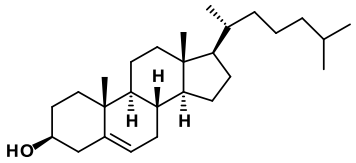
Practice Questions for Chapters 1-8
CHEM 4000A – Medicinal Chemistry

1. The structure of cholesterol is shown below:



(a) Identify all of the endoendo bonds in cholesterol.

(b) Identify all of the exendo bonds in cholesterol.

(c) If we were performing a retrosynthetic analysis on cholesterol and began by making a single disconnection, it should not be one of the endoendo bonds. Why not?

(d) Generally speaking, what would be a better approach to a retrosynthetic analysis of cholesterol?

2.

(a) There are hundreds (possibly thousands?) of ways to oxidize a secondary alcohol to a ketone. Give two examples of reaction conditions that can accomplish this.

(b) Which of your two examples is greener? Explain.

3. We saw two different reactions involving ylides as reagents.

(a) The Wittig reaction involved a phosphonium ylide reacting with a carbonyl. Draw both resonance structures of one example of a phosphonium ylide.

(b) We also saw a reaction involving a sulfonium ylide reacting with a carbonyl. Draw both resonance structures of the sulfonium ylide.

(c) Looking at your answers to (a) and (b), define the term "ylide".

(d) What is the main difference between the reaction of a carbonyl with a phosphonium ylide vs. with a sulfonium ylide?

4. Diethylzinc (Et_2Zn) is often used a source of nucleophilic carbon.

(a) Would you expect this to be a hard nucleophile or a soft nucleophile? Explain.

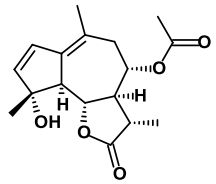
(b) Diethylzinc is pyrophoric (catches fire easily in the presence of water or air). Why?

5. In this course, we discussed three of the four main approaches influencing choice of bond-set. (The fourth approach was "use synthetic methods in which you already have expertise".)

(a) What is a bond-set?

(b) What were the three approaches we discussed? Briefly describe each.

6. The structure of matricin is shown below.



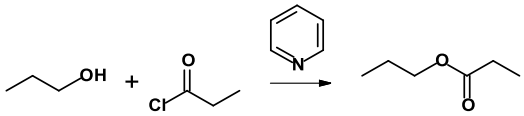
(a) Identify a disconnection that would give an a^1 and a d^2 synthon.

(b) If I'm counting correctly, there are four possible answers to part (a).
Which is/are best? Which is worst? Why?

(c) Identify a disconnection that would give an a^2 and a d^2 synthon.

(d) Why is an a^2-d^2 disconnection usually considered inferior to an a^1-d^2 synthon?

7. When an alcohol is reacted with an acid chloride, an amine such as pyridine is usually included as a nucleophilic catalyst. Propose a mechanism for the reaction below and explain how the inclusion of pyridine accelerates the reaction.

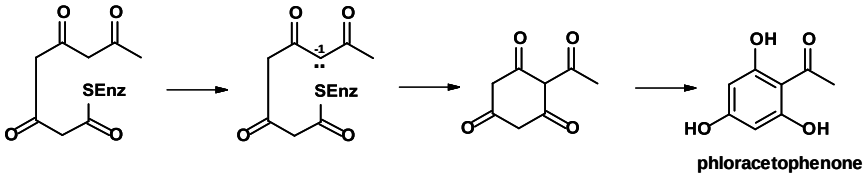


8. LDA is made by reacting diisopropylamine with butyllithium.

(a) Write a balanced chemical reaction for this reaction (including structures of all reactants and products).

(b) Both LDA and butyllithium are strong bases. So, why would we ever want to make LDA instead of just using butyllithium?

9. The biosynthesis of phloracetophenone is shown below.



SEnz stands for a sulfur atom that is part of an enzyme.

Explain what is going on in each step of this biosynthesis. You may use generic acids (HA) and bases (B) in any mechanism as it is reasonable to assume that there are enzymes present with both acidic and basic sites.

10. Propose a synthesis of cinnamyl acetate (shown below). You may use any starting materials that you might reasonably expect to be commercially available as long as no single starting material contributes more than four carbon atoms *or* one benzene ring to the final product.