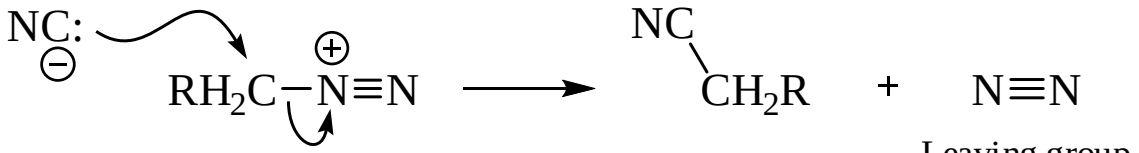
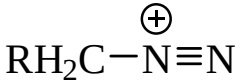
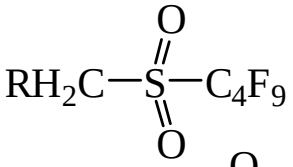
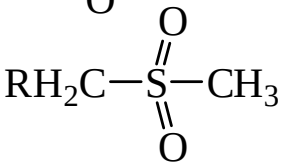
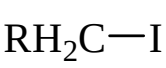
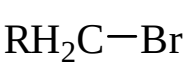
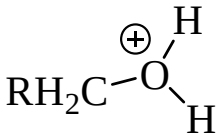
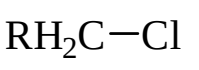
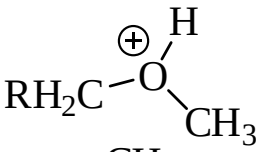
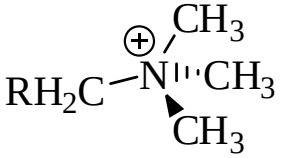
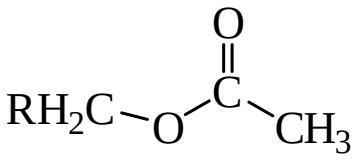
Common Leaving Groups



Class of compound	Leaving group	
 Diazonium salt	N_2	Excellent leaving groups
 Nonaflate	$C_4F_9SO_3^-$	
 Mesylate	$CH_3SO_3^-$	
 Iodides	I^-	
 Bromides	Br^-	
 Protonated alcohols	H_2O	Good leaving groups
 Chlorides	Cl^-	
 Protonated ethers	CH_3OH	
 Quaternary Ammonium Salts	$N(CH_3)_3$	

Poor Leaving Groups

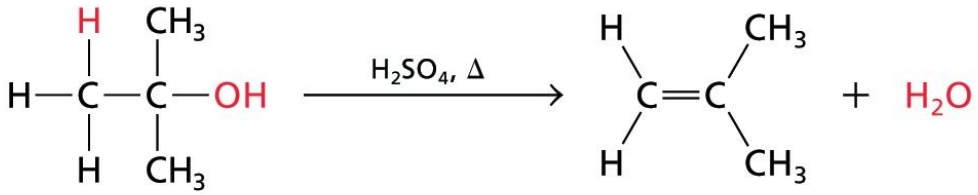
RH_2C-F	Fluorides	F^-
	Acetates	Acetate anion, $CH_3CO_2^-$
RH_2C-OH	Alcohols	Hydroxide, HO^-
RH_2C-H	Hydrides	Hydride, H^-
RH_2C-NH_2	Amines	Amide, NH_2^-
RH_2C-CH_3	Alkanes	CH_3^-

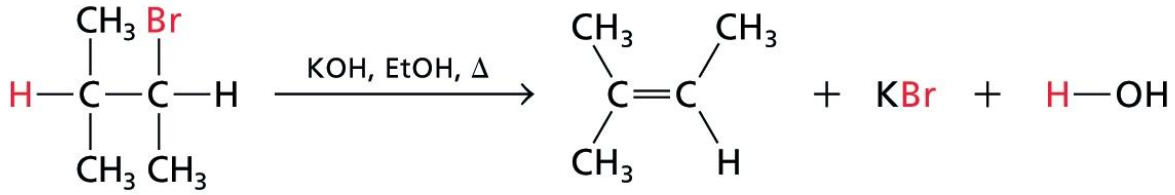
Very poor leaving groups

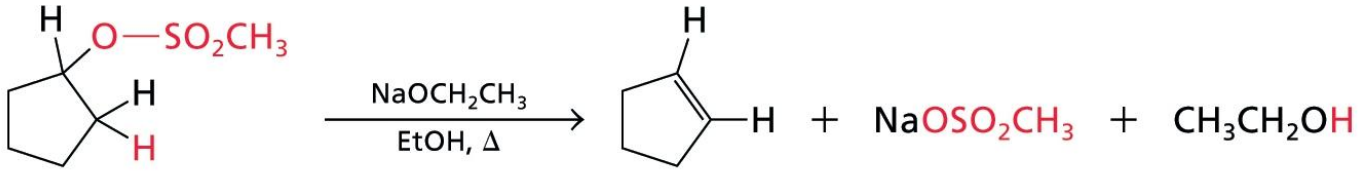
Elimination Reactions

Whenever substitution reactions are possible, we must also consider whether or not elimination reactions might occur under the same reaction conditions.

In elimination reactions, a "neutral" molecule is 'eliminated' from the substrate to form a **π bond**. The π bond is formed between the two carbon atoms that bore the two parts of the eliminated molecule:







Elimination Reactions – The E1 Mechanism

The substrates that favour E1 reactions are the same that favour S_N1 reactions:

- A substrate bearing a good leaving group attached to a tetrahedral carbon atom.
- A substrate that can form a relatively stable carbocation.

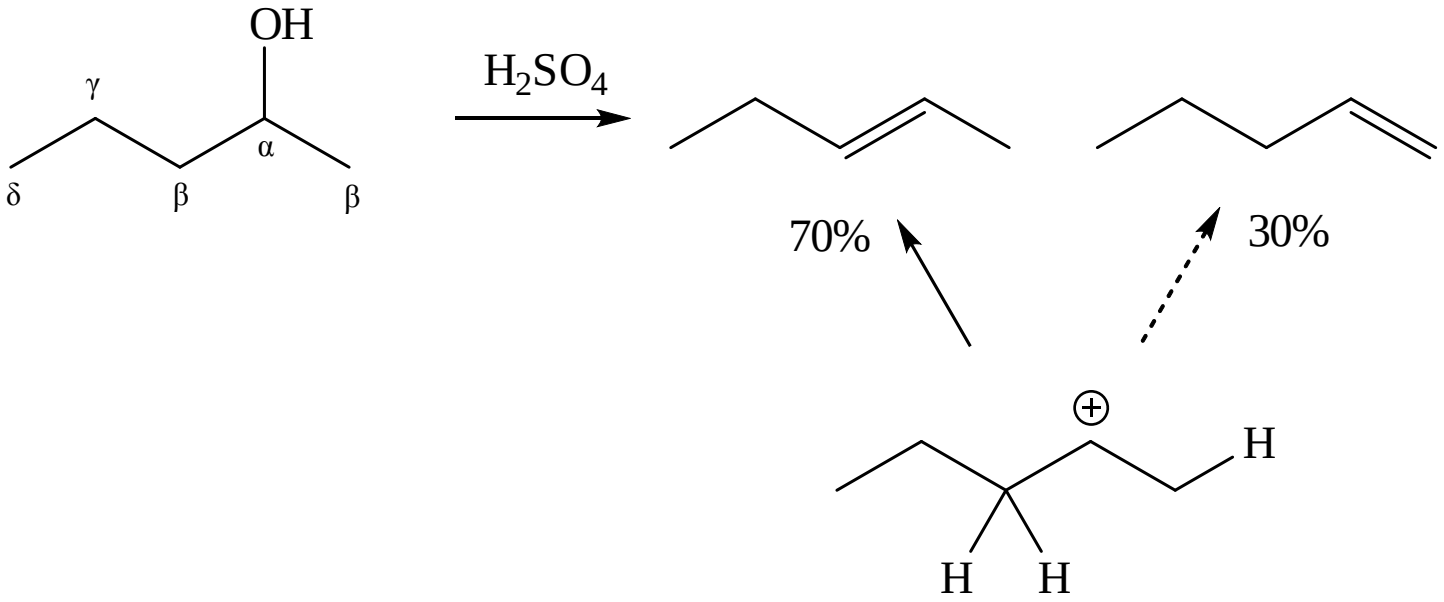
The difference between E1 and SN1 reactions is in the type species which reacts with the substrate. E1 reactions are favoured with:

- Bases that are poor nucleophiles (good nucleophiles will favour substitution reactions).

- **Remember:** Substitution and Elimination reactions are always competing (whenever possible).

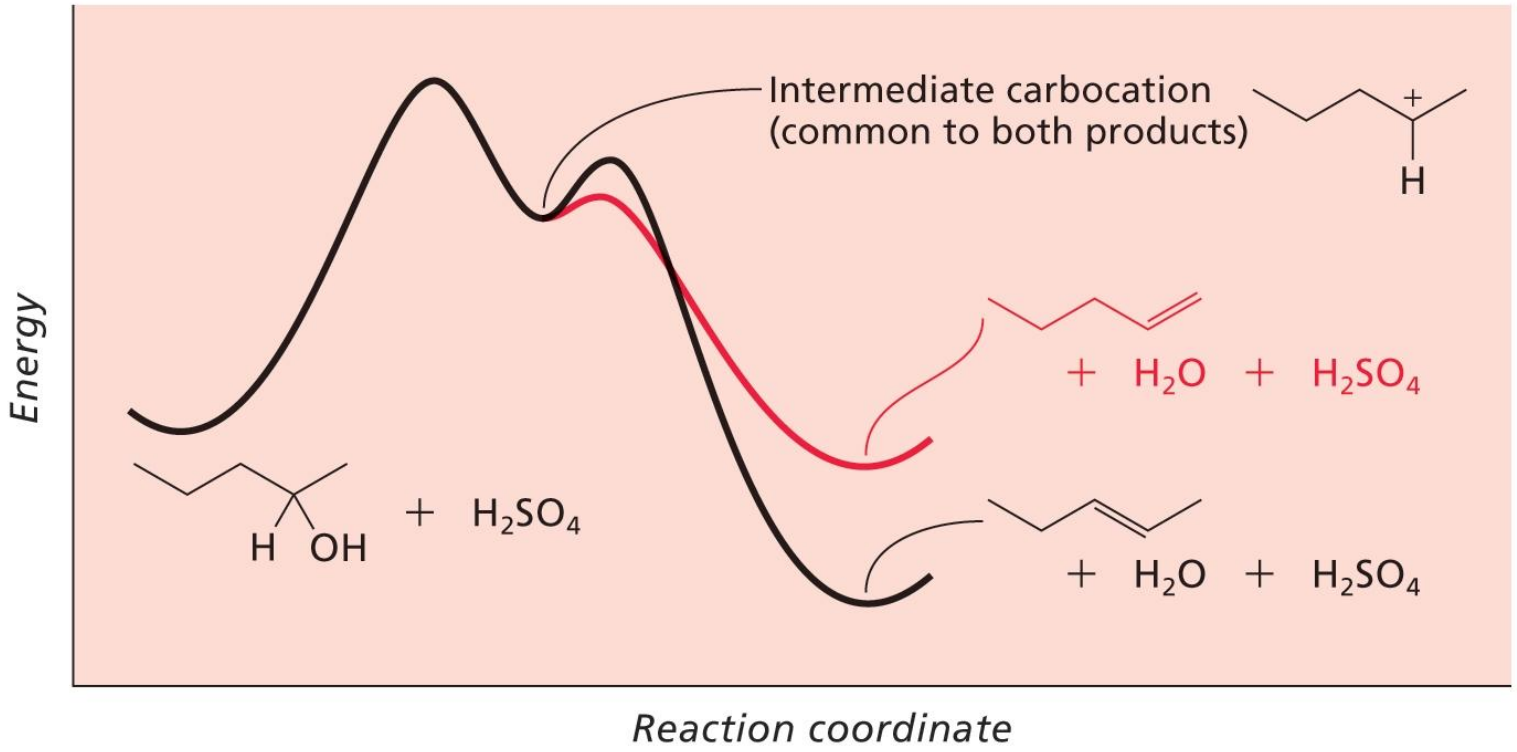
E1 Reactions – Stereochemistry and Regiochemistry

A different elimination product is possible for every unique type of H beta (β) to the carbocation carbon.



Elimination Reactions - Kinetic vs. Thermodynamic Products

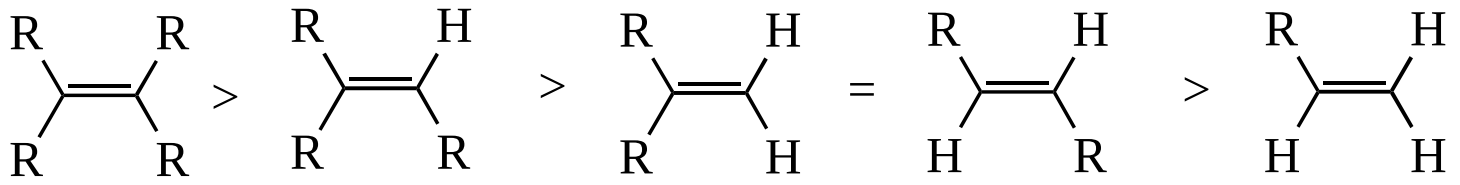
1-pentene is the kinetic product (meaning it is easier to form) and 2-pentene is the thermodynamic product (meaning it is more stable).

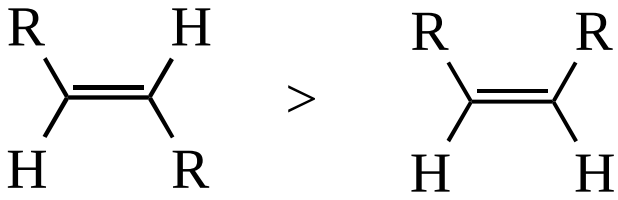


Elimination reactions that occur under thermodynamic control are said to form the **Saytzeff products**.

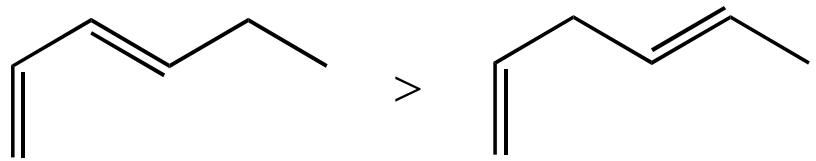
Alkene Stability

C atoms with more s character tend to form stronger bonds with other carbons.

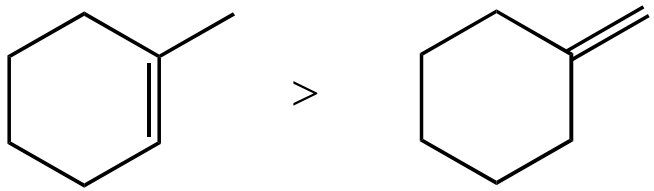




trans > cis



Conjugate > skipped

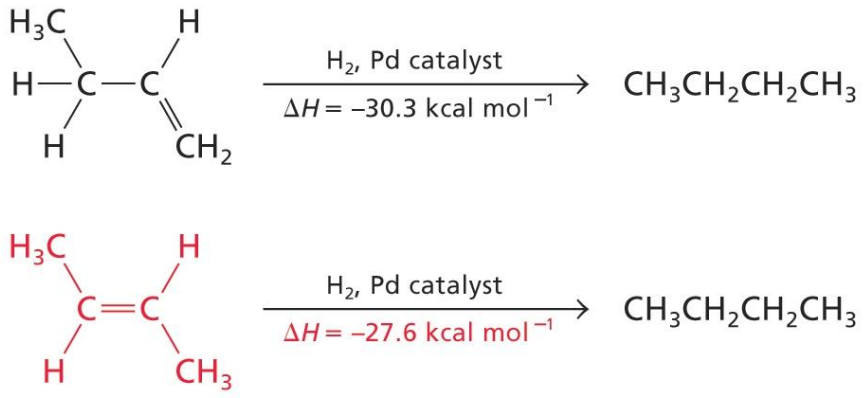


Endocyclic > exocyclic

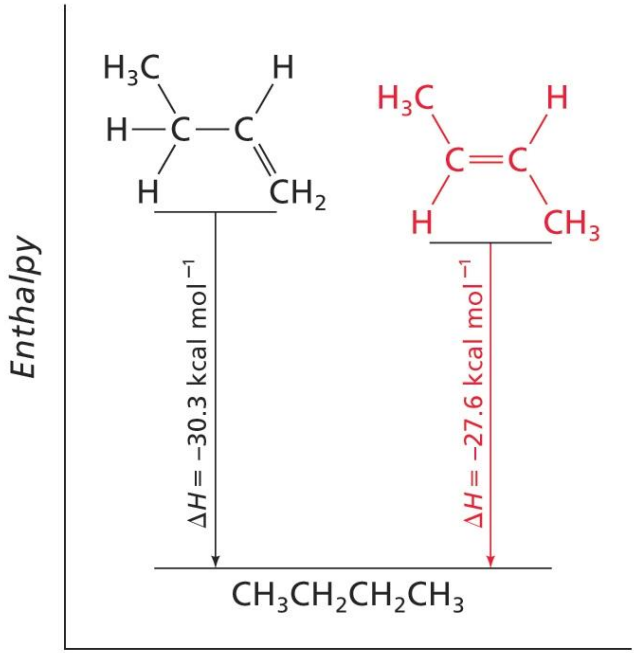
Elimination Reactions - Kinetic vs. Thermodynamic Products

Alkene stability is determined by heats of hydrogenation.

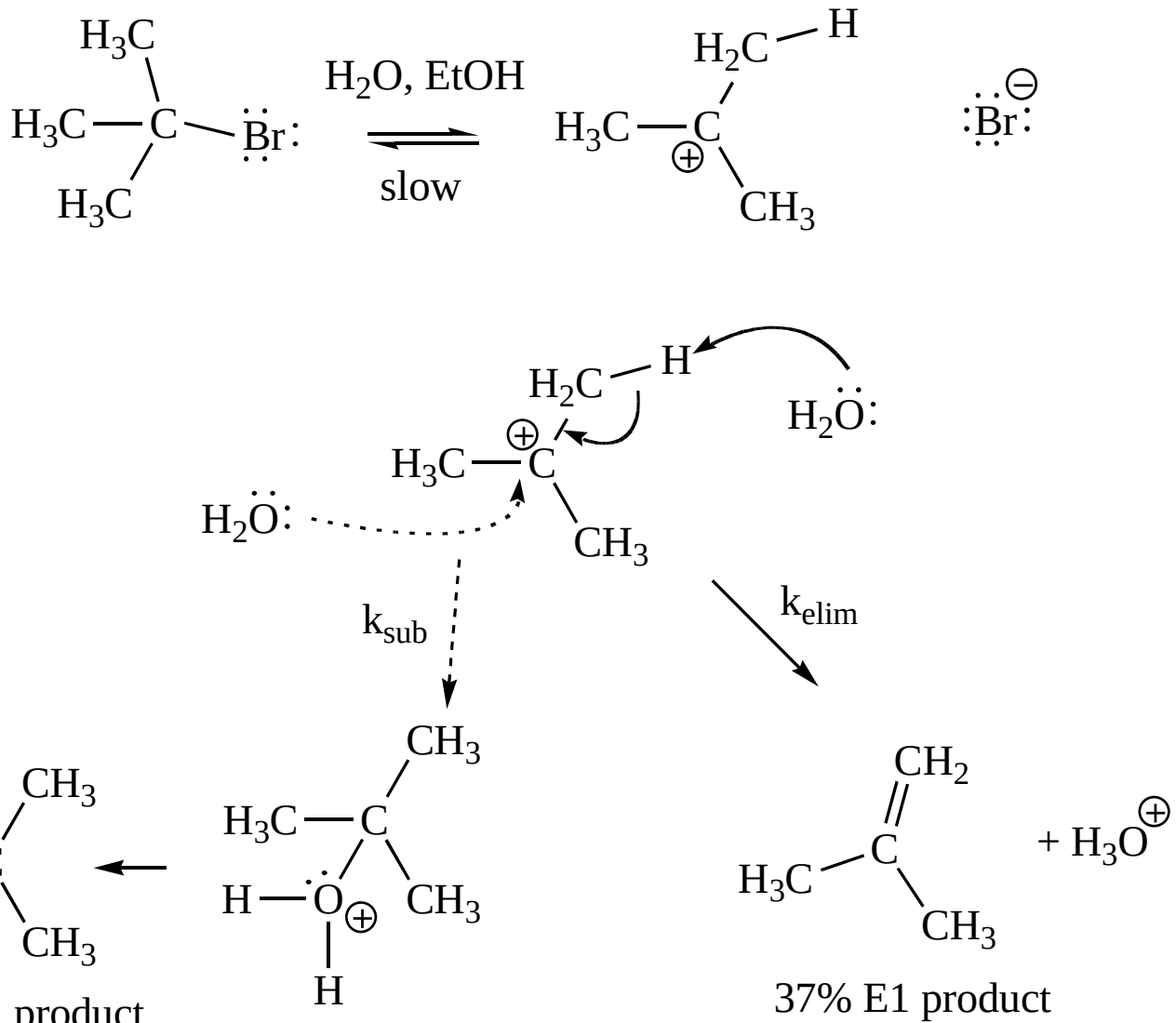
a.



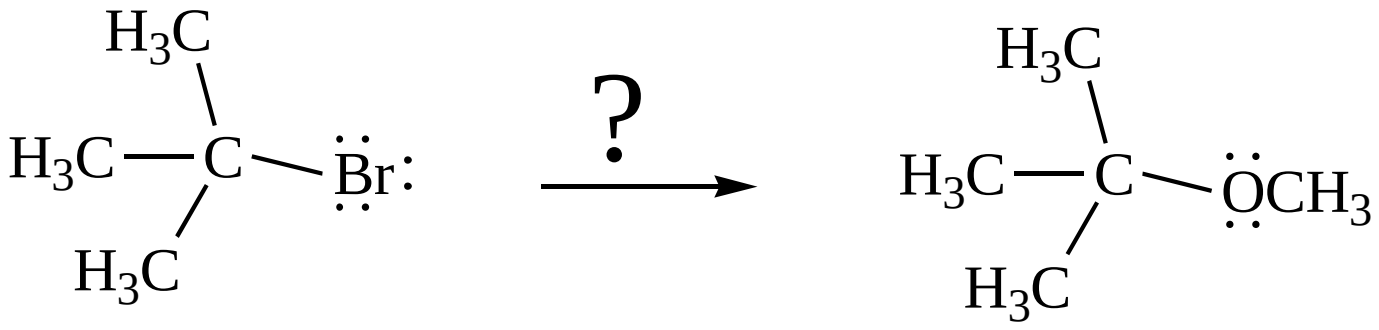
b.



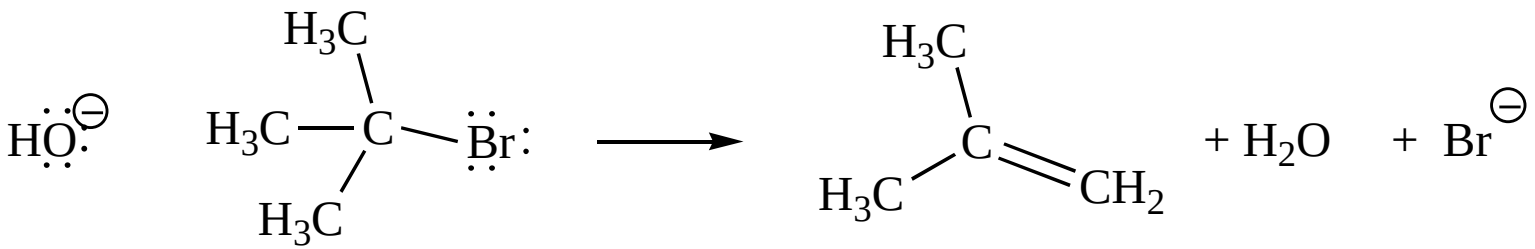
E1 Reactions of Alkyl Halides



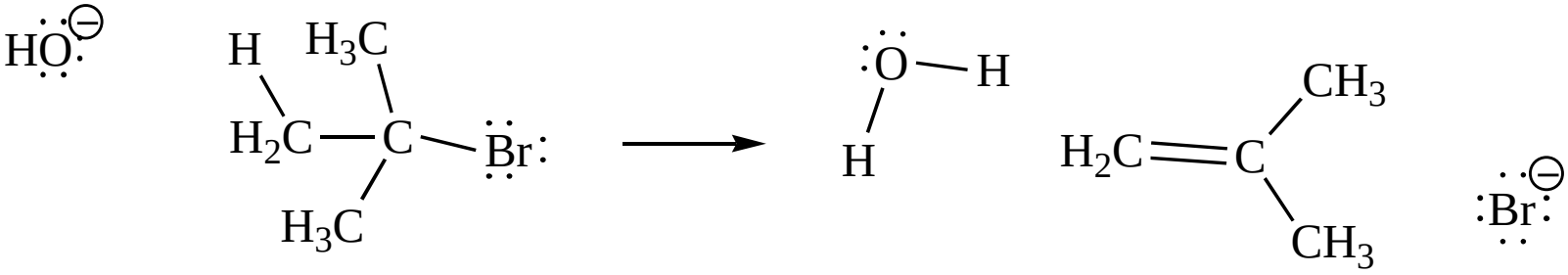
If you want SN1, what nucleophile is best?



The E2 Reaction



The mechanism:

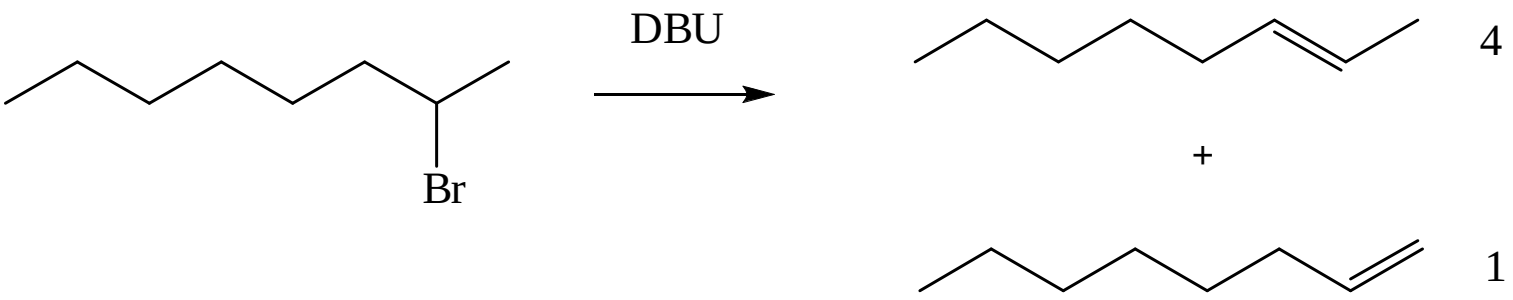


Elimination Reactions – E2 Reaction

E2 reactions are favoured for:

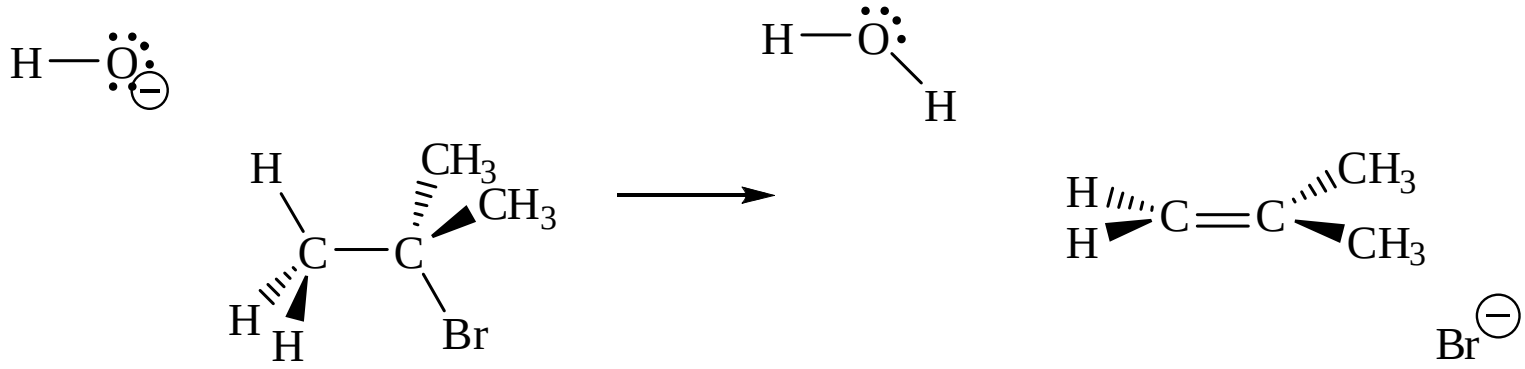
- Substrates bearing a good leaving group attached to a tetrahedral carbon atom.
- Strong non-nucleophilic bases .

The Saytzeff product is generally the major product:



Propose a mechanism to account for the two products formed:

E2 Reactions – Stereochemistry and Regiochemistry

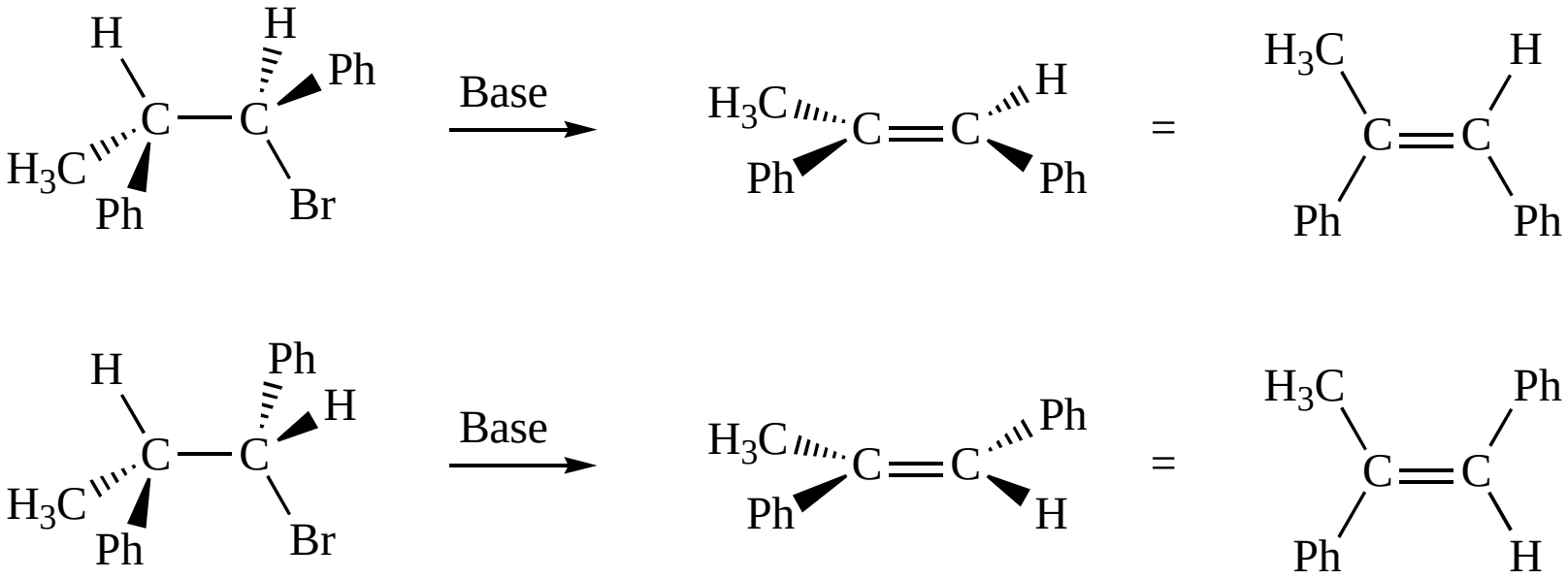


The β-proton pulled off by the base must be anti-periplanar to the leaving group. This reaction is referred to as a "beta-elimination".

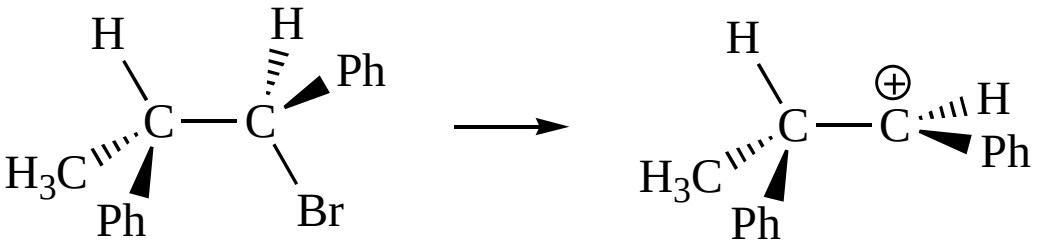
Why?

Stereochemical Consequences

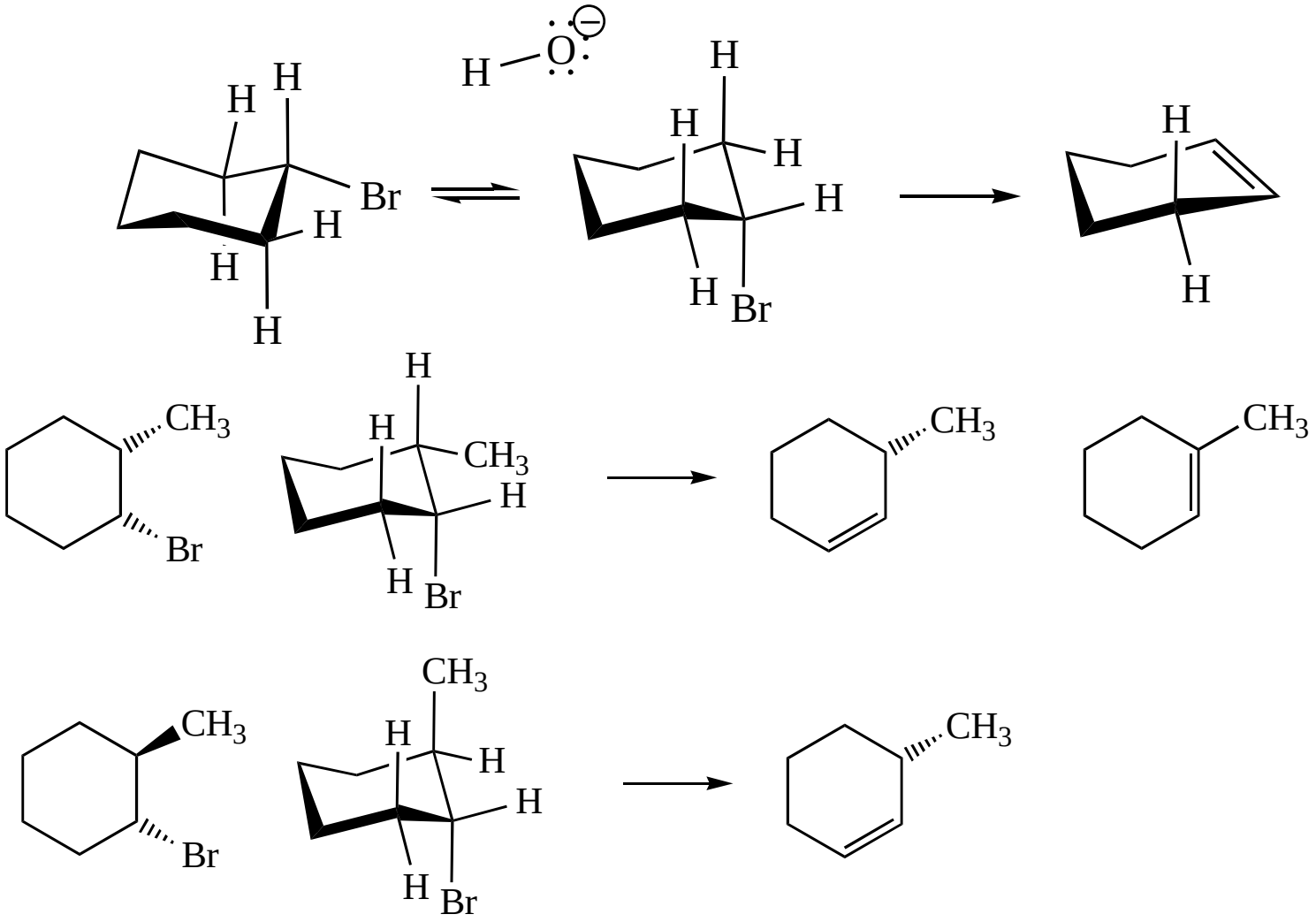
E2:



E1:

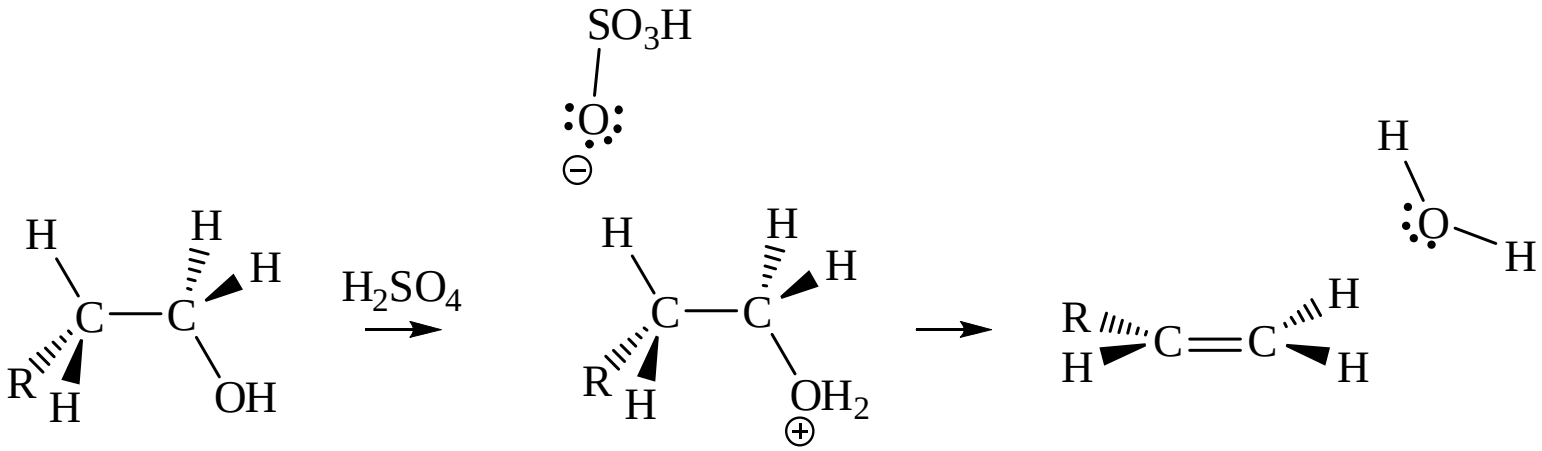


In the E2 reactions of cyclohexyl substrates, the leaving group must be... trans diaxial



E2 Reactions – Elimination of Primary Alcohols

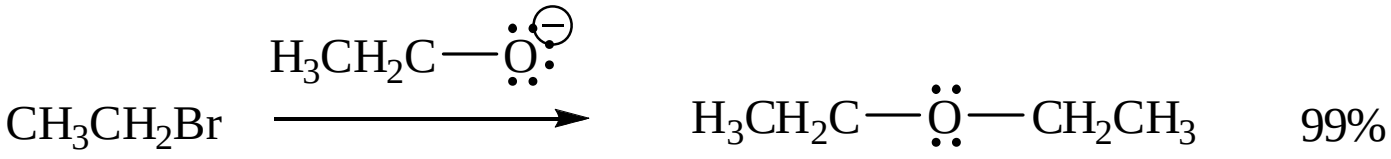
It is possible to convert 1° alcohols to alkenes:

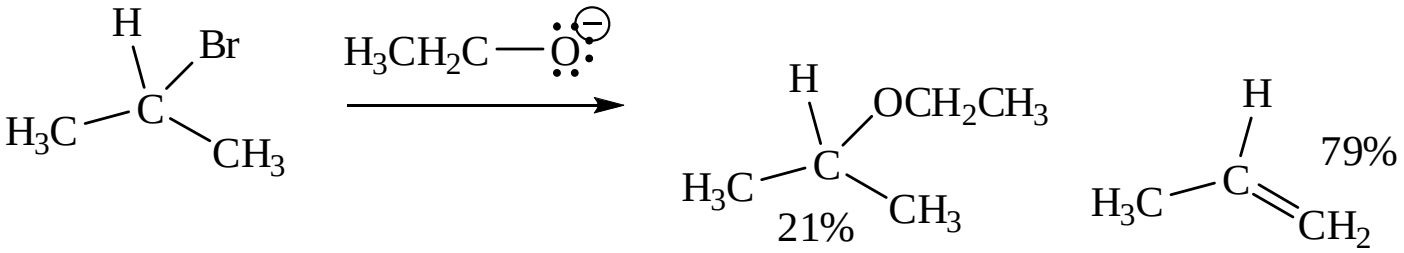


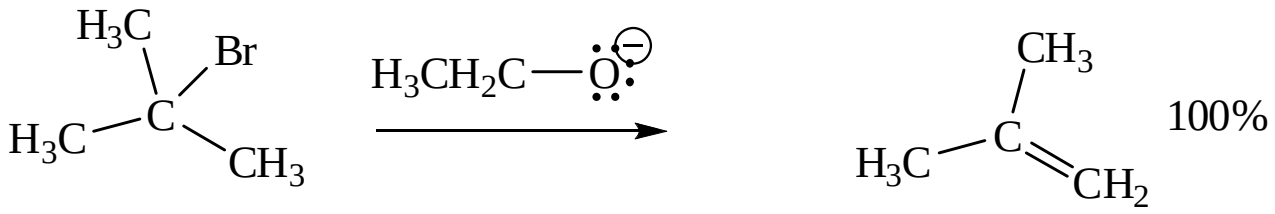
What kind of problems could we expect with the above reaction?

E2 Reactions – E2 vs. S_N2

Because many good nucleophiles are also good bases, S_N2 often competes with E2 for those substrates that are good for S_N2

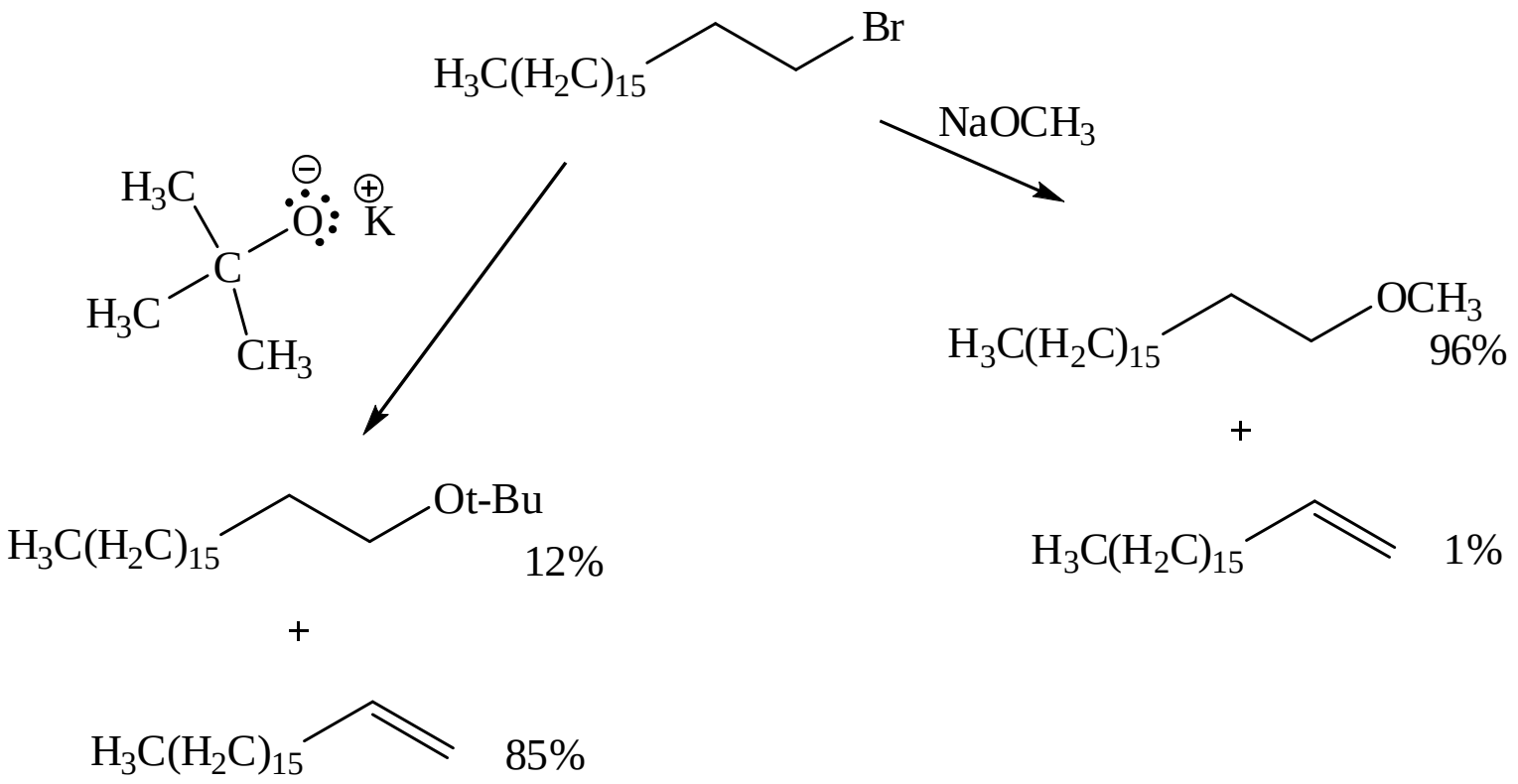






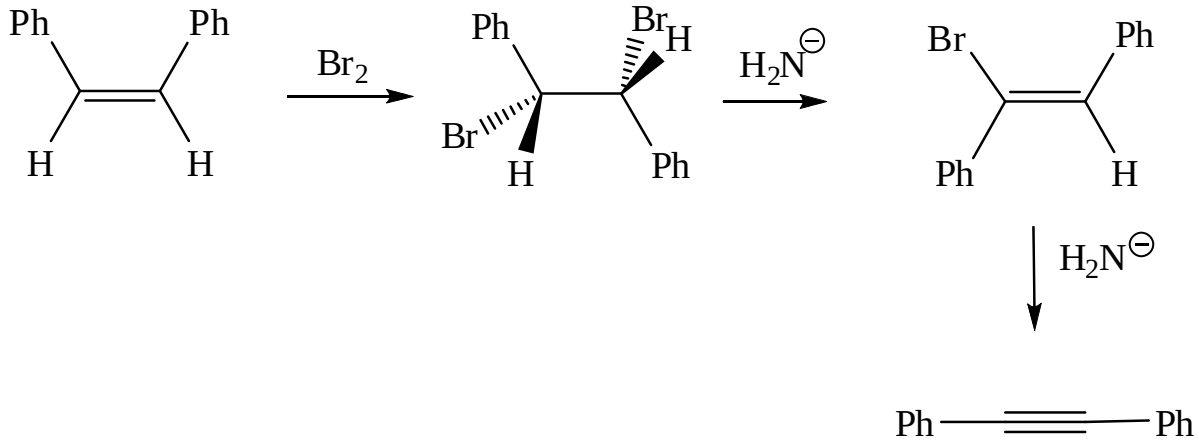
E2 Reactions – E2 vs. S_N2

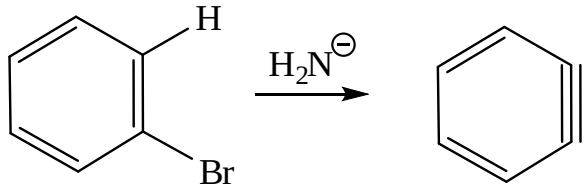
To promote E2 over S_N2 we want to use strong bases that are non-nucleophilic.



E2 Reactions – Preparation of Alkynes

Elimination reactions can be used to prepare alkynes:





E1 vs. E2 vs. S_N1 vs. S_N2 - Summary

•As a general rule, elimination reactions can always compete with substitution reactions. We can, however, alter the reaction conditions to favour one process over another.

•To favour E1 over S_N1 for alcohols, use an acid with a non-nucleophilic conjugate base (H_2SO_4, H_3PO_4). To favour S_N1 over E1, use a good nucleophile.

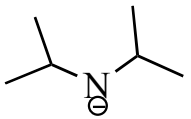
•To favour E2 over S_N2, use a strong, bulky non-nucleophilic base. To favour S_N2 over E2, use good nucleophiles that are relatively weak bases.

•It is important to keep in mind that although you might choose reaction conditions that will favour one reaction over another, more often than not you will still see traces of the competing reaction.

•Before considering the possibility of an elimination reaction, make sure there are β-hydrogen atoms available to eliminate!

SN1, SN2, E1 and E2 - Summary

	SN1	SN2	E1	E2
Mechanism	2 or more steps involving carbocation intermediate	1 step bimolecular process	2 or more steps involving carbocation intermediate	1 step bimolecular process
Kinetics	First order in substrate	Second order, first in substrate and nucleophile	First order in substrate	Second order, first in substrate and base
Substrate Dependence	Those substrates that form stable carbocations. 3°, allylic, benzylic	Those substrates that are uncluttered at the reaction site: 1°, 2°. Good nucleophiles.	Those substrates that form stable carbocations. 3°, allylic, benzylic	Requires strong base and any substrate with beta proton.
Stereochem	Racemization.	Stereospecific inversion.	Usually mixtures.	Stereospecific involving antiperiplanar relationship of beta-proton and leaving group.
Importance of Base/nucleophile	Not involved in RDS, but less basic form of nucleophile will limit E1.	Reactivity of nucleophile is important since it is involved in RDS.	If a good, non-basic nucleophile is present (halides, bisulfate) then SN1.	Strong, non-nucleophilic bases (KOtBu, LDA) best to limit SN2.
Importance of Leaving group	Involved in RDS so is important.	Involved in RDS so is important.	Involved in RDS so is important.	Involved in RDS so is important.
Competes with..	E1 and E2	E2 when basic nucleohiles employed.	SN1	SN2
Solvent	Polar protic best	Polar aprotic best	Polar protic best	Varies.

	Weak base/ poor Nu	**Weak base/ good Nu**	**Moderate/strong base/good Nu**	**Strong base/ poor Nu**
	H_2O, ROH	Br^-, I^-, H_2S	RS^-, NC^-, RNH_2, NH_3 N_3^- HO^-, RO^-	t-Bu—O^-  LDA
Methyl, CH_3X	NR	S_N2	S_N2	S_N2
1°, RCH_2X	NR	S_N2	S_N2	E2
2°, RCHXR	S_N1 E1	S_N2	S_N2 E2	E2
3°, R_3CX	S_N1 E1	S_N1 E1	E2	E2
1° benzylic	S_N1	S_N2	S_N2	S_N2
2° benzylic	S_N1 E1	S_N2	S_N2 E2	E2
3° benzylic	S_N1 E1	S_N1 E1	E2	E2
1° allylic	S_N1	S_N2	S_N2	S_N2
2° allylic	S_N1 E1	S_N2	S_N2 E2	E2
3° allylic	S_N1 E1	S_N1 E1	E2	E2
Aryl, PhX	NR	NR	NR	E2
Alkenyl, H_2C=CHX	NR	NR	NR	E2