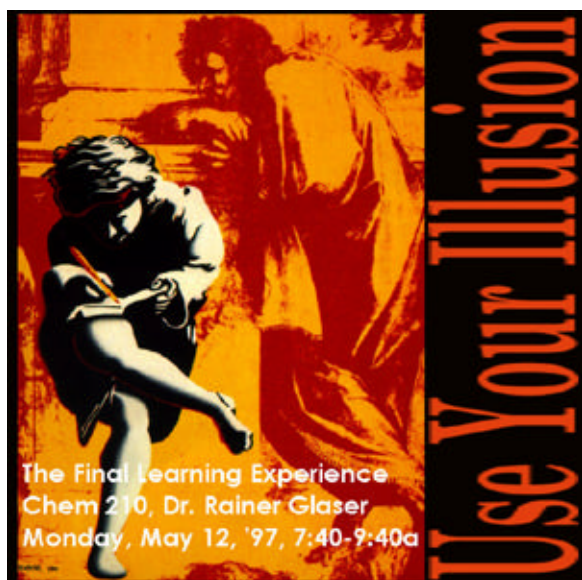


Chemistry 210 — WS '97



The Final Learning Experience

**University of Missouri—Columbia, Prof. Rainer Glaser
Monday, May 12, 1997, Ellis Auditorium, 7:40 - 9:40**

Your Name:

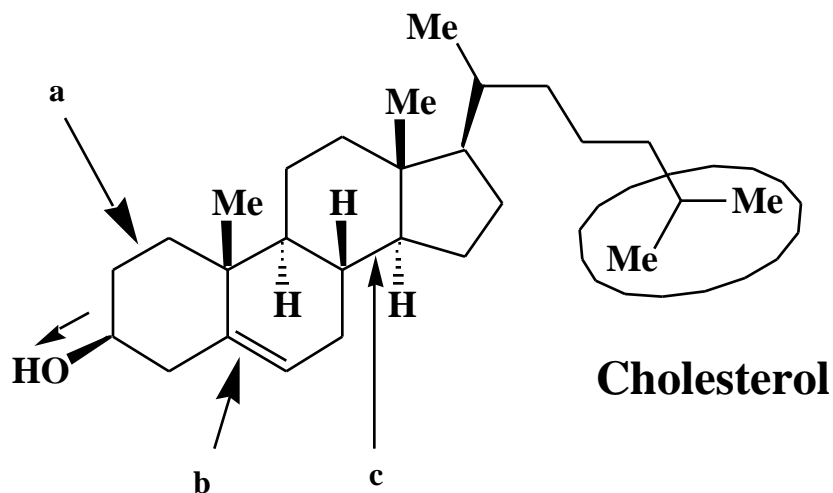
	Max.	Yours
Question 1 (Prop. & Bonding)	32	
Question 2 (Mechanism Concepts)	24	
Question 3 (Alcohols & Ethers)	58	
Question 4 (Epoxides & Diols)	56	
Question 5 (NMR Spectroscopy)	30	
Total	200	



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Question 1. Basic Properties, Bonding and Nomenclature. (32 points)

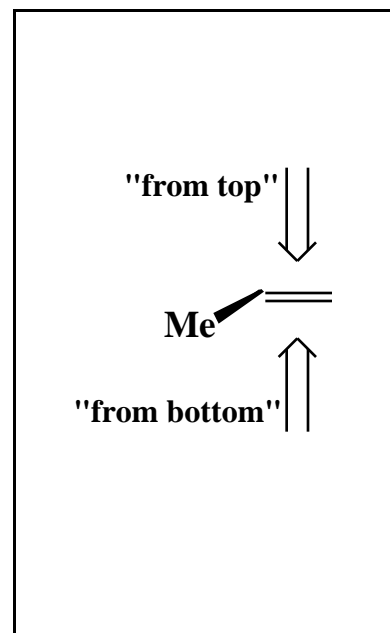


The molecule shown is **cholesterol**. Cholesterol is a soft, waxy substance found among the lipids (fats) in the bloodstream and in all your body's cells. It's an important part of a healthy body because it's used to form cell membranes, some hormones and other needed tissues. But a high level of cholesterol in the blood — hypercholesterolemia — is a major risk factor for heart attack (coronary heart disease).

Chemistry starts with observation and the skills to recognize and to name what has been recognized. So, please exercise your “**skills to observe, recognize & name**”: (a) Cholesterol contains one “iso propyl” group. Find it and circle it. (b) The configuration about the C=C double bond is **Z** (*E*, *Z*) in the Cahn-Ingold-Prelog system. (c) The term “cis” **is not** (is, is not) applicable to this C=C double bond. (d) The “double bond equivalent” (DBE), defined as the sum of rings and unsaturations in a molecule, of cholesterol is **5**. (e) The chirality of the C-atom carrying the alcohol function is **S** (*R*,*S*). (f) The alcohol is **sec.** (primary, secondary, tertiary). (g) Cholesterol **does** (contains, does not contain) a “vinylic hydrogen”. (h) For the C-O bond, indicate the bond dipole moment by drawing (in the above structure) an arrow from the positively charged end to the negatively charged end. (i) Cholesterol is part of the “lipids” since the nonpolar, **lipophilic** (lipophilic, hydrophilic) part of the molecule is much **bigger** (bigger, smaller) than the polar **lipophobic** (lipophobic, hydrophobic) segment of the molecule. (j) The C-C single bond indicated by the arrow “a” is about **1.54** Å long while the C=C bond indicated by the arrow “b” is about **1.34** Å long (1 Å = **100** pm). (k) The H-atoms attached to the bond indicated by the arrow “c” are **trans** (*cis*, *trans*, *gauche*). (l) The C-C single bond is formed by overlap between two **sp³** (sp, sp², sp³) hybrid orbitals.

Question 2. Electrophilic Addition of Bromine to Propene. (24 pts.)

Let's look at the addition of Br_2 to propene. This reaction involves the electrophilic addition of a Br^+ to the $\text{C}=\text{C}$ bond of propene and a bridged **bromonium** ion is formed. This intermediate is then attacked by a bromide ion. The Br^- can attack either at the terminal or at the central C-atom but the attack at the **central** (central, terminal) position will be favored since this carbon carries a **larger** (smaller, larger) positive charge in the intermediate because it is **more** (more, less) substituted. In the end, a 1,2-dibromopropane is formed that contains one $-\text{CH}_2\text{Br}$ group and a $-\text{CHBr}-$ group. Now we note that the central carbon has become chiral as the result of the bromination. The ratio of *R* and *S* centers is, however, exactly unity and the product is **racemic**. To fully realize this stereochemistry, complete the following chart.



<p>Draw the intermediate formed by attack of Br^+ from "the top"</p>	<p>A three-membered ring with a methyl group (Me) on a wedge and a bromine atom (Br^+) on the top vertex.</p>	<p>A three-membered ring with a methyl group (Me) on a wedge and a bromine atom (Br^+) on the bottom vertex.</p>	<p>Draw the intermediate formed by attack of Br^+ from "the bottom"</p>
<p>Draw the product formed by <i>trans</i> addition of Br^-</p>	<p>1,2-dibromopropane with Me on a wedge, H on a dash at C1, and Br on a wedge, H on a dash at C2.</p> <p>R or S: S</p>	<p>1,2-dibromopropane with Br on a wedge, H on a dash at C1, and H on a wedge, Me on a dash at C2.</p> <p>R or S: R</p>	<p>Draw the product formed by <i>trans</i> addition of Br^-</p>

Question 3. Alcohols and Ethers. (58 points)

(a) Show the synthesis of the 1° alcohol $\text{H}_3\text{C}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{OH}$, **1**, from bromopropane using a Grignard reaction. Show the structure of the alkoxide intermediate and indicate how it is worked up. Indicate pertinent bond polarities in the Grignard reagent and the other substrate. (10 points)

draw structure of 1-bromopropane, react with Mg to get PrMgBr
draw PrMgBr and formaldehyde
indicate the bond polarities: Pr negative, MgBr positive; carbonyl-C pos., carbonyl-O neg.
draw the alkoxide
workup with aqueous acid to get **1**.

(b) Now consider the deuterated alcohol **2**, $\text{CH}_3\text{CH}_2\text{CH}_2\text{CHDOH}$, which is optically active and has the R configuration at the chiral C atom. On treatment with thionylchloride, Cl_2SO , **2** gives 1-chlorobutane, **3**. Give perspective drawings of **2** and **3**. What is the configuration of alkylchloride **3**? Show the mechanism of the reaction. (14 p.)



Mechanism: See AK to previous exam! Need to see the inorganic ester and where the HCl is coming from. Need to see the leaving group.

(c) Suggest a synthesis of racemic alcohol $\text{CH}_3\text{CH}_2\text{CH}_2\text{CHDOH}$ from the aldehyde $\text{CH}_3\text{CH}_2\text{CH}_2\text{CHO}$. Be clear about what reagent is used to introduce the deuterium and where the hydroxyl hydrogen comes from. (No need to consider resolution at this point.) (6 points)

1. React with LiAlD_4 in ether. Adds the deuterium anion to the carbonyl-C.
2. Workup the alkoxide with aqueous acid. Adds the proton.

(d) Show how the alcohol (*R*)-**2** can be converted into the ether (*S*)-CH₃CH₂CH₂CHDOCH₃, **4**, and into the ether (*R*)-CH₃CH₂CH₂CHDOCH₃, **5**. One of the ethers is made *via* the Williamson ether synthesis. Be specific about the reagents used to make the alkoxide in that case. Indicate the mechanisms of the reactions (just the type, no details). (12 points)

Synthesis of **4**:

With inversion. Needs S_N2.

Make an ester (carboxylate, sulfonate) from the alcohol (does not change configuration).

Do S_N2 with MeO⁻ and the carboxylate (or other salt) leaves well.

Synthesis of **5**:

This is the WES. Treat the alcohol with base (MeO⁻) and react alkoxide with MeI or MeBr.

(e) Complete the following functional group transformations. (16 points)

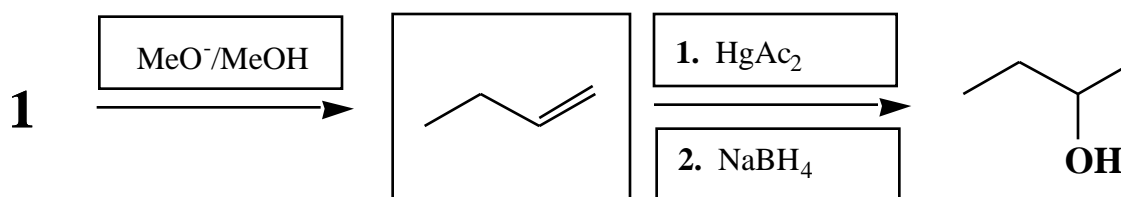
Alcohol **1** is oxidized to the corresponding **aldehyde**: (3 points)

Use PCC. Need to give the structure of PCC or at least the full name.

Alcohol **1** is oxidized to the corresponding **carboxylic acid**: (3 points)

Use any of the Jones reagents.

Alcohol **1** is turned into a secondary alcohol via an **oxymercuration** reaction: (10 points)

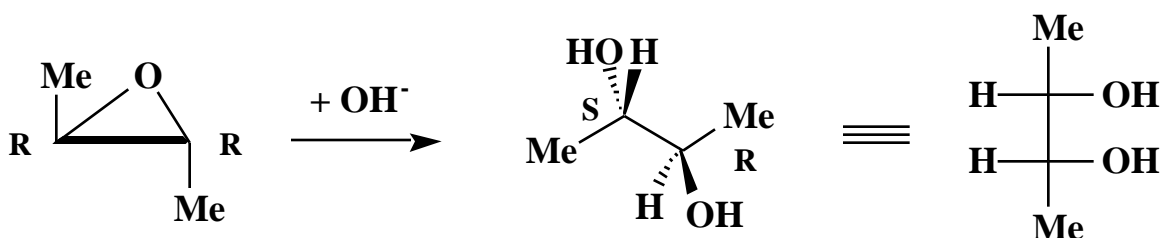


Question 4. Preparations and Reactions of Epoxides (aka oxirane) and Some Related Functional Group Chemistry. (56 points)

(a) (2*R*,3*S*)-3-chloro-2-butanol, **1**, is allowed to react with NaOEt in ethanol to give an optically active oxirane, **2**. Draw the structure of **2**, indicate all chiral carbons and give their configurations with the *R/S* nomenclature. In **2**, the methyl groups are trans (*cis* or *trans*). Use a model set! (10 points)

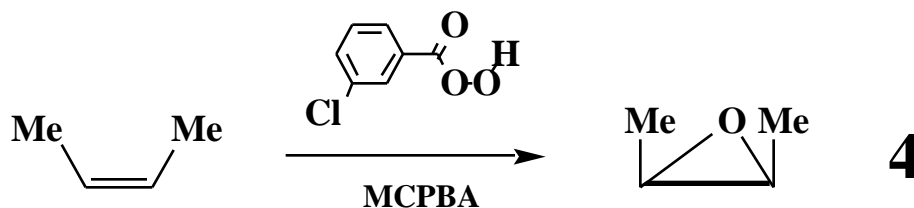


(b) The oxirane **2** is treated with KOH in water to obtain 2,3-butanediol, **3**. Draw the structure of **3** and pay attention to stereochemistry. What can you say about to optical rotation of the product **3**? Remember that the ring opening reaction in alkaline media is an S_N2 (S_N1 , S_N2) process. (10 points)



The product contains two asymmetric centers but it is not chiral; a *meso* form. No optical rotation.

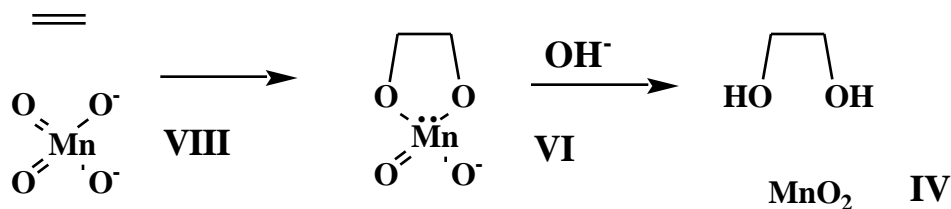
(c) Suggest a synthesis of **4** from an olefine and a peroxyacid. Draw the appropriate geometrical isomer of the olefine. Give the structural formula and the name of a specific peroxyacid. (8 points)



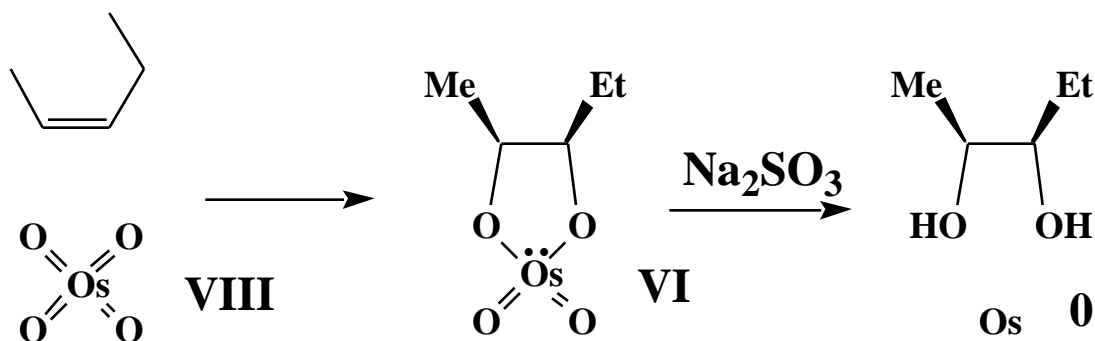
(d) There are several other ways to make 1,2-diols from olefines. One of these methods is called the “**Baeyer Test**” and it involves the oxidation of alkenes with cold, aqueous solutions of potassium permanganate. One of the best modern synthetic methods to obtain diols involves a reaction sequence where **osmiumtetroxide** is used in the first step.

What does the Baeyer Test test for? Explain the principle of the Baeyer Test. (8 points)

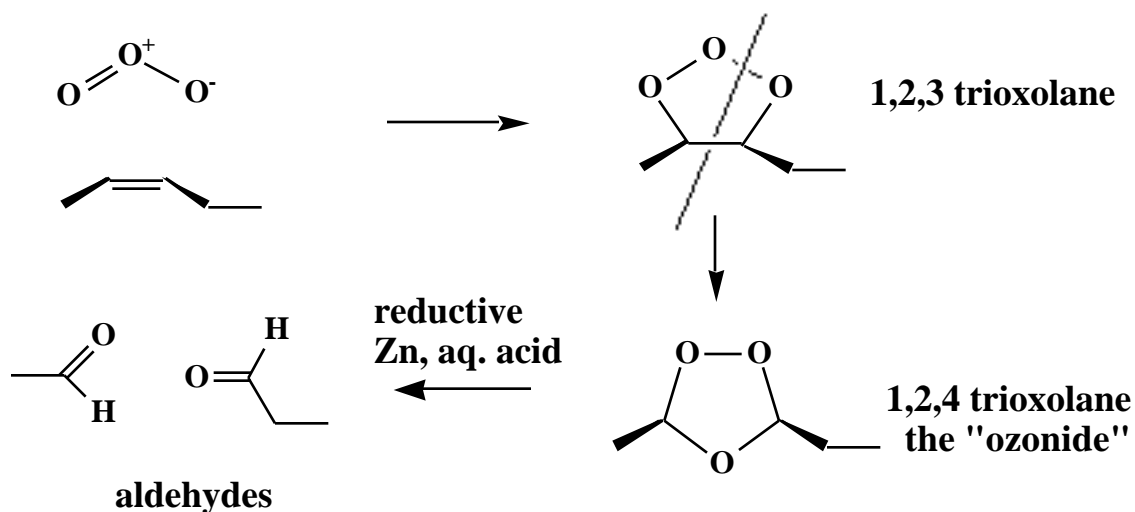
Test for unsaturation: Cold, alkaline, aq. solution of Permanganate. $\text{KMnO}_4 / \text{NaOH}$. Start with purple solution (permanganate) and get a precipitate of “brown stone” (MnO_2).



Show the complete reaction leading to diol formation via OsO_4 oxidation of *cis* pentene-2. (10 points)

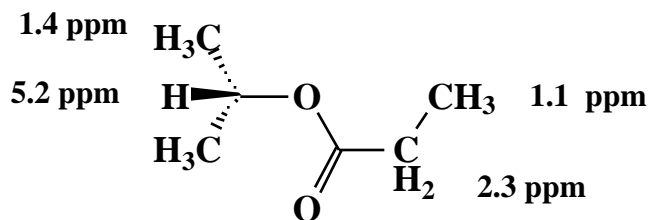


(e) Consider the **ozonolysis** of *cis* pentene-2. Draw the structures of the primary ozonide, of the ozonide, and of the products after reductive workup. Specify the reagent used in the workup. (10 points)



Question 5. Basic ^1H -NMR Spectroscopy.
(30 points)

Consider the NMR spectrum of the ester.



(a) How many **types of protons** are present in the ester and in what **ratio**. (8 points)

4 types: 6 (2 Me in propyl) : 1 (tertiary) : 2 (methylene) : 3 (methyl in ethyl)

(b) Estimate the **chemical shifts** in ppm (reasonable estimates are expected). Write the chemical shifts next to the appropriate H in the above structure. (8 points)

(c) Determine the **splitting pattern** for each signal. Give the multiplicity (singlet, doublet, and so on) and the relative ratios of the lines in each multiplet (e.g. 1:1 for a doublet). (8 points)

Me in Pr: d (1:1); tert. H: septet (1:6:15:20:15:6:1); H in CH_2 : q (1:3:3:1); Me in Et: t (1:2:1).

(d) Now we are ready to draw the spectrum. Do it. Pay attention to chemical shift, multiplicity, and don't forget to reflect the number of absorbing hydrogens correctly in the intensities. Include the signal for the reference material tetramethylsilane (abbreviated TMS). (6 points)



The End

