

Chem 220 - Organic Chemistry

Problem Set 9, Solution Set

Chapters 9 and 10, Alcohols

Due: Monday, November 16, 2009

The alcohol module in [ORGO](#) will give you a good review of some of the fundamental reactions discussed in class and in Chapters 8 and 9. As you master the chemistry of alcohols, you should try the [Web of Reactions](#).



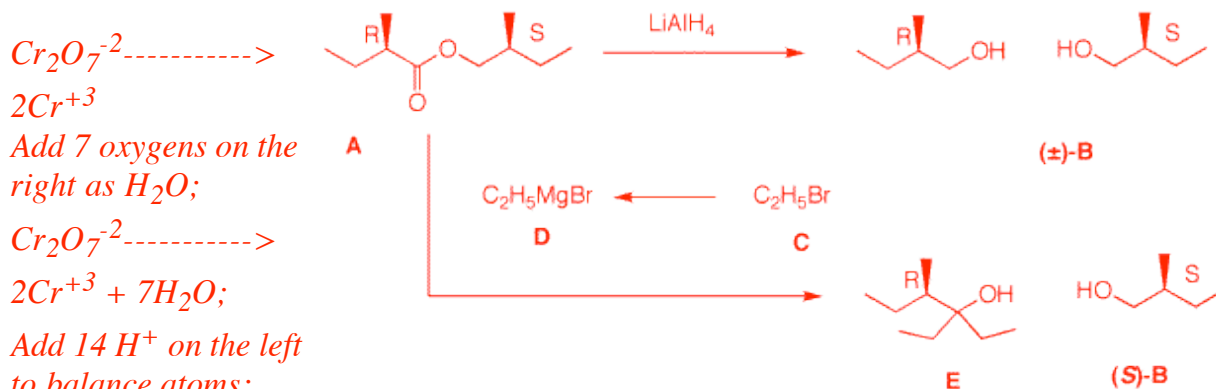
Victor Grignard (1871-1935)

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

1. How many grams of $K_2Cr_2O_7$ in aqueous H_2SO_4 are required to oxidize 30 grams of cyclopentanol to cyclopentanone? [This is a redox reaction from Gen. Chem. Derive the balanced equation and show your work.] this is a reduction-oxidation (redox) reaction. *The alcohol is oxidized; chromium (IV) is reduced to Cr (III). Both electrons and atoms must be balanced.*
a) balance atoms for chromium:

2. Optically-active compound **A** ($C_{10}H_{20}O_2$) reacts with $LiAlH_4$ in ether to form a single optically-inactive compound **B** ($C_5H_{12}O$). Bromide **C** is converted into its Grignard reagent **D**. Reagent **D** reacts with **A** to form optically-active **E** ($C_9H_{20}O$) and (*S*)-**B**. What are the structures **A-E**? Explain and illustrate.

*1 DU. A is C_{10} , 1DU, two oxygens, reacts with $LiAlH_4$ and a Grignard reagent and forms a single C_5 compound after reduction. What is A but an ester whose carboxylic acid and alcohol portions are both C_5 units. The two fragments of A must be branched to allow for optical activity. 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 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*).*



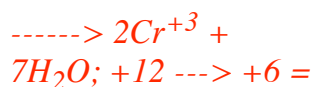
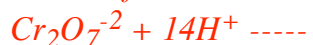
b) Balance atoms for cyclopentanol:



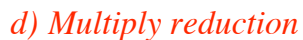
Add 2 H^+ on the right:



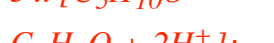
c) Determine the net electron change for each half reaction:

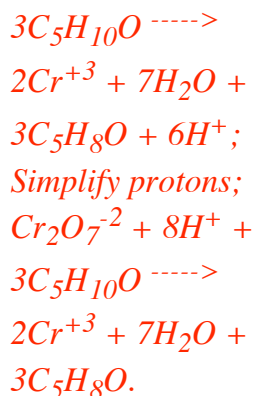


d) Multiply reduction reaction by 3 to balance electron change..



Add half reactions together:





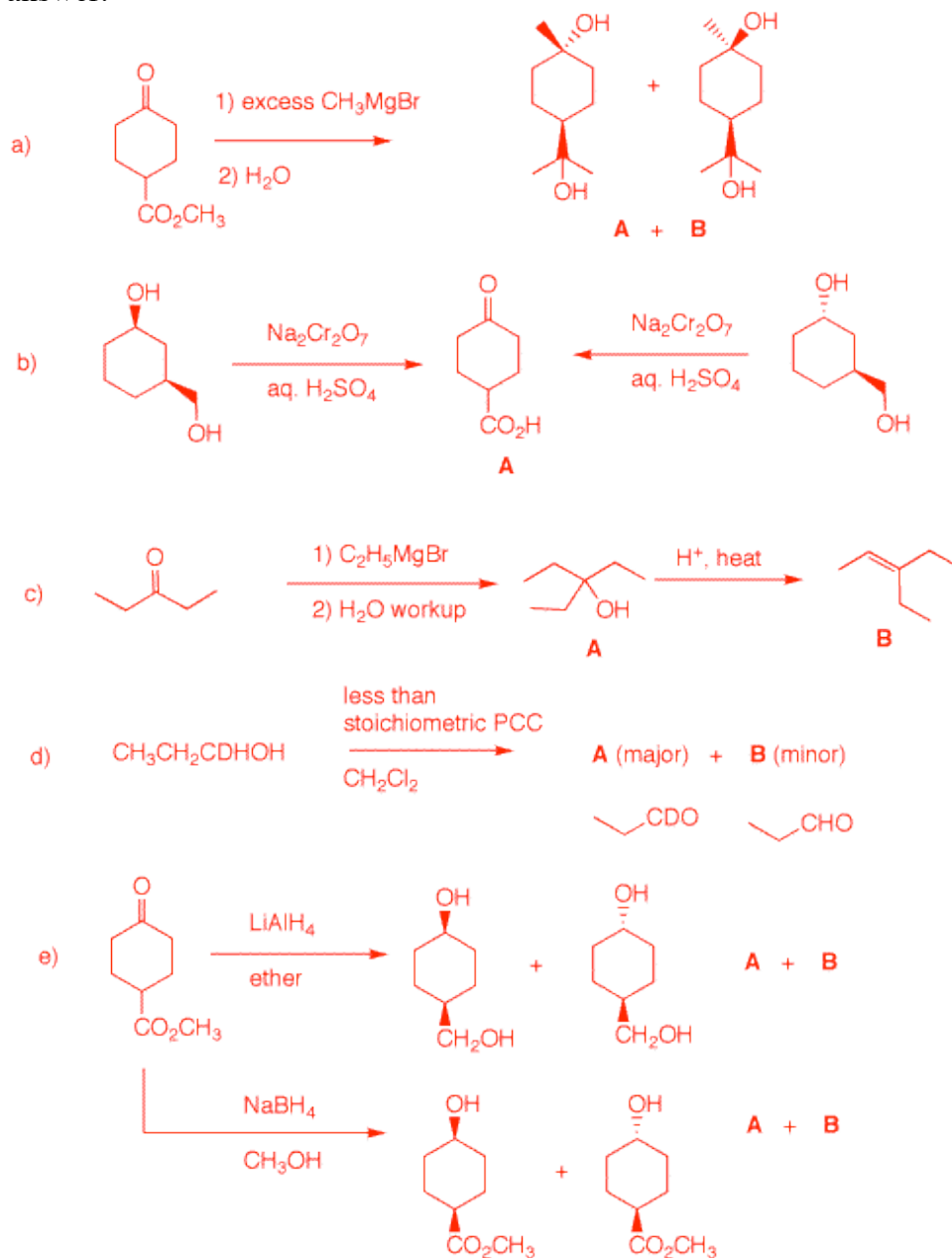
The reaction is balanced in atoms and electrons. Three moles of cyclopentanol are oxidized by one mole of $K_2Cr_2O_7$.

MW cyclopentanol = 86; $30/86 = 0.349$ moles;
 MW $K_2Cr_2O_7 = 294$;
 $294 \times (0.349/3) = 34$ gm.

3a) CH_3MgBr adds twice to the ester and once to the ketone. A stereochemical issue arises because addition to the ketone can be cis- or trans- to the group already in the 4-position. **A** and **B** are indistinguishable.

3b) The cis-diol and the trans-diol give the same product

3. Predict the products in each of the following examples. Justify your answer.



upon aqueous chromium oxidation. The secondary alcohol affords a ketone while the primary alcohol gives an aldehyde, which hydrates, and the hydrate is converted to the carboxylic acid A. For help see Alcohols #2 in ORGO [here](#).

3c) The Grignard reagent adds to 3-pentanone to give 3-ethyl-3-pentanol. Acid-catalyzed dehydration can give but a single alkene B, 3-ethyl-2-pentene.

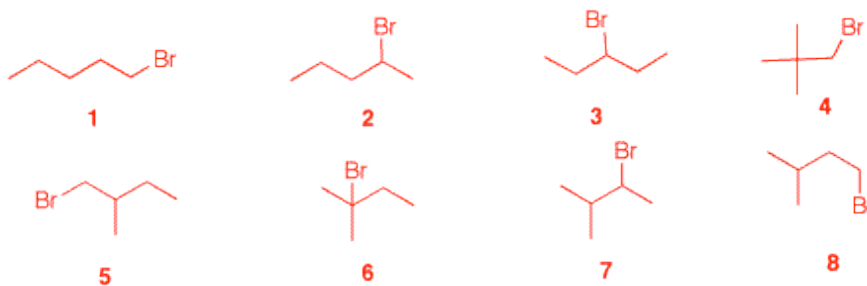
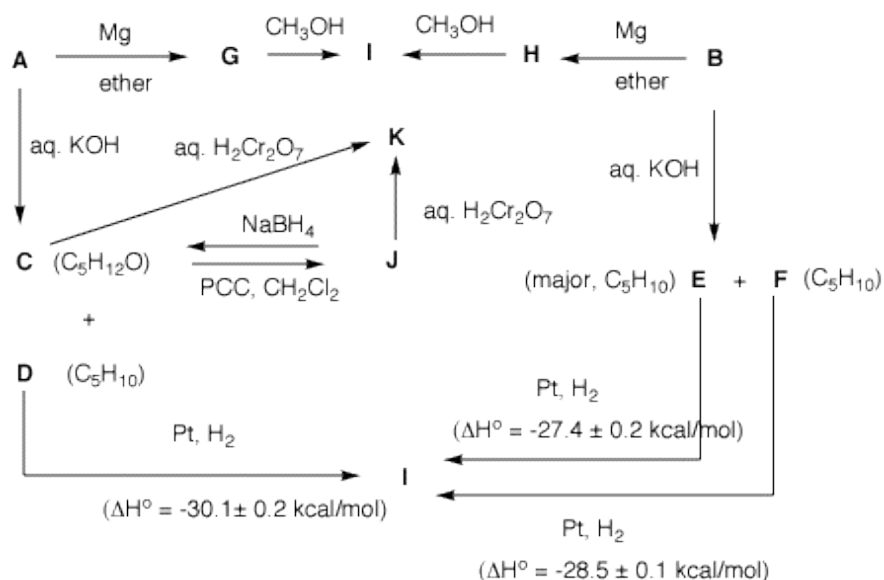
3d) The rate limiting step is removal of the H or D. It is harder to break C-D bonds than C-H bonds. With a limited amount of oxidant, the deuterium-containing aldehyde A will dominate.

3e) As in 3a stereochemical issues arise. The LiAlH_4 reduction

*converts both the ester and the ketone to alcohols. The reduction with NaBH_4 reduces only the ketone. **A** and **B** are indistinguishable*

4. Two bottles on a shelf have had their labels fall on the desktop. 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. She also has access, as do you, to [heats of formation](#).

From the flow chart determine the structure of **A** and **B** and identify **C-I**. [Note: The mixture **C** and **D** is derived from **A**.] Show your reasoning. [Hint: Draw all of the structures of $\text{C}_5\text{H}_{11}\text{Br}$. What does **I** tell you about **A** and **B**?]



*There are 8 possible bromides with the formula, $\text{C}_5\text{H}_{11}\text{Br}$ (on the right). The reactions **A** \rightarrow **G** \rightarrow **I** and **B** \rightarrow **H** \rightarrow **I** tell you that **A** and **B** have the same carbon atom connectivity. Since there is only bromide arising*

from the carbon connectivity of 4, 4 is out of contention. **I** is a saturated alkane. The heat liberated in **D** --> **I** says that **D** is a terminal alkene formed along with alcohol **C** in the base treatment of **A**. There are only two options for **D**: 1-pentene and 3-methyl-1-butene. Oxidation of **C** under aqueous chromic acid conditions gives **K**, which is different from **J**, which is produced from **C** with PCC. Therefore, **K** is a carboxylic acid and **J** is an aldehyde (convertible to **K**). Consequently, **C** is a primary alcohol and **A** is a primary bromide (1, 5 or 8). Bromide **B** gives only alkenes (**E** and **F**) upon base treatment. **B** must be (no alcohol formed) a secondary or tertiary bromide (2, 3, 6 or 7). The difference (~1 kcal/mol) suggests 1,2-disubstituted cis, trans isomers. This info suggests a normal chain. Since there is no terminal alkene formed during the elimination of **B** --> **E** and **F**, 2 is eliminated. **B** is 3-bromopentane (3), **E** is (E)-2-pentene (less heat liberated), **F** is (Z)-2-pentene. Moreover, **A** is

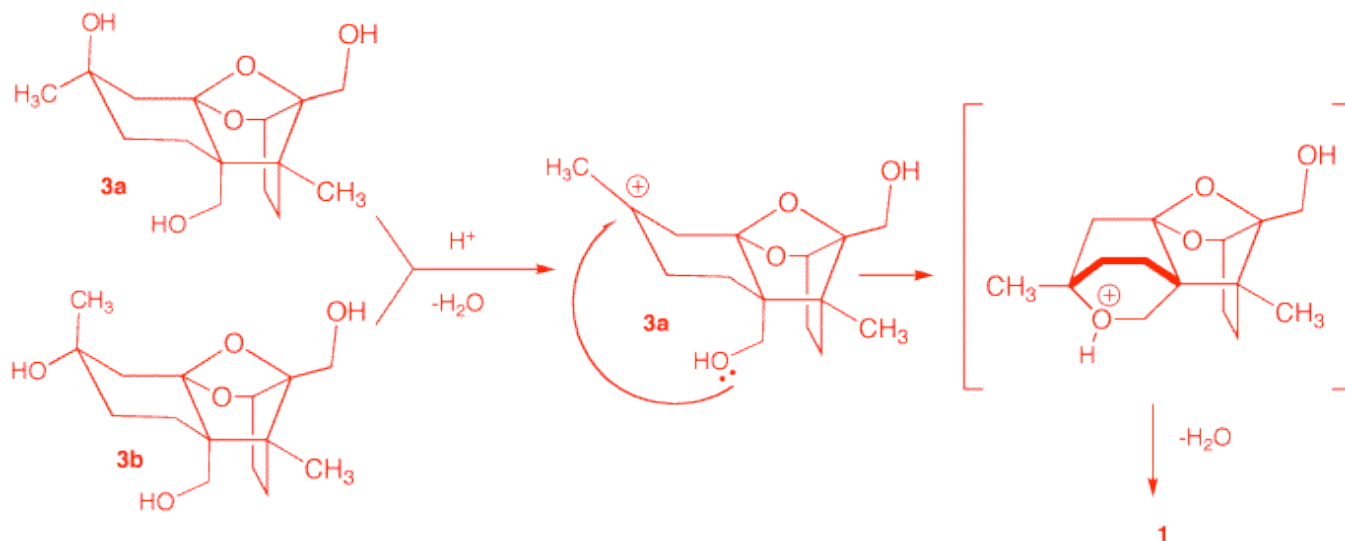
1-bromopentane, C is 1-pentanol, D is 1-pentene, I is n-pentane, J is pentanal and K is pentanoic acid. No other secondary or tertiary halides would lead to only two alkenes whose difference and absolute value of heat of hydrogenation agrees with the data.

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 ketodiol **2** into triol **3**. [The fact-oid-s 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 ketodiol **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**.

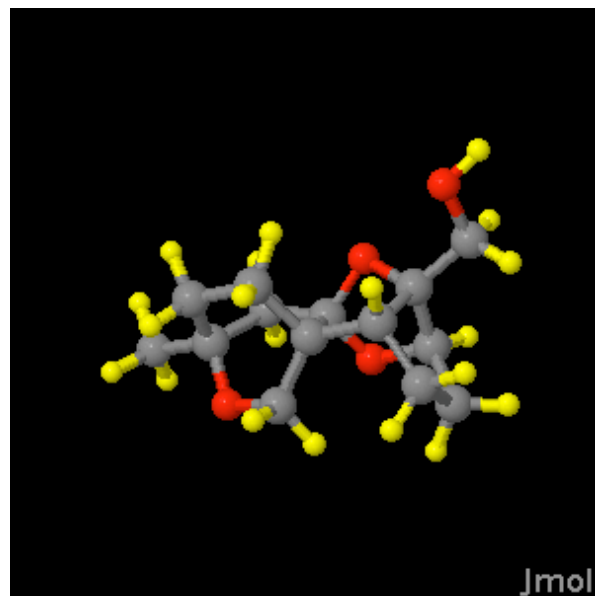
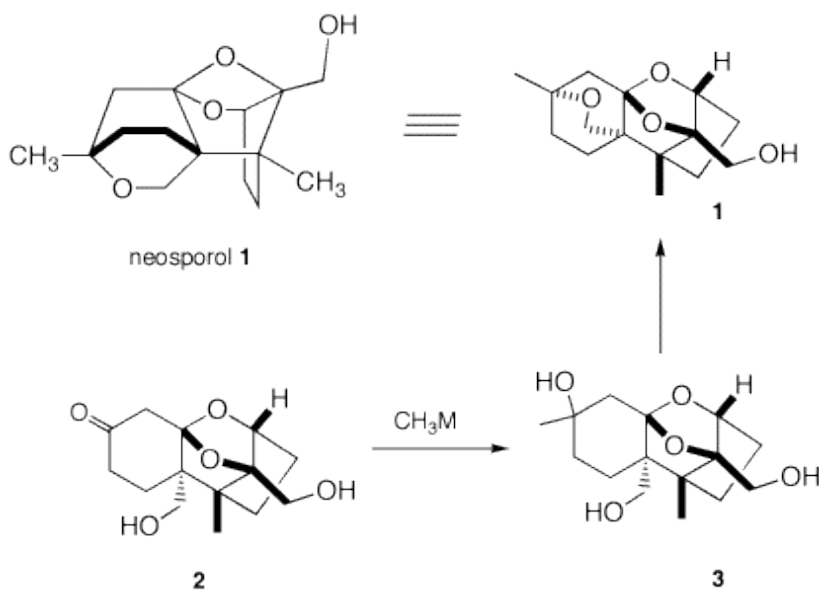
- a) What is the minimum amount of methyllithium required in this reaction? Explain? *Methyllithium reacts with each of the alcohols and the ketone. Three equivalents of methyllithium.*
- b) What events occurred prior to aqueous work up? [Hint: Generally, organolithium and Grignard reagents undergo addition 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 S_N1 reaction followed by loss of a proton to form **1**. No separation of **3a** and **3b** is required.*



Neosporol

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