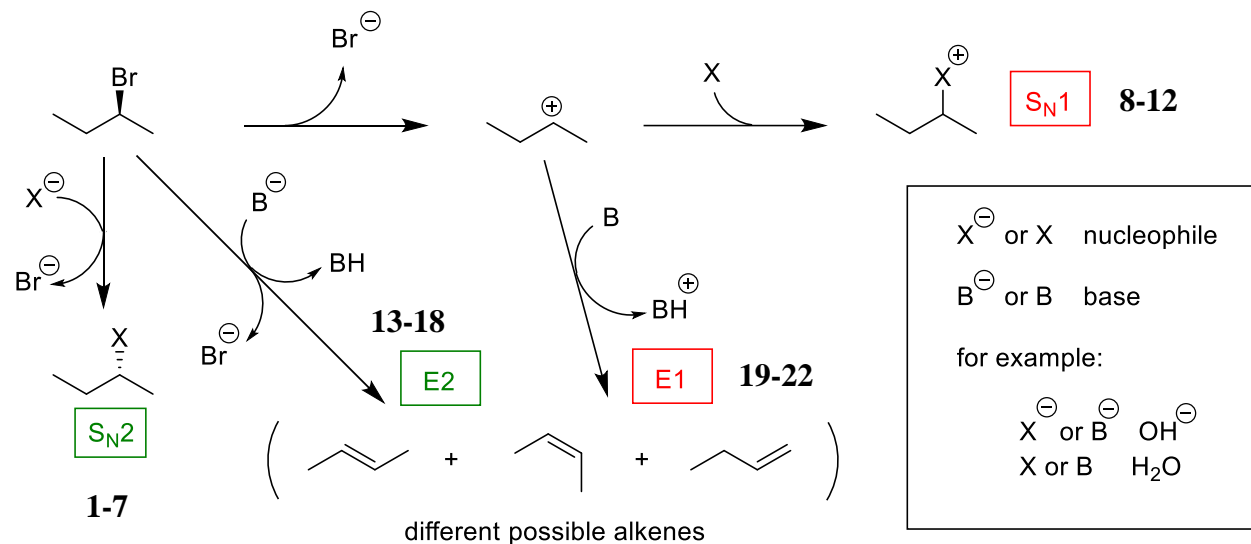


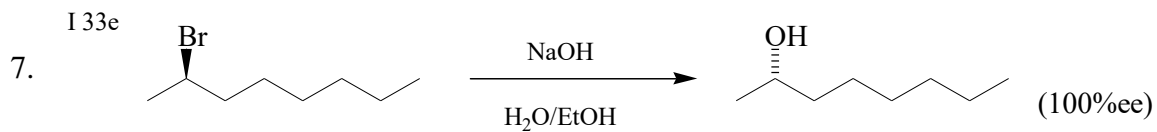
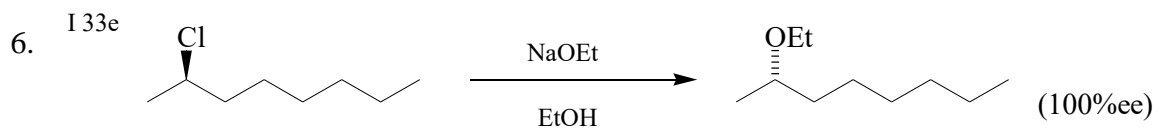
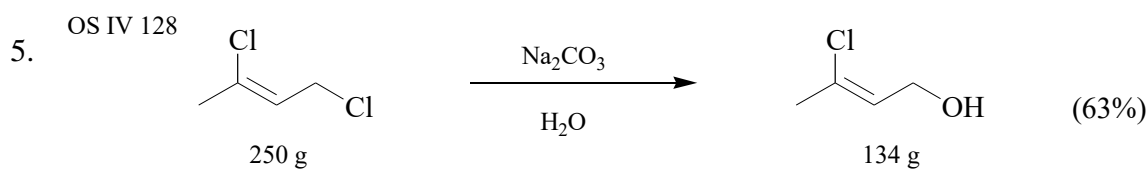
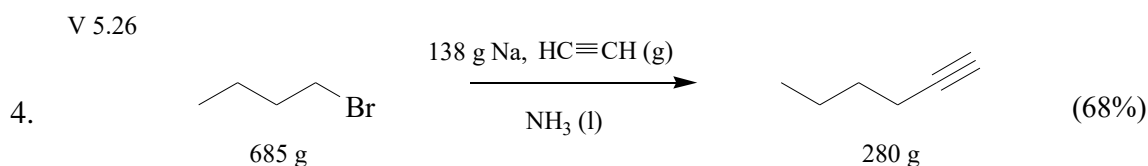
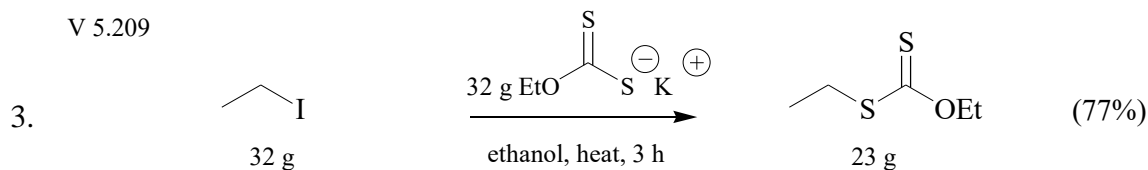
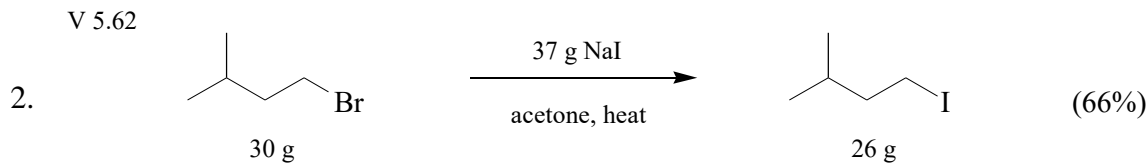
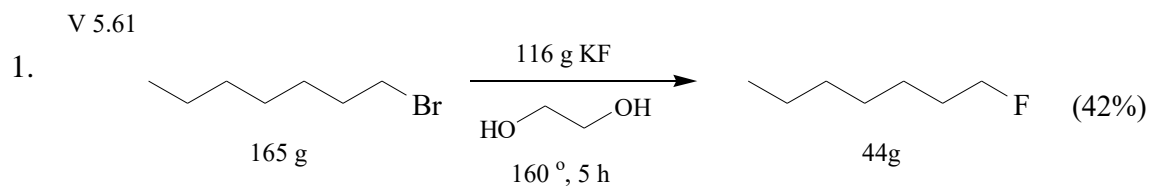
Reactions Overview:

Competition: $E2$ vs S_N2 23-27 $E2$ vs $E1$ vs S_N1 28-31**Topic 33: Substitution mechanisms - unimolecular vs. bimolecular****Topic 34: Substitution - Factors influencing substitution processes - the organic reactant****Topic 35: The Hammond Postulate****Topic 36: Substitution - Factors influencing substitution processes - the nucleophile****Topic 37: Substitution - Factors influencing substitution processes - the solvent****Topic 38: Elimination - Alkenes****Topic 39: Elimination - The $E2$ mechanism****Topic 40: Elimination - the Zaitsev Rule and reaction selectivity****Topic 41: Elimination - The $E1$ mechanism**

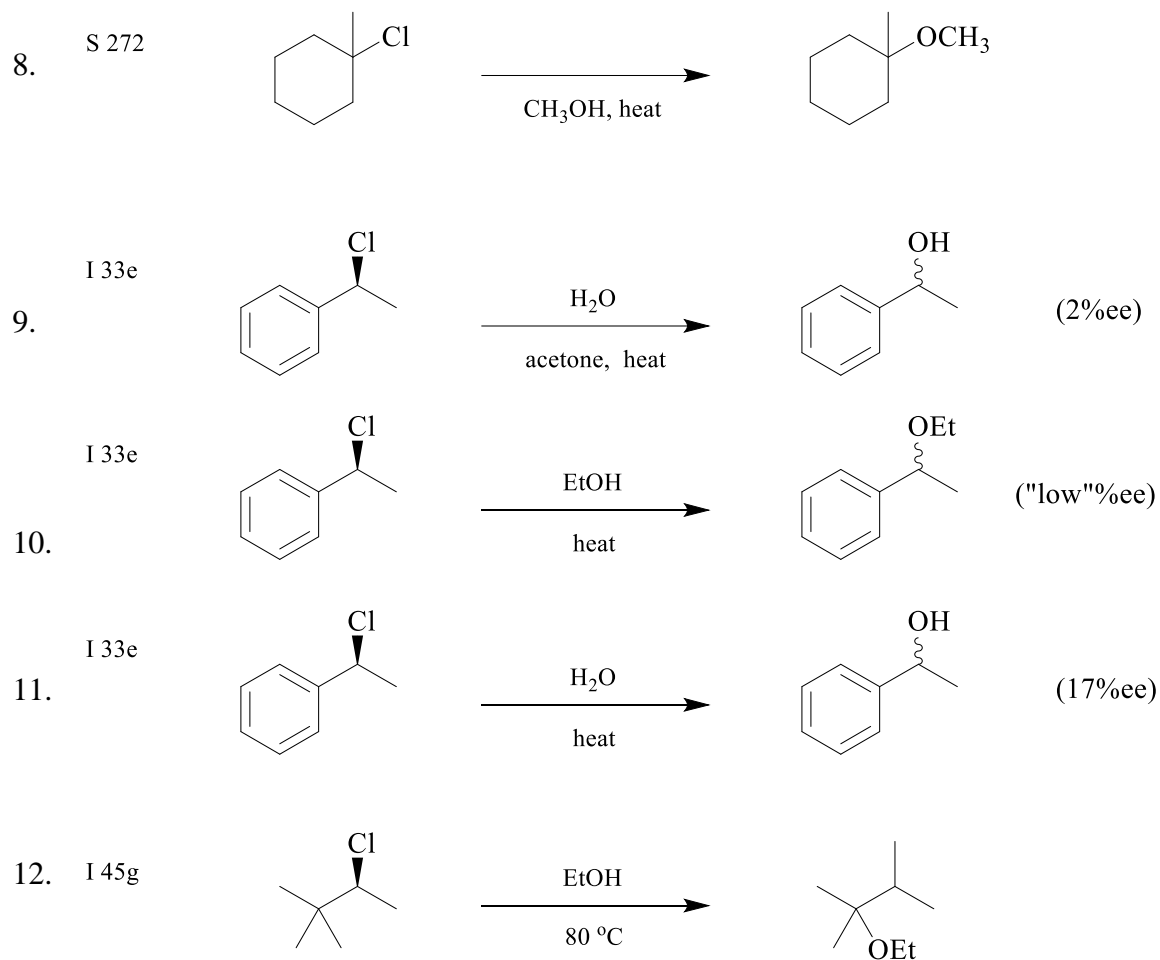
References:

COS: *Compendium of Organic Synthetic Methods*, 1971H: Heathcock, *Introduction to Organic Chemistry*, 1976I: Ingold, *Structure and Mechanism in Organic Chemistry*, 2nd Ed., 1969M: March, *Advanced Organic Chemistry*, 3rd Ed., 1985OS: *Organic Synthesis Collective Volumes*S: Sorrell, *Organic Chemistry*, 1997V: Vogel, *Textbook of Practical Organic Chemistry*, 5th Ed., 1989

Examples of S_N2 Reactions of Alkyl and Allylic Halides



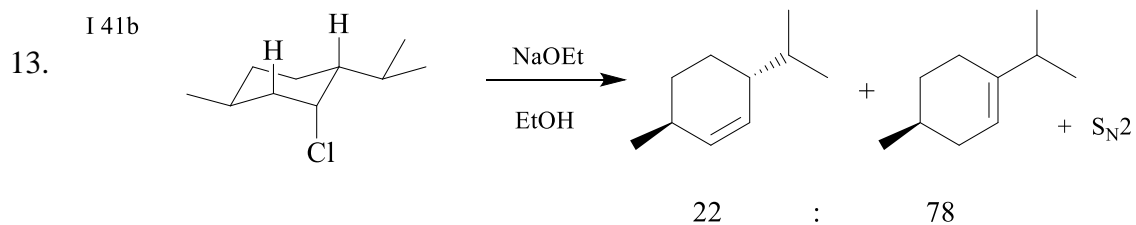
Examples of S_N1 Reactions of Alkyl and Benzylic Halides



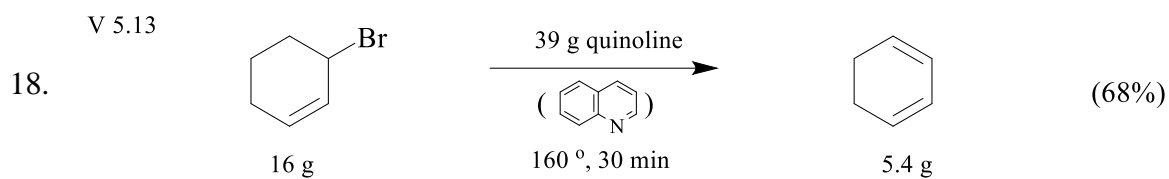
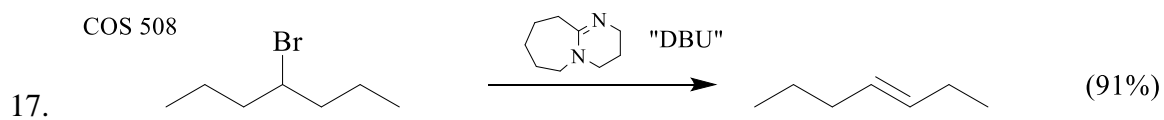
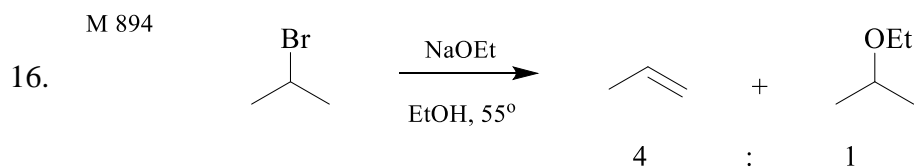
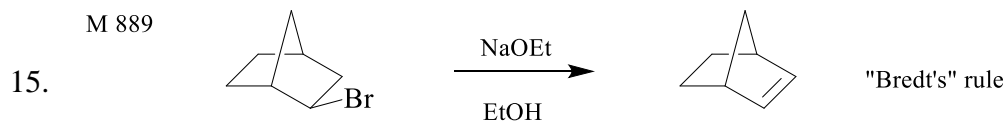
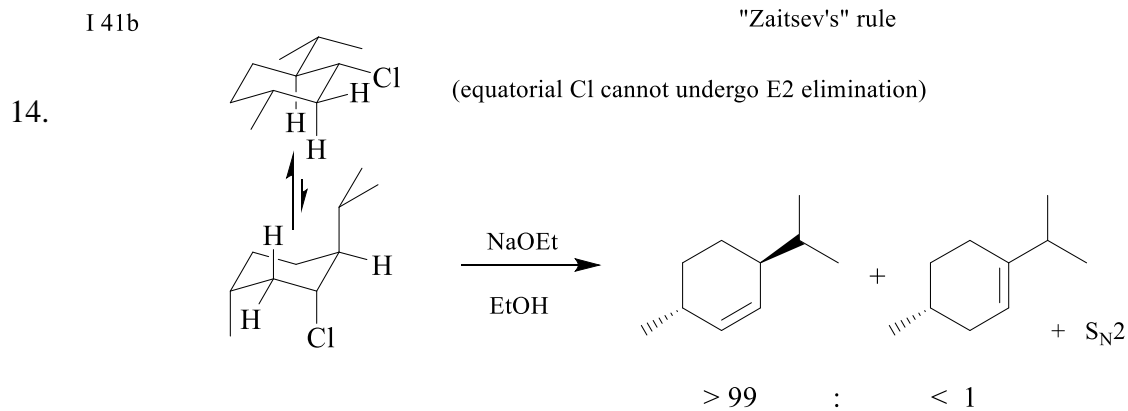
Regarding S_N1 reactions, Ingold states:

It is to be understood that these reactions [in aqueous ethanol] must each give several products, in general, an alcohol, an ethyl ether, and one or more olefins; for the carbonium ion formed by the initial heterolysis can end its life either by the uptake of [a nucleophile] or by the loss of a proton.

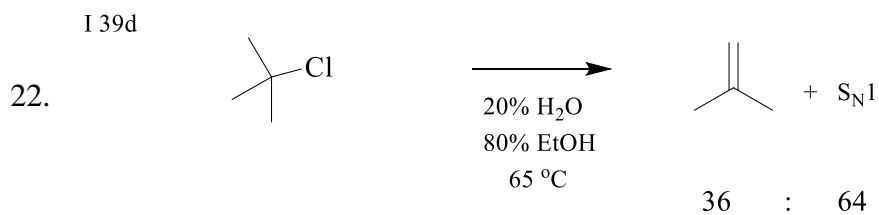
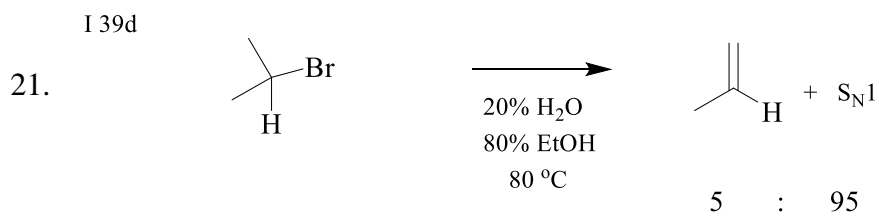
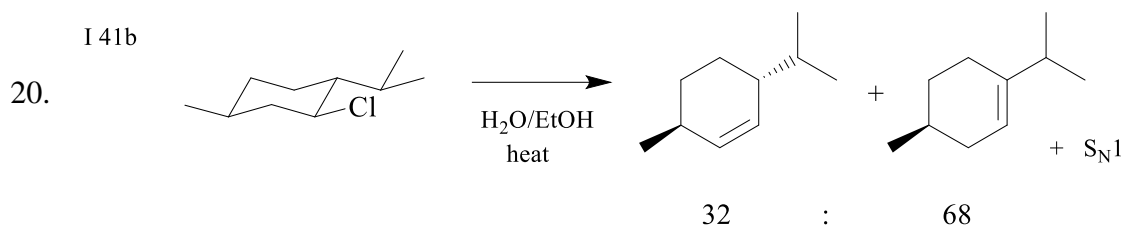
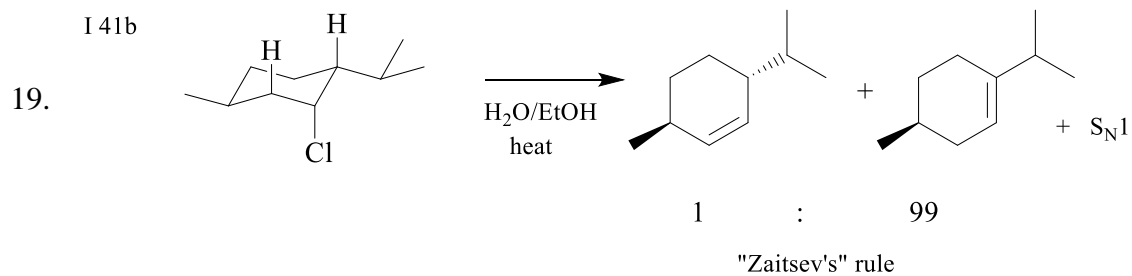
Examples of *E2* Reactions of Alkyl and Allylic Halides



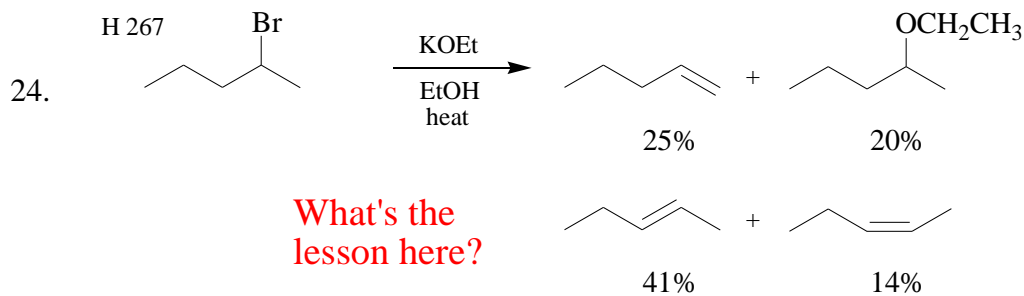
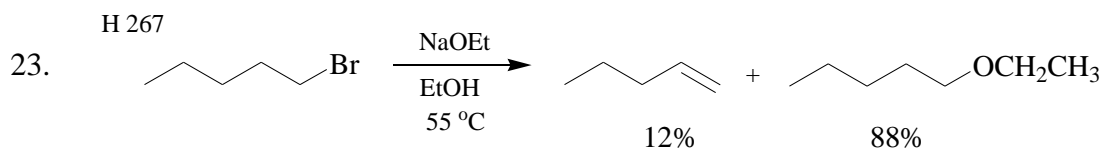
"Zaitsev's" rule



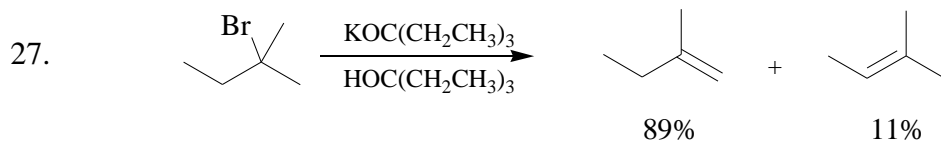
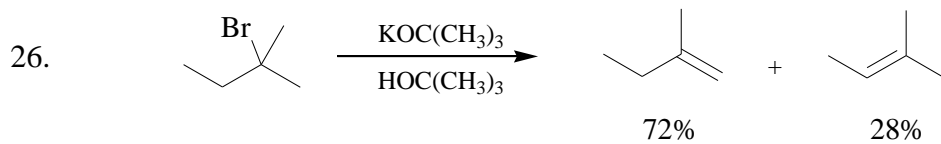
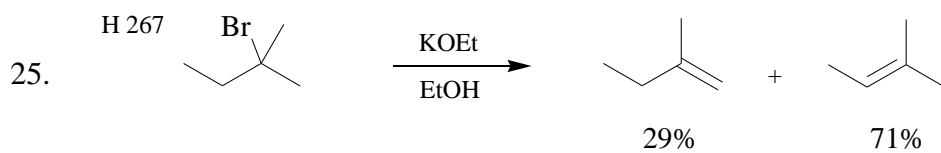
Examples of *E1* Reactions of Alkyl Halides



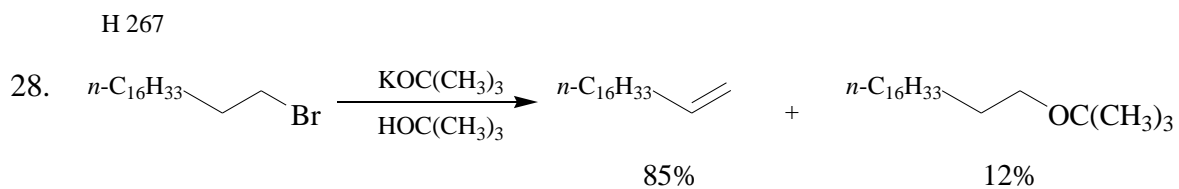
Examples of E2/S_N2 Competition



What's the lesson here?



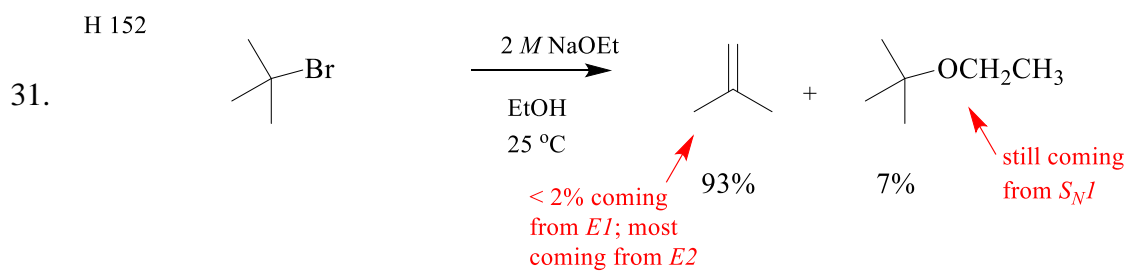
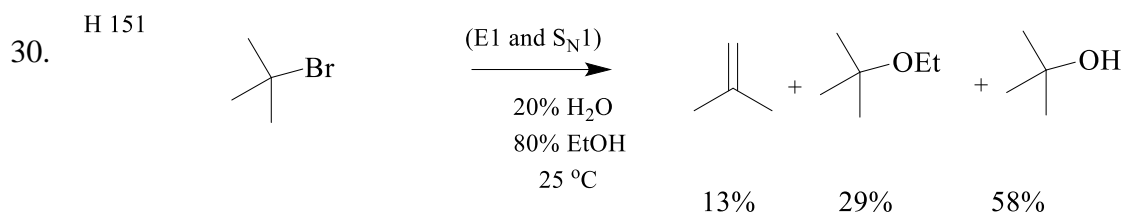
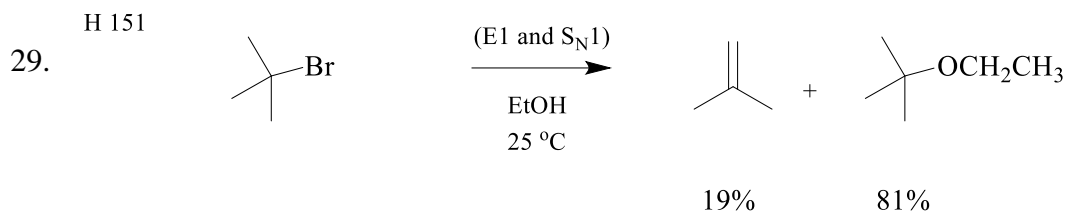
What's the lesson here?



What's the lesson here?

What would you try that might work even better?

Examples of *E2/E1/S_N1* Competition



The point: Increasing the concentration of a strong base accelerates the *E2* reaction. The *E1* and *S_N1* reactions still occur, but they become only minor pathways to product.

Topic 33: Substitution mechanisms - unimolecular vs. bimolecular

- 33.1 What does *concerted* mean in the context of mechanistic steps?
- 33.2 What do S_N1 and S_N2 stand for?
- 33.3 Why must an S_N1 reaction involve at least two mechanistic steps, by definition?
- 33.4 Why is it particularly common for an S_N1 reaction to involve three mechanistic steps?
- 33.5 What are three characteristics of an S_N1 reaction?
- 33.6 What are three characteristics of an S_N1 reaction?
- 33.7 How are p atomic orbitals involved in both S_N1 and S_N2 mechanisms? (In which mechanism is the p orbital empty, and in which is it full?)
- 33.8 Why are S_N1 reactions prone to producing mixtures of several products?
- 33.9 Why is it much less likely for a reaction with an S_N2 mechanism to produce a mixture than one with an S_N1 mechanism?

Topic 34: Substitution - Factors influencing substitution processes - the organic reactant

- 34.1 Why are S_N1 reactions never observed for primary alkyl halides?
- 34.2 Why are S_N2 reactions never observed for tertiary alkyl halides?
- 34.3 What does the stability of carbocations have to do with the preference for S_N2 and S_N1 reaction at primary and tertiary carbons, respectively? (And why is there this difference in stability in the first place?)
- 34.4 What does steric hindrance have to do with the preference for S_N2 and S_N1 reaction at primary and tertiary carbons, respectively?
- 34.5 What is the order of reactivity of alkyl halides going down the periodic table - F, Cl, Br, I? How do you explain that?
- 34.6 Why are vinyl halides and aryl halides never involved in S_N1 or S_N2 reactions?

Topic 35: The Hammond Postulate

- 35.1 What was George Hammond's postulate?
- 35.2 How does the Hammond postulate relate to comparisons of endothermic and exothermic mechanistic steps?
- 35.3 Why might the Hammond postulate be useful in discussions of organic reaction mechanisms?
- 35.4 How is the Hammond postulate applicable in a discussion of substitution reactions?
- 35.5 What makes the Hammond postulate a postulate and not a law?

Topic 36: Substitution - Factors influencing substitution processes - the nucleophile

- 36.1 How are basicity and nucleophilicity related to thermodynamics and kinetics?
- 36.2 What characterizes a “good” nucleophile? Examples?
- 36.3 Why are negatively charged nucleophiles (Cl^- , CN^- , $\text{RC}\equiv\text{C}^-$) generally more reactive than neutral nucleophiles, such as H_2O , CH_3OH , NH_3)?
- 36.4 Why are negatively charged species rarely the nucleophile in S_N1 reactions?
- 36.5 What is solvolysis? Which mechanism, S_N1 or S_N2 , is it more closely associated with? Why?

Topic 37: Substitution - Factors influencing substitution processes - the solvent

- 37.1 What does aprotic mean?
- 37.2 What are several examples of protic and aprotic solvents?
- 37.3 Why might the choice of an aprotic solvent make an S_N2 reaction more likely to happen, whereas choice of a protic solvent would slow it down?
- 37.4 Why is it common to use protic solvents for S_N2 reactions even though they are not as “good” solvents for that type of reaction?
- 37.5 Why does the order of reactivity of halide nucleophiles reverse in going from a protic to aprotic solvents?
- 37.6 What is the “catch” in relation to using protic solvents in S_N1 reactions?
- 37.7 Why is a protic solvent necessary for a solvolysis reaction?

Topic 38: Elimination - Alkenes

- 38.1 What constitutes a β -elimination reaction?
- 38.2 What are the three types of disubstituted alkenes?
- 38.3 Why do we classify cis and trans isomers as diastereomers?
- 38.4 What is the trend in stability of alkenes, based on substitution (mono, di, tri, tetra)?
- 38.5 What is the general “explanation” for this trend (using Google)? Is this the explanation your author gives?
- 38.6 What is hyperconjugation, and how might it explain the trend in stability of substituted alkenes?

Topic 39: Elimination - The *E2* mechanism

- 39.1 What are the essential features of the *E2* mechanism? Why “2” here?
- 39.2 What special alignment of atoms is necessary for (or at least, strongly favors) an *E2* mechanism?
- 39.3 Besides strong RO⁻ bases, what nitrogen-containing weak bases are popular for effecting *E2* reactions? Your author may refer to these as strong bases, but technically they are not strong bases; all amines are weak bases.]
- 39.4 Which nitrogen atom of DBN accepts the proton? Why this one and not the other?
- 39.5 What is so special about DBN and DBU? [HINT: What makes them poor nucleophiles? And what does that have to do with this question?]
- 39.6 Which solvent - nonpolar, polar aprotic, or protic - best promotes *E2* reactions? Why?
- 39.7 What do these abbreviations stand for: DMF, DMSO?
- 39.8 If you needed to carry out an *E2* reaction in the lab, why would you perhaps not choose DMSO as a solvent for an *E2* reaction? (Give two good reasons.)

Topic 40: Elimination - the Zaitsev Rule and reaction selectivity

- 40.1 What is the Zaitsev/Saytzeff/Zaitseff Rule?
- 40.2 Why can't people seem to agree on how to spell Zaitsev's name?
- 40.3 When does the Zaitsev Rule apply? When does it not?
- 40.4 What does it mean for a reaction to be regioselective?
- 40.5 What does it mean for a reaction to be stereoselective?

Topic 41: Elimination - The *E1* mechanism

- 41.1 What are the principal characteristics of the *E1* mechanism?
- 41.2 How it is related to the *S_N1* mechanism?
- 41.3 Can you draw a proper energy diagram (meaning, fully mass-balanced, with energy arrows pointing in the correct direction) for the *E1* elimination of 2-butyl iodide reacting with sodium hydroxide? [Careful! What is the actual base here?]
- 41.4 Why is it safe to say that the base in an *E1* reaction is almost always just the solvent itself?
- 41.5 Why is it safe to say that a reaction involving an *E1* mechanism is certain to give a mixture of several products?
- 41.6 For what two types of alkyl halides is the *E1* mechanism never observed?
- 41.7 Given a 2° alkyl halide, what sorts of things can we do to avoid a reaction proceeding by the *E1* or *S_N1* mechanism?