M.Sc. Semester-IV
Core Course-9 (CC-9)
Synthetic Organic Chemistry

II.Pericyclic Reactions
7. Claisen Rearrangement, The Nazarov Reaction

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II Pericyclic Reactions 20 Hrs

Molecular orbital symmetry, Frontier orbitals of ethylene, 1,3-butadiene, 1, 3, 5-hexatriene, allyl system, Classification of pericyclic reactions. FMO approach, Woodward-Hoffman correlation diagram method and PMO approach for pericyclic reaction under thermal and photochemical conditions.

Electrocyclic reactions: Conrotatary and disrotatary motion, 4n and (4n+2) systems, Cycloaddition reaction: [2+2] and [4+2] cycloaddition reaction, Cycloaddition of ketones, Secondary effects in [4+2] cycloaddition. Stereochemical effects on rate of cycloaddition reaction, Diels-Alder reaction, 1,3-dipolar cycloaddition, Chelotropic reaction, The Nazarov reaction.

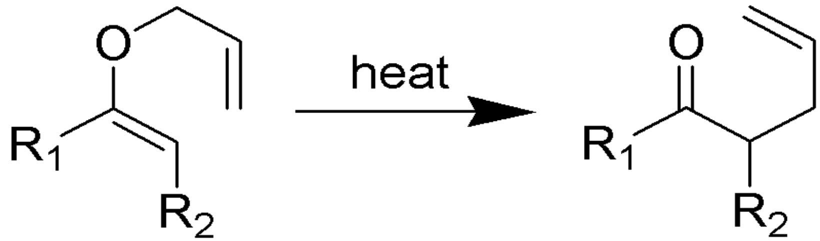
Sigmotropic rearrangement: Suprafacial and antarafacial shift involving H and carbon-moieties, Peripatetic cyclopropane bridge, Retention and inversion of configuration, [3,3]-, [1,5]-, [2,3]-, [4,5]-, [5,5]-, and [9,9]-Sigmatropic rearrangements, Claisen rearrangements (including Aza-Claisen, Ireland-Claisen), Cope rearrangements (including Oxy-Cope, Aza-Cope), Sommelet-Hauser rearrangements, Group transfer reaction, Ene reaction, Mislow - Evans rearrangement, Walk rearrangement.

Coverage:

1.Claisen Rearrangement
2.The Nazarov Reaction

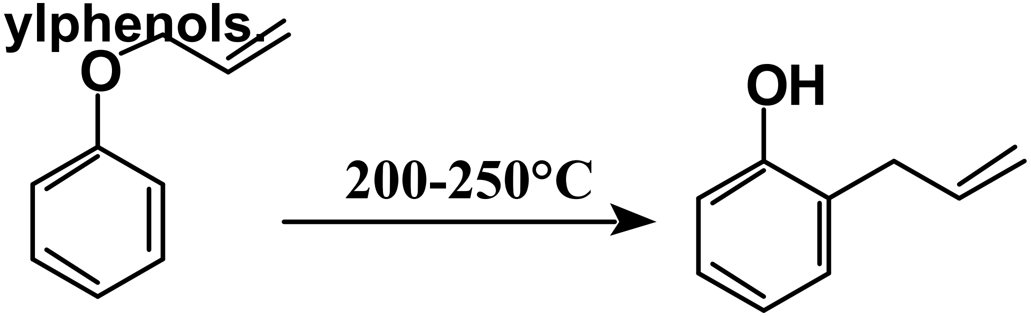
Claisen Rearrangement : [3, 3] Sigmatropic Rearrangement

Rainer Ludwig Claisen
1851-1930

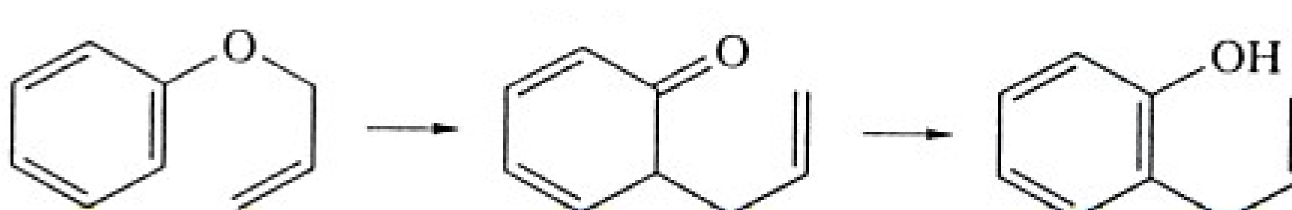


How and Why?

Claisen rearrangement: **A thermal rearrangement of allyl phenyl ethers to form 2-allylphenols.**

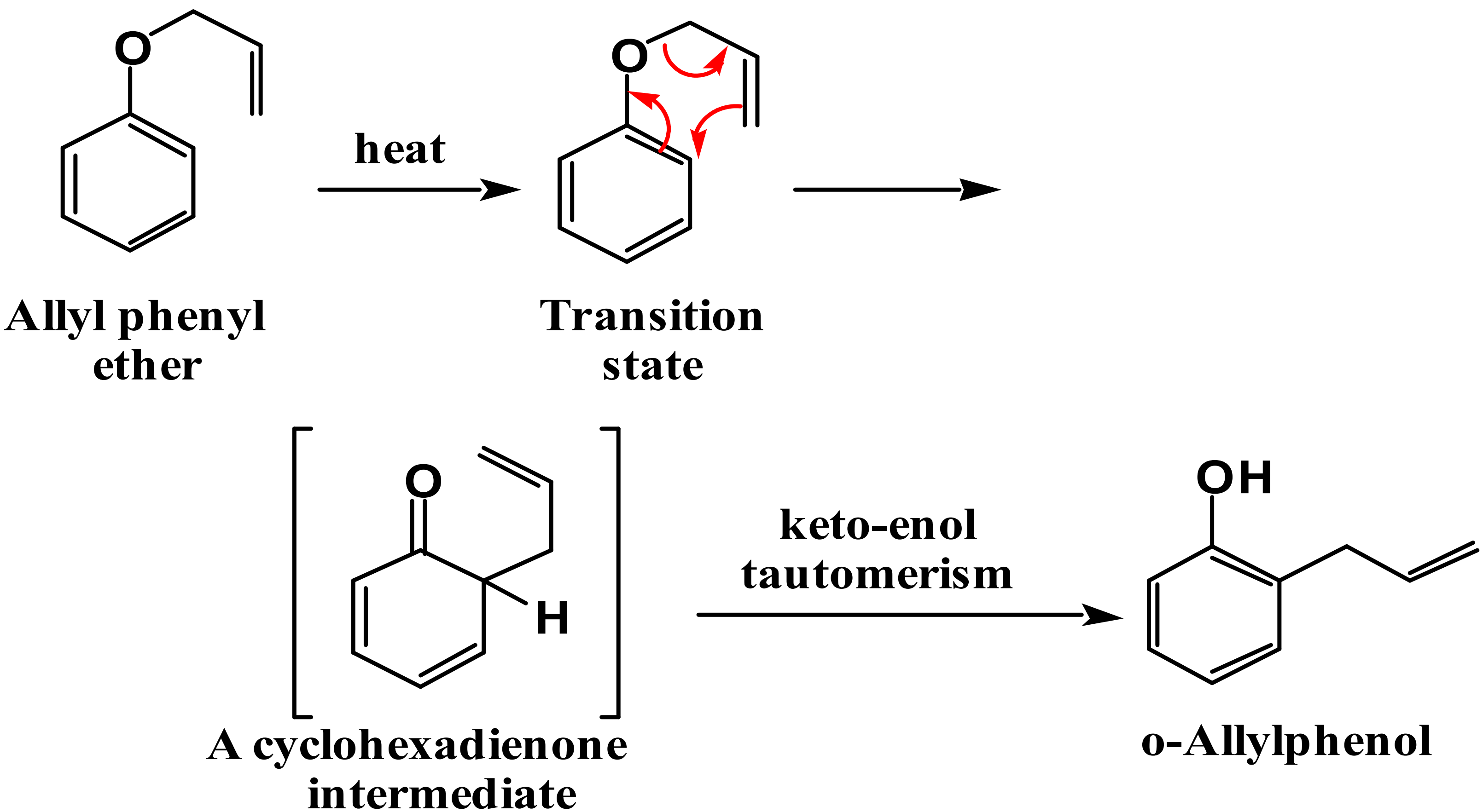


Allyl phenyl ether **2-Allylphenol**



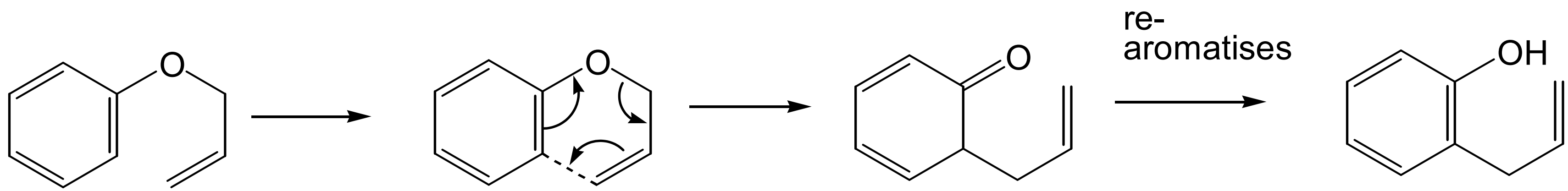
Claisen Rearrangement : [3, 3] Sigmatropic Rearrangement

Mechanism:

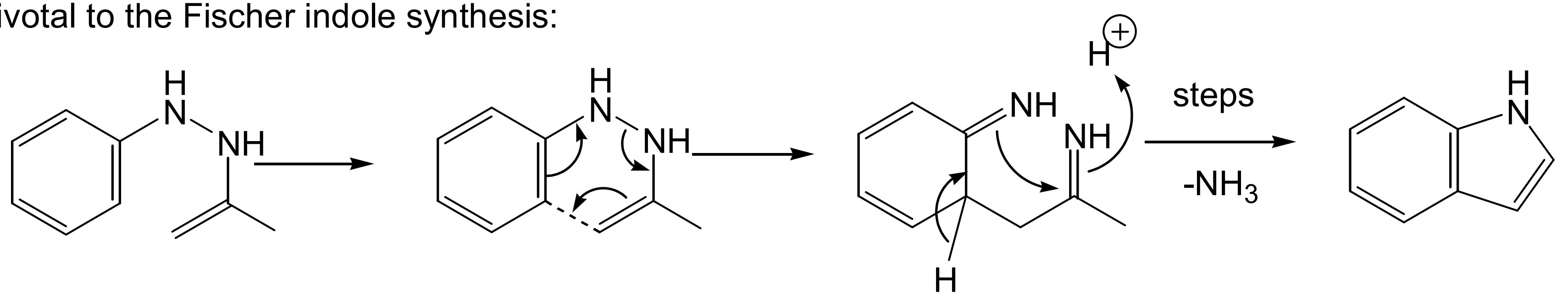


Claisen Rearrangement : [3, 3] Sigmatropic Rearrangement

Claisen reactions are generally irreversible and synthetically useful:



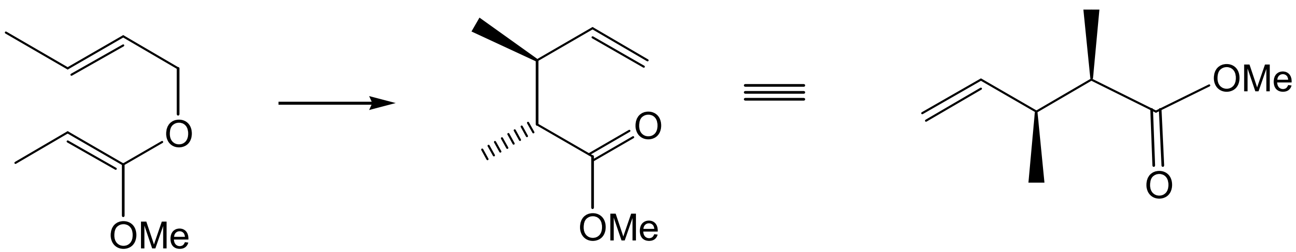
A [3,3]-sigmatropic reaction is
pivotal to the Fischer indole synthesis:



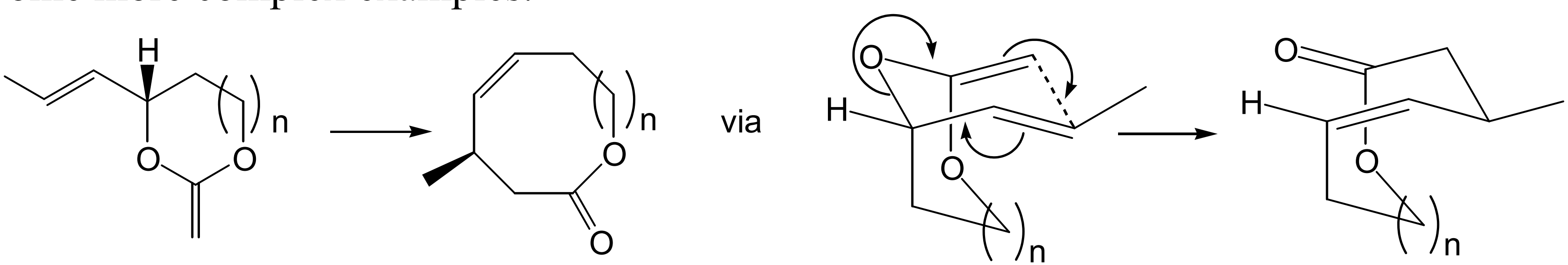
Important: Don’t get confused with the Claisen Reactions of esters.

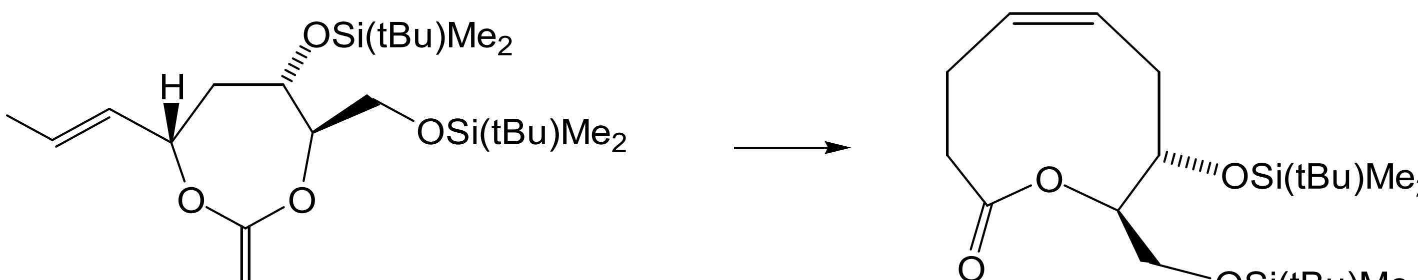
Claisen Rearrangement

The Ireland-Claisen reaction is a useful method for constructing esters, particularly of difficult medium-ring products, with high stereoselectivity.



Some more complex examples:

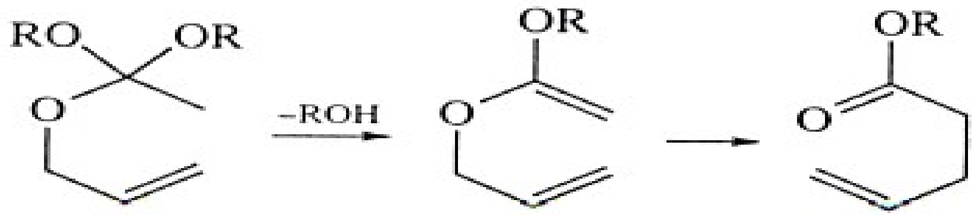




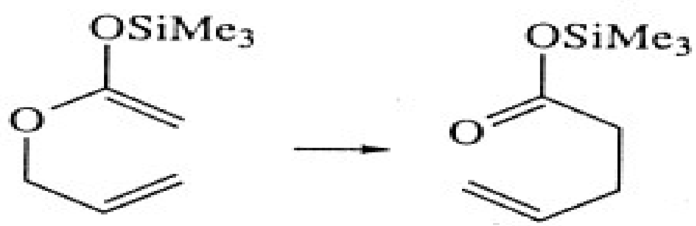
Application to the synthesis of ascidialactone, a marine natural product.

Claisen Rearrangement : Examples

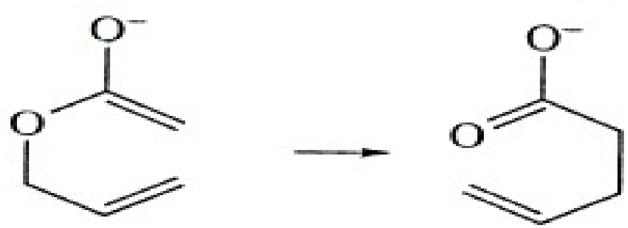
1. Ortho ester Claisen rearrangement



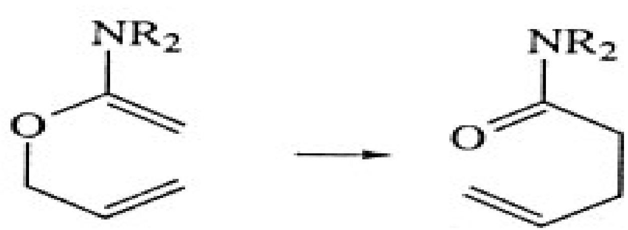
2. Claisen rearrangement of *O*-allyl-*O′*-trimethylsilyl ketene acetals



3. Ester enolate Claisen rearrangement

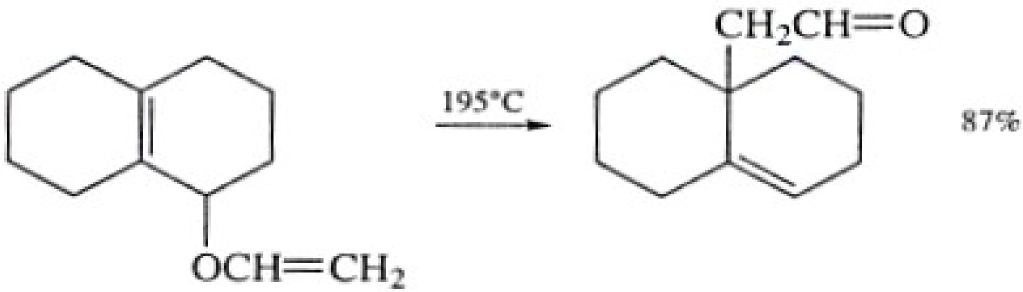


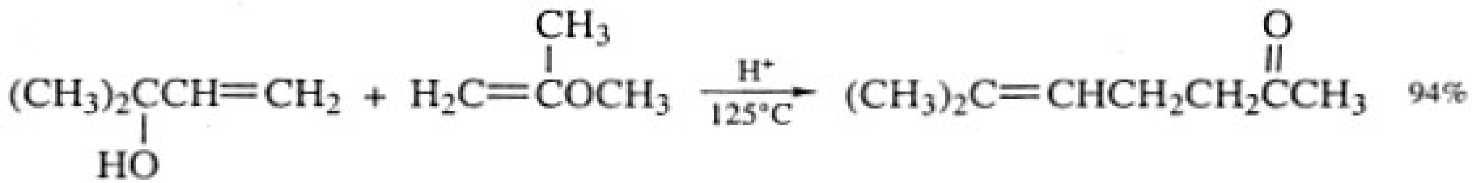
4. Claisen rearrangement of *O*-allyl-*N*,*N*-dialkyl ketene aminals

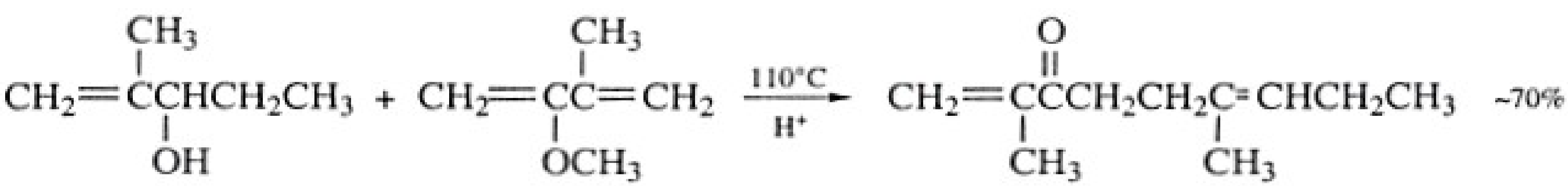


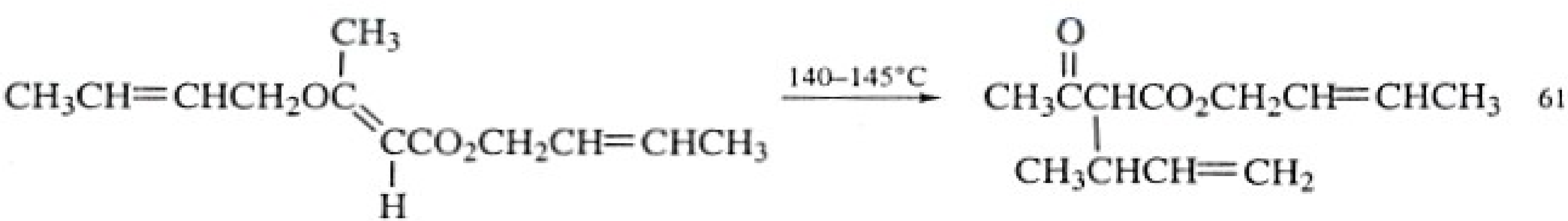
Claisen Rearrangement: Examples

Rearrangement of allyl vinyl ethers

5. 

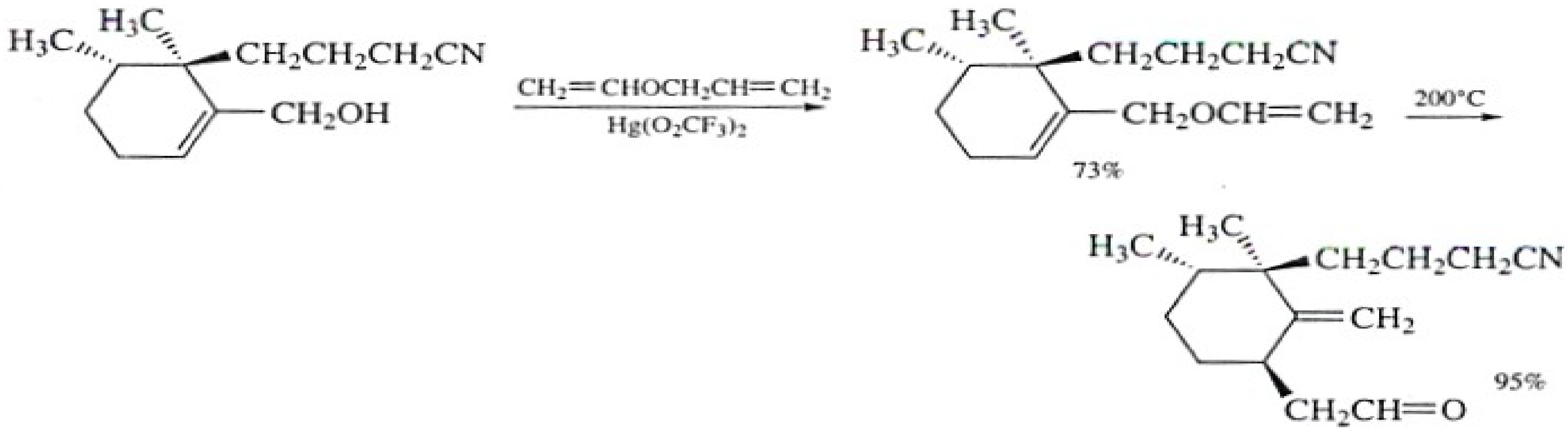
6. 

7. 

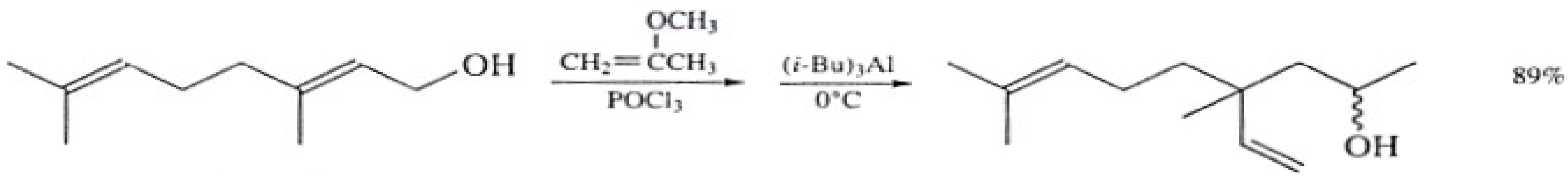
8. 

Claisen Rearrangement: Examples

9.

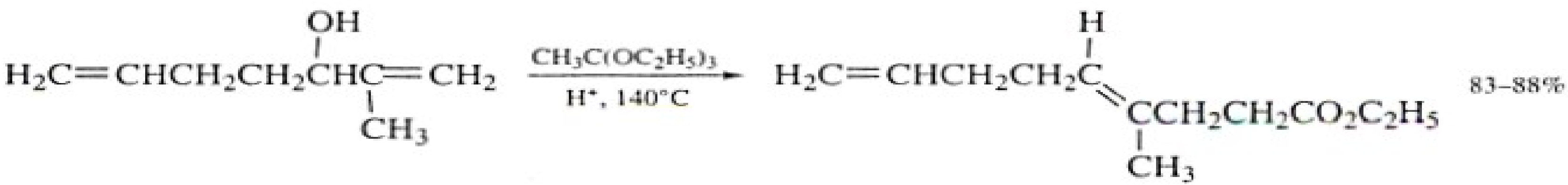


10.

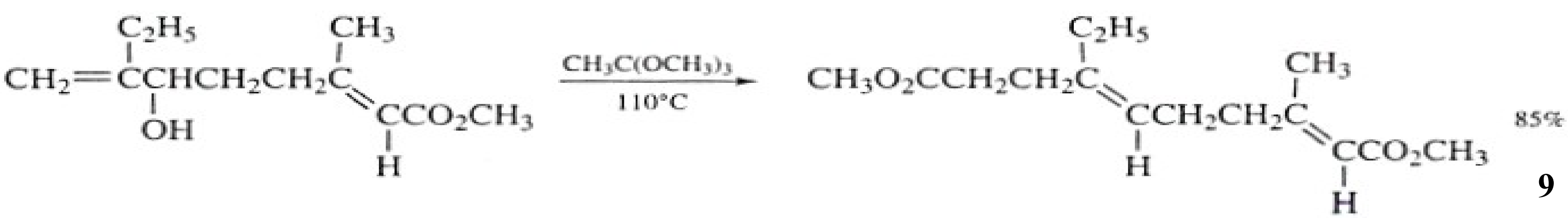


Rearrangement via Ortho Esters

11.

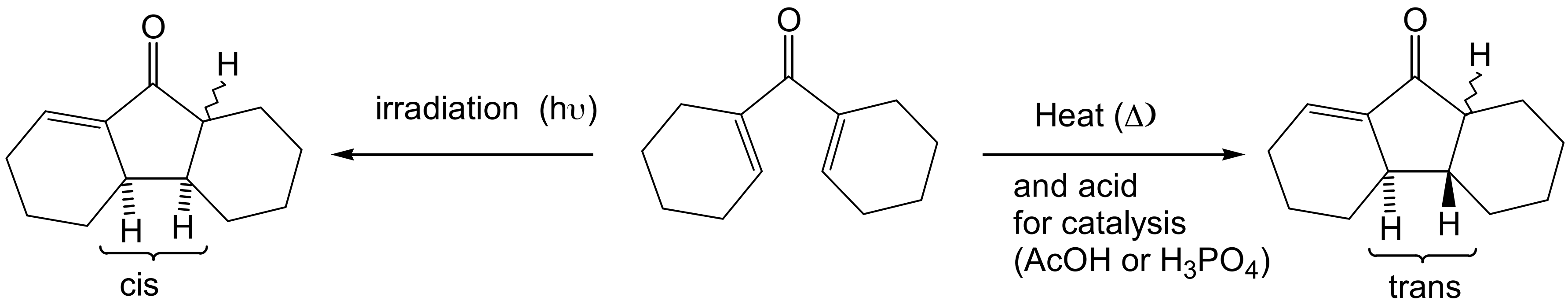


12.



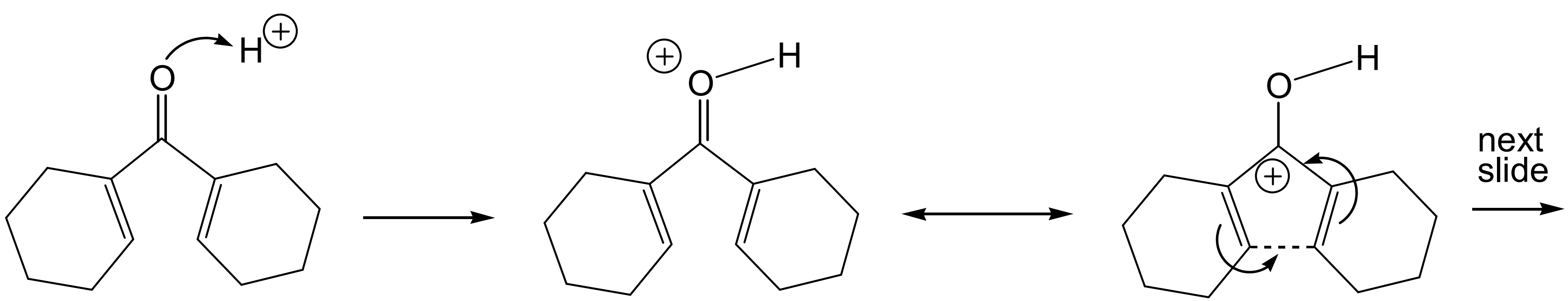
The Nazarov Cyclisation Reaction :

The Nazarov cyclisation usually carried out under acidic/thermal conditions. The position adjacent to the ketone is a mixture of isomers in each case. Only the relative stereochemistry between the lower hydrogens is controlled.

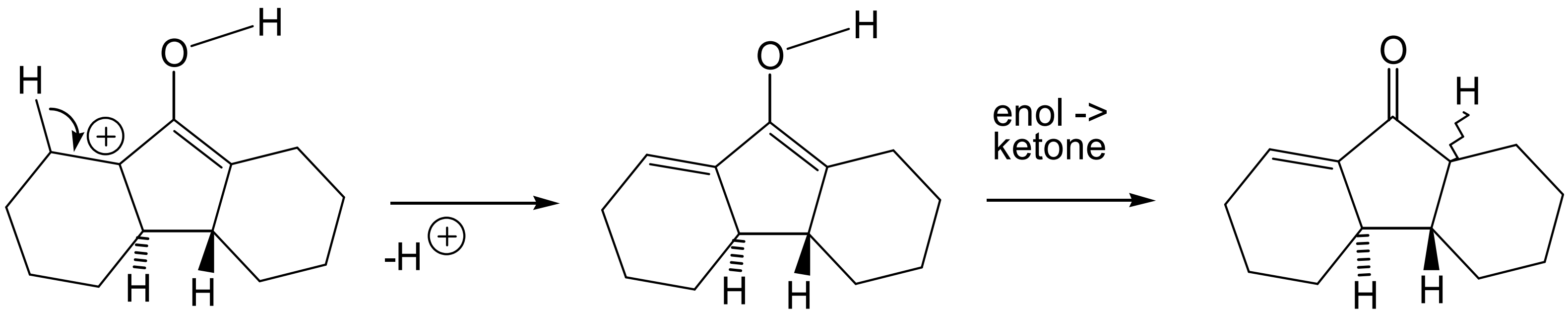


All we need to know is the number of electrons involved (i.e. 4n or 4n+2) and whether the reaction is photochemical or thermal:

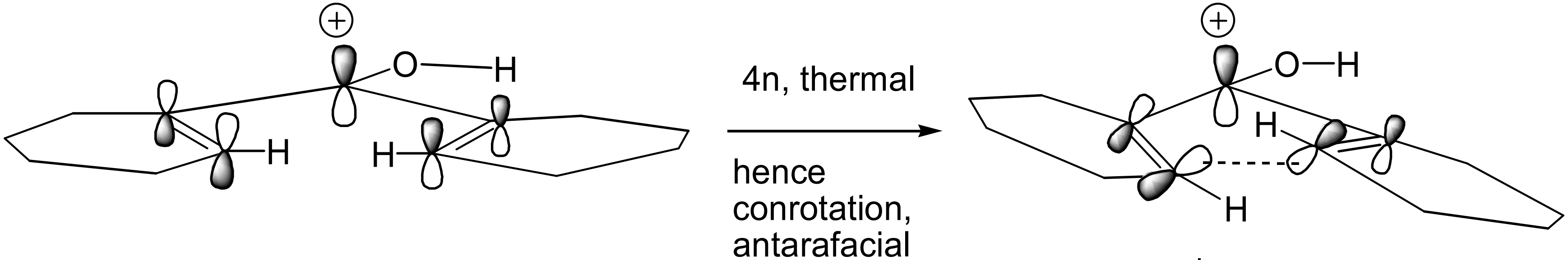
Mechanism:

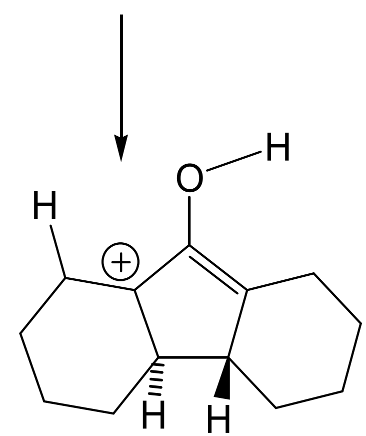


The Nazarov Cyclisation, cont....



Stereochemistry in the key cyclisation step:





Note: although drawn as a localised cation, the positive charge is spread over five atoms through a delocalised pi system of p-orbitals. There are a total of 4 electrons in the pi system (i.e. two in each alkene), hence it is a 4n electron system, and obeys the rules as usual.

Thank You

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