show all arrow pushing.



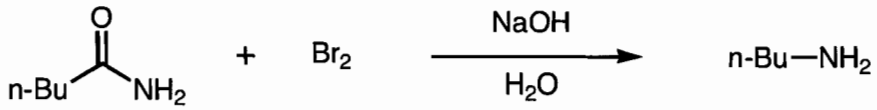
b) Provide a detailed mechanism for the illustrated process. Please show all arrow pushing.

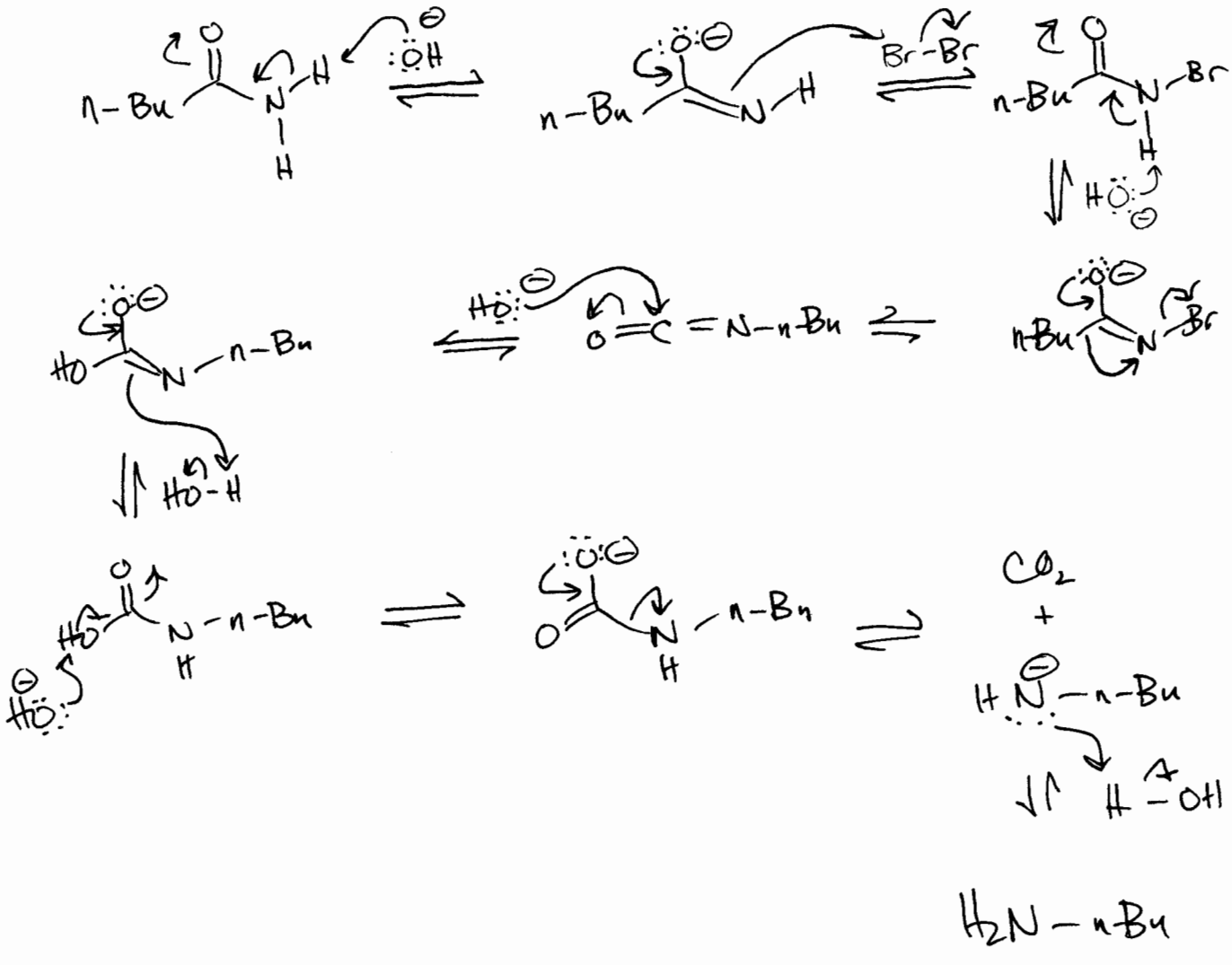


c) Briefly explain why the two reactions provide different products.

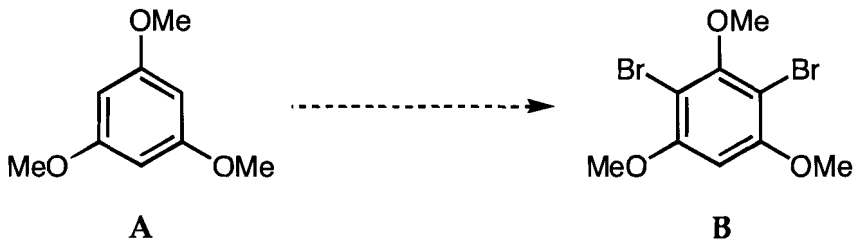
Under basic conditions, $^{\ominus}NH_2$ is a worse LG than $^{\ominus}OMe$, so elimination occurs to give the amide. Under acidic conditions, acid/base equilibrium favors protonation of the nitrogen, making it a good LG. In addition, $^{\oplus}NH_4$ is not nucleophilic, so formation of the ester is irreversible.

7. Provide a mechanism for the Hofmann elimination. Please show all arrow pushing.

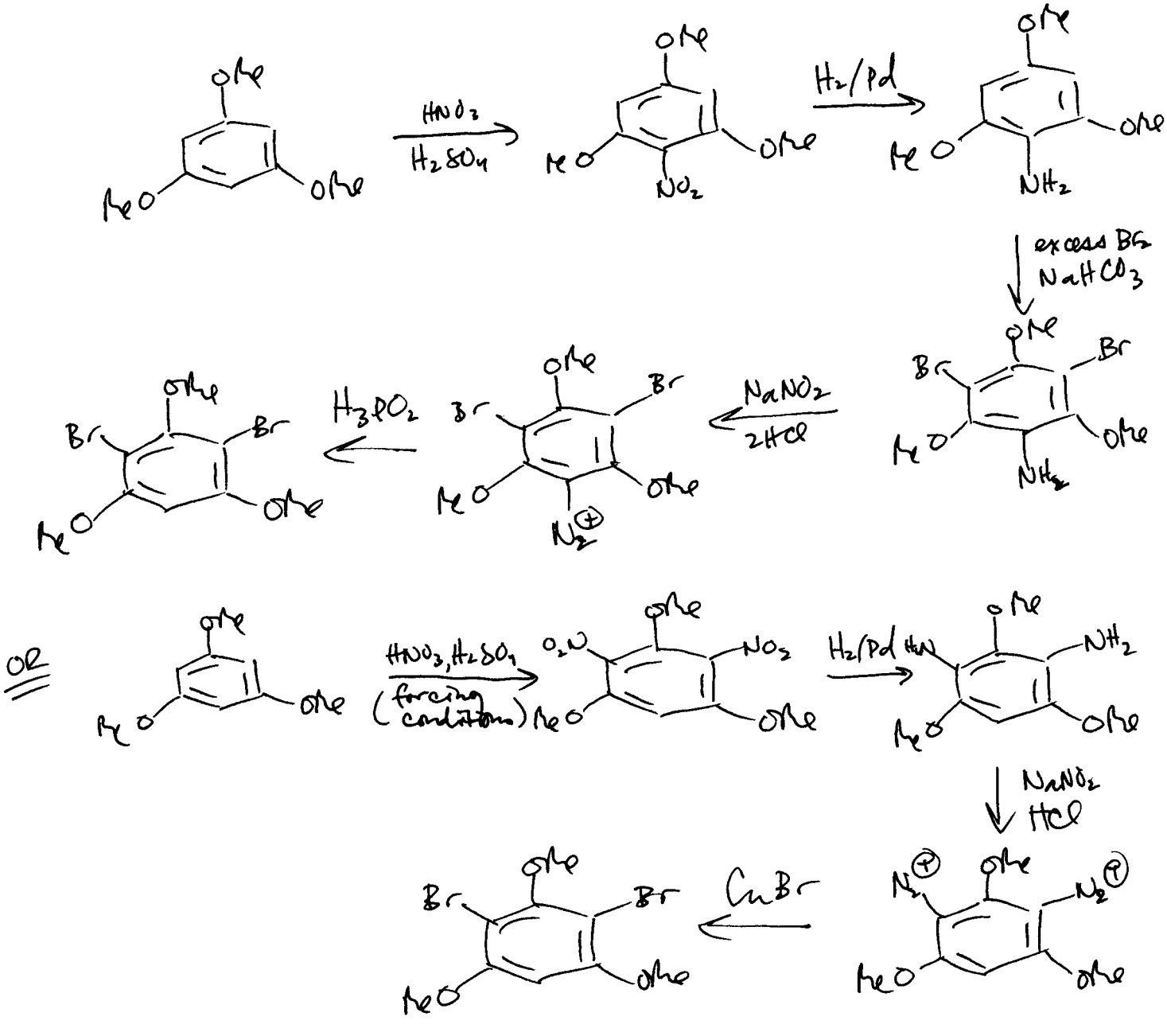




8. Provide a synthesis that will *selectively* convert **A** to **B**. Show all of the key intermediates, and furnish all of the important reagents.

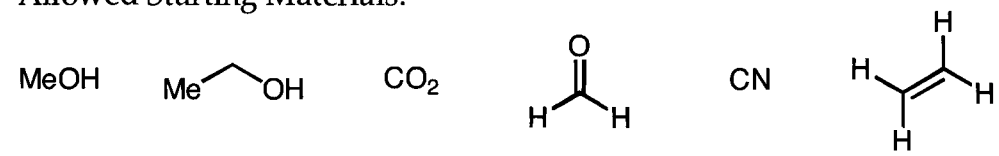


A **B**



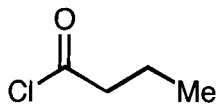
9. Provide syntheses for the following compounds. All of the carbons in the target molecules should be derived from the allowed starting materials. You may use any common reagents.

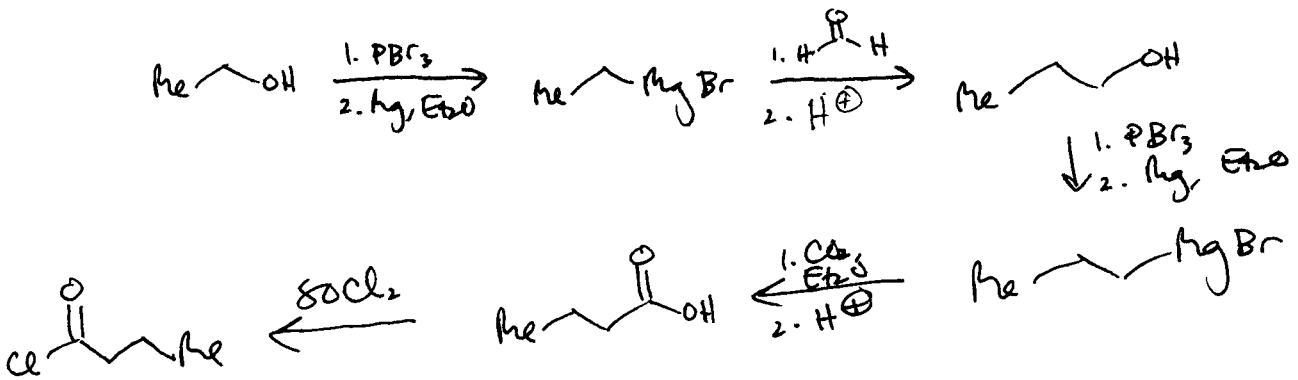
Allowed Starting Materials:



You can put these together in a few different ways.

a)





b)