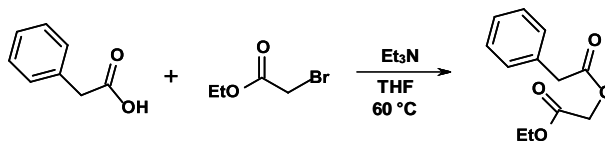
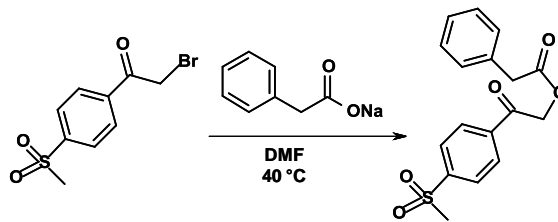


**Practice Questions for Chapters 1-3**  
**CHEM 4000A – Medicinal Chemistry**

1. In the first couple of Friday problem sets, we saw reactions like:



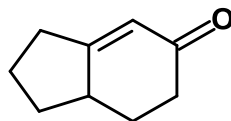
and



At the time, we did not have a good explanation for why the nucleophile attacked the carbon attached to bromine instead of the carbonyl carbon.

Use concepts discussed in class since then to suggest potential reasons for this behavior.

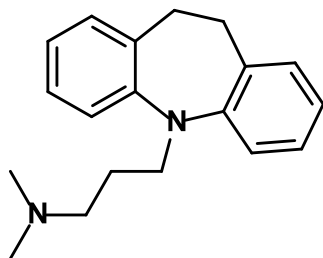
- 2.
- Give an example of an a<sup>1</sup>-synthon.
  - Give an example of a d<sup>1</sup>-synthon.
  - Explain why an a<sup>1</sup>-synthon is usually a better choice than a d<sup>1</sup>-synthon in retrosynthetic analysis.
3. Demonstrate how a Robinson annelation could be used to make the molecule below.



Your answer should indicate all required reagents and include the mechanism for this reaction.

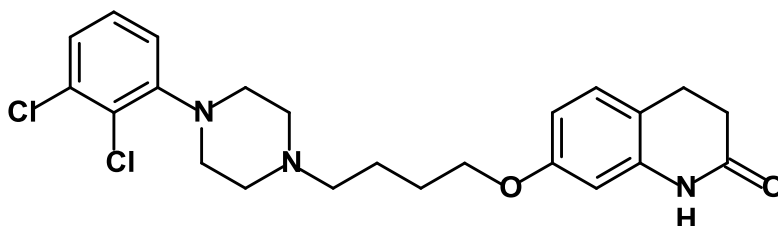
4. We discussed LiAlH<sub>4</sub> and NaBH<sub>4</sub> several times during problem sets.
- In what way are these reagents similar? Give an example of a reaction that could be done using either reagent.
  - In what way are these reagents different? Give an example of a reaction that could only be done using one of these two reagents (and clearly indicate which one).
- 5.
- Under what circumstances is it helpful (or even necessary) to use an auxiliary functional group?
  - Give an example of a reaction using an auxiliary functional group (in which it would have been necessary).
  - Demonstrate how to remove the auxiliary functional group you used in your answer to part (b).

6. Imipramine (Tofranil®) has the structure shown below:



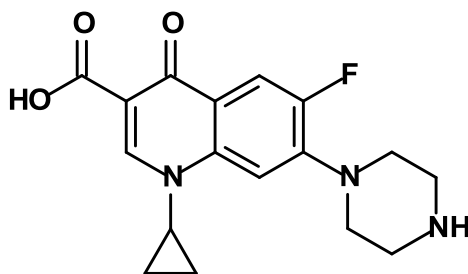
Where is/are the best place(s) to disconnect between the two nitrogen atoms? Explain your choice(s).

7. Aripiprazole (Abilify®) has the structure shown below:



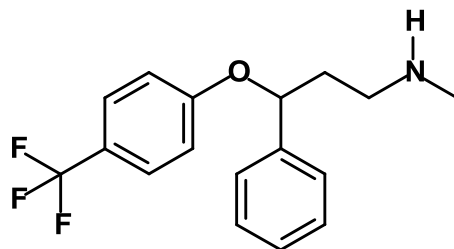
Which of the four main approaches to retrosynthesis would dominate your analysis of this molecule? Justify your choice.

8. Ciprofloxacin (Cipro®) has the structure shown below:



If you wished to take a skeleton-oriented approach to retrosynthesis of this molecule, what disconnections would you make?

9. Fluoxetine hydrochloride (Prozac®) has the structure shown below:



Propose a synthesis of fluoxetine hydrochloride.

4-(trifluoromethyl)phenol is commercially available (and affordable). You may use any other reactants and reagents that you could reasonably expect to be commercially available.