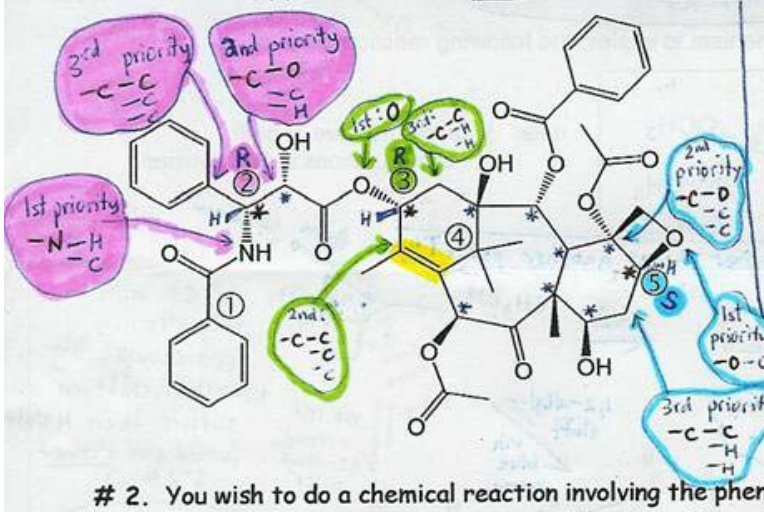
Chem 221 W08 Sect 52 Dr. C. Rogers **NAME:** Rogers (key)

INTRODUCTORY ORGANIC CHEMISTRY I --- PROBLEM SET #2

INSTRUCTIONS: ANSWER ALL QUESTIONS ON THESE PAGES. HAND IN (stapled, with no extra pages please) AT THE BEGINNING OF CLASS on Thursday March 20. LATE SUBMISSIONS WILL NOT BE ACCEPTED (EARLY IS FINE). ALL MATERIAL CAN ALL BE FOUND IN THE CLASS NOTES and/or IN BRUICE CHAPTERS 1-7, 11.

 # 1. The anti-cancer drug Taxol is shown below (recall Problem Set #1). For more about Taxol, and to view this molecule in 3-dimensions, go to: http://www.3dchem.com/molecules.asp?ID=34#
This time, your task involves considering the stereochemical aspects of Taxol.

Your tasks:
(i) Determine if the numbered C atoms are asymmetric (→ 4 different substituents), & if so, label with a *. ~~1~~, 2, 3, ~~4~~, 5
(ii) Label each numbered asymmetric C atom with its R/S configuration. 2 R, 3 R, 5 S
(iii) Determine the E/Z configuration of the alkene unit. E : left sp^2 C vs. right sp^2 C (opposite)
(iv) Label the molecule as chiral or achiral.
(v) Calculate the total # of stereoisomers this molecule could have. Explain briefly.



Max. # stereoisomers = 2^n
where n = # of stereogenic centres
11 asymmetric Cs (C*) R/S
1 alkene unit E/Z
12 total stereogenic centres
∴ $2^n = 2^{12} = 4096$ stereoisomers!
i.e., the 1 shown here + its enantiomer (all C*s inverted) + 4094 others (diastereomers to this one here)

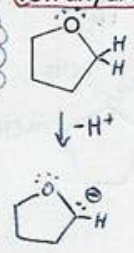
 # 2. You wish to do a chemical reaction involving the phenyl acetylide anion, $C_6H_5{-}C{\equiv}C^{\ominus}$, so you plan to treat phenyl acetylene $C_6H_5{-}C{\equiv}CH$ with sodium amide ($NaNH_2$).

$$C_6H_5{-}C{\equiv}CH + Na^{\oplus}\ {}^{\ominus}{:}NH_2 \longrightarrow C_6H_5C{\equiv}C{:}^{\ominus}Na^{\oplus} + NH_3$$ acid–base rxn

a) Will you need to take precautions to remove traces of water from your solvent before adding your reagents? Why or why not? BASES REACT WITH THE MOST ACIDIC SPECIES PRESENT. ∴ YES. Water has a $pK_a \approx 15.7$, so if there is any water in the solvent, the ${}^{\ominus}{:}NH_2$ will react with the water instead of with the desired reactant $C_6H_5{-}C{\equiv}CH$ ($pK_a \approx 25$? similar to $HC{\equiv}CH$...). We always must be careful to use anhydrous (water-free) solvents when we use strong bases.

b) Which solvent would be better to use, and why? Ethanol (CH_3CH_2OH) or tetrahydrofuran?

	CH_3CH_2OH	THF
pK_a:	16.0	somewhat < 50 (typical sp^3 C-H acidity)
meaning:	easily deprotonated	VERY DIFFICULT TO DEPROTONATE
conclusion:	not suitable as solvent if using a strongly basic reactant	good solvent for use with strong bases (if conj. acid $pK_a \ll 50$!)



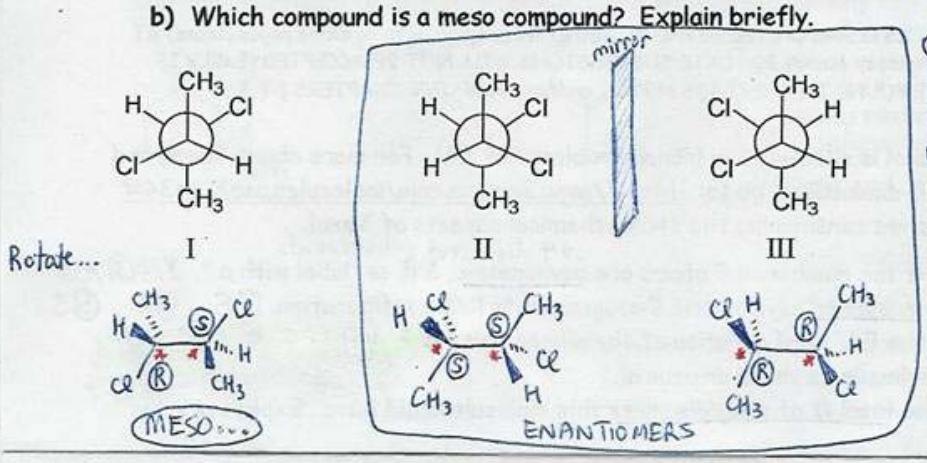
most acidic H is still located on an sp^3 C with NO resonance-stabilization, just slight inductive stabilization.

very reactive!

3. The Newman projections below represent (R,R)- (III), (S,S)- (II) and (R,S)- (I) -2,3-dichlorobutane.

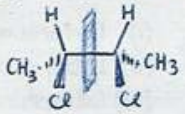
a) Which is which? BUILD MODELS +/- DRAW PERSPECTIVE DRAWINGS TO VISUALIZE!

b) Which compound is a meso compound? Explain briefly.



Compounds II & III are enantiomers (nonsuperimposable mirror images).

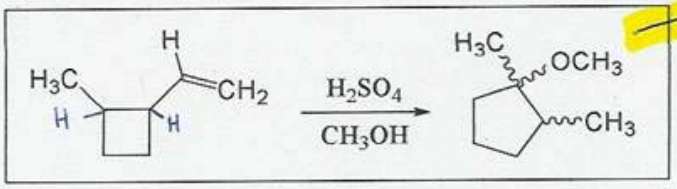
Compound I can be redrawn in a conformation that reveals its INTERNAL MIRROR PLANE:



its 2 asymmetric C's are mirror images...

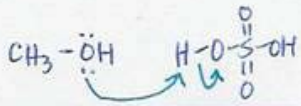
Thus, it is an ACHIRAL, meso compound and would be optically inactive.

 # 4. Write a step-by-step "arrow-pushing" mechanism to explain the following reaction product.

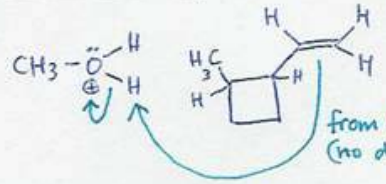


which is not necessarily the only product of this reaction... just the only one we must explain.

note: ≋ means mixture of both configurations at that position

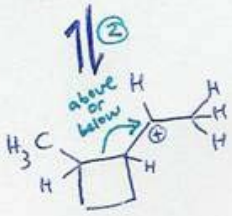


① protonation of solvent



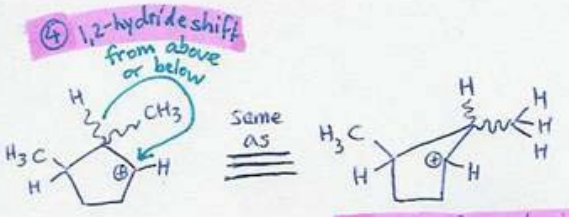
② π-bond attacks acid (either H^+'d solvent, or H_2SO_4 directly)

from above or below (no difference here...)

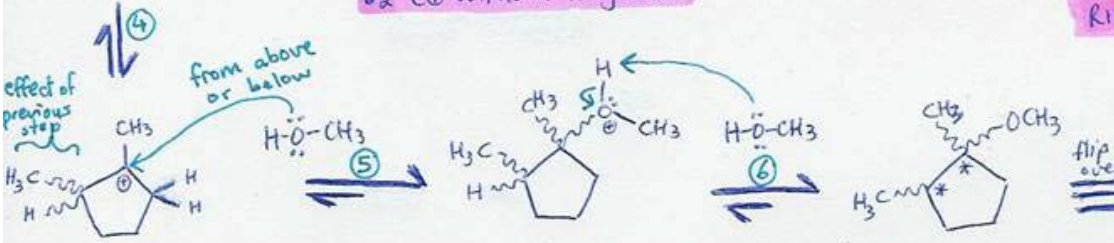


③ 2° C⊕ with ring strain

- rearranges by 1,2-alkyl shift that yields RING EXPANSION

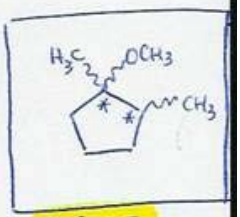


- 2° C⊕ without ring strain



- 3° C⊕
- most stable intermediate... gets attacked by nucleophilic ⑤ solvent CH_3OH

⑥ H^+ transfer to solvent



TARGET PRODUCT.

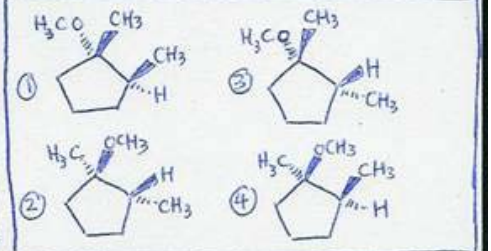
Note: stereochemical outcome

- 2 stereogenic centres (C*'s)

⇒ $2^2 = 4$ possible stereoisomers

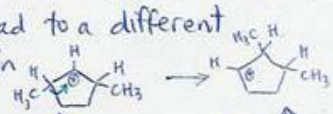
enant. pair: ① CH_3's cis "up" / ② CH_3's cis "down"

enant. pair: ③ CH_3's trans "up" "down" / ④ CH_3's trans "down" "up"

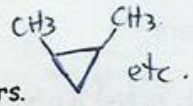


Note: alternative pathway at step ③

- other C–C bond (shown vertical) could have shifted to lead to a different 2° C⊕ without ring strain

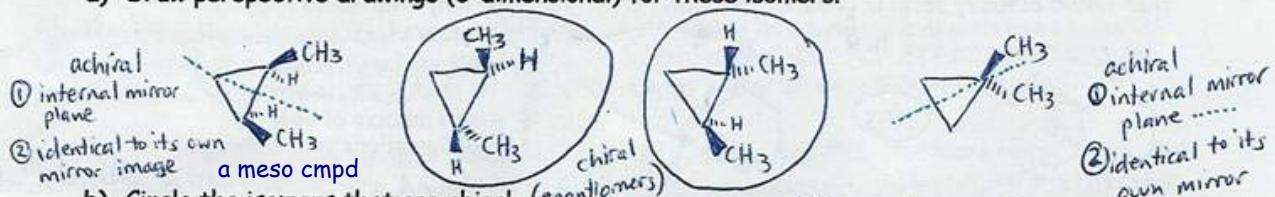


- But, this could rearrange via 1,2-methyl shift to yield our 2° C⊕ above (step ③'s product) on way to forming 3° C⊕ (most stable...)
- Note that we were asked to explain ONE product, so that's where we aimed our attention in the mechanism



 # 5. There are four dimethylcyclopropane isomers.

a) Draw perspective drawings (3-dimensional) for these isomers.



b) Circle the isomers that are chiral.

c) If a mixture of 1 mole of each of these isomers were subjected to simple gas chromatography (which separates compounds based on their boiling points), how many fractions would be obtained? Which compounds would each fraction contain?

3 fractions: (unknown order of b.p.s)
① containing cis-1,2-dimethylcyclopropane
② containing enantiomer pair trans-1,2-dimethyl....
③ containing 1,1-dimethylcyclopropane

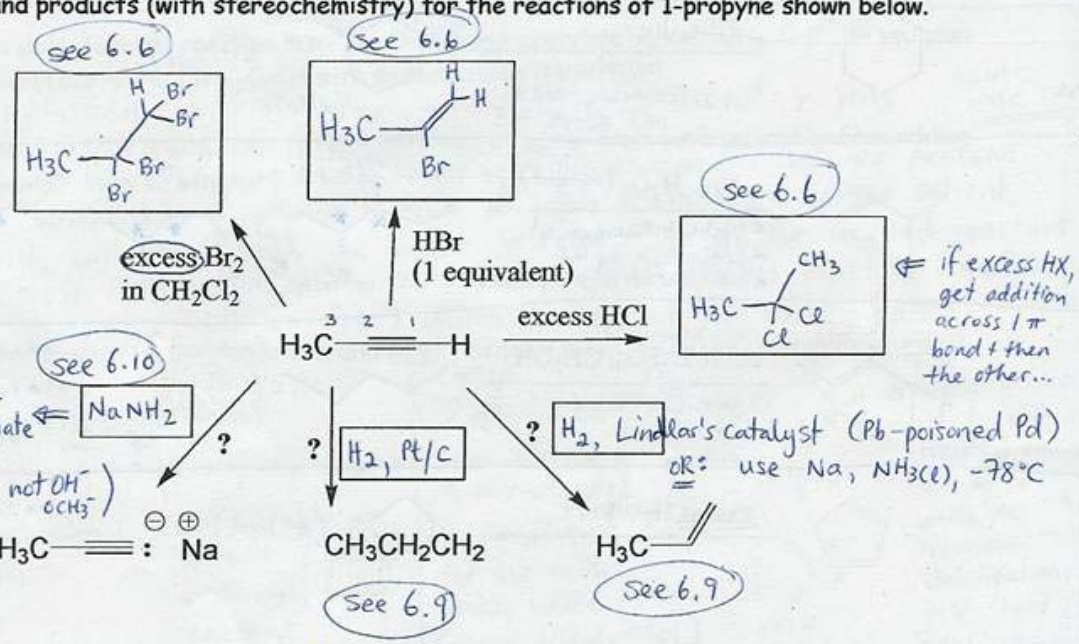
because enantiomers have identical PHYSICAL PROPERTIES.

d) How many of these fractions would be optically active? Explain briefly.

None!

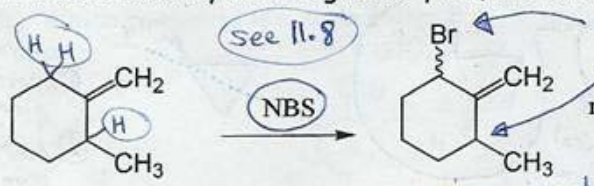
- Achiral molecules do not rotate plane polarized light at all ∴ not optically active.
- A racemic mixture (equal moles of a pair of enantiomers) does not rotate the plane of PPL either, because the rotation caused by 1 enantiomer is cancelled out by the equal but opposite rotation caused by the other enantiomer.

 # 6. Like alkenes, alkynes undergo electrophilic addition reactions. For example, hydrogen halides, halogens and hydrogen can all be added across the C≡C, with results that we can predict using the same mechanistic thinking we used for alkenes (note: addition of water & ROH are a little more complex). Because there are 2 π-bonds, however, we must be careful to control how much of our electrophilic reagent we use, and sometimes make other modifications. On your own, refer to Bruice Ch.6 sections 6.5, 6.6, 6.9 & 6.10 to learn how to correctly choose the missing reagents and products (with stereochemistry) for the reactions of 1-propyne shown below.



conj. acid	pKa	useful base
H_2	35	NaH, CaH_2
NH_3	36	$NaNH_2$
ⁿbutane	50	ⁿBuLi

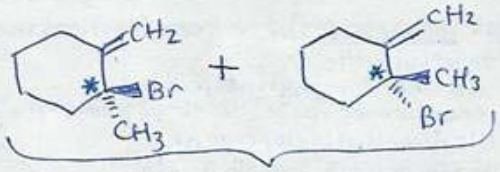
 # 7. The following reaction is unlikely to give a high yield of the product shown. Draw the product(s) that would actually form in greater yield, and briefly explain why this would happen.



• NBS preferentially brominates at allylic positions (as shown here with arrows)

minor product: produced via a 2° radical intermediate

vs.



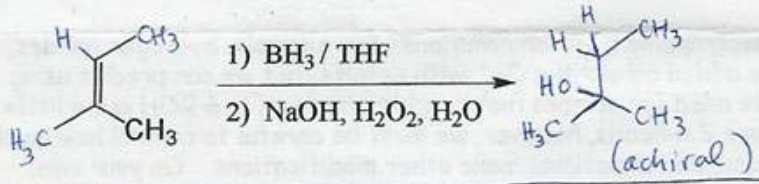
major products racemic mixture

The bromination with NBS occurs via a radical mechanism, and the most stable allylic radical intermediate will be the dominant intermediate. Thus, the 3° carbon would preferentially be attacked by the Br• radical. The radical int. is planar so leads to the racemic 3° bromide shown.

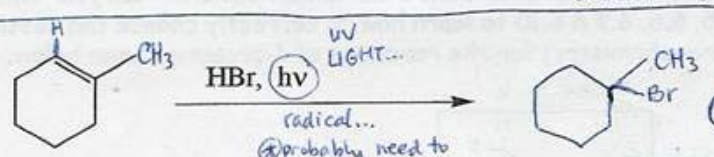
 # 8. Draw line structures of the major product(s) of the reactions below. For each, also include:

i. the expected stereochemistry (i.e. draw dashes/wedges for all asymmetric centres)

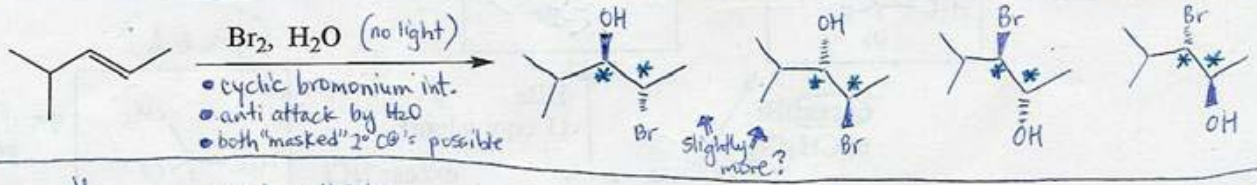
NOTE: error in parts a & b: Text is correct, but structures are WRONG because not anti-Markovnikov! I was working too quickly! This effects the stereochemistry aspect immensely. See corrections - next page.

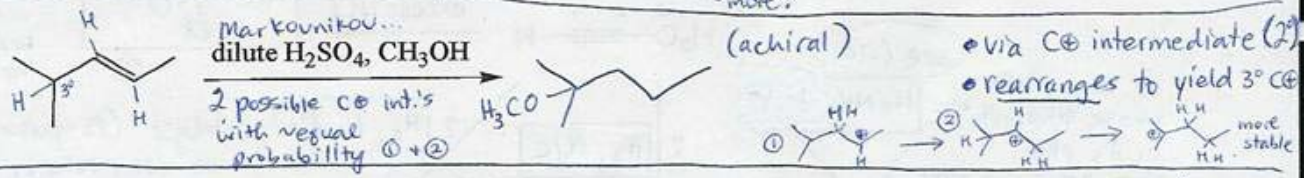


• antiMarkovnikov addition of H_2O
• concerted syn addition of B-H
• B replaced by OH with no change in stereochemistry

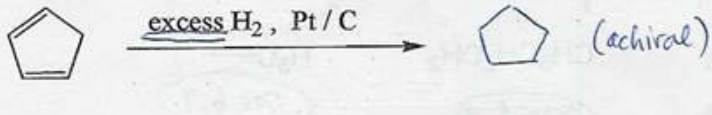


• antiMarkov. addn of HBr
• radical intermediate (planar!)
• if chiral centre made, would be racemic





• via C⊕ intermediate (2°)
• rearranges to yield 3° C⊕



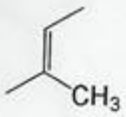
• syn addition of H_2 across BOTH double bonds since have excess H_2.

8. Draw line structures of the major product(s) of the reactions below. For each, also include:

i. the expected stereochemistry (*i.e.*, draw dashes/wedges for all asymmetric centres)

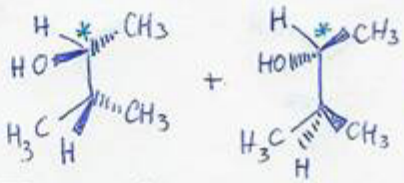
ii. a few keywords about the mechanism that explain the stereochemistry (*e.g.*, C+ intermediate, concerted syn addition, radical intermediate, anti addition, *etc.*).

Corrected



1) BH_3 / THF

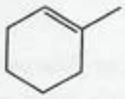
2) NaOH, H_2O_2, H_2O



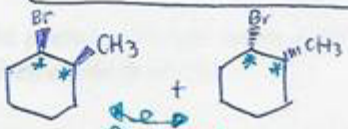
enantiomers

antiMarkovnikov addition of H_2O

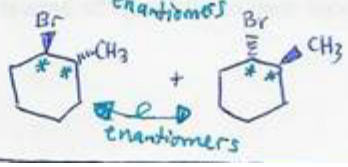
- concerted, syn addition of B-H
- B replaced by OH with no change in stereochemistry.



HBr, hν



enantiomers



enantiomers

antiMarkovnikov addition of HBr

- radical intermediate
- planar
- each C* RACEMIZED