Names: _____ *Section_____*

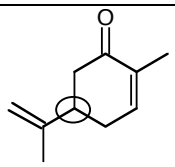
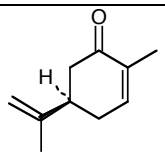
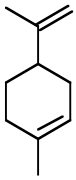
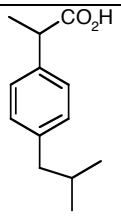
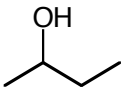
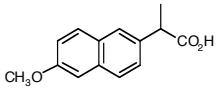
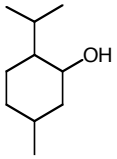
Chem 226/ Fall 2009 *Dr. Rusay*

Optical Rotation: PART 2

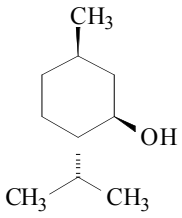
Structure & Configuration; Refer to:

http://chemconnections.org/organic/chem226/Labs/opt-rotation/opt-rot-II.html

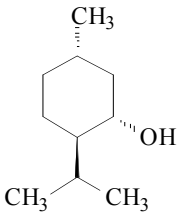
In Part 2, you will examine several chiral molecules using *jmol*. Some molecules are NSAIDs and others are odorants whose olfactory properties have been studied by smell panels. Complete the following table. Carvone is given as an example. Circle all of the chiral atoms in the general structure. Under comments, if it is an NSAID, indicate if the stereochemistry of the Web molecule is the correct absolute configuration of the active drug (ACTIVE) or its enantiomer (NOT ACTIVE). If it is an odorant, list the type of smell, eg. MINT. For smell information refer to the attachment: M. Laska and P. Teubner, *Chemical Senses*, 24, 161-170 (1999) and M. Laska, *Chemical Senses*, 29, 143-152 (2004).

	Name	General Structure	Stereo Structure	Funct-ion(s)	Abs. Config	Rel. Config + or -	Comments
A	l-carvone			ketone; alkene	R-	(-)	MINT
B							
C			Fisher Drawing:				
D			Fisher:				
E			Fisher:				
F							

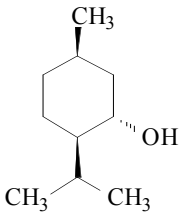
(-)-Menthol is a naturally occurring compound found in peppermint leaves and other plants in the mint family. It is widely used in cough drops, lip balms, nasal inhalers, liqueurs, perfumery, and cigarettes. Since menthol has three stereocenters, there are eight possible stereoisomers in total. Unlabeled samples were found, which contained four of the eight isomers: (-)-menthol, (+)-menthol, (+)-isomenthol, and (+)-neomenthol. Compound F is among the four. The four compounds include a pair of enantiomers and two diastereomers. Circle the chiral carbons in each of the four and provide the absolute configuration (R-) or (S-) for each chiral carbon.



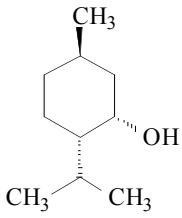
(-)-menthol



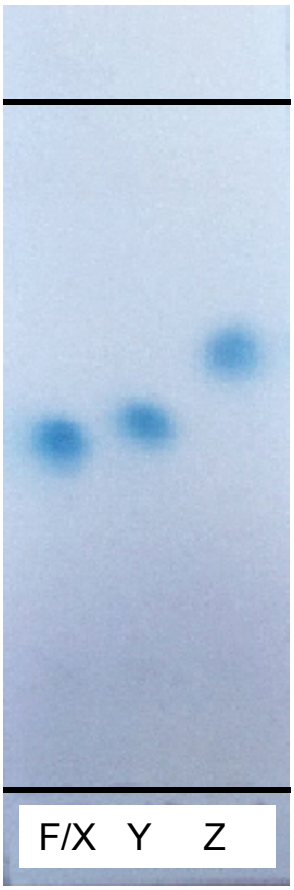
(+)-menthol



(+)-isomenthol



(+)-neomenthol



TLC plate of the four stereoisomers
4:1 hexanes:EtOAc

F /X were spotted on top of each other.
F and X melt at 43-45 °C
Y is a liquid at room temperature
Z melts at 77-83 °C

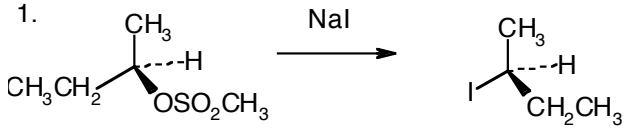
Identify the stereoisomers.
F: _____ X: _____

Y: _____ Z: _____
Briefly explain the reasons for your assignments.

Bonus Question: Briefly describe how menthol relates to the leading cigarette brand "Newport" and the marketing of the brand to teens.

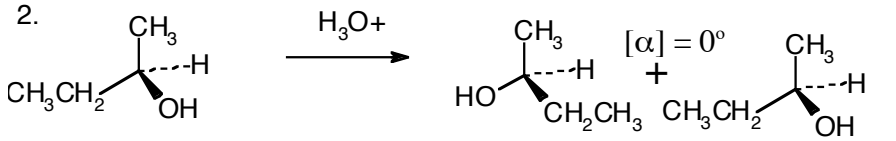
Circle each chiral carbon atom in the reactant and product(s); indicate the absolute configuration (R- or S-) next to each. If additional chiral carbons are introduced in the product(s) circle all of them and indicate R- or S- for each. In ques. #2 and #3 identify the pair as enantiomers or diastereomers. For ques. #1, #2, & #4 consider the stereochemistry of the reactant and compare it to the product(s): does the chiral center of the reactant remain the same (retention), change to the other configuration (inversion) or racemize (i.e., give a 50:50 mixture of both enantomers)?

1.



retention or inversion or racemization

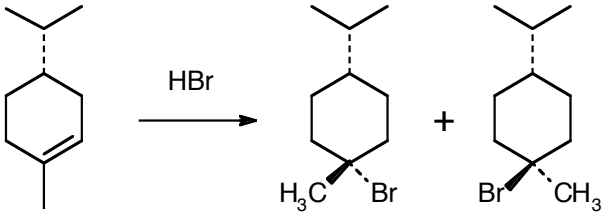
2.



[α] = -13.52°

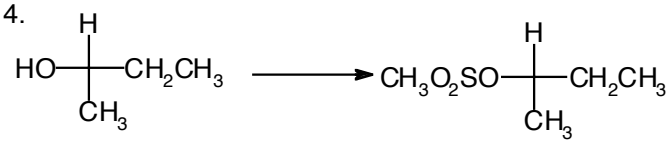
retention or inversion or racemization

3.



retention or inversion or racemization

4.



retention or inversion or racemization

10. *(Refer to the following two references. The complete articles are available on-line.)* Is chiral recognition by smell universal, i.e., is it possible for anyone to distinguish between the enantiomers of any chiral odor molecule? Briefly explain your answer on the basis of the information in the articles.

http://chemse.oxfordjournals.org/cgi/content/full/29/2/143

Chem. Senses 29: 143–152, 2004

Olfactory Discrimination Ability of Human Subjects for Enantiomers with an Isopropenyl Group at the Chiral Center
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Abstract

The ability of 20 human subjects to distinguish between nine enantiomeric odor pairs sharing an isopropenyl group at the chiral center was tested in a forced-choice triangular test procedure. I found (i) that as a group, the subjects were only able to significantly discriminate the optical isomers of limonene, carvone, dihydrocarvone, dihydrocarveol and dihydrocarvyl acetate, whereas they failed to distinguish between the (+)- and (–)-forms of perillaalcohol, perillaaldehyde, isopulegol and limonene oxide; (ii) marked interindividual differences in discrimination performance, ranging from subjects who were able to significantly discriminate between eight of the nine odor pairs to subjects who failed to do so with six of the nine tasks; and (iii) that with none of the nine odor pairs the antipodes were reported to differ significantly in subjective intensity when presented at equal concentrations. Additional tests of the chemesthetic potency and threshold measurements of the optical isomers of dihydrocarvone, dihydrocarveol, and dihydrocarvyl acetate suggest that the discriminability of these three enantiomeric odor pairs is indeed due to differences in odor quality. Analysis of structure–activity relationships suggest that the combined presence of (i) an isopropenyl group at the chiral center; (ii) a methyl group at the para-position; and/or (iii) an oxygen-containing group at the meta-position allows for the discrimination of enantiomeric odor pairs.

Key words: discrimination ability, enantiomers, humans, odor structure–activity relationships, olfaction
http://chemse.oxfordjournals.org/cgi/content/full/24/2/161

Chem. Senses 24: 161–170, 1999

Olfactory Discrimination Ability of Human Subjects for Ten Pairs of Enantiomers
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Abstract

We tested the ability of human subjects to distinguish between enantiomers, i.e. odorants which are identical except for chirality. In a forced-choice triangular test procedure 20 subjects were repeatedly presented with 10 enantiomeric odor pairs and asked to identify the bottle containing the odd stimulus. We found (i) that as a group, the subjects were only able to significantly discriminate the optical isomers of {alpha}-pinene, carvone and limonene, whereas they failed to distinguish between the (+) and (–)-forms of menthol, fenchone, rose oxide, camphor, {alpha}-terpineol, ß-citronellol and 2-butanol; (ii) marked individual differences in discrimination performance, ranging from subjects who were able to significantly discriminate between 6 of the 10 odor pairs to subjects who failed to do so with 9 of the 10 tasks; (iii) that with none of the 10 odor pairs were the antipodes reported to differ significantly in subjective intensity when presented at equal concentrations; and (iv) that error rates were quite stable and did not differ significantly between sessions, and thus, we observed a lack of learning or training effects. Additional tests of the degree of trigeminality and threshold measurements of the optical isomers of {alpha}-pinene, carvone and limonene suggest that the discriminability of these three enantiomeric odor pairs is indeed due to differences in odor quality. These findings support the assumption that enantioselective molecular odor receptors may only exist for some but not all volatile enantiomers and thus that chiral recognition of odorants may not be a general phenomenon but is restricted to some substances.