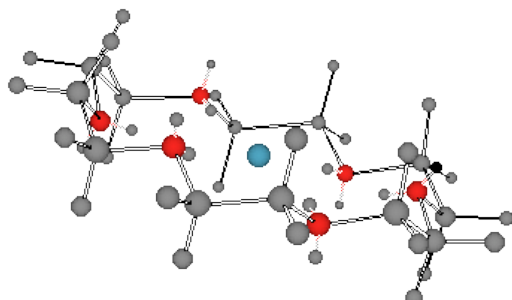


Chem 220 - Organic Chemistry

Problem Set 10

Chapter 14 - Ethers and Epoxides

Due: Monday, November 30, 2009

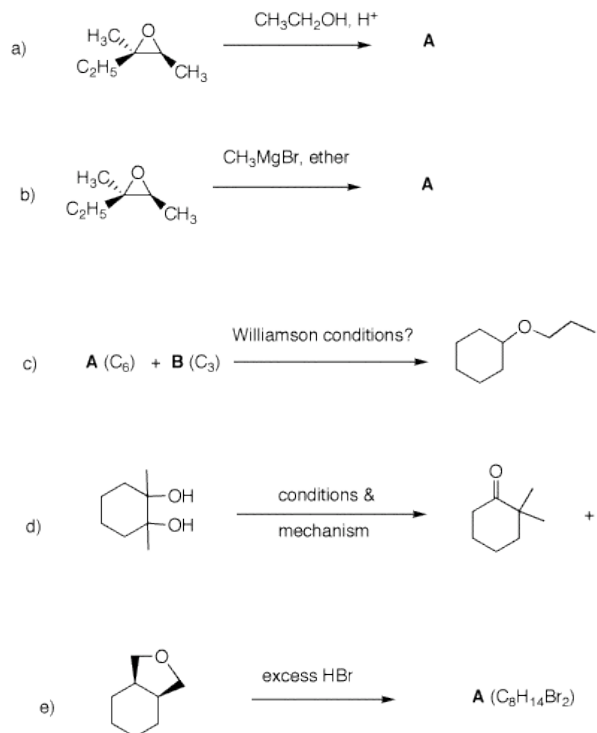


- Potassium cation solvated by the cyclic polyether, 18-crown-6 [18-membered ring; 6 oxygen atoms]. Each of the ethano groups is in a staggered conformation with each of the O-C-C-O dihedral angles at $\sim 60^\circ$ [gauche]. For a dynamic version, [click here](#). Note that the six oxygen atoms occupy the same spatial arrangement as do the six carbon atoms in chair cyclohexane. The discovery of the crown ethers by [Charles Pedersen](#) of DuPont earned him a share in the 1987 Nobel Prize in Chemistry.
- Diethyl ether (ether) may well be the first organic compound prepared that does not appear in Nature. For a chemical history of ether [click here](#). A different Powerpoint version is [here](#).
- *Theory of Etherification*, A. W. Williamson, *Quarterly J. Chem. Soc.*, **1852**, *4*, 106. [See page 23 in the .pdf file.]

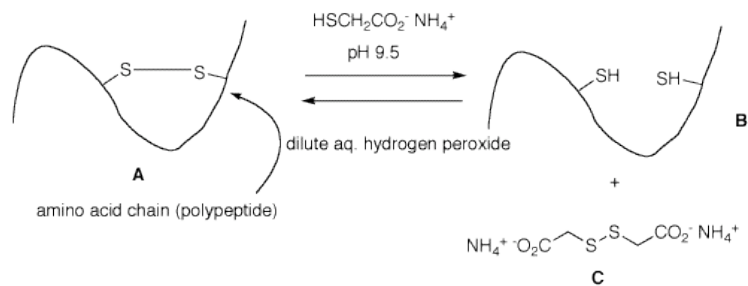
"The following experiments were made with the view of obtaining new alcohols, by substituting carburetted hydrogen for hydrogen in a known alcohol. Iodide of potassium was readily formed on the application of a gentle heat, and the desired substitution was effected; but, contrary to expectation, the compound thus formed had none of the properties of an alcohol -- it was nothing else than common ether, $C^4H^{10}O$."

- *On Etherification*, A. W. Williamson, *Quarterly J. Chem. Soc.*, **1852**, *4*, 229.

1. In the following problems, provide the missing information. Provide explanations for your choices. **Pay attention to stereochemistry.**



2. Cartoon **A** represents the cross-linking a disulfide bond in hair. This property gives hair its natural curl or an artificial "permanent wave". When a solution of ammonium thioglycolate at alkaline pH is applied to the hair, it goes straight to form a dithiol (cartoon **B**) and disulfide **C**, which is water soluble and is rinsed away. To restore the curl, the hair is washed with a mild oxidant. Provide a mechanism for the formation of **B** and **C** from **A**, and the formation of **A** from **B**.



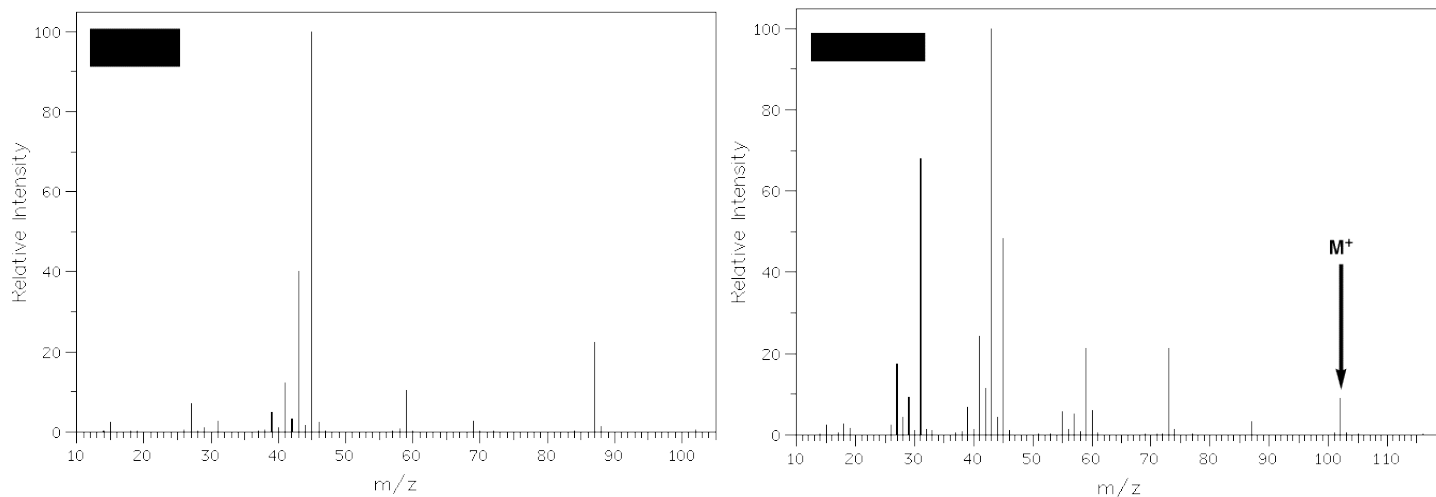
3. Compounds **A** and **B** are constitutionally, isomeric ethers (see spectra). Compound **A** cannot be prepared by the Williamson method. Compound **B** can be prepared only one way by the Williamson method and conveniently by classical acid catalysis.

a) What are the structures of **A** and **B**? Explain the how the spectra distinguish them.

b) Show how you would best prepare the mixed ether **C** that is related to **A** and **B**.

Spectrum A: ([larger version](#))

Spectrum B: ([larger version](#))



4. Design three independent syntheses of 2,3-dimethyl-3-pentanol using three different disconnections. Your sources of carbon contained in the product are limited to methanol, ethylene and propene. All other reagents are available to you. What can you say about the optical rotation of 2,3-dimethyl-3-pentanol in each of your syntheses?

5. Toprol (**4**; Lopressor; Metoprolol) is a β -blocker for the treatment of hypertension. It is racemic drug sold as its monosuccinate salt. A seasoned chemist wants to prepare Toprol as its (*R*)-enantiomer using the synthesis of the racemate. She follows the steps shown on the right.

a) Why is Toprol a racemate?

b) Draw a structure of the (\pm)-succinate salt.

c) What is the role of aq. NaOH?
[Check here.](#)

d) What is the structure and CIP designation for **3**?

e) What does the sequence of reactions and their chirality tell you about the mechanism of the double S_N2 reaction sequence? e) Write mechanisms for the two reactions.

f) How can she prepare (*S*)-**4** without resorting to the use of (*R*)-**1**?

