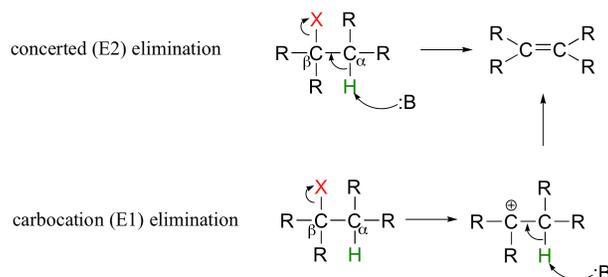


8.1: General Features of Elimination

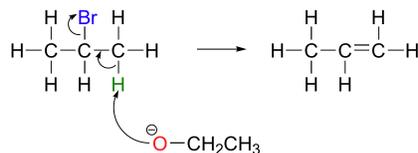
So far in this chapter, we have seen several examples of carbanion-intermediate (E1cb) beta-elimination reactions, in which the first step was proton abstraction at a carbon positioned to an electron-withdrawing carbonyl or imine. Elimination reactions are also possible at positions that are isolated 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).



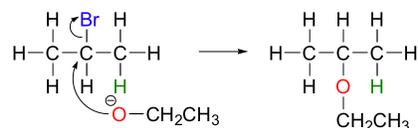
These mechanisms, termed E2 and E1, respectively, are important in laboratory organic chemistry, but are less common in biological chemistry. As explained below, which mechanism actually occurs in a laboratory reaction will depend on the identity of the R groups (ie., whether the alkyl halide is primary,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

E1 and E2 reactions in the laboratory

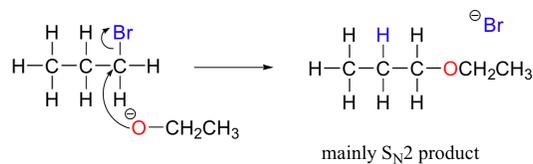
E2 elimination reactions in the laboratory are carried out with relatively strong bases, such as alkoxides (deprotonated alcohols). 2-bromopropane will react with ethoxide, for example, to give propene.



Propene is not the only product of this reaction, however - the ethoxide will also to some extent act as a nucleophile in an S_N2 reaction.

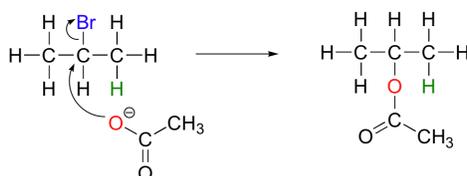


Chemists carrying out nonenzymatic nucleophilic substitution or elimination reactions always have to be aware of the competition between the two mechanisms, because bases can also be nucleophiles, and vice-versa. However, a chemist can tip the scales in one direction or another by carefully choosing reagents. Primary carbon electrophiles like 1-bromopropane, for example, are much more likely to undergo substitution (by the S_N2 mechanism) than elimination (by the E2 mechanism) - this is because the electrophilic carbon is unhindered and a good target for a nucleophile.

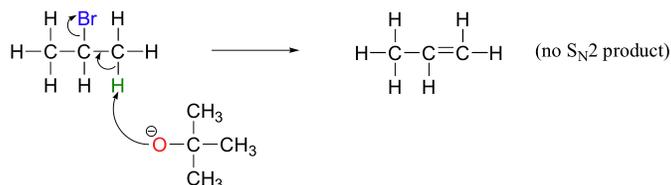


S_N1 and E1 mechanisms are unlikely with such compounds because of the relative instability of primary carbocations.

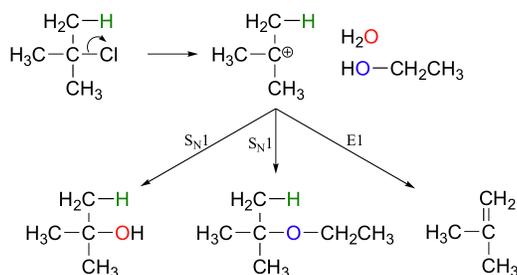
The nature of the electron-rich species is also critical. Acetate, for example, is a weak base but a reasonably good nucleophile, and will react with 2-bromopropane mainly as a nucleophile.



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 S_N1 reactions (section 9.4): a secondary or tertiary substrate, a protic solvent, and a relatively weak base/nucleophile. In fact, E1 and S_N1 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 S_N1 products (tert-butyl alcohol and tert-butyl ethyl ether) and E1 product (2-methylpropene) results.

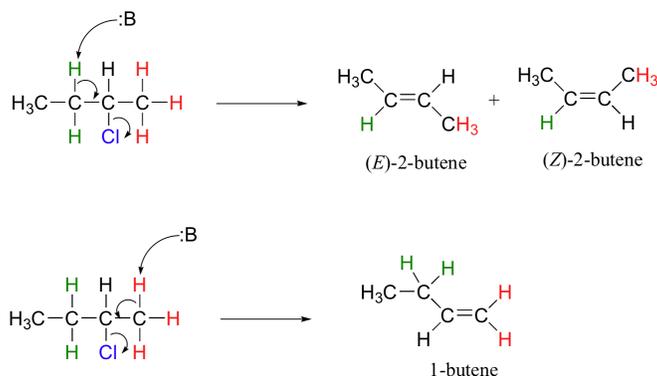


Template:ExampleStart

Exercise 14.4: 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 °C, significantly lower than that of anything else in the reaction solution). Any cyclohexyl phosphate that might form from the competing S_N1 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.

Template:ExampleEnd

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:

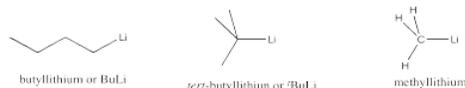


This reaction is both regioselective and stereoselective. In general, *more substituted alkenes are more stable*, and as a result, the product mixture will contain less 1-butene than 2-butene (this is the regiochemical aspect of the outcome, and is often referred to as **Zaitsev's rule**). In addition, 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.

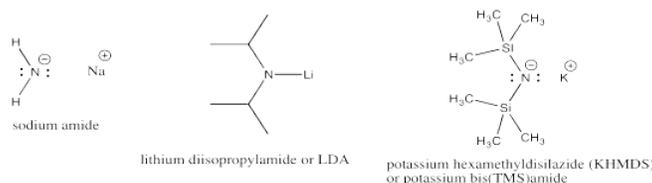
Why might a reaction undergo elimination rather than substitution? The most important reason concerns the nature of the nucleophile. The more basic the nucleophile, the more likely it will induce elimination.

- Basic nucleophiles lead to elimination.

Very strong bases include carbon and nitrogen anions and semi-anions. Examples include butyllithium and sodium amide. Very strong bases are highly likely to engage in elimination, rather than substitution.



Strong bases include non-stabilized oxygen anions. Examples include sodium hydroxide as well as alkoxides such as potassium *tert*-butoxide or sodium ethoxide. Strong bases favour elimination, too. Nevertheless, they can sometimes undergo either elimination or substitution, depending on other factors (see below).



Weak bases include cyanide, stabilized oxygen anions such as carboxylates and aryloxides, fluoride ion and neutral amines. Weak bases are much more likely to undergo substitution than elimination.



Very weak bases include heavy halides such as chloride, bromide or iodide, as well as phosphorus and sulfur nucleophiles. Very weak bases undergo elimination only rarely.

Organic Chemistry With a Biological Emphasis by Tim Soderberg (University of Minnesota, Morris)

- Prof. Steven Farmer (Sonoma State University)

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