

## CFQ & PP: Multi-step Organic Synthesis

### Reading

Brown and Foote: Sections 10.10

Appendix 7: Reagents and Their Uses

Appendix 8: Summary of Methods for the Synthesis of Functional Groups

### Lecture Supplement

Multistep Organic Synthesis (page 9 of this Thinkbook)

### Optional Web Site Reading

The 1990 Nobel Prize in Chemistry (<http://www.nobel.se/chemistry/laureates/1990/index.html>)

### Review

Topics to review from Chem 30A, as needed:  $S_N2/S_N1$ , elimination, radical halogenation, addition to carbon-carbon bonds

### Suggested Text Exercises

Brown and Foote: Chapter 8: 46, 50

Chapter 9: 41, 43, 46

Chapter 10: 6, 19 - 31

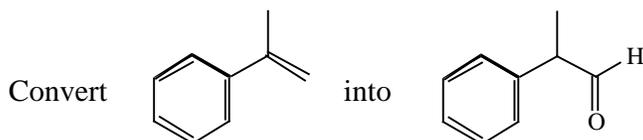
Chapter 11: 32 - 39

### Miscellaneous Projects

Create reaction flash cards (Brown and Foote Appendix 8 very useful for this!)

### Concept Focus Questions

1. Define "retrosynthesis."
2. Describe the retrosynthesis process used to design a multi-step organic synthesis. Use the example shown below.



### Concept Focus Questions Solutions

1. Retrosynthesis is the process of thinking backwards in synthesis design. We consider how a given target molecule is made from some precursor molecule, instead of starting with the given starting material.
2. We start by examining the aldehyde target structure.

Can it be made in a single step from the given starting material? No.

Therefore we must decide what sequence of reactions is appropriate. There is no chance in the basic carbon skeleton (number or sequence of carbons), so we need only be concerned with functional group changes. What functional group(s) are in the product, and how are they prepared?

- Benzene ring: A benzene ring is present in the target and the starting material, so we don't have to be concerned about adding it.
- Aldehyde: We know several ways to make an aldehyde.

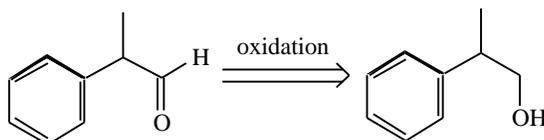
Alkene ozonolysis: Alkene ozonolysis involves changing the carbon skeleton. Since the carbon skeleton is unchanged in this synthesis problem, ozonolysis would require adding this extra carbon at some point. The route employs extra steps and is therefore less efficient.

Alkyne hydroboration: Alkyne hydroboration cannot be used here, because the alkyne that would lead to this aldehyde would have to have a pentavalent carbon.

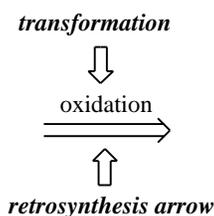
Primary alcohol oxidation: The only viable choice left.

***The more reactions you know, the more flexibility you have, and thus synthesis problems are easier. This is an excellent time to bring your flash cards up to date, and start using them every night!***

We have identified a primary alcohol as a reasonable precursor to the aldehyde target. This is written as:

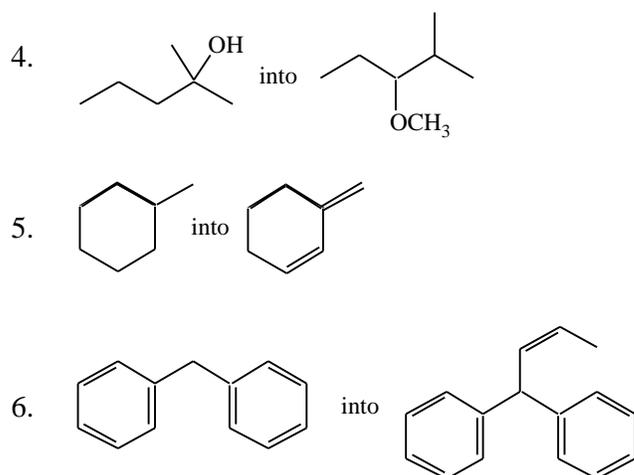


The fat retrosynthesis arrow means "the aldehyde can be made from the alcohol by oxidation." While it is not necessary to write the reaction above the retrosynthesis arrow, it helps you to remember what you planned to do.



Now we repeat the process, with the primary alcohol as the new target molecule.

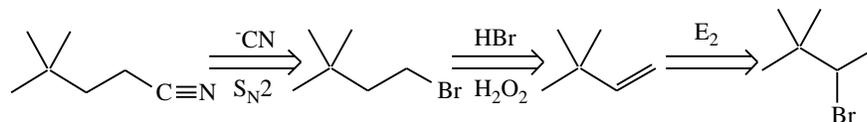




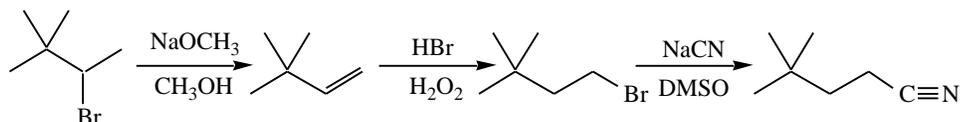
### Practice Problems Solutions

There may be more than one solution to each synthesis problem. If you have questions about the viability of your synthesis, consult a TA or Dr. Hardinger.

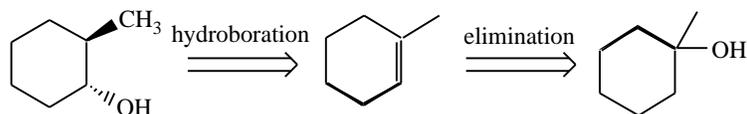
#### 1. Retrosynthesis:



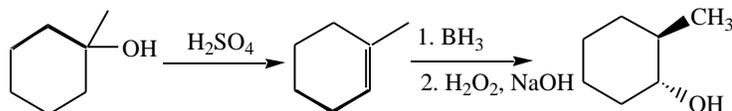
#### Forward direction:



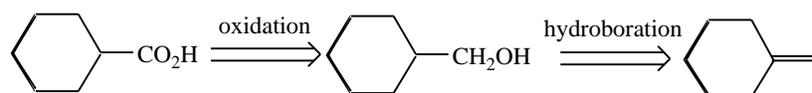
#### 2. Retrosynthesis:



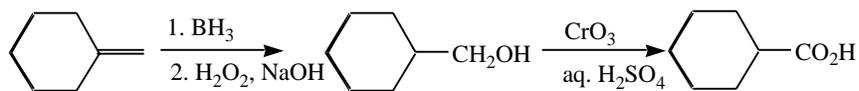
#### Forward direction:



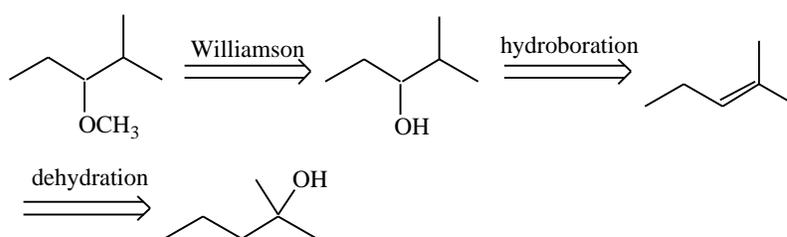
3. Retrosynthesis:



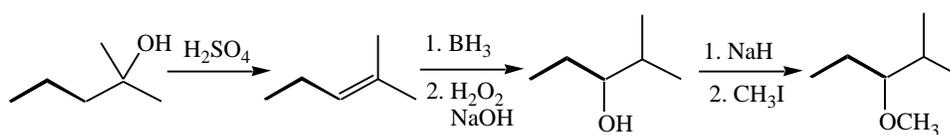
Forward direction:



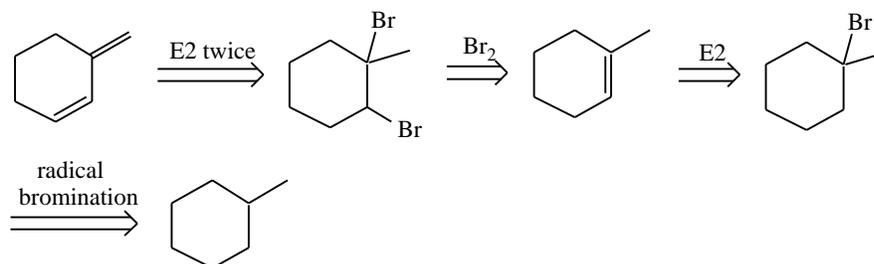
4. Retrosynthesis:



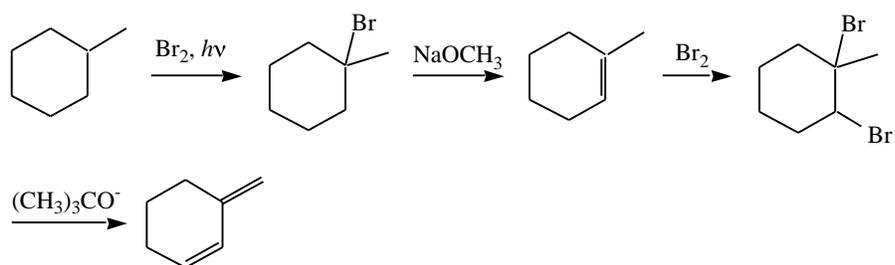
Forward direction:



5. Retrosynthesis:

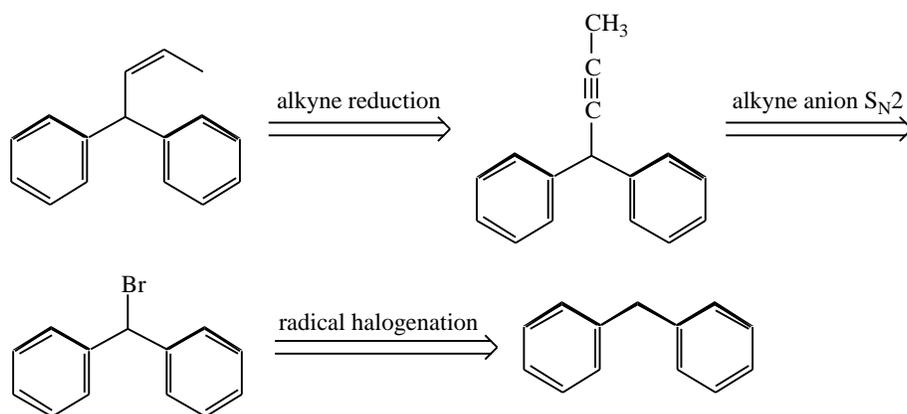


Forward direction:



In the last step, use of a sterically hindered base such as  $(\text{CH}_3)_3\text{CO}^-$  helps ensure that the less substituted alkene is formed.

6. Retrosynthesis:



Forward direction:

