Problem Set 2

Out: November 5, 1999 Due Back: November 12, 1999

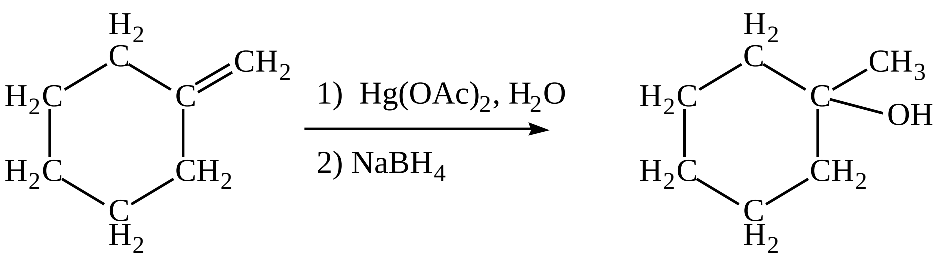
Chemistry 221, 1999

Answers to the following problems should be written, in order and labeled, on 8 1/2 x 11 inch paper. Answers written on the problem set itself will not be graded.
Questions with a bold asterisk **(*)** with them have 3D structures on the web. Check the problem set page for a link.

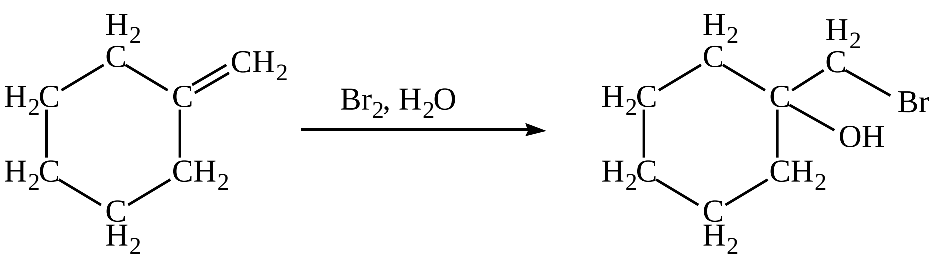
Section A

Predict the product for the following reactions. Provide a structure which shows precise *cis/trans* relationships where appropriate. It is not necessary to show intermediates or mechanisms.

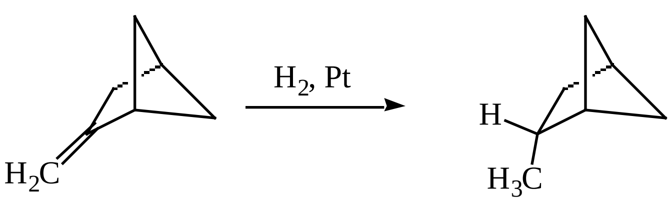
1)



2)

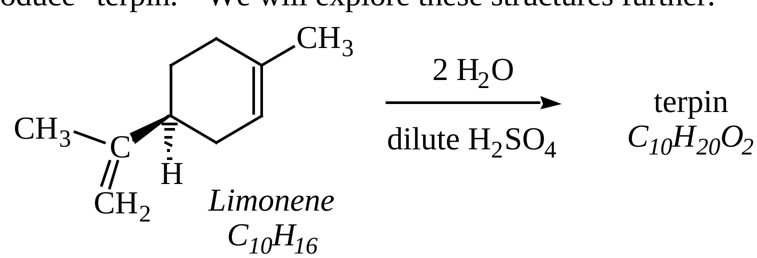


3)*



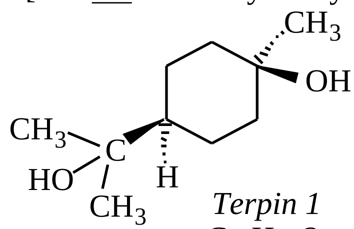
Section B

Sulfuric acid catalyzes a hydration of limonene **(*)** (a fragrance element found in citrus fruits) to produce "terpin." We will explore these structures further.

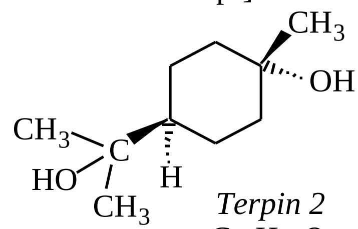


1) Terpin is reported to have only two isomers, one with a melting point of 104° and one with a melting point of 158°. Both isomers would be considered "major" products of

this reaction (there are other minor products). Show the structures for the two isomers of terpin. [It is <u>not</u> necessary to say which isomer has which mp!]



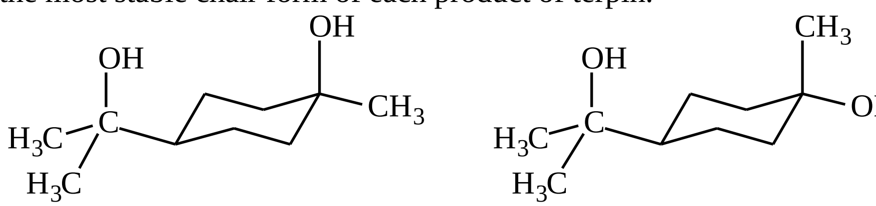
Terpin 1
$C_{10}H_{20}O_2$



Terpin 2
$C_{10}H_{20}O_2$

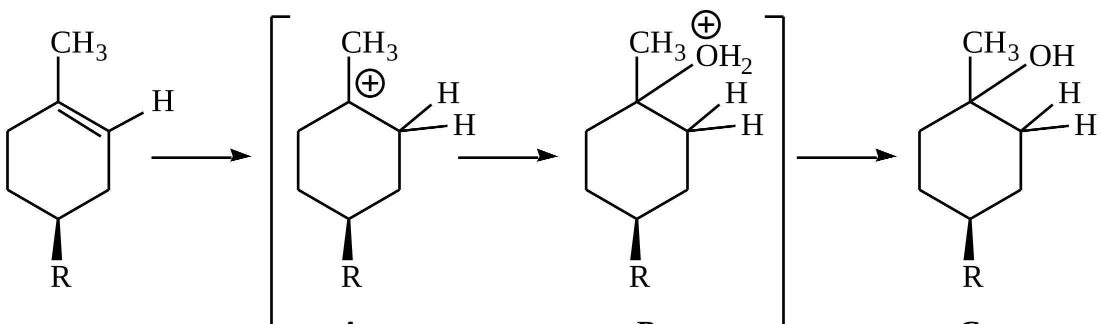
These are the cis and trans isomers of the product. Note that the hydration of the double bond has destroyed the chirality of the molecule, and neither isomer of terpin is optically active, even though limonene is.

2) Draw the most stable chair form of each product of terpin.

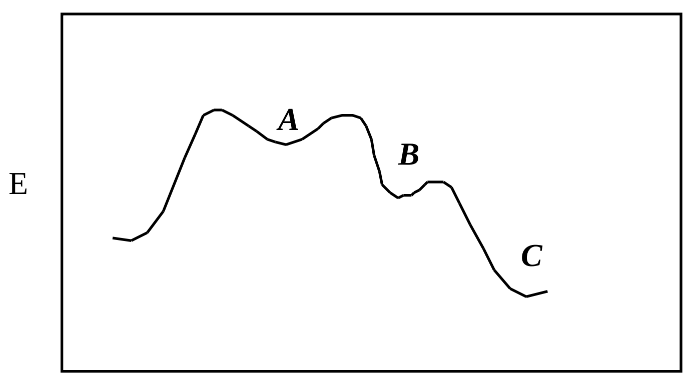


While you don't have a value for the alcohol containing 3-carbon side chain on the left of each molecular drawing above, you should be able to guess that it's pretty bulky--looks a lot like a *t*-butyl group. It will need to be equatorial in the more stable chair form.

3) Show the stepwise mechanism for the hydration of the C=C bond <u>in the ring</u> in limonene.



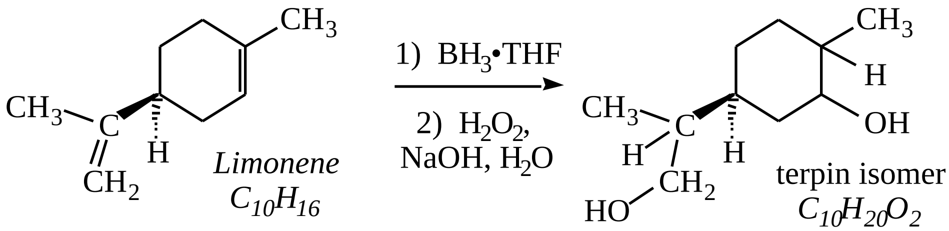
4) Draw the reaction energy diagram for your mechanism.



Reaction Coordinate

The letters refer to intermediates and product from the mechanism above. A stepwise mechanism requires the writing of all intermediates, but not the transition states.

5) The hydroboration/oxidation of limonene shown below gives a several compounds which are constitutional isomers of terpin. Virtually no terpin is formed in this reaction. Draw a structure for the most favored product of this reaction, without specifying the stereochemical relationships.



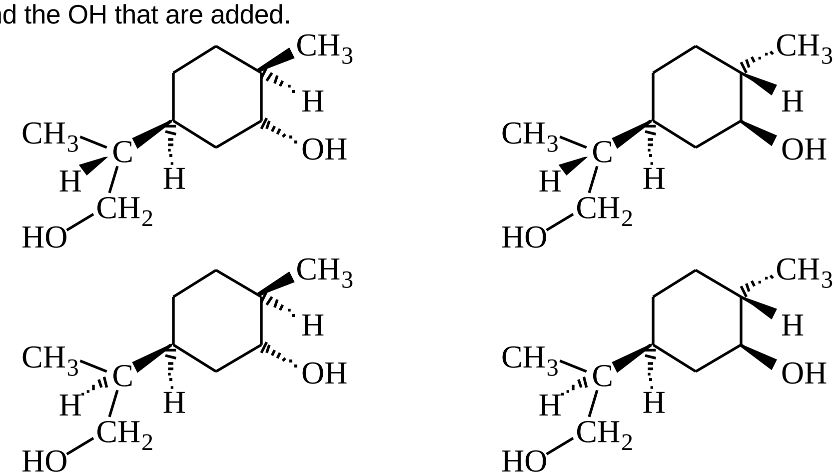
Remember that the hydroboration/oxidation gives the anti-Markovnikov product! There are two clues to that in the question as it's written.

6) How many stereoisomers are possible for the product you drew in the previous question?

There are 4 chiral centers in the molecule, so there should be $2^4 = 16$ possible stereoisomers of the compound.

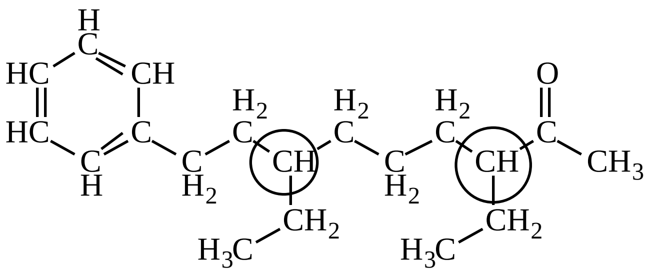
7) Draw all of the stereoisomers that are likely to be formed in this reaction. Remember, each double bond could be attacked from either side.

Note that the underlined section of the question indicates that you don't have to write all of the 16 structures mentioned above. In fact, you only have to draw the 4 that are actually formed in the reaction. Hydroboration/oxidation gives a strict *cis* relationship between the H and the OH that are added.



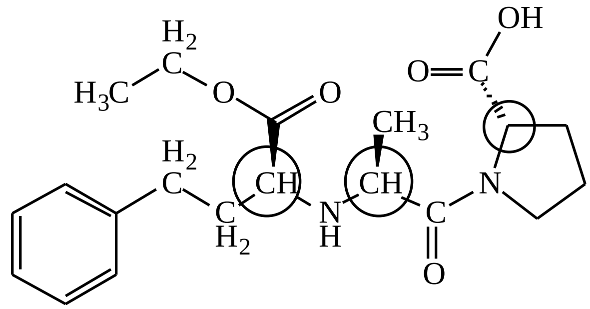
Section C

1)* Redraw each of the compounds shown on the below, circling the chiral centers. How many possible stereoisomers are there (include all possible stereoisomers)? Explain briefly how you chose how many stereoisomers there are.



Dianeackernone[1]

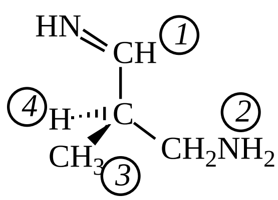
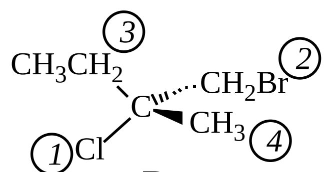
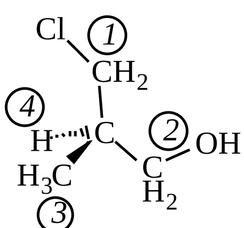
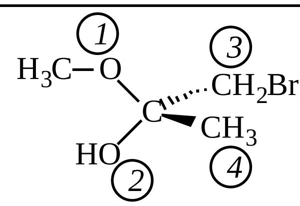
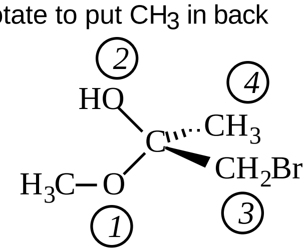
$2^2 = 4$ stereoisomers



Enalapril[2]

$2^3 = 8$ stereoisomers

2)* Redraw each compound shown below, in any orientation you'd like, on your answer page. Determine configuration (R/S) for the following compounds, and show your priority assignments.

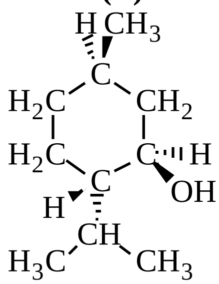
 ***R***	 ***R***
 ***R***	 ***R*** rotate to put CH_3 in back  ***R***

[1] Named for the natural history author Diane Ackerman, this recently discovered compound is secreted by the skins of adult crocodiles. A crocodile pheremone, perhaps? We don't know yet. The authors of the study are making this compound available to those brave souls who study crocodile behavior. *PNAS,* ***96****, 12246 and 12251 (1999).*

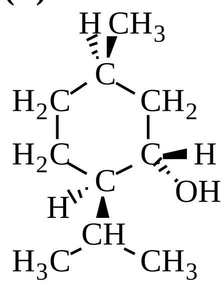
[2] An antihypertensive drug for humans and dogs. It acts as an angiotensin-converting enzyme (ACE) inhibitor by mimicking angiotensin I, but not allowing the cleavage reaction to proceed.

Section D

Show below are menthol **(*)** and an isomer of menthol **(*)**

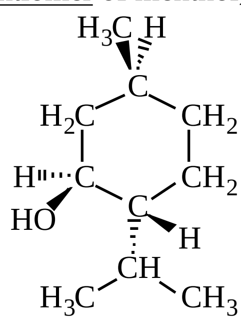


Menthol
BP: 216.5°C
$[\alpha]_D$ = -50°



Isomenthol
BP: 218.5°C

1) Draw the <u>enantiomer</u> of menthol, and give its $[\alpha]_D$ value.



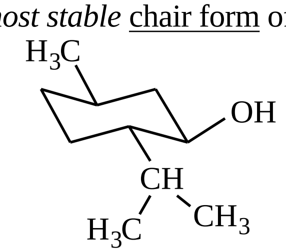
Menthol Enantiomer
BP: 216.5°C
$[\alpha]_D$ = + 50°

2) How many stereoisomers of menthol are possible? Explain briefly.
   There are 3 chiral centers in menthol, so there are 8 possible stereoisomers

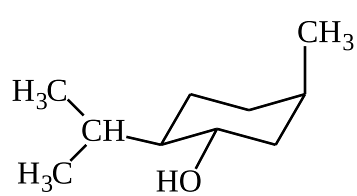
3) What is the isomeric relationship between isomenthol and menthol?
   They are diastereomers.

4) Can you tell the $[\alpha]_D$ value of isomenthol from the information given? Why or why not?
   No. There is no predictable relationship between diastereomers regarding optical activity as there is for enantiomers.

5) Draw the *most stable* <u>chair form</u> of menthol <u>and</u> of isomenthol:



Menthol



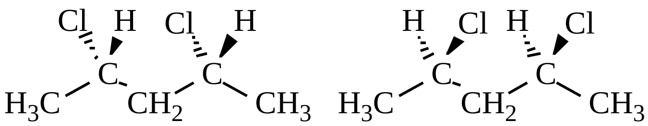
Isomenthol

6) Is menthol more stable than isomenthol? Explain briefly.
   Menthol is more stable because all of the substituents are equatorial. In isomenthol, there is an axial methyl group, leading to a destabilization of about 1.8 Kcal/mole compared to menthol.

Section E

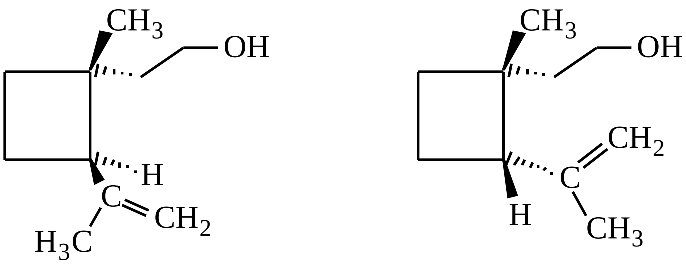
For each pair of compounds, indicate which term best indicates the kind of relationship between the compounds. The choices are: <u>identical,</u> <u>enantiomer,</u> <u>diastereomer,</u> <u>constitutional isomer,</u> <u>not an isomer.</u>

1)*



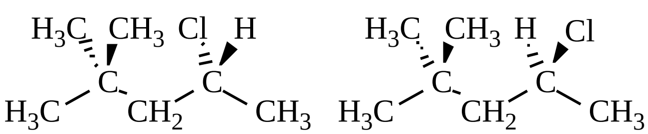
These are identical.

2)[1]



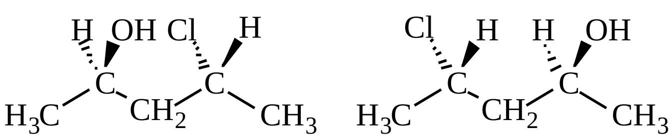
These are diastereomers (cis/trans isomers, in this case).

3)



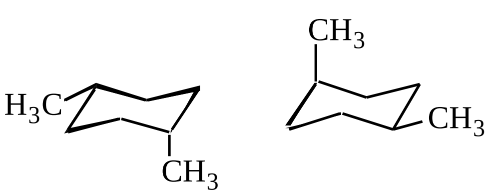
These are enantiomers.

4)



These are enantiomers.

5)



These are identical. Note the plane of symmetry through the methyl groups.

[1]Grandisol: a boll weevil sex attractants.