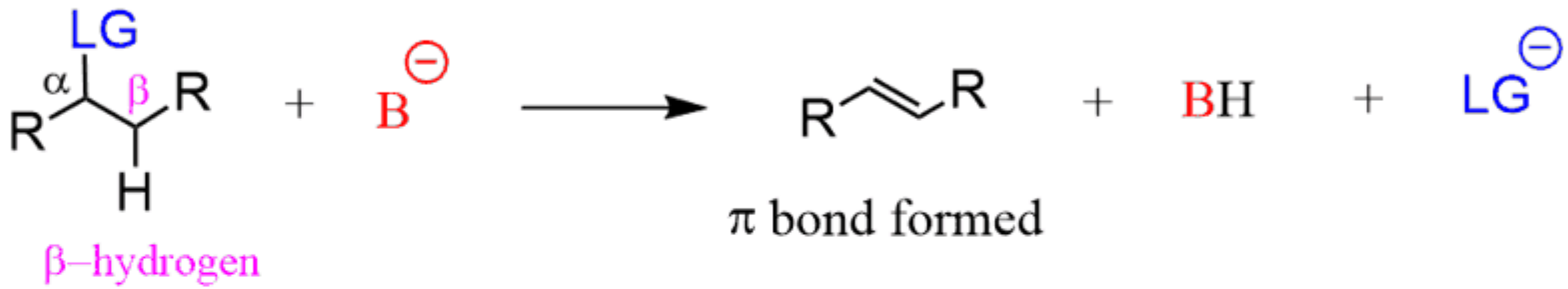
Elimination Reactions

General Features of Elimination Reactions for E1 and E2 mechanisms

In an **elimination reaction**, a new π bond is formed by a loss of elements from the substrate.



The carbon bonded to the leaving group is called α-carbon. The adjacent carbon(s) is called a β–carbon. The hydrogen(s) on the β-carbon is called a ***β-hydrogen****.*

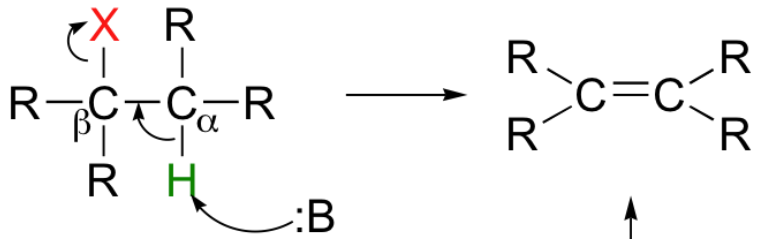
The presence of a β-hydrogen is a must *(unless rearrangements are possible) and because of this, they are called* ***β-elimination*** *or* ***1,2-elimination*** *reactions.*

If the leaving group is a halogen, the elimination is also called ***dehydrohalogenation****.*

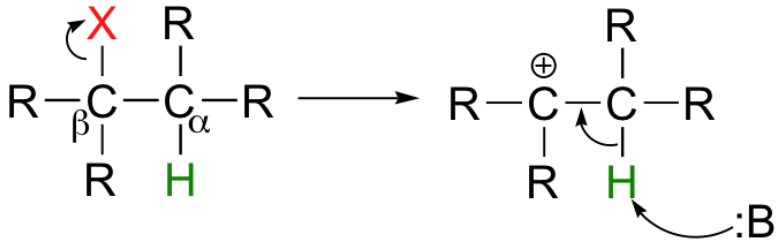
Like in substitution, there is a bimolecular ***(E2)*** *and a unimolecular mechanism* ***(E1)****.*

Elimination reactions are also possible at positions that are isolated from carbonyls or any other electron-withdrawing groups. This type of elimination can be described by two model mechanisms: it can occur in a single concerted step (proton abstraction at C_α occurring at the same time as C_β-X bond cleavage), or in two steps (C_β-X bond cleavage occurring first to form a carbocation intermediate, which is then 'quenched' by proton abstraction at the alpha-carbon).

concerted (E2) elimination

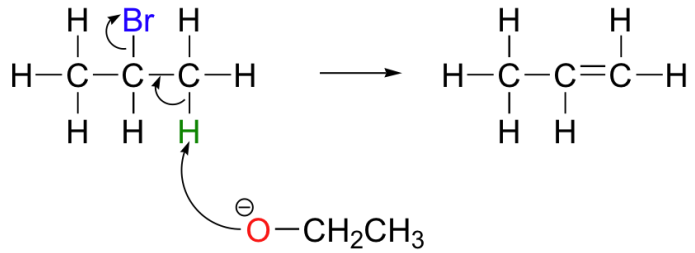


carbocation (E1) elimination

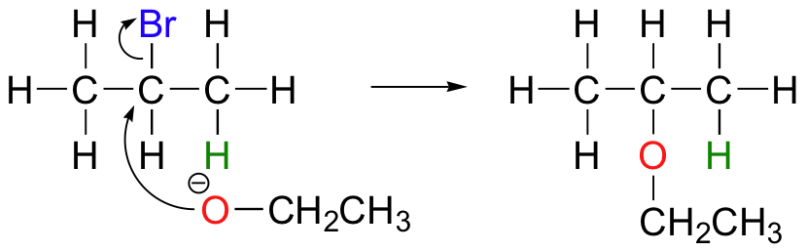


These mechanisms, termed E2 and E1, respectively, are important in laboratory organic chemistry, but are less common in biological chemistry. As explained below, which mechanism actually occurs in a laboratory reaction will depend on the identity of the R groups (ie., whether the alkyl halide is primary, secondary, tertiary, etc.) as well as on the characteristics of the base.

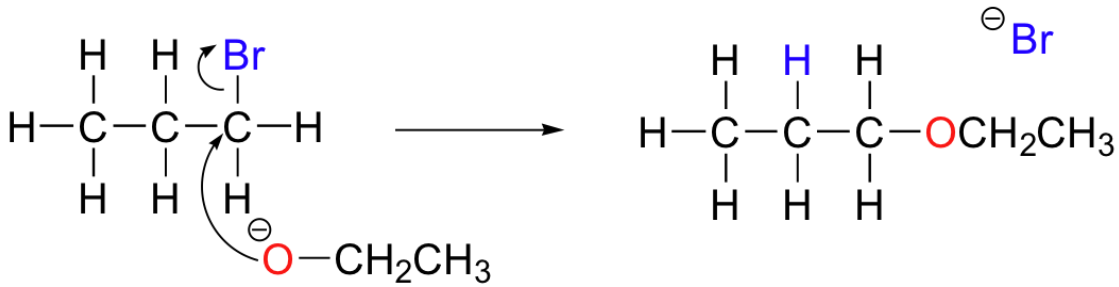
E2 elimination reactions in the laboratory are carried out with relatively strong bases, such as alkoxides (deprotonated alcohols). 2-bromopropane will react with ethoxide, for example, to give propene.



Propene is not the only product of this reaction, however - the ethoxide will also to some extent act as a nucleophile in an SN2 reaction.



Chemists carrying out nonenzymatic nucleophilic substitution or elimination reactions always have to be aware of the competition between the two mechanisms, because bases can also be nucleophiles, and vice-versa. However, a chemist can tip the scales in one direction or another by carefully choosing reagents. Primary carbon electrophiles like 1-bromopropane, for example, are much more likely to undergo substitution (by the SN2 mechanism) than elimination (by the E2 mechanism) – this is because the electrophilic carbon is unhindered and a good target for a nucleophile.

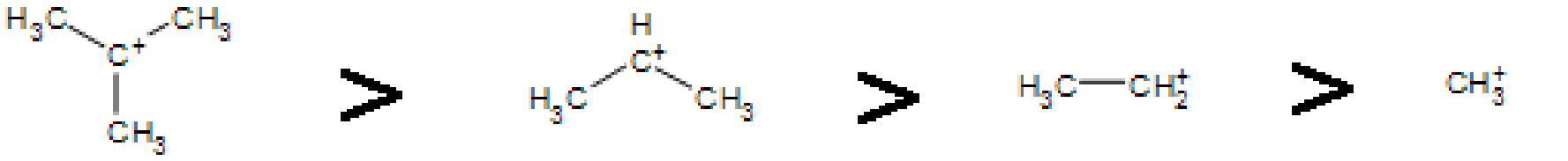


mainly S_N2 product

E1 reactions

Reactivity

Due to the fact that E1 reactions create a carbocation intermediate, rules present in SN1 reactions still apply.

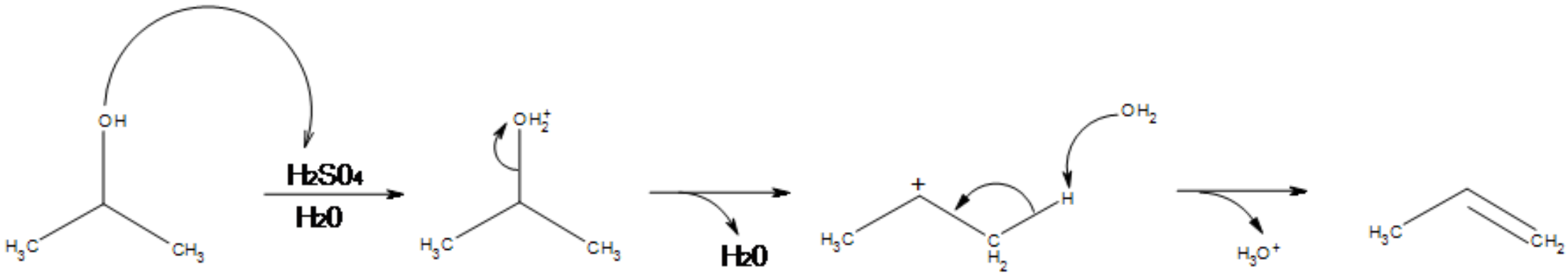


As expected, tertiary carbocations are favored over secondary, primary and methyl's. This is due to the phenomena of hyperconjugation, which essentially allows a nearby C-C or C-H bond to interact with the p orbital of the carbon to bring the electrons down to a lower energy state. Thus, this has a stabilizing effect on the molecule as a whole. In general, primary and methyl carbocations do not proceed through the E1 pathway for this reason, unless there is a means of carbocation rearrangement to move the positive charge to a nearby carbon. Secondary and Tertiary carbons form more stable carbocations, thus this formation occurs quite rapidly.

Secondary carbocations can be subject to the E2 reaction pathway, but this generally occurs in the presence of a good / strong base. Adding a weak base to the reaction disfavors E2, essentially pushing towards the E1 pathway. In many instances, solvolysis occurs rather than using a base to deprotonate. This means heat is added to the solution, and the solvent itself deprotonates a hydrogen. The medium can effect the pathway of the reaction as well. Polar protic solvents may be used to hinder nucleophiles, thus disfavoring E2 / SN2 from occurring.

Acid catalyzed dehydration of secondary / tertiary alcohols

We'll take a look at a mechanism involving solvolysis during an E1 reaction of Propanol in Sulfuric Acid.

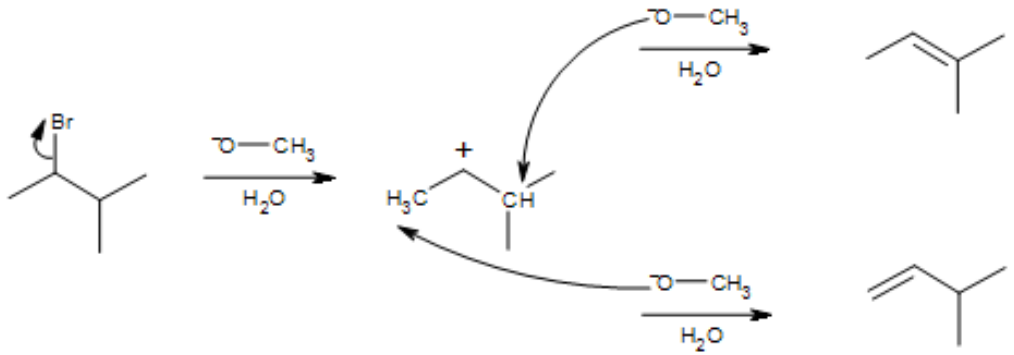


Step 1: The OH group on the 2-propanol is hydrated by H2SO4. This allows the OH to become an H2O, which is a better leaving group.

Step 2: Once the OH has been hydrated, the H2O molecule leaves, taking its electrons with it. This creates a carbocation intermediate on the attached carbon.

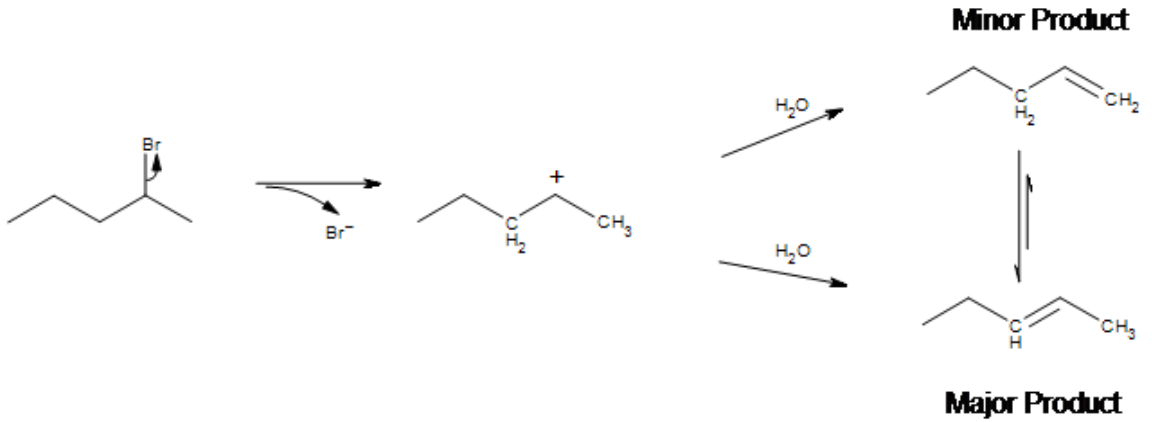
Step 3: Another H2O molecule comes in to deprotonate the beta carbon, which then donates its electrons to the neighboring C-C bond. The carbons are rehybridized from sp3 to sp2, and thus a pi bond is formed between them.

Mechanism for Alkyl Halides



Once again, we see the basic 2 steps of the E1 mechanism.

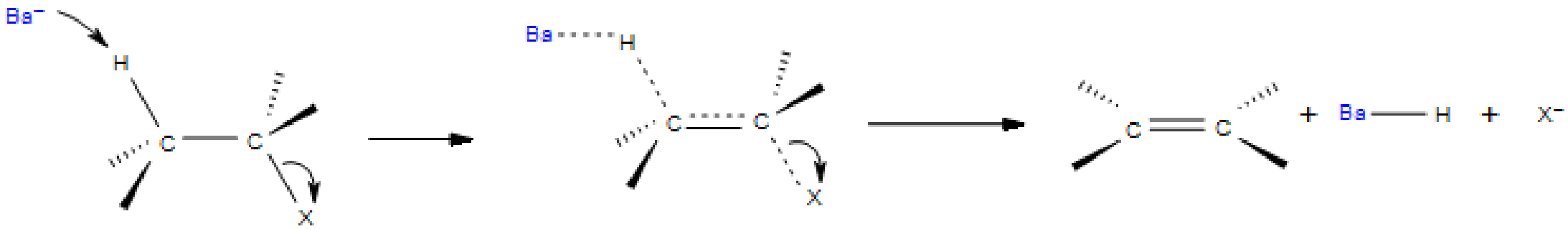
The leaving group leaves along with its electrons to form a carbocation intermediate.
A base deprotonates a beta carbon to form a pi bond.
In this case we see a mixture of products rather than one discrete one. This is the case because the carbocation has two nearby carbons that are capable of being deprotonated, but that only one forms a major product (more stable).



E2 Reactions

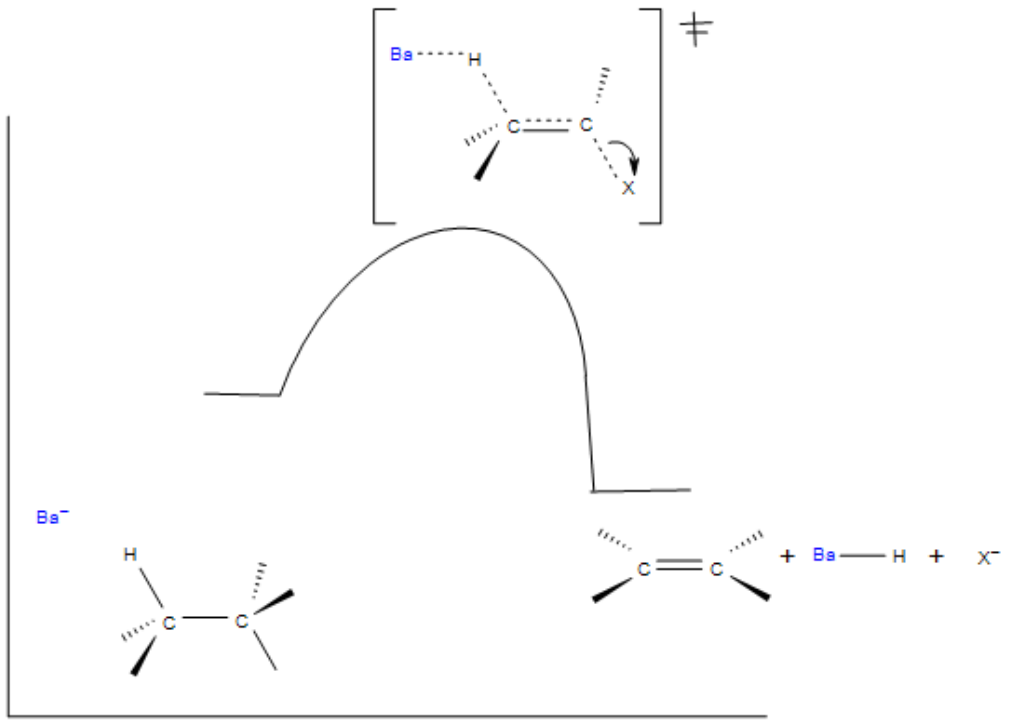
E2 reactions are typically seen with secondary and tertiary alkyl halides, but a hindered base is necessary with a primary halide. The mechanism by which it occurs is a single step concerted reaction with one transition state. The rate at which this mechanism occurs is second order kinetics, and depends on both the base and alkyl halide. A good leaving group is required because it is involved in the rate determining step. The leaving groups must be coplanar in order to form a pi bond; carbons go from sp3 to sp2 hybridization states.

In this reaction Ba represents the base and X represents a leaving group, typically a halogen. There is one transition state that shows the concerted reaction for the base attracting the hydrogen and the halogen taking the electrons from the bond. The product be both eclipse and staggered depending on the transition states. Eclipsed products have a synperiplanar transition states, while staggered products have antiperiplanar transition states. Staggered conformation is usually the major product because of its lower energy confirmation.



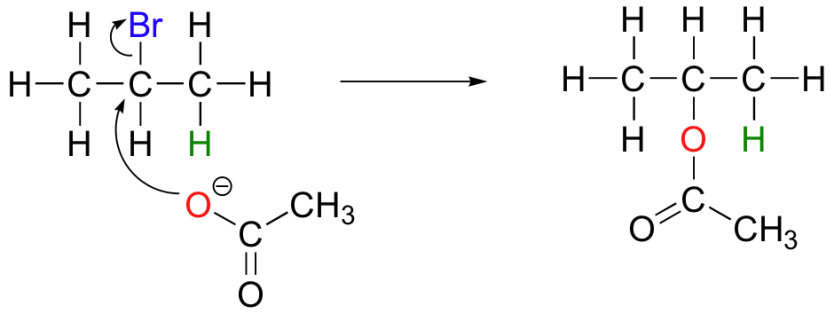
An E2 reaction has certain requirements to proceed:

Secondary and tertiary alkyl halides will proceed with E2 in the presence of a base (OH-, RO-, R2N-)
Both leaving groups should be on the same plane, this allows the double bond to form in the reaction. In the reaction above you can see both leaving groups are in the plane of the carbons.
Follows Zaitsev's rule, the most substituted alkene is usually the major product.
Hoffman Rule, if a sterically hindered base will result in the least substituted product.

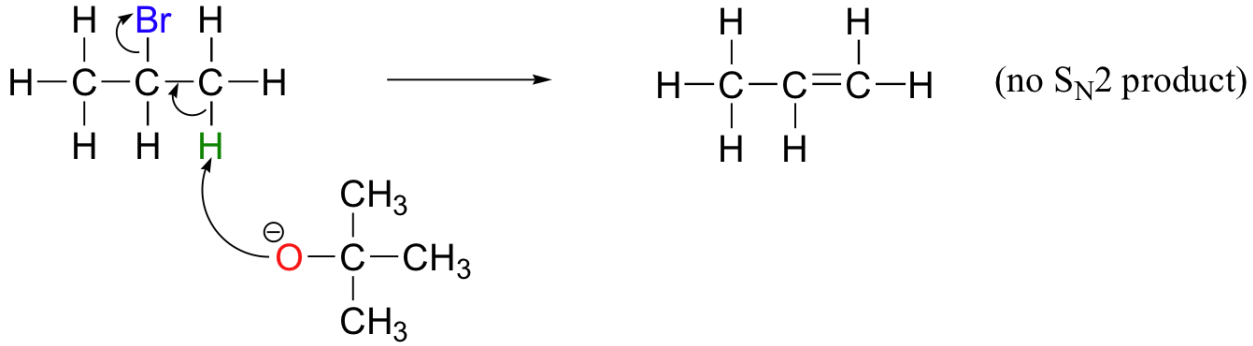


SN1 and E1 mechanisms are unlikely with such compounds because of the relative instability of primary carbocations.

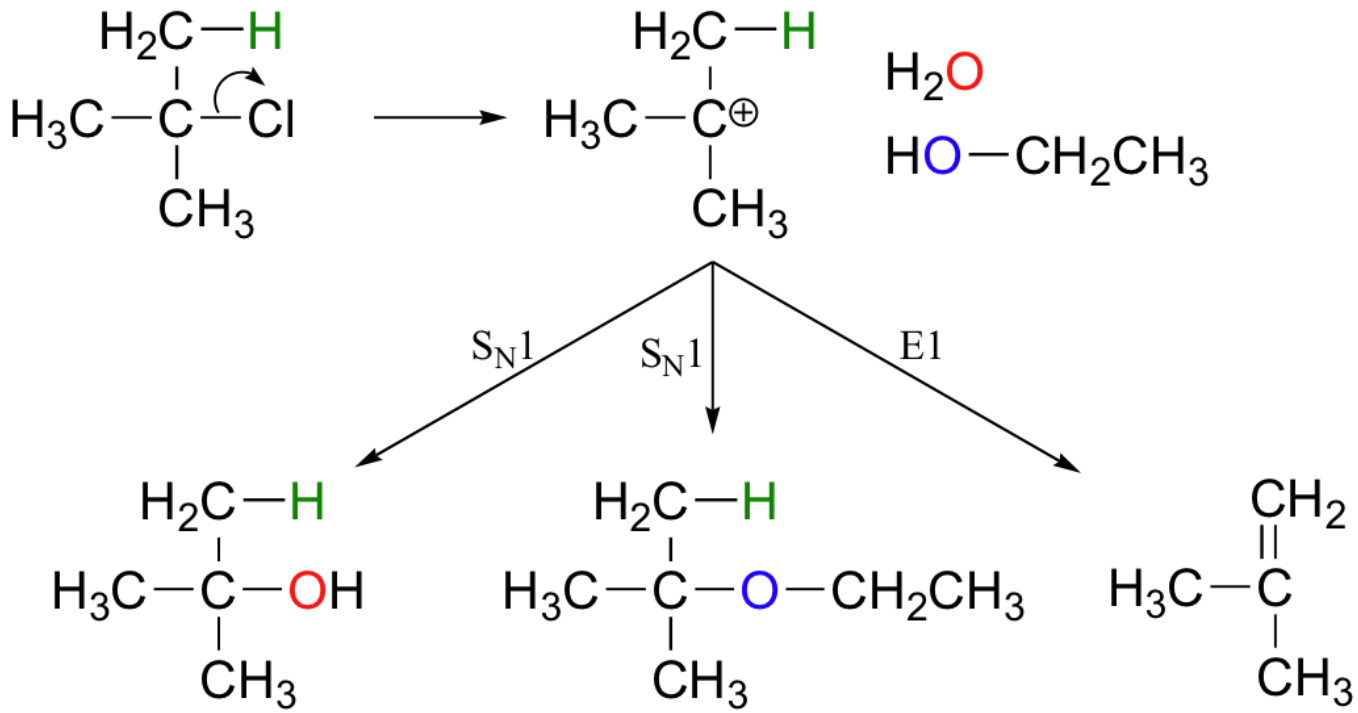
The nature of the electron-rich species is also critical. Acetate, for example, is a weak base but a reasonably good nucleophile, and will react with 2-bromopropane mainly as a nucleophile.



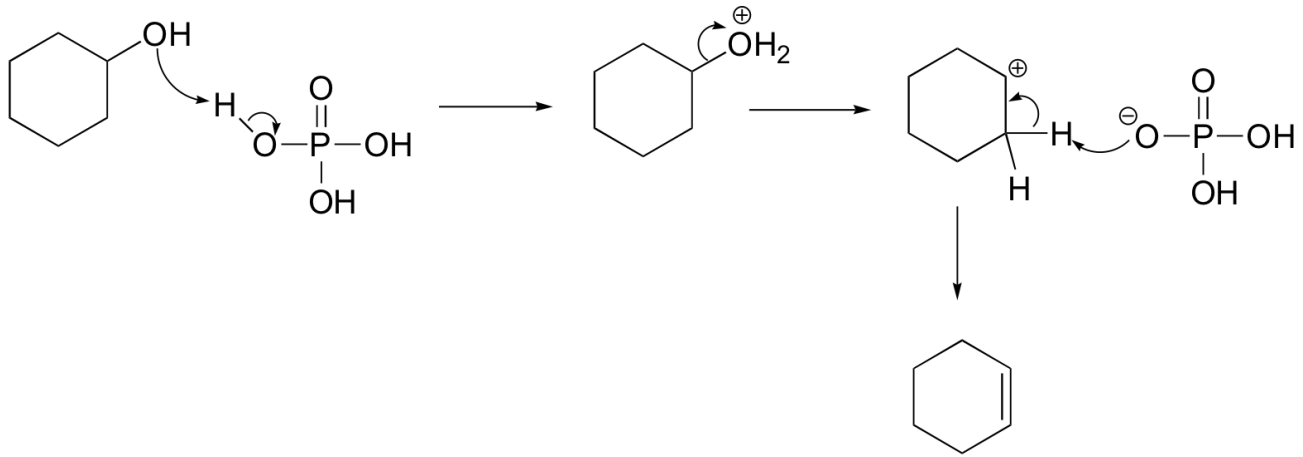
In order to direct the reaction towards elimination**, a strong hindered base** such as tert-butoxide can be used. The bulkiness of tert-butoxide makes it difficult for the oxygen to reach the carbon (in other words, to act as a nucleophile). It is more likely to pluck off a proton, which is much more accessible than the electrophilic carbon).



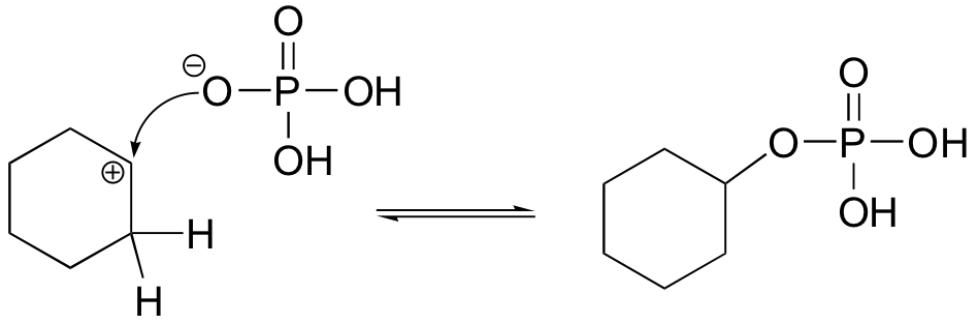
E1 reactions occur by the same kinds of carbocation-favoring conditions that have already been described for SN1 reactions : a secondary or tertiary substrate, a protic solvent, and a relatively weak base/nucleophile. In fact, E1 and SN1 reactions generally occur simultaneously, giving a mixture of substitution and elimination products after formation of a common carbocation intermediate. When tert-butyl chloride is stirred in a mixture of ethanol and water, for example, a mixture of SN1 products (tert-butyl alcohol and tert-butyl ethyl ether) and E1 product (2-methylpropene) results.



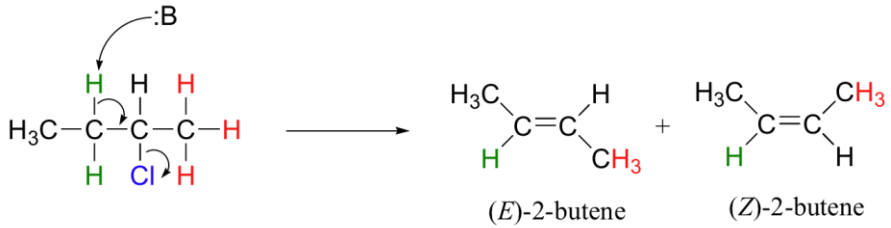
A straightforward functional group conversion that is often carried out in the undergraduate organic lab is the phosphoric acid-catalyzed dehydration of cyclohexanol to form cyclohexene. No solvent is necessary in this reaction - pure liquid cyclohexanol is simply stirred together with a few drops of concentrated phosphoric acid. In order to drive the equilibrium of this reversible reaction towards the desired product, cyclohexene is distilled out of the reaction mixture as it forms (the boiling point of cyclohexene is 83 oC, significantly lower than that of anything else in the reaction solution). Any cyclohexyl phosphate that might form from the competing SN1 reaction remains in the flask, and is eventually converted to cyclohexene over time. Draw a mechanism for the cyclohexene synthesis reaction described above. Also, draw a mechanism showing how the undesired cyclohexyl phosphate could form.

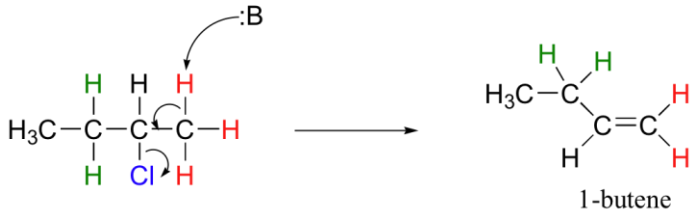


The cyclohexyl phosphate could form if the phosphate attacked the carbocation intermediate as a nucleophile rather than as a base:



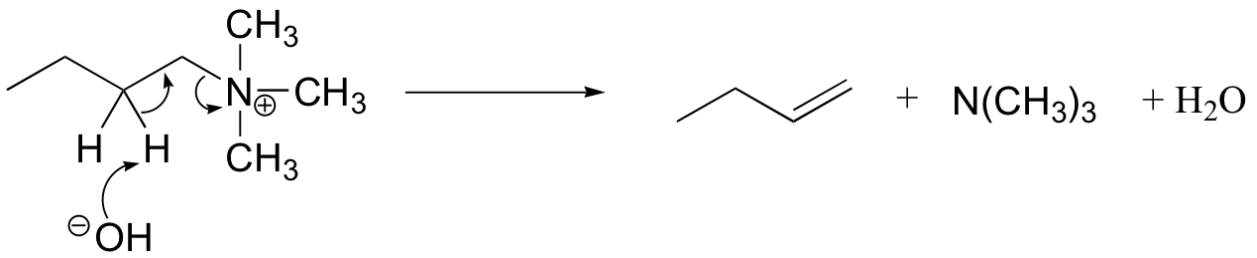
Next, let's put aside the issue of competition between nucleophilic substitution and elimination, and focus on the **regioselectivity** of elimination reactions. In many cases an elimination reaction can result in more than one constitutional isomer or stereoisomer. The elimination products of 2-chloropentane provide a good example:



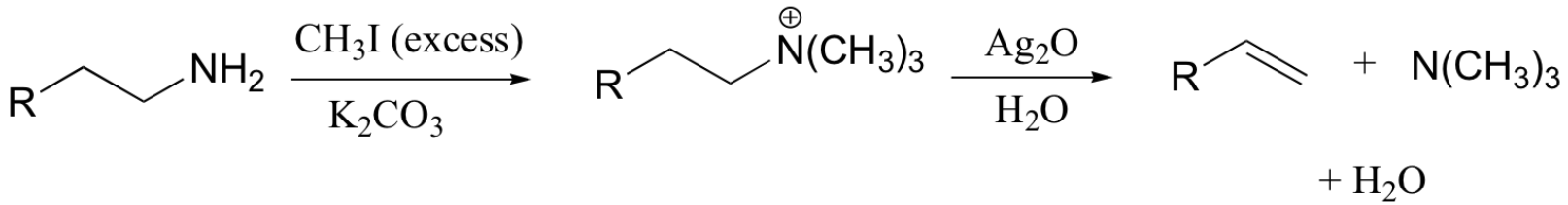


This reaction is both regiospecific and stereospecific. In general, more substituted alkenes are more stable, and as a result, the product mixture will contain less 1-butene than 2-butene (this is the regiochemical aspect of the outcome, and is often referred to as Zaitsev's rule). In addition, we already know that trans (E) alkenes are generally more stable than cis (Z) alkenes (section 3.7C), so we can predict that more of the E product will form compared to the Z product.

The Hoffman elimination is a well-studied E2 elimination in which the leaving group is a quaternary amine - note that there is no proton on the quaternary amine that could protonate the base in the reaction:

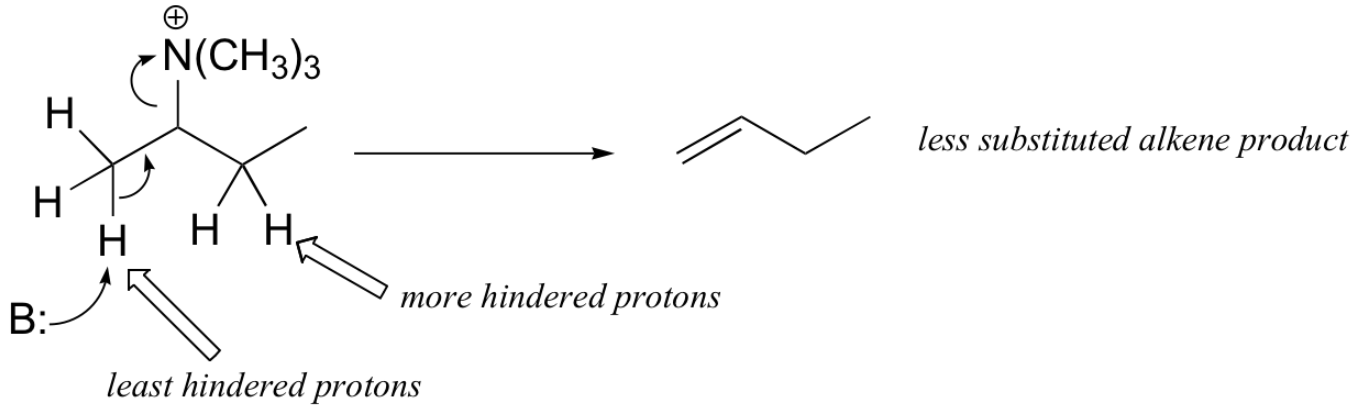


In practice, the quaternary amine is made by treating a primary or secondary amine with excess methyl iodide and weak base. Silver oxide in water generates the necessary hydroxide ion.

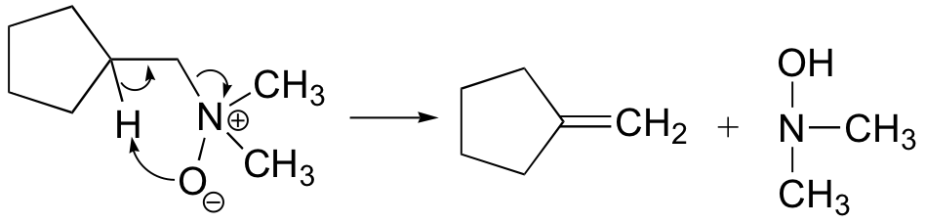


There is very little competing substitution under these conditions.

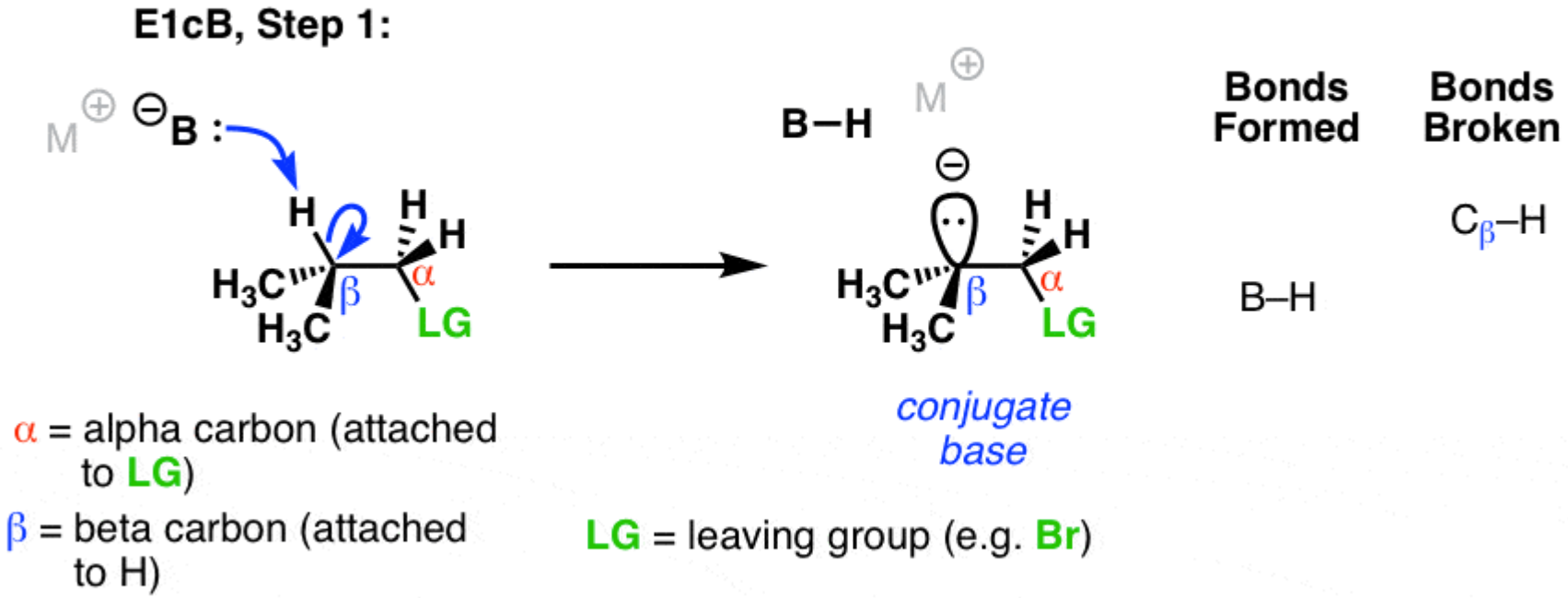
The Hoffman elimination is somewhat unique in that, unlike other elimination reactions, it is usually the least substituted alkene that is the predominant product. This is due to steric factors: the large size of the quaternary ammonium leaving group results in the most accessible (least hindered) proton being abstracted - meaning the proton from the least substituted carbon.



The Cope elimination is another well-known laboratory E2 reaction involving an amine oxide:



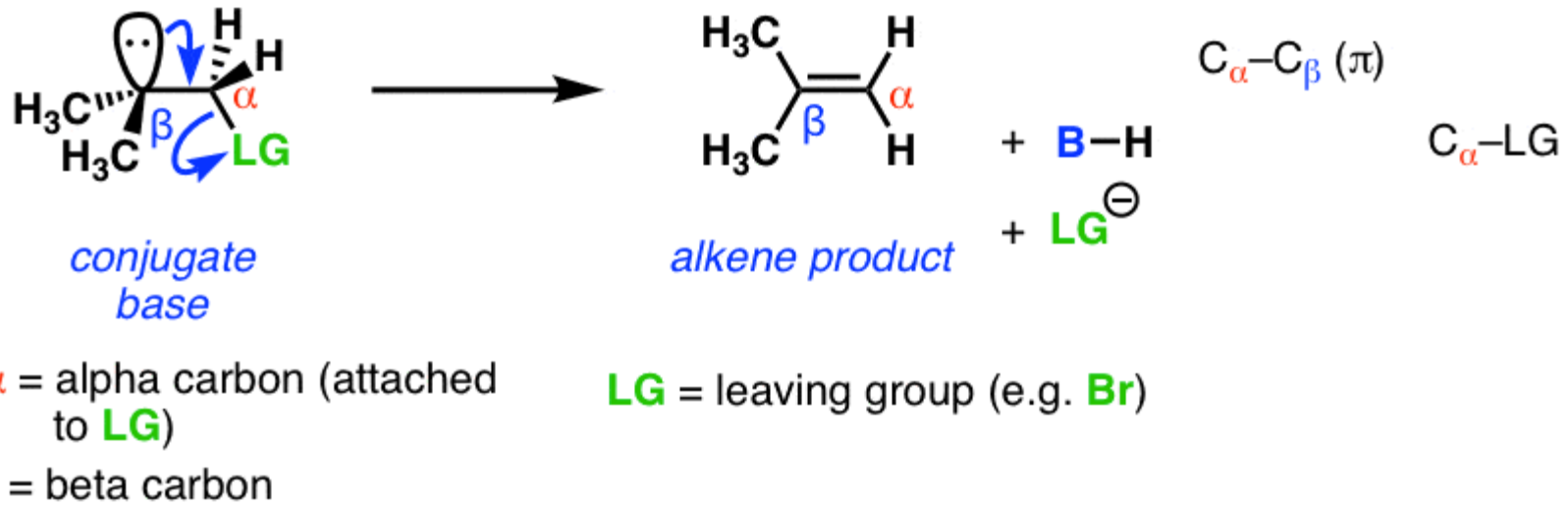
In the E_1cB Mechanism of Elimination, The β-Carbon Is Deprotonated First, To Give The "Conjugate Base" Of The Substrate



Since the first step is deprotonation to give an anion, then you would be right to guess that this mechanism is more likely to occur when the C–H bond is relatively acidic, as when the alpha carbon is adjacent to an electron withdrawing group like a ketone, nitrile (CN), or nitro group (NO2). These groups stabilize negative charge.

In the second step of the E_1cB mechanism, a new C–C pi bond is formed and the C–LG bond breaks

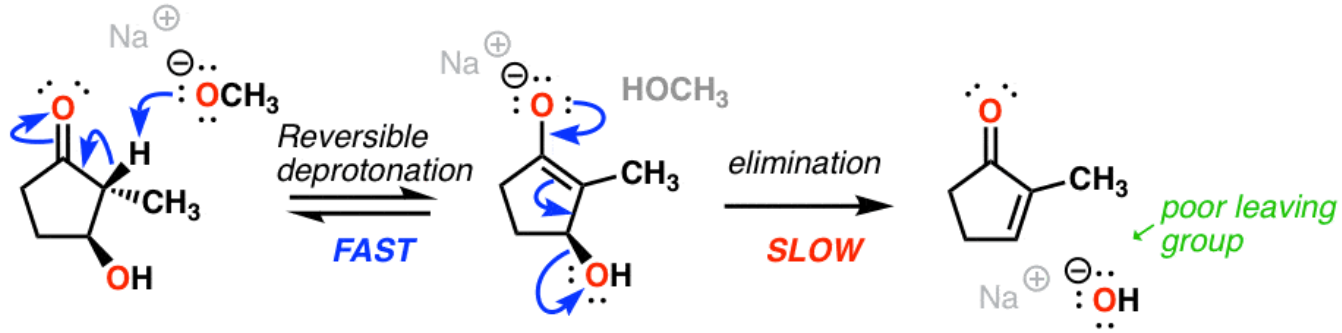
E1cB, Step 2:



In the second step, the pair of electrons from the conjugate base then displaces the leaving group, forming a pi bond [form C–C pi, break C–LG].

In the (many) cases of the E1cB where the second step is the slow step, you can imagine that this step would be made slower by a relatively poor leaving group like (HO-), (CH3O-) or even (believe it or not!) fluorine.

Example of an E_1cB Mechanism: Formation of an Aldol Condensation Product



Product of aldol addition reaction

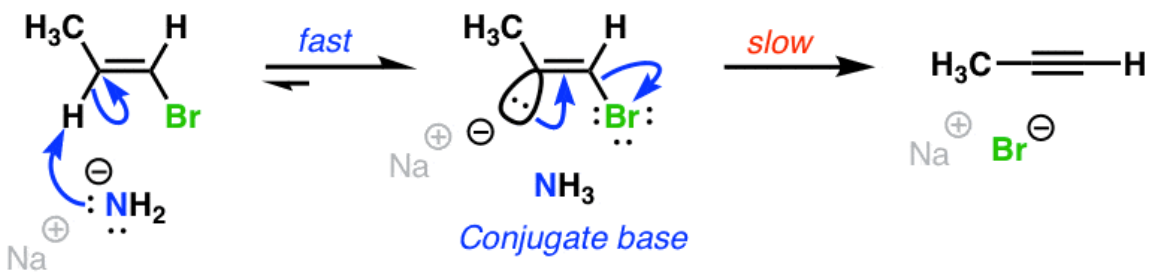
Conjugate base

*Product of aldol **condensation** reaction*

Another Example of an E1cB process: Elimination Of Alkenyl Halides To Alkynes

Step 1: Deprotonation of alkenyl halide

Step 2: Elimination to give alkyne

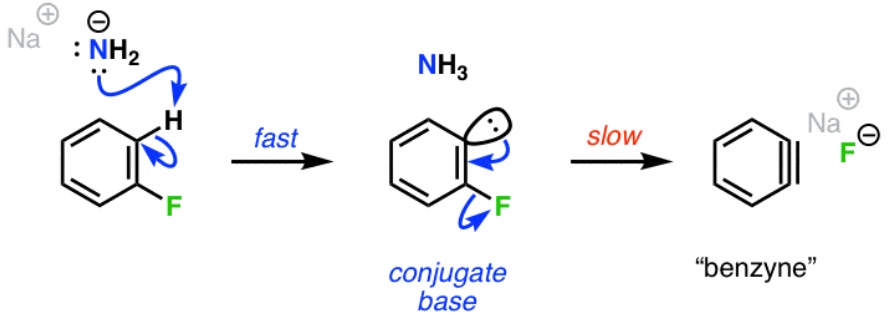


Conjugate base

(a relatively stable anion)

*note: elimination of the *trans* alkenyl halides is *much* faster

Formation of "Benzyne" - Another Example of an E1cB Process



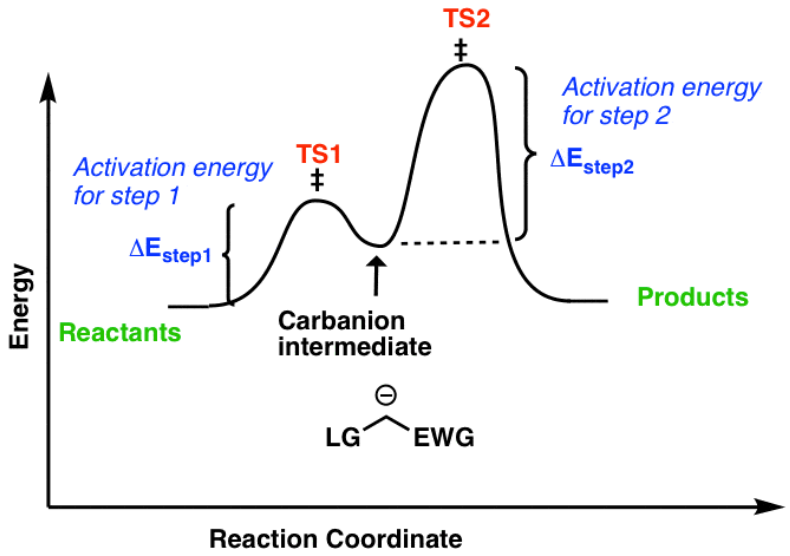
Formation of arynes from phenyl halides:

A related situation to alkenyl halides where the E1cB mechanism can arise is in the formation of benzyne and other "arynes" [See: Nucleophilic Aromatic Substitution – The Benzyne Mechanism]. Although benzyne does not have a "true" pi bond, many of the same principles of the E1cB still apply.

Deprotonation of the aryl fluoride by the strong base (NaNH2) occurs first, giving a carbanion. In this specific case, the second step is loss of the bad leaving group, fluorine.

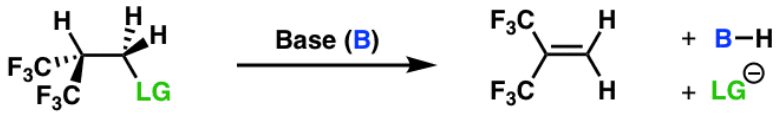
Reaction Coordinate Diagram For An E_1cB Reaction

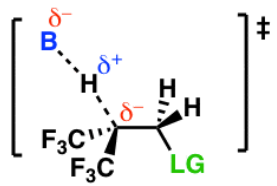
•*for a case where deprotonation is fast, and elimination is slow*



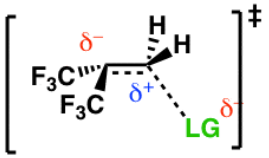
• **Step 2 is rate determining.** The activation energy for Step 2 (elimination, ΔE_{step2}) is greater than that for Step 1 (deprotonation to give carbanion, ΔE_{step1})

For example



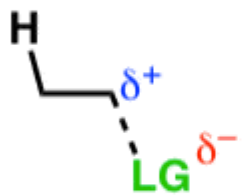
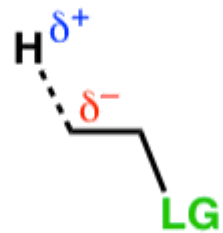


*Transition state 1 (**TS1**)*
Deprotonation to give carbanion (fast step)



*Transition state 2 (**TS2**)*
Formation of pi bond with loss of leaving group
(rate determining step)

Comparing the E1, E2, and E1cB Mechanisms

E1	E2	E1cB
Two steps	**One** step	**Two** steps
1) C–LG breaks 2) C–H breaks C–C (pi) forms	C–H breaks, C–C (pi) forms C–LG breaks, all at same time	1) C–H breaks 2) C–LG breaks C–C (pi) forms
		
Carbocation intermediate	**No** intermediate (concerted)	**Carbanion** intermediate
Carbocation stabilized by electron **donating** groups		Carbanion stabilized by electron **withdrawing** groups
Assisted by **good** leaving groups		Assisted by **poor** leaving groups
No strict requirement on stereochemistry of C–H and C–LG	C–H and C–LG are **anti**	No strict requirement on stereochemistry of C–H and C–LG