

Summary of Organic Reaction Mechanisms

The Twelve Elementary Processes of Organic Chemistry

Organic reactions will either occur in a single concerted step, or will require a sequence of elementary processes and thus pass through one or more intermediate species. There are 12 common processes, and a further 8 that are less significant. Each of these processes occurs synchronously, that is, they cannot be further subdivided in time.

The product of an elementary process is a stable structure that persists for a finite period of time. It may be a reaction intermediate and thus be consumed as the starting point for a subsequent elementary process, or it may be the endpoint of the overall transformation. The distinction between intermediates and products is purely one of lifetime under the specified conditions of the reaction; there is no intrinsic difference between them.

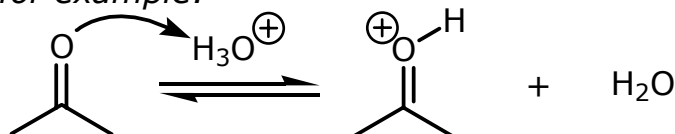
An elementary process either forms a new bond (i.e., it is Associative, labeled **A**) or it breaks an existing bond (i.e., it is Dissociative, labeled **D**) at the central atom of interest. The process may involve a Nucleophile (or a leaving group; both are labeled **N**), an Electrophile (labeled **E**) or a proton (labeled **H**), or a Radical (labeled **R** – we are not discussing these processes here). These labels permit each process to be given a simple symbolic name. You do not need to know these names at this stage, but they are included here for completeness.

1. Proton transfer to/from a lone pair or anion (**A_H/D_H**)

This process is the Bronsted Acid/Base equilibrium

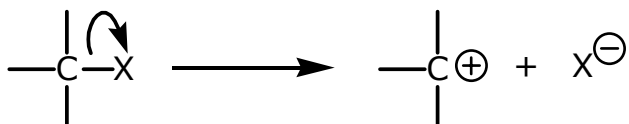


for example:

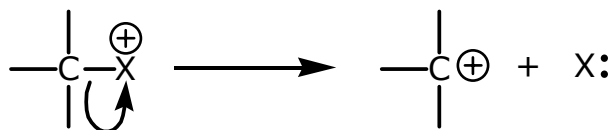


2. Ionization (dissociation) of a leaving group (**D_N**)

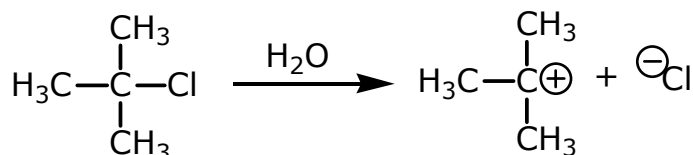
Heterolytic cleavage of a bond



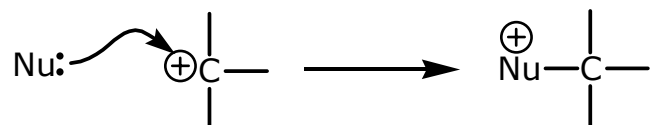
This can also involve a cationic group leaving



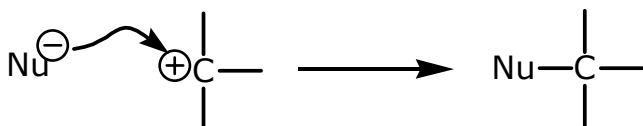
for example:



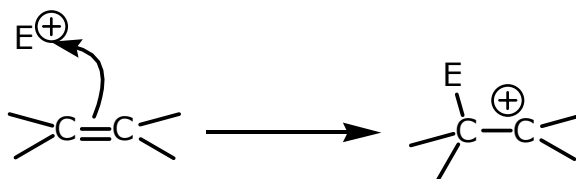
3. Trapping of an electron source (A_N ; reverse of process 2)



or:

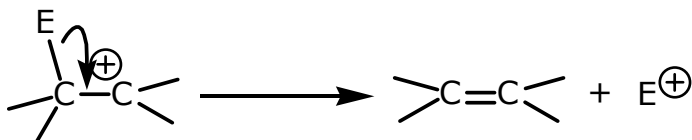


4. Electrophilic addition to multiple bond (A_E or A_H)

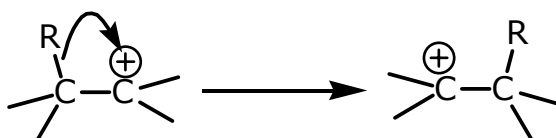


The electrophile may be a proton, or any other electron-deficient species such as a carbocation, or even a Lewis acidic metal.

5. Electrophile loss from a carbocation to form a π bond (D_E ; reverse of process 4)



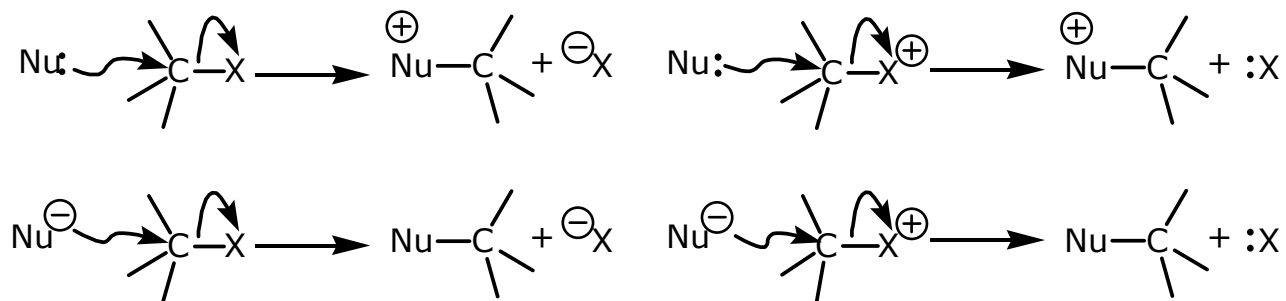
6. 1,2 Rearrangement (shift) of a carbocation (*intramol.*- D_NA_N)



This is the fundamental process in Wagner-Meerwein rearrangements and other 1,2-shift processes that do not involve a leaving group.

7. Bimolecular nucleophilic substitution (A_ND_N ; S_N2)

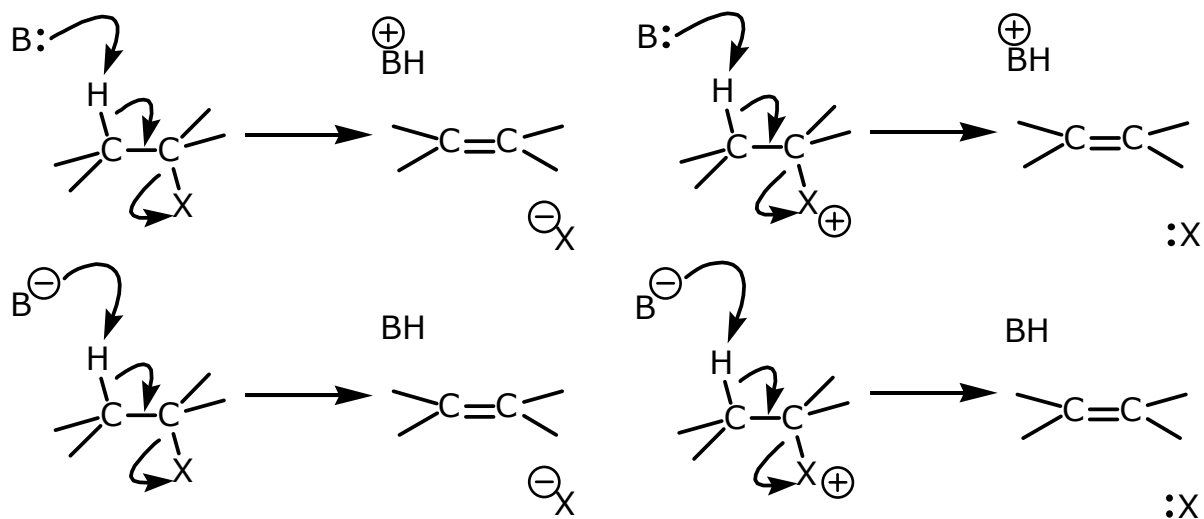
Concerted bimolecular substitution of a leaving group proceeds with stereochemical inversion. The nucleophile may be neutral or anionic, and the leaving group may depart as an anion or a neutral species.



Note that substitution reactions of this kind may occur at heteroatom centres as well as at carbon.

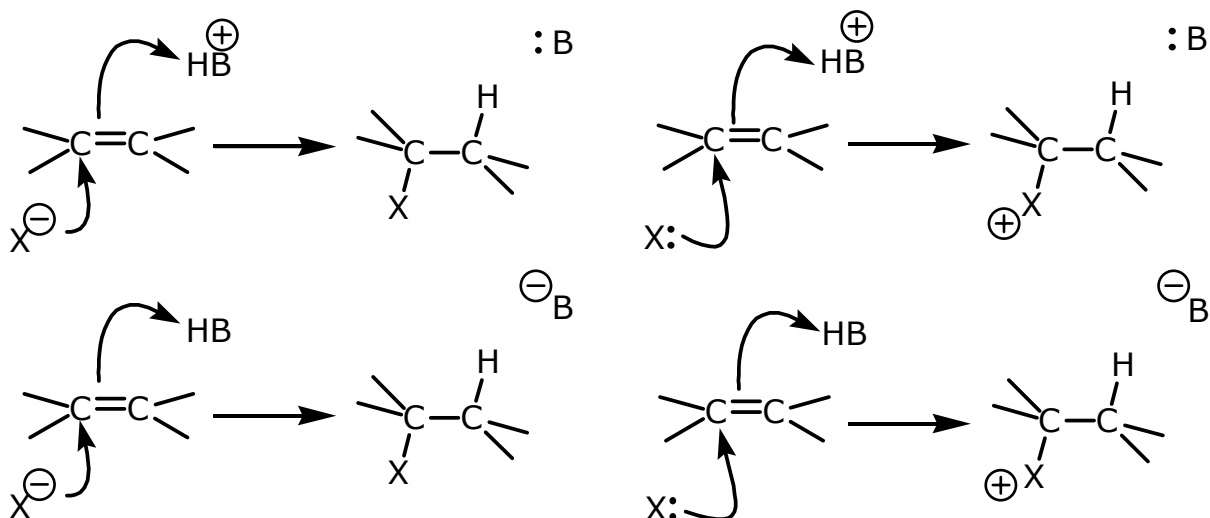
8. Bimolecular elimination (D_HD_N ; E_2)

Concerted bimolecular elimination may also occur at heteroatom centres. The base may be either neutral or anionic, while the leaving group may depart as an anion or a neutral species.



9. Trimolecular electrophilic addition to multiple bond (A_NA_H ; reverse of pathway 8)

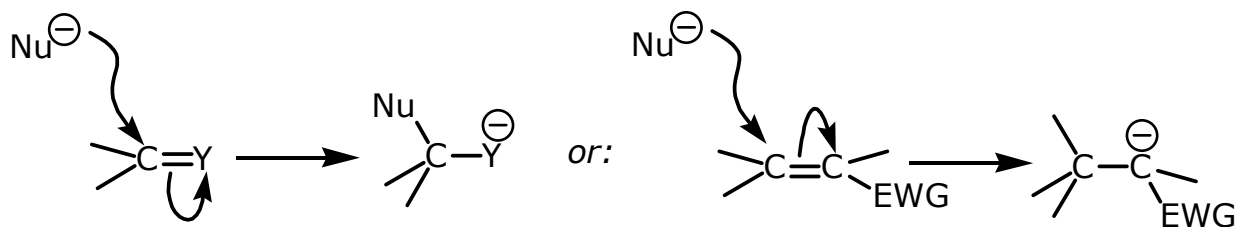
This is the reverse of the E_2 elimination. Note that in this process, there is NO intermediate cation - addition of the nucleophile and electrophile (proton) is simultaneous. Because this reaction is trimolecular, it is statistically less probable than the more-common multi-step addition process.



Note that this pathway can also involve heteroatom centres (e.g. carbonyls) and Lewis acids.

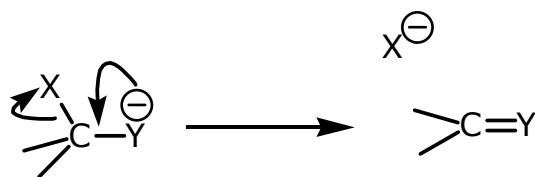
10. Nucleophilic addition to a polarized multiple bond (A_N)

Polarized multiple bonds include carbonyls, imines etc. and also alkenes substituted by electron withdrawing groups. All the variations in charge shown for previous reactions apply here as well, but are omitted for simplicity.

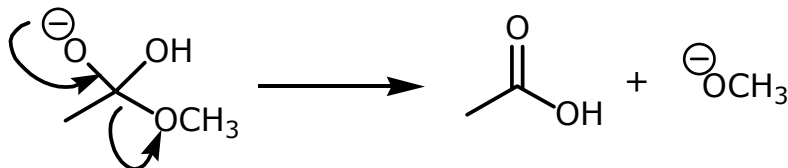


This process is involved in nucleophilic carbonyl additions, and conjugate additions such as Michael addition to α,β -unsaturated carbonyls.

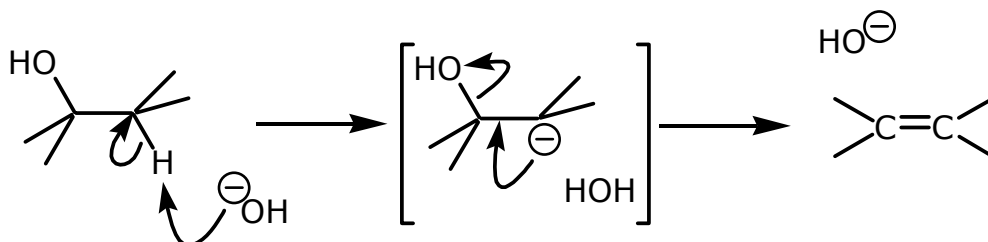
11. β -Elimination from an anion or a lone pair (D_N ; reverse of process 10)



This process is observed in the collapse of tetrahedral intermediates:

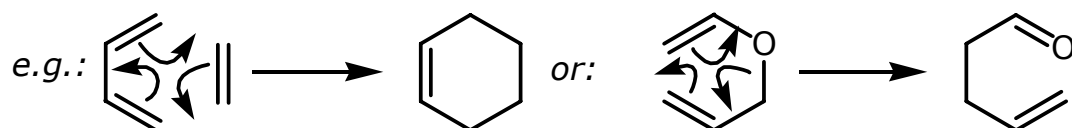


It is also seen in an anionic unimolecular elimination pathway called $E1c_b$.



12. Concerted pericyclic reactions (designation varies depending on number of electrons involved; six-electron pericyclic processes are labeled "6e")

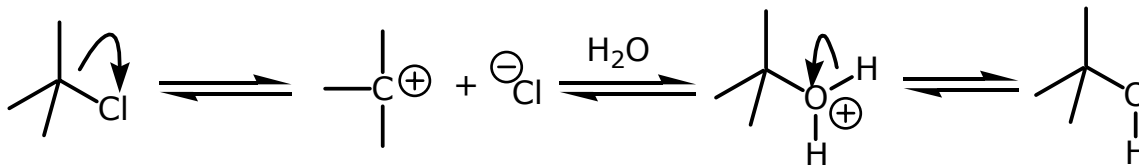
These processes are concerted migrations of multiple electrons, usually involving π and σ bonds and proceeding through aromatic transition structures. They are a diverse set, but are characterized by "merry-go-round" mechanisms.



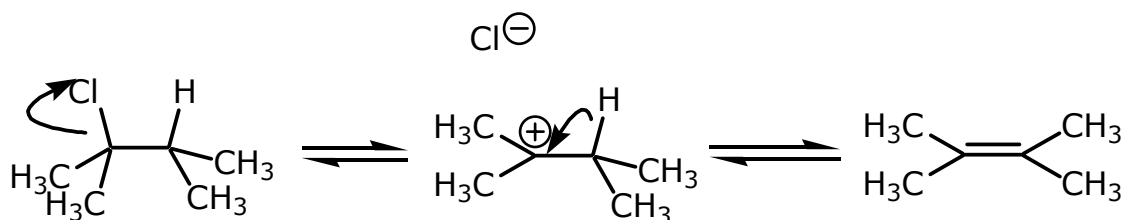
Common Path Combinations

Several well-known organic reactions are simple combinations of only two elementary processes. A few common examples are listed here.

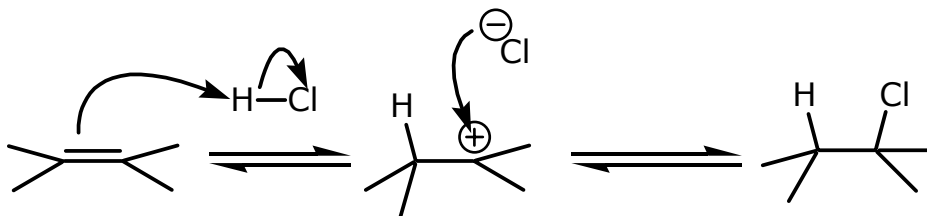
1. Unimolecular nucleophilic substitution ($S_N1 = D_N + A_N$)



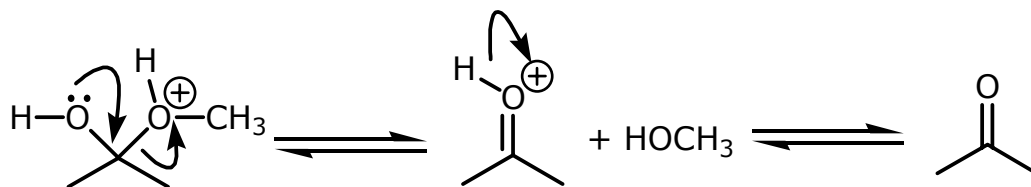
2. Unimolecular elimination ($E1 = D_N + D_E$)



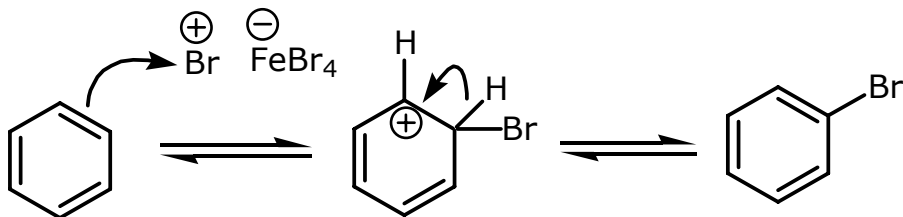
3. Bimolecular electrophilic addition ($A_H + A_N$)



4. Lone pair assisted unimolecular elimination ($D_N + D_H$)



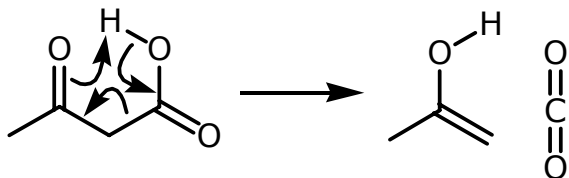
5. Electrophilic aromatic substitution ($A_E + D_E$)



The Eight Minor Pathways

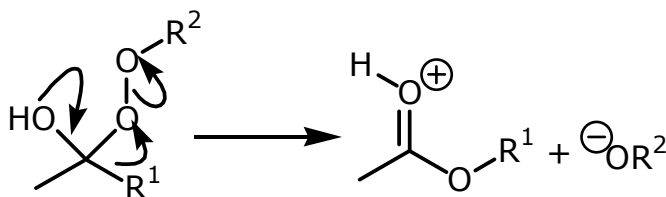
These minor processes are combinations of elementary processes that are sufficiently unique to warrant being treated separately. We have not seen examples of all eight minor pathways in 2.222. Only the three that we have encountered are listed here.

1. Internal *syn* elimination

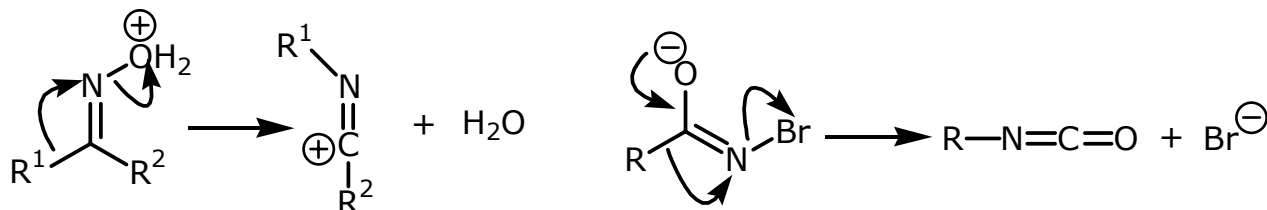


2. 1,2 Rearrangement to an electron deficient center with loss of Nu, a special case of the 1,2R pathway

This pathway is seen in the Baeyer-Villiger reaction:



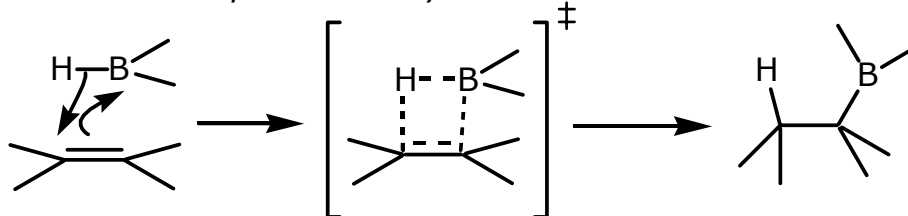
as well as in the Beckmann and Hoffmann rearrangements:



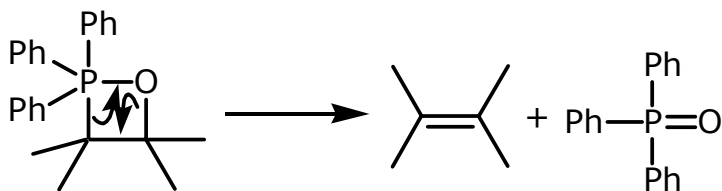
3. Electrocyclic ring closure/opening

Recall that electrocyclic reactions involve a change in the total number of π and σ bonds in the system, in contrast to pericyclic processes.

We have seen this process in hydroboration:



and also in the Wittig reaction:



as well as in Chapter 14:

