CHM 2120 – Assignment #2 – ANSWERS

Additions:

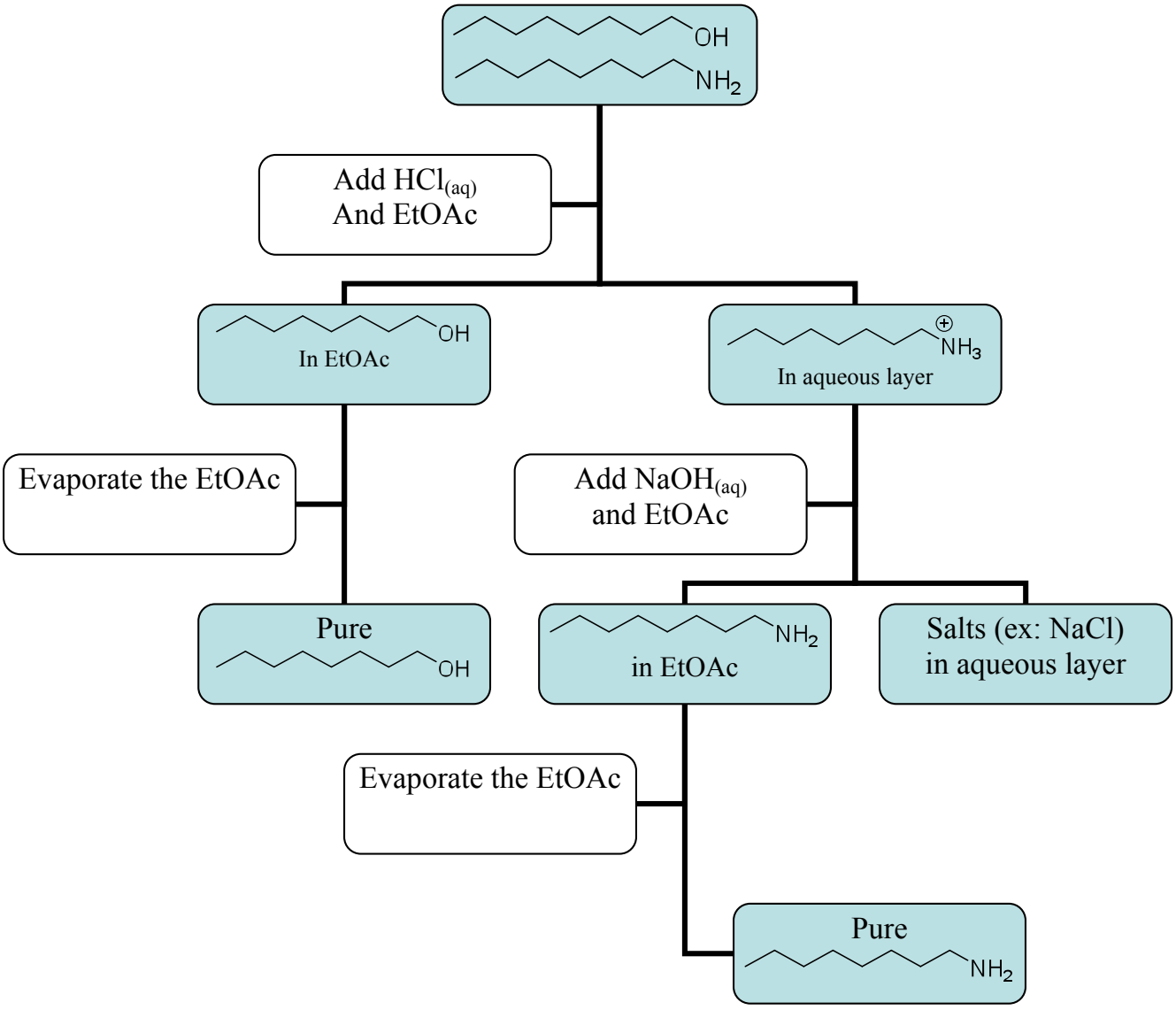
- Addition to the answer of 6f

In this assignment:

- Separation of organic compounds using acid/base techniques
- Acids/Bases
- S_N2, S_N1, E2, E1

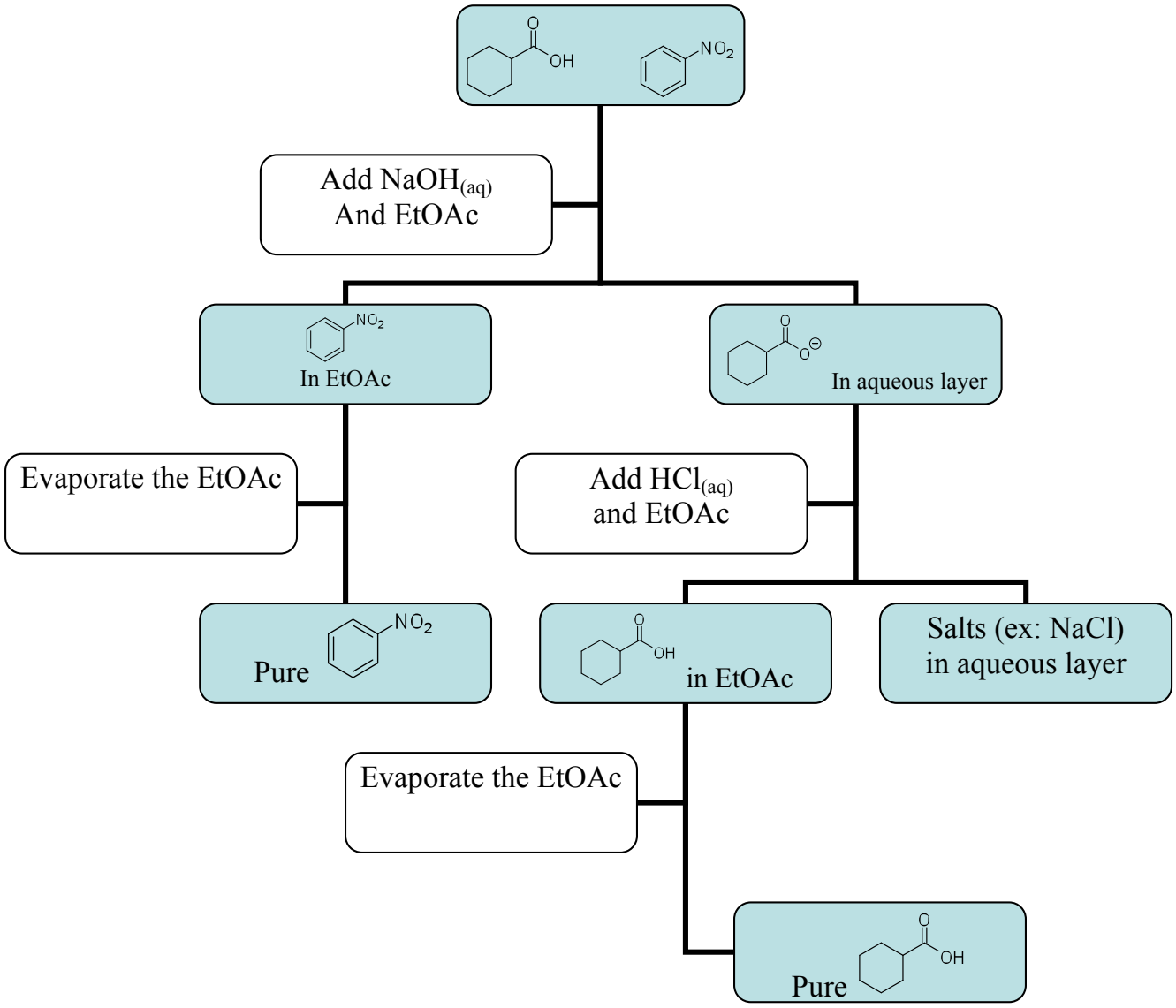
1. How would you separate the following mixtures of compounds?
   a. Octan-1-ol and octan-1-amine

Dissolve both in EtOAc. Add a 10% HCl solution in H_2O, which protonates the amine. Now the octan-1-ol is in the EtOAc, and the protonated (charged) amine is in the aqueous layer. Separate the organic and aqueous layers. Evaporate the organic layer to obtain pure octan-1-ol. Deprotonate the amine to make it neutral by adding a 10% NaOH solution in H_2O. Extract the aqueous layer with EtOAc. The neutral amine dissolves best in the organic layer. Separate the layers and evaporate the EtOAc to obtain pure octan-1-amine.

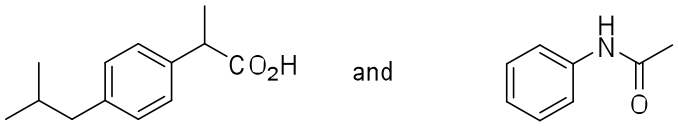


b. Cyclohexanecarboxylic acid from nitrobenzene

Dissolve both in EtOAc. Add a 10% NaOH solution in H_2O, which deprotonates the carboxylic acid. Now we have nitrobenzene in the organic layer, and the deprotonated (charged) cyclohexanecarboxylic acid (a carboxylate) in the aqueous layer. Separate the organic and aqueous layers. Evaporate the organic layer to obtain pure nitrobenzene. Protonate the carboxylate by adding a 10% HCl solution in H_2O. Extract the aqueous layer with EtOAc. The neutral acid dissolves best in the organic layer. Separate the layers and evaporate the EtOAc to obtain pure cyclohexanecarboxylic acid.

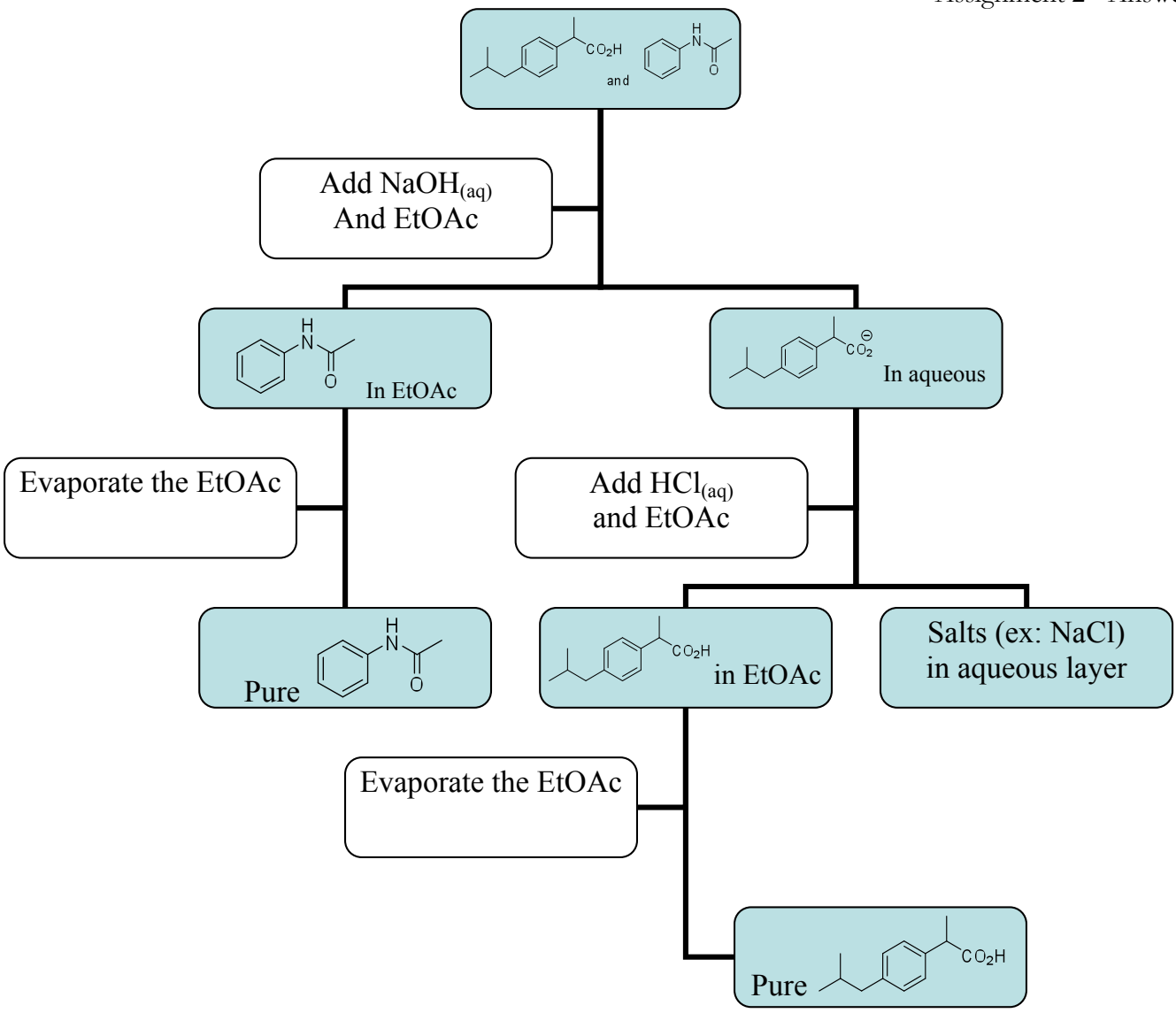


c.



Ibuprofen (advil)

Same procedure as in part B.



2. Which of the following is the strongest, and which is the weakest base?

   a) $CH_3CH_2O^-$ b) CH_3CH_2OH; c) $CH_3CH_2S^-$ d) $CH_3CH_2CO_2^-$ e) $CH_3CH_2NH_2$

Strongest base: a; Weakest base: b

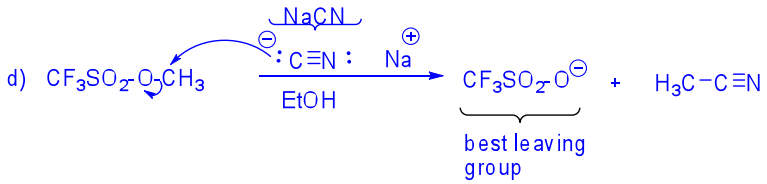
3. Which of the following is the strongest, and which is the weakest nucleophile?

a) $CH_3CH_2O^-$ b) CH_3CH_2OH; c) $CH_3CH_2S^-$ d) $CH_3CH_2CO_2^-$ e) $CH_3CH_2NH_2$

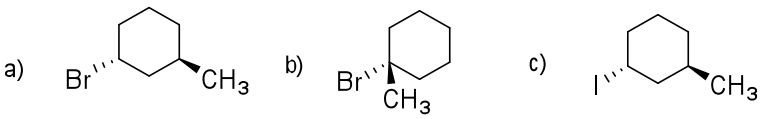
Strongest nucleophile: c; Weakest Nucleophile: b

4. Which of the following will react most rapidly with NaCN in ethanol to give a substitution product? Give the structure of the product.

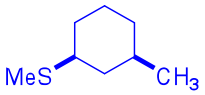
a) $CH_3-CH_2-SO_2-O-CH_3$ b) $CH_3-SO_2-O-CH_3$ c) $CCl_3SO_2-O-CH_3$ d) $CF_3SO_2-O-CH_3$



5. Which of the following will react most rapidly with $Na^{(+)\,(-)}S\text{-}CH_3$ in acetone to give a substitution product? Give reasons for your choice. What is the structure of the product resulting from the fastest reaction?



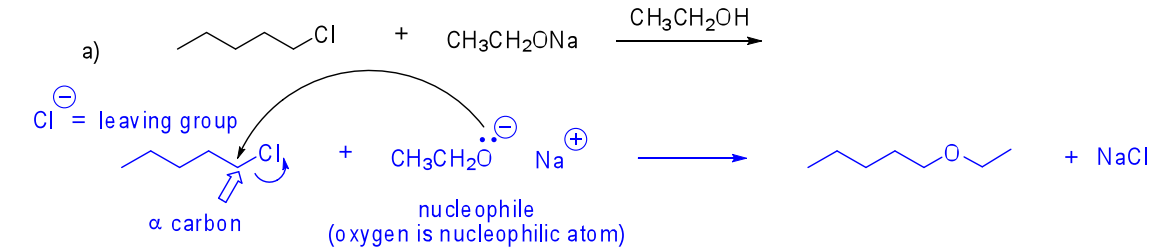
c) reacts fastest since I(-) is the better LG , then a) then b) [S_N2 reactions are very slow if the LG is on a tertiary carbon as in b)].

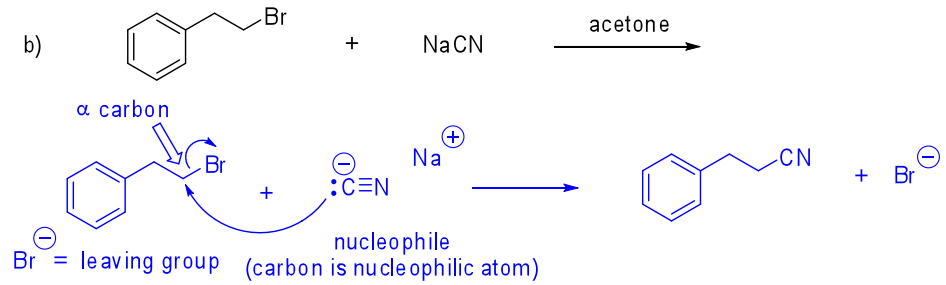


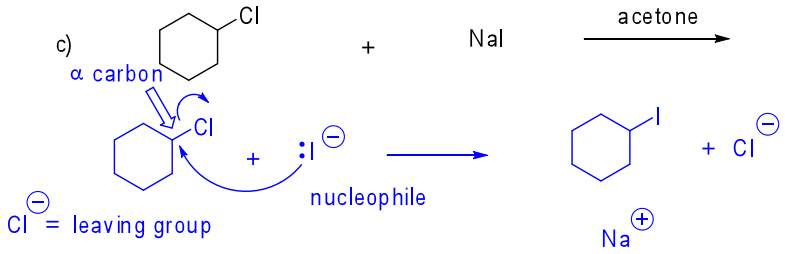
S_N2 occurs with inversion of configuration.
In the starting material the LG was *trans* to the CH_3.
In the product the incoming group [Nu] and CH_3 are now cis

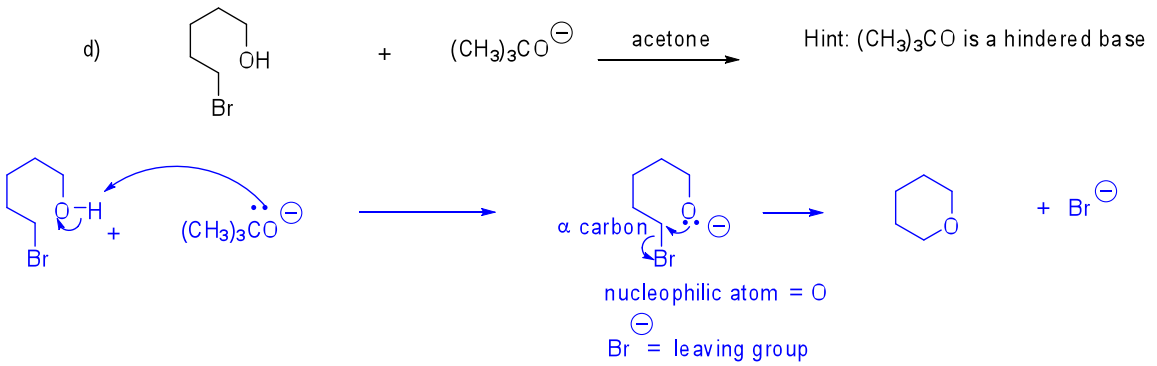
6. Use arrow notation to show the mechanisms of the following reactions. Use your mechanism to predict the product of the reaction. Identify the nucleophile, its nucleophilic atom, the α carbon of the electrophile and the leaving group.

Note: Spectator ions such as Na^+ are commonly omitted from products.



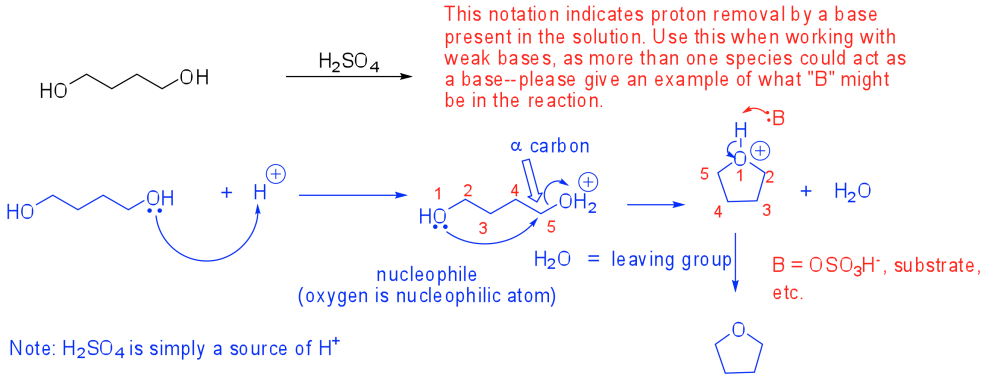






Tip: When bases are present, compare the strength of the base and the conjugate base (just like a typically acid/base reaction). If the base is stronger than the conjugate base that would result, then deprotonate first. This will help tell you whether to deprotonate first or second. Typiclaly, when using strong bases, deprotonate first then diplace/react. When weak bases are present, do the nucleophilic reaction first, then deprotonate. When acids are present, you will usually protonate a basic atom to start the reaction.

e)



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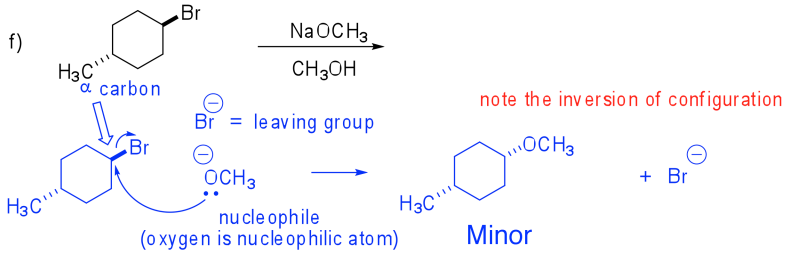
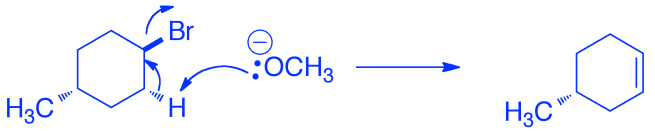
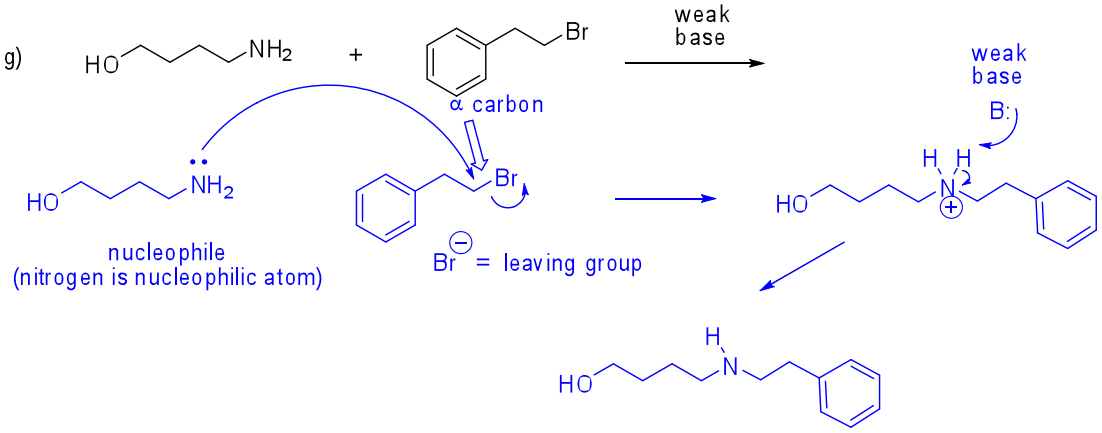




Major product

Note: methoxide is both a good nucleophile and a strong base. Because the alpha carbon is secondary, an E2 reaction mechanism dominates.

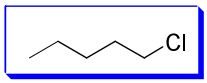
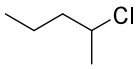
g)



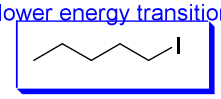
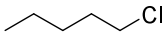
Note: In this reaction, 2 nucleophiles are present. N is the better nucleophile since is lies furthest left in the periodic table. It will be less electronegative than O and is therefore better able to donate electrons.

Because the base is weak, it cannot deprotonate RNH_2, therefore the H^+ is removed after the S_N2 displacement takes place.

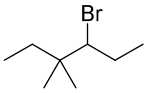
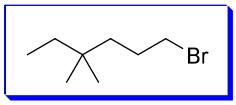
7. Circle the most reactive species in each of the following pairs of compounds based on S_N2 reactivity and explain your choices.

a)  vs 

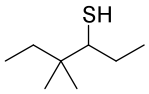
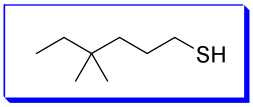
reacts faster as an electophile
the α carbon is less substituted.
Therefore the transition state will be less crowded and lower energy.
A lower energy transition state means a faster reaction

b)  vs 

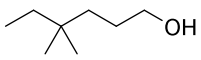
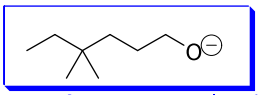
reacts faster as an electophile
iodine is lower in the periodic table than chlorine
this means that iodide will be a larger anion than chloride
a larger anion will have lower energy since the charge is dispersed
therefore iodide is a better leaving group than chlorine
Since this compound has a better leaving group, it will react faster

c)  vs 

reacts faster as an electophile
the α carbon is less substituted.
Therefore the transition state will be less crowded and lower energy.
A lower energy transition state means a faster reaction

d)   (as nucleophiles)

reacts faster as a nucleophile
sulfur is is less crowded (primary)
Therefore the transition state will be less crowded and lower energy.
A lower energy transition state means a faster reaction

e)  vs  (as nucleophiles)

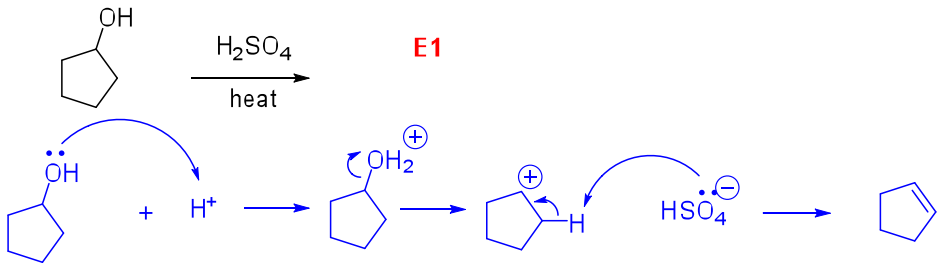
reacts faster as a nucleophile
conjugate bases are better nucleophiles than their conjugate acids since they are better able to donate electons.
The charge on the conjugate base raises the energy of the starting materials relative to the conjugate acids. This nucleophile will give a lower activation energy and faster reaction

f)  vs  (as nucleophiles)

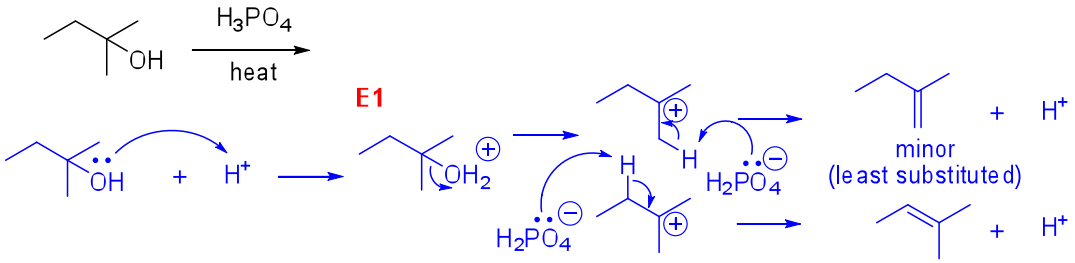
I^- reacts faster as a nucleophile
iodine is lower in the periodic table and therefore holds less tightly to its electrons. It is therefore a better electron donor than chloride

8. Predict the major product of elimination for the following compounds and give a mechanism for each transformation.

a)



b)



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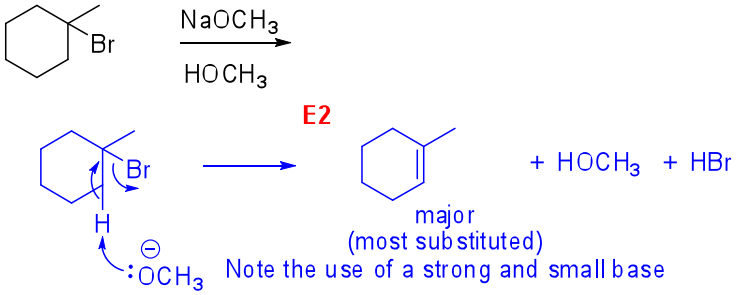

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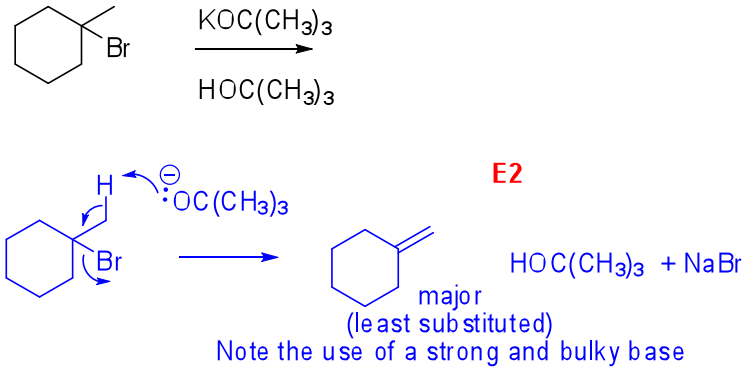

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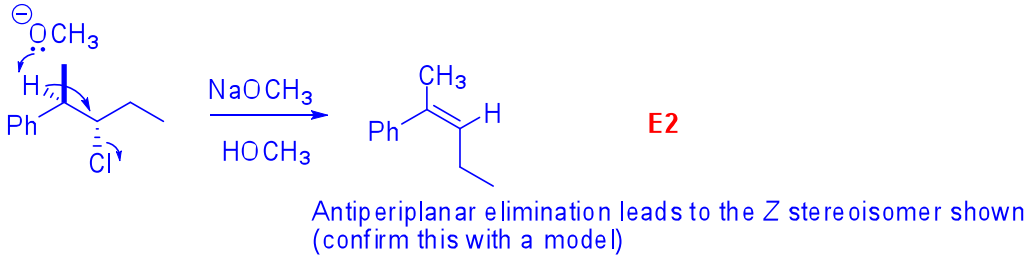
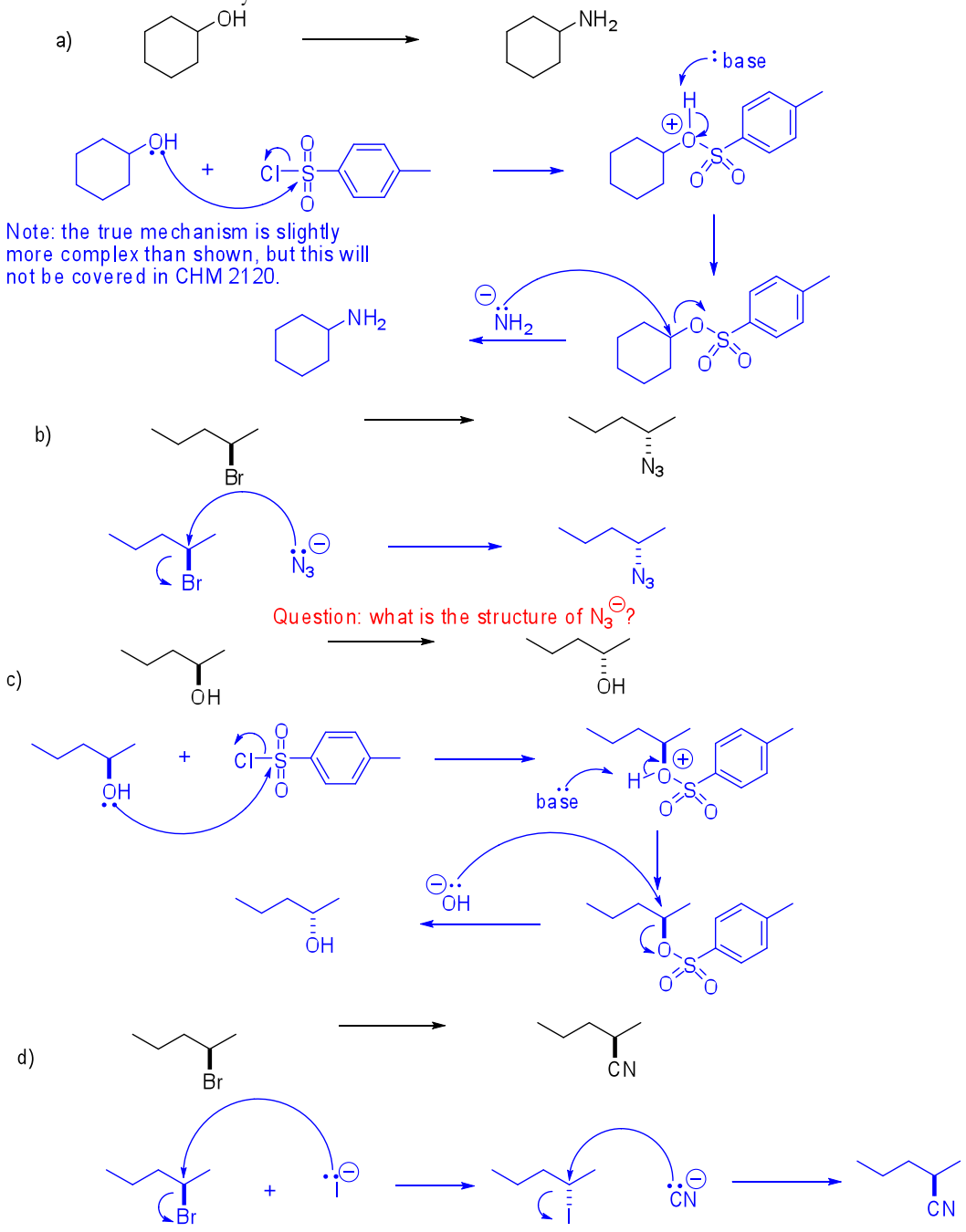


9. Show how each of the following transformations could be achieved. Give reagents and solvents. You may have to use more than one reaction to do some of these.



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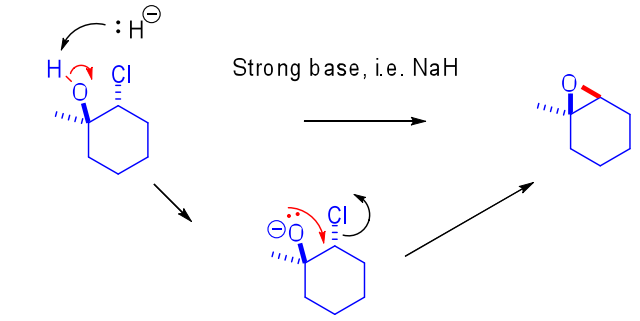

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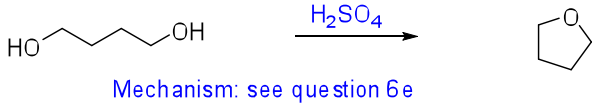

Mechanism: see question 6e

10. Give a mechanism and the product for each of the following transformations:

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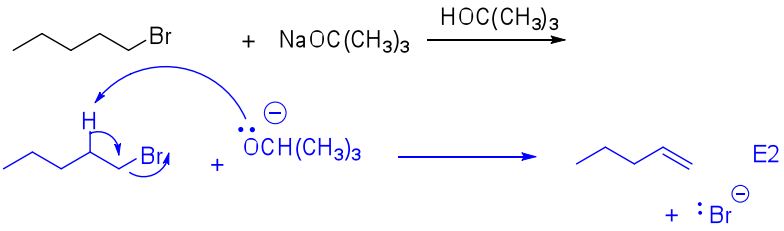

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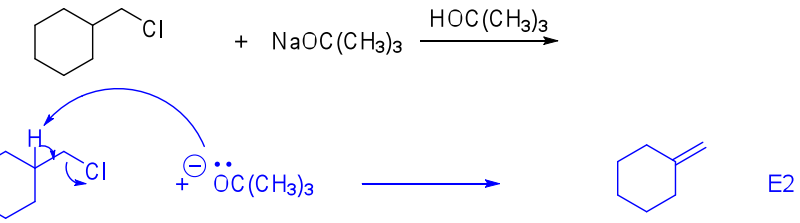

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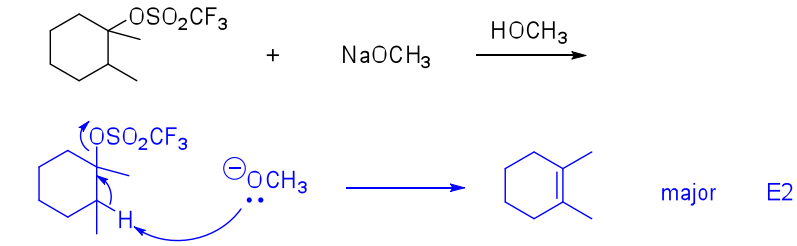

d)