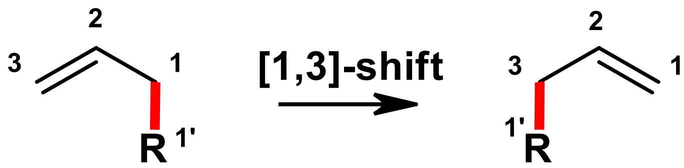
SIGMATROPIC REARRANGEMENTS

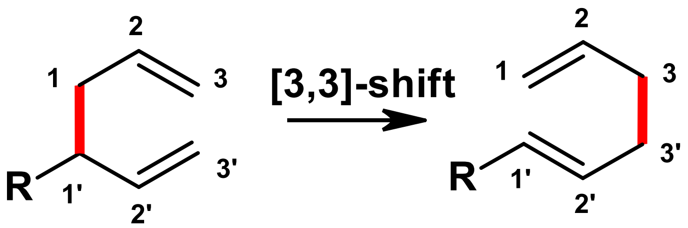
Sigmatropic rearrangements

- pericyclic reaction
- *tropos* (turn)
- migration of a σ-bond across a conjugated π-system

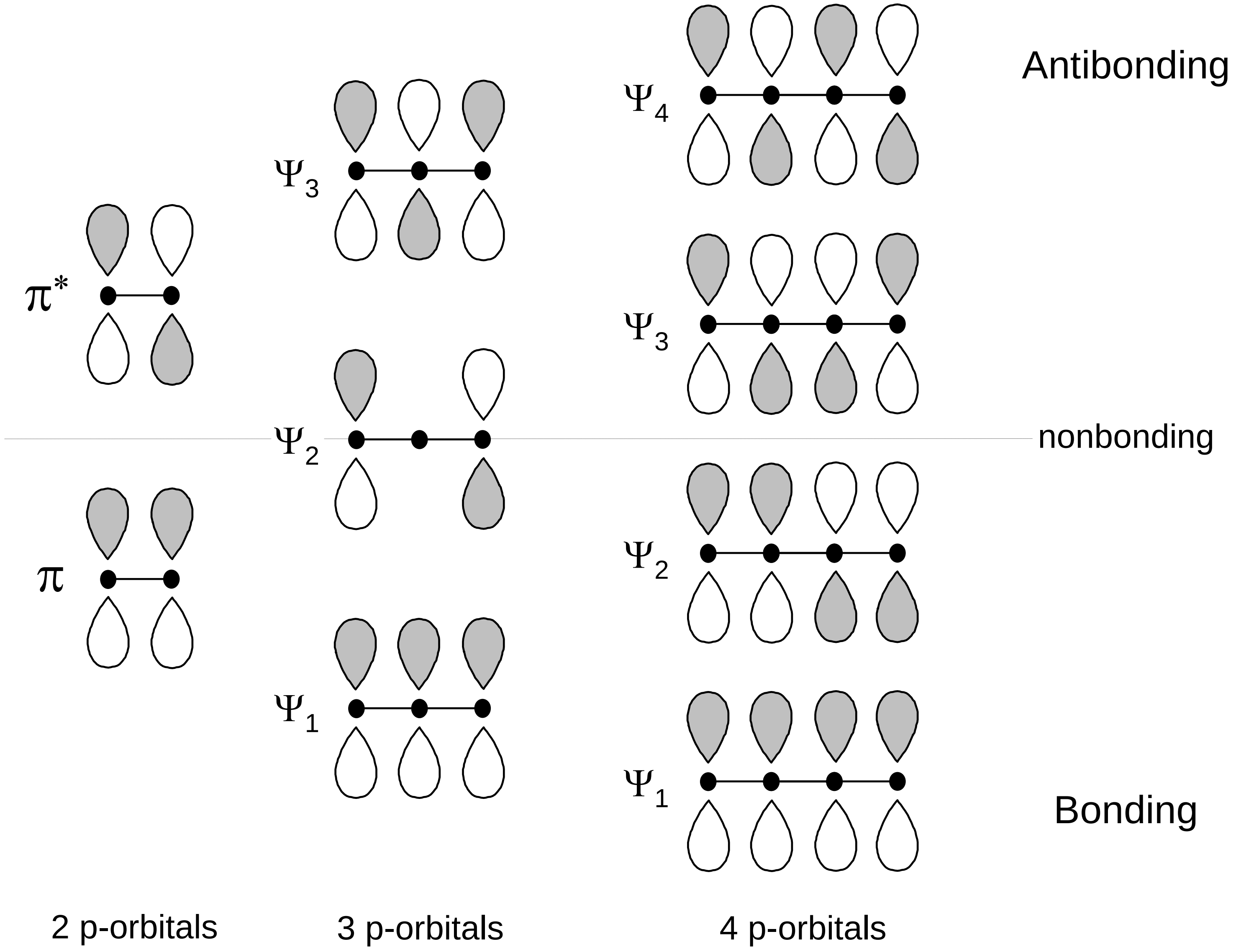
- substituent moves from one part of a π-bonded system to another part in an intramolecular reaction with <u>simultaneous</u> rearrangement of the π systém

- [**m**,**n**] shift when the σ-bond migrates across **m** atoms of one system and **n** of another



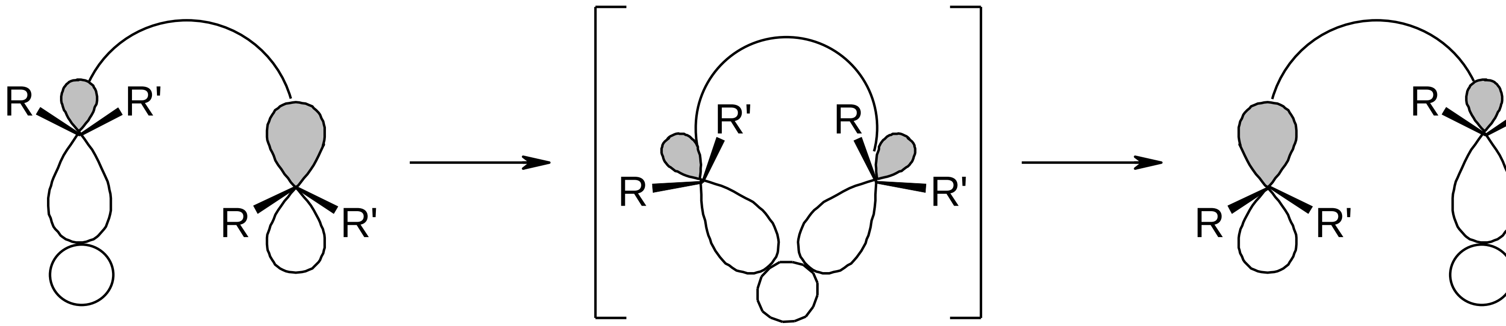


SIGMATROPIC REARRANGEMENTS

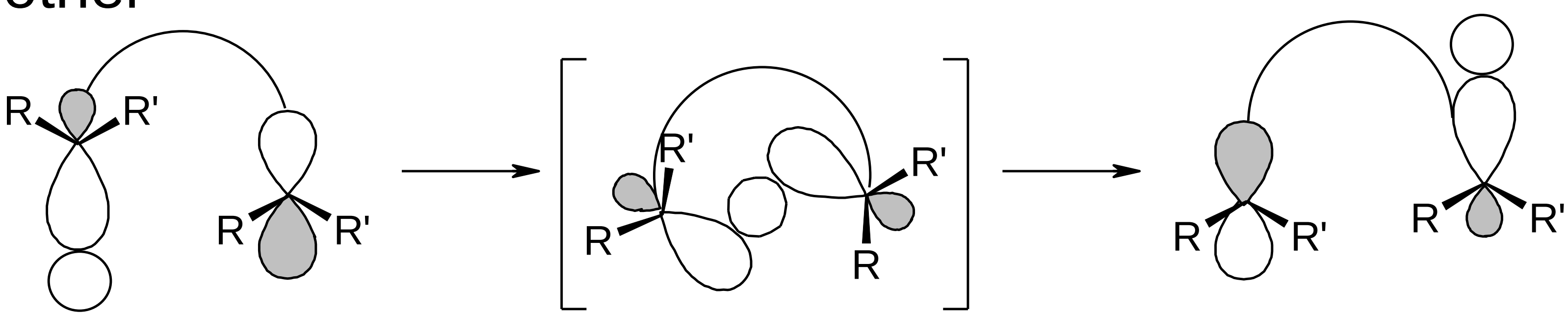


SIGMATROPIC REARRANGEMENTS

- Suprafacial migration: Group moves across same face

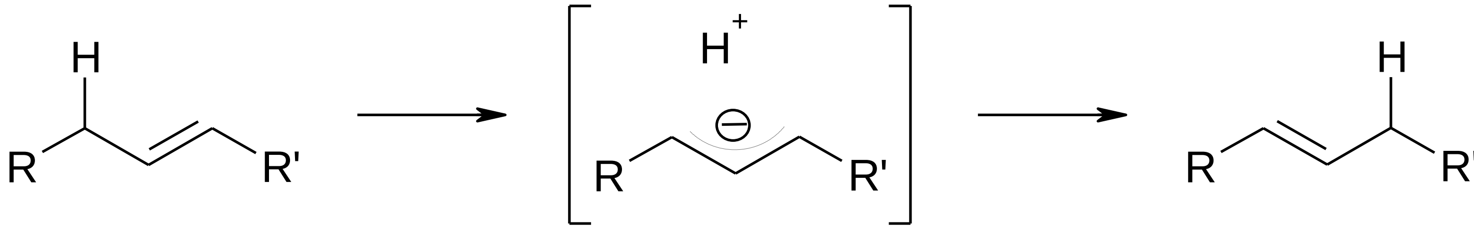


- Antarafacial migration: Group moves from one face to the other



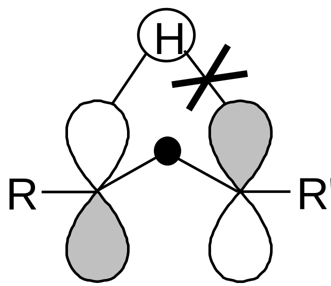
SIGMATROPIC REARRANGEMENTS

- [1,3] Sigmatropic Rearrangements: H migration



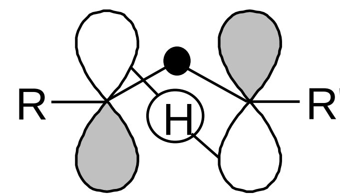
1s proton LUMO

Ψ_2 allyl anion HOMO



Suprafacial migration

FORBIDDEN

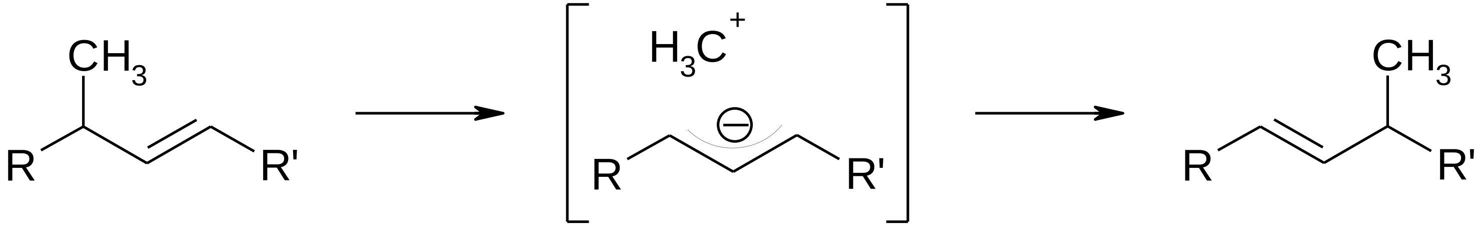


Antarafacial migration

ORBITALLY ALLOWED BUT
H CANNOT BRIDGE DISTANCE

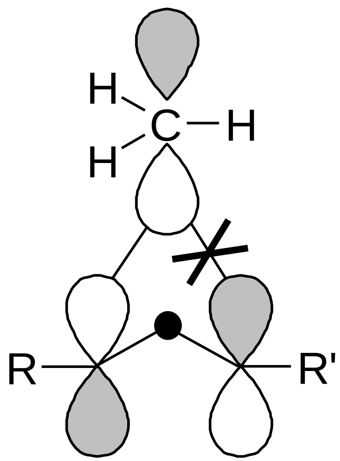
SIGMATROPIC REARRANGEMENTS

- [1,3] Sigmatropic Rearrangements: C migration



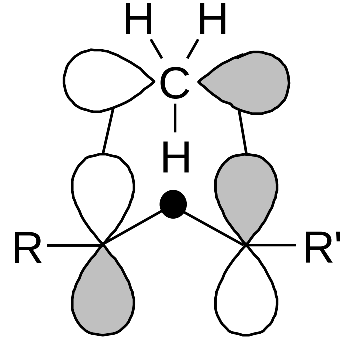
2p Carbon LUMO

Ψ_2 allyl anion HOMO



Suprafacial migration
Retention at carbon

FORBIDDEN

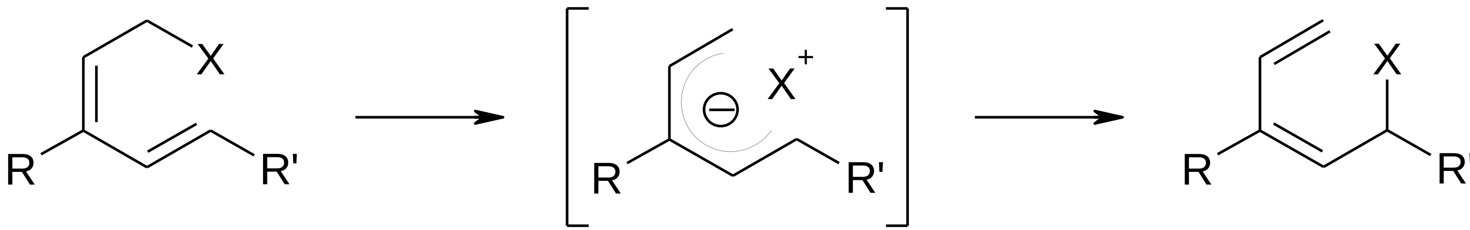


Suprafacial migration
Inversion at carbon

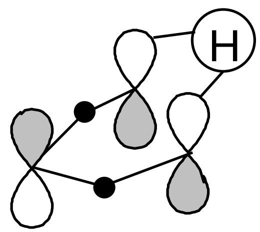
ALLOWED

SIGMATROPIC REARRANGEMENTS

- [1,5] Sigmatropic Rearrangements



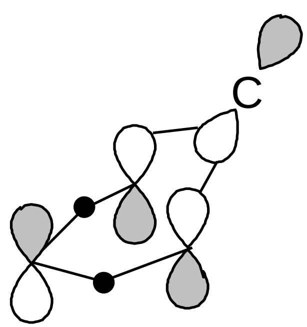
Ψ_3 pentadienyl anion HOMO



1s proton LUMO

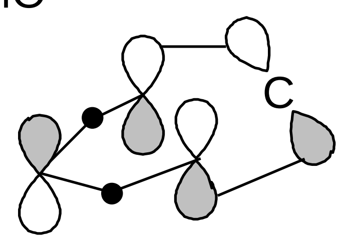
Suprafacial migration	Antarafacial migration
ALLOWED	**FORBIDDEN**

Ψ_3 pentadienyl anion HOMO



2p carbon LUMO

Suprafacial migration
Retention at Carbon
ALLOWED



Antarafacial migration
Inversion at Carbon
ALLOWED

SIGMATROPIC REARRANGEMENTS

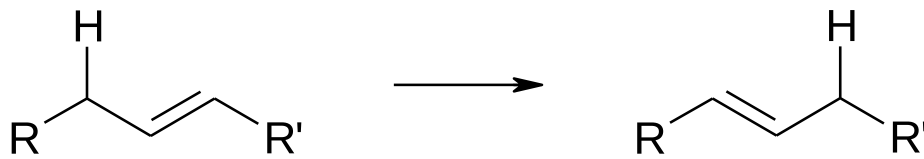
- Dewar-Zimmerman model:
  - Choose a set of 2p atomic orbitals and arbitrarily assign phase
  - Connect the orbitals in the starting material
  - Allow reaction to proceed according to postulated geometry and connect reacting lobes.
  - Count number of phase inversions: Odd = Möbius, Even = Hückel
  - Assign transition state as aromatic or antiaromatic based on number of electrons:

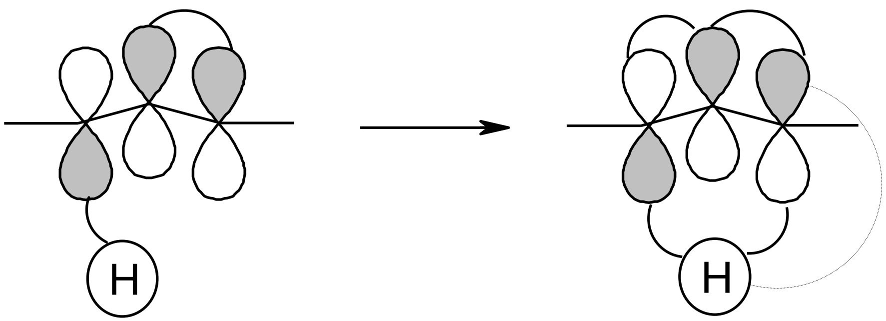
System	Aromatic	Antiaromatic
Hückel	4n + 2	4n
Möbius	4n	4n + 2

  - Aromatic = Thermally allowed (Photochemically forbidden)
  - Antiaromatic = Thermally forbidden (Photochemically allowed)

SIGMATROPIC REARRANGEMENTS

- [1,3]-H shift

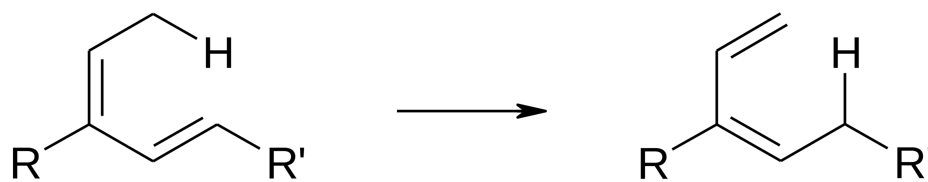


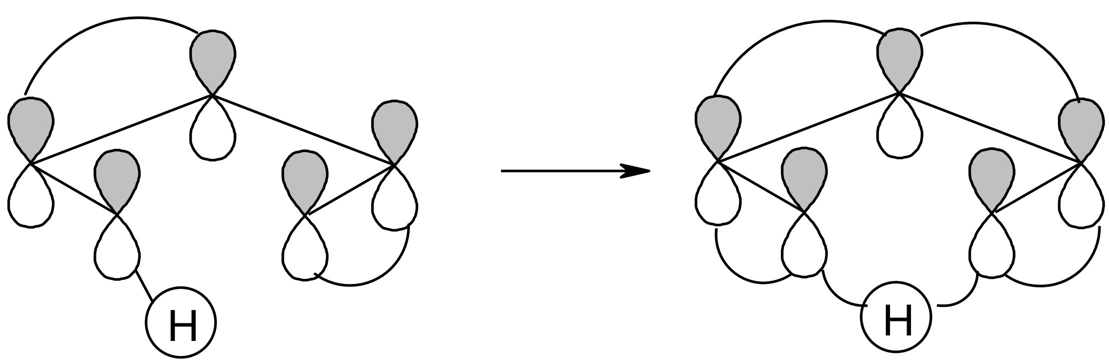


Suprafacial:
Two Phase Inversions
Hückel Topology
Four electrons
FORBIDDEN

Antarafacial:
Three Phase Inversions
Möbius Topology
Four electrons
ALLOWED

- [1,5]-H shift

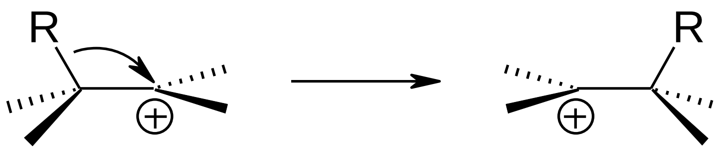


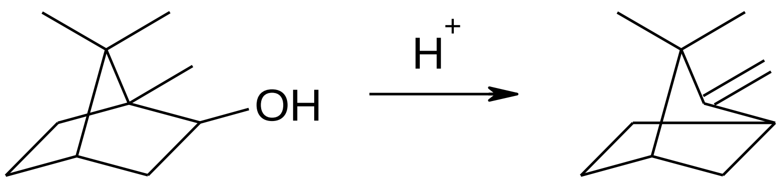


Suprafacial:
Zero Phase Inversions
Hückel Topology
Six electrons
THERMALLY ALLOWED

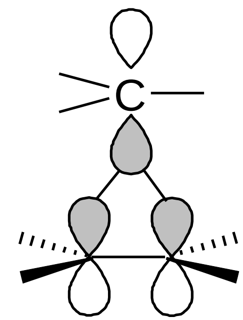
[1,2]-SIGMATROPIC REARRANGEMENTS

- [1,2]-C shift to cation: **Wagner-Meerwein Rearrangement**





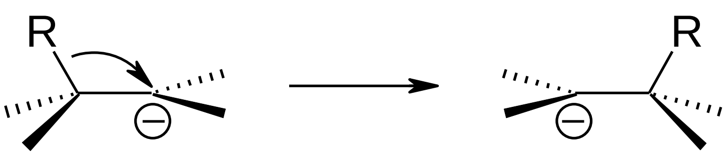
2p Carbon radical

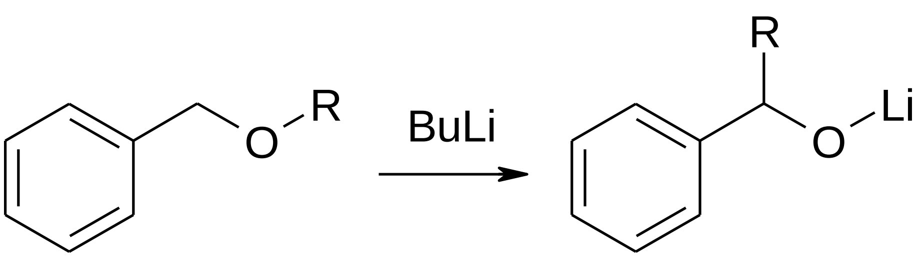


Ψ_1 olefin
radical cation

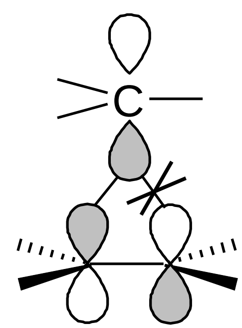
Suprafacial migration: **ALLOWED**

- [1,2]-C shift to anion: **Wittig Rearrangement**





2p Carbon radical

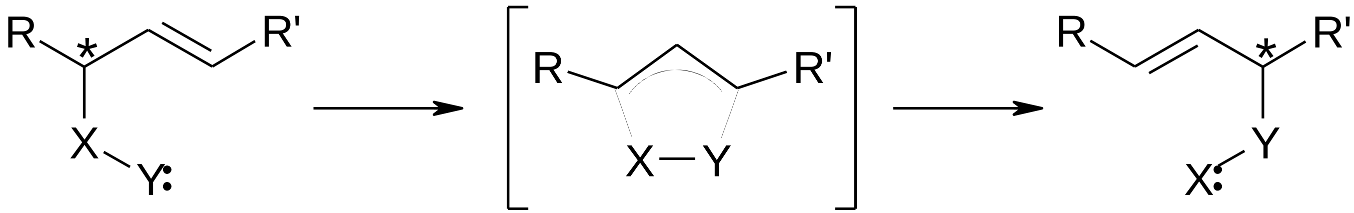


Ψ_2 olefin
radical anion

Suprafacial migration: **FORBIDDEN**
$\therefore$Must be stepwise

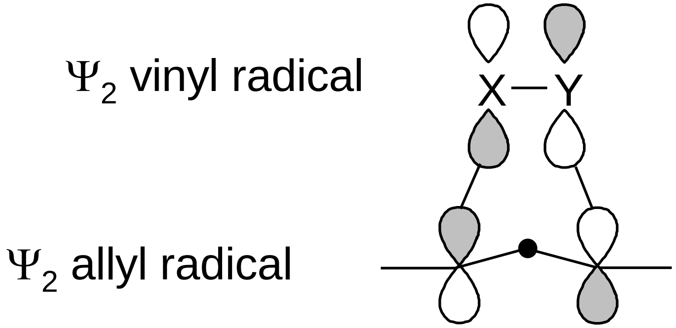
[2,3]-SIGMATROPIC REARRANGEMENTS

- **Stevens, [2,3]-Wittig, Meisenheimer Rearrangement, Ring expansion**



X, Y = C, N, O, S, Se, P

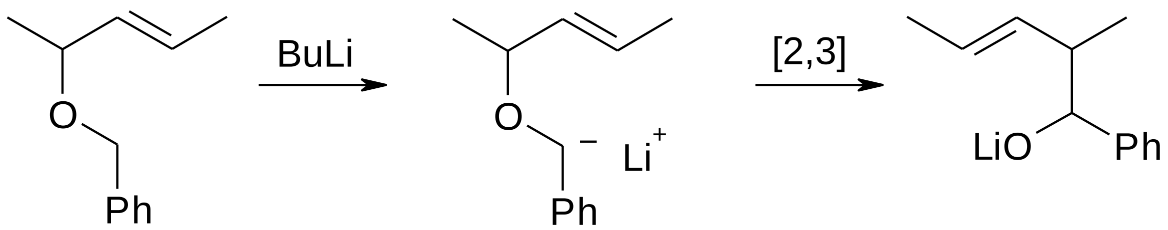
- FMO Analysis



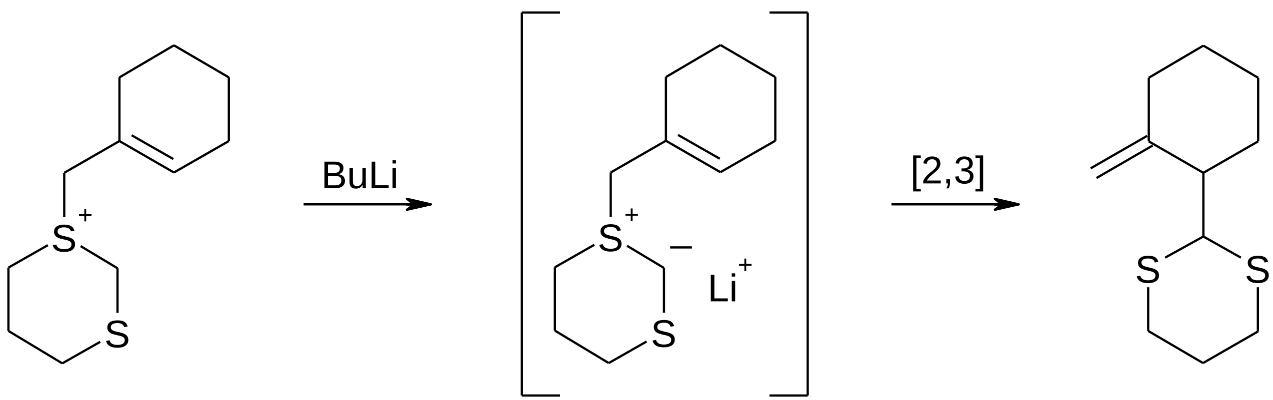
Suprafacial migration
ALLOWED

[2,3]-SIGMATROPIC REARRANGEMENTS

- **Wittig Rearrangement**[1] (X=O, Y=C)



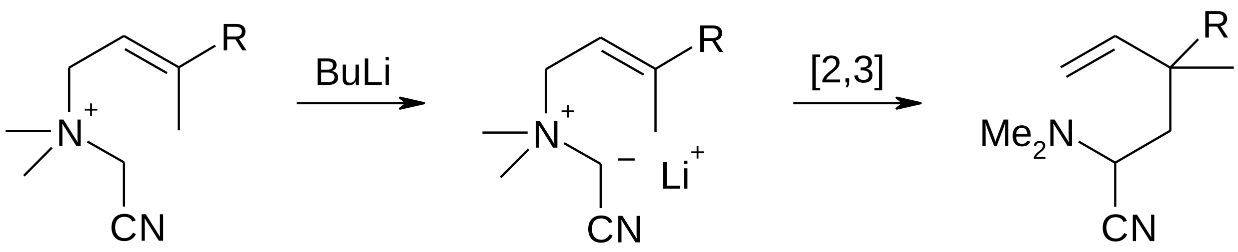
- **Sulfonium Ylide Rearrangement**[2] (X=S, Y=C)



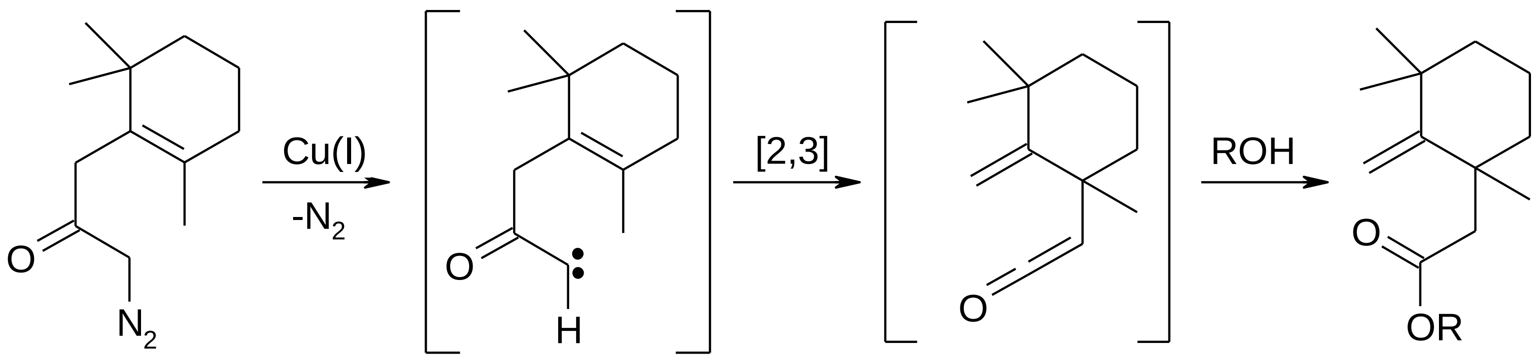
1. Baldwin, *JACS* **1971**, *93*, 3556
2. Lythgoe, *Chem. Comm.* **1972**, 757

[2,3]-SIGMATROPIC REARRANGEMENTS

- **Ammonium Ylide Rearrangement**[3] (**Stevens R.**) (X=N, Y=C)



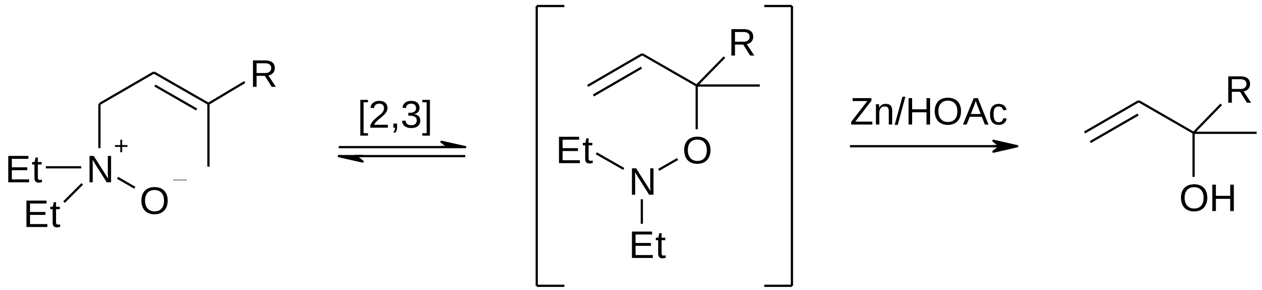
- **All-carbon Rearrangement**[4] (X=C, Y=C)



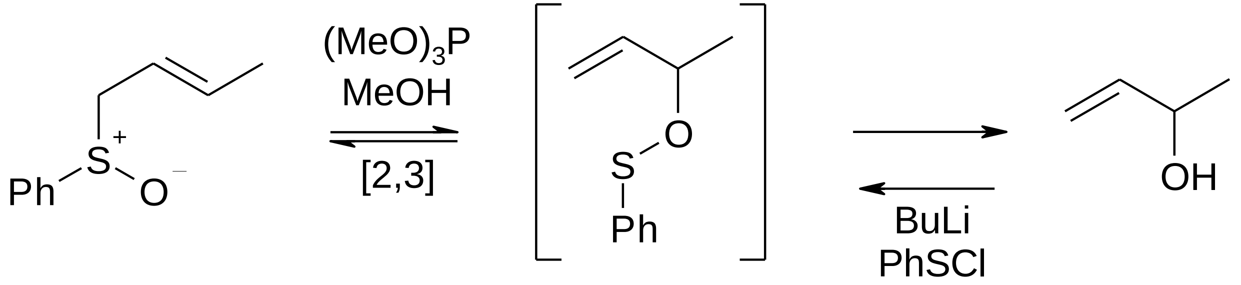
3. Buchi, *J. Am. Chem. Soc.* **1974**, *96*, 7573
4. Smith, *J. Org. Chem.* **1977**, *42*, 3165

[2,3]-SIGMATROPIC REARRANGEMENTS

- **Meisenheimer Rearrangement**[5] (X=N, Y=O)



- **Sulfoxide Rearrangement**[6] (X=S, Y=O)

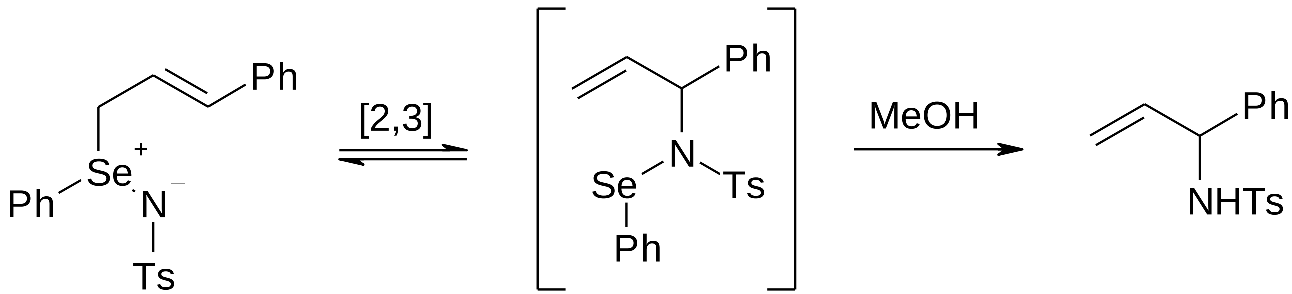


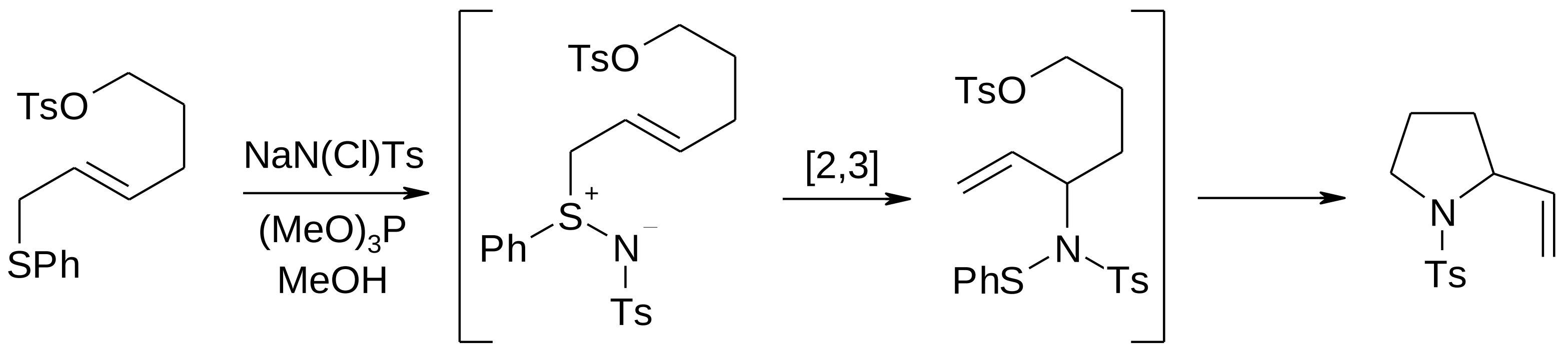
5. Tanabe, *Tet. Lett.* **1975**, 3005

6. Evans, *Acc. Chem. Res.* **1974**, *7*, 147

[2,3]-SIGMATROPIC REARRANGEMENTS

- **Related Rearrangements**[7,8]



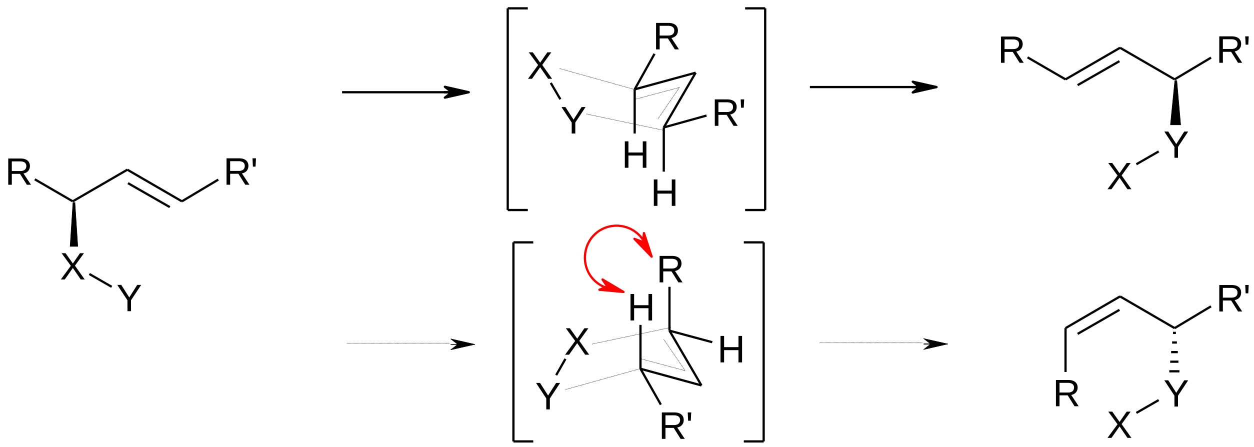


7. Hopkins, *Tet. Lett.* **1984**, *25*, 15

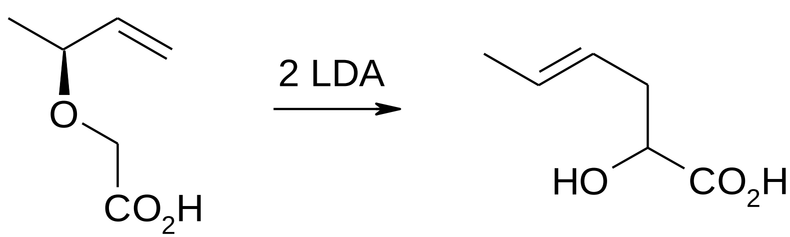
8. Dolle, *Tet. Lett.* **1989**, *30*, 4723

[2,3]-SIGMATROPIC REARRANGEMENTS

- **Olefin Selectivity from starting olefin**
  - 1,2-Disubstitution (*E*)



  - R and R' prefer to sit in pseudo-equatorial positions[9]

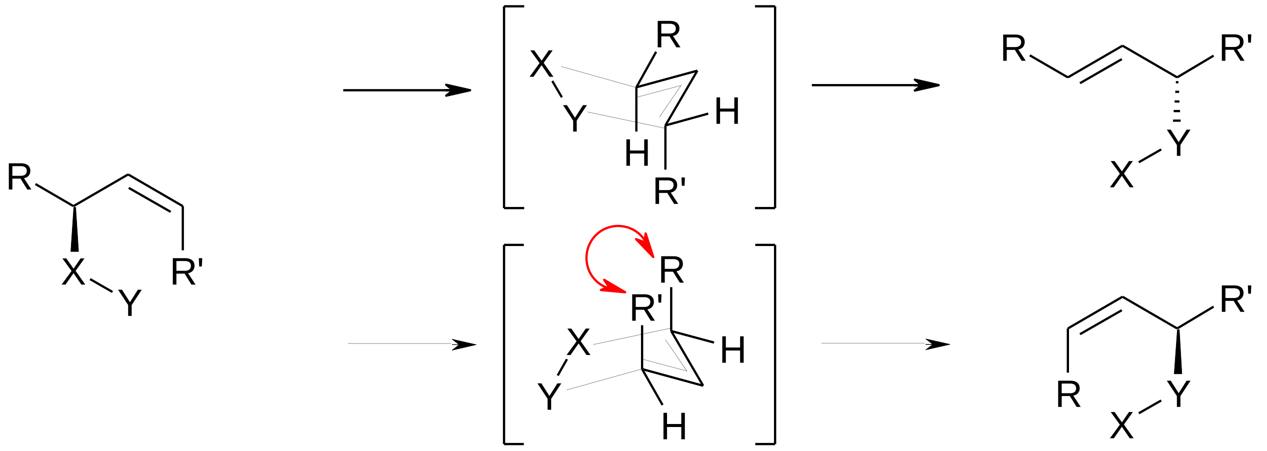


(E) selectivity: 75%

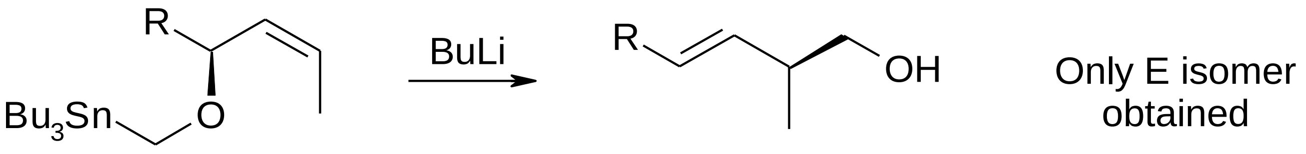
9. Nakai, *Tet. Lett.* **1981**, *22*, 69

[2,3]-SIGMATROPIC REARRANGEMENTS

- **Olefin Selectivity from starting olefin**
  - 1,2-Disubstitution (*Z*)



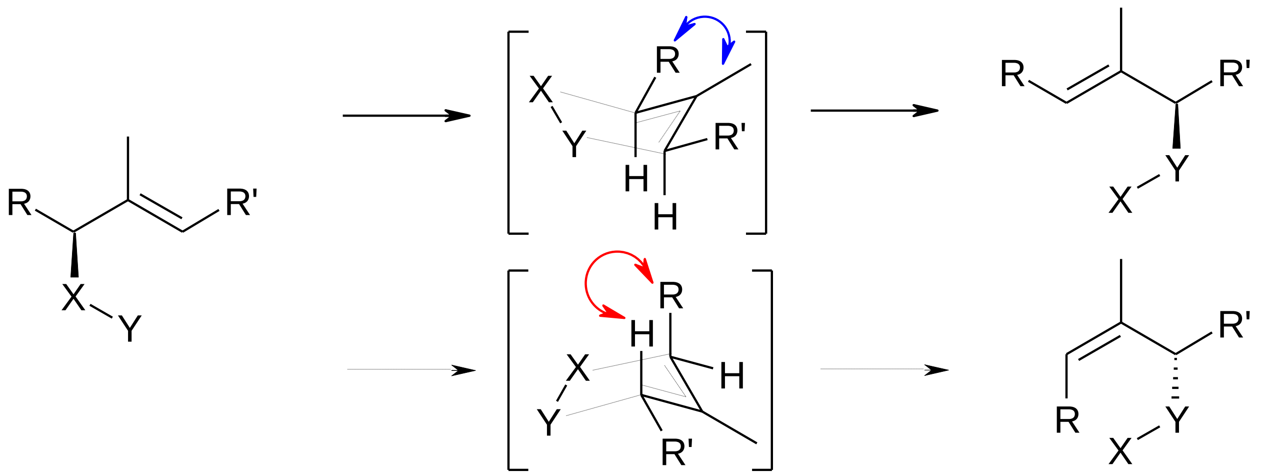
  - Generally, higher levels of 1,3 induction seen with *Z* olefins[10]



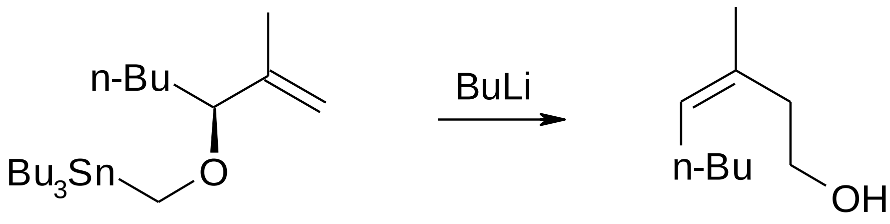
10. Still, *J. Am. Chem. Soc.* **1978**, *100*, 1927

[2,3]-SIGMATROPIC REARRANGEMENTS

- **Olefin Selectivity from starting olefin**
  - (*E*)-Trisubstituted

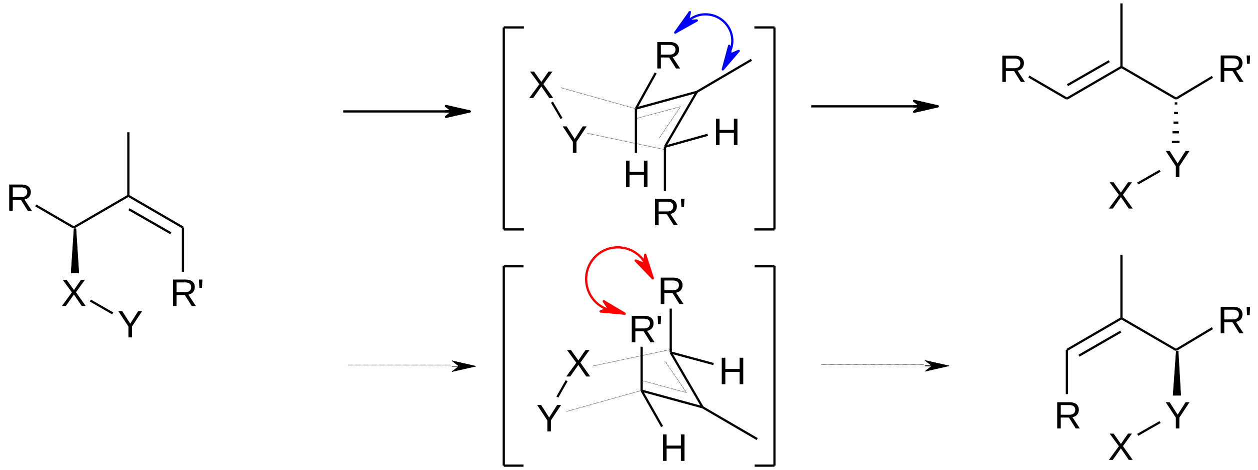


  - *E* transition state still generally preferred but R-Me interaction may cause significant destabilisation[10]



[2,3]-SIGMATROPIC REARRANGEMENTS

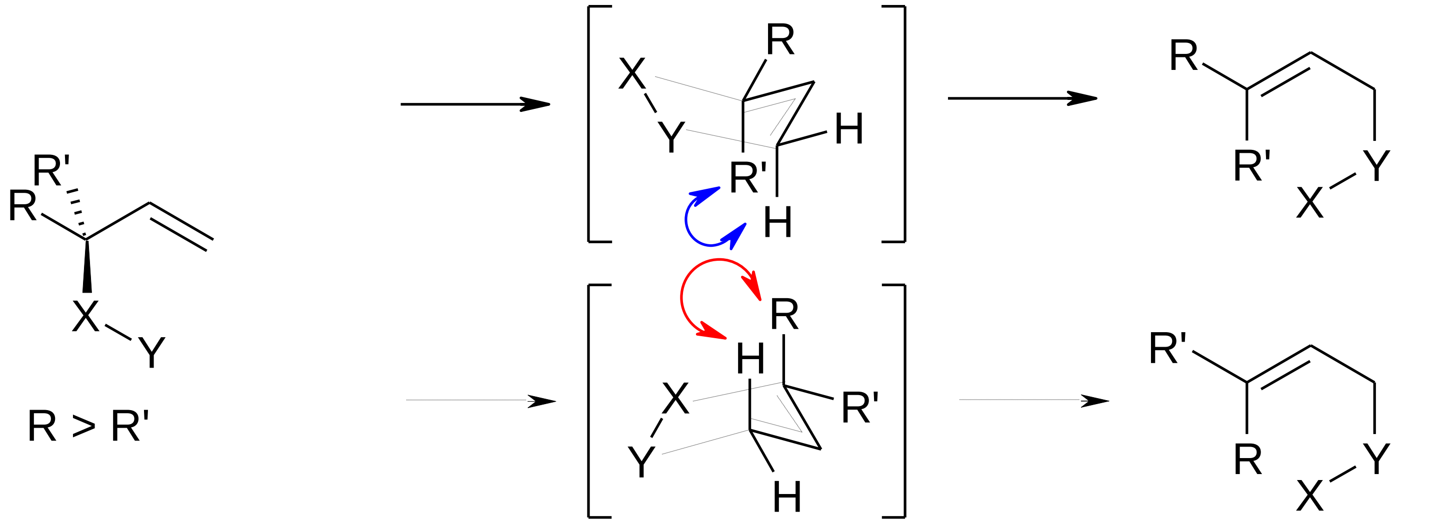
- **Olefin Selectivity from starting olefin**
  - (*Z*)-Trisubstituted



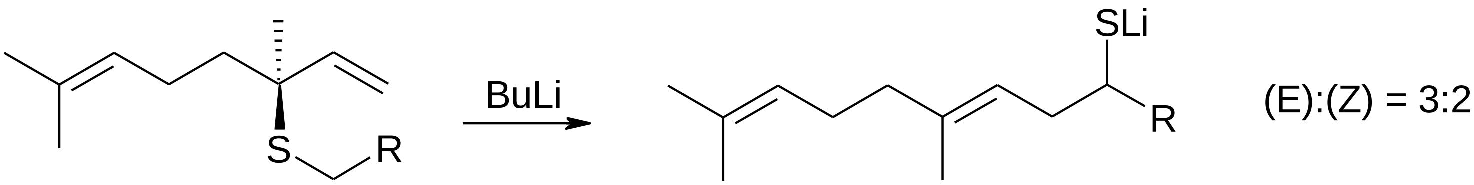
  - Generally higher levels of 1,3 induction seen with *Z*-olefins due to highly destabilising R-R’ interaction

[2,3]-SIGMATROPIC REARRANGEMENTS

- **Olefin Selectivity from allylic position**



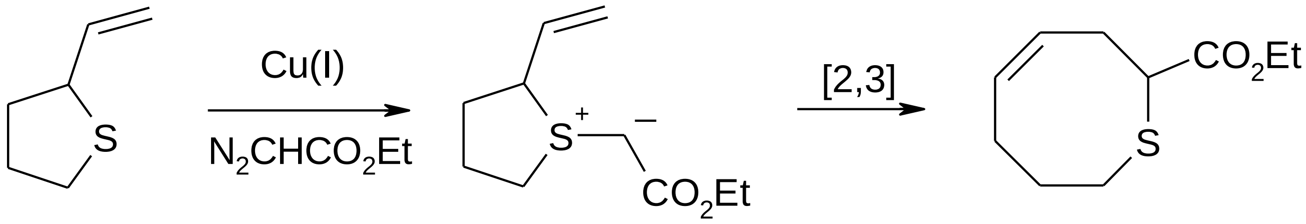
  – May expect selectivity dependent on size difference of R vs. R'[11]



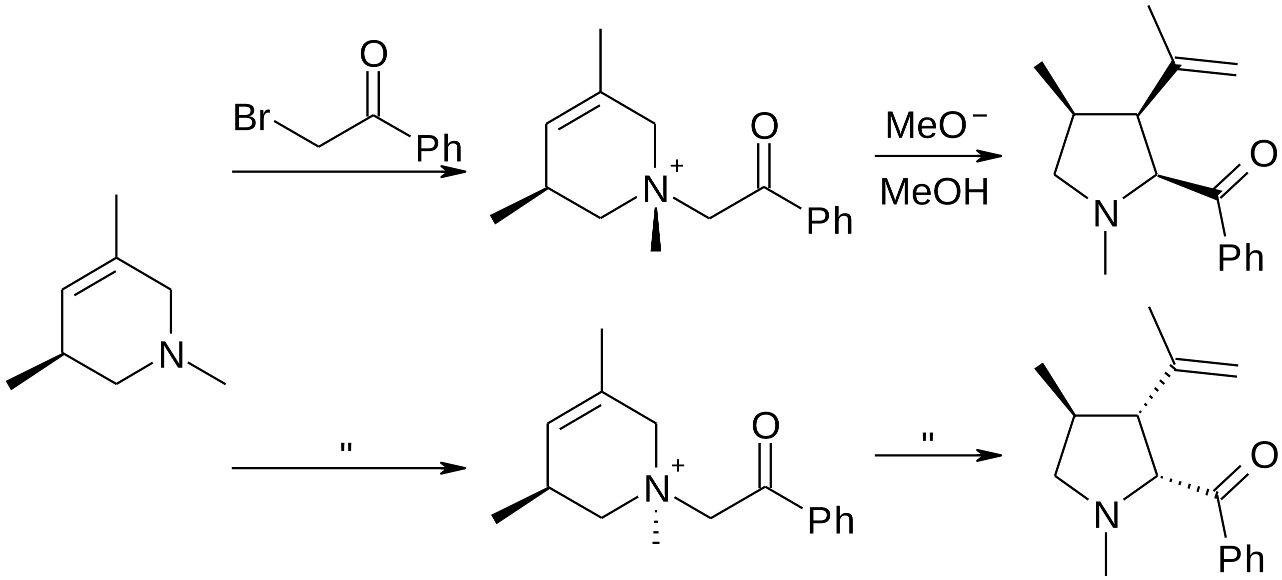
11. Rautenstrauch, *Helv. Chim. Acta* **1971**, *54*, 739

[2,3]-SIGMATROPIC REARRANGEMENTS

- **Ring Expansion**



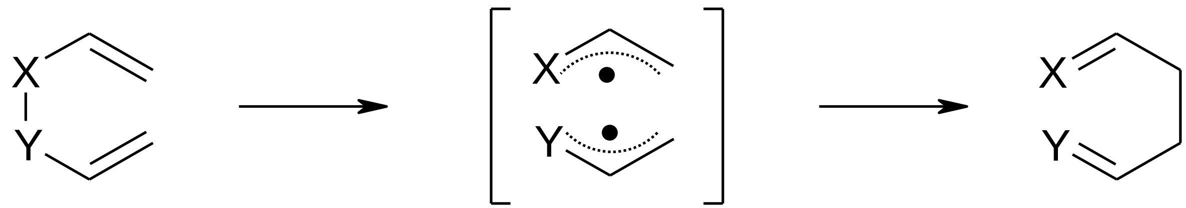
- **Ring Contraction**



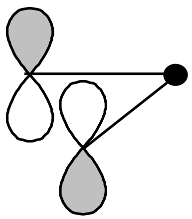
Vedejs, *Acc. Chem. Res.* **1984**, *17*, 358
Stevenson, *Tet. Lett.* **1990**, *31*, 4351

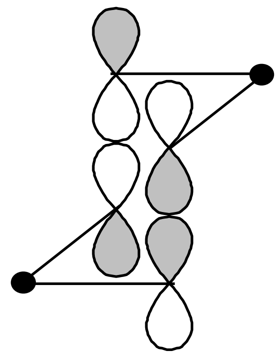
[3,3]-SIGMATROPIC REARRANGEMENTS

- **FMO Analysis**

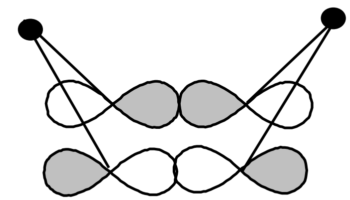


Ψ_2 allyl radical



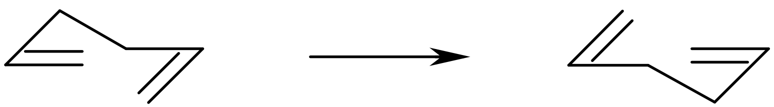


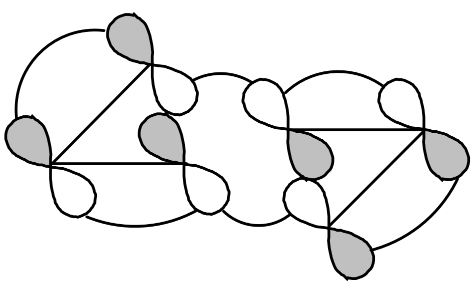
Chair geometry
ALLOWED



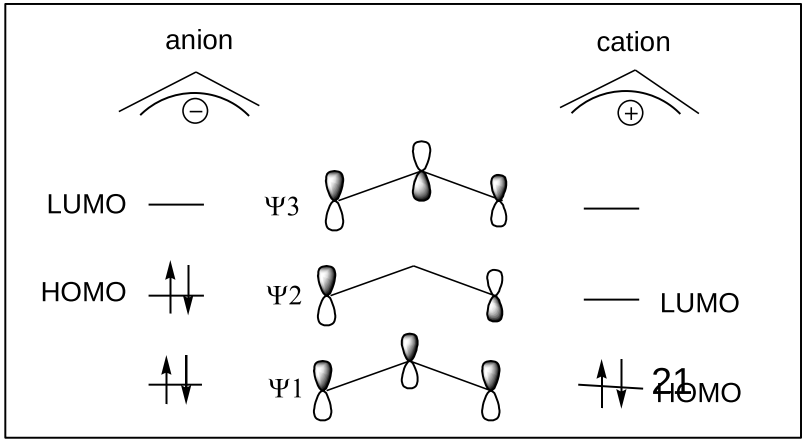
Boat geometry
ALLOWED

- **Dewar-Zimmerman**



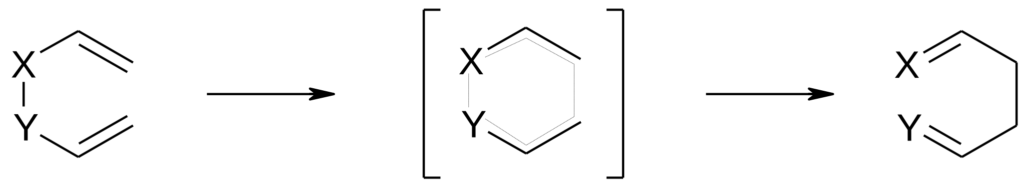


Zero Phase Inversions
Hückel Topology
Six electrons
THERMALLY ALLOWED

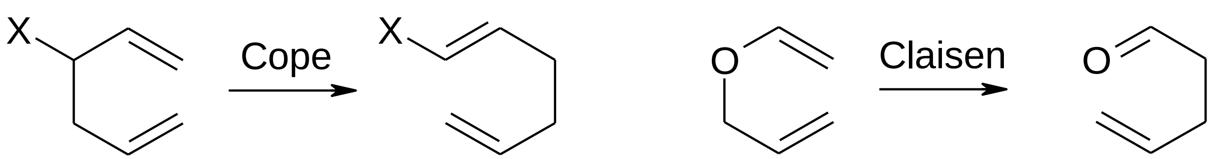


[3,3]-SIGMATROPIC REARRANGEMENTS

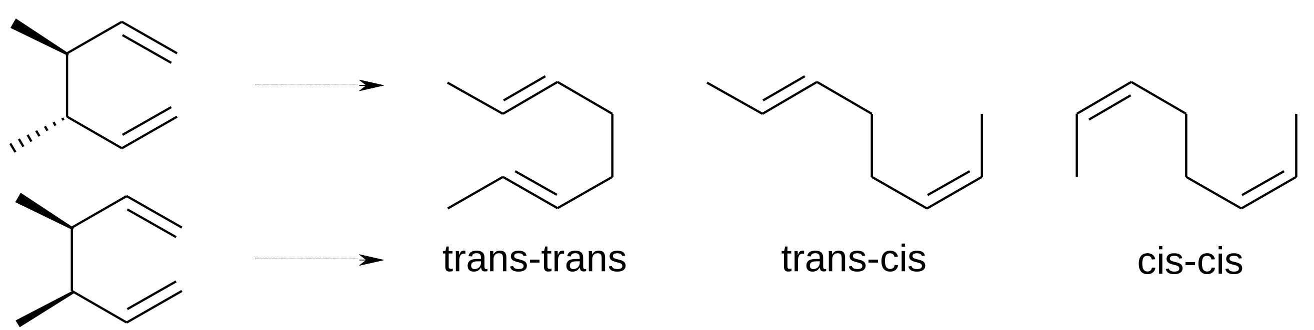
- **Cope** x **Claisen Rearrangement**



X, Y = C, O, N, etc



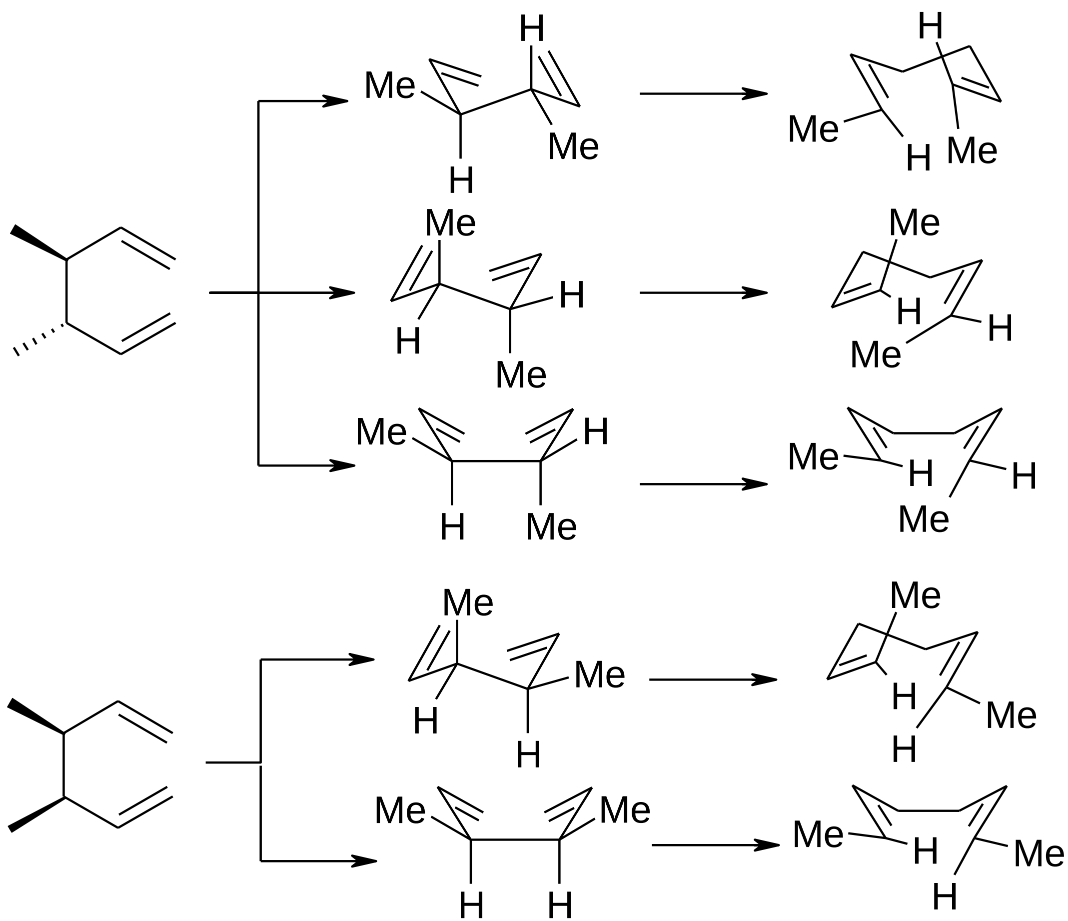
- Cope Rearrangement: Boat vs. Chair Transition State[17]



17. Doering, Roth, *Tetrahedron* **1962**, *18*, 67

[3,3]-SIGMATROPIC REARRANGEMENTS

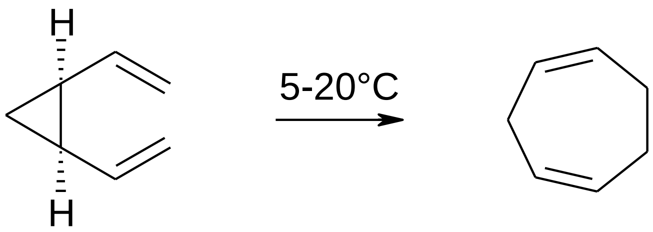
- **Cope Rearrangement: Boat vs. Chair Transition State**

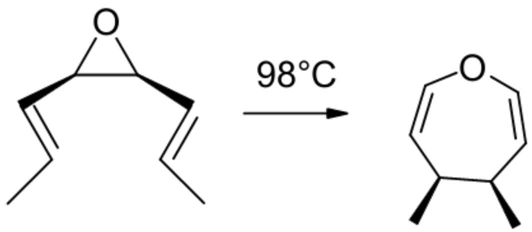


trans-trans	90%
cis-cis	10%
trans-cis	<1%
trans-cis	99.7%
trans-trans	0.3%

[3,3]-SIGMATROPIC REARRANGEMENTS

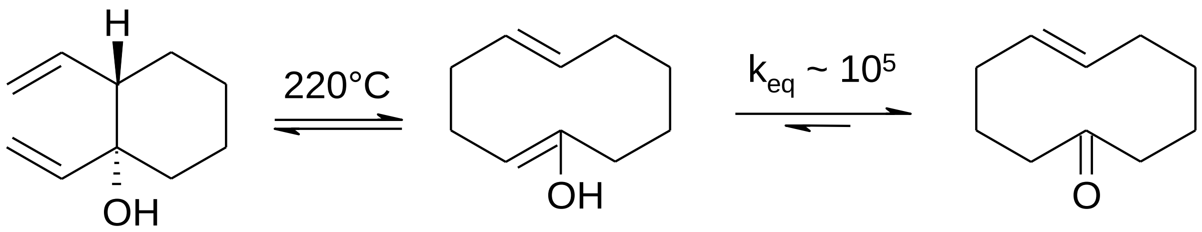
- **Cope Rearrangement: Use of ring strain**[18]





  – Relief of ring strain upon rearrangement

- **Oxy-Cope Rearrangement**[19]

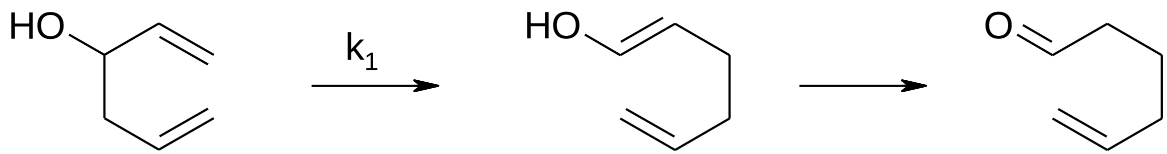


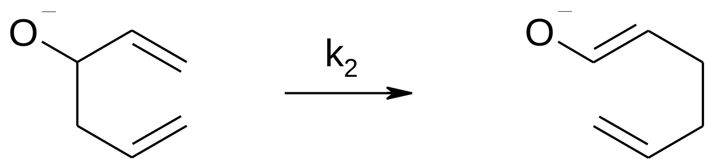
  – Tautomerism shifts equilibrium to right

18. Brown, *Chem. Comm.* **1973**, 319

19. Marvell, *Tet. Lett.* **1970**, 509

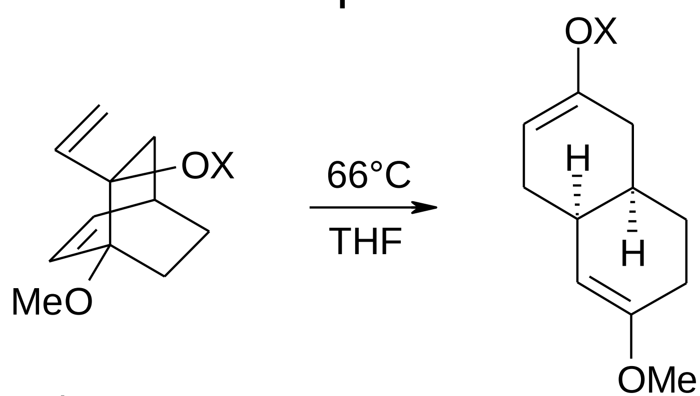
- **Oxy-Cope Rearrangement**





$$10^{10} < \frac{k_2}{k_1} < 10^{17}$$

  - Significant rate acceleration for anionic Oxy-Cope.[20]
  - Counter-ion also important

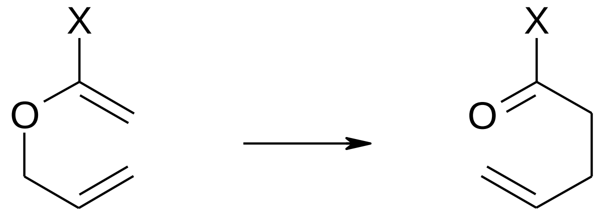


OX	Half-life	T/°C
OH	(66 yrs)	66
OLi	No rxn	
ONa	1.2 hrs	
OK	1.4 min	
OK	11 hrs	10
O^- K^+	4.4 min	

20. Golob, *J. Am. Chem. Soc.* **1975**, *97*, 4765

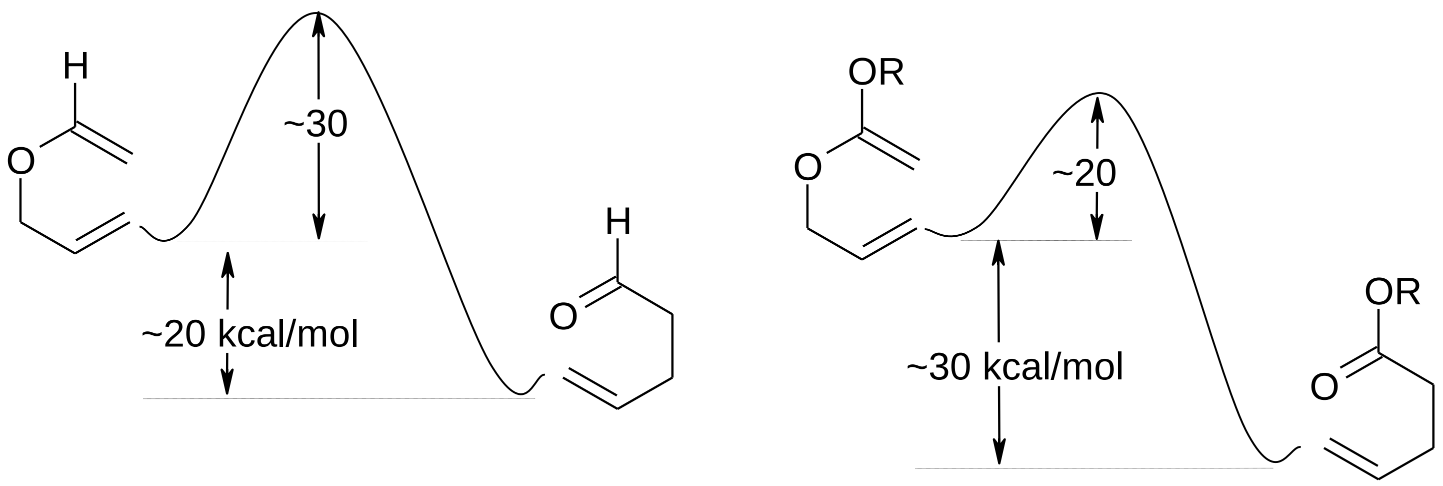
[3,3]-SIGMATROPIC REARRANGEMENTS

- **Claisen Rearrangement**



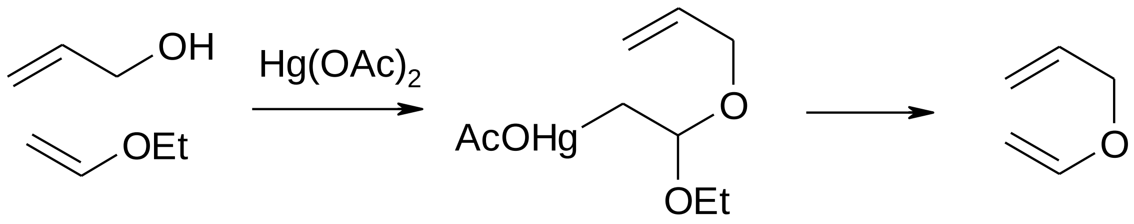
X = C, H, O, N

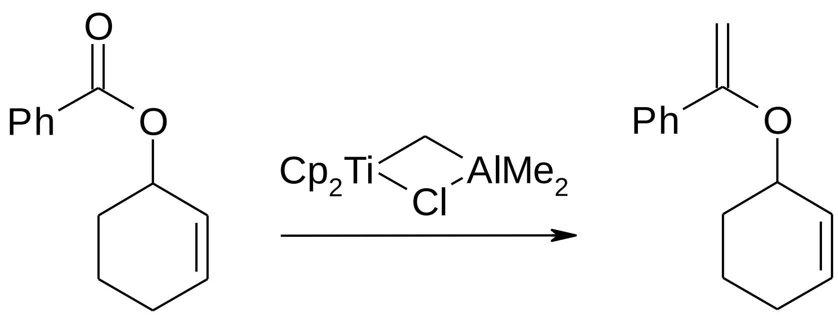
  - Thermodynamic driving force: (C-O) π-bond and (C-C) σ-bond formation
  - X=Heteroatom leads to higher exothermicity and reaction rate



[3,3]-SIGMATROPIC REARRANGEMENTS

- ***Synthesis of allyl vinyl ethers***[21,22]



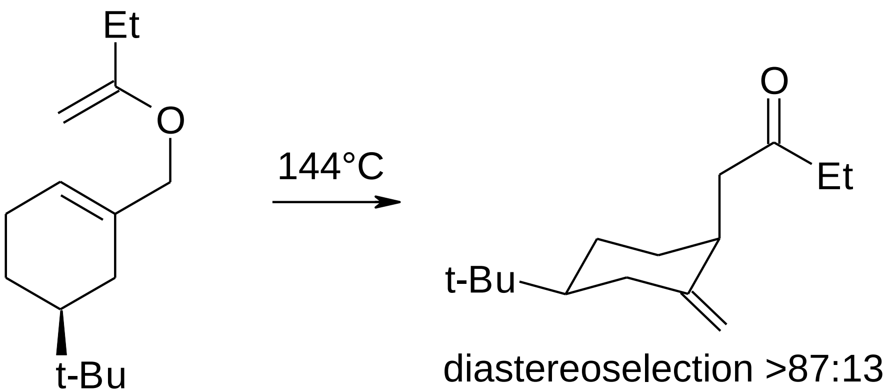


21. Watanabe, Conlon, *J. Am. Chem. Soc.* **1957**, *79*, 2828

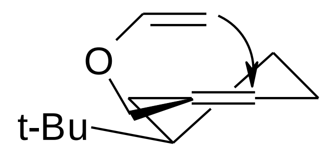
22. Evans, Grubbs, *J. Am. Chem. Soc.* **1980**, *102*, 3272

[3,3]-SIGMATROPIC REARRANGEMENTS

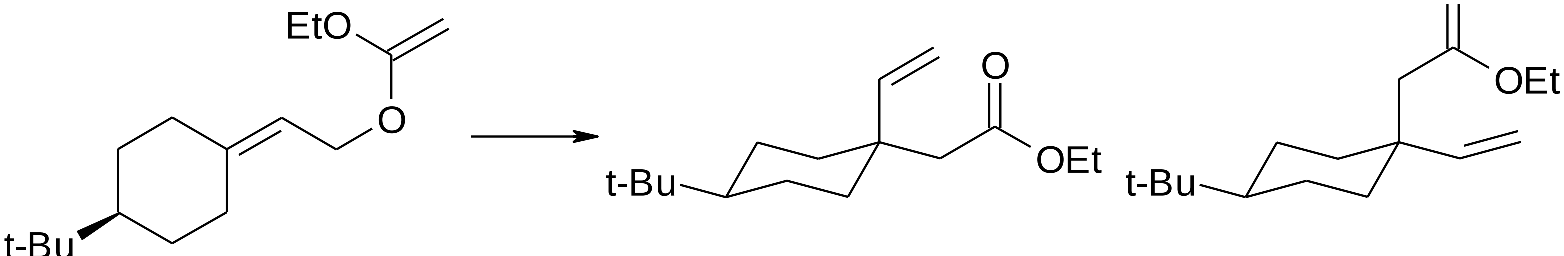
- **Endocyclic Olefins**[23]



Via Chair intermediate:



- **Exocyclic Olefins**[24]



ratio 52:48

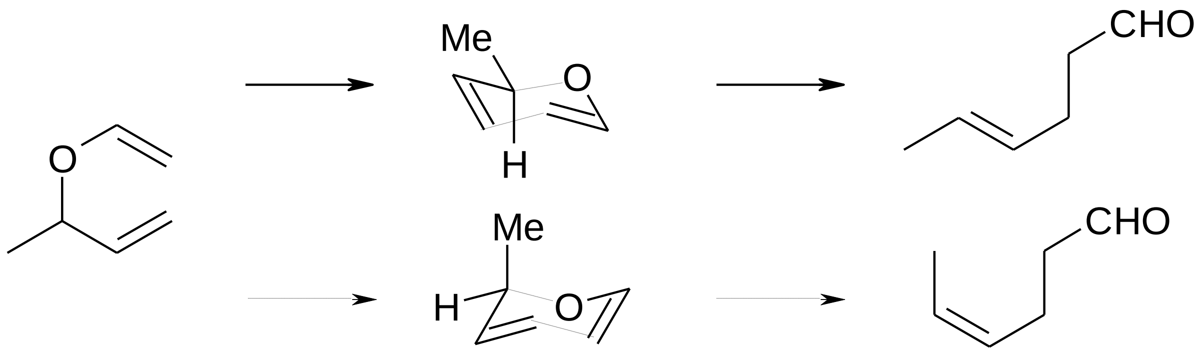
  – Overlap equally good from either face

23. Ireland, *J. Org. Chem.* **1983**, *48*, 1829

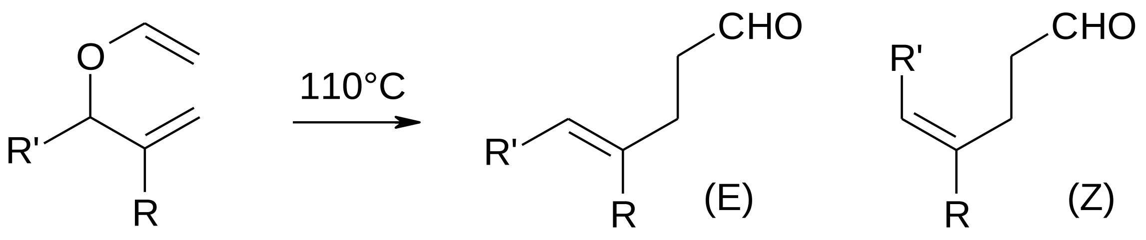
24. House, *J. Org. Chem.* **1975**, *40*, 86

[3,3]-SIGMATROPIC REARRANGEMENTS

- **Olefin Selectivity**



  – R group prefers to sit in pseudo-equatorial position[25]

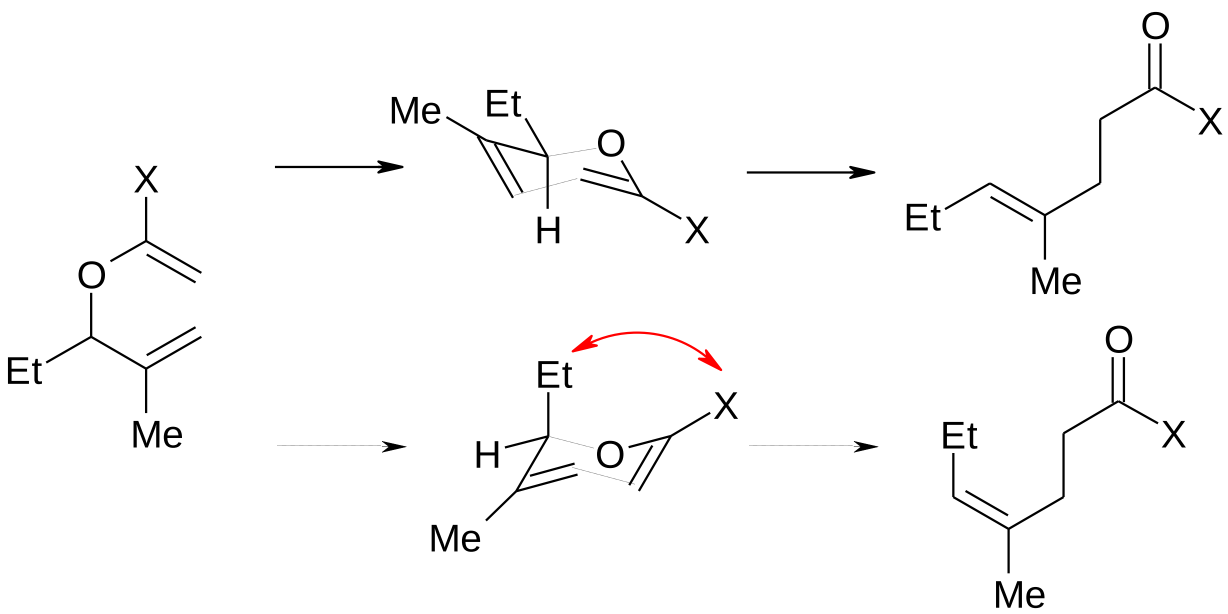


R	R'	(E):(Z)
Me	Et	90:10
Me	i-Pr	93:7
Et	Et	90:10

25. Faulkner, *J. Am. Chem. Soc.* **1973**, *95*, 553

[3,3]-SIGMATROPIC REARRANGEMENTS

- **Olefin Selectivity**

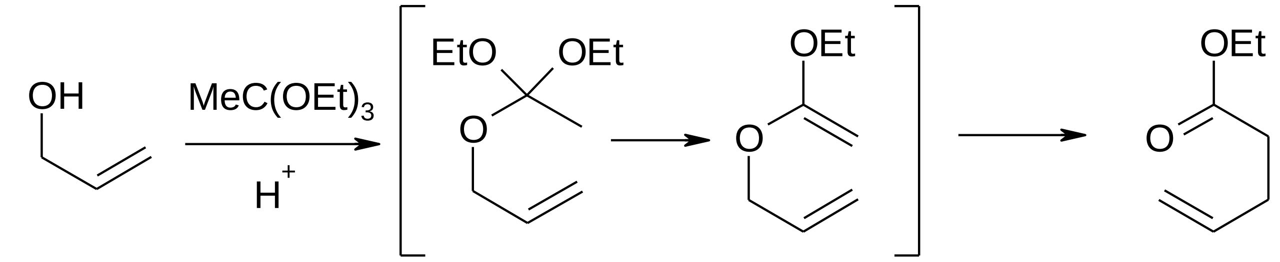


– Extra substituents lead to enhanced diastereoselection[25]
Larger X => better selectivity

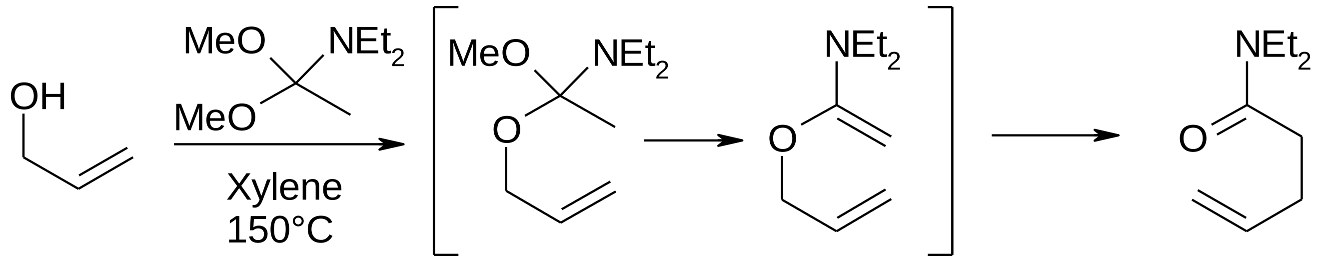
X	(E):(Z)
H	90:10
Me	>99:1
MeO	>99:1
Me_2N	>98:2

[3,3]-SIGMATROPIC REARRANGEMENTS

- Claisen Variants: **Johnson Orthoester Claisen**[26]



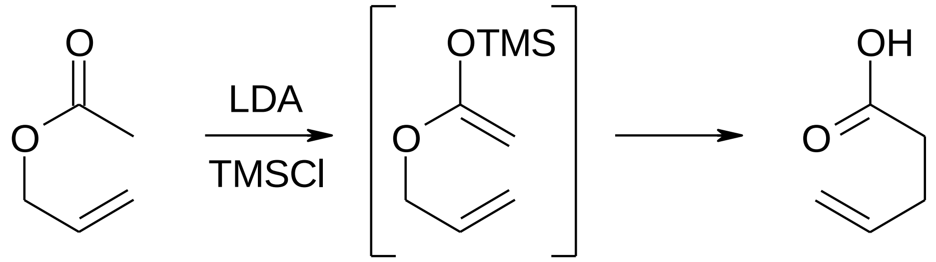
- Claisen Variants: **Eschenmoser Claisen**[27]



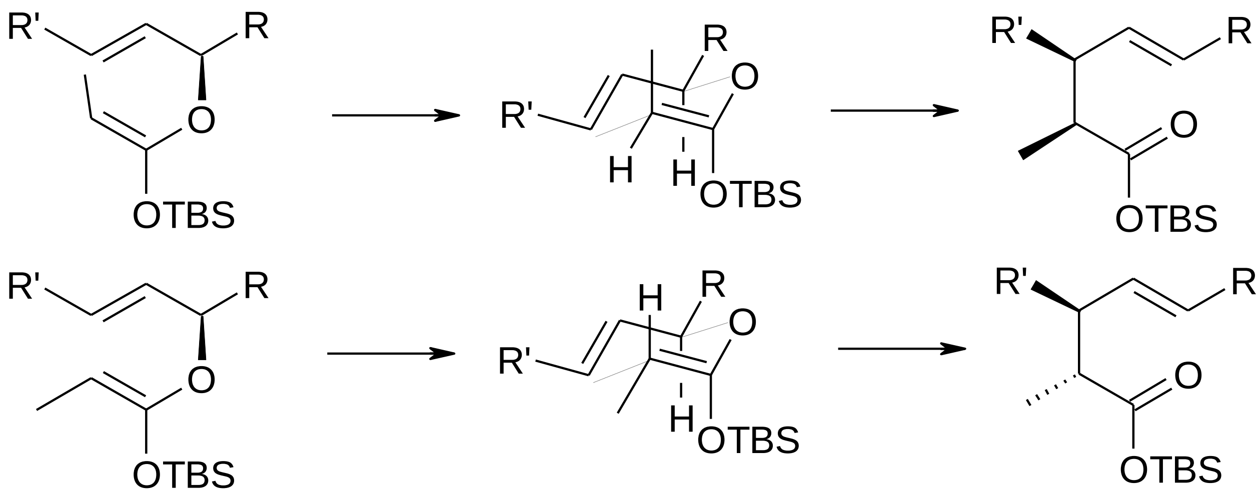
26. Johnson, Faulkner, Peterson, *J. Am. Chem. Soc.* **1970**, *92*, 741
27. Eschenmoser, *Helv. Chim. Acta* **1964**, *47*, 2425

[3,3]-SIGMATROPIC REARRANGEMENTS

- Claisen Variants: **Ireland Enolate Claisen**[28]



  - Substituted enolates afford an additional stereocentre[29]

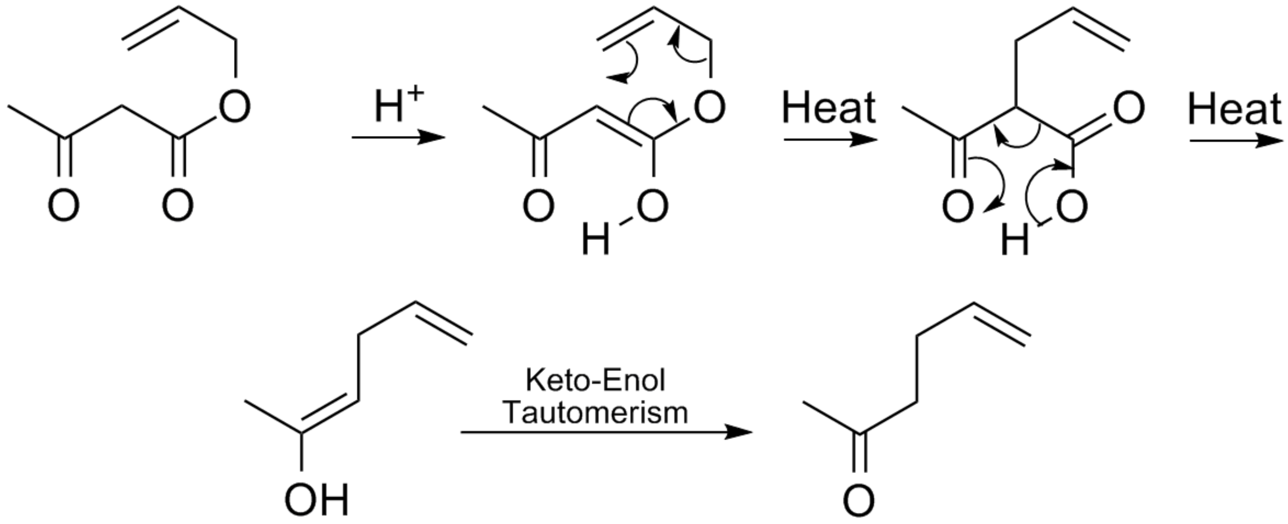


28. Ireland, *J. Am. Chem. Soc.* **1976**, *98*, 2868

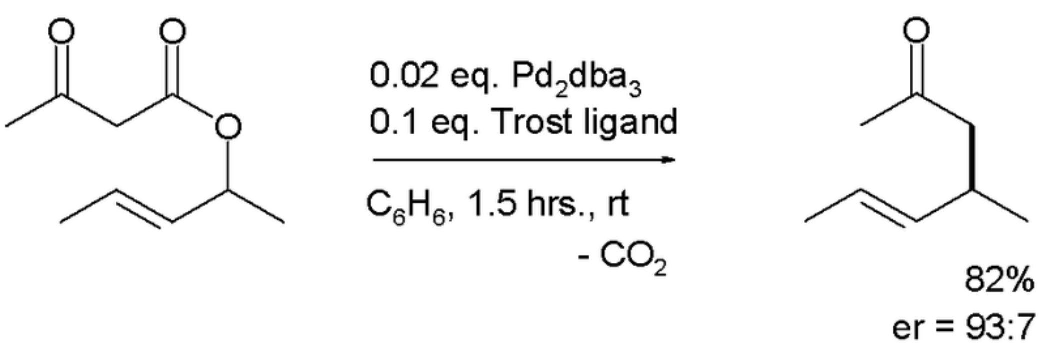
29. Ireland, *J. Org. Chem.* **1991**, *56*, 650

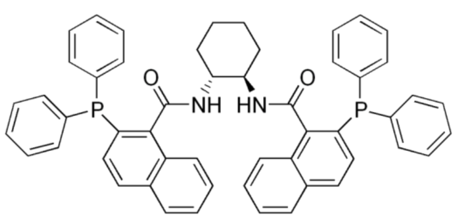
[3,3]-SIGMATROPIC REARRANGEMENTS

- Claisen Variants: **Carroll Rearangement**

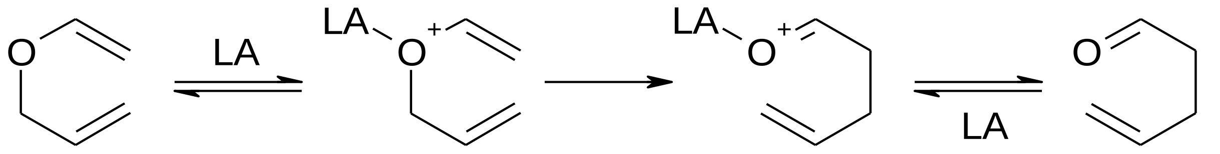


- \- asymmetric version

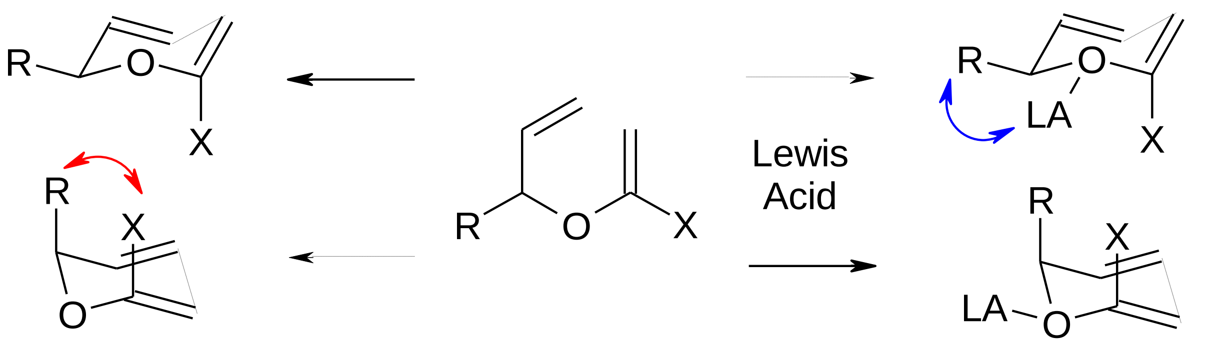




- **Lewis Acid catalysed Claisen rearrangement**



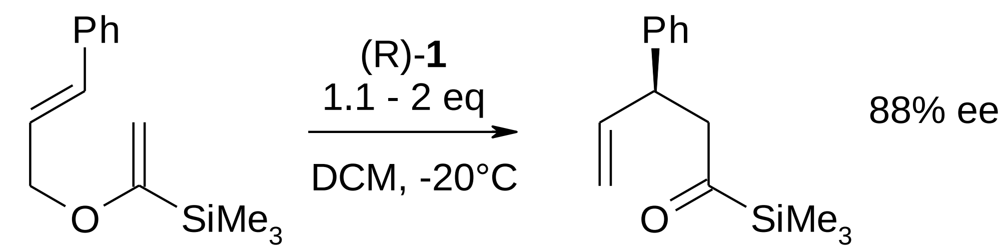
– Presence of Lewis Acid can influence rearrangement[30]

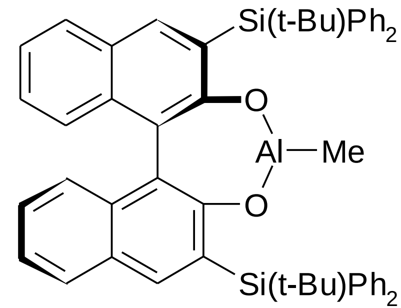


30. Yamamoto, *J. Am. Chem. Soc.* **1990**, *112*, 316

[3,3]-SIGMATROPIC REARRANGEMENTS

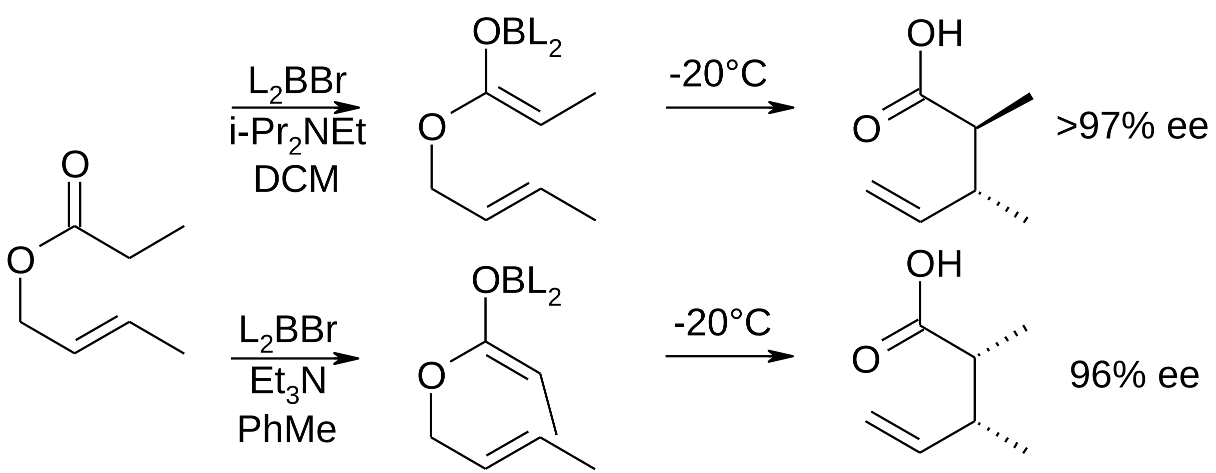
- **Chiral Lewis Acid promoted Claisen rearrangement**[31]

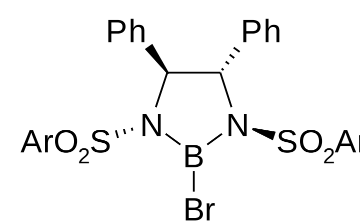




(R)-**1**

- **Enantioselective Claisen Rearrangements**[32]



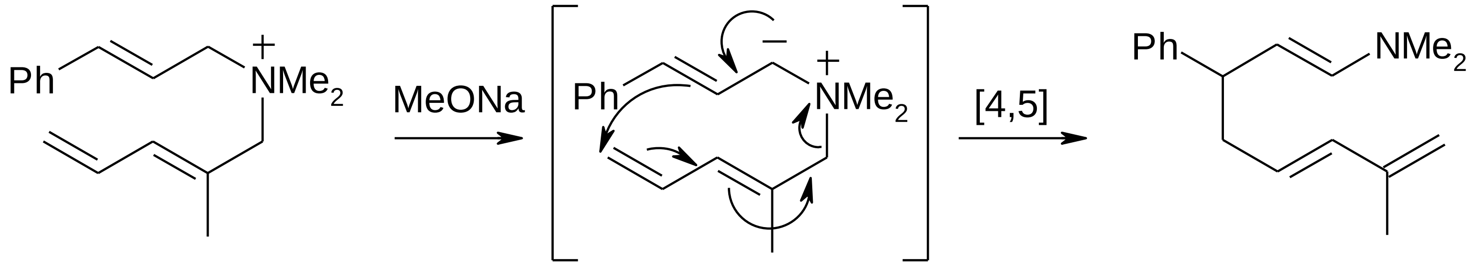


L$_2$BBr

31. Yamamoto, *J. Am. Chem. Soc.* **1990**, *112*, 7791 32. Corey, *J. Am. Chem. Soc.* **1991**, *113*, 4026

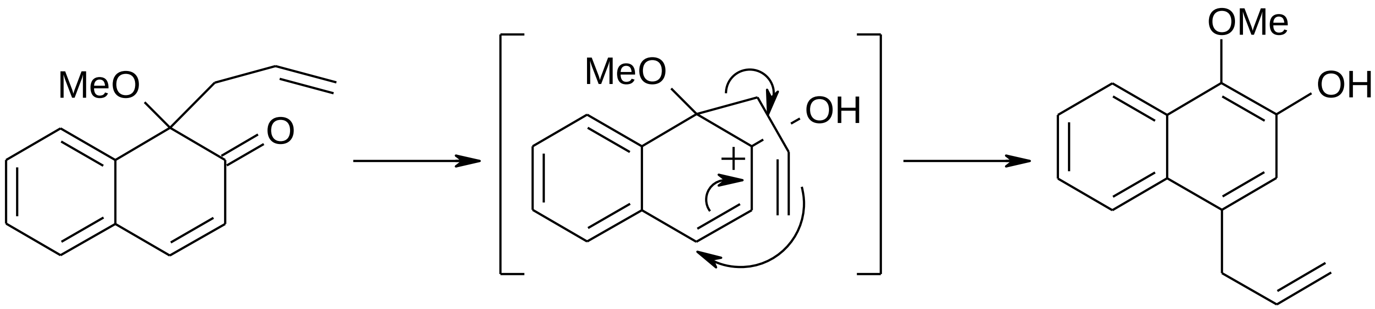
[m,n]-SIGMATROPIC REARRANGEMENTS

- **[4,5] shift**



  – [2,3] possible but [4,5] favoured. [2,5] and [3,4] forbidden

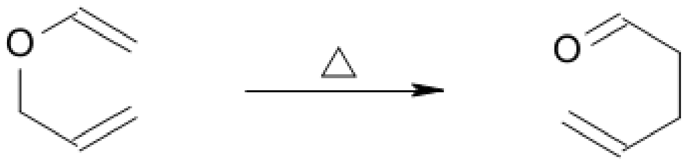
- **[3,4] shift**



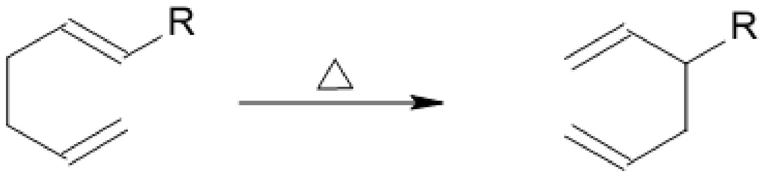
[3,3]-SIGMATROPIC REARRANGEMENTS

- Summary of [3,3] sigmatropic rearrangements

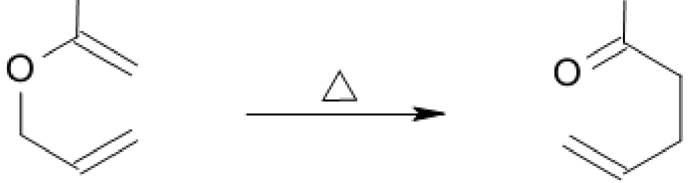
Claisen



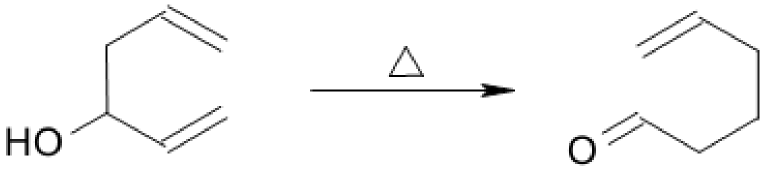
Cope



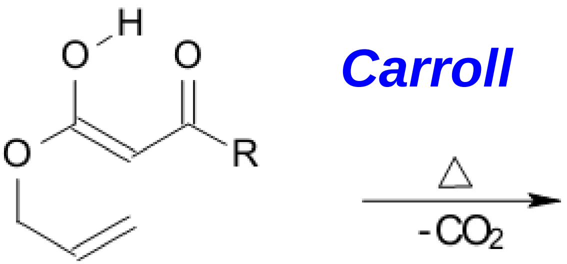
Johnson



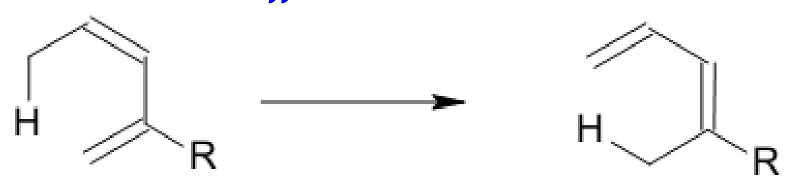
Oxy-Cope



Carroll



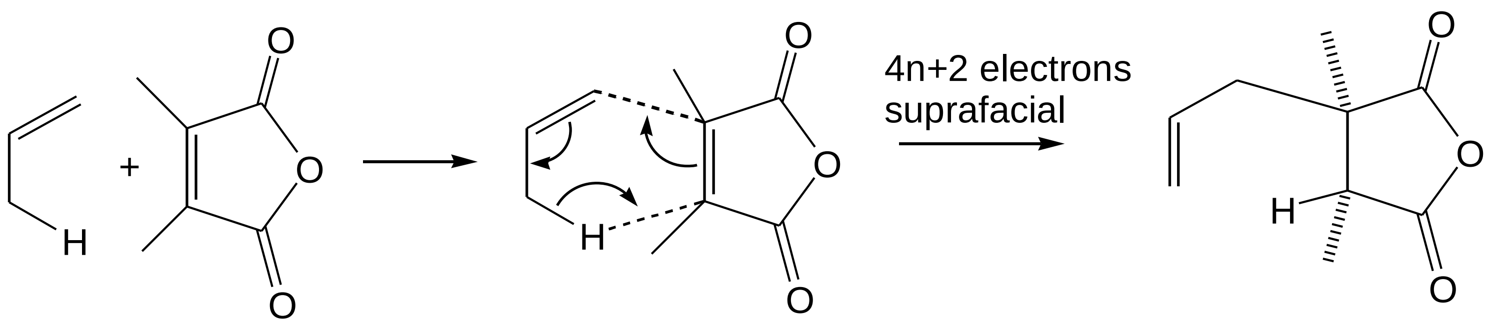
„Ene“



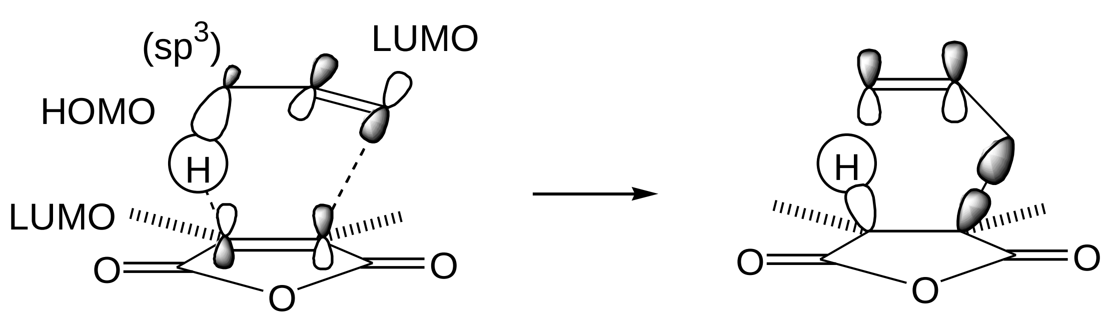
SIGMATROPIC REARRANGEMENTS - App.

- **„Ene“ Reaction**

  - involves a cycloaddition between two alkenes, but with the formation of only a single C-C bond. A C-H bond is also formed in the process:

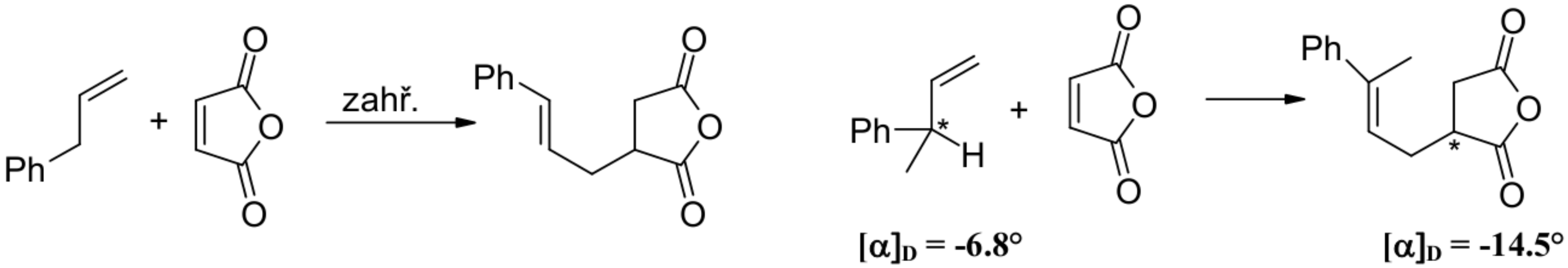


More complex as it involves 3 molecular orbital systems.

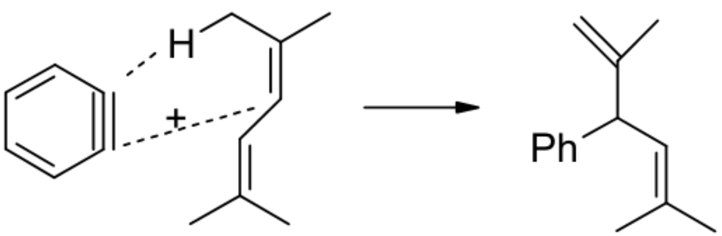


SIGMATROPIC REARRANGEMENTS - App.

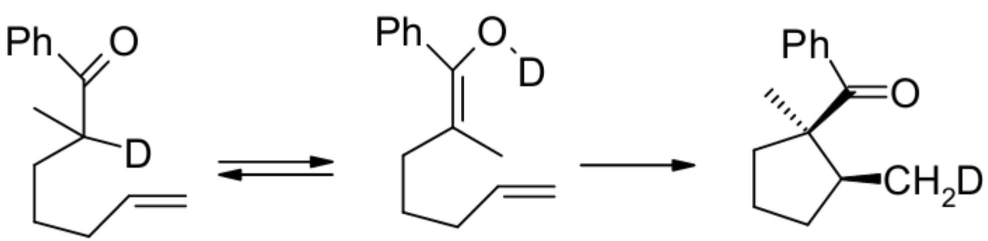
- **„Ene“ Reaction**



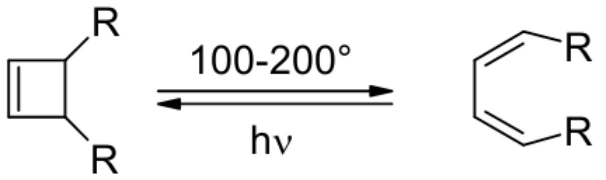
Arynes:

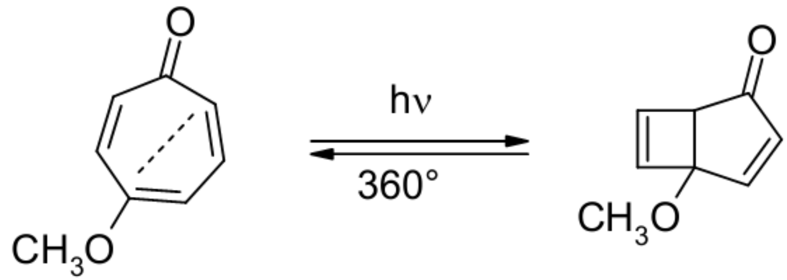


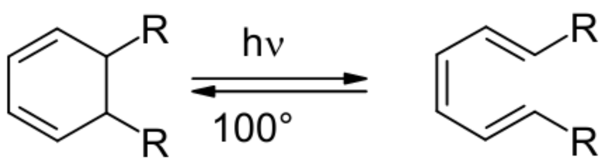
- **Conia-Ene Reaction** (formation of cyclopentanes, cyclohexanes)

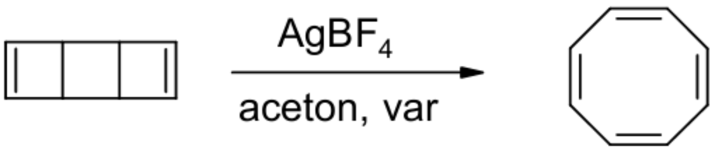


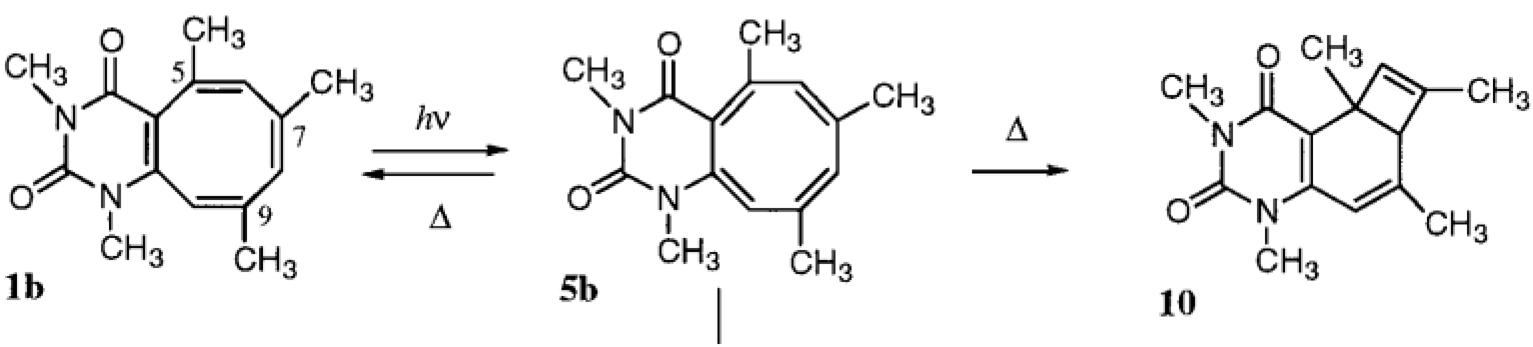
ELECTROCYCLIC REARRANGEMENTS





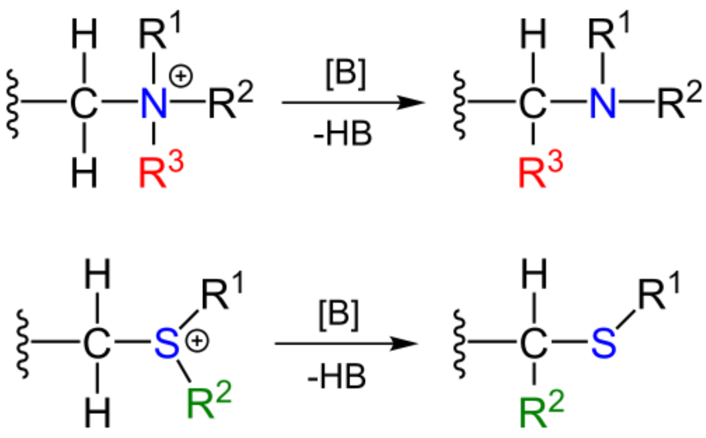






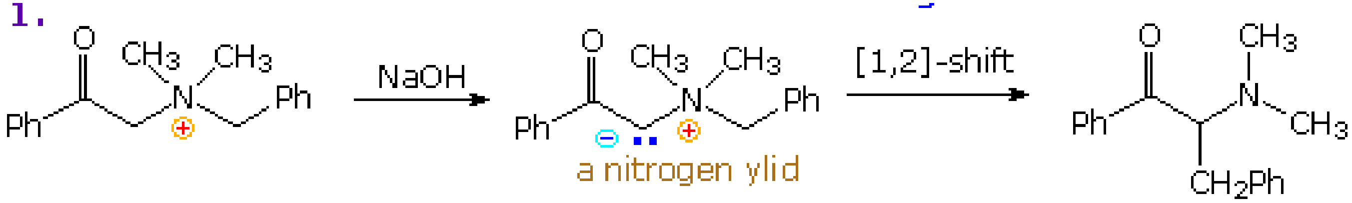
BASE-CATALYZED REARRANGEMENTS

- **Stevens Rearrangement**

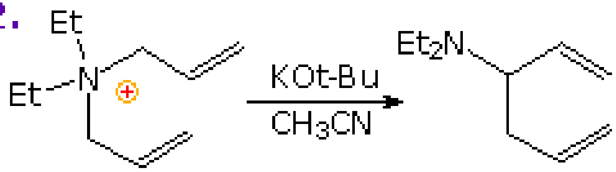


- conversion of quaternary ammonium salts and sulfonium salts to the corresponding amines or sulfides
- in the presence of a strong base
- [1,2]-rearrangement
- Z group: ArCO-, RCO-, ROOC-, NC-,..., Ph.
- R (migration group): All, Bn, Ph_2CH, propargyl, benzoyl....
- Base: $NaNH_2/NH_3$, BuLi, NaOH, tBuOK, etc.

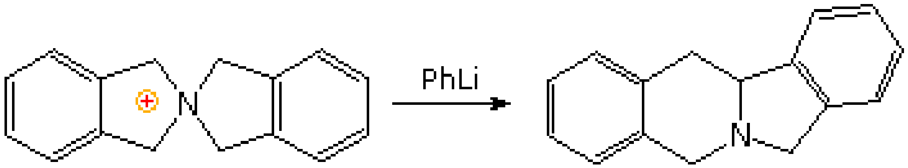
1.



2.



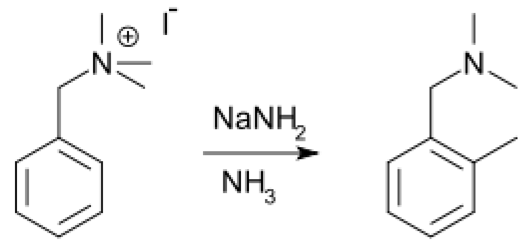
3.



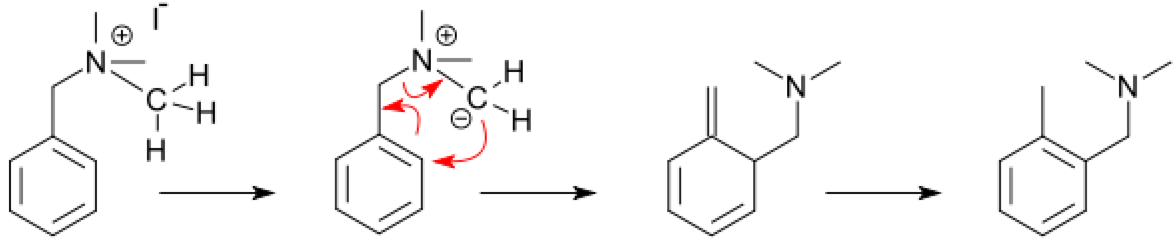
BASE-CATALYZED REARRANGEMENTS

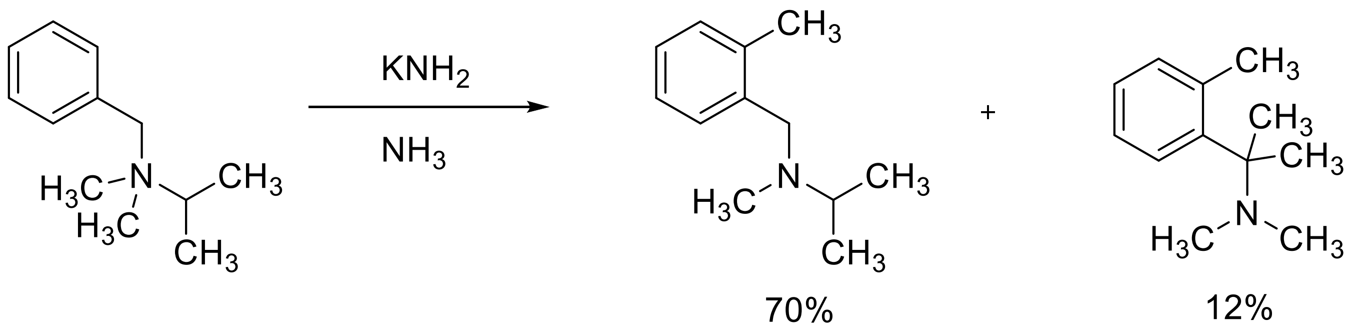
- **Sommelet-Hauser Rearrangement**

- conversion of benzyl quaternary ammonium salts in *N*-dialkyl benzyl amine with *ortho*-alkylated benzyl group



- [2,3]-rearrangement
- Base: $NaNH_2$, $LiNH_2$, etc.
- Mechanism

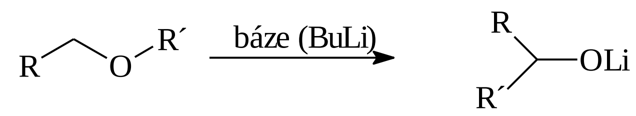




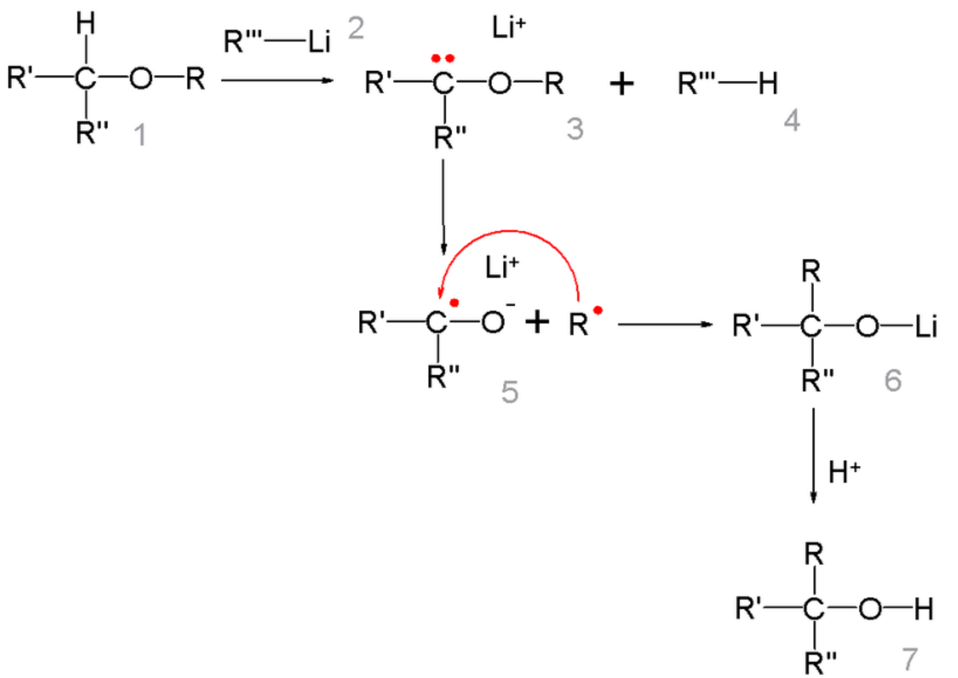
- Stevens R. and S.-H. R - competition

BASE-CATALYZED REARRANGEMENTS

- **Wittig Rearrangement**



- [1,2]-rearrangement
- conversion of an ether with an alkyllithium compound to alkoxides
- **Base**: RLi, $NaNH_2$, etc.
- R, R´ = alkyl, aryl, allyl, vinyl.
- **Migration:** allyl, benzyl > Me > Et > Ar
- **Mechanism:**

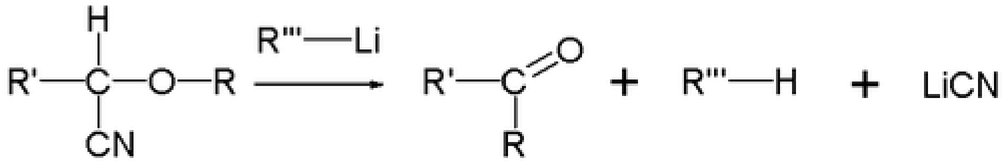


BASE-CATALYZED REARRANGEMENTS

- **Wittig Rearrangement**

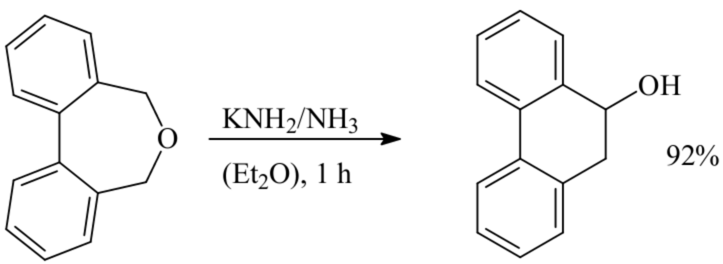
  Wittig Variants

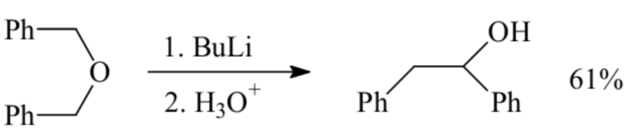
- R´ = good leaving group (CN)



- Competition: low temp (under -60 °C rapid and high selectivity [2,3])

Examples

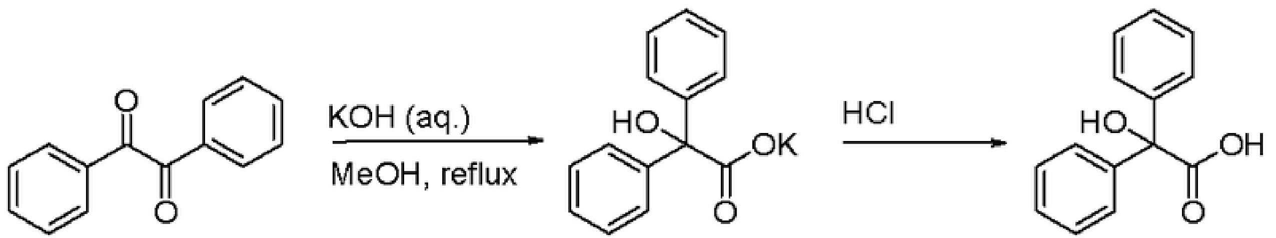




BASE-CATALYZED REARRANGEMENTS

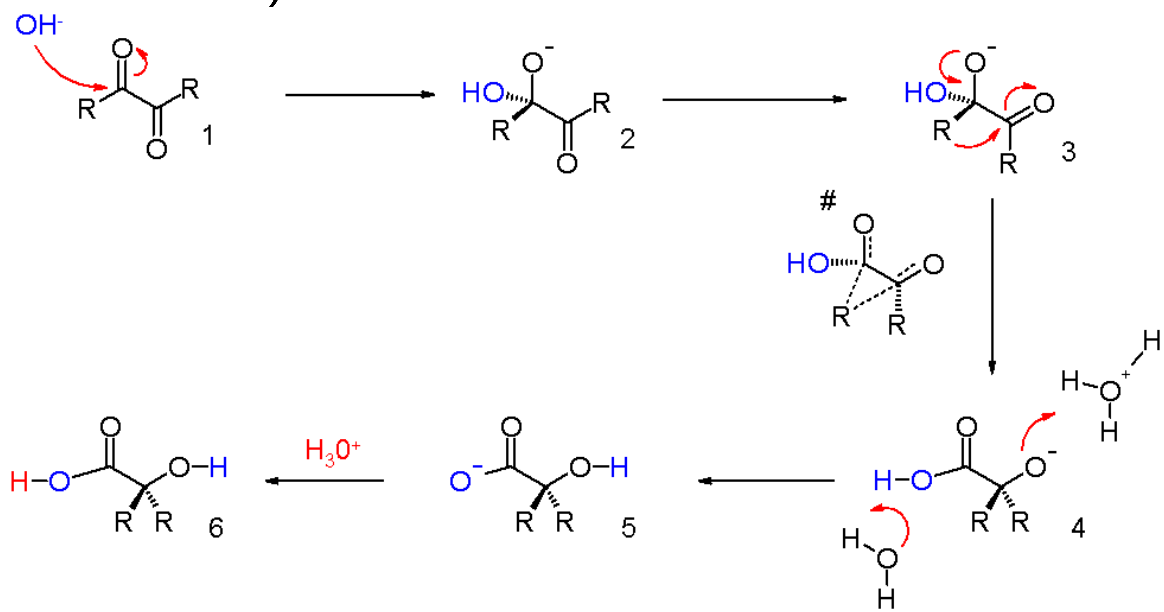
- **Benzilic Acid Rearrangement**

- [1,2]-rearrangement - Liebig (1838)
- conversion of 1,2-diketones to α-hydroxy-carboxylic acids



- Not only aromatic, but also aliphatic 1,2-diketones and α-oxo-carboxylic acids (KOH, t-BuOK-estes)

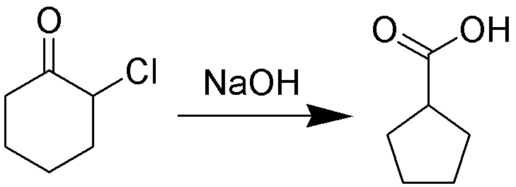
Mechanism



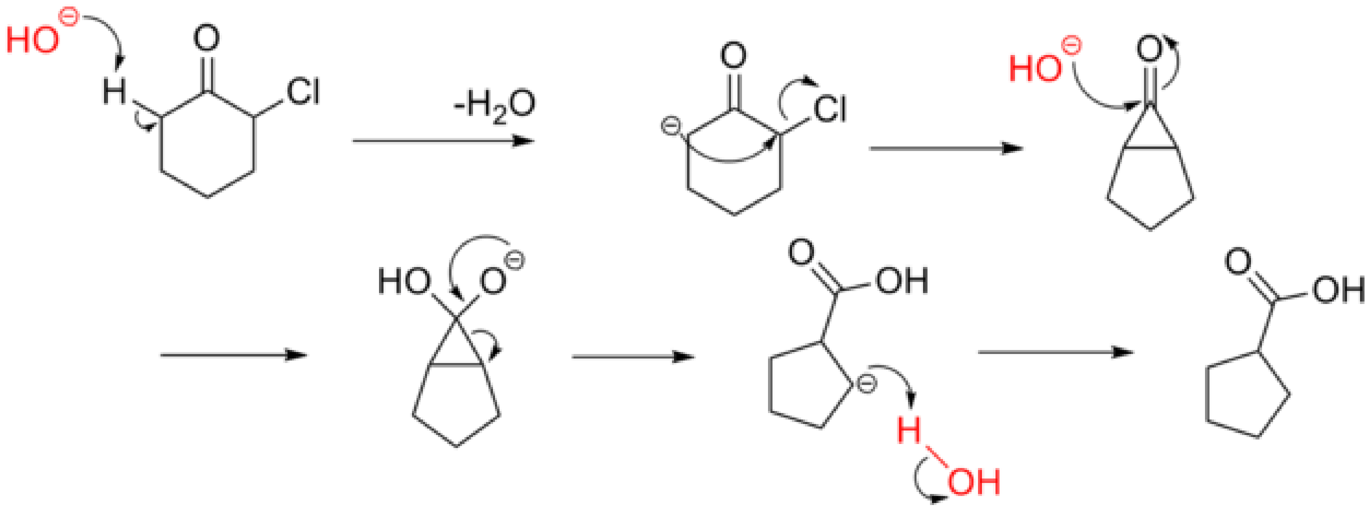
BASE-CATALYZED REARRANGEMENTS

- **Favorski Rearrangement**

- rearrangement of cyclopropanones and α-halo ketones leading to carboxylic acid derivatives
- via enolate

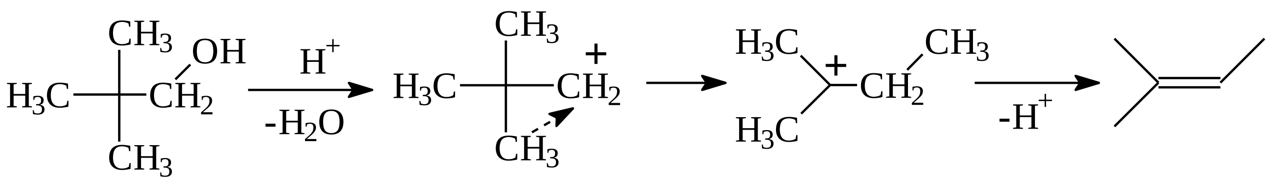


Mechanism:

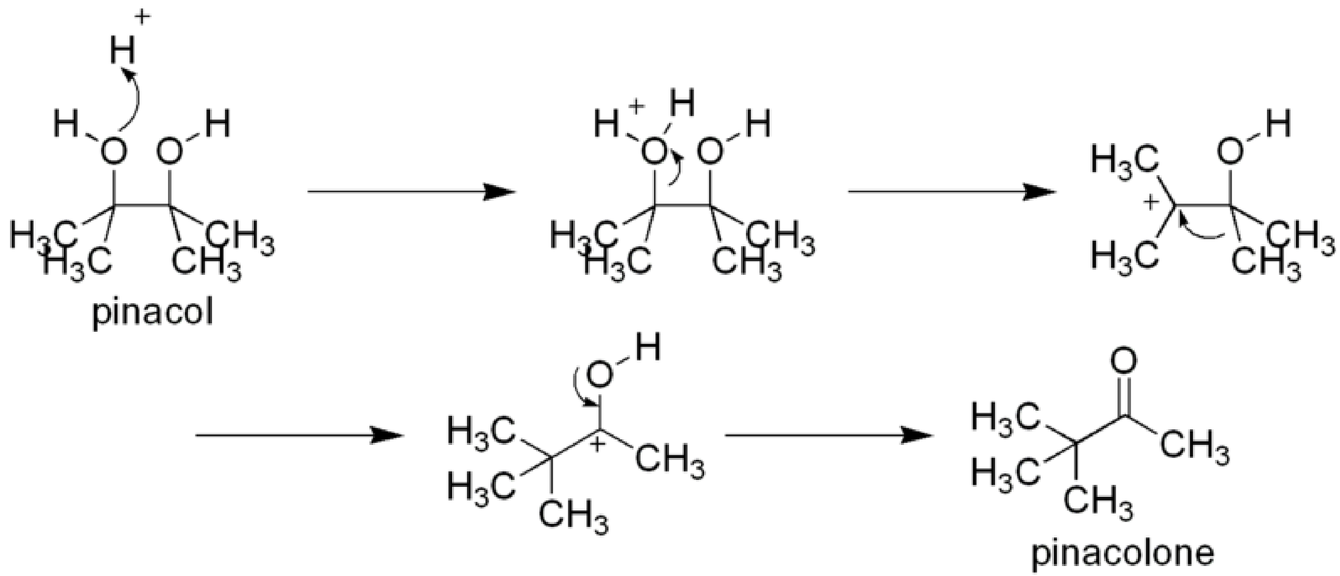


ACID-CATALYZED REARRANGEMENTS

- **Wagner-Meerwein Rearrangement**

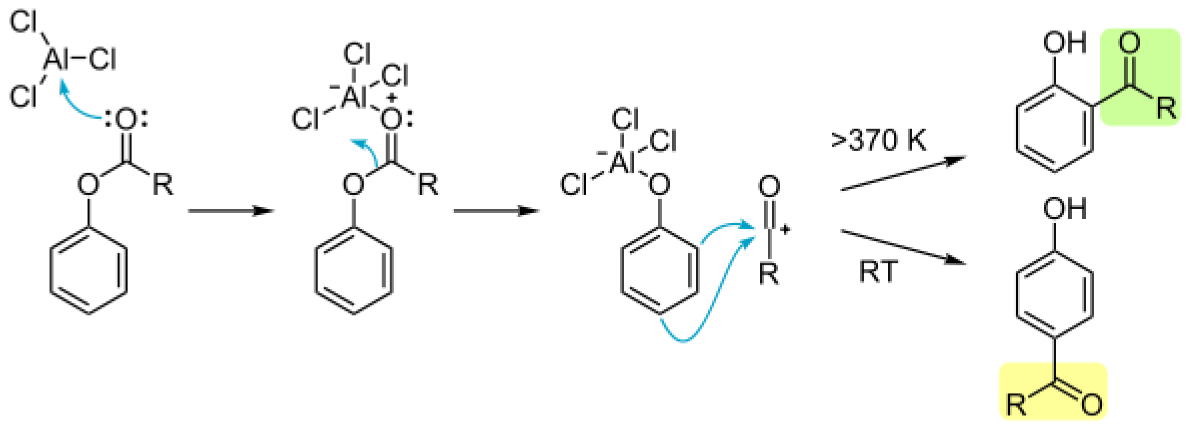


- **Pinacol Rearrangement**

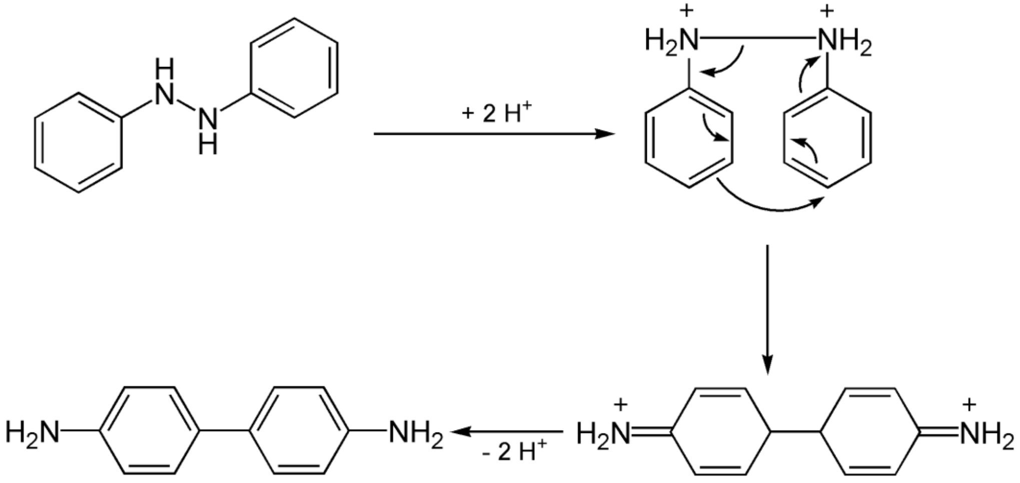


ACID-CATALYZED REARRANGEMENTS

- Fries Rearrangement



- Benzidine Rearrangement



ACID-CATALYZED REARRANGEMENTS

- **Beckmann rearrangement**
- rearrangement used to convert oximes to amides
- trans [1,2]-shift