Chem 220 - Organic Chemistry

Problem Set 9, Solution Set

Chapters 10 and 11, 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.

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-oxidaton (redox) reaction. *The alcohol is oxidized; chromium (IV) is reduced to Cr (III). Both electrons and atoms must be balanced.*

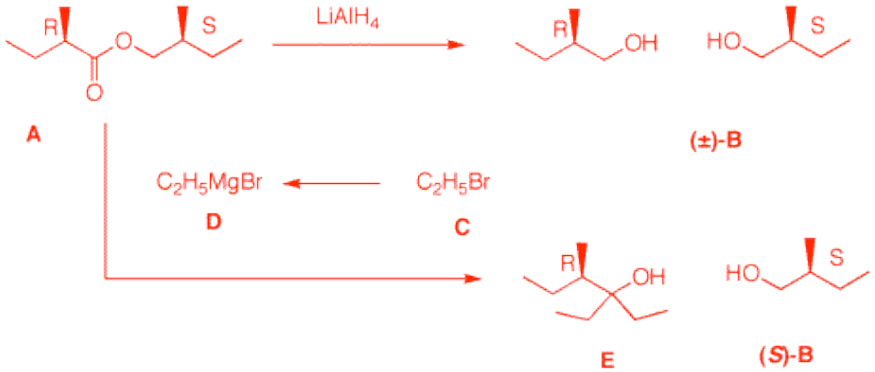
a) balance atoms for chromium:

Victor Grignard (1871-1935)

Co-Nobel Prize in Chemistry (1912)

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).*



$Cr_2O_7^{-2}$-----------> $2Cr^{+3}$

Add 7 oxygens on the right as H_2O;

$Cr_2O_7^{-2}$-----------> $2Cr^{+3} + 7H_2O$;

Add 14 H^+ on the left to balance atoms;

$Cr_2O_7^{-2} + 14H^+$ -----------> $2Cr^{+3} + 7H_2O$.

b) Balance atoms for cyclopentanol:

$C_5H_{10}O$ -------> C_5H_8O;

Add $2H^+$ on the right:

$C_5H_{10}O$ -------> $C_5H_8O + 2H^+$

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

$Cr_2O_7^{-2} + 14H^+$ -----------> $2Cr^{+3} + 7H_2O$; +12 ---> +6 = +6 electrons;

$C_5H_{10}O$ -------> $C_5H_8O + 2H^+$; 0 ---> +2 = -2 electrons.

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

3 x [$C_5H_{10}O$ -------> $C_5H_8O + 2H^+$];

$3C_5H_{10}O$ -------> $3C_5H_8O + 6H^+$;

Add half reactions together:

$Cr_2O_7^{-2} + 14H^+ + 3C_5H_{10}O$ -----> $2Cr^{+3} + 7H_2O$ +

$3C_5H_8O + 6H^+$; Simplify protons; $Cr_2O_7^{-2} + 8H^+ + 3C_5H_{10}O$ -----> $2Cr^{+3} + 7H_2O + 3C_5H_8O$. The reaction is balanced in atoms and electrons. Three moles of cyclopentanol are oxidized by one mole of $K_2Cr_2O_7$.

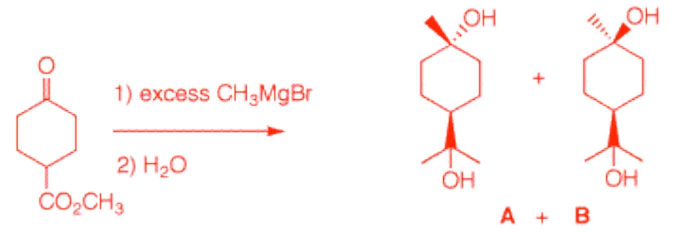
MW cyclopentanol = 86; 30/86 = 0.349 moles;

MW $K_2Cr_2O_7$ = 294; 294 x (0.349/3) = 34 gm.

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

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 upon aqueous chromium oxidation. The a)



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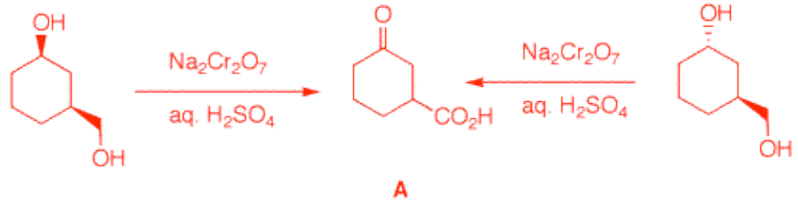
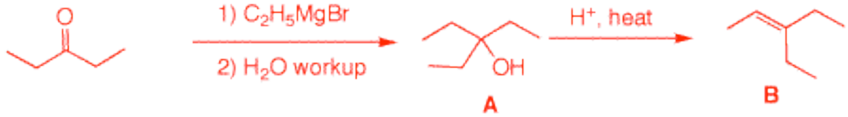
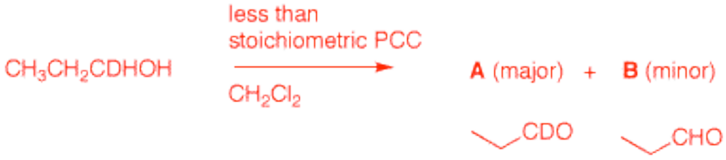


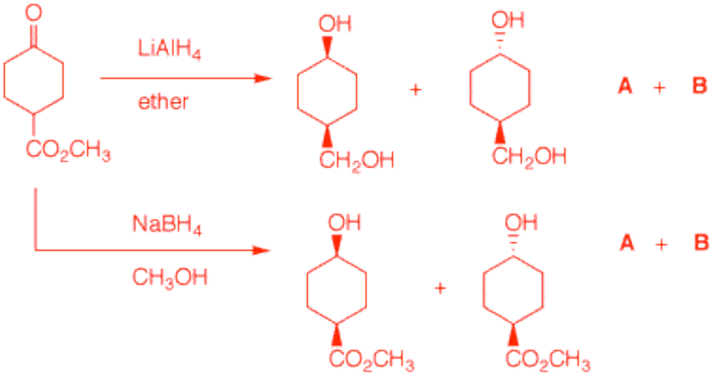
c)



d)



e)



*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.*

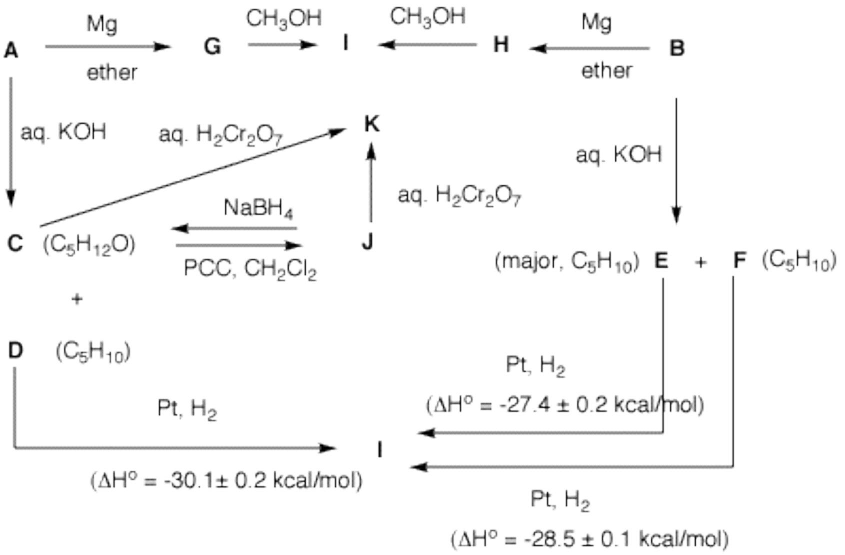
3c) The Grignard reagent adds to 3-pentanone to give 3-ethyl-3-pentanol. Acid-catalyzed dehydration can give but a single alkene B, 3-ethyl-2-pentene.

*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 convers 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 "C$_5$H$_{11}$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 C$_5$H$_{11}$Br. What does **I** tell you about **A** and **B**?]

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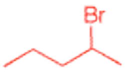
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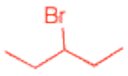
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4


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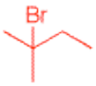
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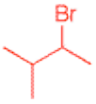
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*There are 8 possible bromides with the formula, C$_5$H$_{11}$Br (on the right). The reactions **A** --> **G** --> **I** and **B** --> **H** --> **I** tell you that **A** and **B** have the same carbon atom connectivity. Since there is only bromide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

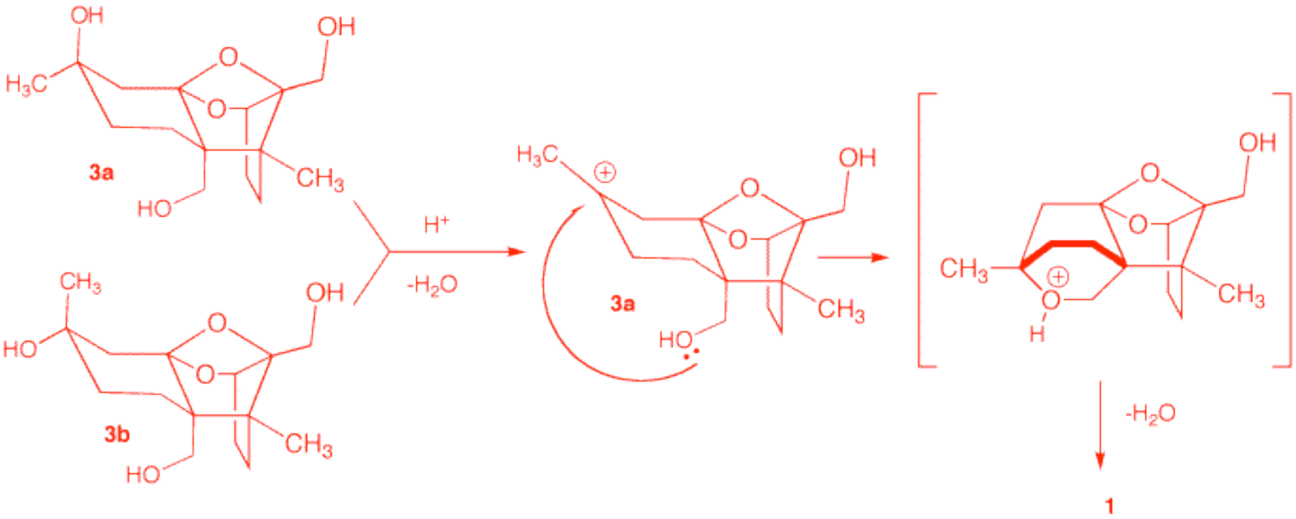
5. Neosporol (**1**), which is shown in two views, was successfully synthesized from racemic ketone **2**, whose synthesis is well beyond the scope of this question. The immediate problem was to convert ketodiol **2** into triol **3**. [The fact-oid-s have been altered slighted to facilitate the question. (*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.*

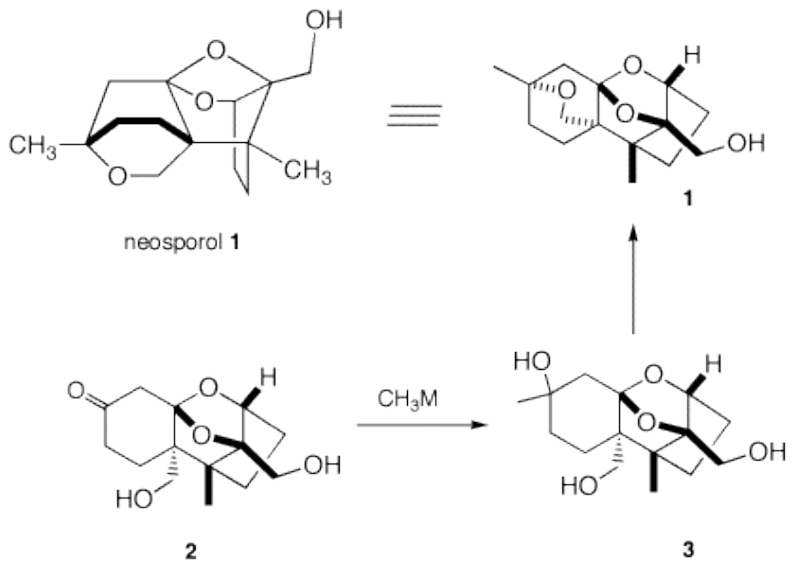
b) What events occurred prior to aqueous work up? [Hint: Generally, organolithium and Grignard reagents undergo addition but they are also the conjugate bases of weak acids.] What was the fate of the ketone group? *Rather than undergoing addition to the ketone, the methyllithium acted as a base, abstracting 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)