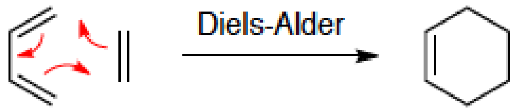
Four major types of pericyclic reactions

Cycloadditions

Cycloadditions are characterized by formation of a cyclic product when two components come together. In these reactions, two new σ bonds are formed between the ends of the π systems of the two components. The Diels-Alder reaction is one of the most well know example of cycloadditions.

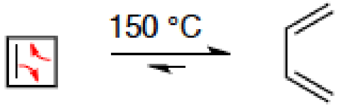
Example:



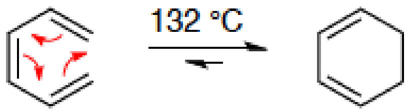
Electrocyclic reactions

Electrocyclic reactions are unimolecular pericyclic reactions characterized by ring closing or ring opening. In an electrocyclic ring closing reaction, a σ bond is formed between the ends of a conjugated π system. In an electrocyclic ring opening reaction (the reverse), a C–C σ bond breaks to give a conjugated π system. Electrocyclic reactions are further described by the number of electrons participated, such as 2 π electrocyclic, 4 π electrocyclic and etc.

Examples:



4 π electrocyclic ring opening

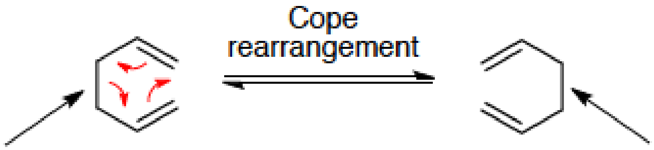


6 π electrocyclic ring closing

Sigmatropic rearrangements

Sigmatropic rearrangements are also unimolecular pericyclic reactions. They involve breaking a σ bond at one place and forming a new σ bond at another place within the molecule. There is no net change in the number of σ and π bonds in a sigmatropic rearrangement.

Example:



+ Group transfer reaction

Electrocyclic rearrangements

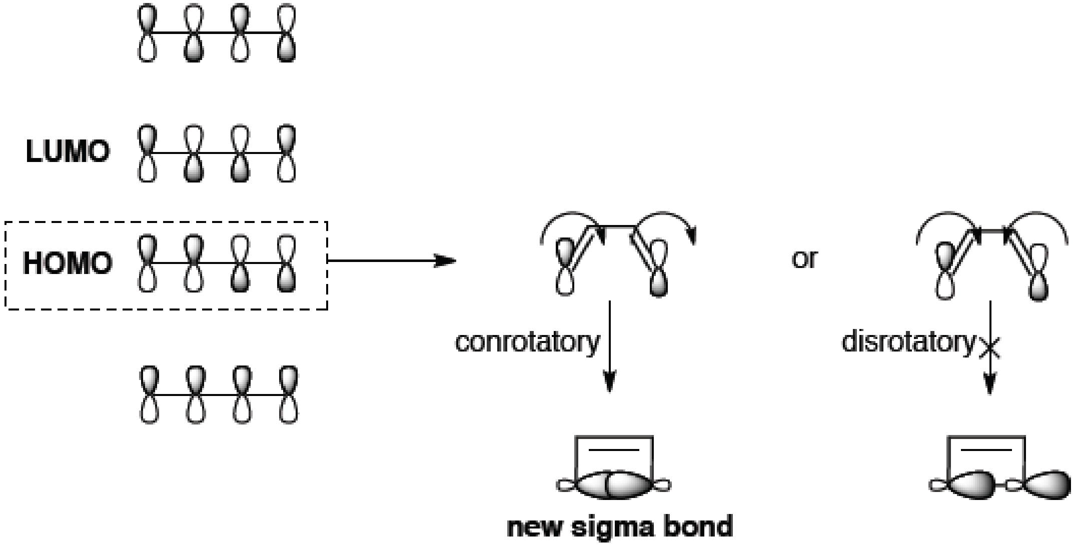
In an electrocyclic reaction a ring is always broken or formed across the ends of a single conjugated π-system. The difference between a cycloaddition and an electrocyclic reaction is that in an electrocyclic reaction just one new σ-bond is formed (or broken) whereas in cycloadditions two new σ-bonds are formed (or broken).

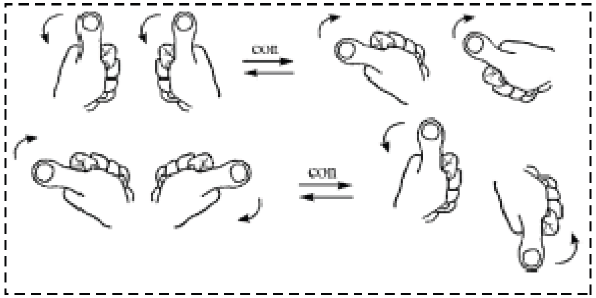
1,3 diene

The ring closure of a 1,3-diene is a typical example of an electrocyclic reaction.

Conrotatory vs Disrotatory

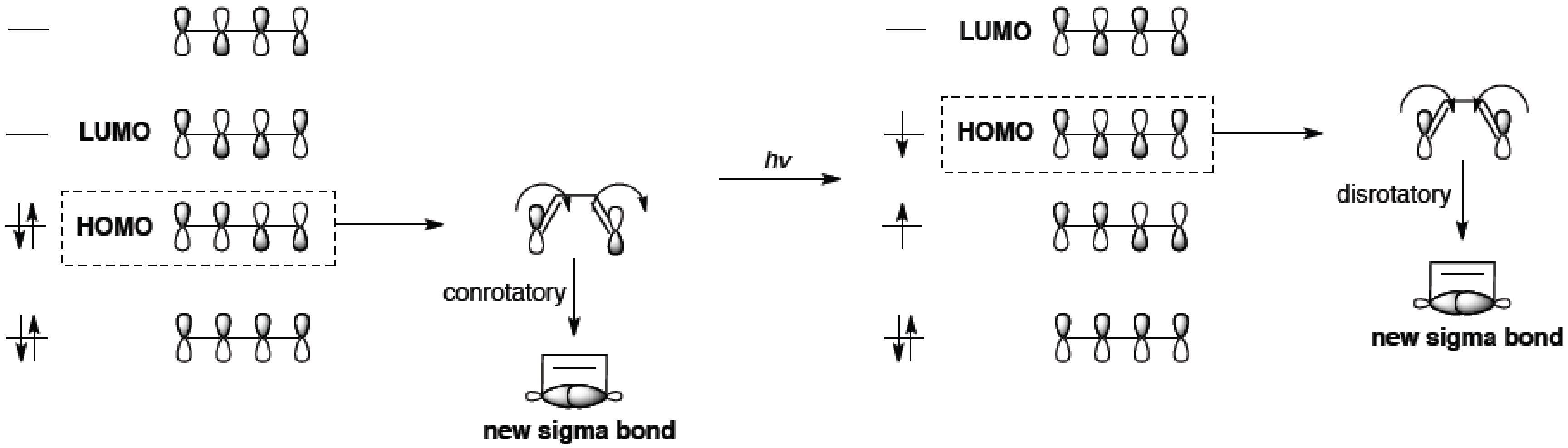
In an electrocyclic reaction the end two orbitals of a conjugated π-system have to form a new σ-bond. As you need electrons to form a new σ-bond, the HOMO of the 1,3-diene determines the outcome of the reaction. In order to overlap the two end orbitals of the HOMO to form the new σ-bond, they can be turned in two different directions: In conrotatory mode, both end groups turn in the same direction (clockwise). In disrotatory mode, the groups turn in opposite directions (one clockwise and one counter-clockwise).





Thermal vs Photochemical

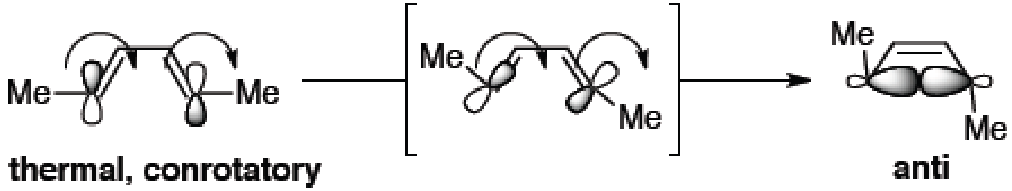
As already showed above, in the thermal electrocyclic ring closure of 1,3-diene the orbitals have to be turned in a conrotatory fashion to form the new σ-bond (4n, thermal, conrotatory). In the photochemical case the disrotation leads to the desired ring closure (4n, photochemical, disrotatory)



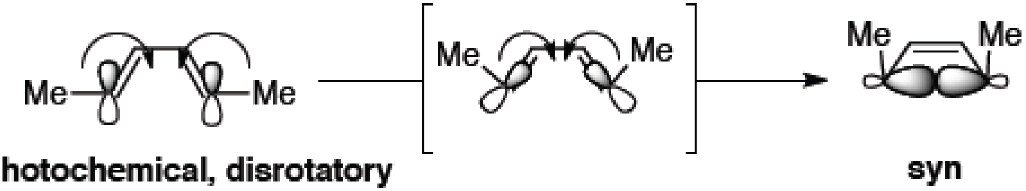
Stereochemical outcome

The ring closure of 2,4-hexadiene could provide the *cis* or the *trans* product.

To predict the stereochemical outcome of this reaction you just have to apply the rules from above. In the thermal case, the conrotation of the orbitals flips one methyl group above the plane and the other underneath. In the photochemical reaction the orbitals have to be turned in disrotatory fashion and both methyl group end up on the same side.

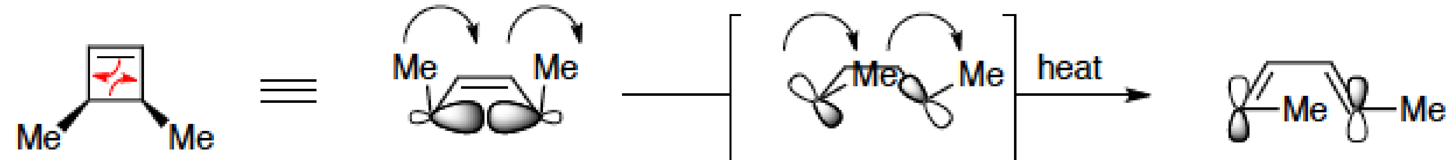


4n, thermal, conrotatory

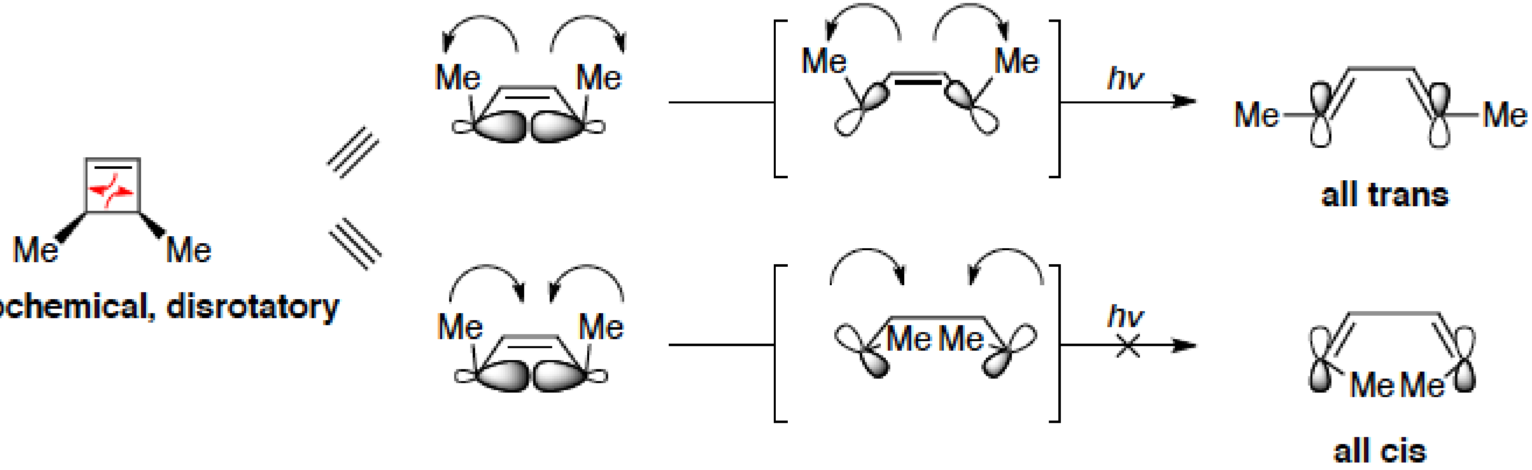


4n, photochemical, disrotatory

The ring opening of 1,2-dimethylcyclobutane is the reverse reaction of the electrocyclic ring closure of 2,4-hexadiene. The rules are exactly the same: under thermal conditions the ring has to be opened in a conrotatory way, therefore the product has a cis,trans configuration. Under photochemical conditions the ring is opened via disrotation. This could lead to two different products: The all-cis and the all-trans. In fact only the all-trans product is obtained, because there are severe steric interactions in the transition state leading to the all-cis product.



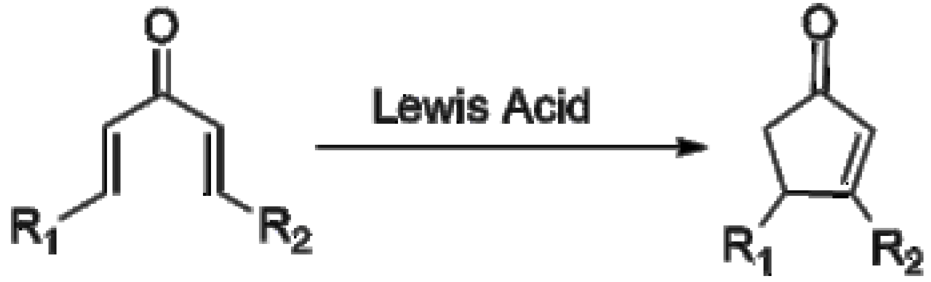
4n, thermal, conrotatory

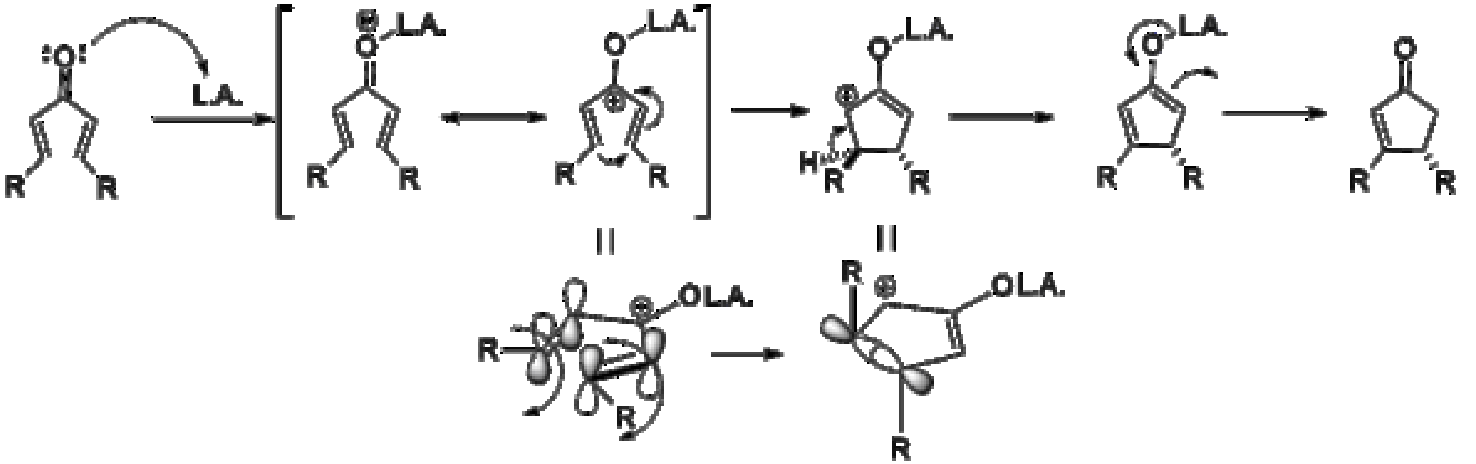


4n, photochemical, disrotatory

Nazarov cyclization reaction

cationic 4π-electrocyclic ring closure





The success of the Nazarov cyclization as a tool in organic synthesis stems from the utility and ubiquity of cyclopentenones as both motifs in natural products (including jasmone, the aflatoxins, and a subclass of prostaglandins) and as useful synthetic intermediates for total synthesis.
The reaction has been used in several total syntheses and several reviews have been published.

Sigmatropic rearrangements

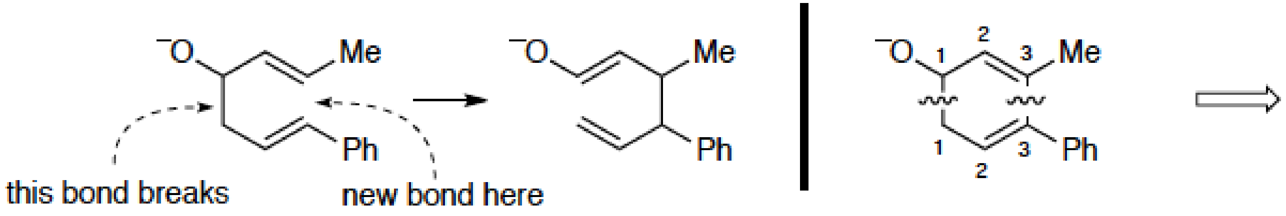
Sigmatropic rearrangements are the most inherently reversible of all pericyclic reactions, since there is not net change in the number of σ and π bonds. The position of the equilibrium depends on the relative thermodynamic and kinetic stability of the starting material and products.

Naming sigmatropic rearrangements

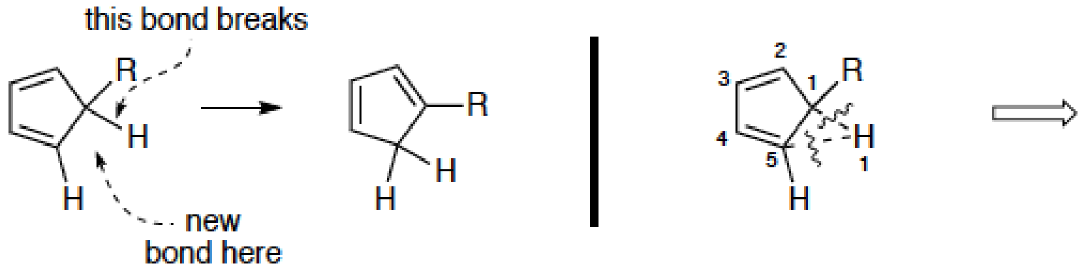
Sigmatropic rearrangements are calssified as [m,n] sigmatropic rearrangements, where m and n are the number of atoms in the fragments in between where the σ bond breaks and forms.

How to classify sigmatropic rearrangements:

1. Locate where σ bond breaks and forms.
2. Draw squiggles through the center of the bonds that breaks and forms.
3. Count the number of atoms in each fragments



[3,3]-sigmatropic rearrangement



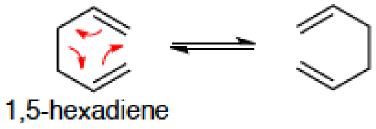
[1,5]-sigmatropic rearrangement

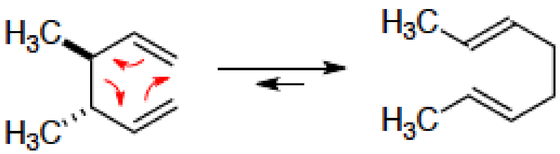
[3,3]-Sigmatropic rearrangements

The [3,3]-sigmatropic rearrangements (Cope and Claisen rearrangements) are the most widely used sigmatropic rearrangements.

Cope rearrangements

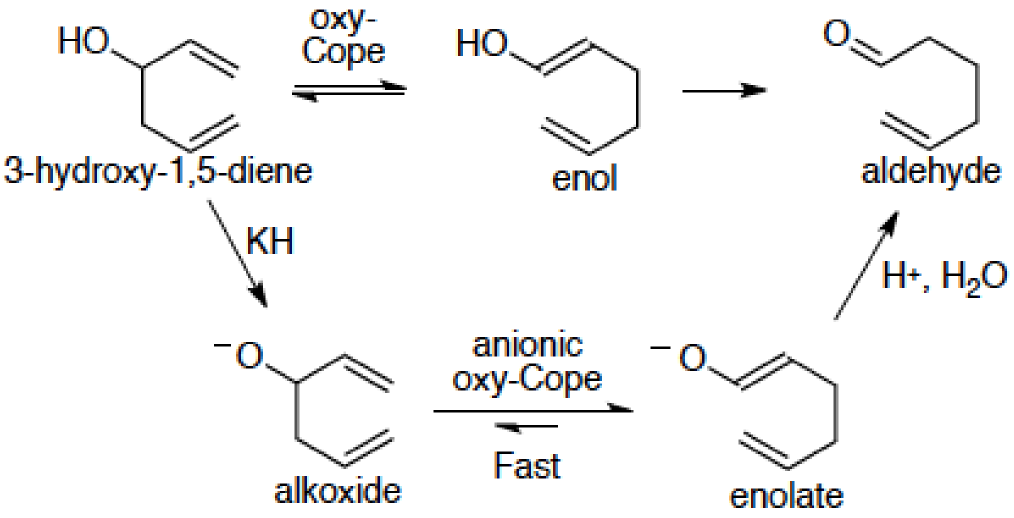
The rearrangement of 1,5-hexadiene is the simplest Cope rearrangement. The reaction is degenerate, meaning that the starting material is identical with the product.





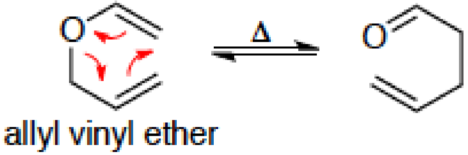
more stable because of
more substituted double
bonds

Substituents can shift the equilibrium to the side with the more substituted π bonds.

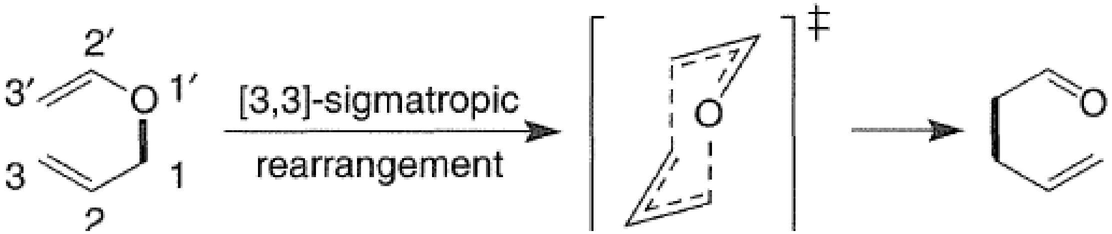


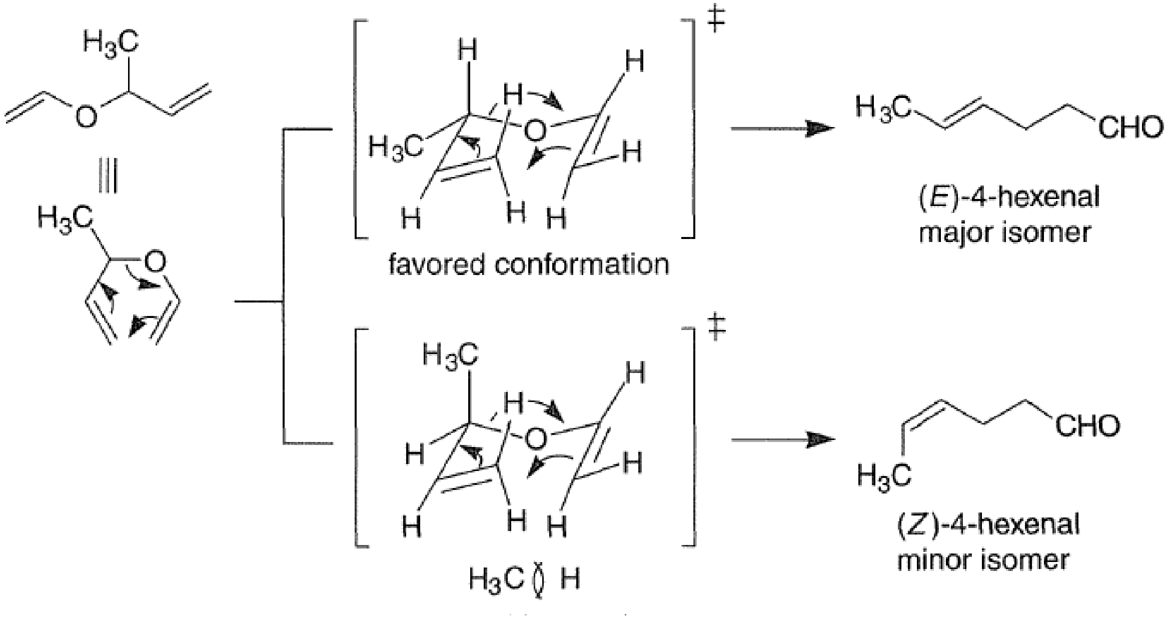
Claisen rearrangements

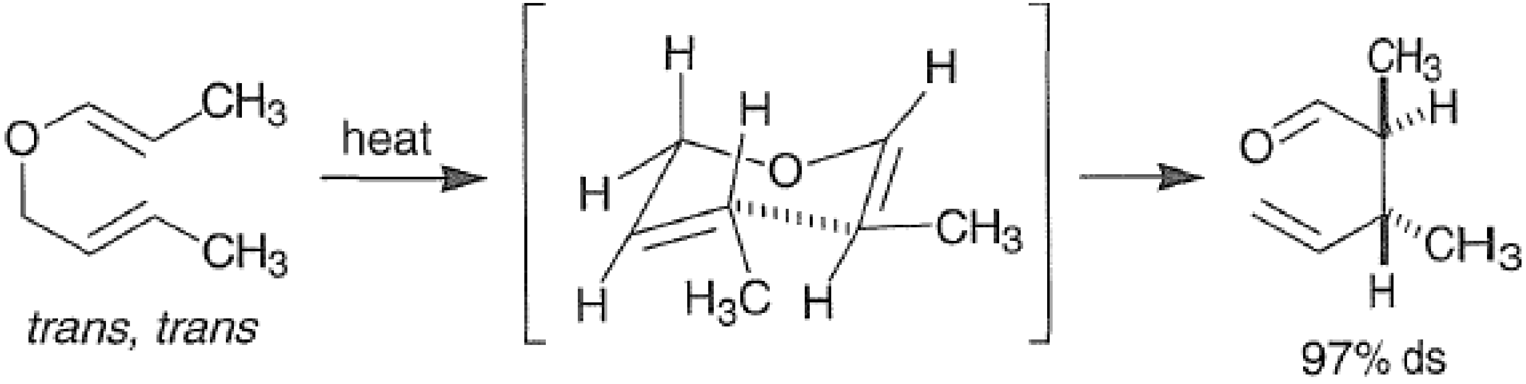
Rearrangement of allyl vinyl ether.

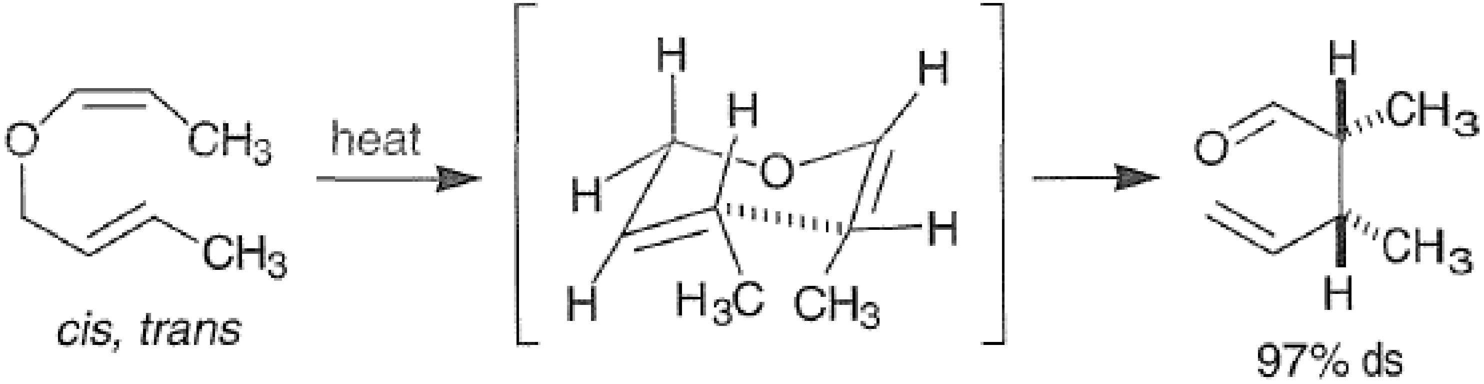


C=O π bond: 79 kcal/mol
C=C π bond: 67 kcal/mol



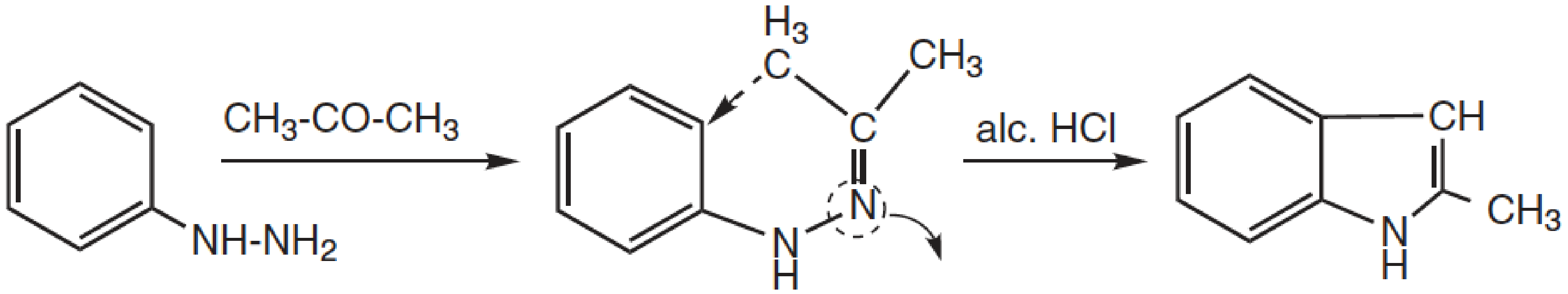


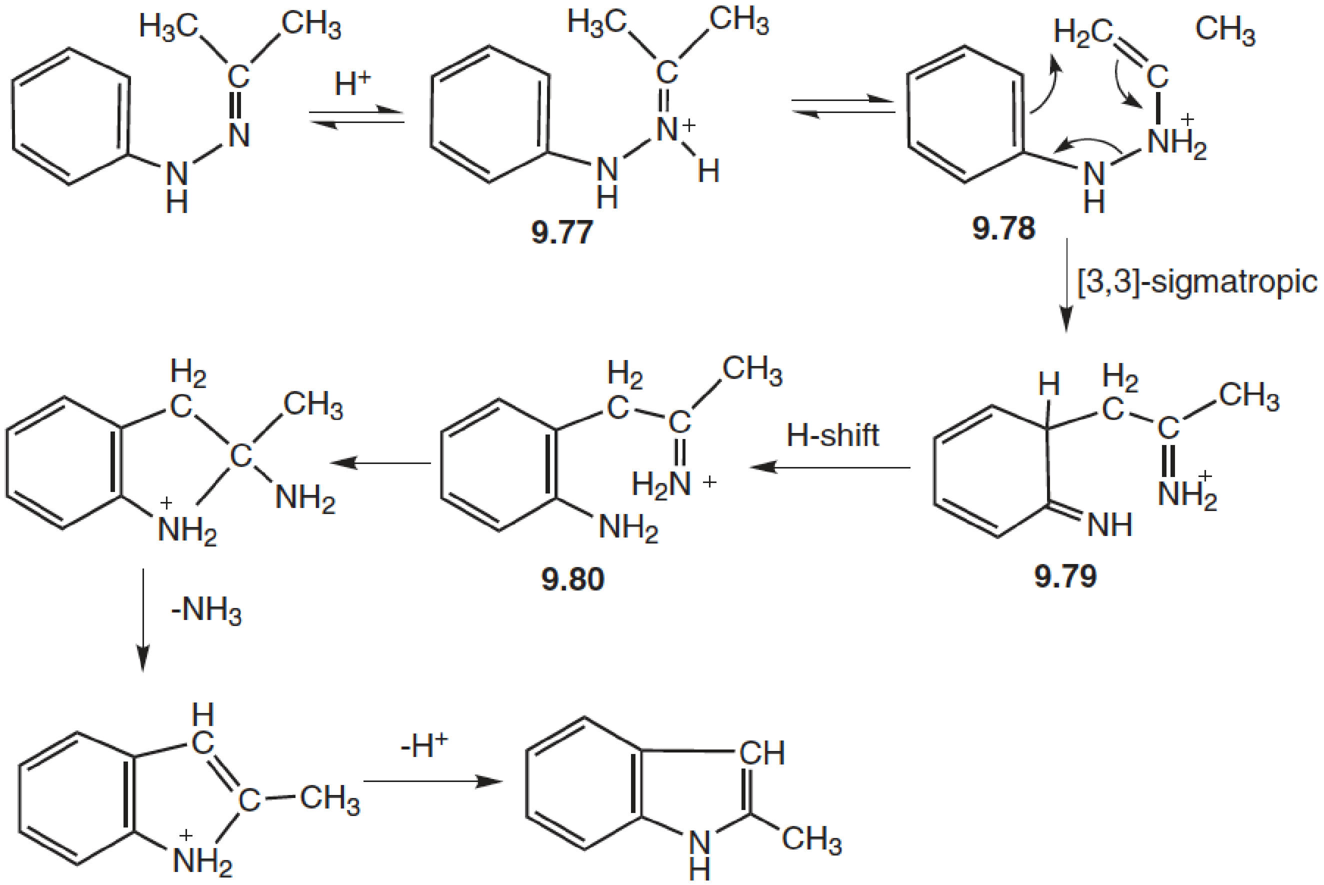




The stereochemical course of the rearrangement is controlled by suprafacial inphase interactions of the participating molecular orbitals and is consistent with that predicted by frontier molecular orbital theory.

Claisen Rearrangements in Heterocyclic chemistry (Fisher Indole synthesis)





Claisen Rearrangements in BIOLOGY

The enzyme Chorismate mutase catalyzes the Claisen rearrangement of chorismate ion to prephenate ion,
a key intermediate in the shikimic acid pathway (the biosynthetic pathway towards the synthesis of phenylalanine and tyrosine).

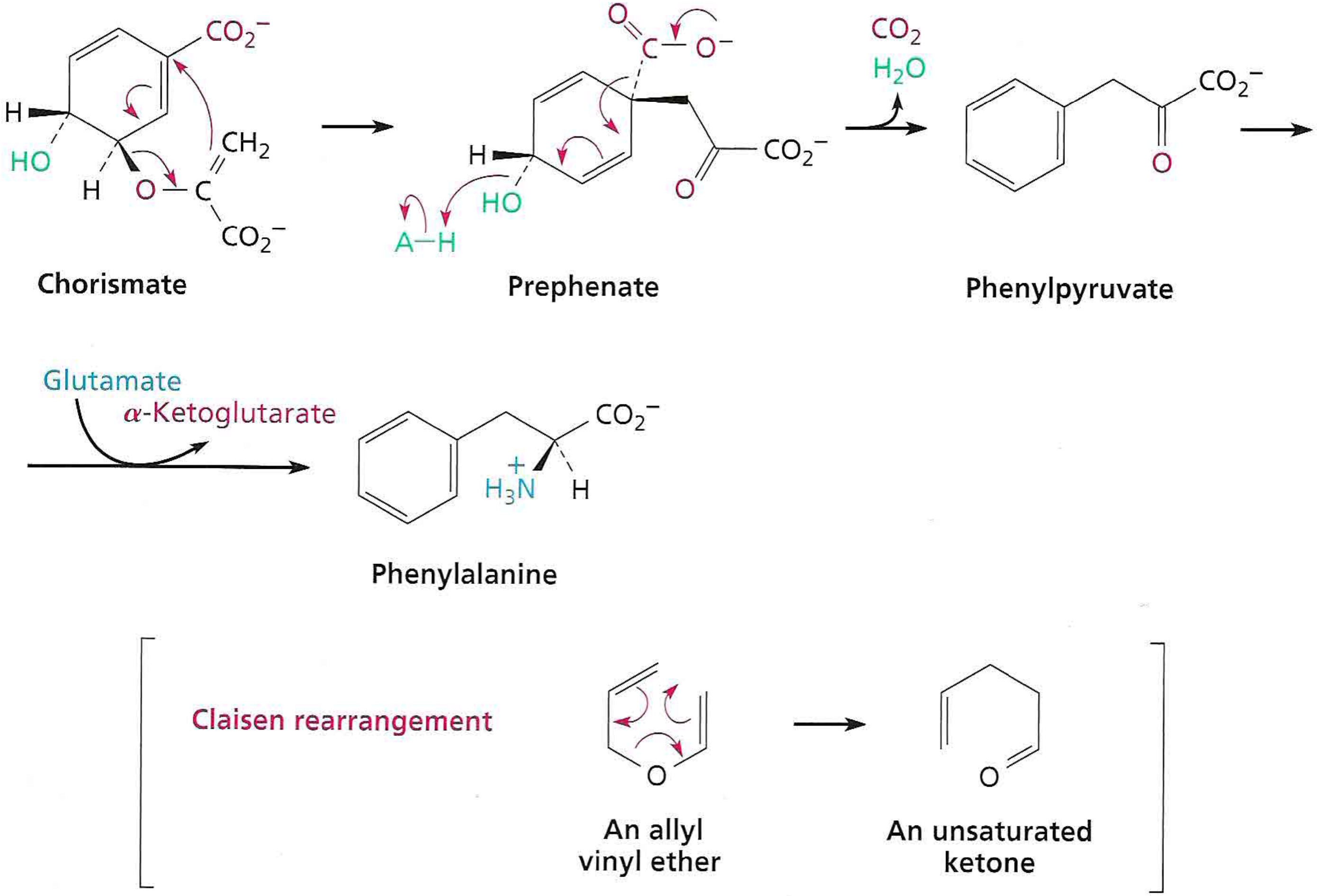
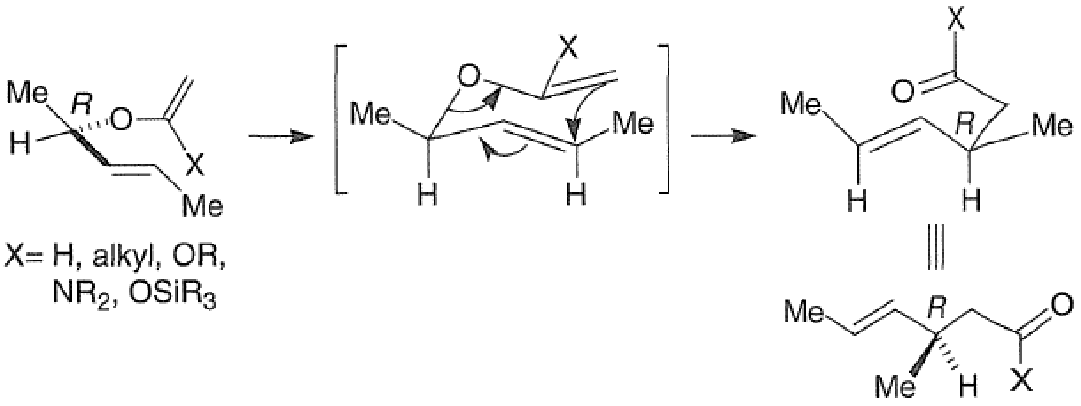
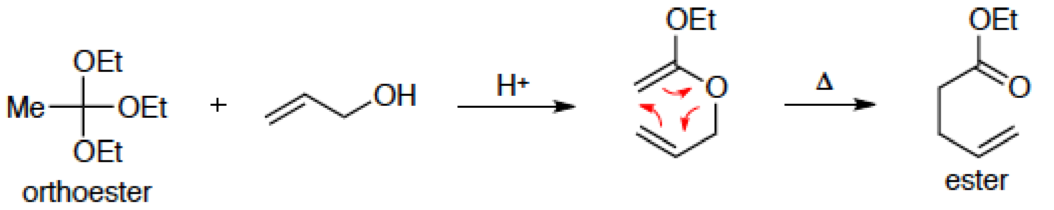


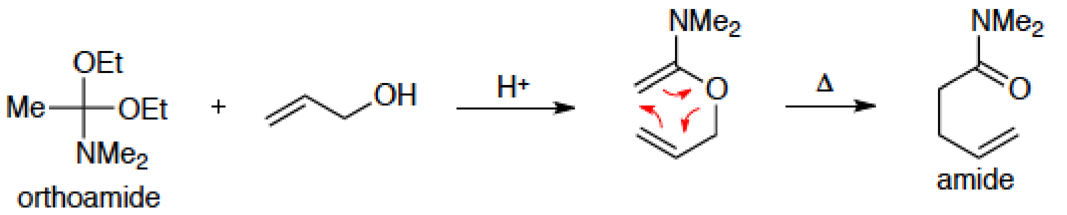
FIGURE 5.47 Pathway for the biosynthesis of phenylalanine from chorismate.



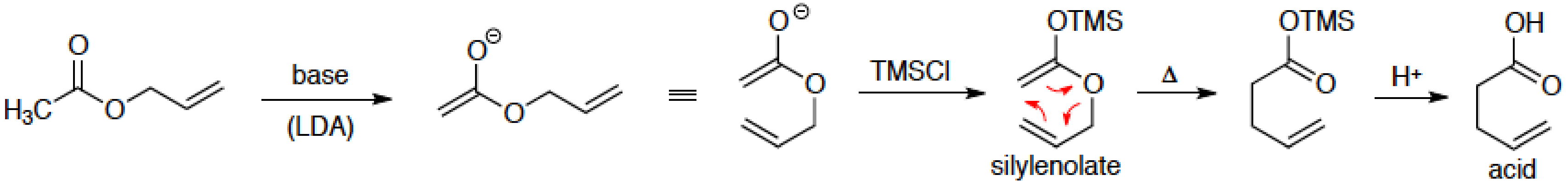
Johnson-Claisen



Eschenmoser-Claisen

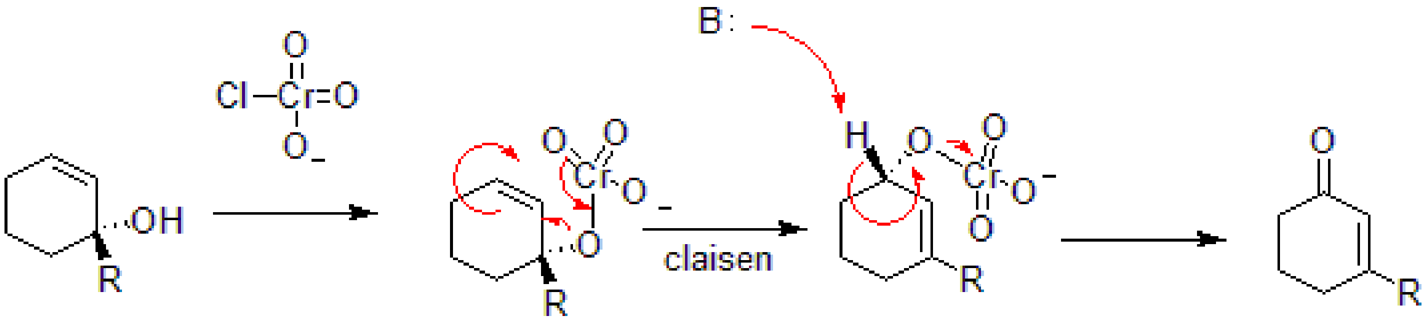


Ireland-Claisen

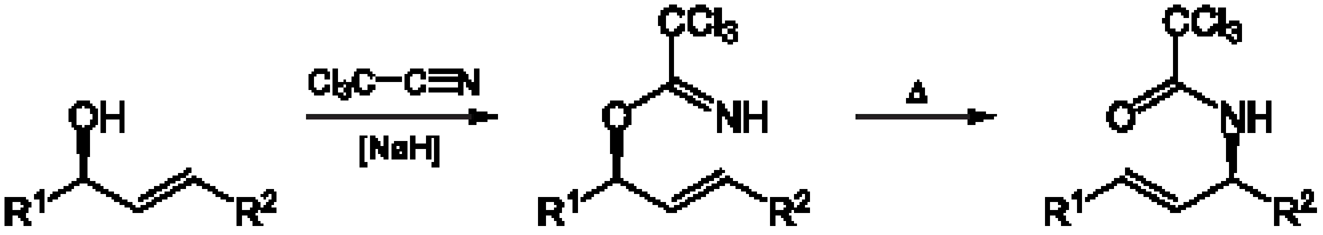


Other examples od Claisen rearrangements

Chromium can oxidize allylic alcohols to alpha-beta unsaturated ketones



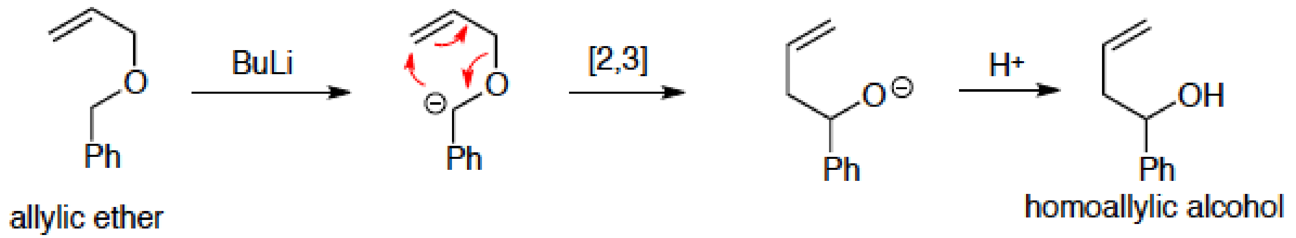
Overman rearrangement

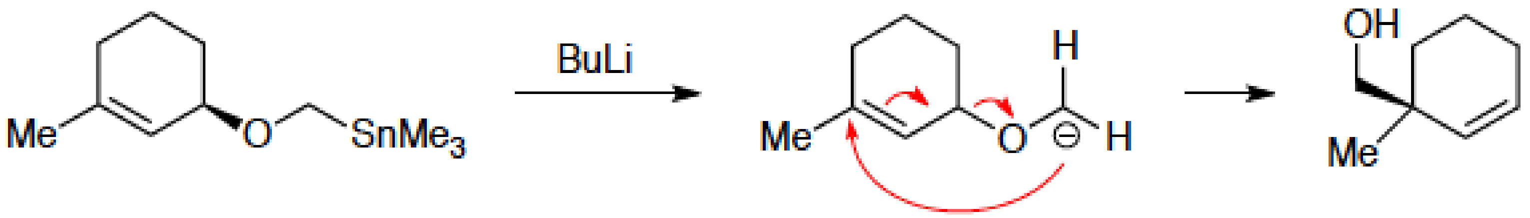


[2,3]-Sigmatropic rearrangements

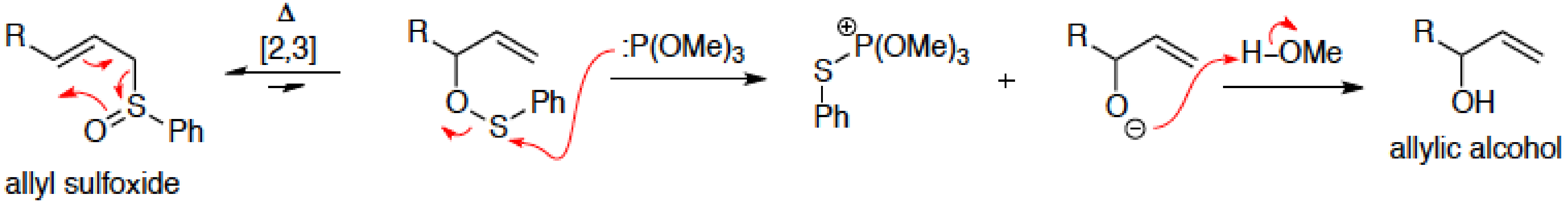
Wittig rearrangement

Transformation of allylic ether into homoallylic alcohol.





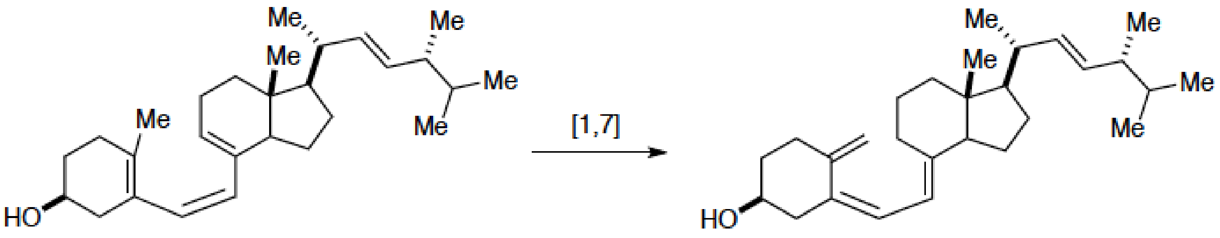
Evans-Mislow rearrangement



[1,n]-Hydride shifts

In these reactions, a hydride is moved from one atom to another atom in the molecule.

A [1,7]-hydride shift occurs in the final stage of the human body’s synthesis of vitamin D from cholesterol.



parcalciferol

ergocalciferol (Vitamin D_2)

Group transfer

Ene reactions/Reaction between allylic hydrogen and an alkene/alkyne.

Alder-ene: