Concordia UNIVERSITY

Rogers MARKING SCHEME

COURSE	ORGANIC CHEMISTRY I	NUMBER	CHEM 221	SECTION	/4 02
EXAMINATION	Final Examination	DATE	April 20, 2005	TIME	0900-1200
INSTRUCTOR	Dr. Cerrie ROGERS				

MATERIALS ALLOWED:	☐ NO	☒	YES (PLEASE SPECIFY)	periodic table & pK_a data table provided non-programmable calculators allowed
CALCULATORS ALLOWED:	☐ NO	☒	YES	molecular model kits allowed

Chem 221 --- ORGANIC CHEMISTRY I

LAST NAME: Rogers FIRST NAME: _____

STUDENT NUMBER: _____ SIGNATURE: _____

Instructions: PLEASE READ THIS PAGE WHILE WAITING TO START!

- ***Make sure your exam has 13 pages, including this cover page.***
- ***You may detach the two pages containing the periodic table and pK_a data if you wish.***
- ***Write your student ID number on all pages.***
- ***Write all answers <u>legibly</u> in the space provided (use the backs of pages for rough work).***
- ***Non-programmable calculators are allowed; cell phones & electronic dictionaries are not.***
- ***Suggestion: if you spend 15 min / page ⇨ you'll have 30 min. extra to check your work.***

<u>Mark breakdown</u>:

Page 2.	/ 16
Page 3.	/ 12
Page 4.	/ 11
Page 5.	/ 12
Page 6.	/ 9
Page 7.	/ 12
Page 8.	/ 10
Page 9.	/ 8
Page 10.	/ 10
Page 11.	/ 5 *BONUS*
TOTAL:	**/ 100 (MAXIMUM MARK = 105)**

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 # 1. (__/ 16 marks) Circle the word(s) that correctly completes each of the following statements.

1 mark each:

a) A molecule or atom that is described as electrophilic is also ((LEWIS ACIDIC) / LEWIS BASIC).

b) If a bonding orbital and its corresponding antibonding orbital are both filled, the bond between the two atoms (FORMS / (BREAKS)).

c) A radical species will be ((STABILIZED) / DESTABILIZED) by the presence of alkyl substituents on the atom carrying the unpaired electron.

d) The rate of a reaction that occurs via an S_N2 mechanism will ((DEPEND ON) / NOT DEPEND ON) the concentration of the nucleophile.

8

e) At room temperature, (SUFFICIENT / (INSUFFICIENT)) thermal energy is available for an alkene to rotate about its π-bond.

f) A molecule with n stereogenic centres will have a maximum of (2n / (2^n)) stereoisomers.

g) Markovnikov's rule works because electrophiles always add to the (MOST / (LEAST)) substituted sp^2 carbon in an alkene.

h) Secondary alkyl halides react faster than primary alkyl halides in (S_N2 / (E2)) reactions.

2 marks each:

i) A reaction pathway with a lower activation energy has a ((MORE STABLE) / LESS STABLE) transition state than another pathway with a higher activation energy.

8

j) When an elimination occurs via the E1 mechanism, (ONLY ANTI / (BOTH SYN AND ANTI)) elimination products are observed.

k) Any species whose conjugate acid has a pK_a (BELOW / (ABOVE)) the pK_a of another substance will be a strong enough base to deprotonate that substance.

l) We would expect a tertiary amine to be (MORE SOLUBLE / (LESS SOLUBLE)) in water than a secondary amine with the same number of carbons.

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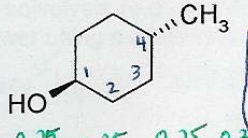
brackets
(-0.25 for extra hyphens or comma problems – once each)

 # 2. (__ / 4 marks) Name the following molecules according to IUPAC conventions; include stereochemistry (*i.e.*, relative orientations and/or absolute configurations as appropriate).

2 EACH

a)



-0.25 if R/S specified
-0.25 if E/Z specified

trans
achiral ∴ no R,S
1,4-disubstituted

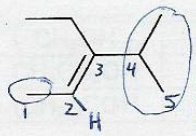
0.5 0.25 0.25 0.25 0.25 0.25

trans-4-methylcyclohexanol

OR trans-4-methylcyclohexan-1-ol

OR trans-4-methyl-1-cyclohexanol

b)



-0.25 if R/S specified
-0.25 for alphab. error Me/Et

3 ethyl
4 methyl
(E) pent-2-ene

(E)-3-ethyl-4-methyl-2-pentene
if wrong longest chain: (total points) -0.5

OR (E)-3-ethyl-4-methylpent-2-ene

0.25 0.25 0.25 0.25 0.25 0.25 0.25 0.25

 # 3. (__ / 4 marks) Draw skeletal (line) structures of the following molecules; include stereochemistry.

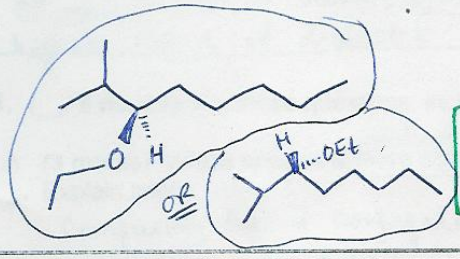
2 EACH

a) (*R*)-3-ethoxy-2-methyloctane

0.5 0.5 0.5 0.5

no part marks there if wrong chain length

0.5 0.5 (isopropyl higher priority than n-pentyl)



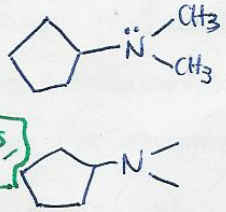
TOTAL: if NOT line structures, -0.5

b) *N*,*N*-dimethylcyclopentanamine

0.5 0.5 0.5 0.5

5C in ring

→ not ammonium! (0)
not diamine (0.25)



either form of methyls is ok.

 # 4. (__ / 4 marks) Draw structures that represent examples of each of the following types of compounds.

a) a primary amine

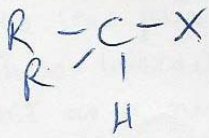
0.5 0.5

$R-NH_2$

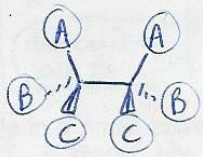
1 each
any example
any style of structure

c) a secondary halide

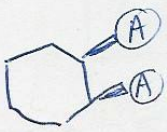
0.5 0.5



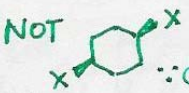
b) a meso compound



need 2 chiral centres ∴ stereochem REQUIRED or no marks



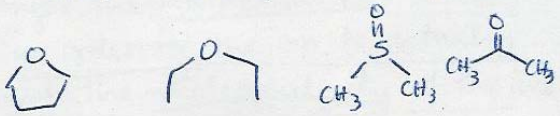
NOT



∵ C's not chiral

d) a polar aprotic solvent

eg. THF, diethyl ether, DMSO, acetone



dichloromethane
CH_2Cl_2

0.5: any other aprotic polar cmpd (solid/gas)
+ 0.25 if mention no NH or OH bonds

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if interpret as "decide SN1 vs E1..." • full marks possible

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 # 5. (__/ 5 marks) Some properties of common alcohol solvents are listed in the table.

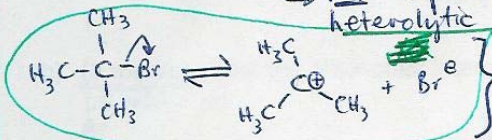
In which of these solvents would *t*-butyl bromide (SN1) most rapidly (RATE) undergo solvolysis (*e.g.*, to form an ether product)? Explain your answer using a discussion of the reaction's mechanism.

Compound	Boiling point b.p. (°C)	Dielectric constant, ε (at 25°C)
CH_3OH	64.7	33
CH_3CH_2OH	78.3	25
$(CH_3)_3COH$	82.3	11

3 mech

• tertiary halide ⇒ ① SN1 mechanism ✓✓

↳ rate depends on rate of heterolytic cleavage of C-Br = RLS



Rate-Limiting step of SN1 solvolysis leading to ether.
Transition state is MORE charged than reactant,
∴ stabilized by a more polar solvent ✓
eg. protic solvent (like any alcohol)

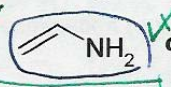
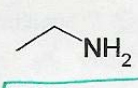
• For higher bp comments: max 1

• If choose SN2: max 1 mark for discussion of MeOH's small size.

2 solvent

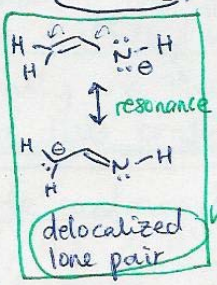
The more polar the alcohol solvent, the stronger the dipole-dipole interactions between the "transition state" and the solvent will be; therefore, the more stabilized the ‡ will be, and the faster the SN1 mechanism will proceed. Of the 3 alcohols shown, methanol is the most polar, as seen by its highest value of dielectric constant ε. ✓ Thus: fastest SN1 in methanol.

 # 6. (__/ 6 marks) For these questions, include any structural drawings that help clarify your explanations.

a) **(3 marks)** Which species is more acidic (weakest conj. base): vinylamine,  **or** ethylamine,  ?
Explain briefly.

3

Comparing the 2 conjugate bases:
Vinylamide is stabilized via resonance; the delocalized lone pair is less reactive than the fully localized lone pair on ethylamide. Thus, vinylamide is less basic ✓ ∴ vinylamine is more acidic



vs.

b) **(3 marks)** Which species is the stronger nucleophile in a protic solvent: fluoride, F^- **or** iodide, I^- ? ✓ 0.5
Explain briefly. F⁻ stronger base than I⁻...]0.5 ∴ poorer Nu here

3

Iodide is the stronger nucleophile in a protic solvent. A protic solvent contains –O–H or –N–H bonds, so has a highly δ+ H that is able to interact strongly with nucleophiles. The smaller the atom carrying the lone pair on a nucleophile, the stronger the interactions (ion-dipole). These interactions must be overcome in order for the ion to actually ACT as a nucleophile, so they diminish the nucleophilicity of the ion. Thus, the large iodide ion is the stronger nucleophile, since it has only weak ion-dipole interactions because of its low charge density. Fluoride (small) has strong ion-dipole interactions (hydrogen bonding, in fact) + is therefore a MUCH weaker nucleophile in a protic solvent.

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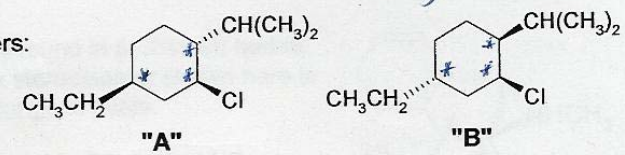
 # 7. (__/ 12 marks) Molecules A & B are stereoisomers:



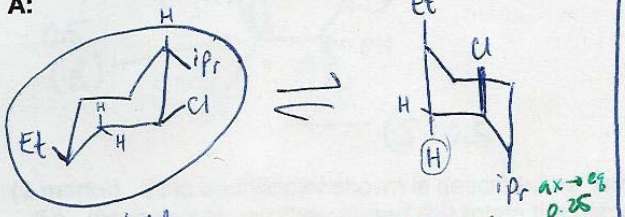
a) **(2 marks)** Are A & B diastereomers or enantiomers? How can you tell?

2 not all 3 stereocentres are inverted in configuration

b) **(3 marks)** Draw the chair-chair interconversion (ring-flipping equilibrium) for each molecule.

1.5 each

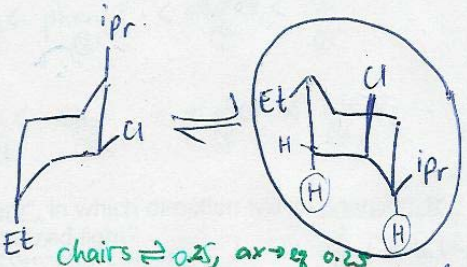
A:



3 more stable
larger groups equatorial

chairs ⇌ 0.25 iPr ax→eq 0.25
Et/Cl cis 0.25 each
Cl/iPr trans 0.25 each

B:



chairs ⇌ 0.25, ax→eq 0.25
Et/Cl trans 0.25 each more stable
Cl/iPr cis 0.25 each

c) **(2 marks)** Circle the more stable chair conformation of each molecule.

2 (each) ⇒ no mention of rel. confo. [ ]'s ⇒ max 3.

d) **(5 marks)** Which molecule will undergo more rapid E2 elimination (under the same conditions)? Explain.

1.5 The rate of E2 elimination depends on the concentration of both the nucleophile (assume same here) AND the alkyl halide. However, because E2 elimination occurs predominantly via the anti-periplanar β-H–LG conformation, the abundance of this conformation is important.

5 1.5 For molecule A: the more stable conformation has Cl in the equatorial position; therefore, the β-H's are NOT oriented ANTI to the Cl. Only the less stable conformation has a β-H anti to the Cl, so the rate of E2 elimination from molecule A would be small. ie: β-H and LG both axial, & trans/anti. ✓

1.5 For molecule B: the more stable conformation has 2 β-H's that are anti to the Cl. Thus, the majority of the molecules will exist in a conformation that can easily undergo E2 elimination, so the rate of E2 should be large.

0.5 Thus: molecule B will undergo more rapid E2.

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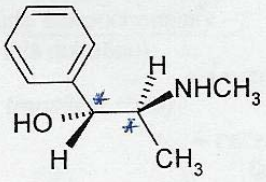
 # 8. (__/ 9 marks) Ephedrine is a compound originally found in a Chinese herbal remedy for asthma that is now marketed as a drug. The stereoisomer shown here is the one that is active in causing the air passages in the lungs to dilate.

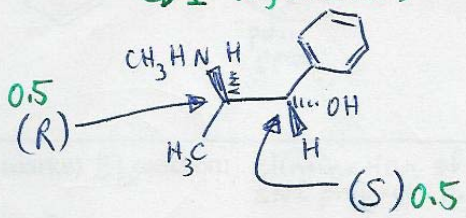


a) **(1 mark)** How many stereogenic carbons are present in this molecule?

1 — 2 (ignore the N!)

b) **(2 marks)** Draw the molecule's enantiomer, and label its stereogenic carbons as *R* or *S* as appropriate.

2 — ↳ 1 (any orientation)



PRIORITIES (no marks for this)

H < phenyl < other C* < OH
④ ③ ② ①

H < CH_3 < other C* < $NHCH_3$
④ ③ ② ①

c) **(2 marks)** If the enantiomer shown is described as "levorotatory", in which direction will its enantiomer *(i.e., the molecule you drew in part (b))* rotate the plane of polarized light?

counterclockwise

opposite to levo! ∴ dextro. ∴ clockwise

2 — no part marks.

CIRCLE ONE: (clockwise) *OR* counterclockwise

d) **(4 marks)** Imagine you prepare a sample of synthetic ephedrine in a pharmaceutical lab, and the compound must contain less than 0.5% of the (+) enantiomer in order to sell it as a drug. If a sample of pure (−) enantiomer yields a specific rotation of −10.0°, and your sample has an optical rotation of −9.5°, what percentage of the sample is composed of the (+) enantiomer? Is your sample pure enough to sell?

pure (−) enantiomer: $\alpha = -10.0°$
sample: $\alpha = -9.5°$

$$\%\ e.e. = \frac{-9.5°}{-10.0°} \times 100\%$$ 0.5

= 95% ee, (−) in excess (0.5)

4 — Meaning of 95% e.e.:

95% pure (−) ← 0.5 / 0.25 / 0.25

0.5 → 5% racemic = 2.5% (−) + 2.5% (+)

TOTAL (−) = 97.5%
(+) = 2.5% } 0.5

Sample can contain a maximum of 0.5% (+) } conclusion 1
∴ it is not pure enough to sell as a drug.

9

1.

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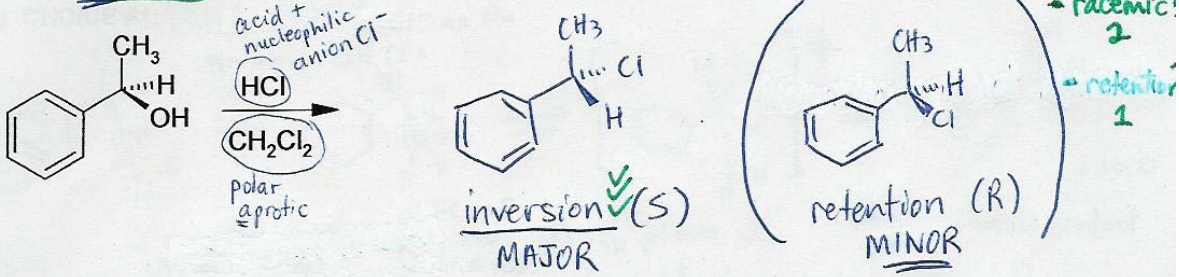
 # 9. (__/ 12 marks) REACTIONS: Predict the major product for **EACH** reaction; include stereochemistry. (labels not required)
(Note: read Question # 10 before you start this question).

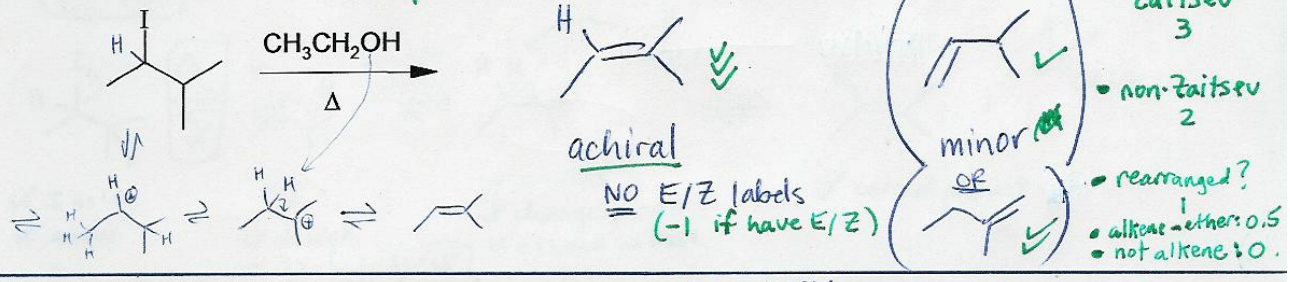
a) **(3 marks)** S_N2 reaction (*Note: if choosing this for Q.# 10, please include the S_N2 transition state*)

substitution by Cl : 1



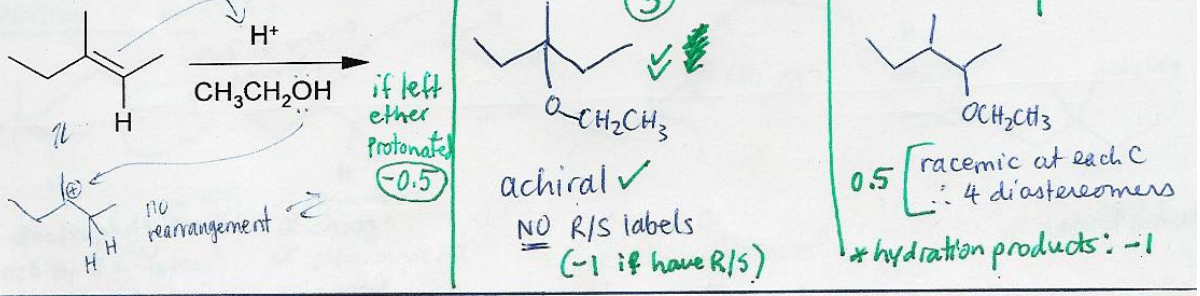
- inversion 3
- racemic 2
- retention 1

b) **(3 marks)** E1 reaction: elimination of HI : 1
SN1 product : 0.5



- Zaitsev 3
- non-Zaitsev 2
- rearranged? !
- alkene - ether: 0.5
- not alkene: 0.

c) **(3 marks)** Acid-catalyzed addition of an alcohol: MARKOVNIKOV. (3)

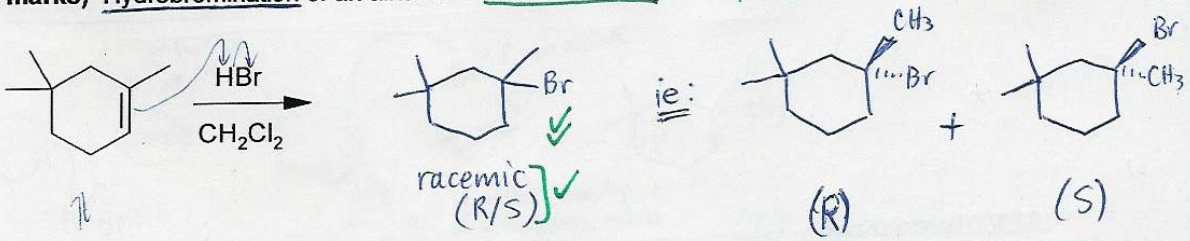


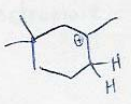
anti-Markov. X
1

0.5 [racemic at each C ∴ 4 diastereomers

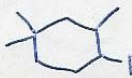
* hydration products: -1

d) **(3 marks)** Hydrobromination of an alkene: MARKOVNIKOV. – mystery rxn via Markov. regio : 0.5





Antimarkov X
1



0.5 [4 diastereomers

if tried to use CH_2Cl_2 as Nu: ~~max 1~~
1 if Markov.
0.5 if antiMarkov.

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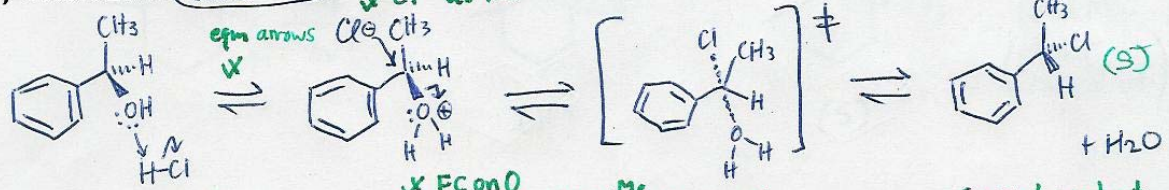
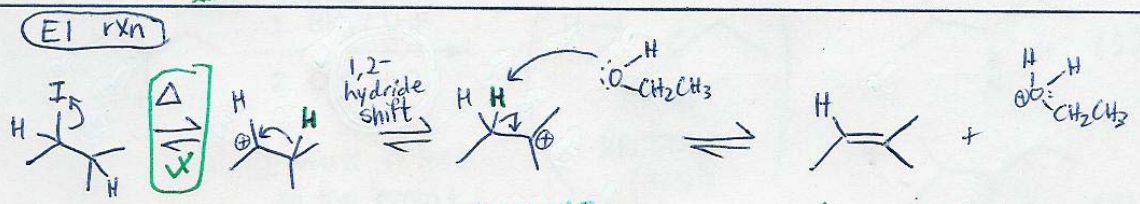
 # 10. (__/ 10 marks) MECHANISMS: For any **TWO** of the reactions from **Question # 9**, write complete step-by-step "arrow-pushing" mechanisms to explain how the predicted major product was formed. For each of your choices, please write the name of the reaction at the top of the mechanism.

(5 marks) CHOICE #1: SN2 rxn ✓ backside attack ✓ Cl⁻ as Nu



✓ rxn c HCl
0.25 ea ✓ [arrow from: ✓] arrow from bond

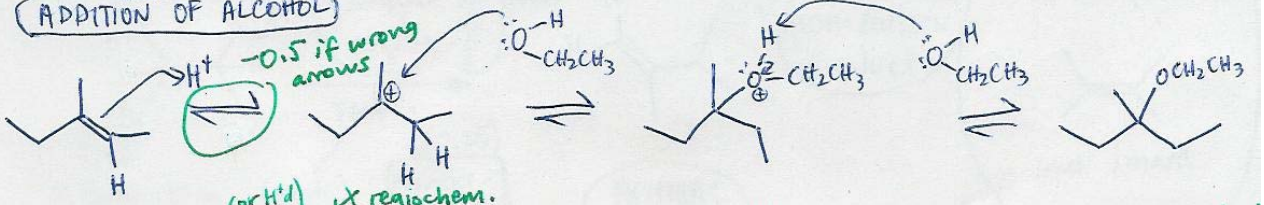
E1 rxn



✓ I as LG
✓ arrow
✓ charge
✓ 1,2-hydride shift ✓ arrow
✓ arrows
✓ charge moved
✓ ethanol as base
✓ correct product.

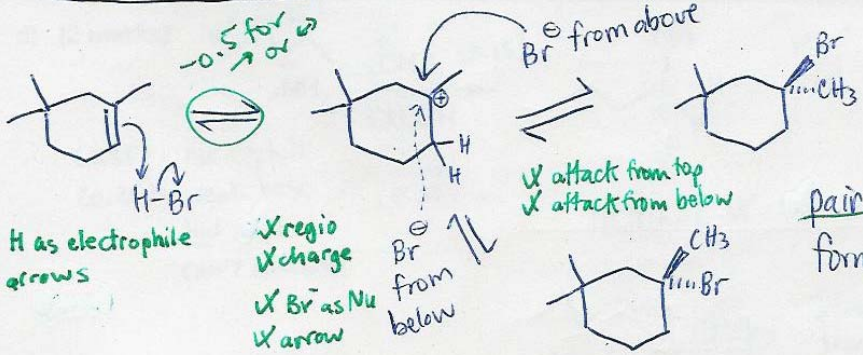
(5 marks) CHOICE #2:

ADDITION OF ALCOHOL



✓ H⁺ electrophile (or H⁺d ethanol)
✓ attack by π e⁻s (arrow)
✓ regiochem.
✓ charge
✓ ethanol as Nu
✓ arrow
✓ FC on O
✓ ethanol as base
✓ arrows
✓ correct product

HYDROBROMINATION



✓✓ H as electrophile
✓✓ arrows
✓ regio
✓ charge
✓ Br⁻ as Nu
✓ arrow
✓ attack from top
✓ attack from below

pair of enantiomers form with equal probability

If in brackets: can give part marks if final answer wrong but have made some correct observations.

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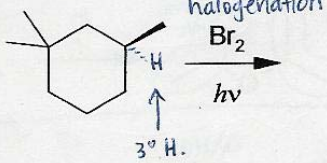
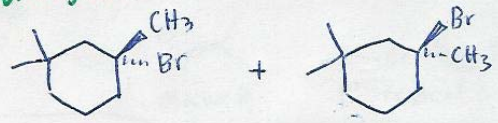
labels not required.

 # 11. (__/ 8 marks) REACTIONS: Predict the major product(s) for each reaction; include stereochemistry.

a) **(2 marks)**



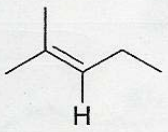


✓✓ monohalogenated (✓ if diBr'd) ✓ regiochem. ✓ stereochem

(R) (S)

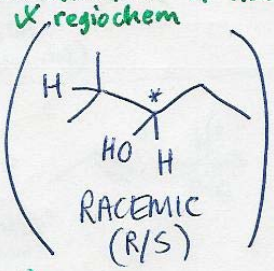
RACEMIC. (planar radical int.)

b) **(2 marks)**

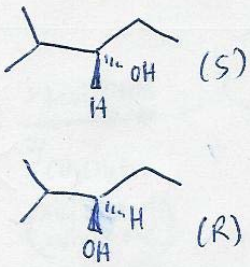


hydroboration = anti-Markovnikov addition of H_2O

1. BH_3 / THF
2. OH^-, H_2O_2

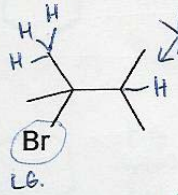


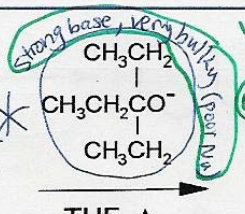
✓✓ addition of H_2O ✓ regiochem ✓ stereochem



1 mark if leave on the boron + do stereo (0.5 if B only).

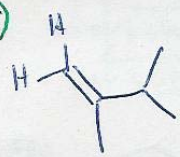
c) **(2 marks)**





3° favours E1 too but base is STRONG ∴ E2 faster (0.25)

✓✓ elimination (0.5 only if not one of the products below)



✓ non-Zaitsev product

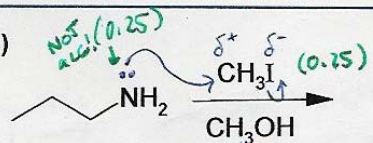
Will not see: Zaitsev product

max 1 mark

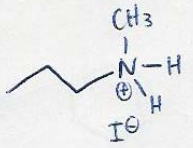
ACHIRAL (no E/Z) ✓

If substitution: must be SN1... max. 0.5

d) **(2 marks)**



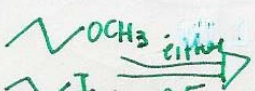
(0.25) • nucleophile
(0.25) • weak base but CH_3I CAN'T eliminate!



✓✓ substitution product ✓ with quaternary N

ACHIRAL ✓

1.5 assuming they thought MeOH could deprotonate it (wrong)



either 0.5. assuming they thought $RN^+(CH_3)H_2$ would lose $RNHCH_3$ via attack by MeOH.

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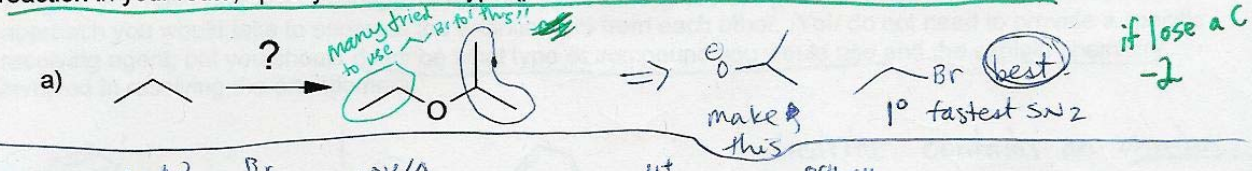
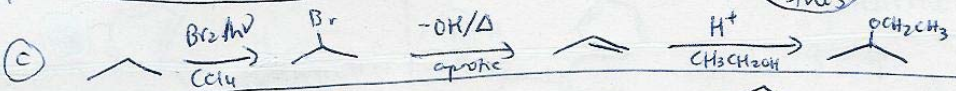
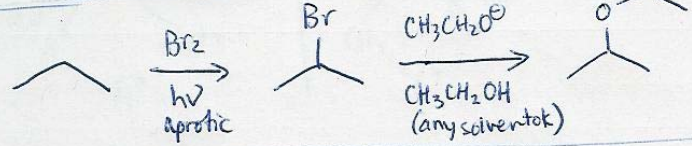
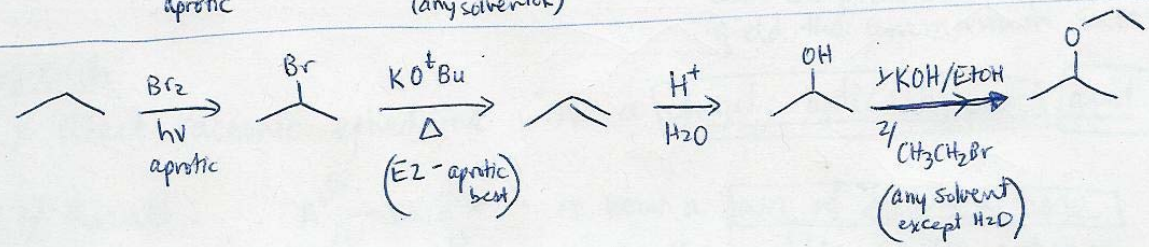
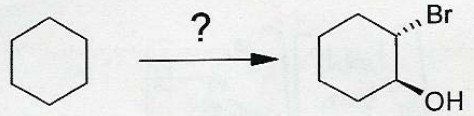
 # 12. (__/ 10 marks) CHOICE OF SYNTHESIS: Provide a synthetic route to **ONE** of the following target compounds. Start from the suggested starting material and use any other reagents you need. For each reaction in your route, specify the solvent type (protic *vs.* aprotic) and temperature (hot *vs.* cold).

a) 

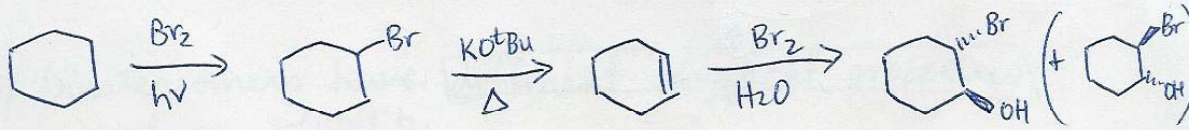
c) 

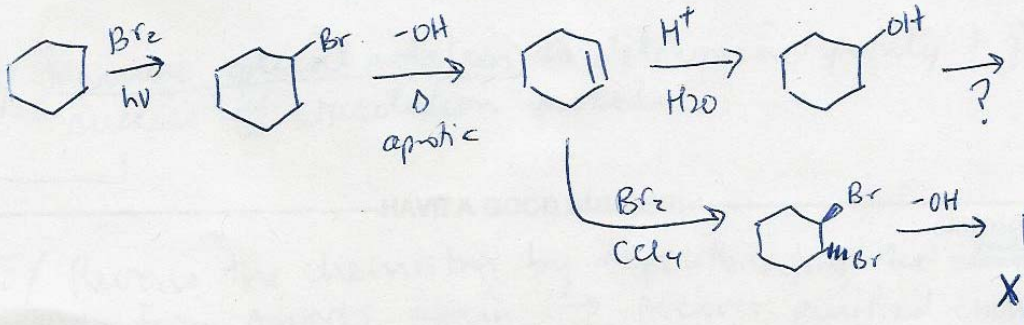
A) 

B) 

b) 

	reagents / products	regio/stereo	solv/T
2×3.25 = 3.5 ← 3 steps	2 or 1.75	0.75	0.75
2.5 ← 4 steps	1.25	0.75	0.75
5 ← 2 steps	2.5	1.25	1.25

A) 



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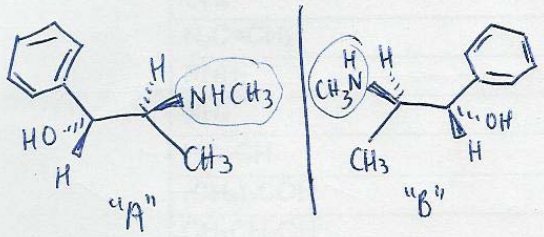
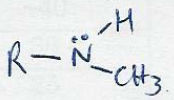
BONUS QUESTION: (__/ 5 marks)

Imagine you have prepared a sample of racemic ephedrine (structure given in Question # 8). Describe the approach you would take to separate the enantiomers from each other. You do not need to provide a specific resolving agent, but you should describe what type of compound you would use and the explain chemistry involved in resolving the enantiomers.



Ephedrine contains an amine group:



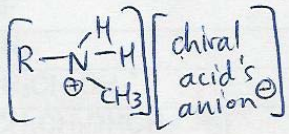
Therefore, it is a weak base & can be protonated by an acid to yield the ammonium salt.

Approach:

✓✓ 1/ React racemic ephedrine with a chiral, optically pure acid.

✓ 2/ Result: "A"$^{\oplus}$ — acid$^{\ominus}$ *
"B"$^{\oplus}$ — acid$^{\ominus}$ *

is now a pair of diastereomers since the acid's configuration is the SAME in each, but the ephedrine's chiral centres are all opposite.

ie: 

✓✓ 3/ Diastereomers have different physical properties such as solubility
∴ find a recrystallization solvent where one of the 2 salts precipitates out preferentially
→ repeat until pure!

✓ 4/ measure optical rotation to determine purity + gauge success of resolution process.

---HAVE A GOOD SUMMER!---

5 ✓ 5/ Reverse the chemistry by deprotonating the ~~amine~~ ammonium salt back to form AMINES again → recover purified enantiomers.

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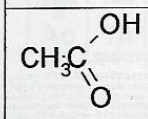
pK_a VALUES

Compound	pK_a
$CH_3CH_2CH_2CH_3$	>50
CH_4	50
$H_2C{=}CH_2$	44
RNH_2	~40
NH_3	36
$HC{\equiv}CH$	25
$(CH_3)_3COH$	18
CH_3CH_2OH	16
CH_3OH	15.5
H_2O	15.7
RNH_3^+	~10
HCN	9
	4.7
HF	3.2
HN_3	3
$CH_3CH_2OH_2^+$	-2.4
$[CH_3CH_2OHCH_2CH_3]^+$	-3.6
H_2SO_4	-5
HCl	-7
HI	-10