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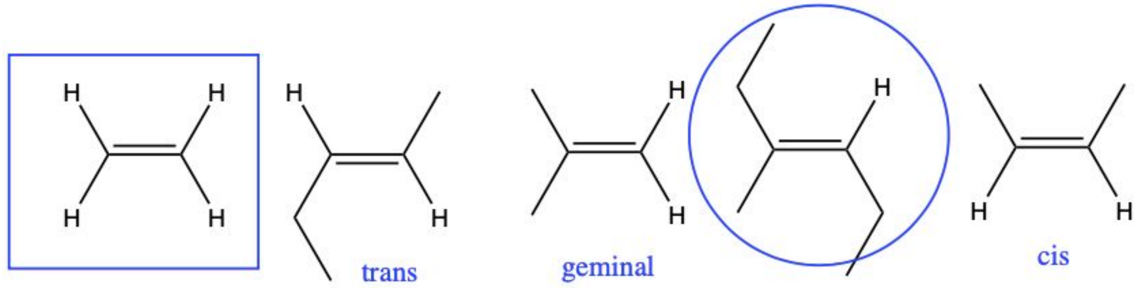
CHEM 51B
Professor King
https://sites.uci.edu/ochemtutors/

Midterm 1 Review Packet

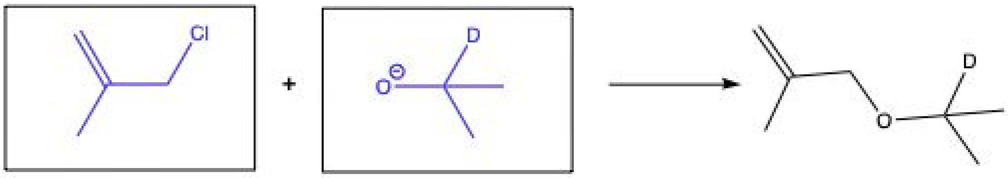
1. Label whether the following alkenes are cis, trans, or geminal. Circle the most stable alkene and draw a square around the least stable alkene.



Disubstituted alkenes can be categorized as either trans, cis, or geminal. **Trans** alkenes have the 2 R groups on opposite sides of the double bond. **Cis** alkenes have the 2 R groups on the same side of the double bond. **Geminal** alkenes have the 2 R groups attached to the same C of the double bond.

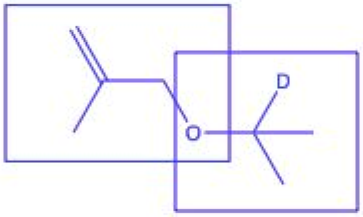
REMEMBER: More R groups = more stable

2. Show the alkyl halide and alkoxide that could be used to synthesize the following ether by a williamson ether synthesis.

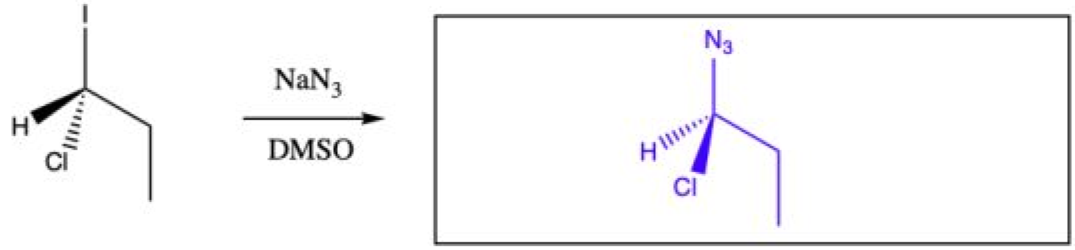


alkyl halide alkoxide

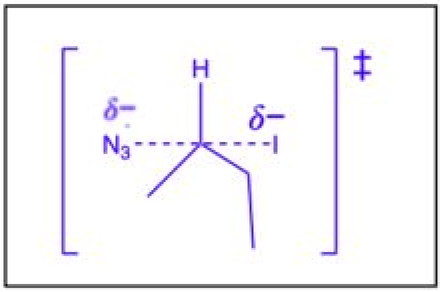
In a williamson ether synthesis reaction, the alkyl halide is preferentially an unhindered 1° or methyl halide. This is due to the fact that 2° alkyl halides will predominantly lead to elimination and 3° will only result in eliminations. When choosing the reagents, group the oxygen into 2 separate groups in order to decide which would be best as the alkyl halide.



3. Predict the major product of the following reaction. Additionally, draw the structure of the transition state, including any partial charges.



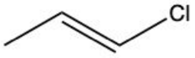
transition state:



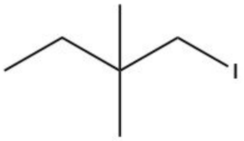
As the solvent for this reaction is a polar aprotic solvent, an SN1 reaction can immediately be ruled out since SN1 reactions require a polar protic solvent. Since N_3^- is a strong nucleophile and SN2 reactions run best in PA solvents, this reaction is an SN2 reaction. SN2 reactions occur in one step, so the transition state includes 5 groups. (SN2 is a second order reaction & bimolecular → electrophile & nucleophile collide in the rate determining step)

REMEMBER: SN2 reactions follow a **backside attack**. As such, always remember **inversion of configuration** at the stereocenter.

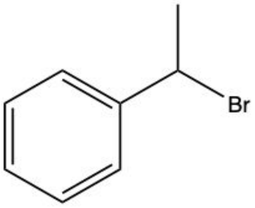
4. Identify whether each of the following substrates favor an SN2 or E2 reaction. The nucleophile is a strong base.



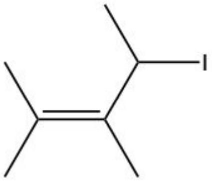
A



B



C



D

E

A: **NR**

Elimination and substitution reactions cannot occur with sp2 carbons

B: **NR**

SN2 and E2 reactions can both occur with 1° alkyl halides, but in this case, neither can occur. SN2 cannot occur because of steric hindrance and E2 cannot occur because there are no β hydrogens.

C: **E2**

SN2 and E2 reactions can both occur with 2° alkyl halides, but E2 is favored because the nucleophile is a strong base.

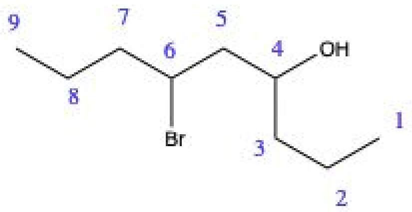
D: **E2**

SN2 and E2 reactions can both occur with 2° alkyl halides, but E2 is favored because the nucleophile is a strong base.

E: **SN2**

SN2 reactions are favored with unhindered 1° alkyl halides.

5. Name the following alcohols using IUPAC nomenclature.



a.

Answer: 6-bromo-4-nonanol or 6-bromononan-4-ol

1. Choose the longest continuous carbon chain to be the parent

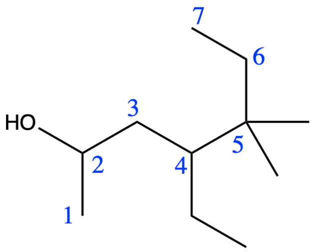
   Parent chain has 9 carbons → nonane

2. Drop the -e for -ol

   Nonane → nonanol

3. The parent chain should be numbered so that the -OH has the lowest number. Name the substituents.

   Subsituents: 6-bromo



b.

Answer: 4-ethyl-5,5-dimethyl-2-heptanol or 4-ethyl-5,5-dimethylheptan-2-ol

4. Choose the longest continuous carbon chain to be the parent
   Parent chain has 7 carbons → heptane
5. Drop the -e for -ol
   heptane → heptanol
6. The parent chain should be numbered so that the -OH has the lowest number. Name the substituents.
   Substituents: 4-ethyl , 5,5-dimethyl

6. Predict what happens to the reaction rate in each of the following instances:

a. The leaving group changes from Cl- to I-

   Answer: speeds up

   Good leaving groups are weak bases. I- is the best leaving group because it is the weakest base.

   Remember the trend for LG: -I > -Br > - Cl > ~~-F~~ (NR)

b. The solvent of an SN1 reaction changes from H_2O to DMSO

   Answer: no reaction

   SN1 reactions require a polar protic solvent in order for the reaction to occur. DMSO is a polar aprotic solvent, so the reaction will not occur.

c. The solvent of an SN1 reaction changes from H_2O to ethanol

   Answer: slows down

   SN1 reactions are the fastest in H_2O and water has a higher dielectric constant than ethanol.

d. The nucleophile in an SN2 reaction F- to Cl-

   Answer: depends on solvent; PP - speeds up PA - slows down

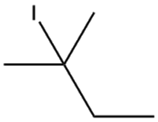
   For PP solvents, nucleophilicity increases as you **go down the row** of a periodic table. This is due to the fact that solvation weakens nucleophiles and impedes their ability to atack. If nucleophiles are weakly solvated, they will more easily shed the solvent molecules in order to attack. Going down the periodic table, atomic size increases, thus decreasing solvation.

   For PA solvents, nucleophilic strength increase as base strength increases.

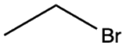
7. Draw both of the E2 products for the following reaction. Identify the Zaitsev and Hoffman product and the major product .

In an E2 reaction, 2 or more elimination products can be possible, depending on which adjacent carbon the nucleophile . When this happens, the most stable alkene predominates. The **Zaitsev** product is the more substituted product and is usually the more stable product, while the **Hoffman** product is the less substituted product and usually the minor product. However, in this reaction, the nucleophile is DBN, which is a **strong bulky base.** Due to its bulkiness, DBN will remove the **most accessible hydrogen** to give the **least substituted** alkene as the major product.

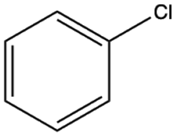
8. Given the following set of compounds, choose a compound letter or letters that correctly answers each question.



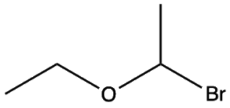
A



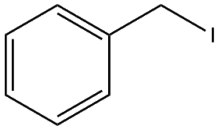
B



C



D

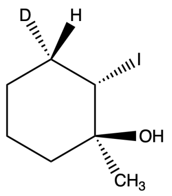


E

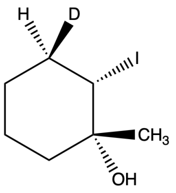
a. Which compound gives the fastest SN1 reaction? D — it forms a **secondary resonance-stabilized** carbocation!
   Remember the carbocation stability: 2° resonance-stabilized > 3° > 1° resonance-stabilized > 2° > 1°
b. Which compound has the fastest reaction with NaBr in acetone? B — primary alkyl halide in SN2 reaction conditions (strong nucleophile & PA solvent!)
c. SN1, SN2, E1, and E2 reactions are impossible with which compound? C — **aryl halides** cannot undergo any of these reactions; forms an **extremely unstable carbocation** (SN1, E1, E2) + the nucleophile is repelled by the electron cloud (SN2)
d. Which compound forms the most stable carbocation after ionization? D — look at the carbocation stability ranking

e. Which compound(s) **do not** undergo E2 reaction? B, C, E — they all have no β-H's so elimination cannot occur!

9. Consider the following stereoisomers:



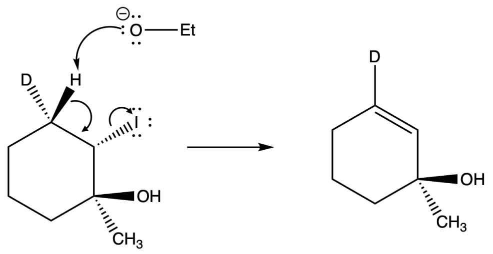
A



B

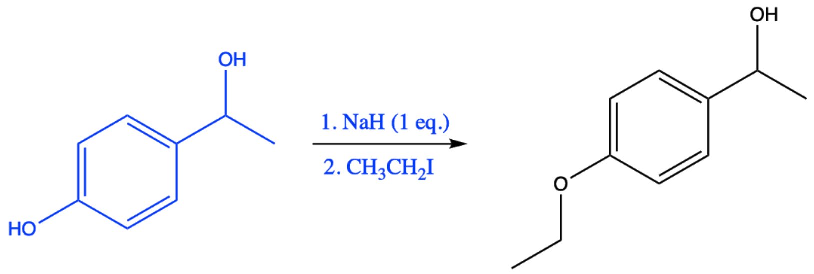
a. Which stereoisomer has the faster rate for an E2 reaction?
   i. Stereoisomer A; **kinetic isotope effect** states that it takes longer to break a C-D bond than a C-H bond (breaking C-H bond = r.d.s.)
      1. Note: E2 reactions are **anti-periplanar** (β-H and L.G. are in the same plane + anti)! In a **cyclohexane ring**, anti-periplanar means they have to be **trans-diaxial**.
      2. Stereoisomer A: H comes off; Stereoisomer B: D comes off

b. Draw the product that forms when the stereoisomer A undergoes E2 elimination.
   i. Note: alkenes do not have dashed/wedged bonds because all of the participating atoms are in the same plane.

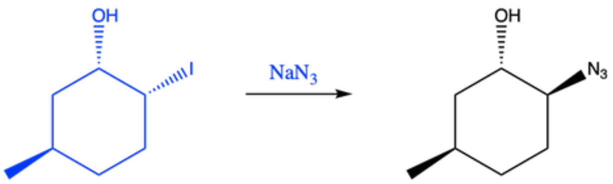


10. Predict the major product or provide the reagents in the following reactions.

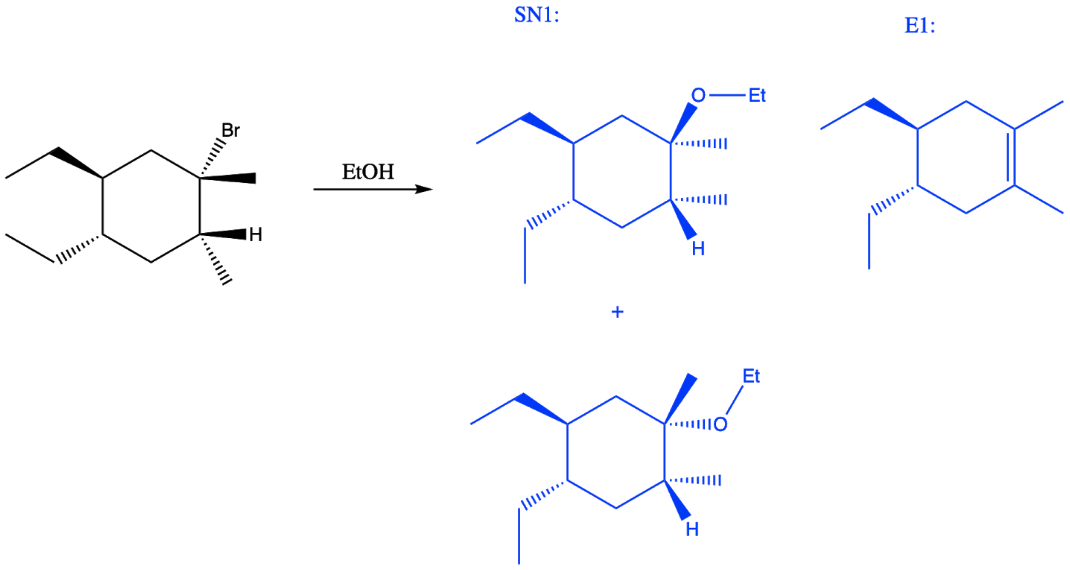
a. This is a Williamson ether synthesis reaction.



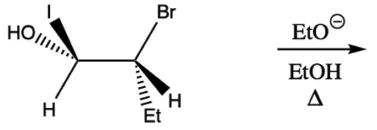
b. SN2 reaction → **inversion of configuration!**

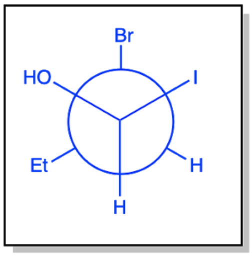


c. Remember that SN1 results in **racemization** because the formation of the carbocation allows nucleophilic attack from both sides.

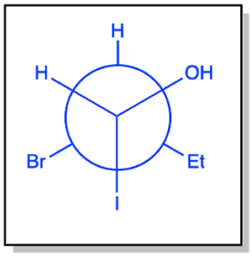


11. For the following E2 reaction, draw the Newman projection of the alkyl halide (view from the left) & the rotated Newman projection in which the reaction occurs. Then predict the product.

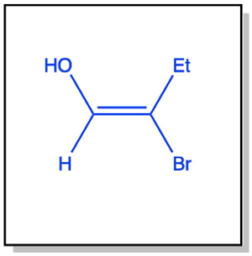




Newman projection

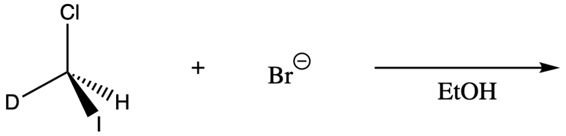


Rotated Newman projection

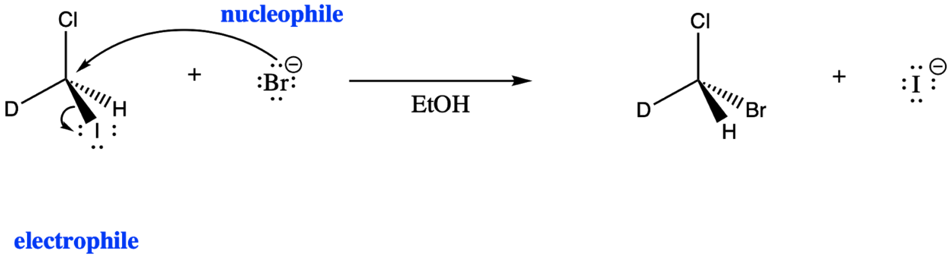


Alkene product

12. Consider the following reaction:



a. Predict the type of reaction & product. Draw the mechanism and label each reagent as a nucleophile or electrophile. This is an SN2 reaction!



Note: this should be a backside attack!

b. Is this a reversible reaction? Yes; both leaving groups have similar leaving group abilities.

c. Considering **nucleophilic strength** only, which direction is favored at equilibrium? EtOH is a **polar protic** solution. In PP solutions, I^- is the stronger nucleophile. Therefore, the reaction will favor the left side.

d. If Ag^+ is added to the reaction mixture, which direction will this drive the equilibrium? Note: Ag^+ forms insoluble precipitate with I^-. According to Le Chatelier's principle, equilibrium will be driven to the right. The formation of AgI(s) means I^- is being depleted.

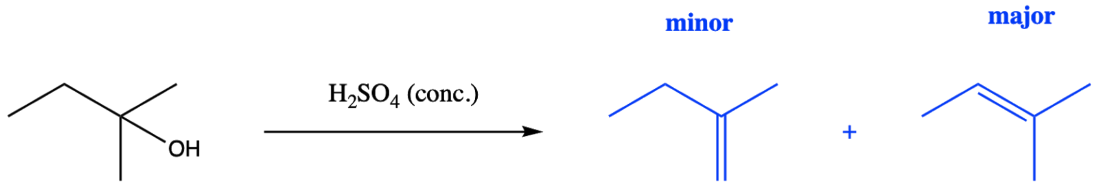
13. Rank the following nucleophiles from strongest to weakest in a polar aprotic solution (1 = best nucleophile). Note: (pKa $HN_3 = 4.6$)

	CH_3OH	$CH_3S^{\ominus}$	$CH_3O^{\ominus}$	$CH_3C\equiv C^{\ominus}$	$^{\ominus}N_3$
	$\boxed{5}$	$\boxed{3}$	$\boxed{2}$	$\boxed{1}$	$\boxed{4}$
pKa:	<0		15	25	4.6

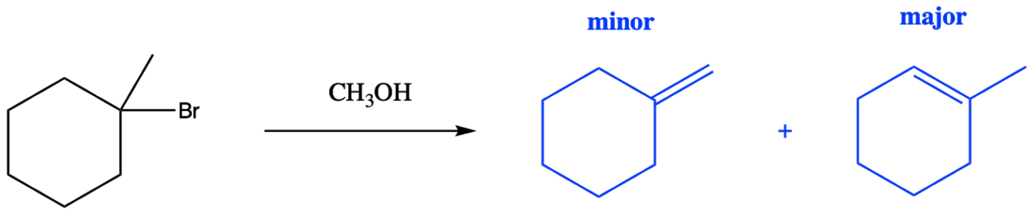
Note: Remember the following good nucleophiles that are weak bases: I^-, Br^-, Cl^-, N_3^-, HS^-

14. Predict the major and minor products for each of the following **elimination** reactions:

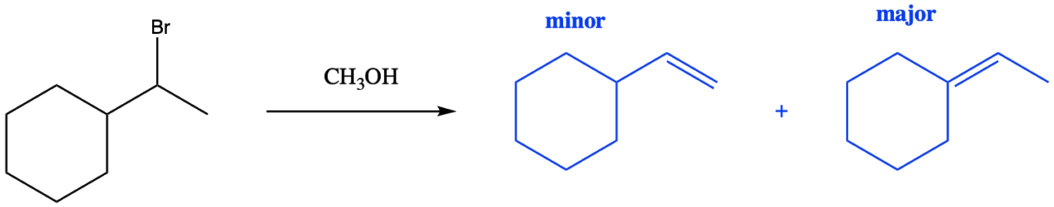
a. This is a dehydration reaction!



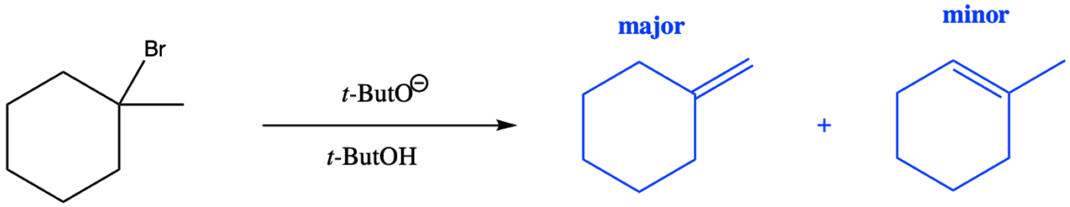
b. This is an E1 reaction!



c. This is another E1 reaction! However, you need to remember that any reaction where a carbocation forms can undergo **carbocation rearrangement!**

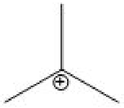


d. This is an **E2** reaction! Note: the bulky base prevents the most substituted alkene from being the major product.

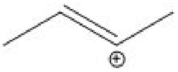


15. Rank the following carbocations from least stable to most stable

A

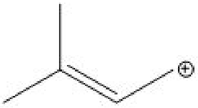


B

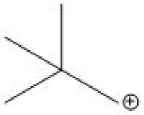


C

D

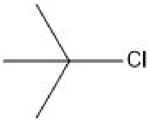


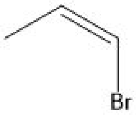
E

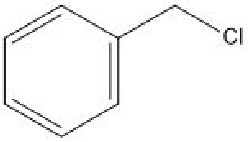


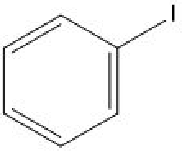
Answer:
B (vinyl), E (primary), C (secondary), D (resonance-stabilized primary), A (tertiary)

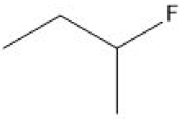
16. Classify the following alkyl halides (e.g. primary, secondary, vinyl, etc.)









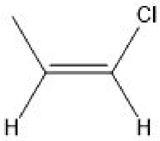


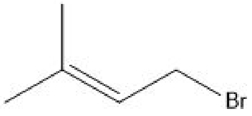
H_3C-Br

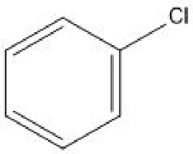
Answers:

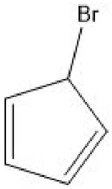
tertiary	vinyl	benzylic
aryl	secondary	primary
allylic	methoxymethyl	methyl

17. Which of these molecules will not be able to participate in SN1 or SN2 reactions?

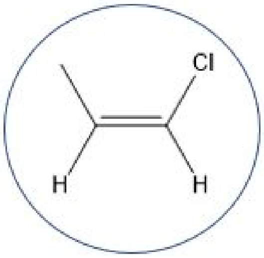


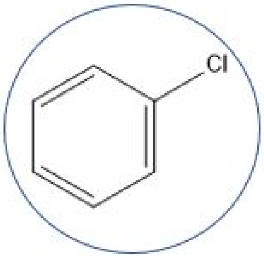


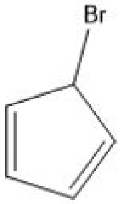




Answer:







Vinylic and aryl halides will not undergo SN1 and SN2 reactions
SN1: vinylic and aryl carbocations are too unstable
SN2: The pi electron cloud of nearby double bonds will block the backside attack of the nucleophile

18. Fill out the following table about SN1 and SN2 reactions

	SN1	SN2
Kinetics (unimolecular vs bimolecular)	Unimolecular	Bimolecular
Effect of alkyl halide	tertiary>secondary>primary (primary = no SN1 unless resonance stabilized) More stable carbocation intermediate = faster reaction rate	methyl>primary>secondary (tertiary = no SN2) Less steric hindrance = faster reaction rate
Effect of nucleophile	Weak nucleophiles are okay since the nucleophile does not appear in the rate law	Strong nucleophile required
Effect of solvent	Requires PP solvent to stabilize the carbocation intermediate	Can be done in PP or PA solvent, but nucleophile will be stronger in PA solvent
Stereochemistry	Racemization due to planar carbocation intermediate; nucleophile can attack from both sides	Backside attack results in inversion of configuration at the stereocenter

19. Fill out the following table about E1 and E2 reactions

	E1	E2
Kinetics (unimolecular vs bimolecular)	Unimolecular	Bimolecular
Effect of alkyl halide	tertiary>secondary>primary since the stability of the carbocation intermediate is important	tertiary>secondary>primary More substitution can often mean a more stable alkene, which makes E2 more favorable Steric bulk also allows E2 to outcompete SN2 reaction
Effect of nucleophile/base	Weak base is favored. Base does not appear in the rate law, and a weak base will allow E1 to outcompete E2, which requires a strong base	Strong base required
Effect of solvent	PP solvent required	Can be done in PP and PA solvent, but PA solvent will solvate base less
Stereochemistry	No special stereochemistry	Beta-hydrogen and LG must be antiperiplanar If looking at a chair, beta-hydrogen and LG must both be axial (trans diaxial)

20. Which of the following SN2 reactions is reversible?

(a) $CH_3CH_2I + Br^- \rightarrow CH_3CH_2Br + I^-$

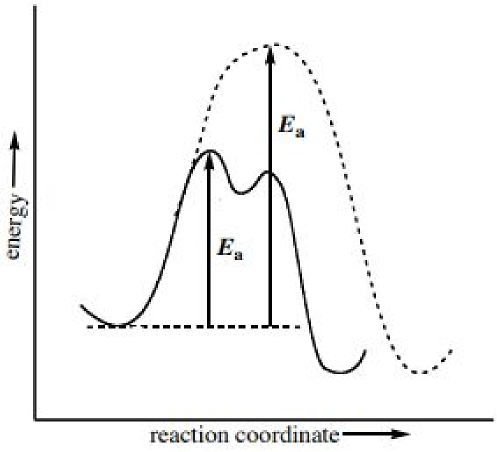
(b) $CH_3CH_2Br + NaCN \rightarrow CH_3CH_2CN + Br^-$

Answer:

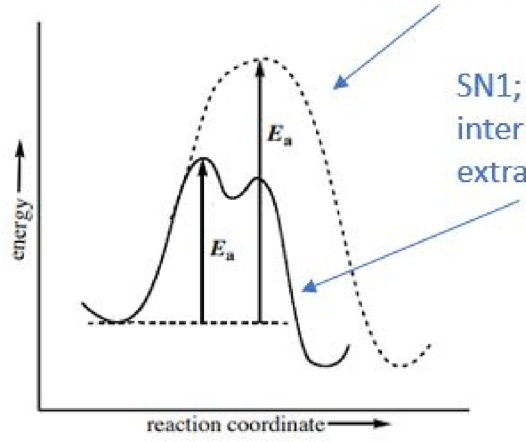
When looking for reversibility of SN2 reactions, compare the basicity of the two potential leaving groups. If they have similar basicities, the reaction will likely be reversible since the kicked-off leaving group can attack the alkyl halide again.

(a) Conjugate acids: HBr (pKa = -9), HI (pKa = -10) → pKa are similar, so reaction is **reversible**
(b) Conjugate acids: HBr (pKa = -9), HCN (pKa = 9) → pKa are very different, so reaction is **irreversible**

21. Based on the following reaction coordinate, which of the curves corresponds to an SN1 reaction? Which corresponds to an SN2 reaction? Is the alkyl halide used in this reaction more likely to be primary or tertiary?



SN2; this mechanism is concerted (all bond breaking and forming happens in a single step)



SN1; this mechanism involves an intermediate, so there will be an extra peak compared to SN2

The SN1 reaction coordinate has a lower energy of activation, so the alkyl halide is **tertiary**