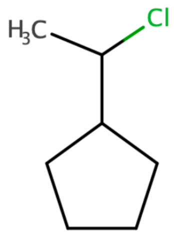
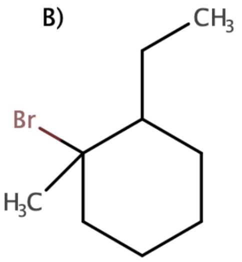
7.1 **Elimination by the E1 mechanism**

A) Draw the structures of all possible E1 products starting with the compounds below, and rank them in order of highest to lowest abundance.

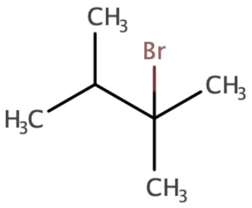
A)



B)



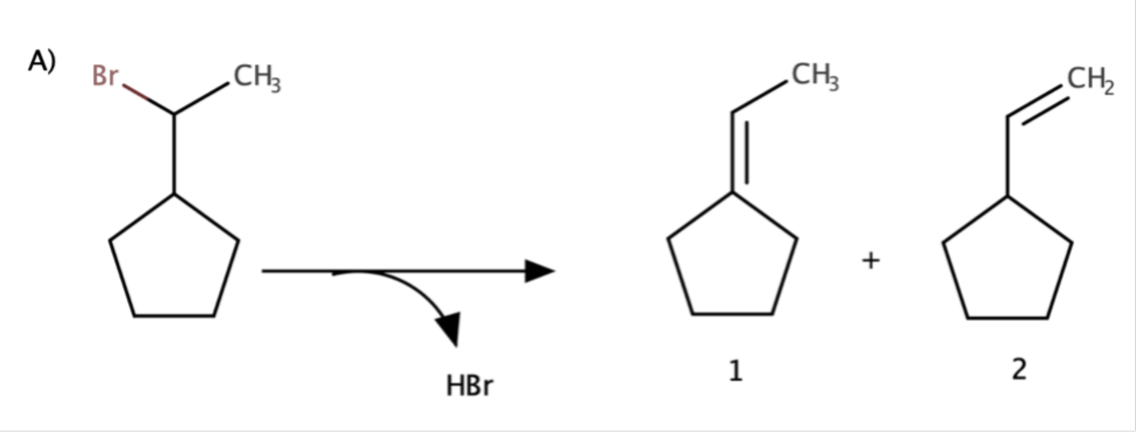
C)



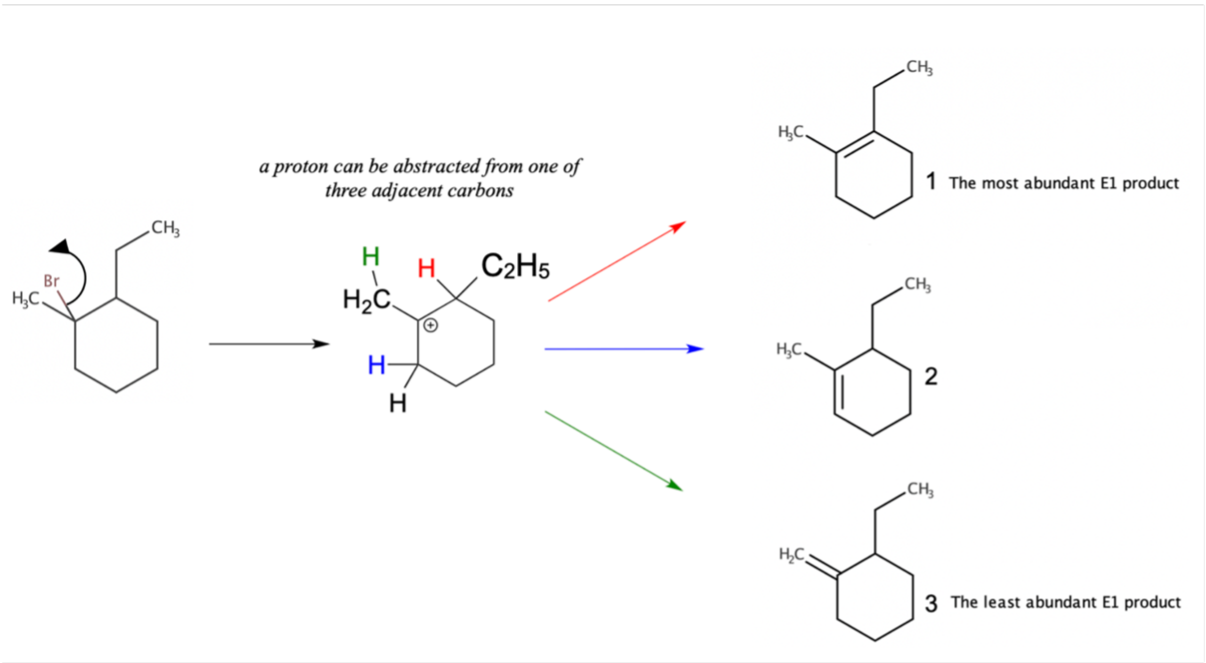
Answer:

Zaitsev's rule : The most abundant alkene product is that which is most substituted: in other words, the alkene in which the two sp2 carbons are bonded to the fewest hydrogen atoms.

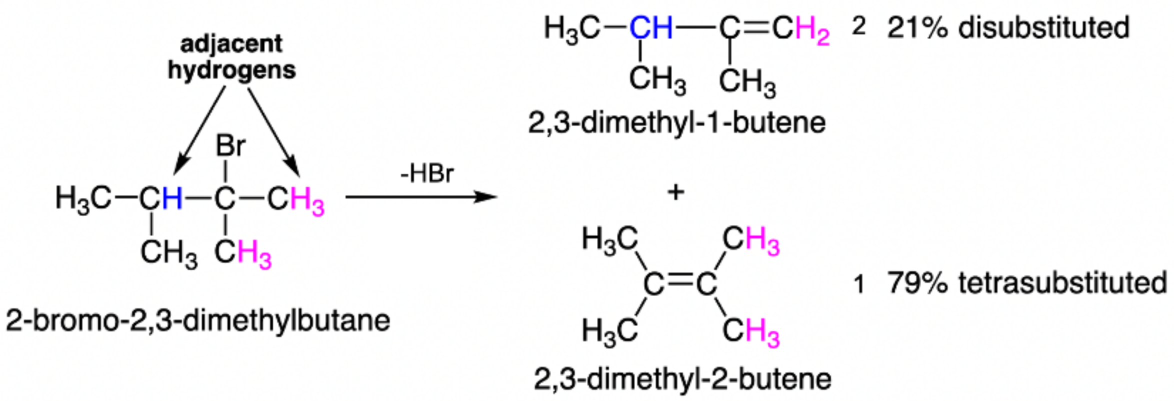
A)



B)



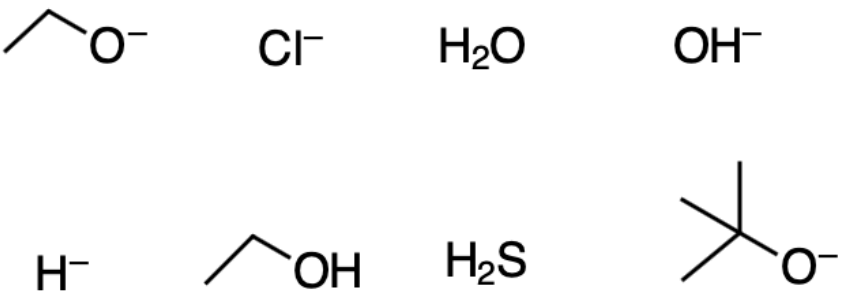
C)



7.2 Substitution vs. elimination

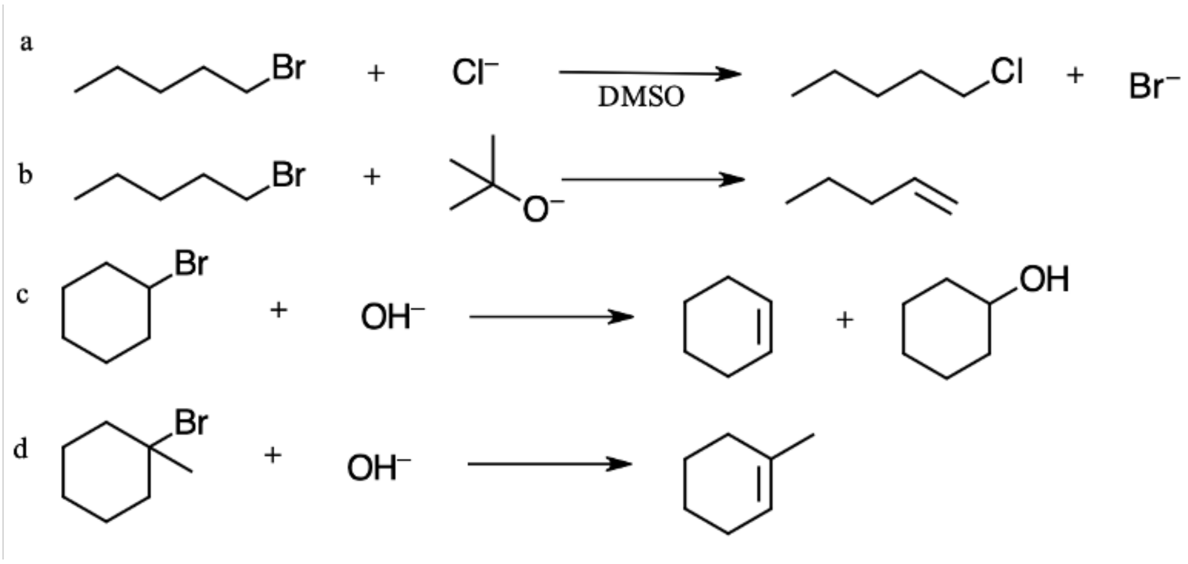
A) When both elimination and substitution products are possible, however, we can often predict which reaction will predominate. In general, strong bases and hindered carbons favor elimination, while powerful nucleophiles and unhindered carbons favor substitution. Let's start with rating the following compounds into four groups:

- nucleophile only
- base only
- strong nucleophile & strong base
- and weak nucleophile & weak base



- Methoxide anion = strong nucleophile/strong base
- Chloride ion = nucleophile only (high electron density => good nucleophile; weak base as it has a strong conjugate acid)
- Water molecule = weak nucleophile/weak base (partial negative charge and, thus, low electron density on Oxygen; H3O+ is a fairly strong acid)
- Hydroxide ion = strong nucleophile/strong base (high electron density on Oxygen; H2O is a weak acid)
- Hydrogen anion = base only (tiny atom size, thus, not polarizable; H2 is a weak acid)
- Ethanol = weak nucleophile/weak base
- Hydrogen sulfide = nucleophile only (strong Nu due to polarizability: Sulfur is a large atom, and electrons are far away from the nucleus; weak base as it has a strong conjugate acid)
- Tert-butoxide ion = strong base only (hindered as a nucleophile)

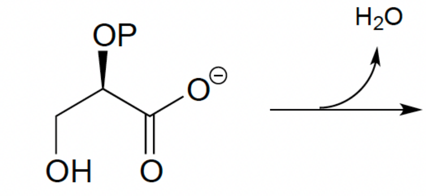
B) Now, draw products of the following reactions. Explain your reasoning:



For **a**, keep in mind the nucleophilicity of halides in aprotic solvent (F−>Cl−>Br−>I−). Cl is more nucleophilic than Br, so the SN2 reaction will take place.

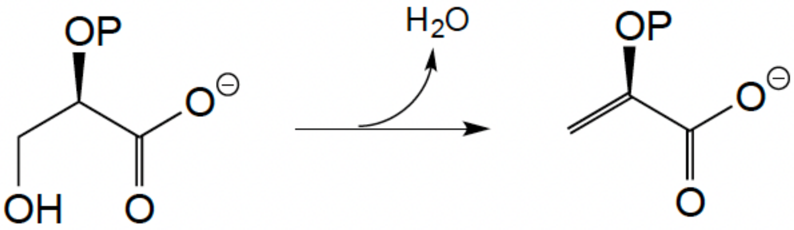
7.3 E1cb Elimination

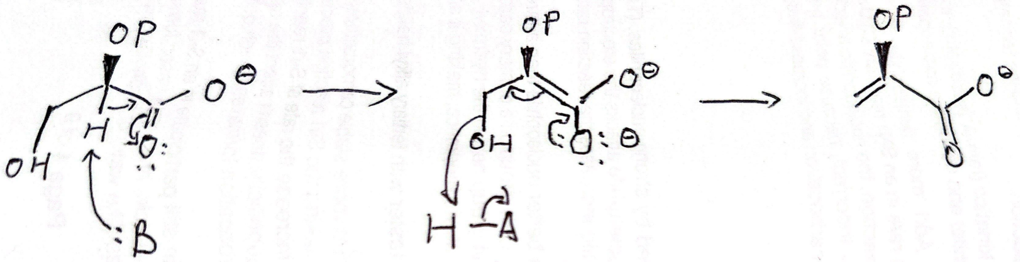
(A) In the glycolysis pathway, the enzyme 'enolase' (EC 4.2.1.11) catalyzes the E1cb dehydration of 2-phosphoglycerate. Predict the product of this enzymatic step.



2-phosphoglycerate

Answer:



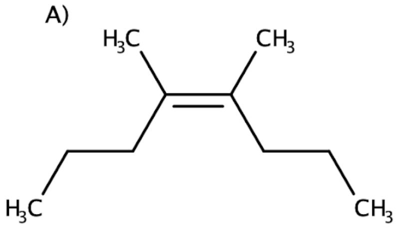


7.4 Mechanism of electrophilic addition of HBr to symmetric alkenes and its stereochemistry

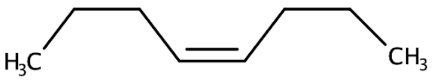
Draw the mechanism and predict the product(s) of of electrophilic addition of HBr to the following alkenes. Draw all possible stereoisomers that could form, and take care not to draw identical structures twice.

A) *cis*-4,5-dimethyl-4-octene B) *cis*-4-octene C) cyclohexene

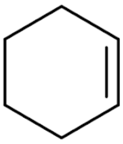
A)



B)



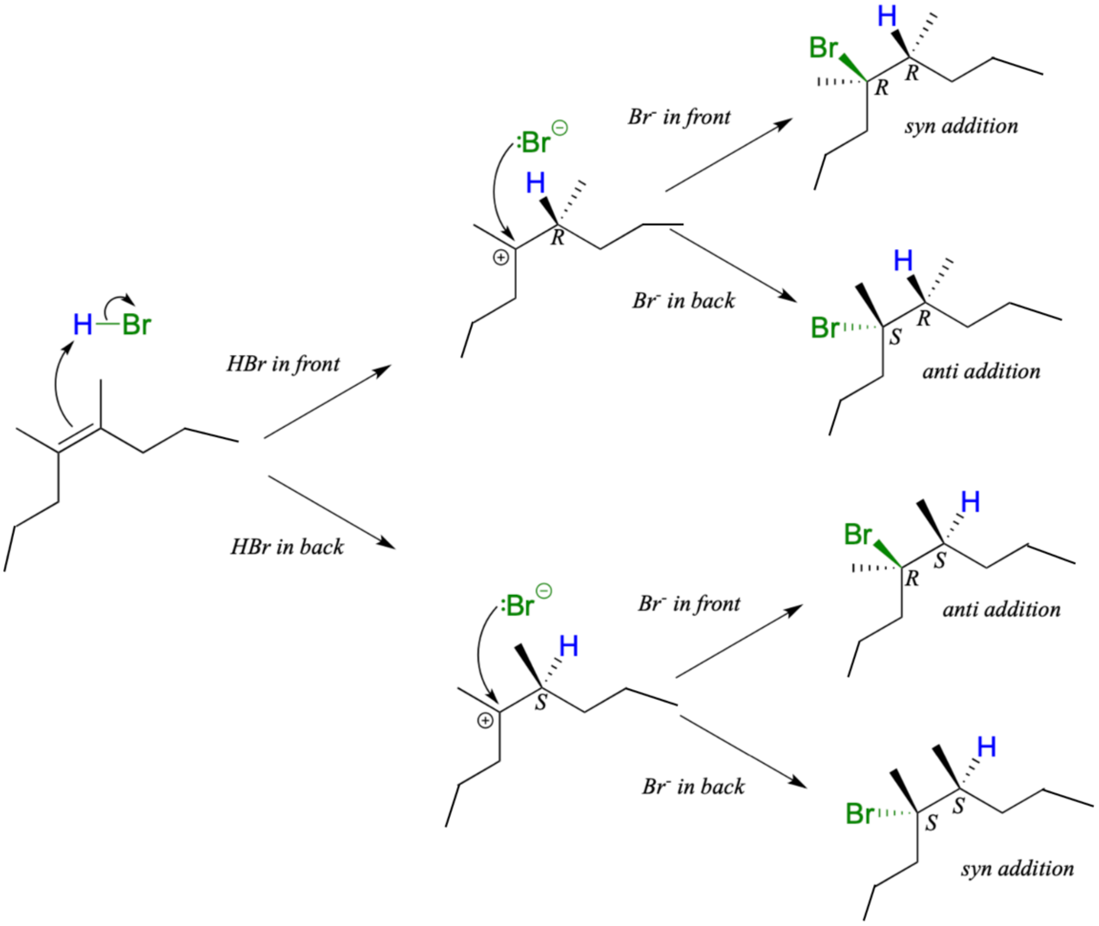
C)



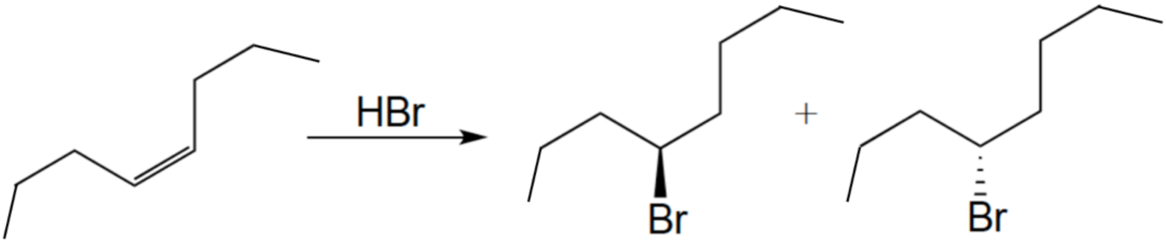
Answer:

Addition of HBr to an alkene is *not* stereoselective: the reaction results in racemization at *both* of the alkene carbons. The initial proton abstraction step creates a new chiral center, and because the acidic proton could be added to either side of the planar alkene carbon with equal probability, the center could have either *S* or *R* configuration

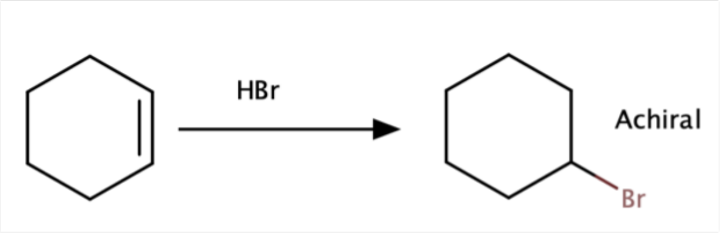
A)



B)

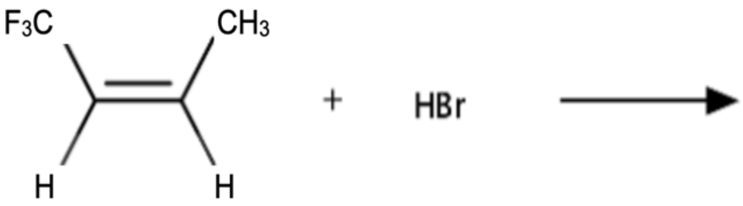


C)

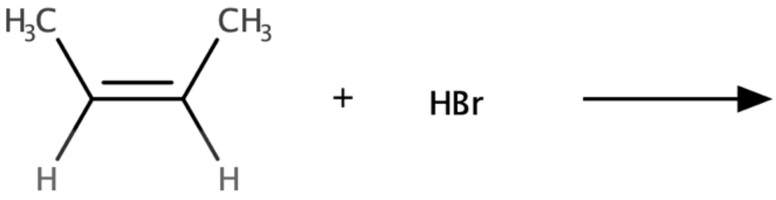


7. 5 Electrophilic addition of HBr, water, to non-symmetric alkenes: Markovnikov rule

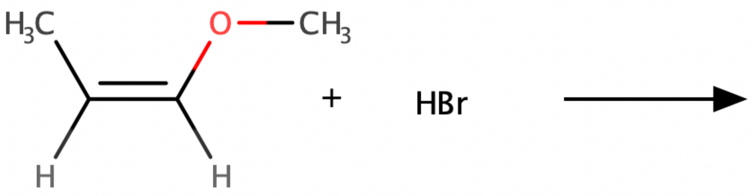
Predict the major product(s) of the following reactions. Draw all possible stereoisomers, and take care not to draw the same structure twice.



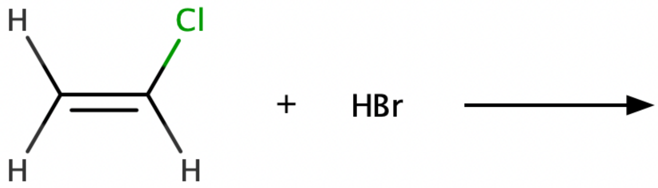
A)



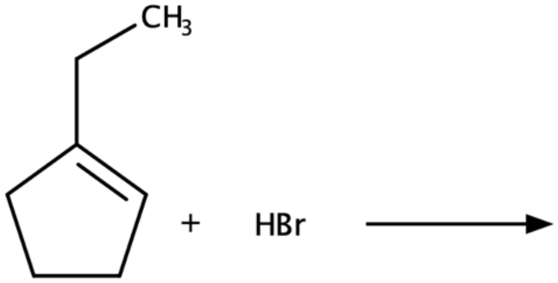
B)



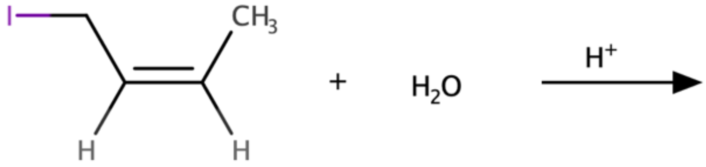
C)



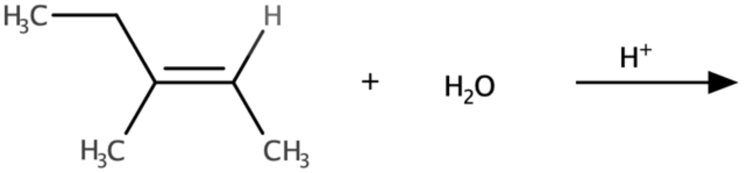
D)



E)



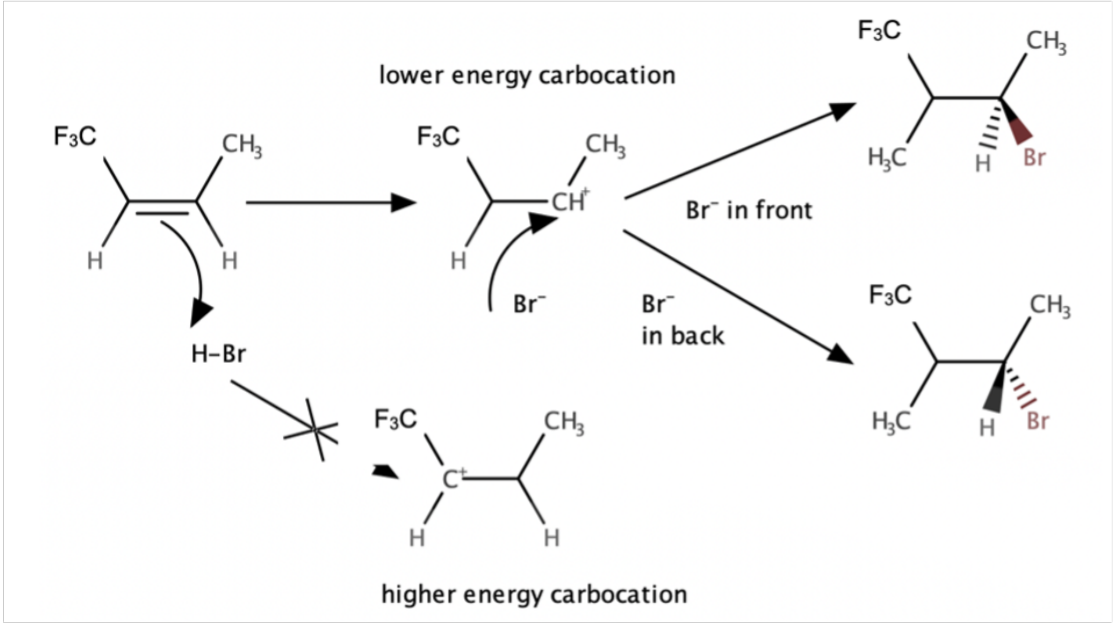
F)



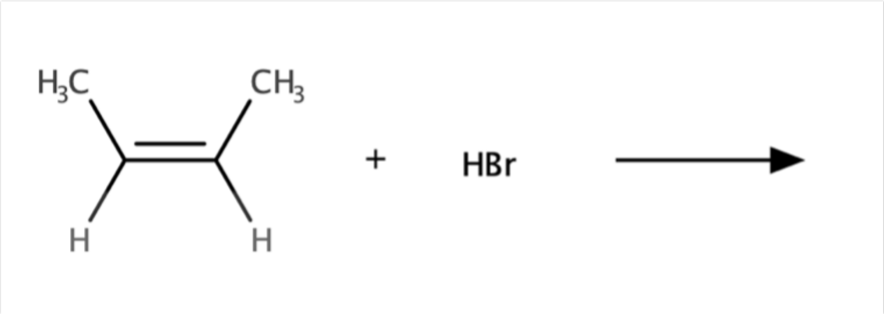
G)

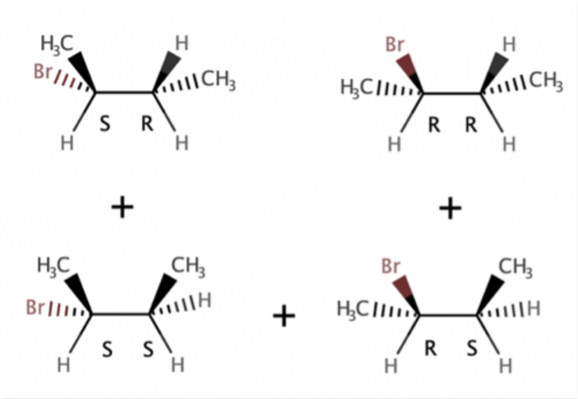
The regioselectivity of electrophilic addition rule: When an asymmetrical alkene undergoes electrophilic addition, the product that predominates is the one that results from the more stable of the two possible carbocation intermediates.

A) When HBr is added, it is the *less* substituted carbocation that forms faster in the rate- determining protonation step, because in this intermediate the carbon bearing the positive charge is located further away from the electron-withdrawing, cation-destabilizing fluorine (CF_3).

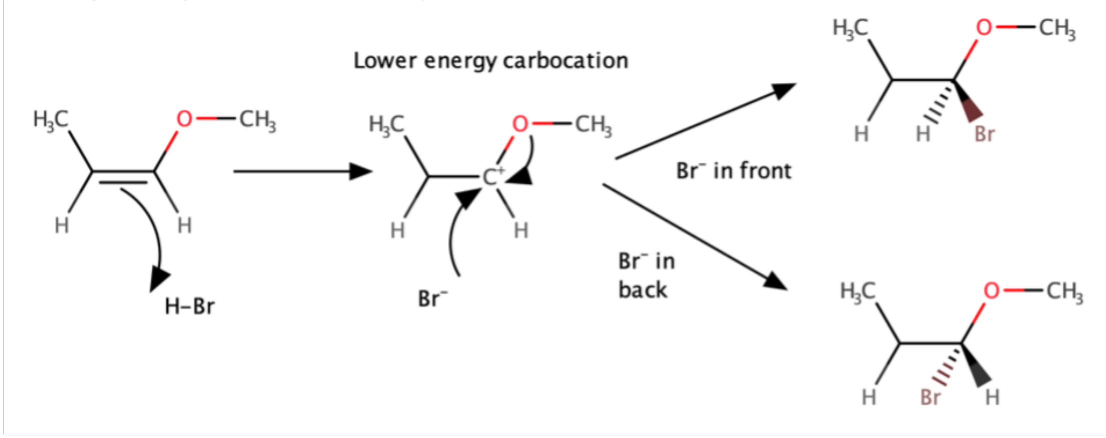


B)

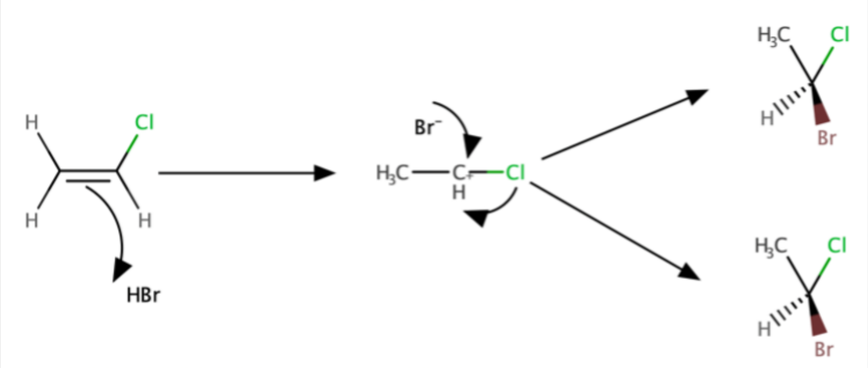


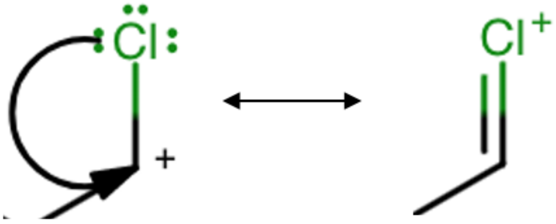


C) OCH_3 group (has +M effect) stabilizes more the neighboring carbocation center than CH_3 group (has low +I effect).



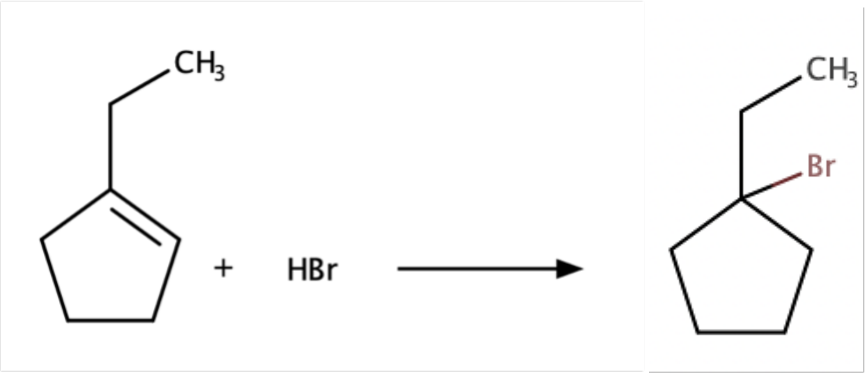
D) The secondary carbocation is more stable due the better stabilization from Cl, and reaction much faster through the secondary carbocation.



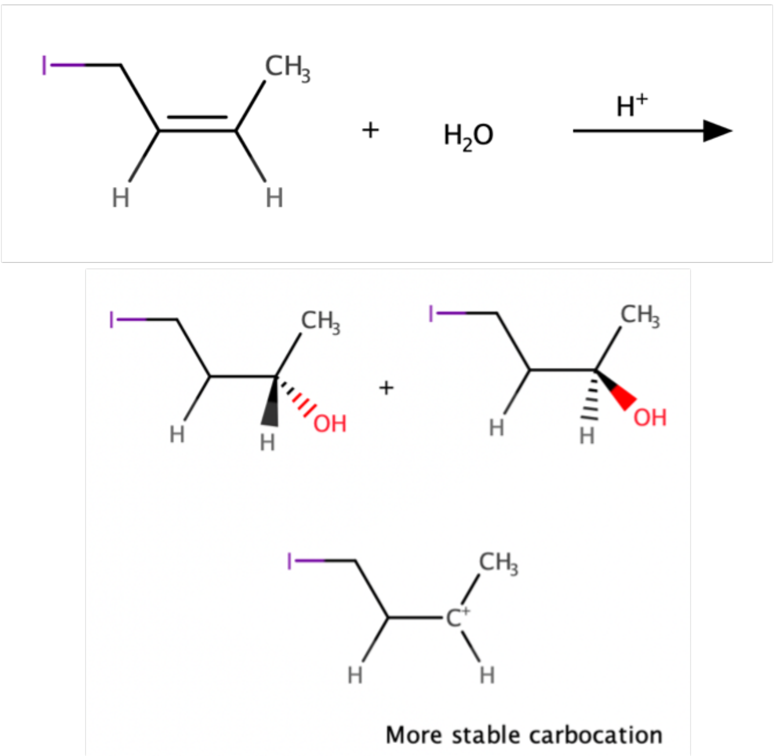


Cl can stabilize the carbocation through resonance.

E)

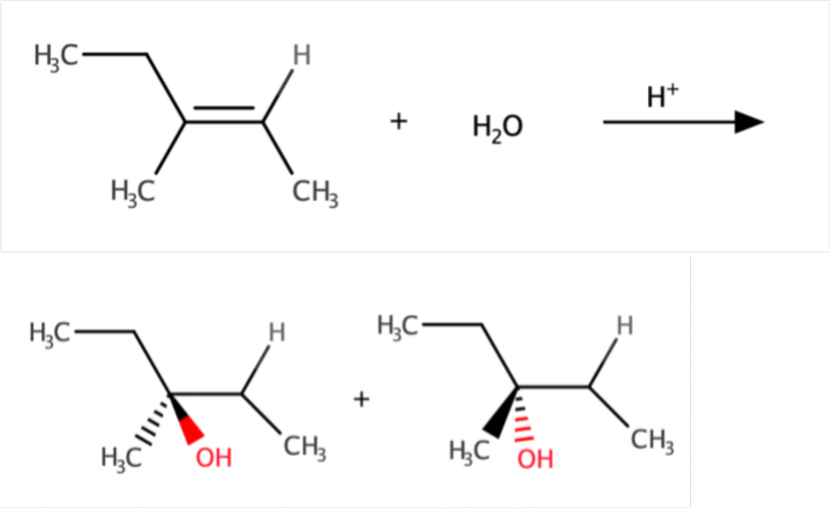


F)



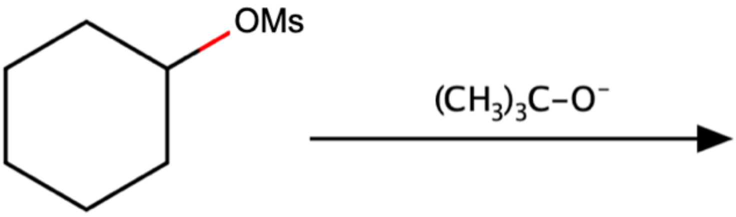
More stable carbocation

G)



7.6 Competition between elimination and substitution E2/SN1/E1/SN2

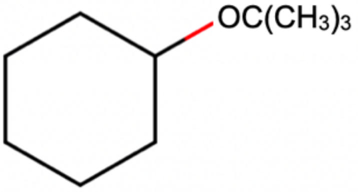
A. Consider the following:



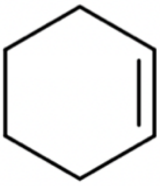
Where OMs is a good leaving group.

Which among the following reactions: SN1, SN2, E1, E2 is MOST likely to dominate? What is the major product formed in the given reaction? What is the mechanism?

A)



B)

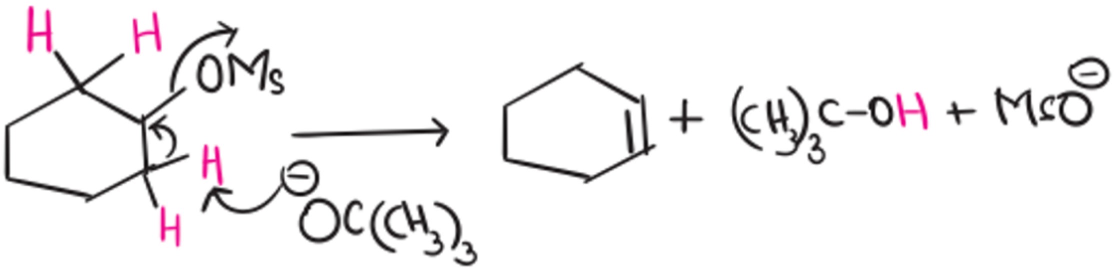


To decide if a reaction proceeds via SN1/SN2/E1/E2, we need to look at multiple factors and rule them out one-by-one. The deciding factors are:

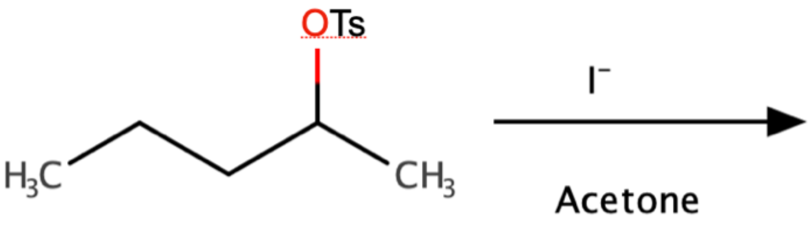
Substrate: Here, we have a secondary substrate. We cannot say for sure which reaction it would undergo without looking at other parameters.

Reagent: (CH3)3CO$^-$ is a **strong base and a very poor nucleophile** owing to its bulkiness and steric hindrance. As a poor nucleophile, we can rule out both SNI and SN2 substitution reactions. A strong base will also favour E2 reaction.

Meaning, it is going to be an E2 reaction:

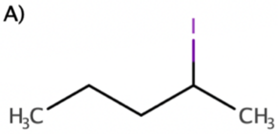


B. Consider the following:



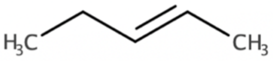
Which among the following reactions: SN1, SN2, E1, E2 is MOST likely to dominate? What is the major product formed in the given reaction? What is the mechanism?

A)



B)

C)

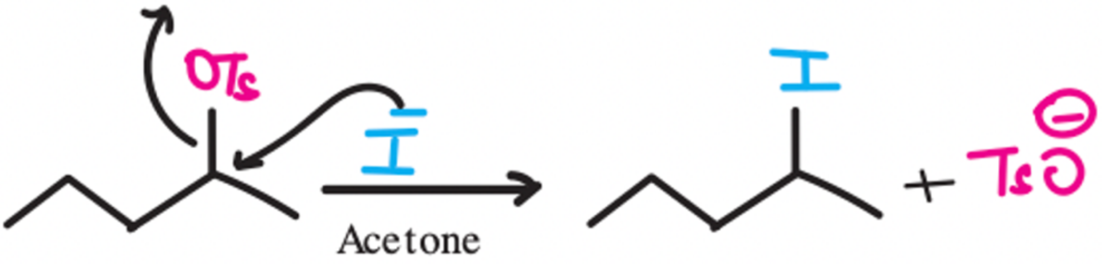


Substrate: Here, we have a secondary substrate. We cannot say for sure which reaction it would undergo without looking at other parameters.

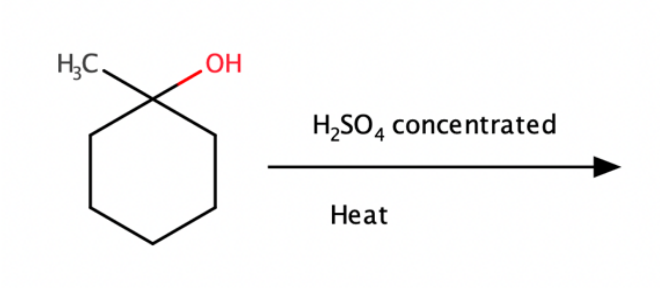
Reagent: I^- is a highly polarisable ion. It is also the weak conjugate base of a strong acid (HI). That means, it is **a good nucleophile but a poor base**. SN1, SN2, ~~E1~~, ~~E2.~~

Solvent: We know that **polar aprotic solvents** like acetone and DMSO would tip the reaction in favour of substitution (SN2) more than elimination (E2).

Meaning, it's going to be an SN2 reaction:

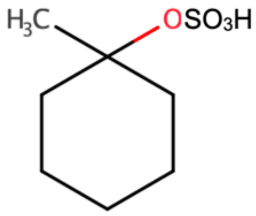


C. Consider the following:

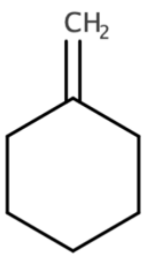


Which among the following reactions: SN1, SN2, E1, E2 is MOST likely to dominate? What is the major product formed in the given reaction? What is the mechanism?

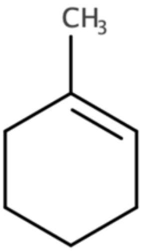
A)



B)



C)

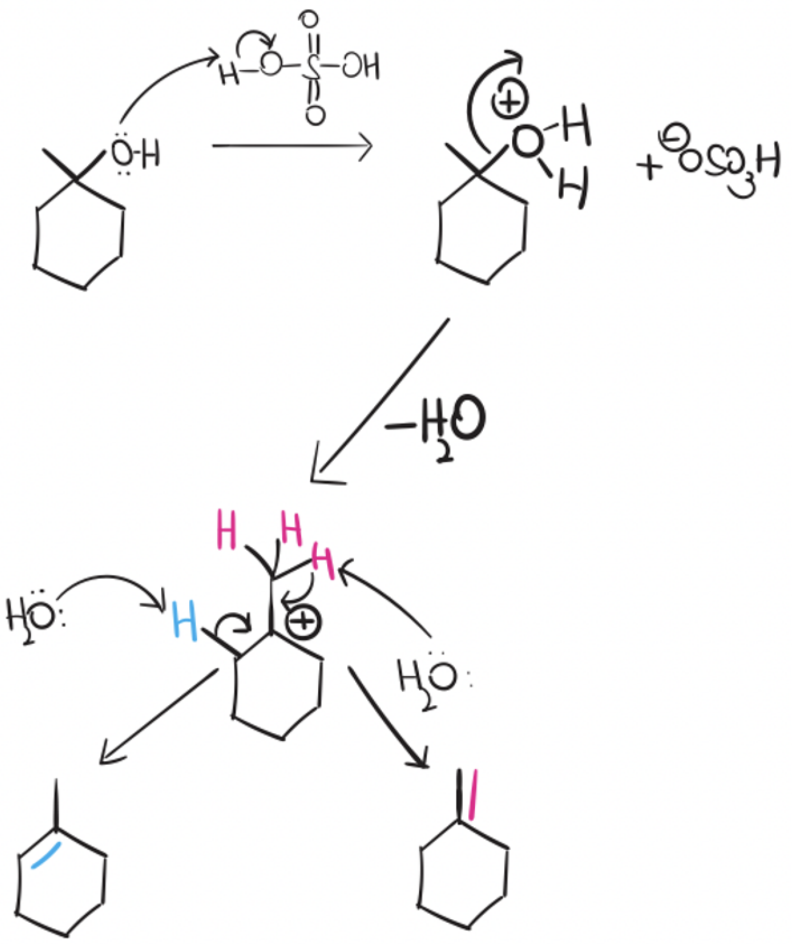


Substrate: Here, we have a secondary alcohol. We cannot say for sure which reaction it would undergo without looking at other parameters.

Reagent: Conc H2SO4 is a **strong acid**. In the presence of a strong acid, the alcohol will most likely undergo SN1 or E1 reaction.

Heat favors elimination reaction over substitution.

Meaning, it's going to be an E1 reaction:

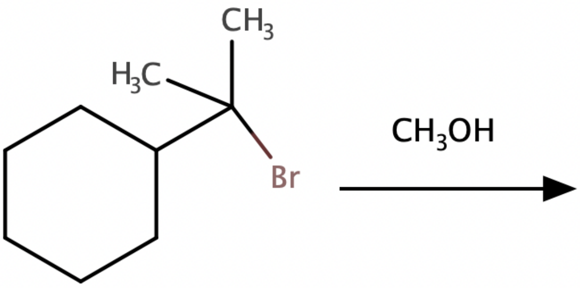


Major product
(Zaitsev)

In a strongly acidic medium, the -OH group gets protonated converting it into a good leaving group. Once the carbocation is formed, it becomes a good candidate for both substitution (SN1) as well as elimination (E1).

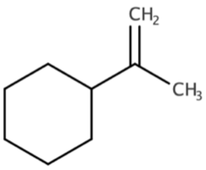
However, HSO30 anion is a poor nucleophile as it is resonance stabilised. This makes SN1 reaction very very slow. In addition to it, elimination product is favoured at higher temperatures.

D. Consider the following:

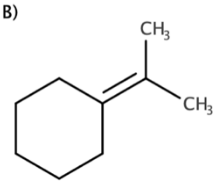


Which among the following reactions: SN1, SN2, E1, E2 is MOST likely to dominate? What is the major product formed in the given reaction?

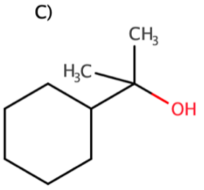
A)



B)

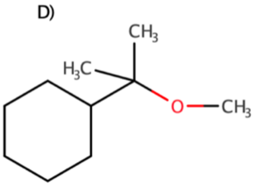


C)



+

D)

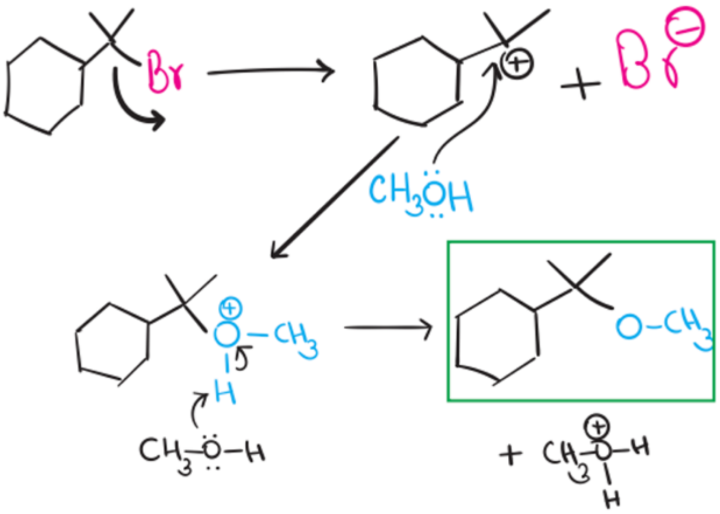


Substrate: Here, we have a tertiary alkyl halide. Being a bulky substrate, we can easily rule out the SN2 reaction. SN1, ~~SN2~~, E1, E2

Reagent: CH3OH is a neutral molecule. It is a weaker nucleophile/base compared to its charged counterpart. Neutral reagents favour SN1 or E1 reactions.

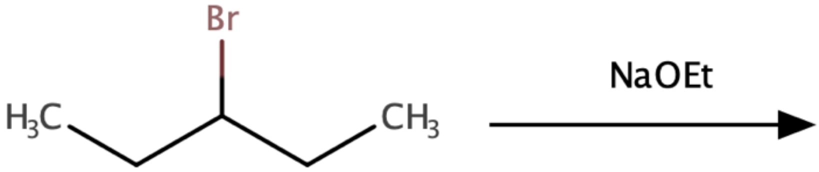
Heat: Largely favours elimination over substitution. Since there is no heat, SN1 is more likely to predominate at lower temperatures.

Meaning, it's going to be an SN1 reaction:



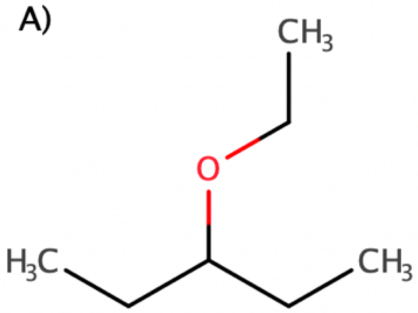
Note: This reaction would likely give a mixture of SN1 and E1 products with the SN1 product being formed in major amounts at lower temperatures.

E. Consider the following:

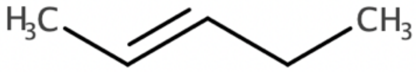


Which among the following reactions: SN1, SN2, E1, E2 is MOST likely to dominate?
What is the major product formed in the given reaction?

A)



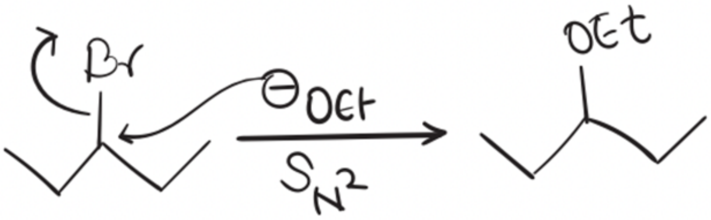
B)



Substrate: Here, we have a secondary substrate. We cannot say for sure which reaction it would undergo without looking at other parameters.

Reagent: Ethoxide ion (OEt) or CH3CH2O is a strong base as well as a strong nucleophile. And we know that, in the presence of such a strong reagent, the alkyl halide can undergo an SN2 as well as an E2 reaction. ~~SN1~~, SN2, ~~E1~~, E2

Meaning, it is going to be both SN2 and E2 reactions:



Note: A polar aprotic solvent would tip the reaction towards an SN2 reaction while a polar protic solvent would favour E2. Even then, with secondary substrates, a mixture of products is quite common.