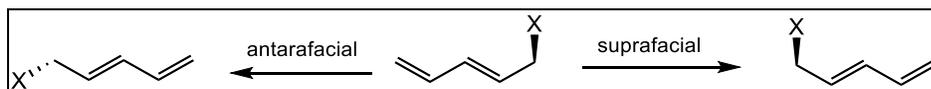


Sigmatropic Rearrangements

1. Introduction

- A class of concerted pericyclic reactions governed by orbital symmetry.
- One bond is being broken while another bond is being formed across a π system.
- Migrating group remains the same face with the system: suprafacial. Migrating group moves to opposite face of the system: antarafacial.

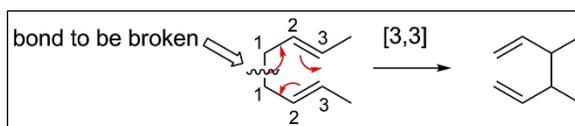


- Processes with 2- and 6-electron (Huckel, $4n+2$) are allowed suprafacially, 4-electron processes must occur antarafacially (Möbius, $4n$).¹

Order [1,j] 1+j =	Supra/retention	Supra/inversion	Antara/retention	Antara/inversion
4n	Forbidden	Allowed	Allowed	Forbidden
4n + 2	Allowed	Forbidden	Forbidden	Allowed

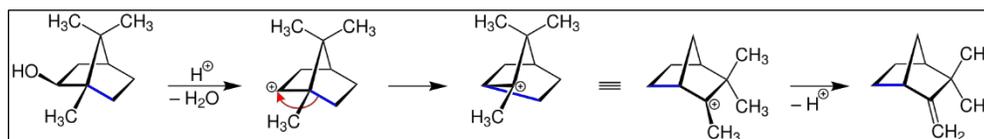
Order [i,j] i+j =	Supra/supra	Supra/antara	Antara/antara
4n	Forbidden	Allowed	Forbidden
4n + 2	Allowed	Forbidden	Allowed

- Nomenclature of [n,m] sigmatropic rearrangement: numbering the atoms of the bond being broken as atom 1, then count the atoms from the broken bond in each direction to the atoms (n, m) of the new bond.



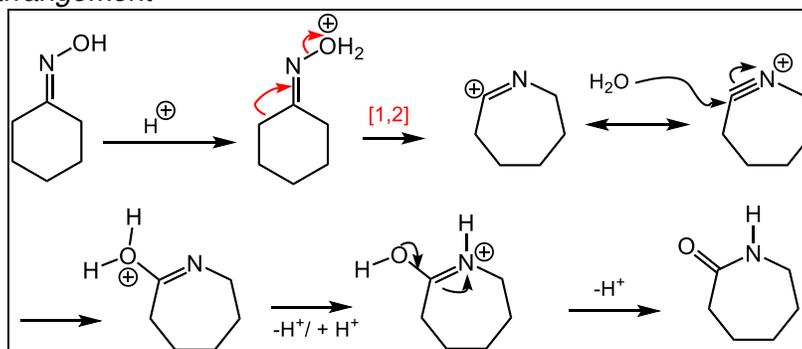
- ### 2. [1,2] Sigmatropic rearrangement:
- Often initialized by the formation of a reactive intermediate such as a carbocation or a carbanion to form a more stable intermediate. Many name reactions involve a [1,2] shift such as Wagner-Meerwein, Beckmann, or Stevens rearrangement.

- *Wagner-Meerwein rearrangement* in bicyclic terpenes

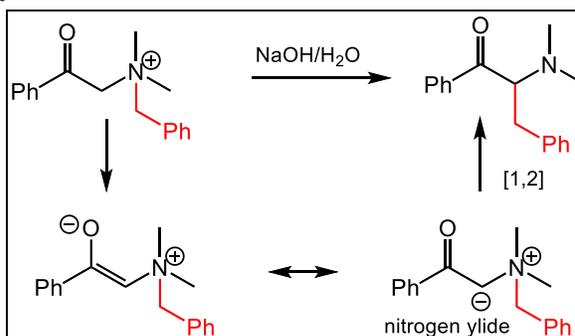


¹ R. B. Woodward and R. Hoffmann, *J. Am. Chem. Soc.*, **1965**, *87*, 2511

- *Beckmann rearrangement*

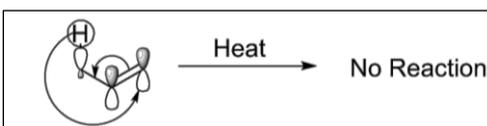


- *Stevens rearrangement*



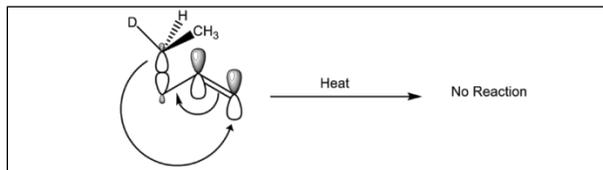
3. **[1,3] Sigmatropic rearrangement**

3.1. **Thermal [1,3] hydride shifts:** The Möbius topology required in the transition state prohibits such a shift because it is geometrically impossible.

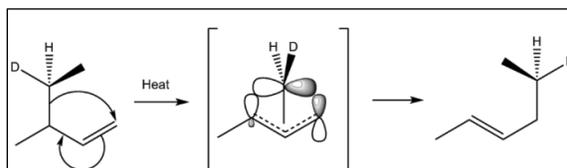


3.2. **Thermal [1,3] alkyl shifts:** Geometry of the transition state is prohibitive, but an alkyl group can invert its geometry, and therefore proceed via a suprafacial shift.

- Antarafacial [1,3] alkyl shift: symmetry allowed, geometrically impossible



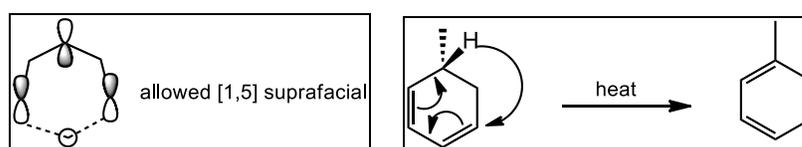
- Suprafacial [1,3] alkyl shift with inversion: symmetry allowed



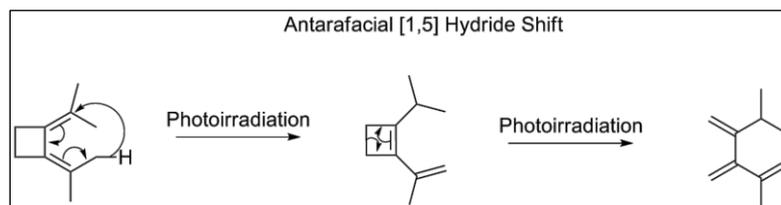
3.3. Photochemical [1,3] shift: should proceed suprafacially; however, most are non-concerted (have a diradical mechanism, to which the Woodward-Hoffmann rules do not apply).²

4. [1,5] Sigmatropic rearrangement: involving the shift of 1 substituent (H, alkyl, or Ar) down 5 atoms of a π system. Suprafacial thermal shifts are quite common, while antarafacial photochemical shifts are rarely observed.

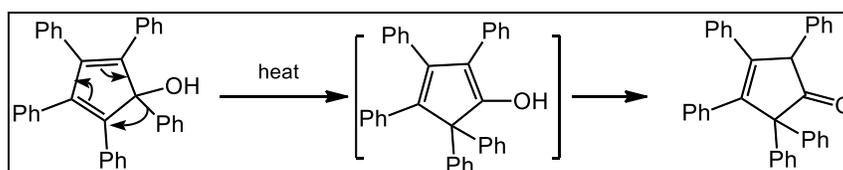
4.1. [1,5] hydride shifts: Hydrogen has been shown to shift in both cyclic and open chain systems at high temperature. These reactions proceed suprafacially, via a Huckel topology transition state.



- Photochemical irradiation allows antarafacial [1,5] hydride shift.³



4.2. [1,5] alkyl shifts: thermally allowed, though very poor, and never been observed in an open-chain system. Studies showed the rate preferences for [1,5] alkyl shift in cyclic system: carbonyl > hydride > phenyl and vinyl > alkyl.⁴

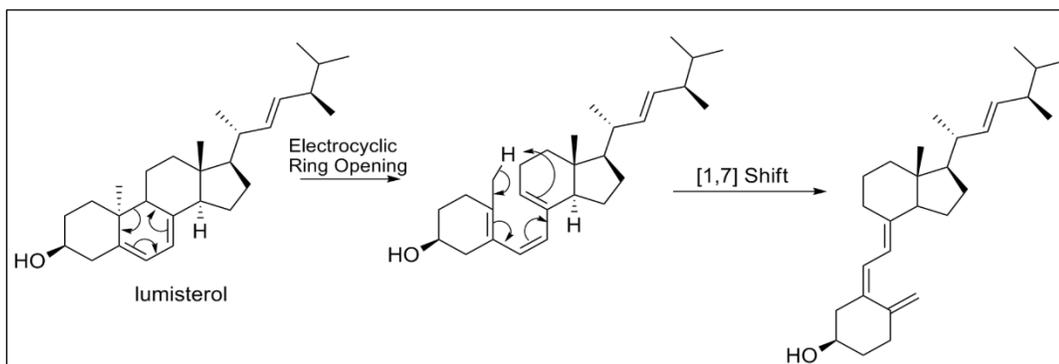


² Miller, Bernard. *Advanced Organic Chemistry*. 2nd Ed. Upper Saddle River: Pearson Prentice Hall. 2004

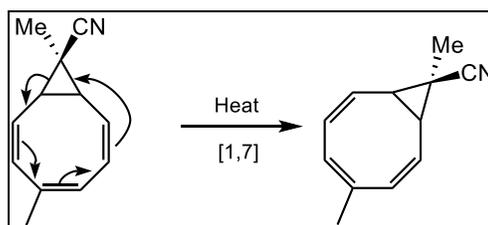
³ Kiefer, E.F.; Tana, C.H. *J. Am. Chem. Soc.*, **1969**, *91*, 4478

⁴ Fields, D.J.; Jones, D.W.; Kneen, G. *Chem. Comm*, **1976**, 873

5. **[1,7] Sigmatropic rearrangement:** proceed through antarafacial fashion, via a Möbius topology transition state (predicted by Woodward-Hoffmann rules), observed in the conversion of lumisterol to vitamin D₂.

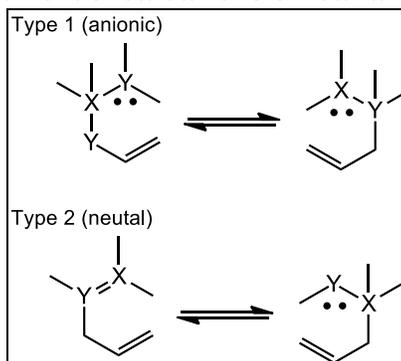


- In a bicyclic molecule, the migration of a divalent group, which is a part of 3-membered ring, is preferred as a "walk rearrangement".

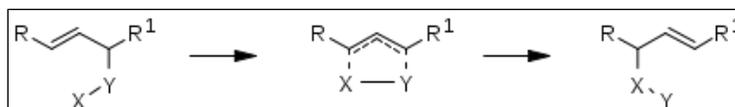


6. **[2,3] Sigmatropic rearrangement:**

- Classified in 2 types: rearrangement of carbanions or rearrangement of ylides



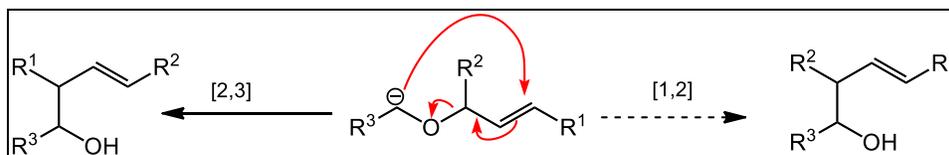
- Proceed through a 5-membered cyclic transition state.



- High stereoselectivity: prefer (*E*)-alkene product. Generally, the (*E*)-alkene will favor the formation of *anti* product, while (*Z*)-alkene will favor formation of *syn* product.

6.1. **Type 1:** encompass anionic rearrangement.

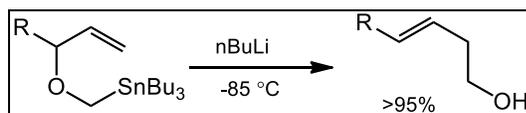
- **[2,3]-Wittig rearrangement:** allylic ether into a homoallylic alcohol via a concerted, pericyclic process. Often competes with [1,2]-Wittig rearrangement. Carbanion is often generated from direct lithiation or tin transmetalation.



- A highly enantioselective [2,3]-Wittig rearrangement using chromium carbonyl complexes.⁵

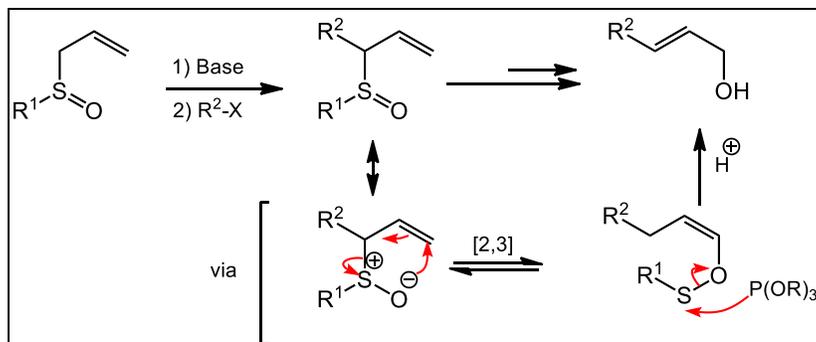


- The substrate must contain acidic hydrogens adjacent to the ether oxygen, which was a significant limitation. The development of transmetalation methods that allowed the selective generation of carbanions represents a profound advance.⁶



6.2. **Type 2:** encompasses ylide formation (carbon ylide or heteroatom ylide)

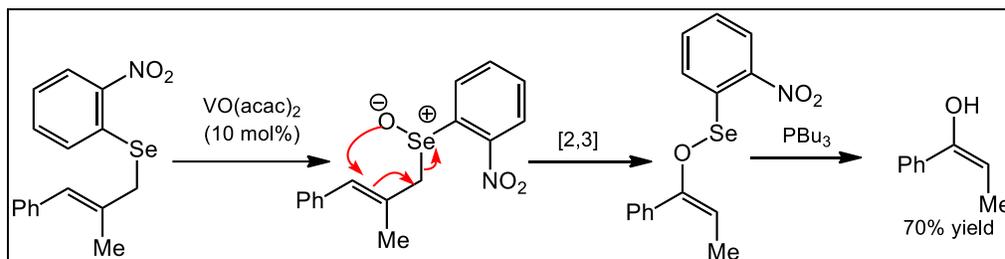
- **Mislow-Evans rearrangement:** allylic sulfoxides to allylic alcohol in a [2,3]-shift as a single-pot reaction



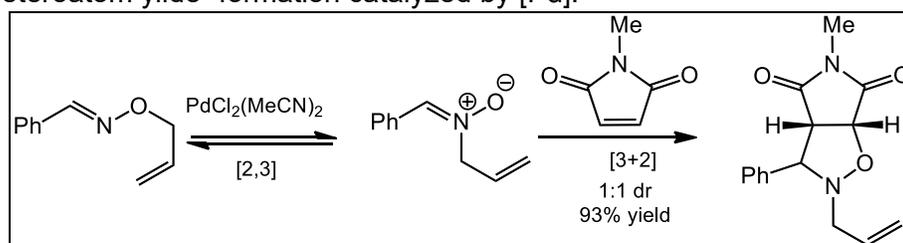
⁵ J. Am. Chem. Soc., 1991, 113, 5402

⁶ Still, W. C.; Mitra, A. J. Am. Chem. Soc., 1978, 100, 1927

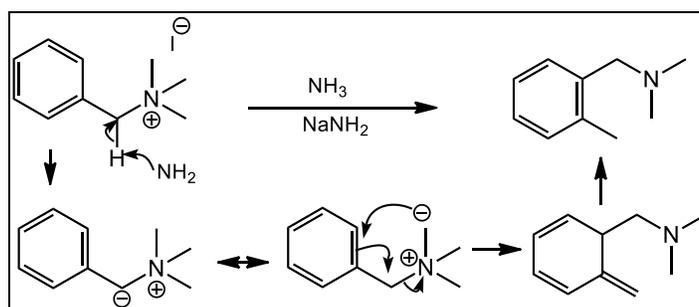
- In a selenium analogue of the Mislow-Evans arrangement, aryl selenides could be oxidized to selenate, which underwent [2,3] rearrangement.⁷



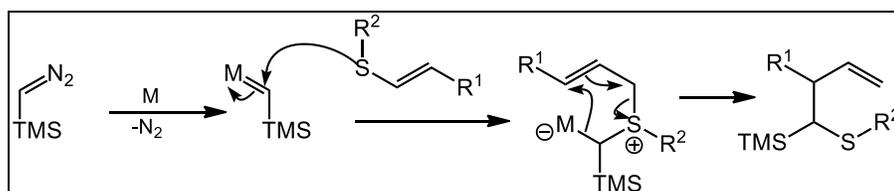
- Another “heteroatom ylide” formation catalyzed by [Pd].⁸



- Sommelet–Hauser rearrangement: forming ammonium ylide.



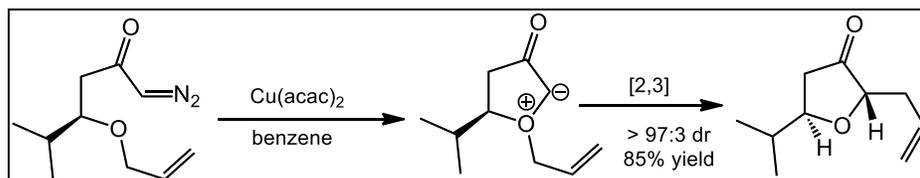
- **Doyle-Kirmse reaction**: an allyl sulfide reacts with diazo compounds to form the homoallyl sulfide compound.



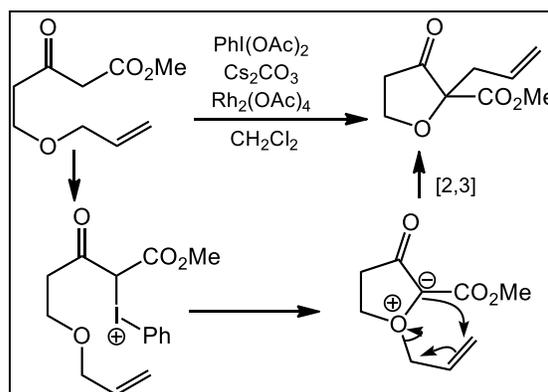
⁷ R. G. Carter, T. C. Bourland, *Chem. Commun.* **2000**, 2031.

⁸ R. Grigg, J. Markandu, *Tetrahedron Lett.* **1991**, 32, 279.

- Many reactions using diazo compounds to generate ylides⁹



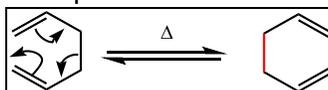
- Hypervalent iodine is an alternative to diazo compounds for use in the tandem ylide formation/[2,3] rearrangement.¹⁰



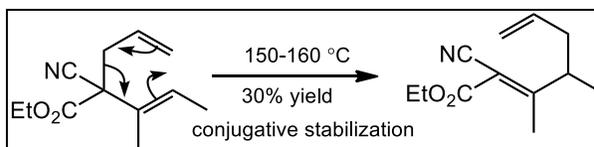
- [3,3] Sigmatropic rearrangement:** proceed suprafacially, via a Huckel topology transition state.

7.1. Cope rearrangement:

- Found by Cope in 1940,¹¹ a reversible process.



- Many strategies employed to drive the rearrangement toward the desired product (introduction of conjugation or aromaticity).



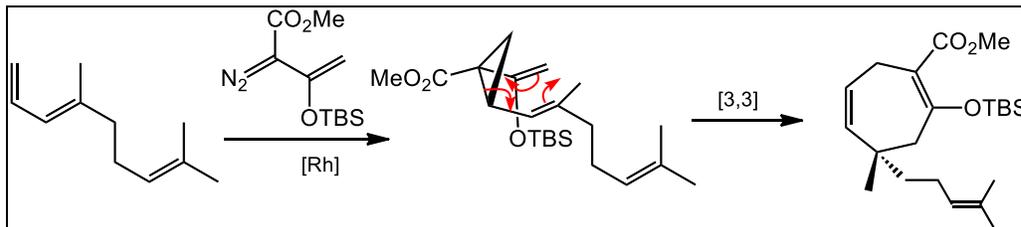
- Introducing a strained-ring (cyclopropane or cyclobutane) makes a Cope arrangement irreversible.

⁹ J. S. Clark, *Tetrahedron Lett.* **1992**, 33, 6193

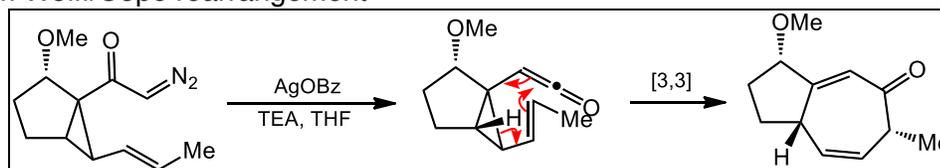
¹⁰ G. K. Murphy, F. G. West, *Org. Lett.* **2006**, 8, 4359

¹¹ A. C. Cope, E. M. Hardy, *J. Am. Chem. Soc.* **1940**, 62, 441

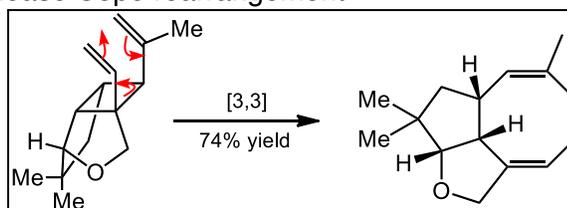
- Rh-catalyzed asymmetric cyclopropanation/Cope arrangement¹²



- Tandem Wolff/Cope rearrangement¹³

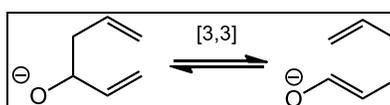


- Cyclobutane strain-release Cope rearrangement¹⁴

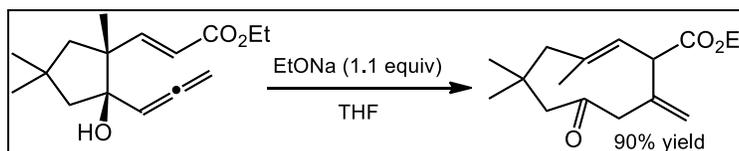


7.2. Oxy-Cope Rearrangement: discovered in 1964 by Jones and Berson.¹⁵

- The product is favored by incorporating an oxygen. Due to keto-enol tautomerization, the reaction is irreversible in most case.



- Anionic alkoxides accelerate the reaction rate: known as “anionic oxy-Cope rearrangement”
- Base-mediated anionic oxy-Cope¹⁶



¹² B. D. Schwartz, J. R. Denton, Y. Lian, H. M. L. Davies, C. M. Williams, *J. Am. Chem. Soc.* **2009**, *131*, 8329

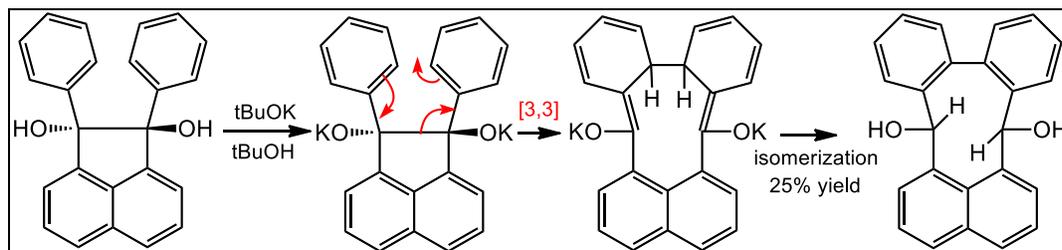
¹³ R. Sarpong, J. T. Su, B. M. Stoltz, *J. Am. Chem. Soc.* **2003**, *125*, 13624

¹⁴ J. Limanto, M. L. Snapper, *J. Am. Chem. Soc.* **2000**, *122*, 8071

¹⁵ J. A. Berson, M. Jones, Jr., *J. Am. Chem. Soc.* **1964**, *86*, 5019

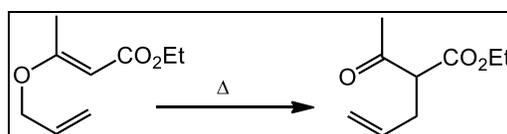
¹⁶ A. Balakumar, J. Seelvasakaran, K. Rajagopalan, *J. Org. Chem.* **1993**, *58*, 5482

- Base-catalyzed dianionic oxy-Cope rearrangement¹⁷



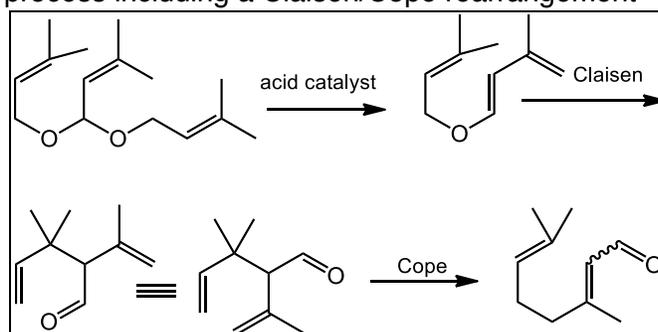
7.3. Claisen rearrangement:

- The first example of a [3,3] sigmatropic rearrangement (1912).¹⁸ A heteroatom variant of the Cope arrangement.
- The formation of carbonyl group makes this reaction, unlike other sigmatropic rearrangements, irreversible.



- Involving in many tandem pericyclic processes, isomerization, and cyclization.

- BASF continuous Citral process including a Claisen/Cope rearrangement¹⁹

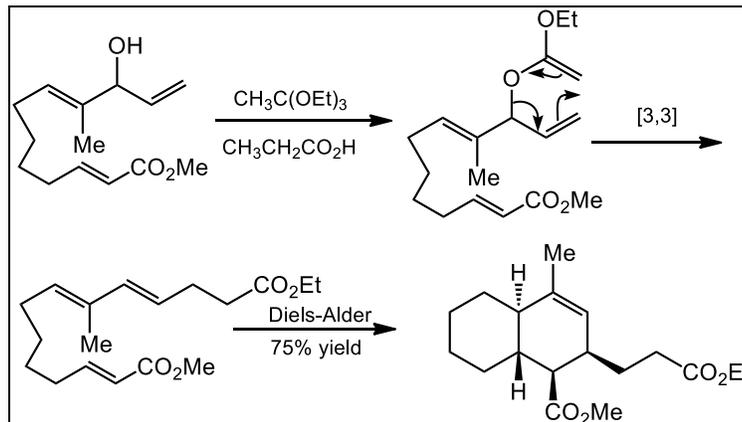


¹⁷ S. S. Hussaini, A. R. N. Raj, C. A. M. A. Huq, *Tetrahedron Lett.* **2007**, *48*, 775

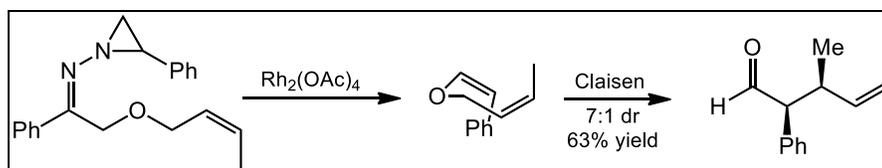
¹⁸ L. Claisen, *Chem. Ber.* **1912**, *45*, 6157

¹⁹ A. Nissen, W. Rebačka, W. Aquila, United States Patent 4288636, 09/08/, **1981**

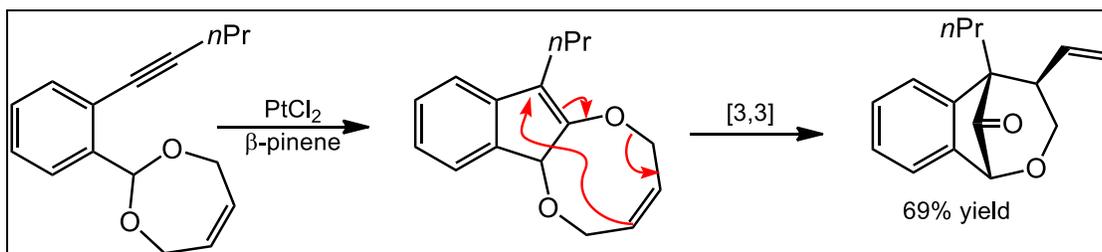
- Acid-catalyzed Johnson-Claisen/Diels-Alder cyclization²⁰



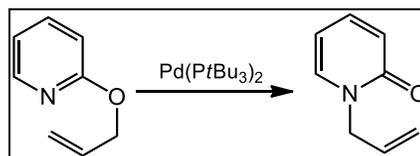
- Rhodium-catalyzed Bamford–Stevens/Claisen rearrangement²¹



- Platinum-catalyzed cycloisomerization/Claisen rearrangement²²



- Palladium-catalyzed aza-Claisen²³



²⁰ J. Mulzer, H. Bock, W. Eck, J. Buschmann, P. Luger, *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 414

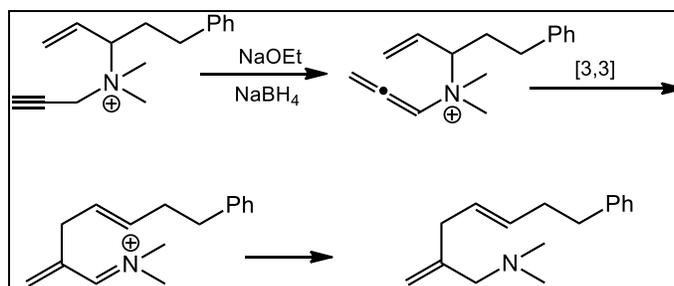
²¹ J. A. May, B. M. Stoltz, *J. Am. Chem. Soc.* **2002**, *124*, 12426

²² I. Nakamura, G. B. Bajracharya, Y. Yamamoto, *Chem. Lett.* **2005**, *34*, 174

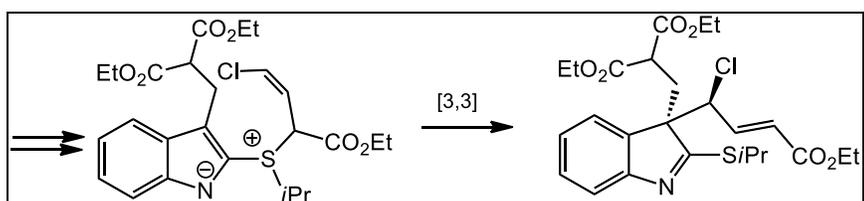
²³ K. Itami, D. Yamazaki, J. Yoshida, *Org. Lett.* **2003**, *5*, 2161

- Charge substrates can accelerate Claisen rearrangement.

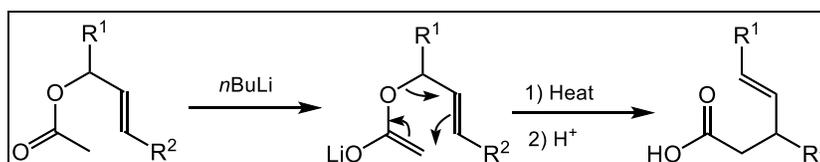
- Ammonium-Claisen rearrangement²⁴



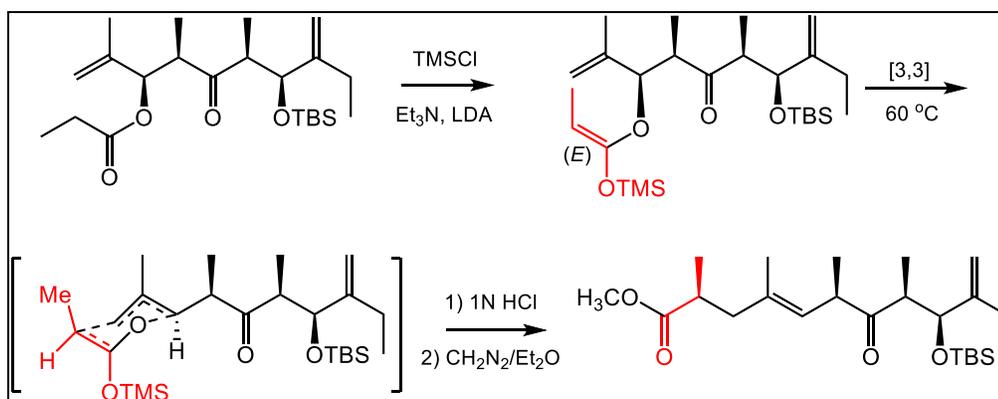
- Thio-Claisen rearrangement²⁵



- Ireland-Claisen rearrangement: convert allylic esters with a strong base to give γ,δ -unsaturated carboxylic acids



- Employed in the synthesis of inhibitor (-)-ebelatone A²⁶

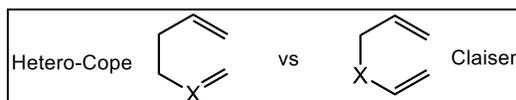


²⁴ K. Honda, H. Yasui, S. Inoue, *Synlett* **2003**, 2380

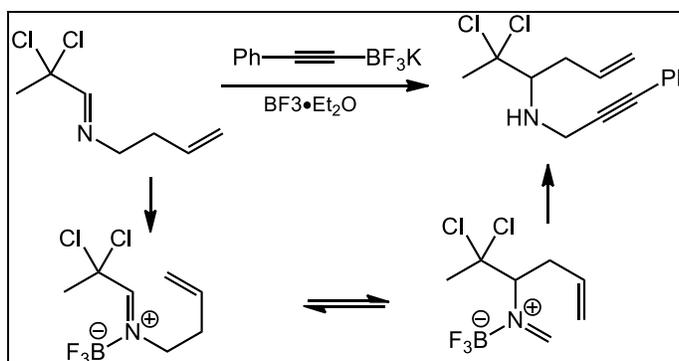
²⁵ V. Boyarskikh, A. Nyong, J. D. Rainier, *Angew. Chem. Int. Ed.* **2008**, *47*, 5374

²⁶ Paterson, I., Hulme, A. N., *J. Org. Chem.* **1995**, *60*, 3288

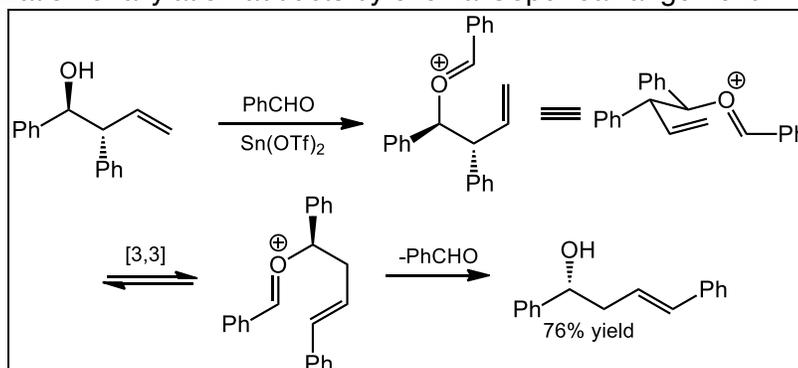
7.4. Hetero-Cope rearrangement



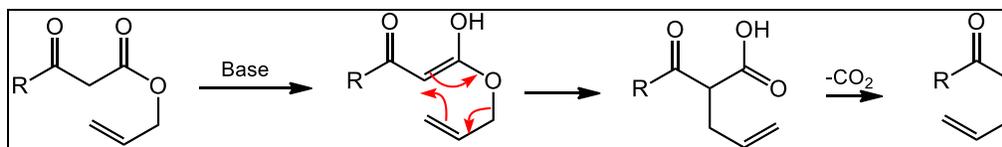
- **Aza-cope rearrangement:** usually initiated by acid-catalyzed condensation to form a reactive iminium ion.
 - Lewis acid-mediated tandem aza-Cope/Petasis-type reaction.²⁷



- **Oxonia-Cope rearrangement:** the oxygen analogue of the aza-Cope rearrangement, often competes with oxocarbenium reactions.
 - Isomerization of allylation adducts by oxonia-Cope rearrangement.²⁸



- 7.5. **Carroll rearrangement:** an analogue of Claisen rearrangement of β -keto allyl ester in the presence of a base, followed by decarboxylation.²⁹



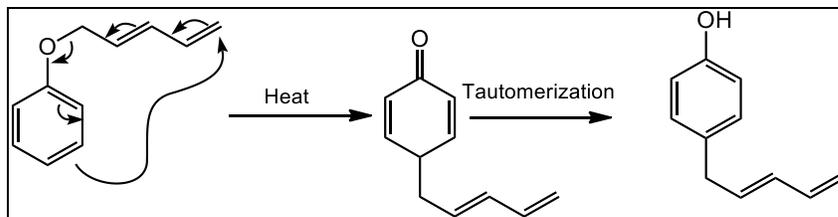
²⁷ S. Stas, K. A. Tehrani, G. Laus, *Tetrahedron* **2008**, *64*, 3457

²⁸ S. Sumida, M. Ohga, J. Mitani, J. Nokami, *J. Am. Chem. Soc.* **2000**, *122*, 1310

²⁹ Carroll, M. F. *J. Chem. Soc.* **1940**, 704

8. **[5,5] Rearrangement:** similar to [3,3] shift, proceed suprafacially, Huckel topology transition state.

- [5,5] shift of Phenyl pentadienyl ether³⁰



The end.

³⁰ Miller, Bernard. *Advanced Organic Chemistry*. 2nd Ed. Upper Saddle River: Pearson Prentice Hall. 2004.