

Chem 220 - Organic Chemistry

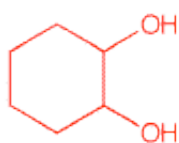
Solution Set - Problem Set 9

Chapters 10 and 11, Alcohols

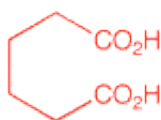
Due: Monday, November 29, 2010

The alcohol module in [ORGO](#) will give you a good review of some of the fundamental reactions discussed in class and in Chapters 10 and 11. As you master the chemistry of alcohols, you should try the [Web of Reactions](#).

1. How many grams of KMnO_4 in aqueous KOH are required to oxidize 20 grams of 1,2-cyclohexanediol to adipic acid? [Note: MnO_2 is the reduction product of permanganate. This is a redox reaction from Gen. Chem. [Go here for help](#). Derive the balanced equation and show your work.].



cyclohexane-1,2-diol
 $\text{C}_6\text{H}_{12}\text{O}_2$



adipic acid
 $\text{C}_6\text{H}_{10}\text{O}_4$

First,



then add two oxygens on the right by using two hydroxyls and one water for each oxygen added on the left.



Now,



requires two oxygens on the left and two hydrogens on the right.
First, the oxygens:



Victor Grignard

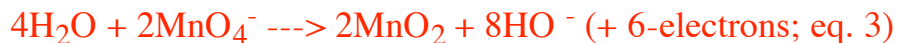
Now the hydrogens:



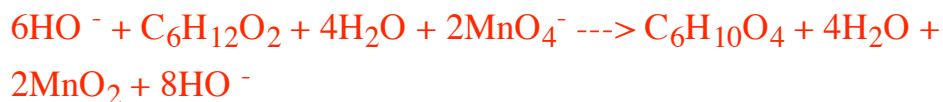
This equation simplifies to



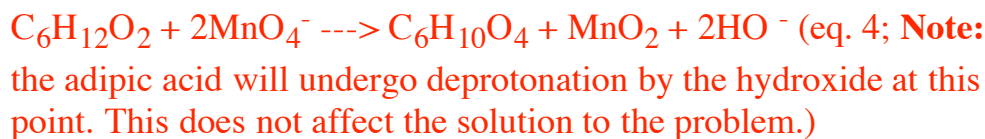
Multiplying eq. 1 by a factor of two to balance the electrons gained and lost, we have



Adding eqs. 2 and 3, we have



Simplifying yields



$$\text{KMnO}_4 \text{ MW.} = 154; \text{C}_6\text{H}_{12}\text{O}_2 \text{ MW} = 116$$

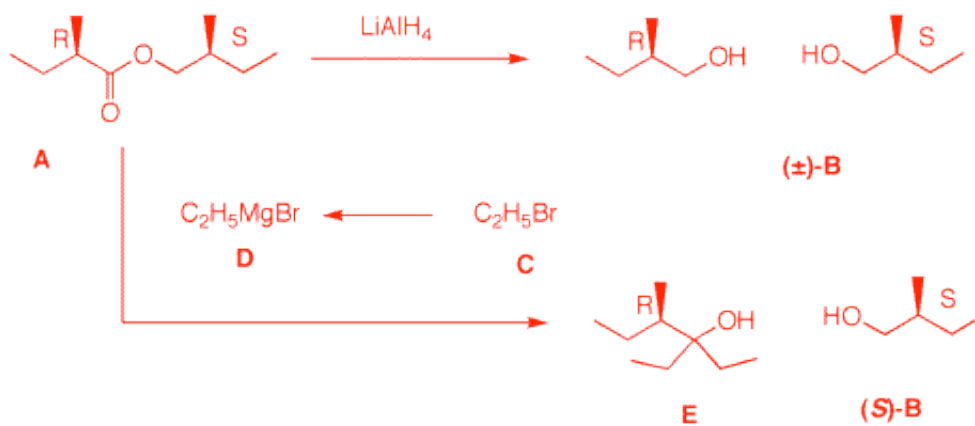
$$\text{Thus, } 2 \times 154/116 = x/20; x = 54.5 \text{ g KMnO}_4$$

2. Optically-active compound **A** ($\text{C}_{10}\text{H}_{20}\text{O}_2$) reacts with LiAlH_4 in ether to form a single optically-inactive compound **B** ($\text{C}_5\text{H}_{12}\text{O}$). Bromide **C** is converted into its Grignard reagent **D**. Reagent **D** reacts with **A** to form optically-active **E** ($\text{C}_9\text{H}_{20}\text{O}$) and (*S*)-**B**. What are the structures **A-E**? Explain and illustrate. *1 DU. A is C₁₀, 1 DU, two oxygens, reacts with LiAlH₄ and a Grignard reagent and forms a single C₅ compound after reduction. What is A but an ester whose carboxylic acid and alcohol portions are both C₅ units. The two fragments of A must be branched to allow for optical activity. The racemic alcohol B must be primary because of the LiAlH₄ reduction. There is only one possibility for a primary alcohol that is C₅ and chiral. At this point the gross structure of A is known. The lack of optical activity in B is due to the presence of a racemate. So the two asymmetric carbons must have opposite handedness. Esters undergo double Grignard*

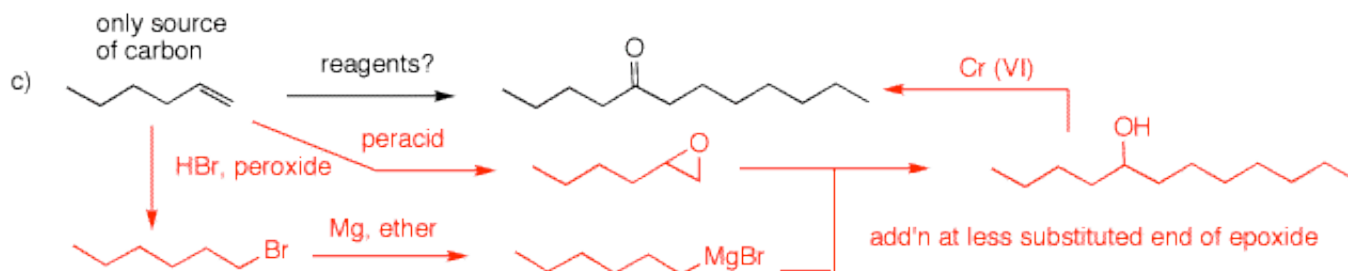
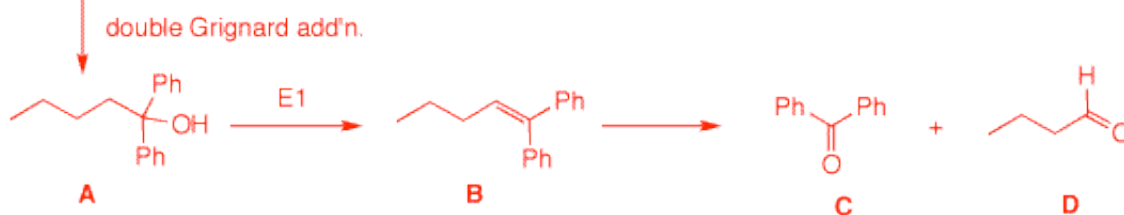
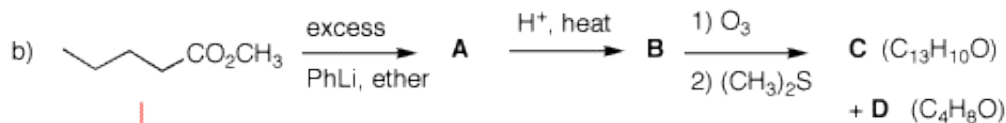
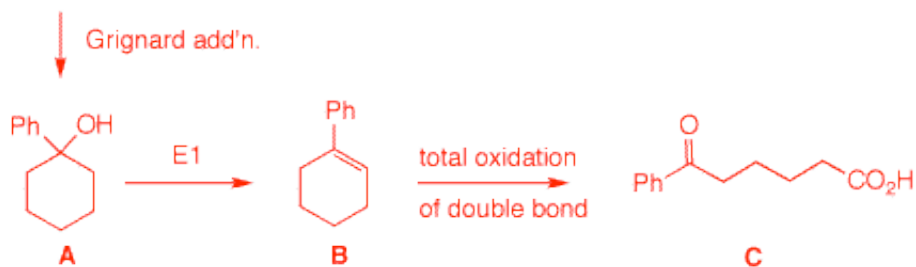
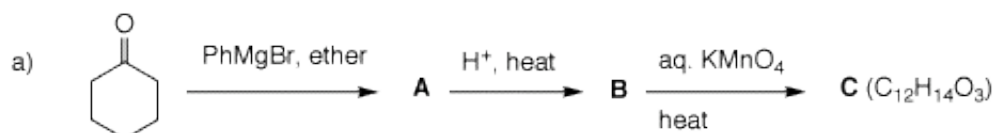
VICTOR CRIGLIANO
(1871-1935)

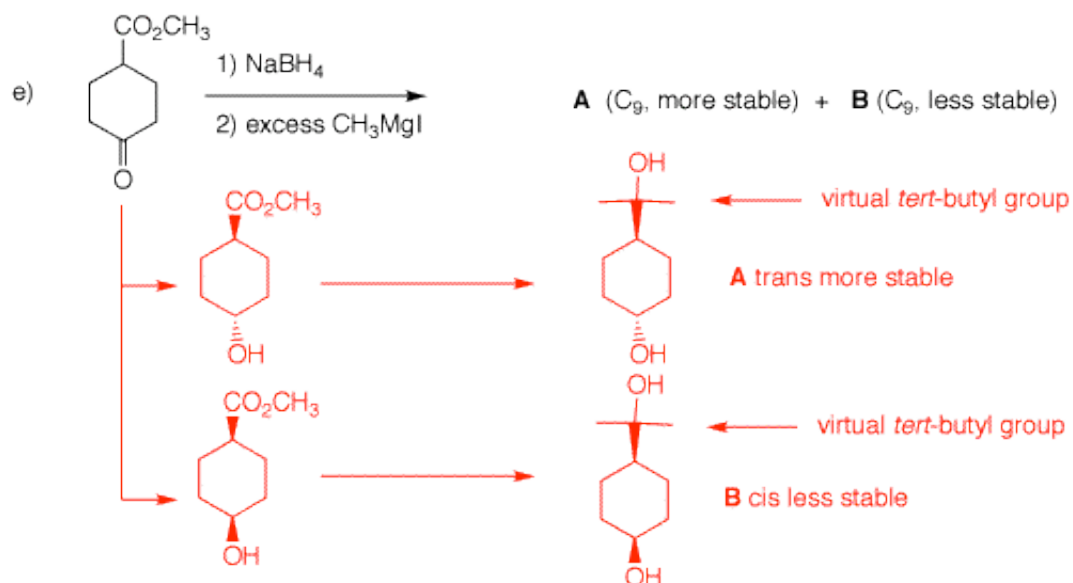
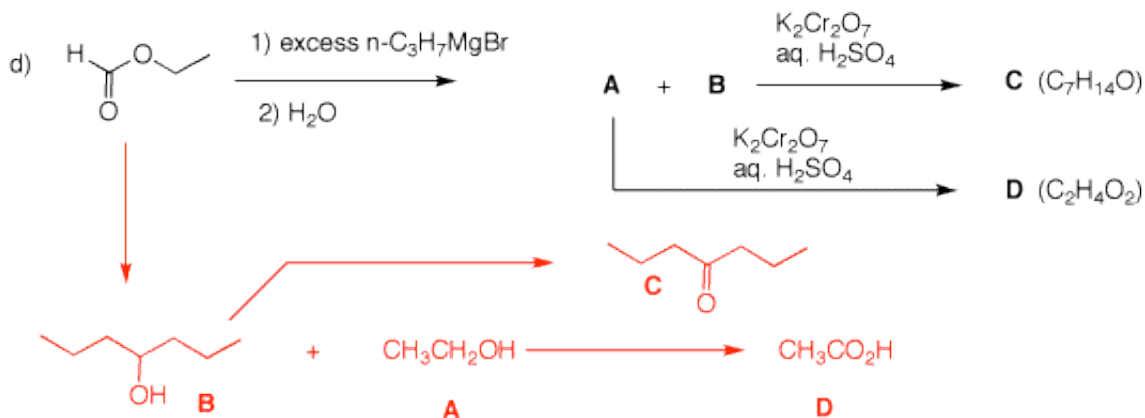
[Co-Nobel Prize in
Chemistry \(1912\)](#)

addition. Since **E** is C_9 (0 DU), the Grignard reagent **D** is ethyl magnesium bromide and **C** is ethyl bromide [$C_5 + (2 \times C_2) = C_9$]. The production of (*S*)-**B** in the Grignard addition means that the alcohol portion of ester **A** is (*S*) and the carboxylic acid portion is (*R*).



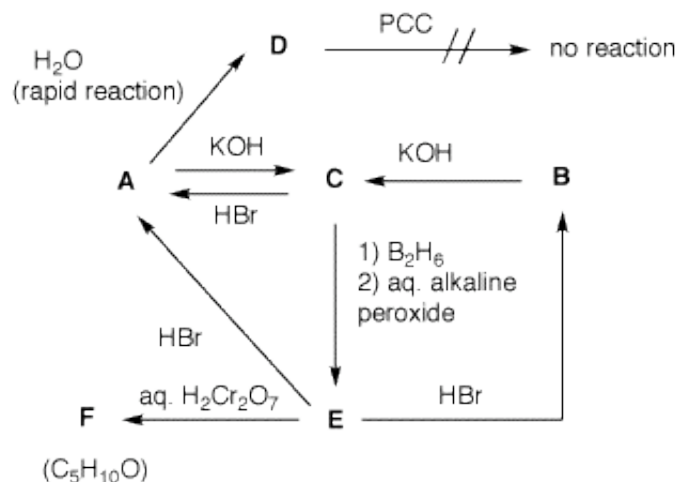
3. Predict the products and/or reagents in each of the following examples. Justify your answers.





4. Two bottles on a shelf have had their labels fall off. Both of the labels read " $\text{C}_5\text{H}_{11}\text{Br}$ ". A student decides to run some reactions on the contents of bottle **A** and **B** to determine the structures of the two compounds. From the flow chart determine the structure of **A** and **B** and identify **C-F**. Show your reasoning. **Hint:** Draw all of

SHOW your reasoning. [Hint: Draw all of the structures of $C_5H_{11}Br$. Eliminate non-contenders? Only the major product in the formation of **C** should be considered.] **A** has no DU. It reacts rapidly with water (S_N1). **A** is a tertiary bromide. One possibility: 2-bromo-2-methylbutane. **B** is 2-methyl-2-butanol. Tertiary alcohols are not oxidized by PCC. KOH causes E2 elimination of **A** to form **C**, 2-methyl-2-butene. Hydroboration of **C** gives anti-Markovnikov addition of water to the alkene. **E** is 3-methyl-2-butanol. Chromic acid oxidation of **E**, a secondary alcohol, provides **F**, 3-methyl-2-butanone. HBr treatment of secondary alcohol **E** afford hydride migration product **A** in addition to direct substitution product **B**. KOH E2 elimination of **B** gives **C**.

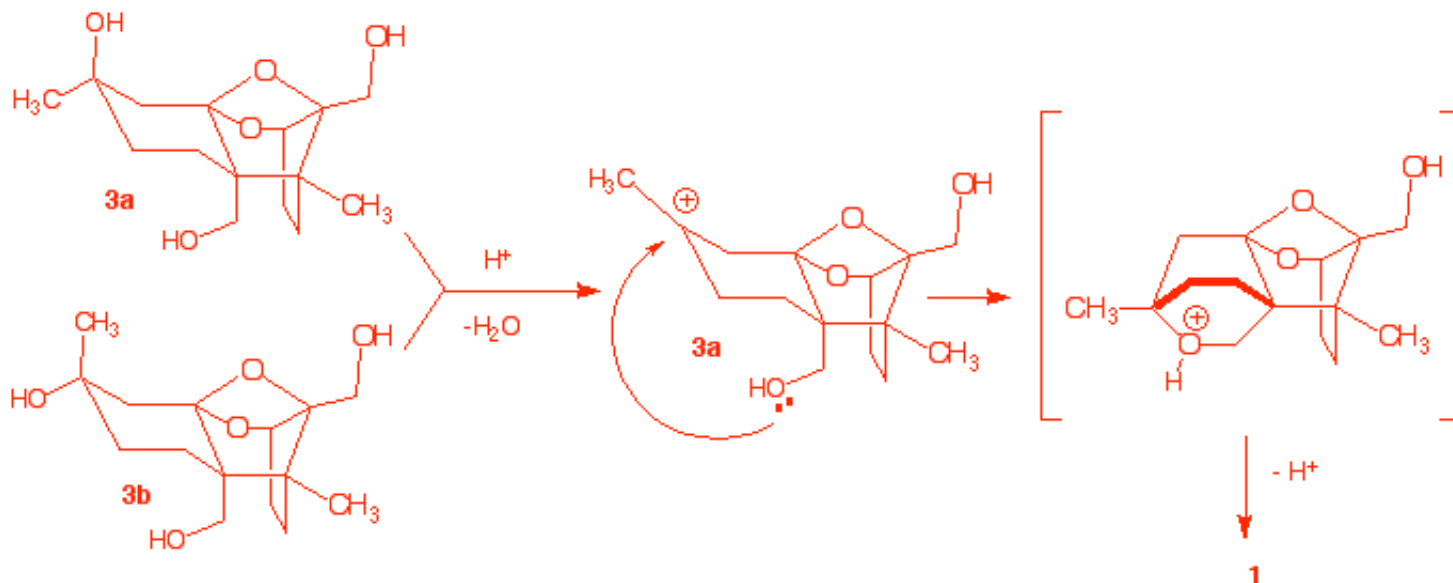


5. Neosporol (**1**), which is shown in two views, was successfully synthesized from racemic ketone **2**, whose synthesis is well beyond the scope of this question. The immediate problem was to convert ketodiols **2** into triol **3**. [The factoids have been altered slightly to facilitate the question. ([J. Am. Chem. Soc., 1993, 115, 2581](#))] When an excess of methyllithium was used to convert the ketone function of **2** into the tertiary alcohol of **3**, only ketodiols **2** was recovered upon aqueous workup. A Jmol structure of neosporol is provided. Move the structure around to compare it with the two views of neosporol **1**.

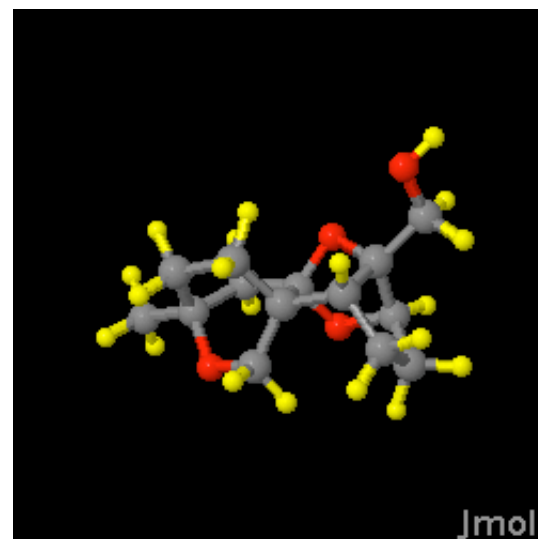
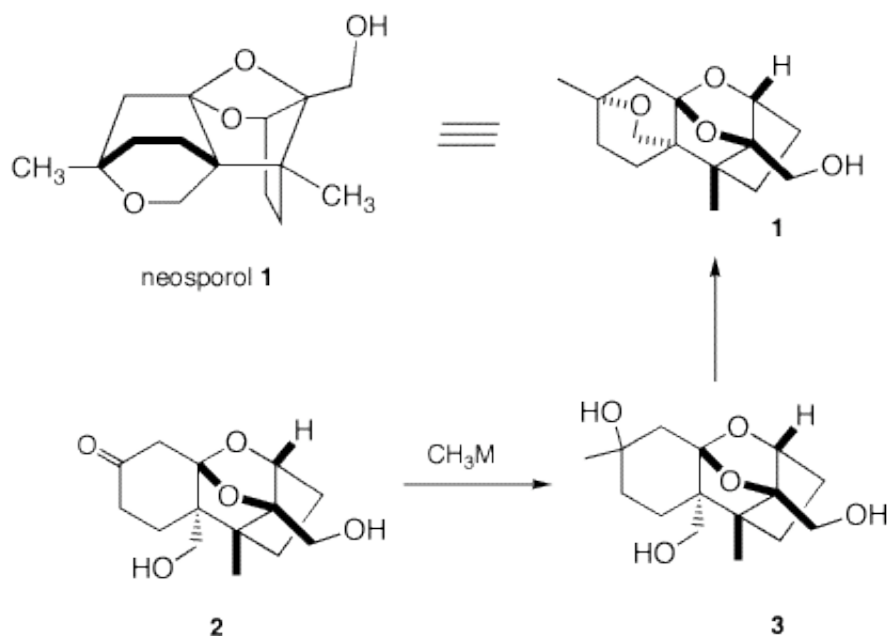
- a) What is the minimum amount of methyllithium required in this reaction? Explain? *Methyllithium reacts with each of the alcohols and the ketone. Three equivalents of methyllithium.*
- b) What events occurred prior to aqueous work up? [Hint: Generally, organolithium and Grignard reagents undergo addition but they are also the conjugate bases of weak acids.] What was the fate of the ketone group? *Rather than undergoing addition to the ketone, the methyllithium acted as a base, abstracting a hydrogen atom adjacent to the ketone forming a ketone enolate. The enolate is stable until it is protonated in the aqueous workup.*

When methyl magnesium bromide was employed, both **2** and a mixture of the diastereomers of **3** were obtained. Complete conversion of **2** to **3** (5/1 mixture of diastereomeric tertiary alcohols) was effected cleanly with the cerium reagent, CH_3CeCl_2 .

- c) Draw the structures of the two diastereomers of **3**, i.e., provide stereochemistry in structure **3**. *See **3a** and **3b** below from addition of the organometallic reagent to either face of the ketone.*



d) Provide conditions and a mechanism for the conversion of **3** to **1**. Is it necessary to separate the diastereomers of **3** prior to forming **1**? *See above. A proton can protonate any of the oxygen atoms of **3a** and **3b**. The only productive event is protonation of the tertiary alcohol, which leads to a tertiary carbocation. The carbocation is captured by an intramolecular $\text{S}_{\text{N}}1$ reaction followed by loss of a proton to form **1**. No separation of **3a** and **3b** is required.*



Neosporol

[\(How to manipulate Jmol structures\)](#)

[\(Larger Version\)](#)