

Outline:

1. Introduction and General Reactivity Paradigms
2. Wagner-Meerwein
3. Pinacol/Semi-Pinacol
4. Dowd-Beckwith
5. Cyclopropanation/Fragmentation
6. Beckmann Rearrangement
7. Grob Fragmentation
8. Sigmatropic Rearrangements

General References:

Definition:

- Unsworth, W. *Chem. Eur. J.* **2017**, 23, 8780.

Wagner-Meerwein:

- Hanson, J. *Comprehensive Organic Synthesis.* **1991**, 705.

Pinacol/Semi-Pinacol:

- Tu, Y-Q. *Chem. Rev.* **2011**, 111, 7523.

Dowd-Beckwith:

- Dowd, P. *Chem. Rev.* **1993**, 93, 2091.

- Zhang, W. *Radicals in Organic Synthesis: Ring Expansions.* **2001**.

- Hari, D. *Chem. Eur. J.* **2022**, 28.

Cyclopropanation/Fragmentation:

- Carreira, E. *Chem. Rev.* **2017**, 117, 11651.

Beckmann Rearrangement:

- Georg, G. *Molecular Rearrangements in Organic Synthesis.* **2016**.

Grob Fragmentation:

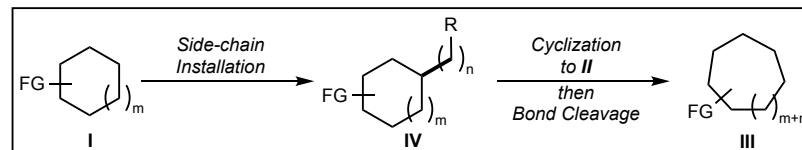
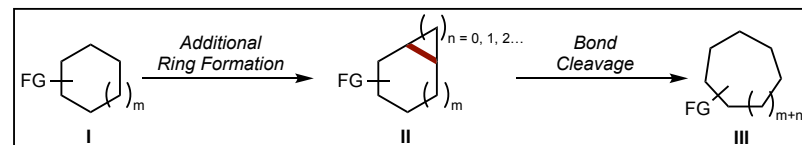
Mulzer, J. *Chem. Rev.* **2010**, 110, 3741.

Sigmatropic Rearrangements:

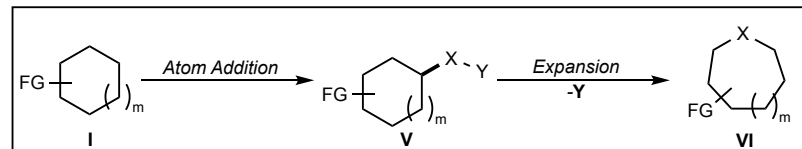
Gaich, T. *Beilstein J. Org. Chem.* **2014**, 10, 163.

Covered Paradigms:

Fragmentation:



Atom Addition, then Expansion:



Disclaimers:

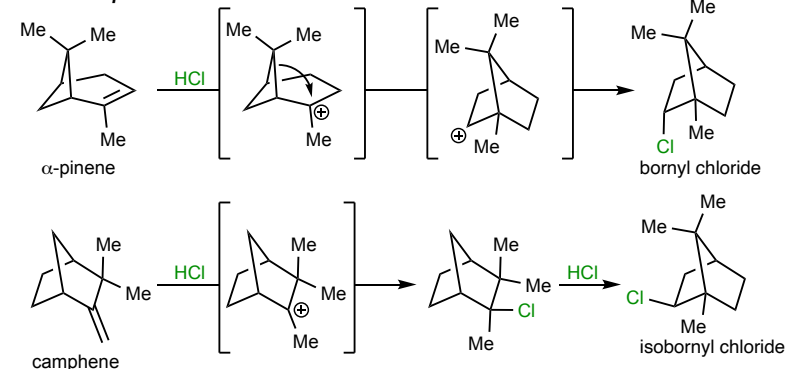
1. This review is not meant to be a comprehensive overview of ring-expansion techniques in total synthesis. Instead, it serves the purpose to quickly provide practitioners with variations of ring-expansions to further facilitate different retrosynthetic analyses.
2. Techniques covered in previous MOTW and CHEM 534 will not be discussed (ie. Baeyer-Villiger, Schreiber fragmentation, etc.)
3. The outline for each technique is presented in the following manner:
 - a. Introduction
 - b. Methodological Advancements
 - c. Applications in Synthesis

Classics in Ring-Expansion: Wagner-Meerwein

Wagner-Meerwein Rearrangement:

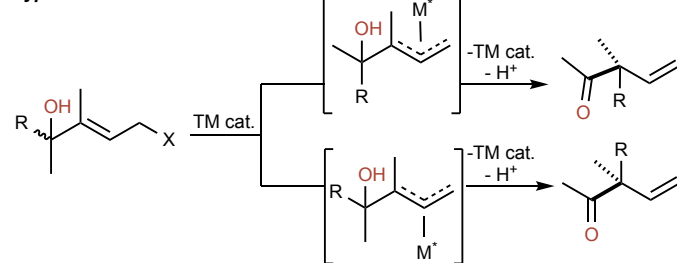
- One of the foundational reactions in organic synthesis identified in the 19th century.
- The reaction is formally defined as follows: **the generation of a carbocation on a bicyclic system followed by the 1,2-shift of an adjacent skeletal C-C bond to generate a new carbocation.**
- If carbocation generation is followed by the migration of a methyl group, the classification diverges to the Nametkin rearrangement.

Seminal Reports:

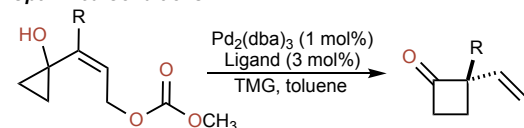


The Wagner-Meerwein process enables the facile formation of quaternary carbon centers as well as the construction of highly difficult carbocyclic frameworks. These advantages have spurred significant interest in stereoselective variants of this process.

Trost (2001): A Catalytic Asymmetric Wagner-Meerwein Shift



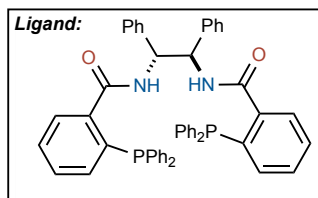
Optimized Conditions:



Reaction discoveries:

1. Toluene - optimal solvent.
2. Addition of organic base such as TMG proved critical in catalytic amounts.
3. Amount of TMG required is substrate dependent.

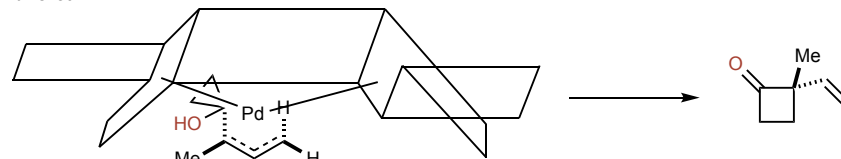
R, yield (%), e.e. (%)
 CH₃, quant, 92%
 n-C₄H₉, quant, 90%
 CH₂CH₂Ph, quant, 92%
 Ph, 62%, 70%
 CC(CH₂)₂OTBDMS, 91%, 89%



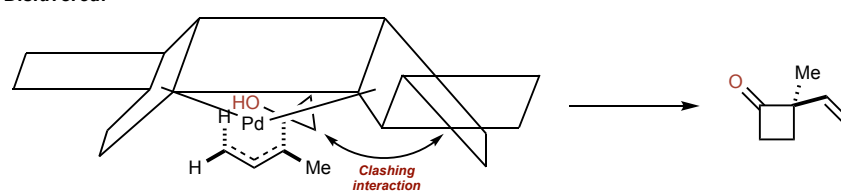
Trost, B. J. Am. Chem. Soc. 2001, 123, 7162. <https://doi.org/10.1021/ja010504c>

Trost (2001): Mechanistic and Stereochemical Rationale

Favored:

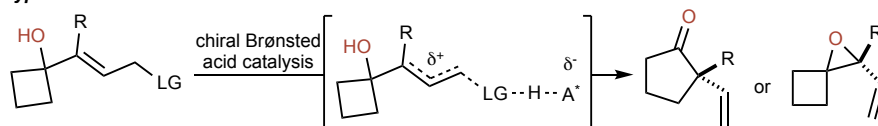


Disfavored:

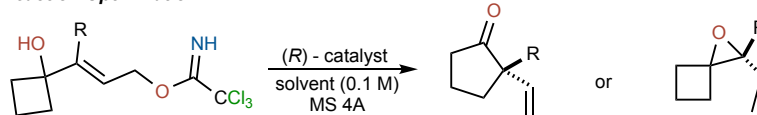


Terada (2019): Organocatalytic Wagner-Meerwein

Hypothesis:

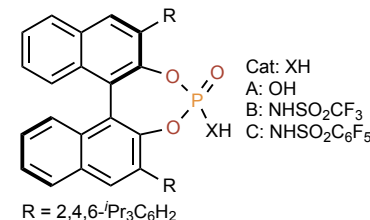


Reaction Optimization:



R = Ph
 catalyst, solvent, conditions, yield (%), isomeric ratio, e.e. (%)

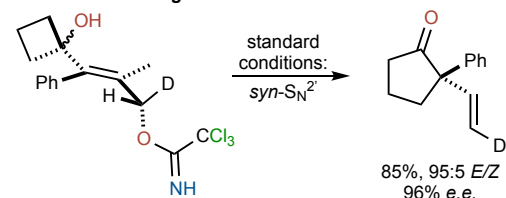
- A, toluene, rt, 48 hrs, 31%, 77 / 23, 4%
 B, toluene, rt, 0.5 hrs, 89%, 96 / 4, 43%
 B, toluene, -40 °C, 0.5 hrs, 90%, 94 / 6, 78% / 77%
 B, Et₂O, -40 °C, 0.5 hrs, 93%, 44 / 56, 72% / 93%
 B, EtOAc, -40 °C, 0.5 hrs, 87%, 32 / 68, 63% / 94%
 B, DCM, -40 °C, 0.5 hrs, 91%, 99 / 1, 69%
 C, CHCl₃, -60 °C, 3 hrs, 84%, 99 / 1, 96%



R, yield (%), isomeric ratio, e.e. (%)

- 4-MeC₆H₄, 85%, 99:1, 94%
 4-MeOC₆H₄, 90%, 99:1, 83%
 4-^tBuC₆H₄, 82%, 99:1, 95%
 3-MeC₆H₄, 95%, 99:1, 95%
 3-MeOC₆H₄, 88%, 99:1, 97%
 2-naphthyl, 85%, 99:1, 95%
 3-thienyl, 83%, 99:1, 79%
 Bn, 70%, 96:4, rac

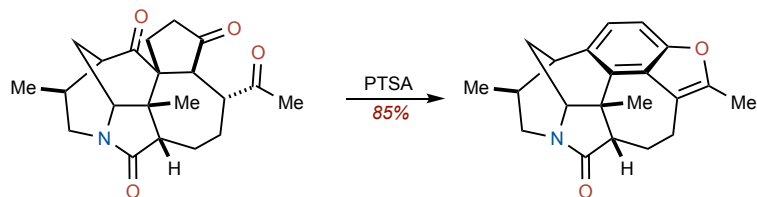
Mechanistic Insight:



Terada, M. ACS Catal. 2019, 9, 6846. <https://doi.org/10.1021/acscatal.9b01780>

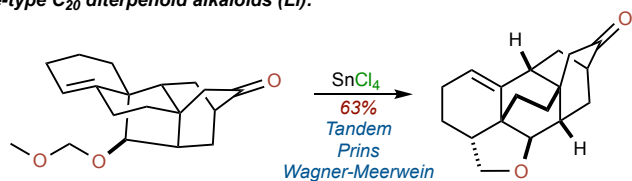
Synthetic Applications:

(-)-daphnilongeranin B (Zhai):



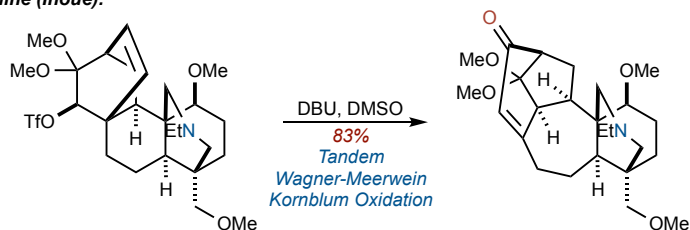
Zhai, H. *Angew. Chem. Int. Ed.* **2018**, *57*, 947. <https://doi.org/10.1002/anie.201709762>

arcutine-type C₂₀ diterpenoid alkaloids (Li):



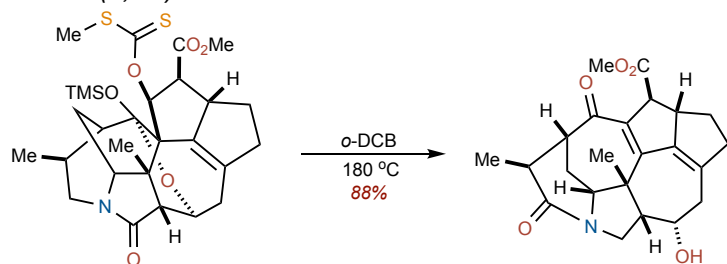
Li, A. *J. Am. Chem. Soc.* **2019**, *141*, 13718. <https://doi.org/10.1021/jacs.9b05818>

talatisamine (Inoue):



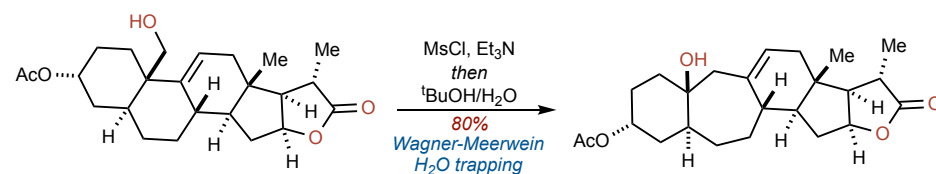
Inoue, M. *Angew. Chem. Int. Ed.* **2020**, *59*, 479. <https://doi.org/10.1002/anie.201912737>

(-)-daphnillonin B (Li, C.C.):



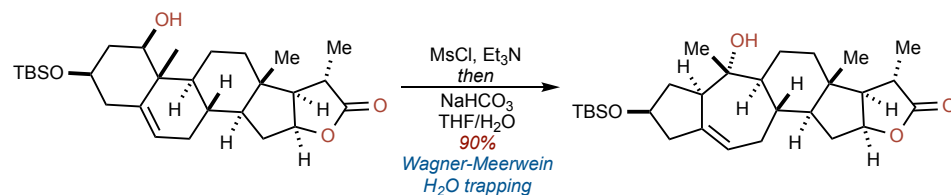
Li, C.C. *J. Am. Chem. Soc.* **2023**, *145*, 10998. <https://doi.org/10.1021/jacs.3c03755>

propindilactone G (Gui):



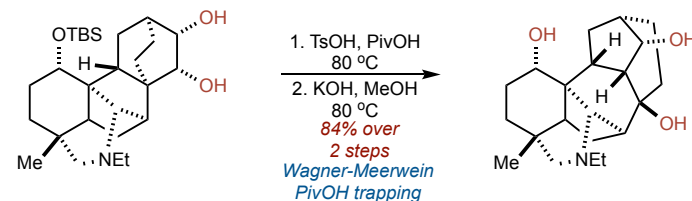
Gui, J. *J. Am. Chem. Soc.* **2020**, *142*, 5007. <https://doi.org/10.1021/jacs.0c00363>

bufospirostenin A (Gui):



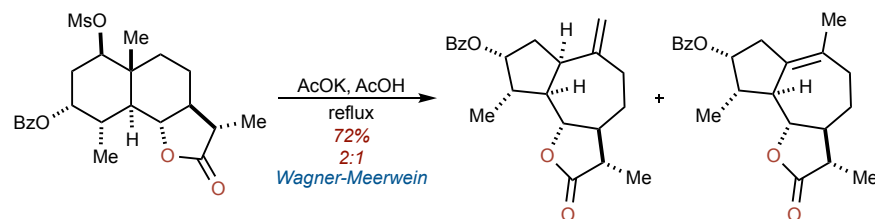
Gui, J. *J. Am. Chem. Soc.* **2021**, *143*, 19576. <https://doi.org/10.1021/jacs.1c10067>

cardiopetaline (Fukuyama):



Fukuyama, T. *Org. Lett.* **2017**, *19*, 5833. <https://doi.org/10.1021/acs.orglett.7b02812>

arborescin (Takase):

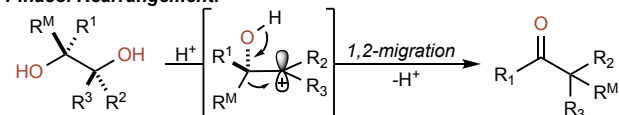


Takase, K. *J. Org. Chem.* **1982**, *47*, 3909. <https://doi.org/10.1021/jo00141a020>

Pinacol Rearrangements:

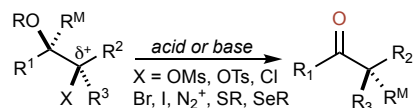
- A specific variation of the Wagner-Meerwein rearrangement involving a 1,2-diol.
- Originally defined in the following manner: **the acid-catalyzed transformation of 1,2-diols to ketones or aldehydes by a 1,2-migration of a C-C or C-H bond toward the vicinal carbocation.**
- In most cases, a pinacol rearrangement lacks regio- and diastereoselectivity. However, the semi-pinacol rearrangement has been extended to include multiple leaving groups instead of the second hydroxyl unit.
- This description gives rise to a new definition: **such processes share a common reactive species in which an electrophilic carbon center, including but not limited to carbocations, is vicinal to an oxygen-containing carbon and can drive the 1,2-migration of a C-C or C-H bond to terminate the process, generating a carbonyl group.**

Pinacol Rearrangement:

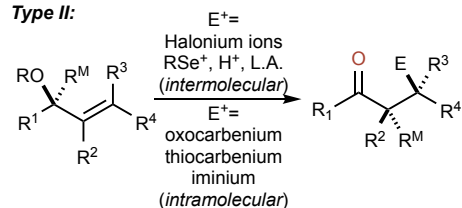


Semi-pinacol Rearrangement:

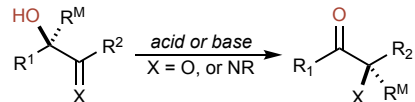
Type I:



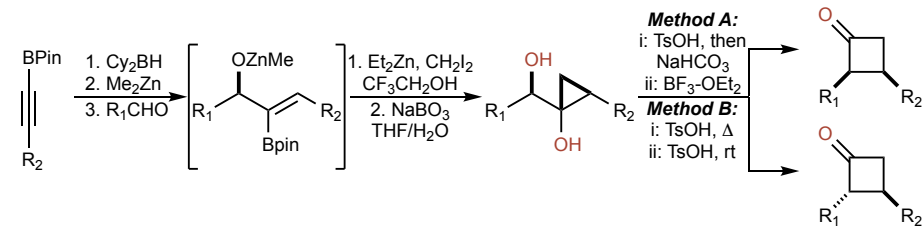
Type II:



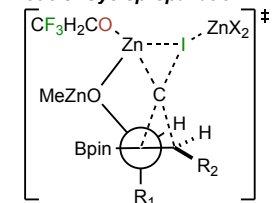
α -ketol rearrangement



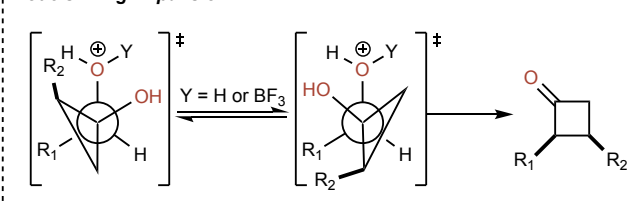
Tandem Carbonyl Addition/Alkoxide-Directed Cyclopropanation/Rearrangement (Walsh, 2009):



Models: Cyclopropanation



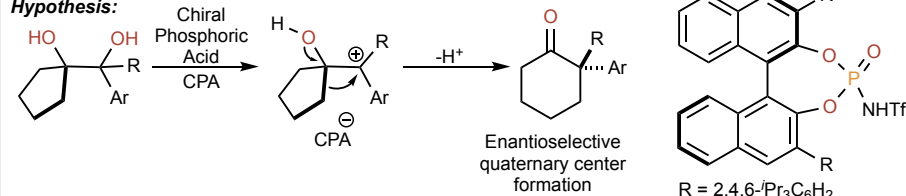
Models: Ring-Expansion



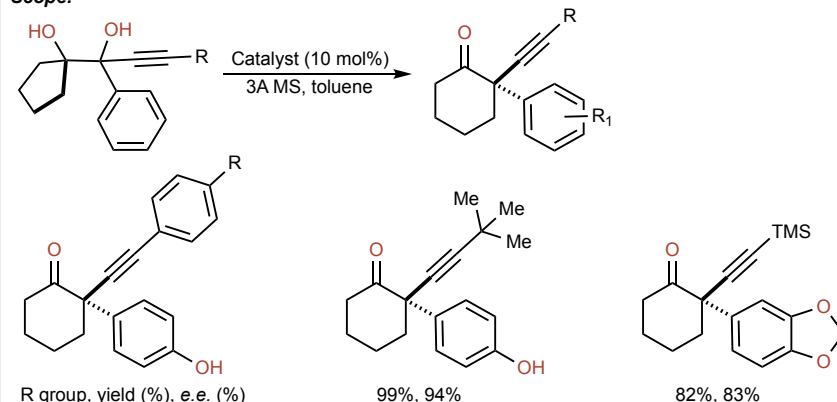
Cis-isomer formation is rationalized by a concerted rearrangement whereas ring-expansion proceeds via an antiperiplanar transition state. A possible isomerization of cis to trans may be involved for the observed outcomes.

Catalytic Enantioselective Pinacol Rearrangements (Zhu, 2019):

Hypothesis:

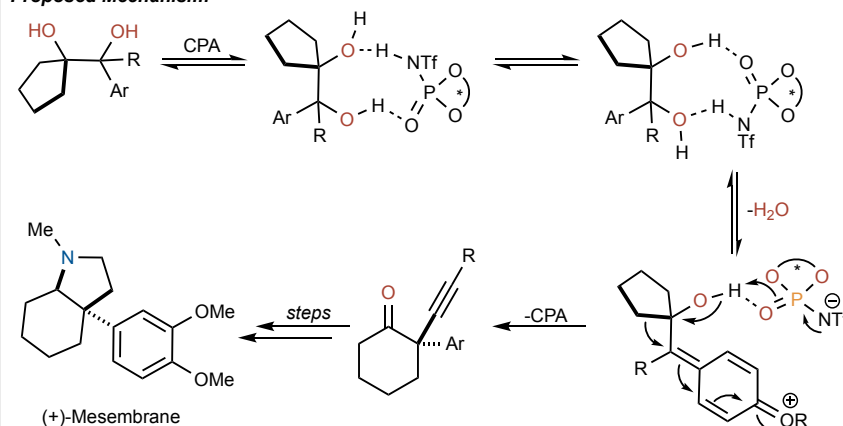


Scope:



R group, yield (%), e.e. (%)
 H, 99%, 90%
 Me, 98%, 94%
 Ph, 75%, 91%
 F, 97%, 92%
 OMe, 81%, 87%

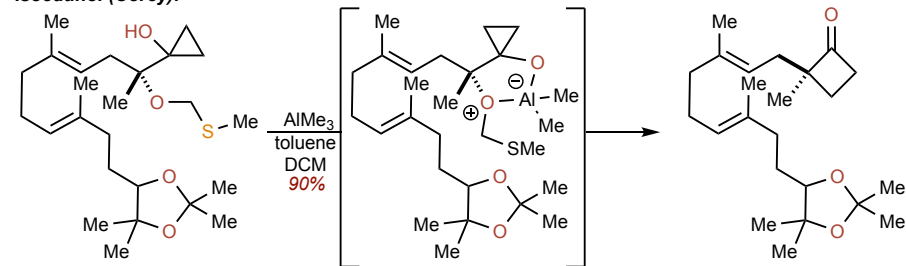
Proposed Mechanism:



Walsh, P. *J. Am. Chem. Soc.* **2009**, *131*, 6516. <https://doi.org/10.1021/ja900147s>
 Zhu, J. *J. Am. Chem. Soc.* **2019**, *141*, 11372. <https://doi.org/10.1021/jacs.9b04551>

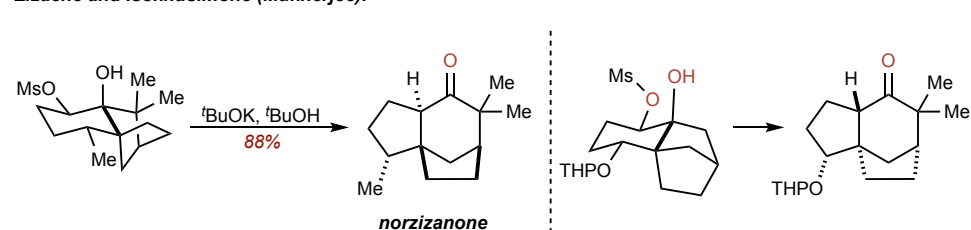
Synthetic Applications:

Isoedunal (Corey):



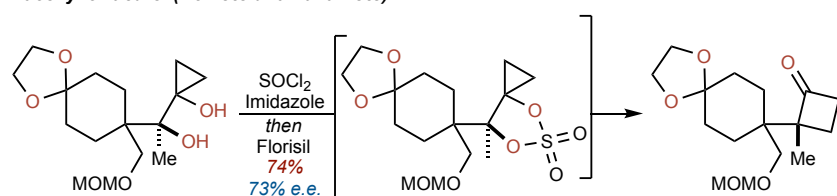
Corey, E. J. *J. Am. Chem. Soc.* **2005**, *127*, 13813. <https://doi.org/10.1021/ja055137+>

Zizaene and Isokhusimone (Mukherjee):



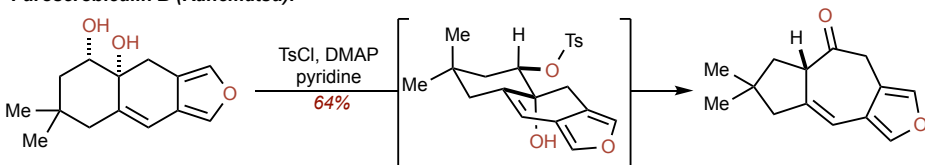
Mukherjee, D. *Tetrahedron.* **2002**, *58*, 1773. [https://doi.org/10.1016/S0040-4020\(02\)00063-7](https://doi.org/10.1016/S0040-4020(02)00063-7)

4-deoxyverrucarol (Nemoto and Fukumoto):



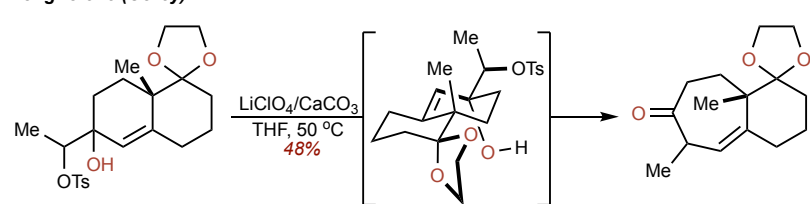
Ihara, M. *J. Org. Chem.* **2000**, *65*, 504. <https://doi.org/10.1021/jo991430e>

Furoscrobiculin B (Kanematsu):



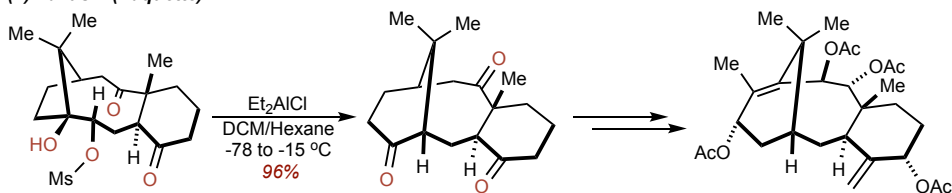
Kanematsu, K. *J. Chem. Soc.; Perkin Trans.* **1997**, 1707. <https://doi.org/10.1039/A607164C>

Longifolene (Corey):



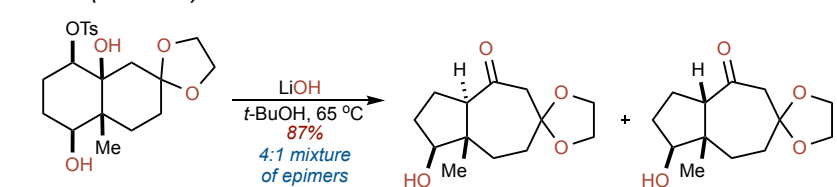
Corey, E. J. *J. Am. Chem. Soc.* **1964**, *86*, 478. <https://doi.org/10.1021/ja01057a039>

(+)-Taxusin (Paquette):



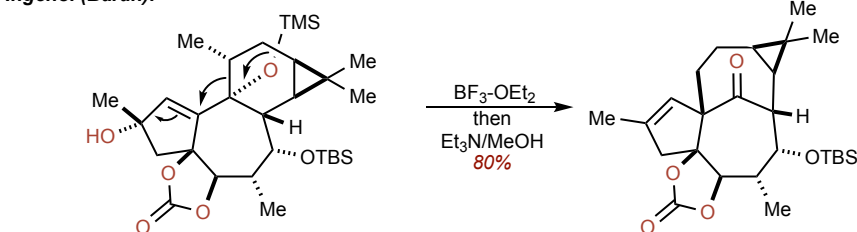
Paquette, L. *J. Am. Chem. Soc.* **1998**, *120*, 5203. <https://doi.org/10.1021/ja9805371>

Confertin (Heathcock):



Heathcock, C. *J. Am. Chem. Soc.* **1982**, *104*, 1907. <https://doi.org/10.1021/ja00371a020>

Ingenol (Baran):



Baran, P.S. *Science.* **2013**, *341*, 878. <https://doi.org/10.1126/science.1241606>

Classics in Ring Expansion: Dowd-Beckwith

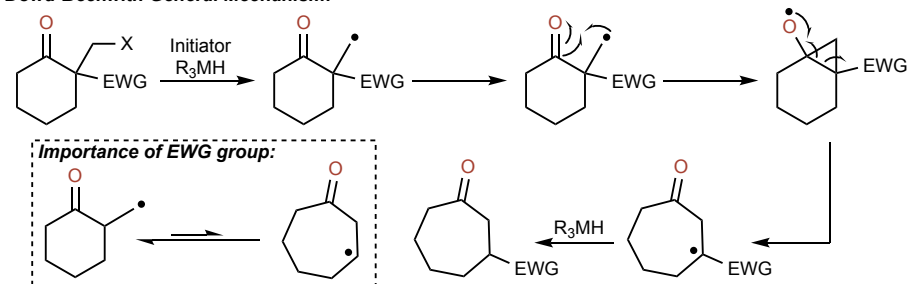
Dowd-Beckwith: *n* - Carbon Ring Expansions

- The Dowd-Beckwith is a radical reaction which incorporates the side-chain into a nearby ring.
- Separately, the overall process can be divided into two phases.

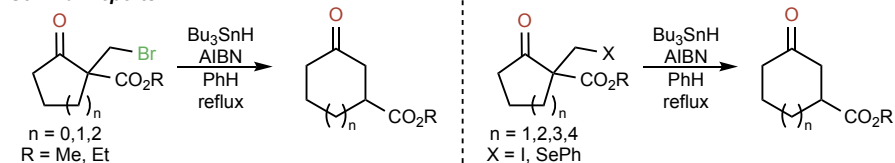
1st Phase: An initially formed alkyl radical adds into a nearby ketone to form an alkoxy radical.
2nd Phase: β -scission of the alkoxy radical results in a ring-expanded product and alkyl radical which further undergoes termination.

- Usually, the EWG plays two critical roles. 1.) It activates the ketone for attack by the formed carbon radical and 2.) alters the equilibrium to favor ring-expansion.

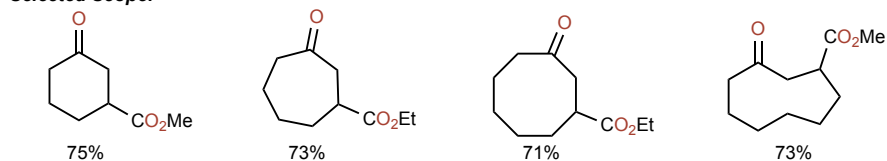
Dowd-Beckwith General Mechanism:



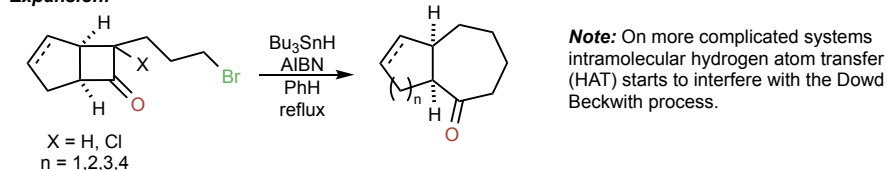
Seminal Reports:



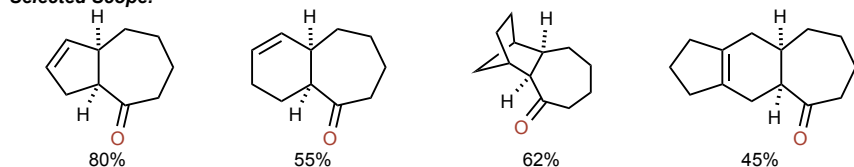
Selected Scope:



Expansion:

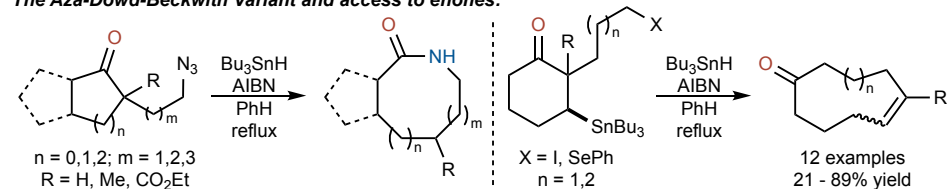


Selected Scope:

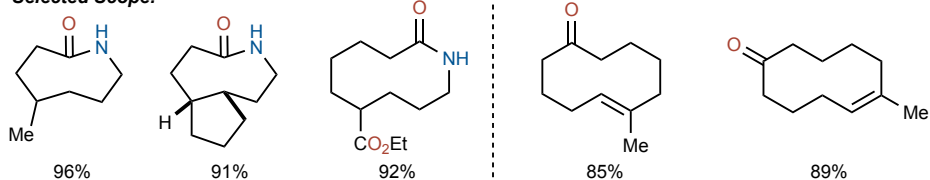


Further Developments:

The Aza-Dowd-Beckwith Variant and access to enones:

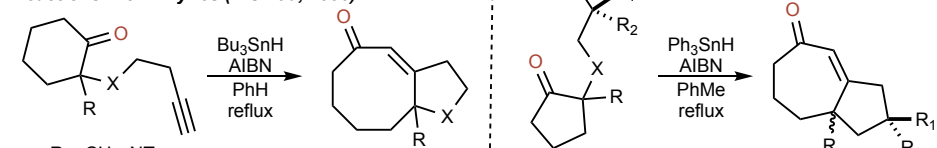


Selected Scope:

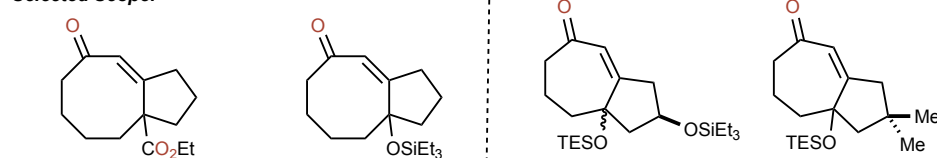


Additional Developments:

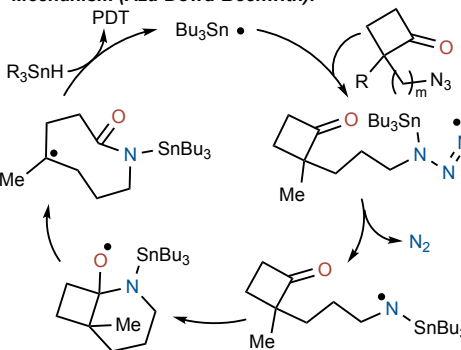
Reactions with Alkynes (Nishida, 1990):



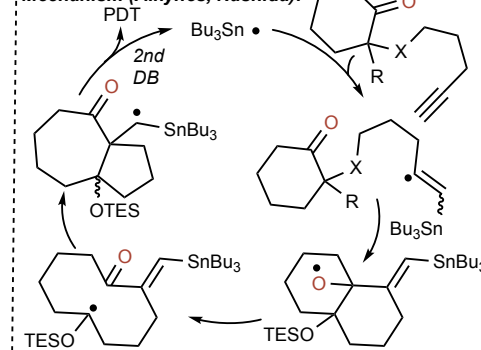
Selected Scope:



Mechanism (Aza-Dowd-Beckwith):



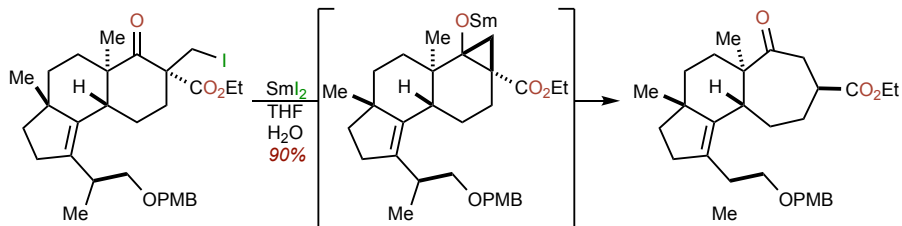
Mechanism (Alkynes, Nishida):



Classics in Ring Expansion: Dowd-Beckwith

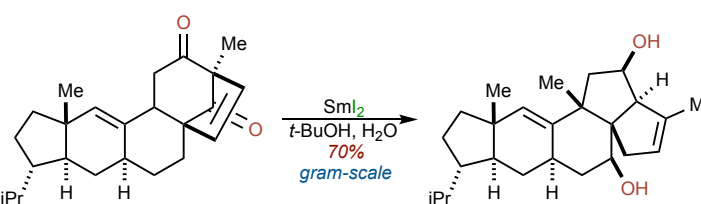
Synthetic Applications:

Sarcodonin G (Pier):



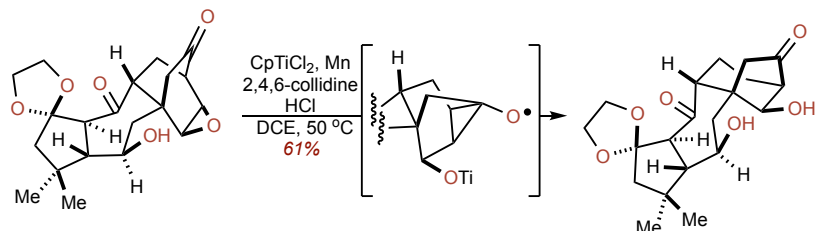
Piers, E. *Org. Lett.* **2000**, 2, 1407. <https://doi.org/10.1021/ol0057333>

(-)-ritgeranic acid A (Ding):



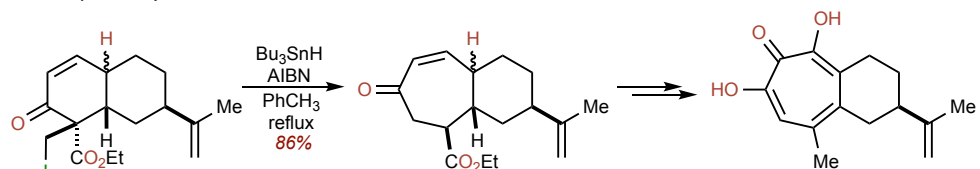
Ding, H. *J. Am. Chem. Soc.* **2023**, 145, 11927. <https://doi.org/10.1021/jacs.3c03178>

Rhodomollein XXII (Ding):



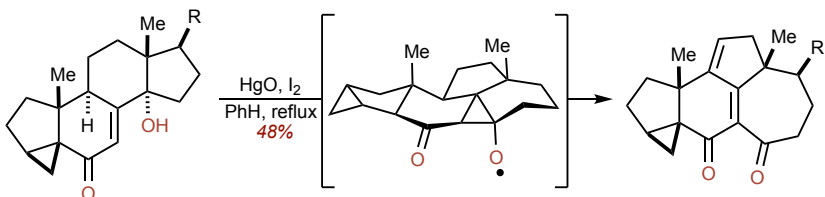
Ding, H. *Angew. Chem. Int. Ed.* **2019**, 58, 8556. <https://doi.org/10.1002/anie.201903349>

Manicol (Banwell):



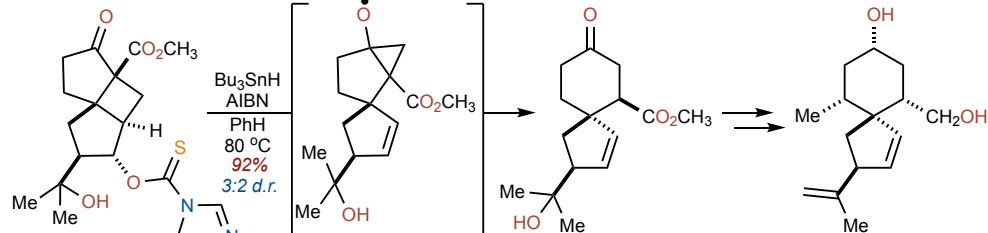
Banwell, M. *Tetrahedron. Lett.* **1996**, 37, 525. [https://doi.org/10.1016/0040-4039\(95\)02178-7](https://doi.org/10.1016/0040-4039(95)02178-7)

Swinhoeisterol A (Heretsch):



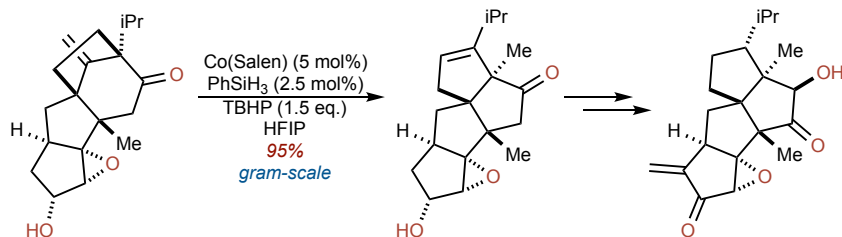
Heretsch, P. *J. Am. Chem. Soc.* **2020**, 142, 104. <https://doi.org/10.1021/jacs.9b12899>

Lubiminol (Crimmins):



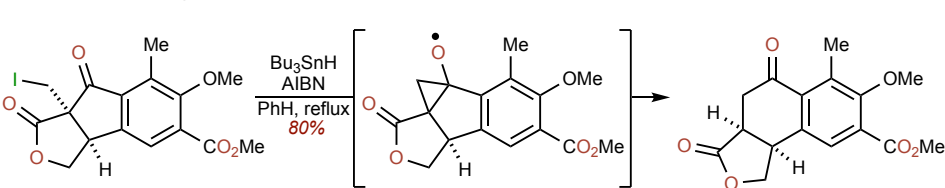
Crimmins, M. *J. Am. Chem. Soc.* **1998**, 120, 1747. <https://doi.org/10.1021/ja973824y>

Crinpellins (Ding):



Ding, H. *J. Am. Chem. Soc.* **2022**, 144, 2495. <https://doi.org/10.1021/jacs.1c13370>

Salvileucalin C (Ding):



Ding, H. *Org. Lett.* **2014**, 16, 3376. <https://doi.org/10.1021/ol501423t>

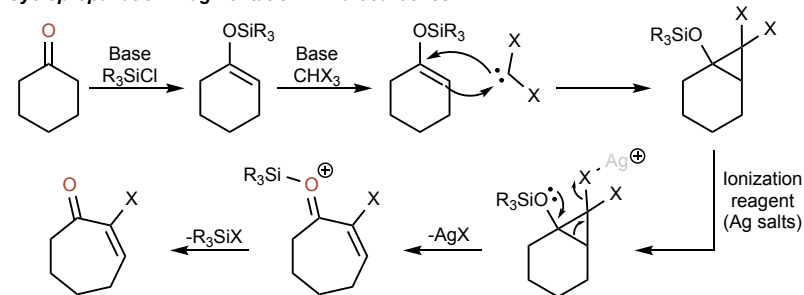
Classics in Ring Expansion: Cyclopropanation/Fragmentation

- A classic approach to a single carbon ring-expansion consists of the process of cyclopropanation followed by fragmentation to produce a (n + 1) carbocycle.

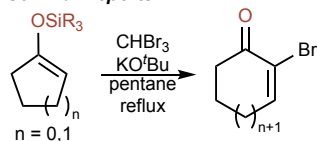
- The versatility of this method ranges due to the multiple reaction circumstances which may be designed due to the incorporation of nearby donor or acceptors.

- Fragmentation occurs in accordance with the appropriate orbital alignment of the cyclopropane (situational dependence). Multiple methods may be used such as ionic or radical pathways.

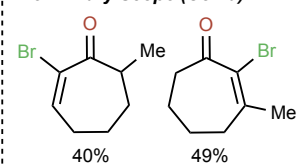
Cyclopropanation/Fragmentation: Dihalocarbenes



Seminal Reports:

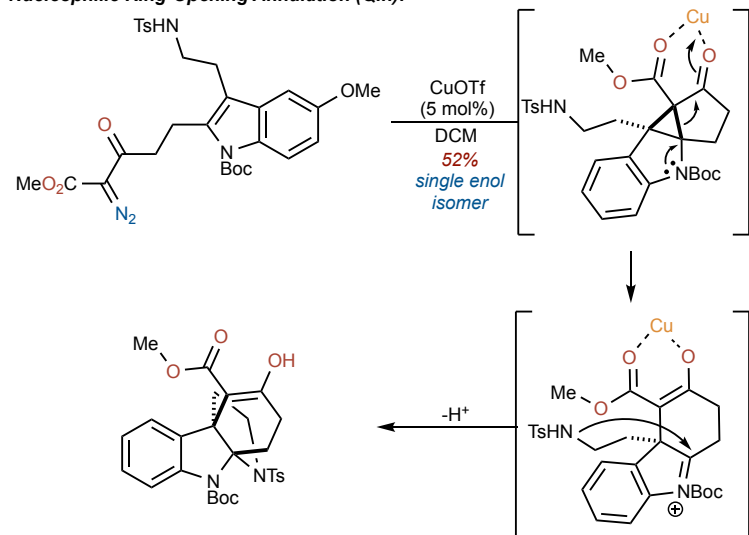


Preliminary Scope (Conia):



Note: This method is very general and does not have many reports specifically outlining it as a methodology. Hence, synthetic examples will be shown in the following.

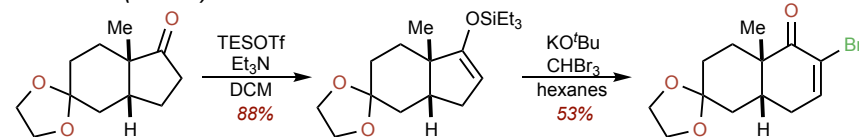
Nucleophilic Ring-Opening Annulation (Qin):



Qin, Y. *J. Am. Chem. Soc.* **2009**, 131, 6013. <https://doi.org/10.1021/ja901219v>

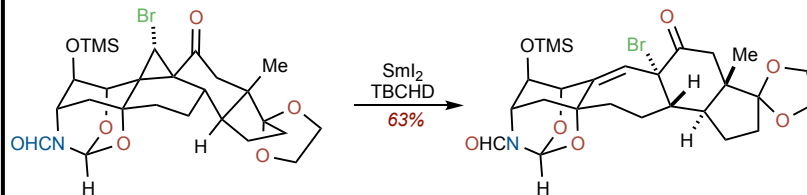
Synthetic Applications:

Batrachotoxin (Du Bois):



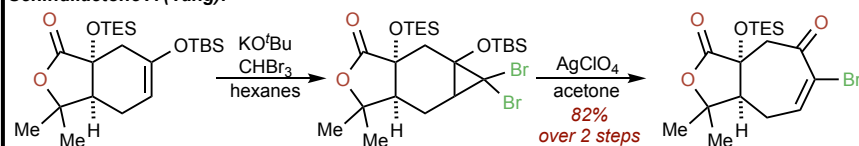
Du Bois, J. *Science*. **2016**, 354, 865. <https://doi.org/10.1126/science.aag2981>

Coristatin A (Baran):



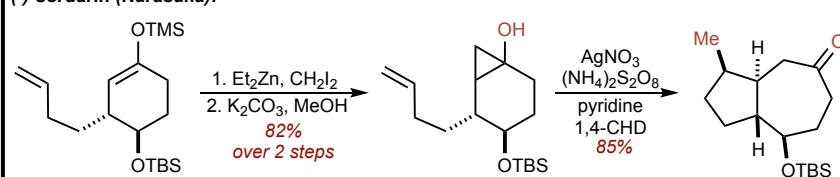
Baran, P.S. *J. Am. Chem. Soc.* **2008**, 130, 7241. <https://doi.org/10.1021/ja8023466>

Schindilactone A (Yang):



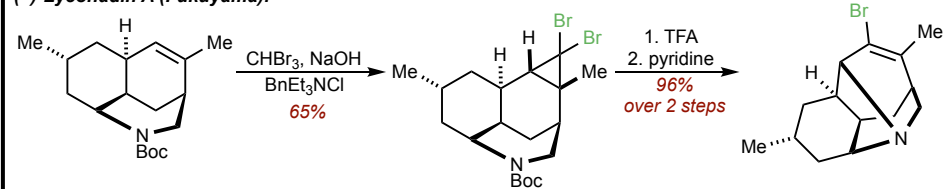
Yang, Z. *Angew. Chem. Int. Ed.* **2011**, 50, 7373. <https://doi.org/10.1002/anie.201103088>

(-)-sordarin (Narasaka):



Narasaka, K. *J. Am. Chem. Soc.* **2006**, 128, 6931. <https://doi.org/10.1021/ja060408h>

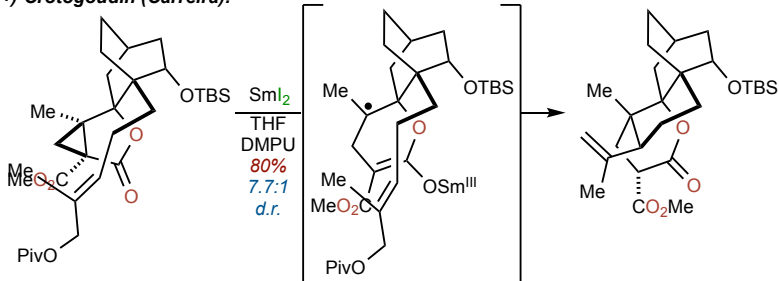
(+)-Lycanadin A (Fukuyama):



Fukuyama, T. *J. Am. Chem. Soc.* **2011**, 133, 418. <https://doi.org/10.1021/ja109516f>

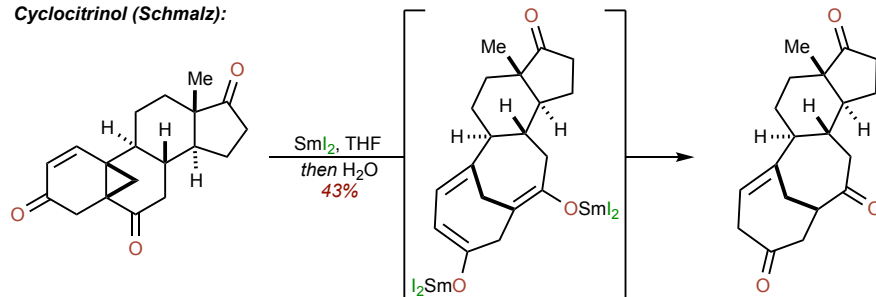
Synthetic Applications:

(+)-Crotogoudin (Carreira):



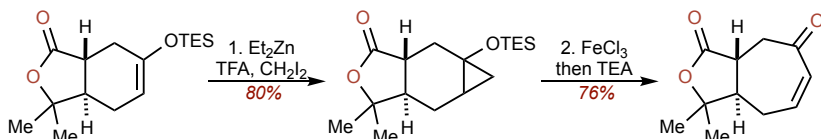
Carreira, E. *Angew. Chem. Int. Ed.* **2013**, *52*, 11168. <https://doi.org/10.1002/anie.201305822>

Cyclocitrinol (Schmalz):



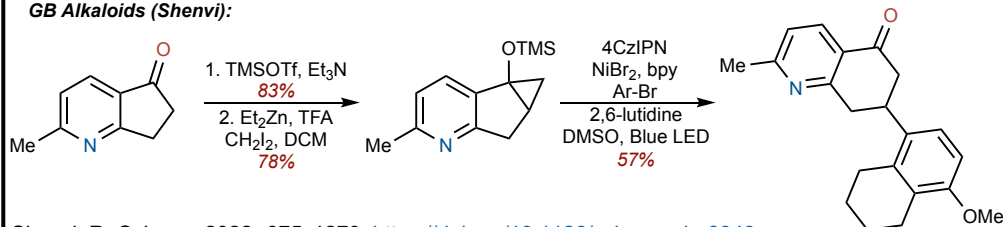
Schmalz, H-G. *Synlett.* **2007**, 1881. 10.1055/s-2007-984521

Pre-schisanartanin C (Yang, Z):



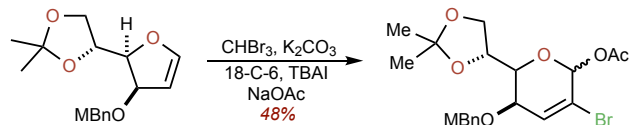
Yang, Z. *J. Am. Chem. Soc.* **2020**, *142*, 573. <https://doi.org/10.1021/jacs.9b11872>

GB Alkaloids (Shenvi):



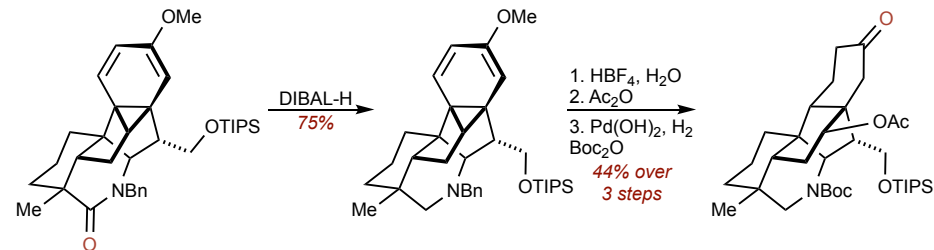
Shenvi, R. *Science.* **2022**, *375*, 1270. <https://doi.org/10.1126/science.abn8343>

(-)-TAN-2483B (Harvey):



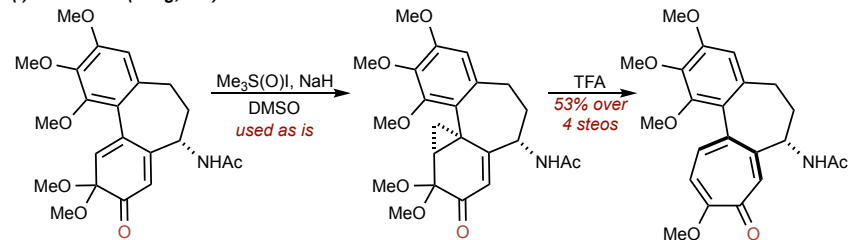
Harvey, J. *Org. Lett.* **2020**, *22*, 9427. <https://doi.org/10.1021/acs.orglett.0c03303>

(+)-Talassimidine (Zhang, Y):



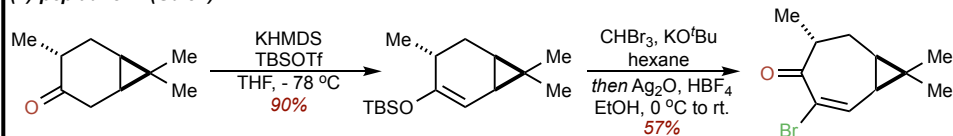
Zhang, Y. *J. Am. Chem. Soc.* **2021**, *143*, 7088. <https://doi.org/10.1021/jacs.1c01865>

(-)-Colchicine (Yang, Y-R):



Yang, Y. *Org. Lett.* **2021**, *23*, 2731. <https://doi.org/10.1021/acs.orglett.1c00638>

(+)-pepluanol A (Gaich):

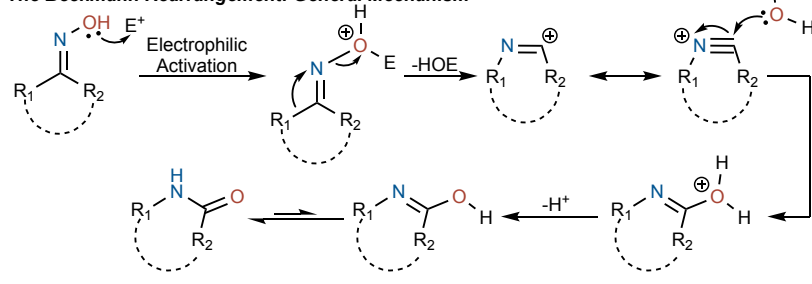


Gaich, T. *J. Am. Chem. Soc.* **2021**, *143*, 11934. <https://doi.org/10.1021/jacs.1c05257>

Classics in Ring Expansion: Beckmann Rearrangement

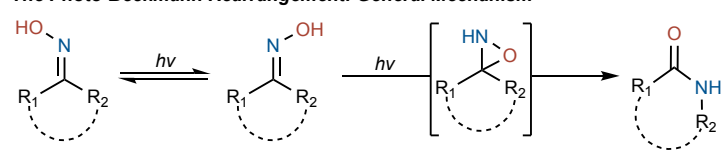
- The Beckmann rearrangement of cyclic ketones, discovered in 1886, is the ring-expansion of cyclic ketones using activated oximes or their activated ester counterparts.
 - Through several decades of mechanistic interrogation, the mechanism is believed to proceed through the ejection of the leaving group with migration of the substituent situated *anti* to the N-O bond. The maximization of antiperiplanar electron delocalization of the C-C bond σ orbital to the antibonding σ^* orbital of the N-O bond is responsible for the observed selectivity.

The Beckmann Rearrangement: General Mechanism



- An alternative to the Beckmann rearrangement is its photochemical counterpart, which was discovered by Mayo and delivers the opposite constitutional isomer in comparison to the traditional conditions.
 - The reaction proceeds under stereoelectronic control, which triggers migration of the group *anti* to the lone pair of the oxaziridine towards nitrogen.

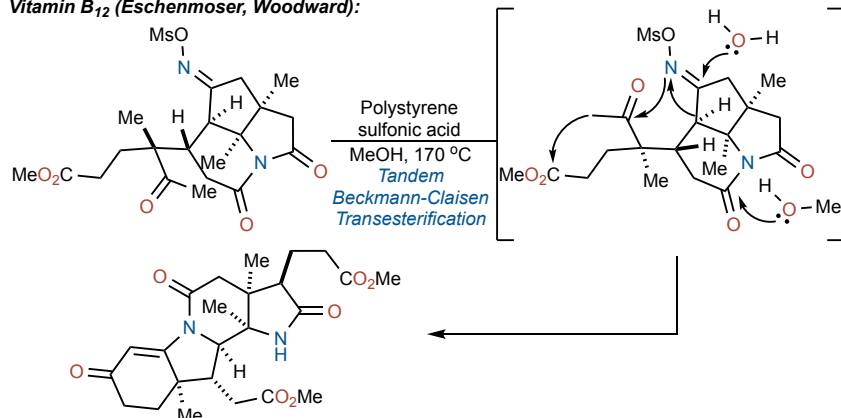
The Photo-Beckmann Rearrangement: General Mechanism



- In general, advances in the Beckmann rearrangement has been met by discovery of multiple activating reagents ranging from tosyl chloride, thionyl chloride, phosphorous chlorides/oxides, Bronsted acids, and Lewis acids.

Synthetic Applications:

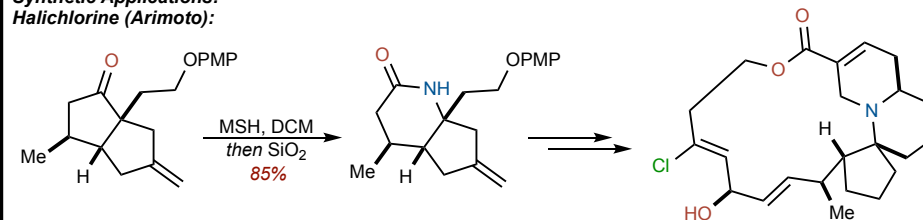
Vitamin B₁₂ (Eschenmoser, Woodward):



Eschenmoser, A.; Woodward, R. *Pure Appl. Chem.* **1973**, *33*, 145.
<http://dx.doi.org/10.1351/pac197333010145>

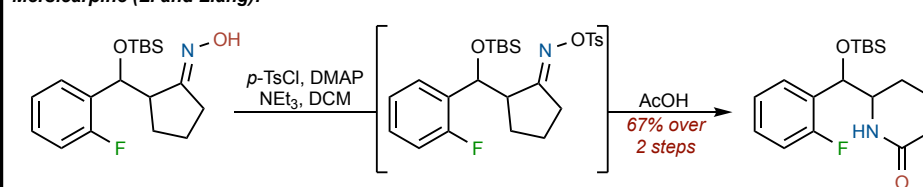
Synthetic Applications:

Halichlorine (Arimoto):



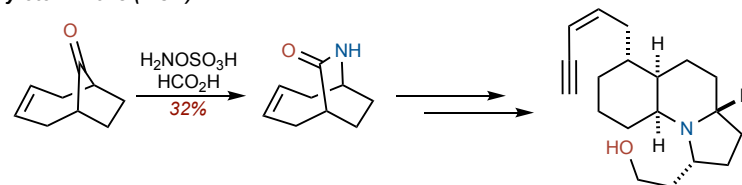
Arimoto, H. *Chem. Asian. J.* **2014**, *9*, 367. <https://doi.org/10.1002/asia.201301248>

Mersicarpine (Li and Liang):



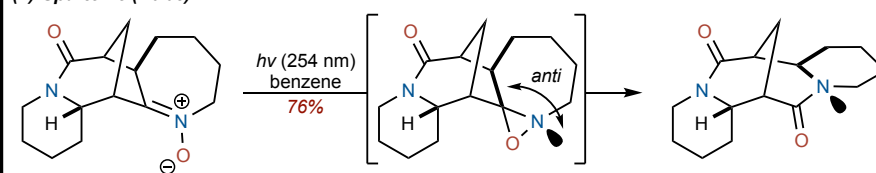
Liang, G. *Chem. Org. Lett.* **2014**, *16*, 1653. <https://doi.org/10.1021/ol500308e>

(-)-Gephyrotoxin 287C (Kishi):



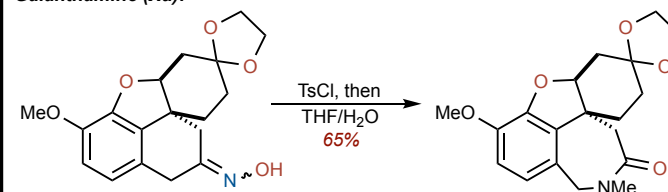
Kishi, Y. *J. Am. Chem. Soc.* **1980**, *102*, 7154. <https://doi.org/10.1021/ja00543a067>

(+)-Sparteine (Aubé):



Aubé, J. *Org. Lett.* **2002**, *4*, 2577. <https://doi.org/10.1021/ol026230y>

Galanthamine (Xu):



Xu, T. *Org. Lett.* **2020**, *22*, 1244. <https://doi.org/10.1021/acs.orglett.9b04337>

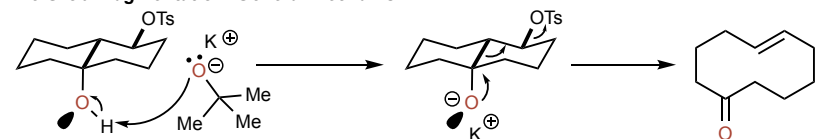
Classics in Ring Expansion: Grob Fragmentation

- One of the classical methods of generating medium to large rings is through the implementation of the Grob fragmentation.

- The Grob fragmentation is defined as the following: a heterolytic fragmentation in a molecule where a certain carbon-heteroatom (N, O, S, P, Si, B, or halogen) combination is cleaved under specific mechanistic principles.

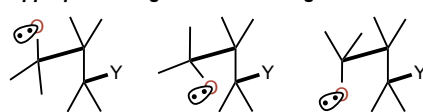
- Typically, the fragmentation substrates exhibit a 1,3-diheterofunctionalization, where one is a nucleophilic atom with a negative charge or lone pair, while the other is a leaving group.

The Grob Fragmentation: General Mechanism



Note: also undergoes fragmentation due to the all-*anti*-periplanar relation.

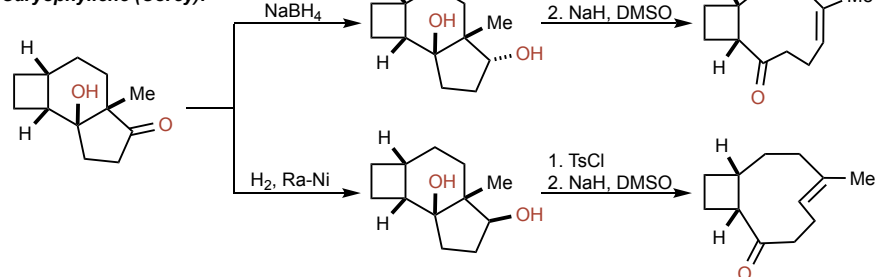
Appropriate Fragmentation Arrangements:



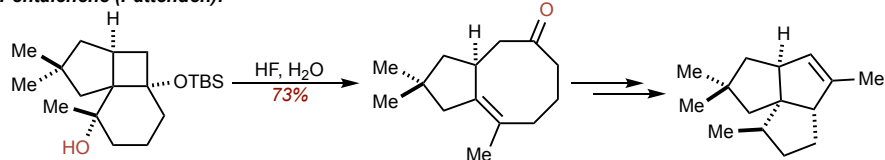
The generality of this method can be extended to many systems and is exemplified by the examples below:

Synthetic Applications:

Caryophyllene (Corey):

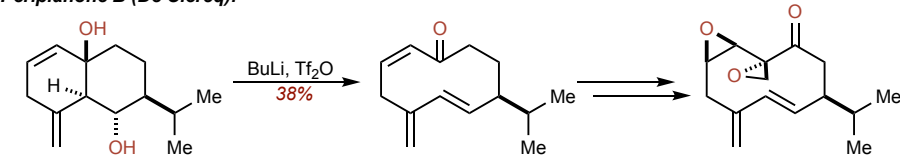


Pentalenene (Pattenden):



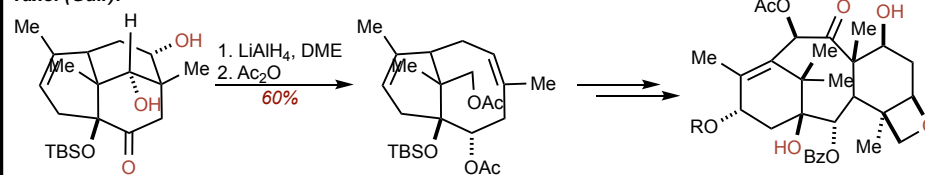
Pattenden, G. *Tetrahedron Letters*. **1984**, 25, 3021. [https://doi.org/10.1016/S0040-4039\(81\)018354-X](https://doi.org/10.1016/S0040-4039(81)018354-X)

Periplanone B (De Clercq):



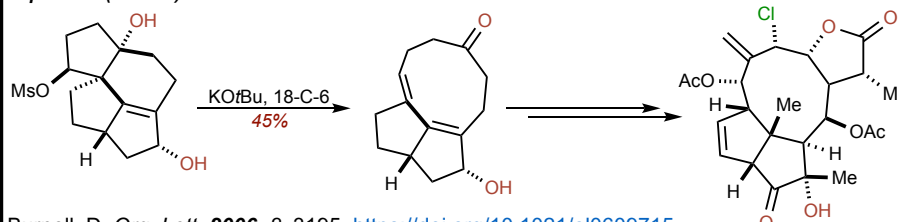
De Clercq, P. J. *Tetrahedron Letters*. **1984**, 29, 6501. [https://doi.org/10.1016/S0040-4039\(00\)82384-9](https://doi.org/10.1016/S0040-4039(00)82384-9)

Taxol (Guir):



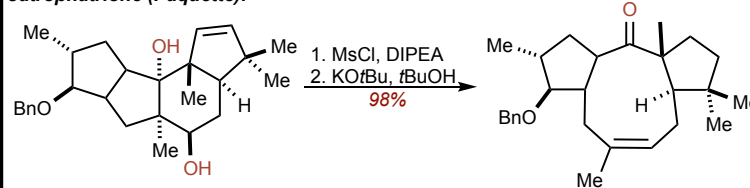
Guir, F. *Tetrahedron Letters*. **1997**, 38, 3223. [https://doi.org/10.1016/S0040-4039\(97\)00583-2](https://doi.org/10.1016/S0040-4039(97)00583-2)

Aquarane (Burnell):



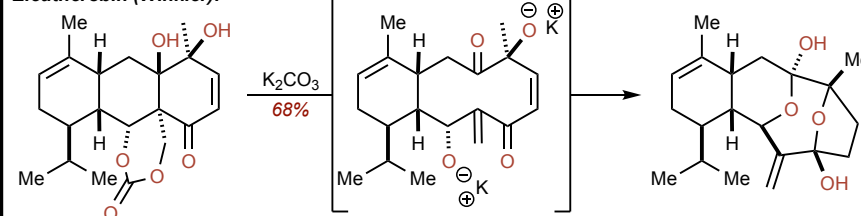
Burnell, D. *Org. Lett.* **2006**, 8, 3195. <https://doi.org/10.1021/ol0609715>

Jatrophatrione (Paquette):



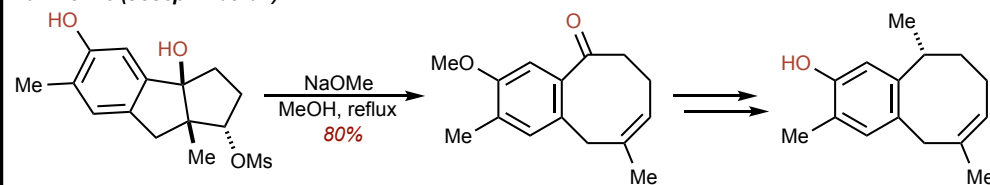
Paquette, L. *J. Am. Chem. Soc.* **2002**, 124, 6542. <https://doi.org/10.1021/ja020292z>

Eleutherobin (Winkler):



Winkler, J. *Org. Lett.* **2003**, 5, 1805. <https://doi.org/10.1021/ol0345226>

Parvifoline (Joseph-Nathan):



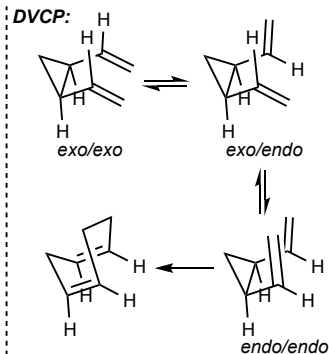
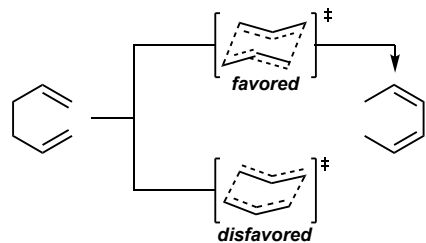
Joseph-Nathan, P. *Tetrahedron*. **1995**, 51, 9285. [https://doi.org/10.1016/0040-4020\(95\)00517-C](https://doi.org/10.1016/0040-4020(95)00517-C)

Classics in Ring Expansion: Sigmatropic Rearrangements

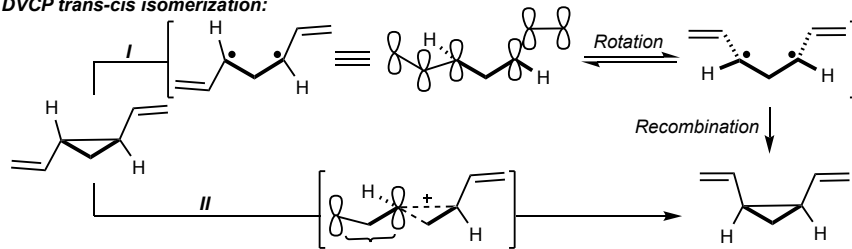
- An alternative pathway for ring expansion to medium and macrocyclic rings is through the sigmatropic rearrangements of cyclic systems.
- Namely, the Cope and divinylcyclopropane (DVCP) rearrangements are frequently employed.
- The traditional Cope rearrangement proceeds through either a chair or boat transition state, with the chair being favored by 11 kcal/mol.
- In contrast, the DVCP rearrangement proceeds through only through the boat transition state, with both vinyl substituents in the *endo*-orientation.

General Mechanism:

Cope:

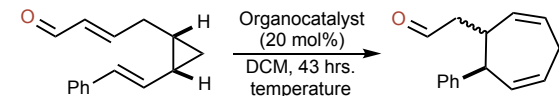


DVCP *trans-cis* isomerization:

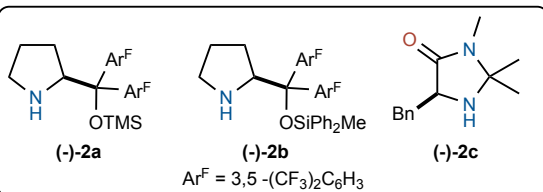


Methodological Developments:

Organocatalytic DVCP Rearrangement (Christmann):

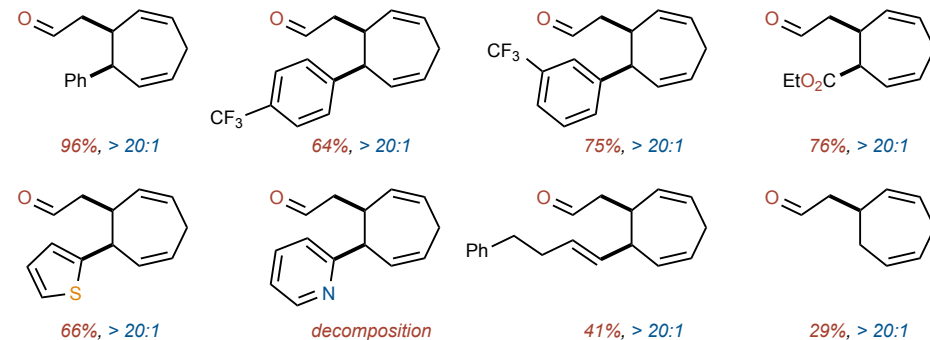


via:

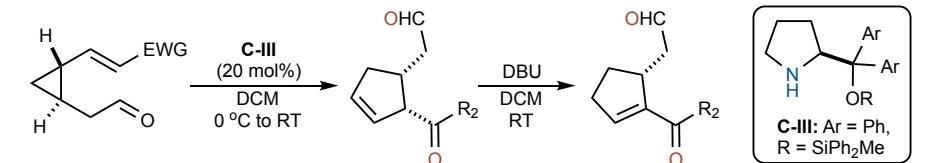


catalyst, temperature, yield, *cis:trans*
 pyrrolidine, 20 °C, 31%, 3:1
 piperidine, 20 °C, 38%, 3:1
 morpholine, 20 °C, 7%, 2:1
 (-)-2a, 20 °C, 96%, > 20:1
 (-)-2a, 40 °C, 72%, > 20:1
 (-)-2b, 20 °C, 60%, > 20:1
 (-)-2c, 20 °C, 2%, > 20:1
 with 10% AcOH and (-)-2a:
 83%, 4 hours, > 20:1

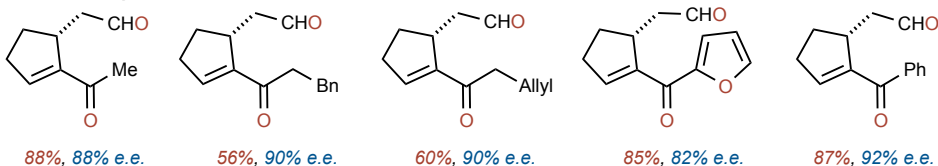
Organocatalytic DVCP Rearrangement Selected Scope (Christmann):



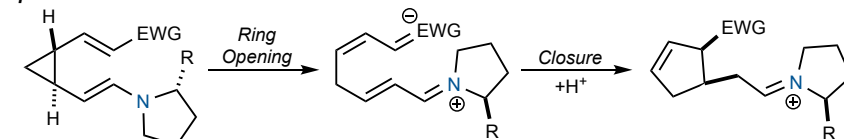
Organocatalytic Enantioselective Vinylcyclopropane-Cyclopentene (VCP-CP) Rearrangement (Vicario):



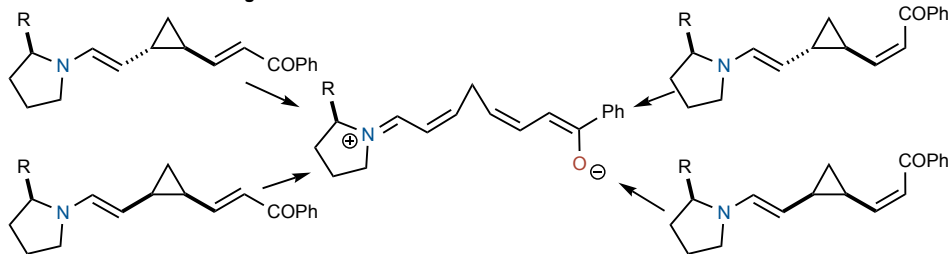
Selected Scope:



Simplified Mechanism:

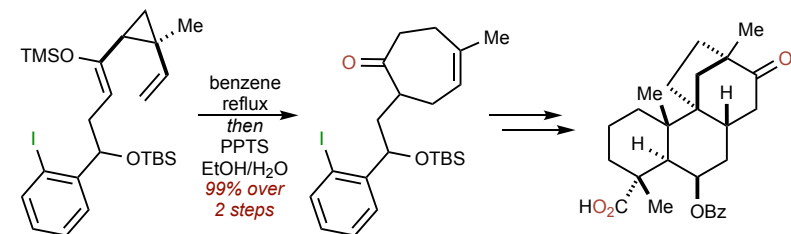


Further Mechanistic Findings:



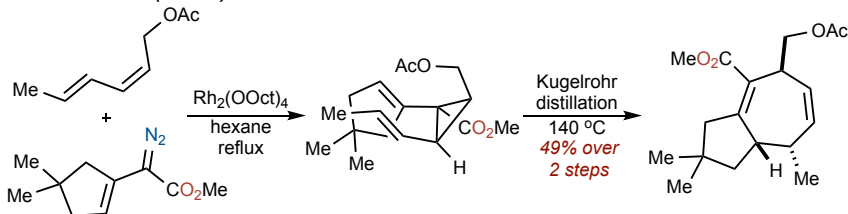
Synthetic Applications:

Scopadulcic Acid B (Overman):



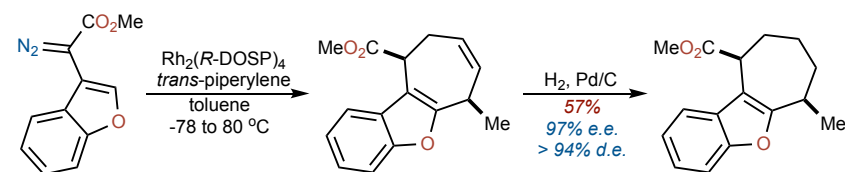
Overman, L. *J. Am. Chem. Soc.* **1993**, *115*, 2042. <https://doi.org/10.1021/ja00058a064>

Tremulenolide A (Davies):



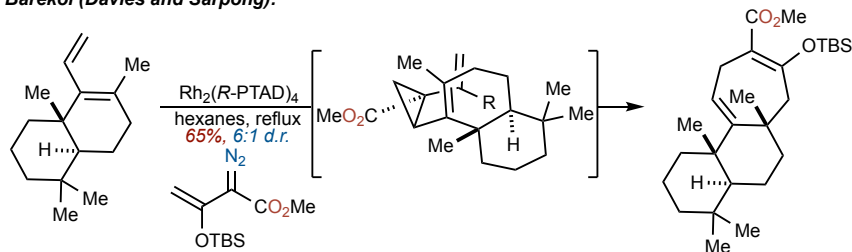
Davies, H. *J. Org. Chem.* **1998**, *63*, 657. <https://doi.org/10.1021/jo971577a>

Frondosin B (Davies):



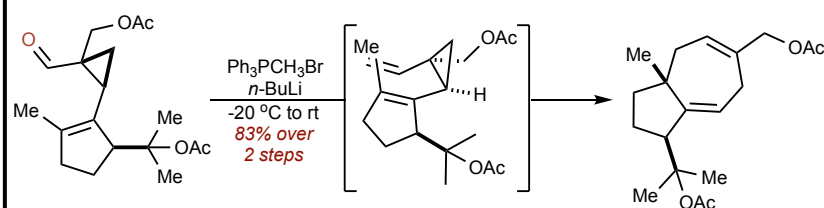
Davies, H. *Org. Lett.* **2008**, *10*, 573. <https://doi.org/10.1021/ol702844g>

Barekol (Davies and Sarpong):



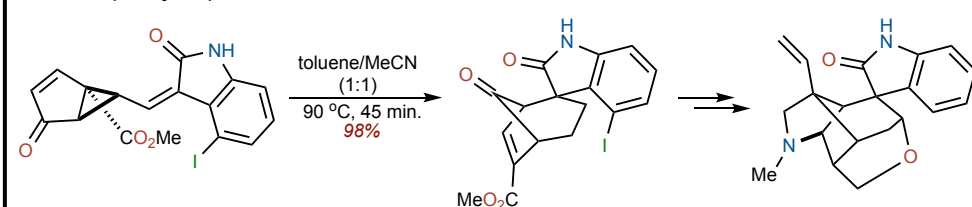
Davies, H. *J. Am. Chem. Soc.* **2010**, *132*, 12422. <https://doi.org/10.1021/ja103916t>

Schisanwilsonene A (Echavarren):



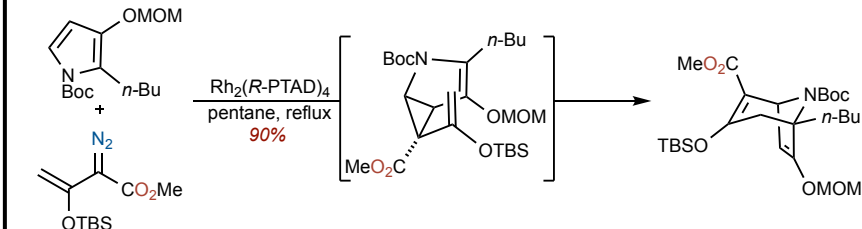
Echavarren, A. *Angew. Chem. Int. Ed.* **2013**, *52*, 6396. <https://doi.org/10.1002/anie.201302411>

Gelsemine (Fukuyama):



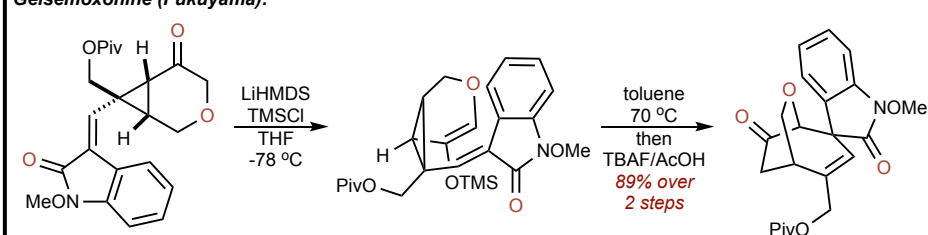
Fukuyama, T. *J. Am. Chem. Soc.* **1996**, *118*, 7426. <https://doi.org/10.1021/ja961701s>

Isostemofoline (Kende):



Kende, A. *J. Am. Chem. Soc.* **1999**, *121*, 7431. <https://doi.org/10.1021/ja991528a>

Gelsemoxonine (Fukuyama):



Fukuyama, T. *J. Am. Chem. Soc.* **2011**, *133*, 17634. <https://doi.org/10.1021/ja208617c>