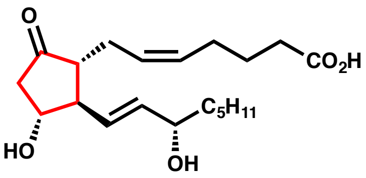
Shenvi Lab Group Meeting
June 19, 2017

Synthesis of 5-membered Carbocycles

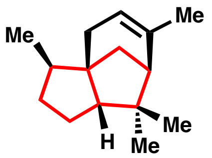
S. Crossley

This group meeting presents a survey of common strategies and tactics for the synthesis of 5-membered carbocycles in the context of natural products synthesis.

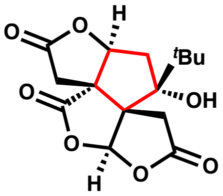
Selected examples of natural products containing 5-membered carbocycles.



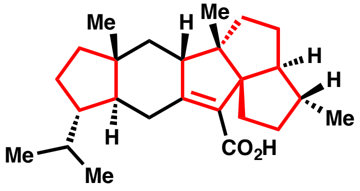
$PGF_{2\alpha}$



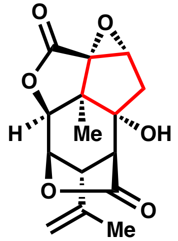
cedrene



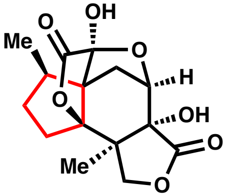
bilobalide



retingeranic acid



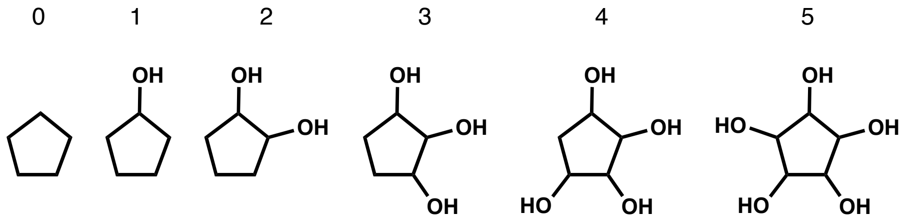
picrotoxinin



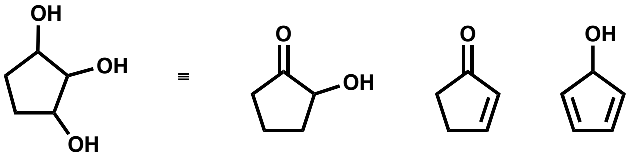
jiadifenolide

Structural Considerations.

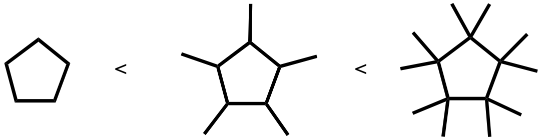
1) *Oxidation state* (0 to 10, but > 4 is rare). e.g.



Most of these have several redox equivalent structures/hydration levels. For example, when the degree of oxidation = 3:



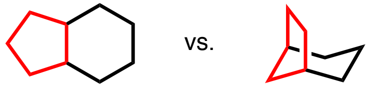
2) *Degree of Substitution*, e.g.



These structural considerations determine which *strategies* and *tactics* should be selected retrosynthetically.

3) *Nature of Substitution*, e.g.

a) Fused vs. Bridged ring systems



b) Identity of substitution

- EWGs, EDGs, Ar, Alkyl, Halogen, etc.

c) stereochemistry
Both the absolute and relative stereochemistry of the substitutents

4) Physical organic chemistry considerations

a) Cyclization to form 5-membered rings is the fastest of any size (in general, > 100x than 6-membered rings). For this reason, 5-membered rings are frequently formed in the construction of adjacent ring systems.

b) 5-membered rings are thermodynamically less stable than 6-membered rings. Be aware of this fact when both cyclization modes are viable and the reaction pathway is reversible.

c) Relay of stereochemical information about a 5-membered ring is often challenging, and far less predictable than in 6-membered rings.

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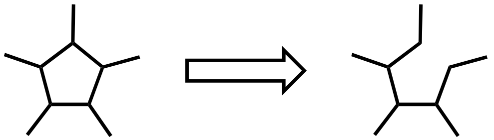
Disconnection Strategies and Common Tactics

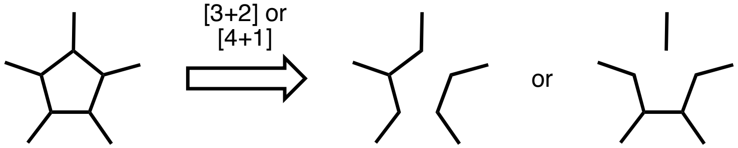
S. Crossley

Strategies

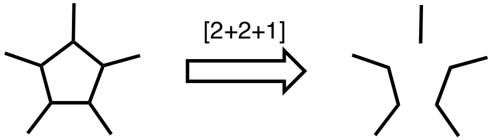
1) Make 1 bond (most common, by far)



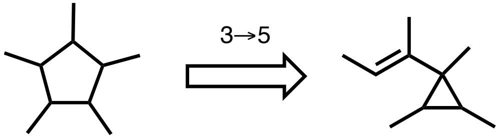
2) Make 2 bonds

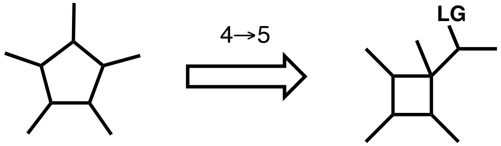


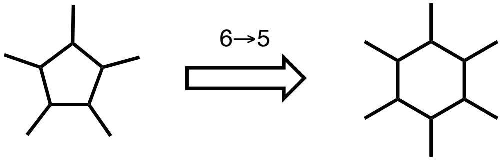
3) Make 3 bonds



4) Rearrangements (very common)







Tactics (not exhaustive)

Make 1 bond
- as tethers in the process of making other rings, especially cycloadditions reactions
- intramolecular S_N2/alkylation
- intramolecular Wittig
- classic carbonyl chemistry: aldol, Michael, Claisen, Dieckmann, Mannich, etc.
- Friedel-Crafts
- Nazarov
- Piancatelli
- vinylidine/carbenoid C-H insertions
- radical cyclizations
- cycloisomerizations
- π-philic metal-mediated/catalyzed cyclization (more recent development)
- ring closing metathesis
- Prins/Ene
- - many others...

Make 2 bonds
- stabilized dipole and photo [3+2]
- phosphine catalyzed [3+2]
- arene-alkene *meta*-photocycloadditon
- double alkylation (formal [4+1])
- radical cascades
- [5+2] cycloadditions

Make 3 bonds
- Pauson-Khand

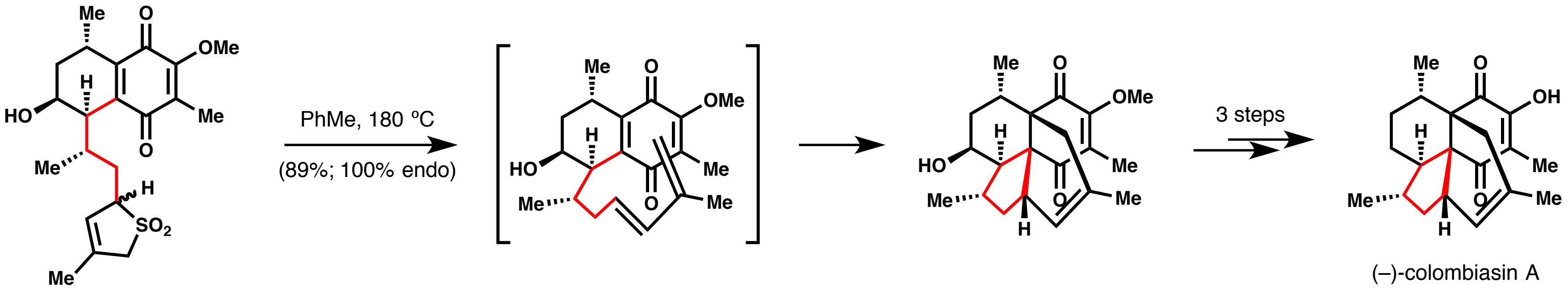
Rearrangements
- 3→5 (vinyl-cyclopropane rearrangement)
- 4→5 (Tiffeneau-Demjanov; pinacol, semi-pinacol, etc.)
- 6→5 (oxidative cleavage, aldol; Favorskii; α-santonin di-π-methane)

- α-ketol rearrangement

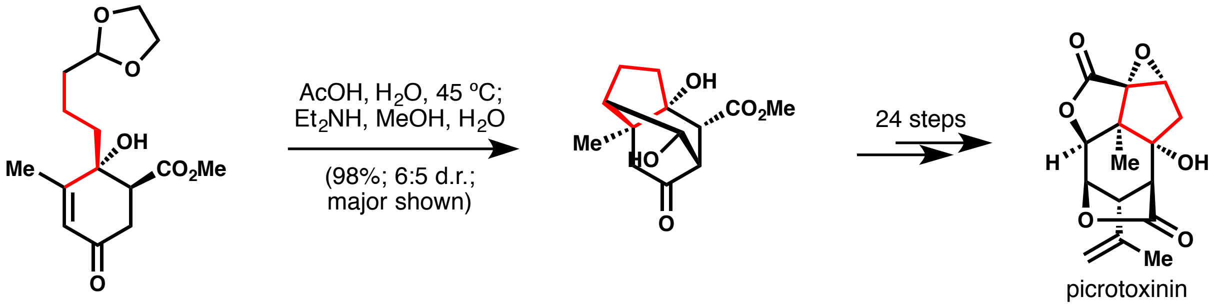
Make 1 bond

A) As a tether in the formation of other rings, especially cycloadditions

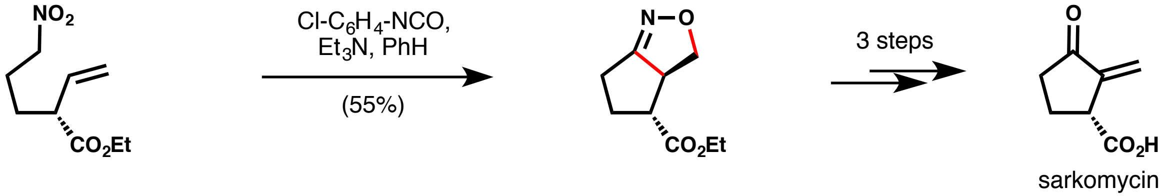
Since cyclization to form 5-membered rings is kinetically fastest of any cyclization (> 100x faster than 6-membered ring cyclization), 5-membered rings are frequently formed in the process of forming fused and bridged polycyclic systems. (eg. *JACS* **1984**, *106*(4), 1051). Cycloaddition reactions are particularly common in this regard.



Nicolaou and co. *AC* **2001**, *113*, 2543; *Chem. Eur. J.* **2001**, *7*, 5359.



Yamada and co. *JACS* **1984**, *106*, 4547. (*Tet. Lett.* **1973**, 4963.)



Kozikowski, A.P.; Stein, P.D. *JACS* **1982**, *104*(14), 4023.

Make 1 bond

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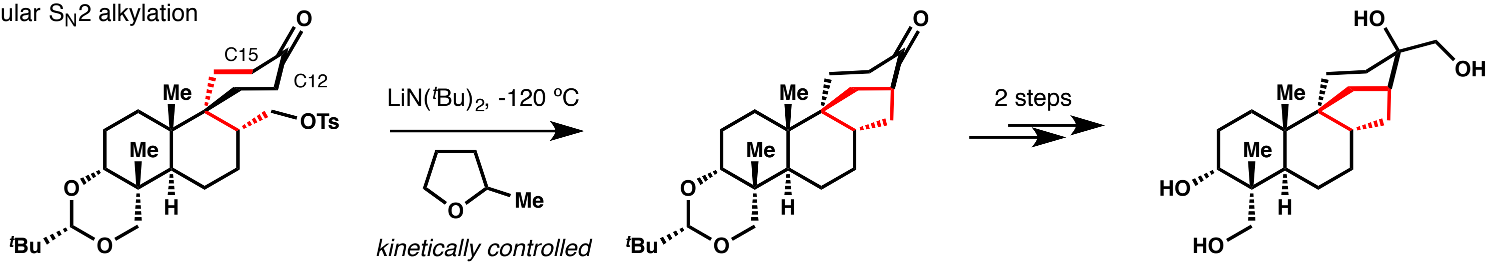
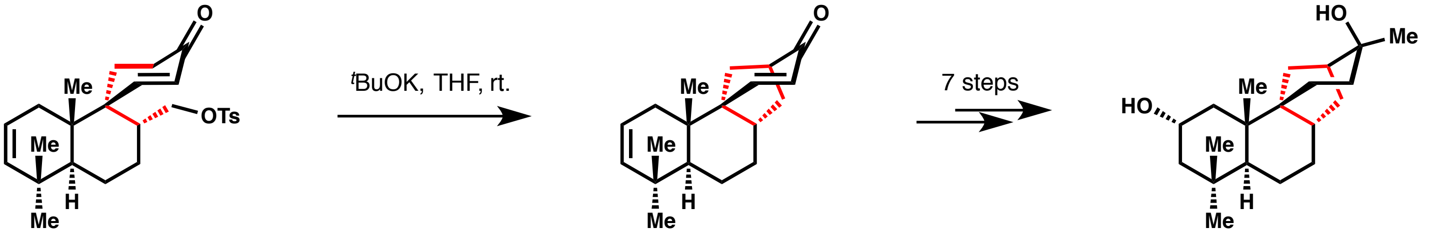
B) Intramolecular S_N2 alkylation



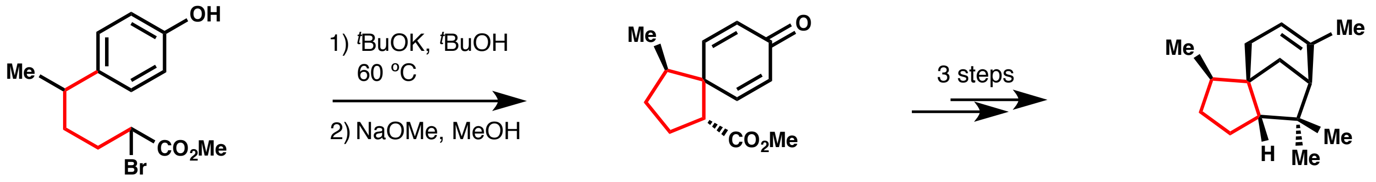
aphidicolin

Corey and co. *JACS* **1980**, *102*, 1742.



stemodin

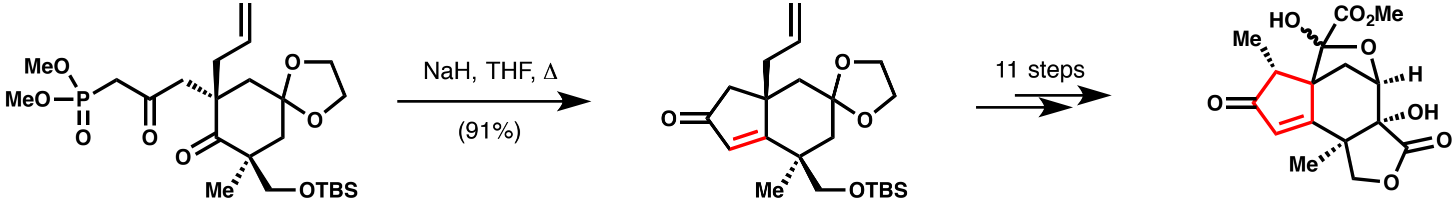
Corey and co. *JACS* **1980**, *102*, 7612.



cedrene

Corey and co. *JACS* **1969**, *91*, 1557; *JACS* **1955**, *77*, 1072; *JACS* **1961**, *83*, 3114; *Tetrahedron Lett.* **1973**, 3153.

B) Wittig, HWE, etc. type olefinations



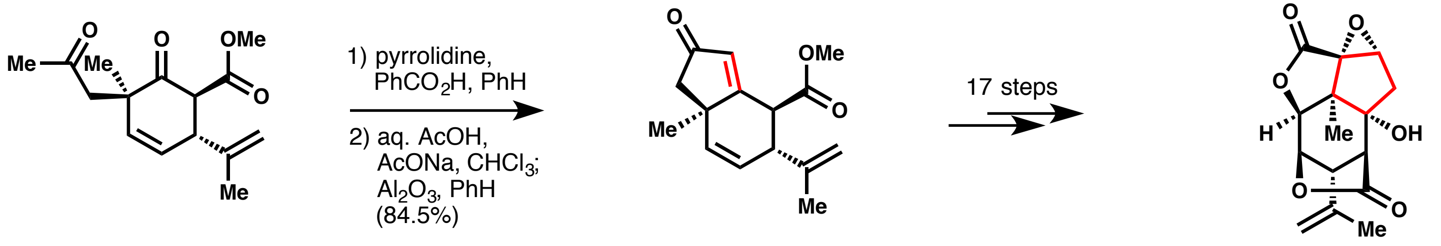
(–)-jiadifenin

Danishefsky and co. *JACS* **2006**, *128*, 1016.

Make 1 bond

C) Classic carbonyl chemistry

aldol condensation



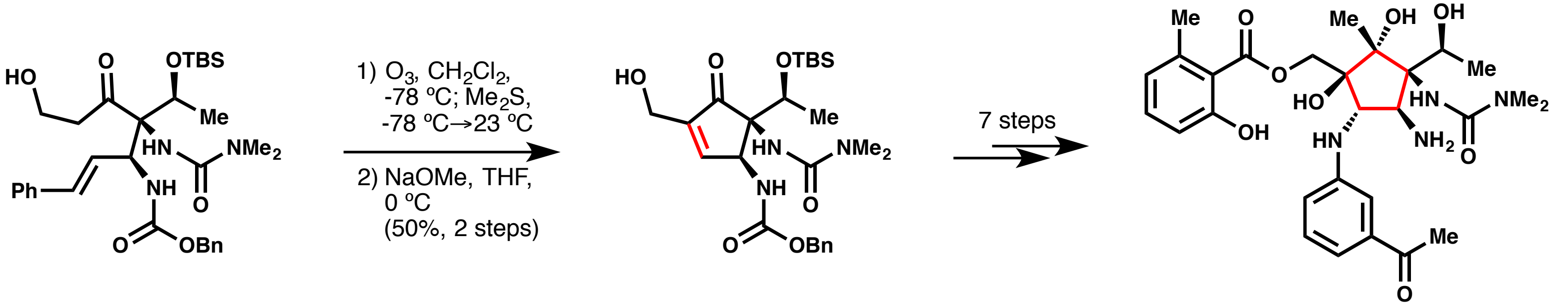
1) pyrrolidine, $PhCO_2H$, PhH

2) aq. AcOH, AcONa, $CHCl_3$; Al_2O_3, PhH (84.5%)

17 steps

picrotoxinin

Miyashita, Suzuki and Yoshikoshi. *JACS* **1989**, *111*, 3728. (*JOC* **1985**, *50*(18), 3377.)



1) O_3, CH_2Cl_2, -78 °C; Me_2S, -78 °C→23 °C

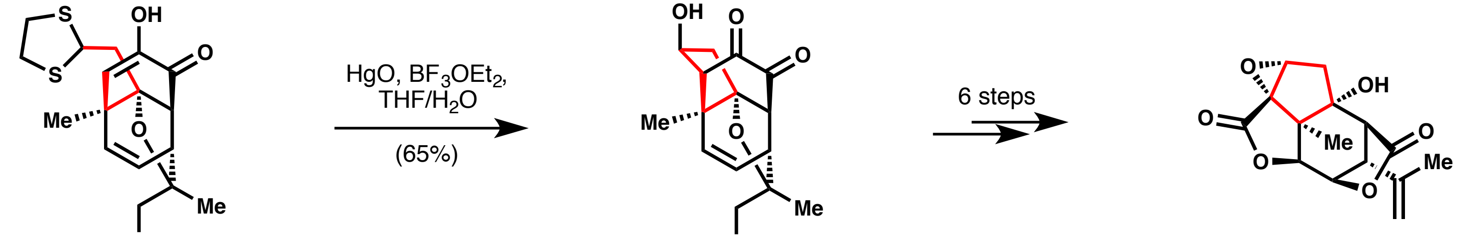
2) NaOMe, THF, 0 °C (50%, 2 steps)

7 steps

pactamycin

Johnson, J.S. and co. *Science* **2013**, *340*(6129), 180; *JACS* **2013**, *135*(*47*), 17990.

aldol addition



HgO, BF_3OEt_2, THF/H_2O

(65%)

6 steps

picrotoxinin

Corey and co. *JACS* **1979**, *101*, 5841; *Tet. Lett.* **1980**, *21*, 1823.

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Make 1 bond

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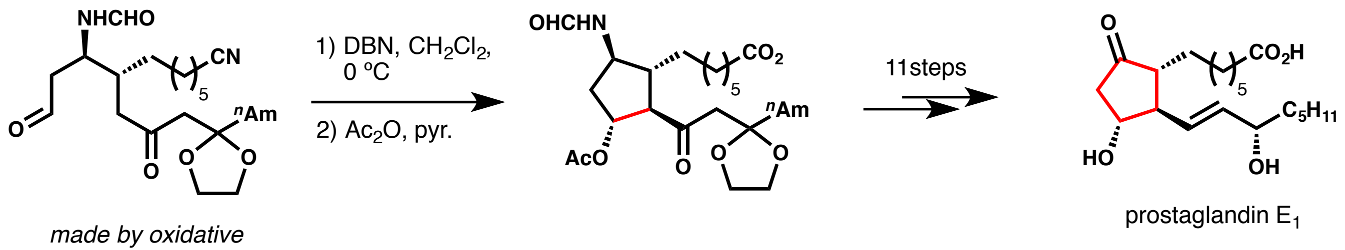
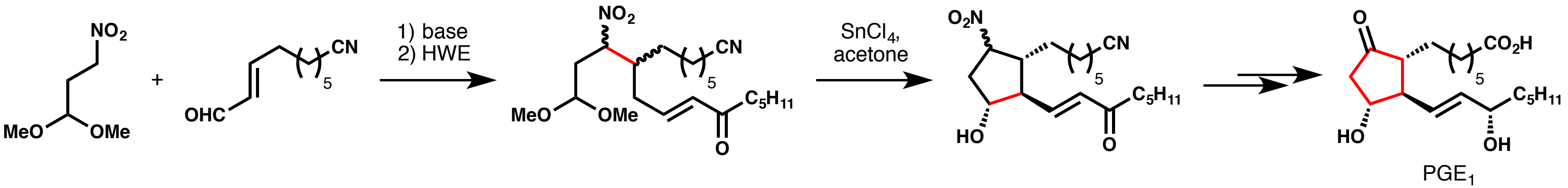
aldol addition



made by oxidative cleavage of a DA adduct

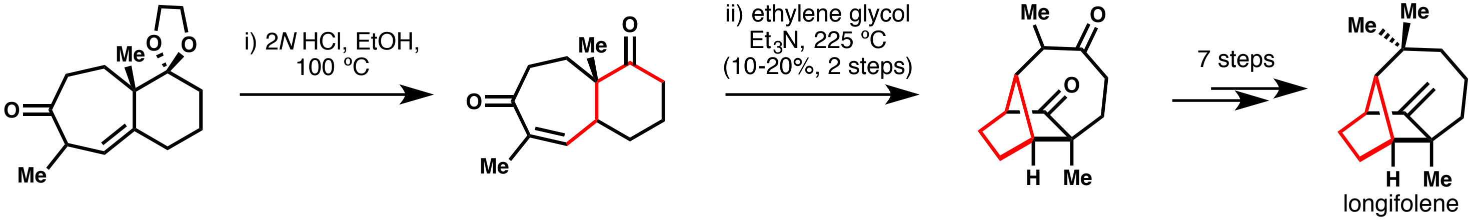
Corey and co. *JACS* **1968**, *90*, 3245.

Michael/aldol addition

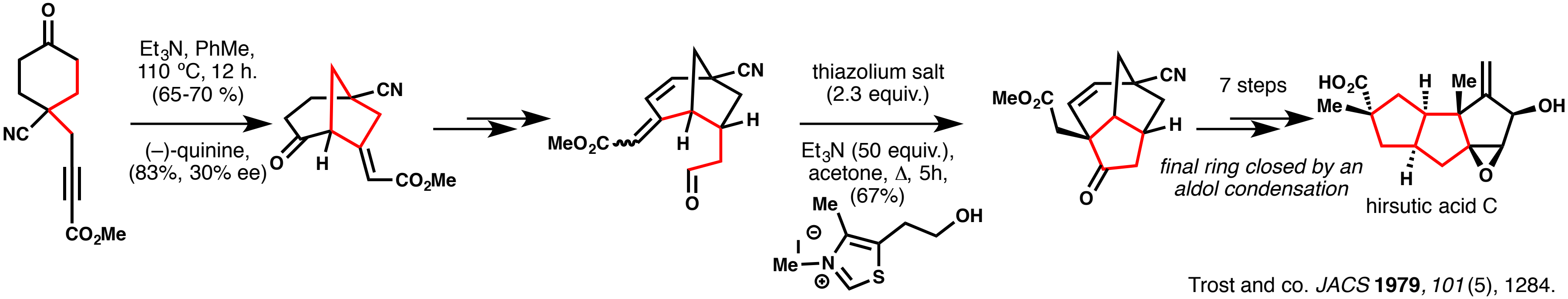


Corey and co. *JACS* **1968**, *90*, 3247; *JACS* **1969**, *91*, 535; *JACS* **1969**, *91*, 5675.

Michael addition



Corey and co. *JACS* **1961**, *83*, 1251; *JACS* **1964**, *86*, 478.

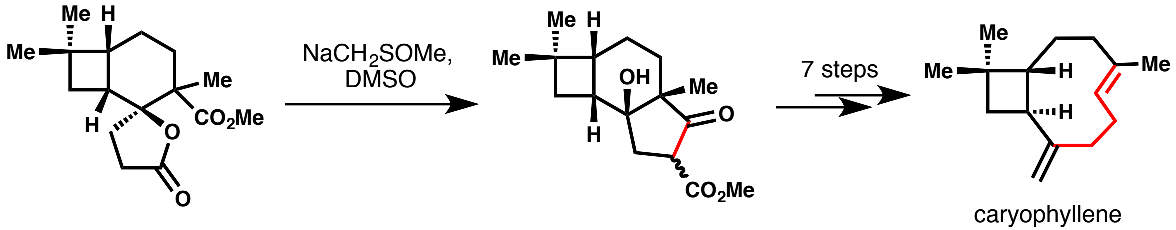


final ring closed by an aldol condensation

Trost and co. *JACS* **1979**, *101* (5), 1284.

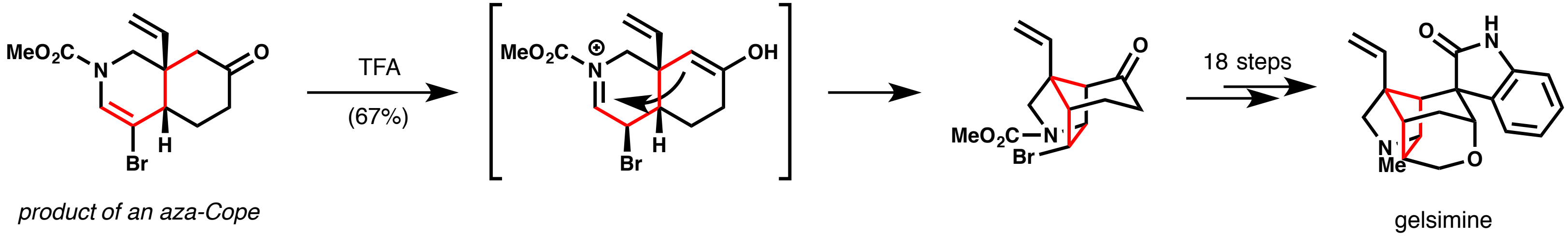
Make 1 bond

Dieckmann



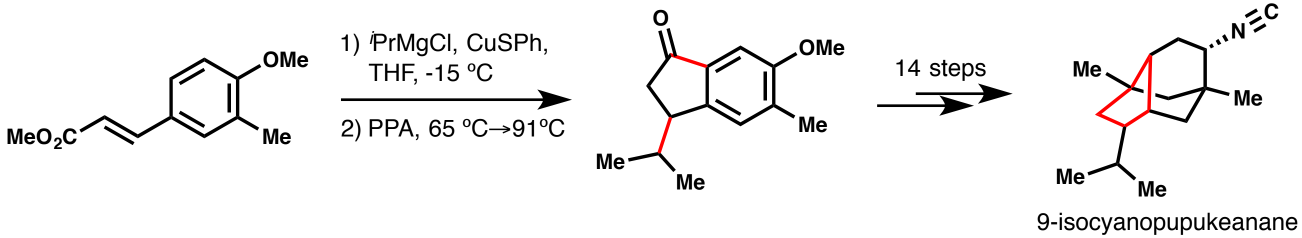
Corey and co. *JACS* **1963**, *85*, 362; *JACS* **1964**, *86*, 485.

Mannich



Overman, L. and co. *JACS* **2005**, *127*, 18046.

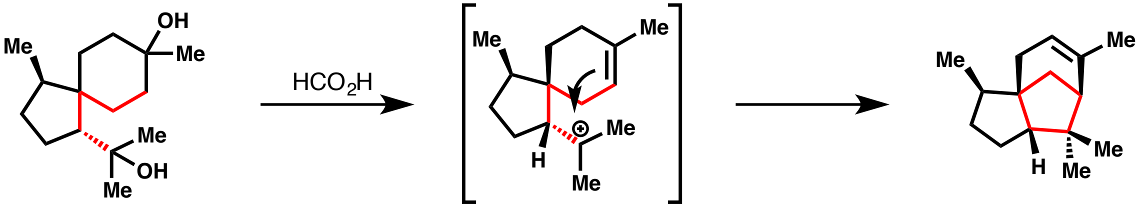
D) Friedel-Crafts



Corey and co. *JACS* **1979**, *101*, 1608; *Tet. Lett.* **1979**, 2745.

E) Cationic

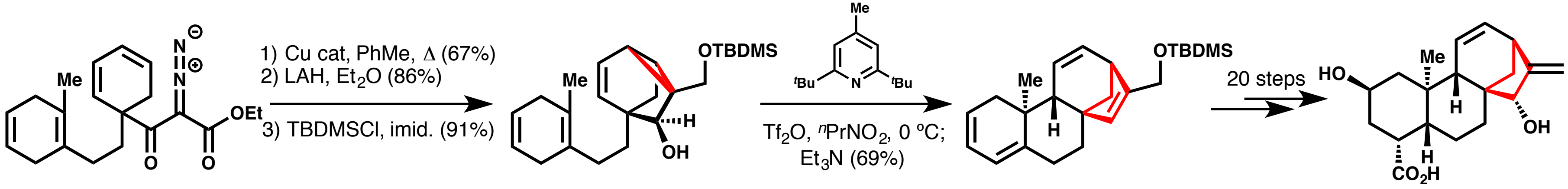
cation-olefin cyclization



cedrene

Corey and co. *JACS* **1969**, *91*, 1557; *JACS* **1955**, *77*, 1072; *JACS* **1961**, *83*, 3114

cyclopropanation, then cationic ring opening strategy

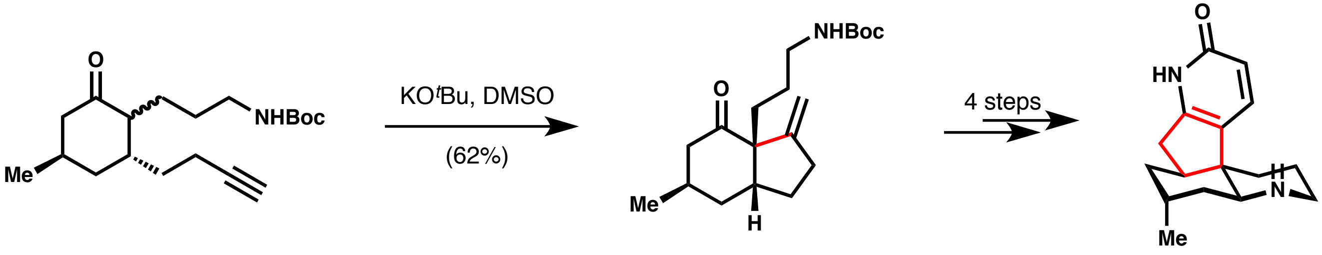


atractyligenin

Corey and co. *JACS* **1987**, *109*, 6187; For a similar strategy in cafestol and kahweol syntheses, see *JACS* **1987**, *109*, 4717; *Tetrahedron Lett.* **1987**, *28*, 5403.

E) Pericyclic

metallo-ene



lycoposerramine R

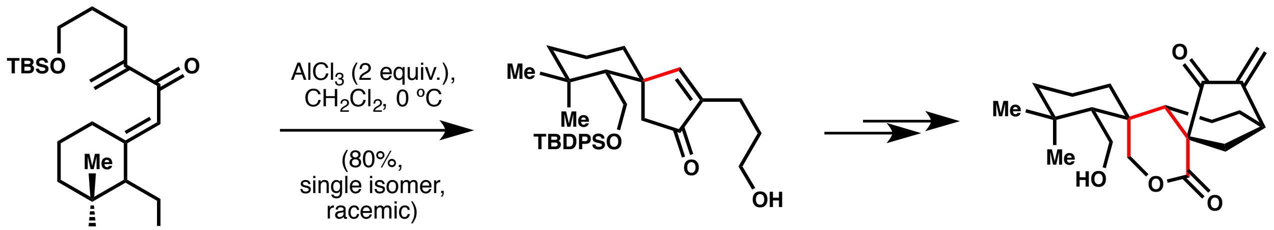
Trauner and co. *ACIE* **2017**, *56*, 893. See also: Pronin and co. *JACS* **2016**, *138*, 12316.

Bases with K$^+$ as a counterion were optimal for this reaction. Yields and reaction times with Na$^+$ counterions were lower, and Li$^+$ gave no product. (i.e. 71%:57%:0% yields on test substrate.)

Make 1 bond

Nazarov

(Use of AIBN/$HSnBu_3$ was used to form the other 5-membered ring)

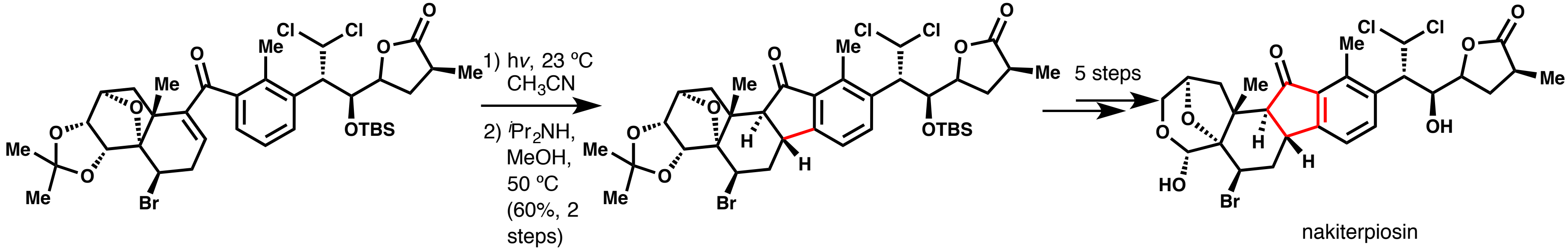


sculponeatin N

Thomson, R. and co. *ACIE* **2014***, 53*, 2988.

Photo-Nazarov

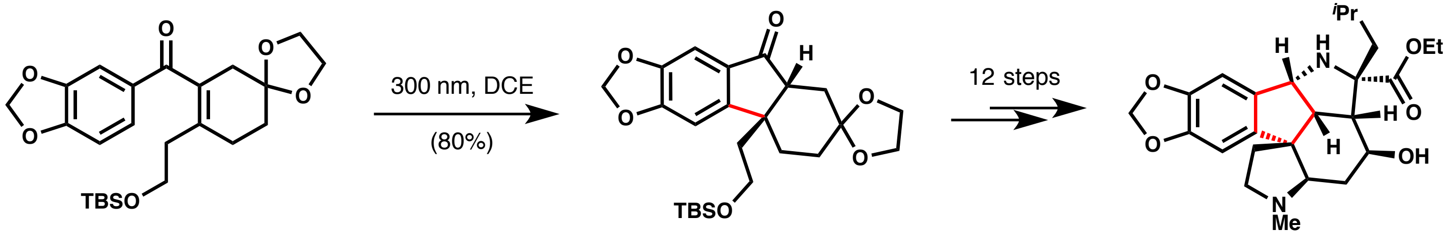
A carbonylative Stille coupling was used to join the left and right halves.



nakiterpiosin

Chen, C. and co. *JACS* **2009**, *131* , 1410.

The photo-Nazarov is commonly used when aromatic rings are involved, and can occur at neurtral or basic pH.



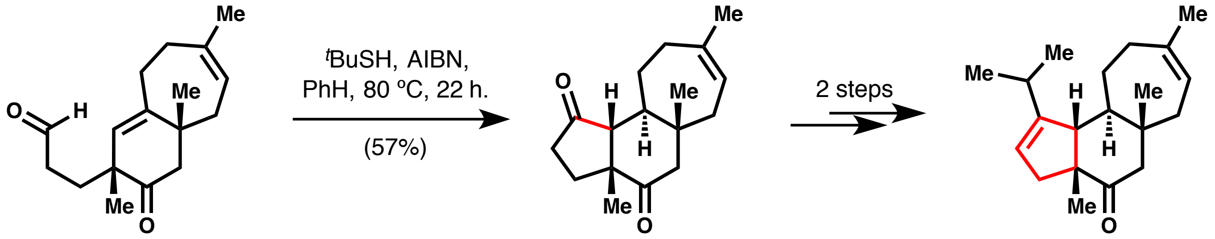
gracilamine

Gao, S. and co. *ACIE* **2014**, *53*, 9539.

Make 1 bond

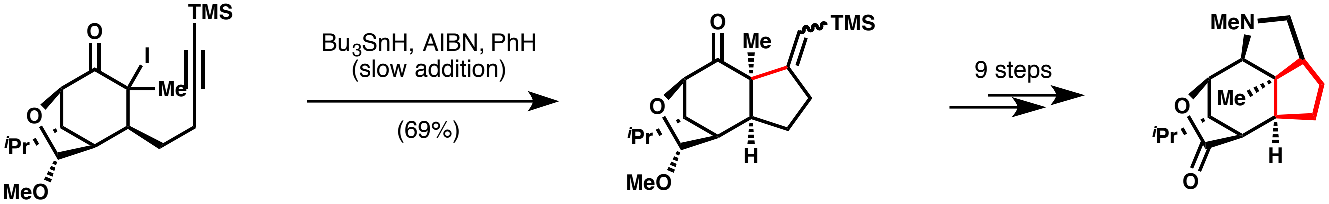
F) Radical Methods

Tin radical examples



cyanthiwigin F

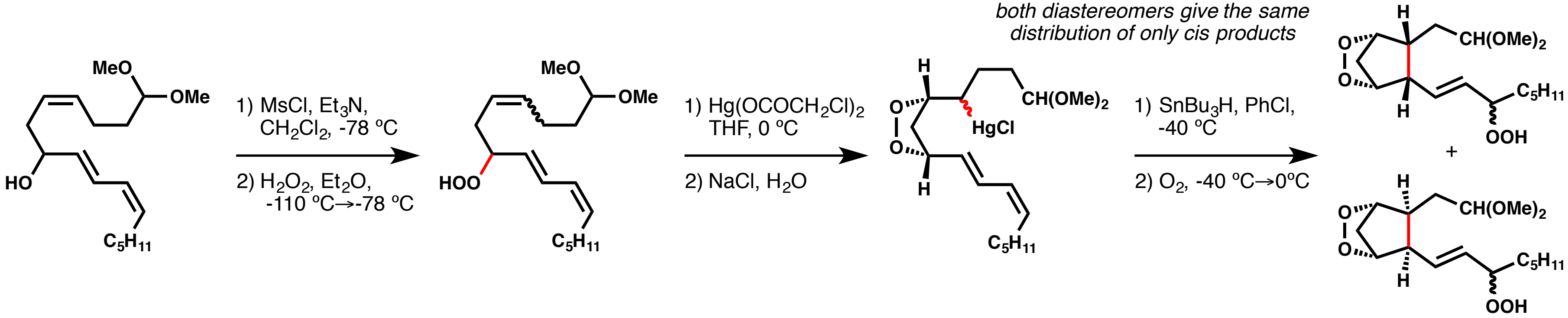
Stolz, B.M. and co. *Nature* **2008**, *453*, 1228.



(–)-dendrobine

Sha, C.-S. and co. *JACS* **1997**, *119* (18), 4130.

both diastereomers give the same distribution of only cis products

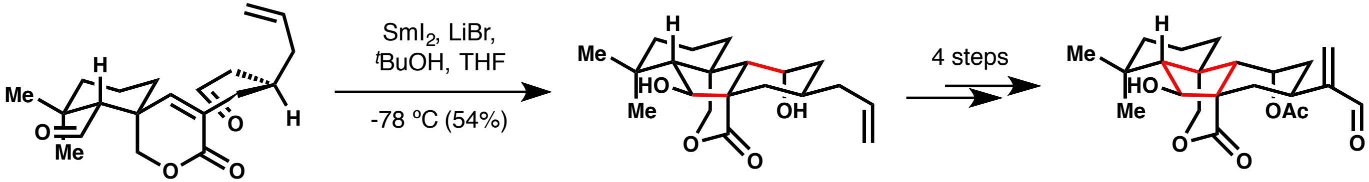


elaborated to various prostaglandins

Corey and co. *JACS* **1984**, *106*, 6425; *Tetrahedron Lett.* **1970**, 311; *Tetrahedron Lett.* **1984**, *25*, 5013; *Tetrahedron Lett.* **1982**, *23*, 719.

Make 1 bond

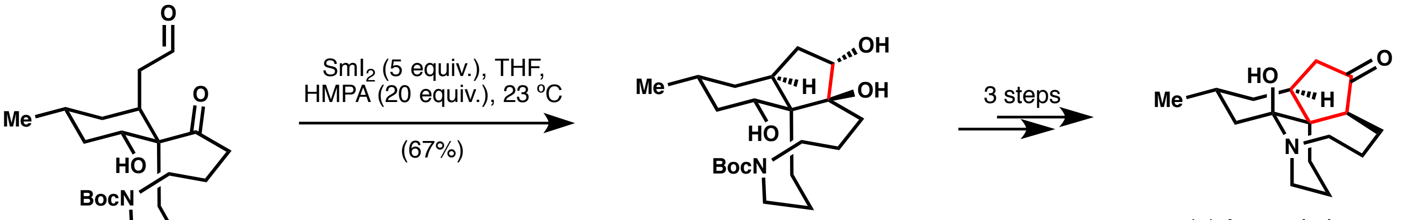
SmI$_2$ cyclization



(–)-macocrystal Z

Reisman and co. *JACS* **2011**, *133*, 14964.

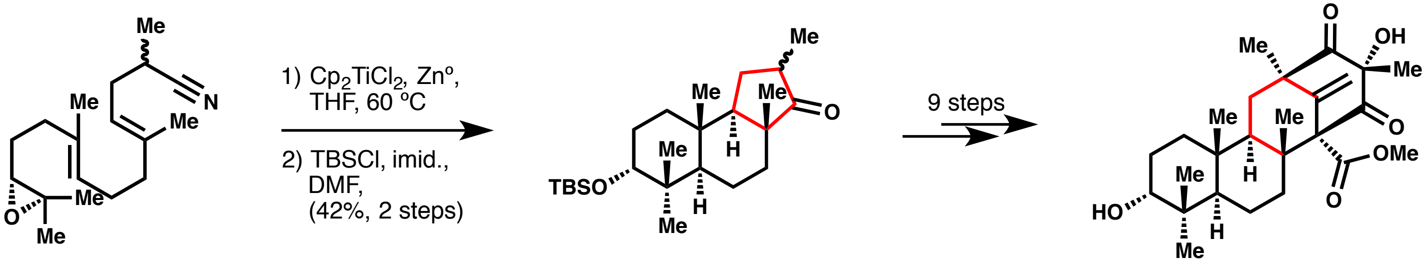
SmI$_2$ mediated pinacol coupling. Reduction of the aldehyde to the hydroxyl followed by ketalization is a competitive pathway.



(+)-fawcettimine

Lei, X. and co. *ACIE* **2012**, *51*, 491.

Ti(III) initiated

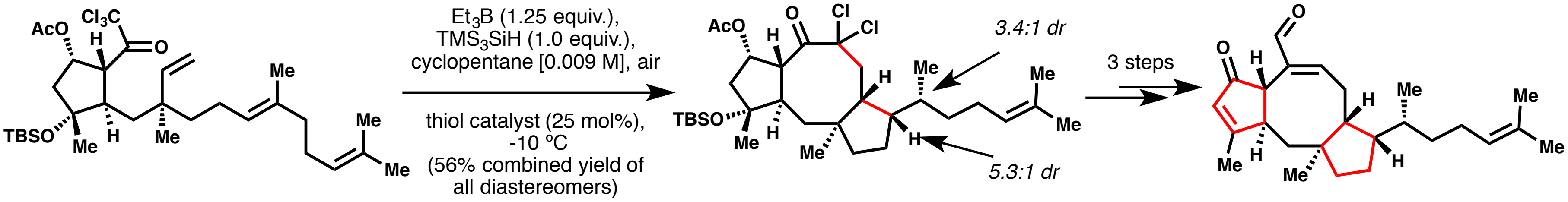


berkeleyone A

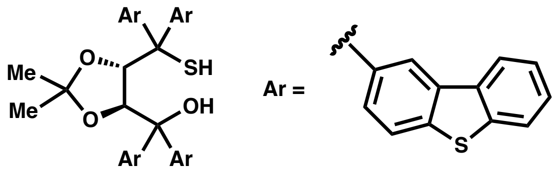
Fernandez-Mateos *et al. Synlett*, **2007**, *2007*, 2718.; Maimone and co. *JACS* **2016**, *138*, 14868.

Make 1 bond

polarity-reversal + asymmetric catalysis



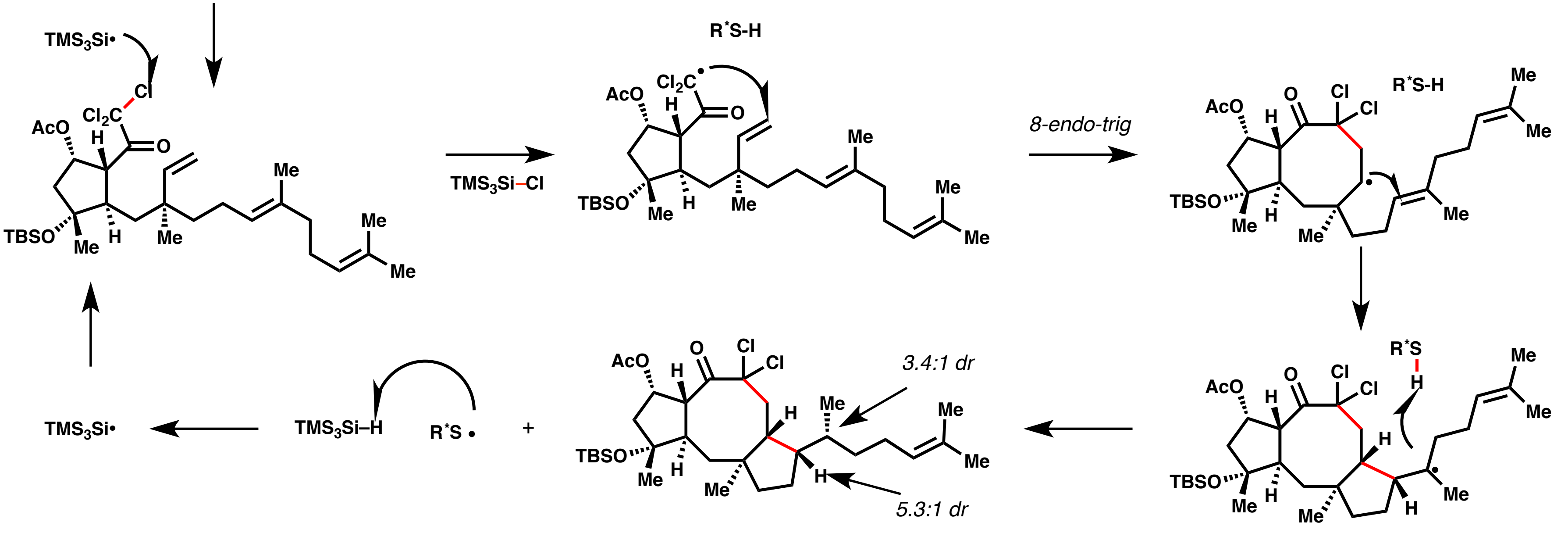
(–)-6-*epi*-ophiobolin N



Plausible mechanism based on literature precedence:

Maimone, T. and co. *Science* **2016**, *138*, 14868

$Et_3B + O_2 \rightarrow Et\bullet + Et_2BOO\bullet \rightarrow$ radical initiation
$Et_2BOO\bullet + TMS_3Si\text{-}H \rightarrow Et_2BOOH + TMS_3Si\bullet$

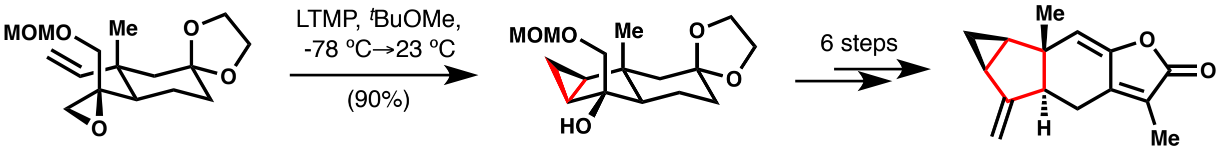


chirality in the final step is enabled by a terminating H• abstraction from the chiral thiol by the tertiary carbon radical

polarity-reversal conditions
Roberts, B.P. and co. *Chem. Soc. Rev.* **1999**, *28*, 25.; *J. Chem. Soc., Perkin Trans. 1* **1991**, 103.

G) Carbene/Carbenoid

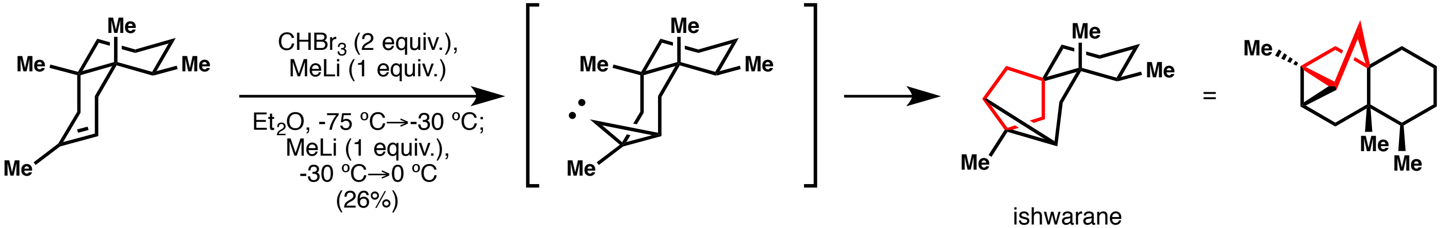
Hodgson cyclopropanation.



chloranthalactone A

Liu, B. and co. *Org. Lett.* **2011**, *13*(19), 5406.

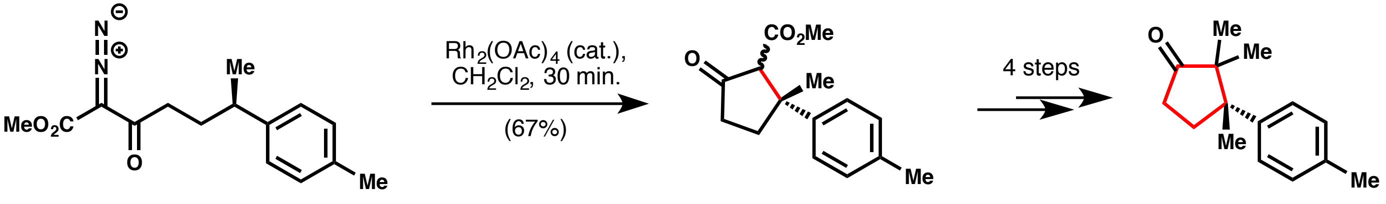
Carbene: C-H insertion



ishwarane

Cory, R.; McLaren, F.R. *J. Chem. Soc., Chem. Comm.* **1977**, 587.

Benzylic C-H insertion of a Rh-carbenoid. An example of enantioselective quaternary carbon formation.

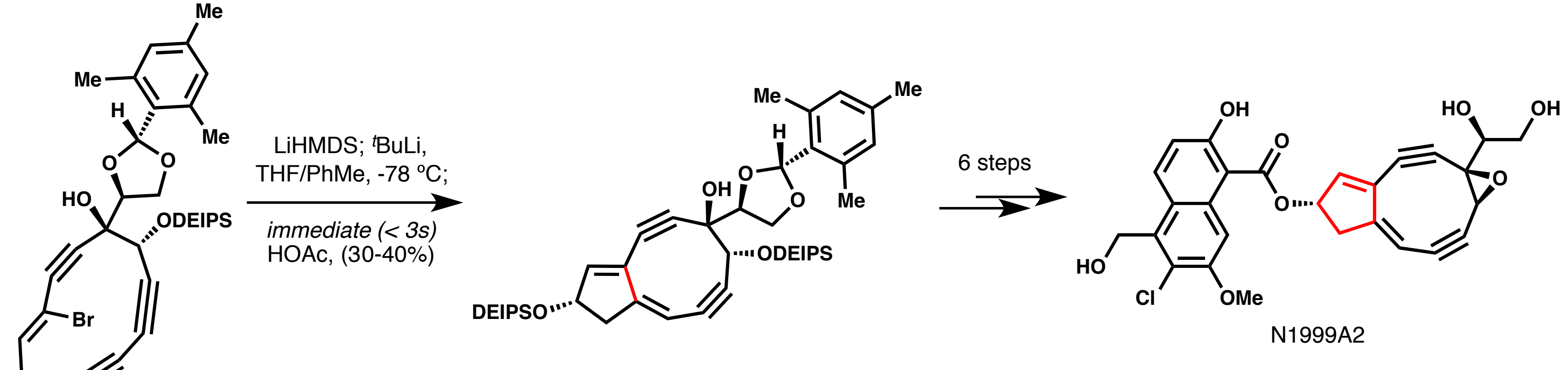


α-cuparenone

Taber, D.F. and co. *JACS* **1985**, *107*(1), 196.

Make 1 bond

Formation of 9-membered enediyne macrocyclic natural products. *The high strain of a 9-membered enediyne macrocycle necessitated intial formation of a 12-membered macrocycle (by an Eglinton Cu-mediated alkyne-alkyne coupling), followed by 5-membered ring closure to access the challenging 9-5 fused ring system.*

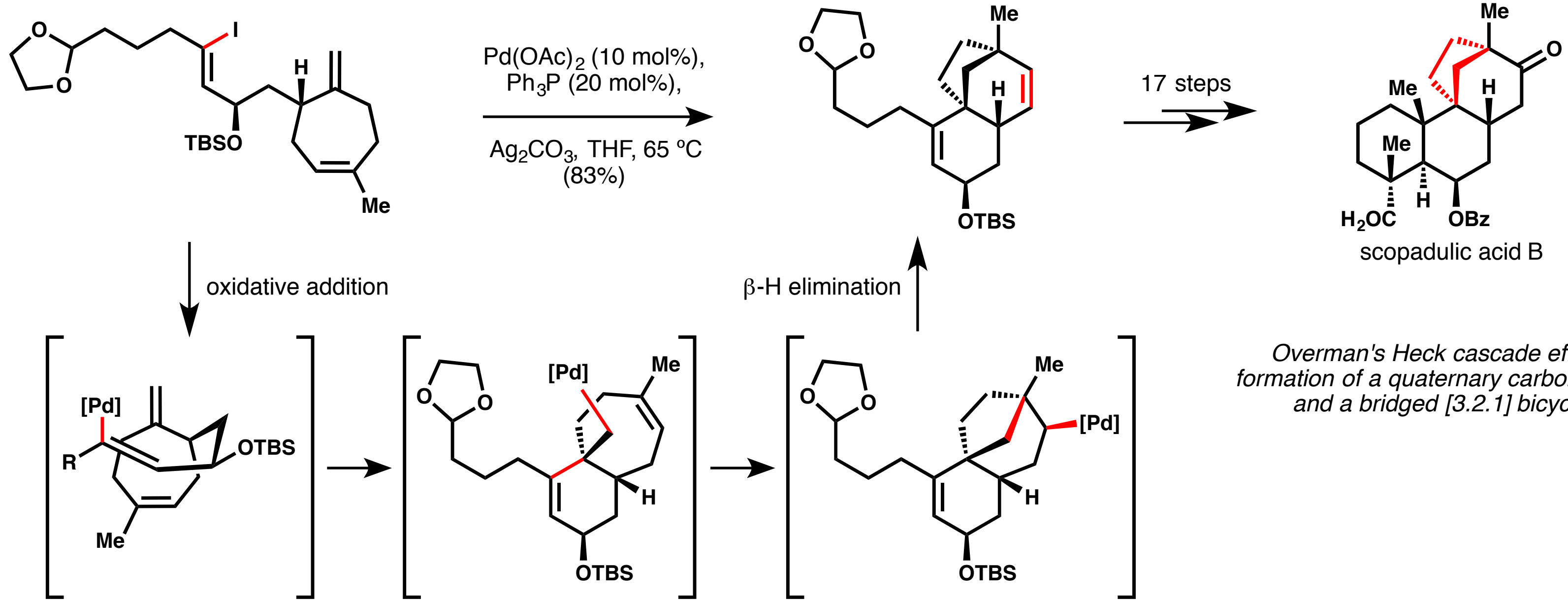


N1999A2

Myers and co. *JACS* **2006**, *128* (46), 14825; *ACIE* **2000**, *39*, 2932, *ACIE* **2002**, *41*, 1062.

H) Metal catalyzed/mediated anulation methods. *The power of metal mediated/catalyzed cyclizations may be attributed to their capacity to form multible ring systems in a cascade sequence, forge highly substituted stereocenters, effect enantioselective transformations through catalyst control, and exhibit good chemoselectivity.*

Heck annulation



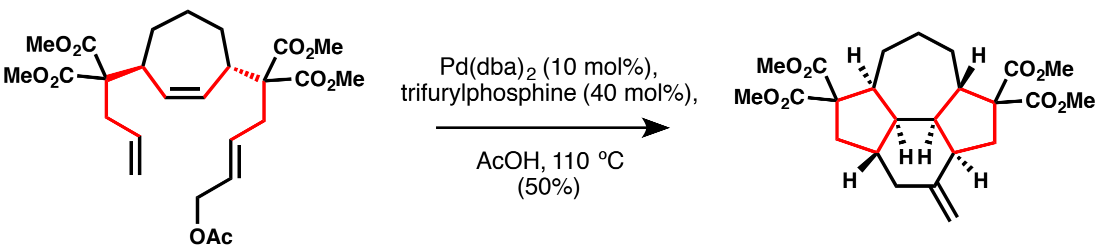
scopadulic acid B

Overman's Heck cascade effects formation of a quaternary carbon center and a bridged [3.2.1] bicycle.

Overman, L.E. and co. *JACS* **1993**, *115*, 2042; *JOC* **1993**, *58*, 5304.

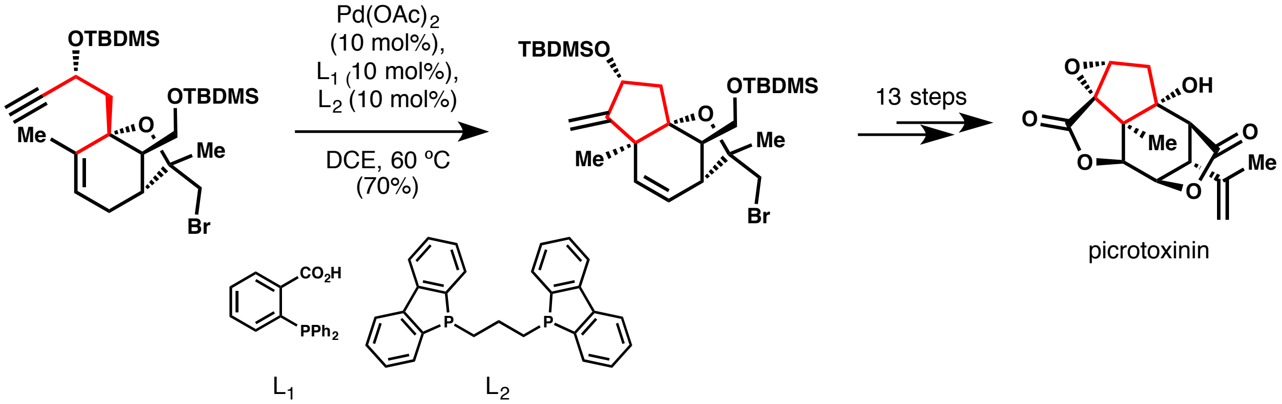
Make 1 bond

Oppolzer's palladium-ene/Heck annulation.



Oppolzer, W. and co. *JOC* **1991**, *56*, 6256; *Pure and Appl. Chem.* **1990**, *62*, 1941; **1988**, *60*, 39; *ACIE* **1991**, 32, 131.

Trost's Pd-catalyzed Alder-ene reaction effectively forges the cis-fused 5-6 ring system of picrotoxinin.

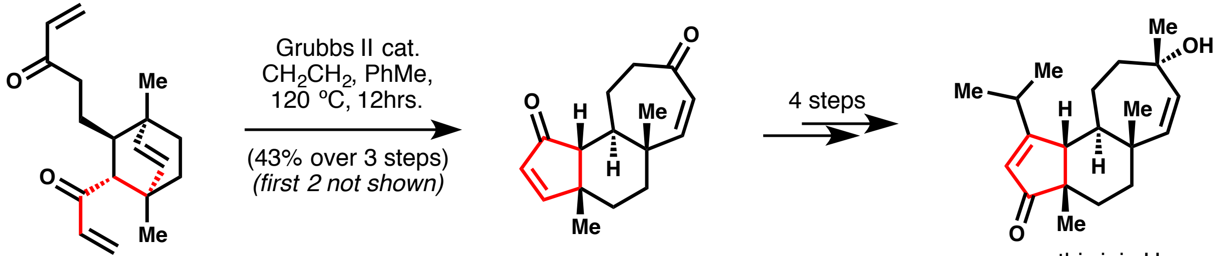


picrotoxinin

L_1 L_2

(M. Krische's graduate work) Trost and co. *JACS* **1996**, *118*, 233; *JACS* **1999**, *121*, 6183

Ring closing metathesis

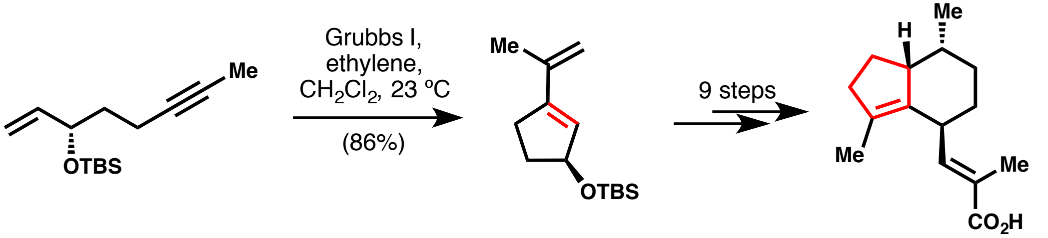


cyanthiwigin U

Pfeiffer, M. B.; Phillips, A.J. *JACS* **2015**, *127*(15), 5334.

Make 1 bond

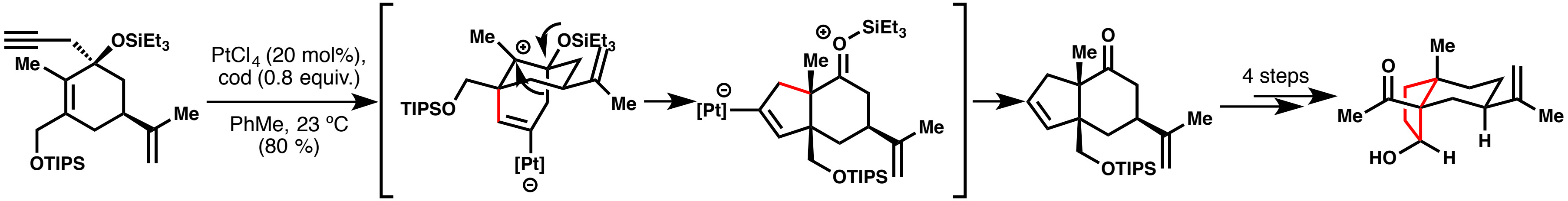
Enyne RCM



valerenic acid

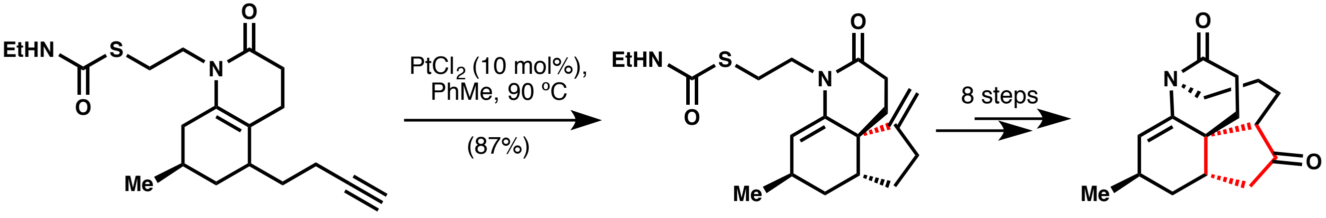
Ramharter, J.; Mulzer, J. *Org. Lett.* **2009**, *11*, 1151.

electrophilic Pt-catalyzed cycloisomerization



cyperolone

Kirsch, S.F. and co. *OL* **2012**, *14*(5), 1250.

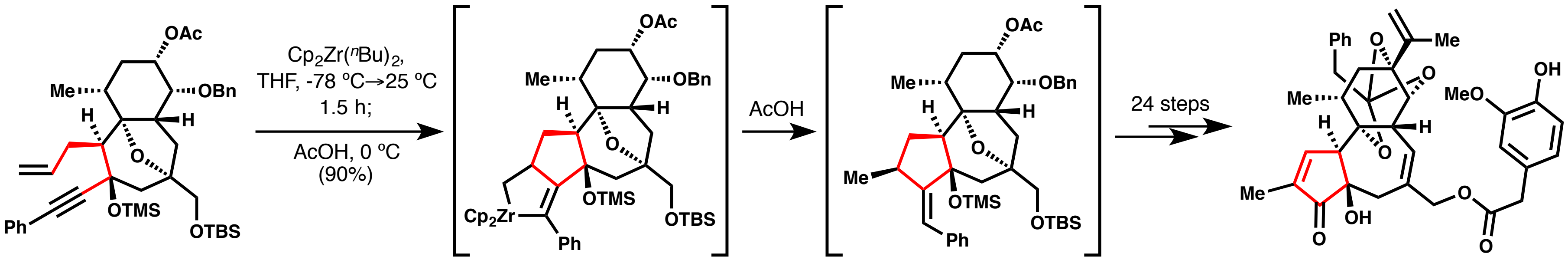


(+)-fawcettidine

Kozak, J.A.; Dake, G.R. *ACIE* **2008**, *47*, 4221.

Make 1 bond

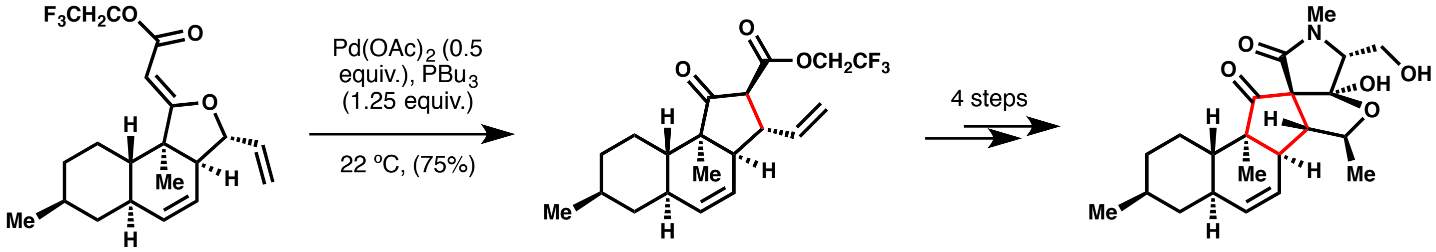
Wender's use of a zirconium-mediated enyne ring closure.



resiniferatoxin

Wender and co. *JACS* **1997**, *119*, 12976. For Zr chemistry: Nugent and co. *JACS* **1984**, *106*, 6422; *JACS* **1988**, *110*, 7128,; Negishi and co. *JACS* **1989**, *111*, 3336; *Tetrahedron Lett.* **1986**, *27*, 2829.

Pd-catalyzed isomerization.

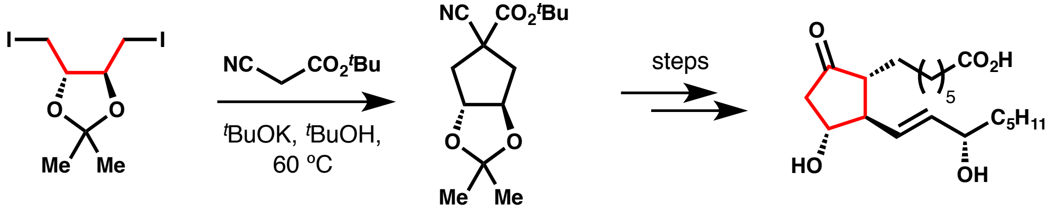


"Considering that the basicity and leaving ability of β-ketoester enolate are similar to those of phenoxide, we rationalized that a transition metal complex that promotes the substitution of a phenyl ally ether would fit the requirement."

(–)-fusaretin A

Li, A. and co. *JACS* **2012**, *134*, 920.

[4+1] double alkylation strategy



prostaglandin E_1

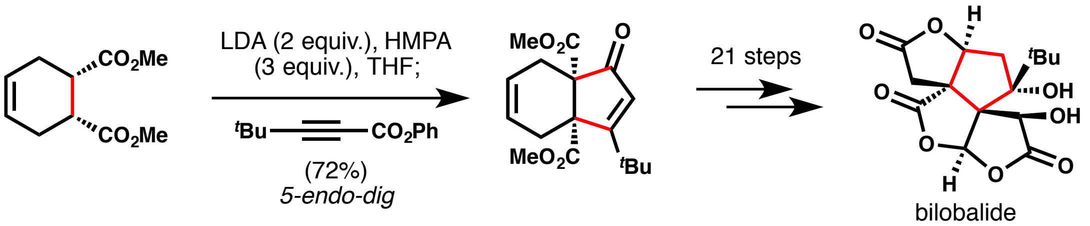
Tetrahedron Lett. **1986**, *27*, 2199, 3556; **1983**, *24*, 5571.

Shenvi Lab Group Meeting
June 19, 2017

Make 2 bonds

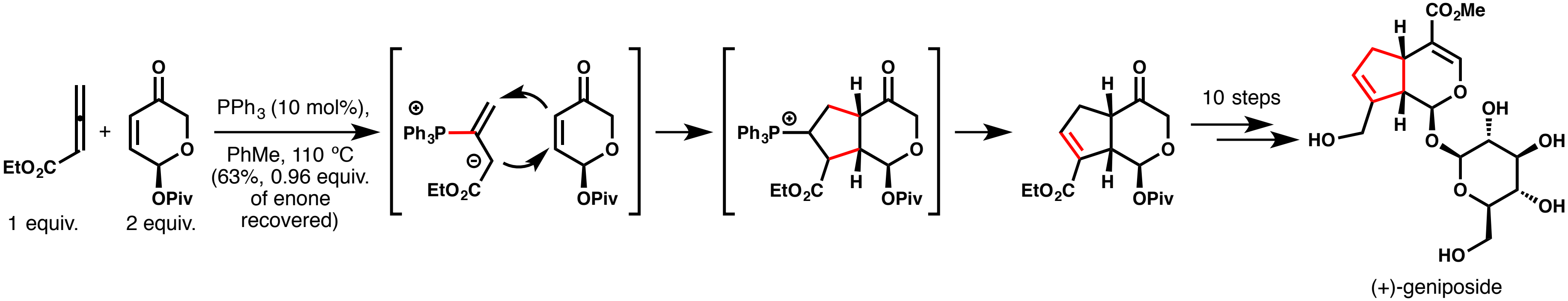
S. Crossley

A Claisen-Michael cascade



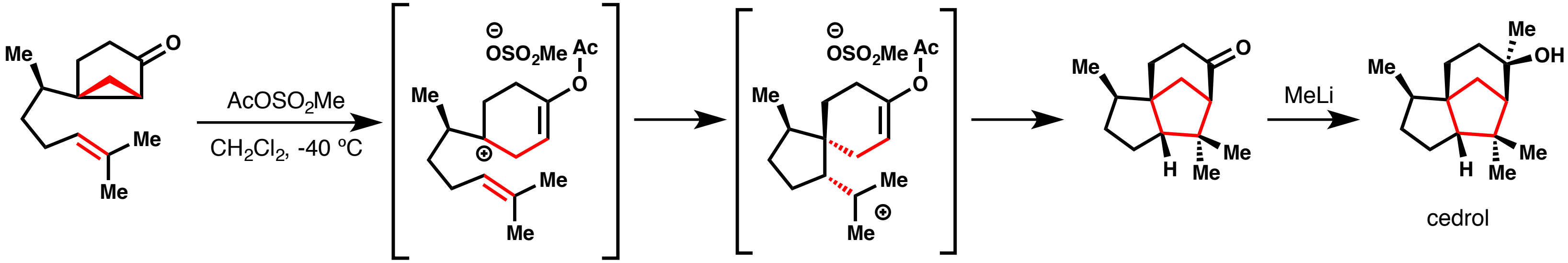
Corey and co. *JACS* **1988**, *110*, 3672; *Tetrahedron Lett.* **1988**, *29*, 3423; *Tetrahedron Lett.* **1986**, *27*, 5951.

Phosphine catalyzed [3+2]. *Not (yet) commonly used in total synthesis, but is an active area of research. See G. Fu's work for extensive developments.*



Jones, R.A; Krische, M.J. *OL* **2009**, *11* (8), 1849.

Stabilized cation-olefin [3+2]

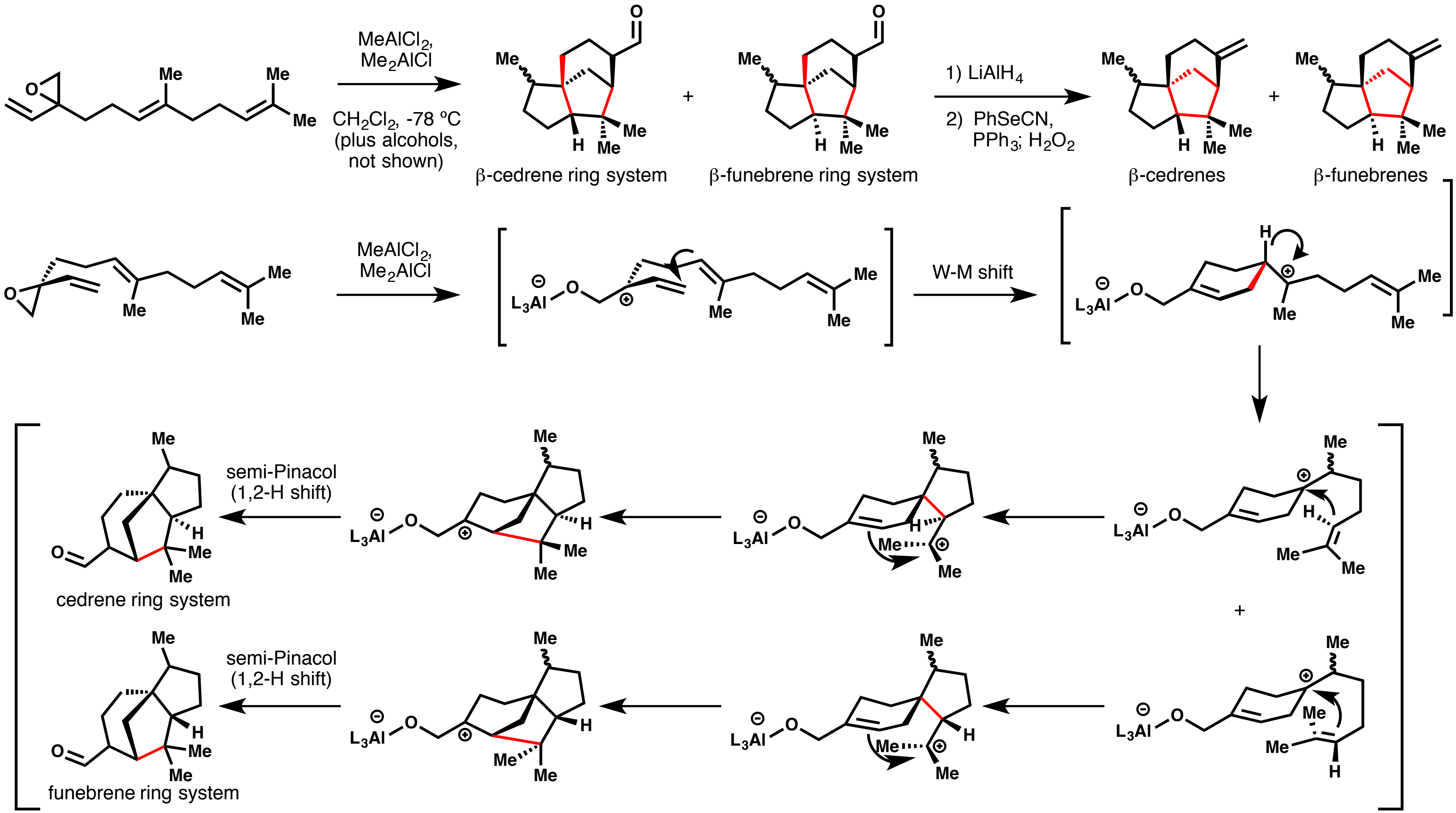


Corey and co. *Tetrahedron Lett.* **1973**, 3153.

Make 2 bonds

cation-olefin cyclization

Biosynthetically, many 5-membered ring containing terpenes and terpenoids arise from tail-to-head cation-olefin cyclization cascades. This paper demonstrates that these cyclization pathways are viable in a flask by sequestration of the counterion away from the propagating cation to make a number of highly strained terpenes, includeing cedrenes, funebrenes and cumacrenes.

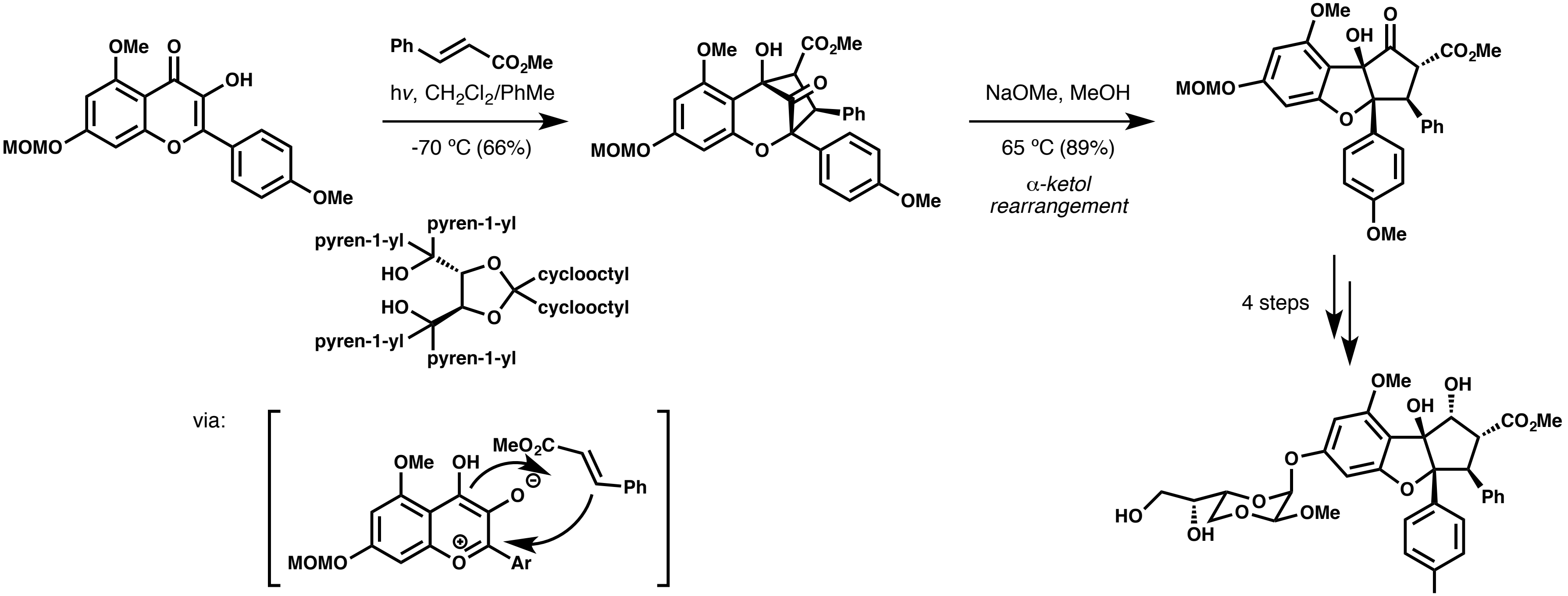


- tail-to-head cyclization can lead to remarkably strained ring systems, such as β-funebrene, cumacrene, and taxa-4,1-diene

Pronin and Shenvi *Nat. Chem.* **2012**, *4*, 915.

Make 2 bonds

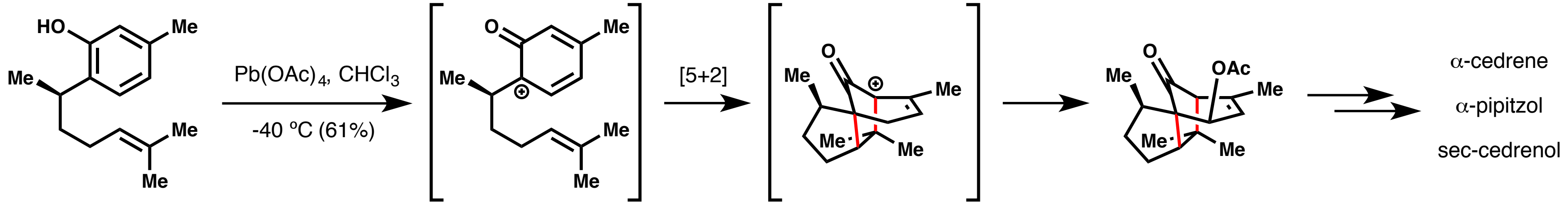
[3+2] photocycloaddition



(–)-silvestrol (87% ee)

Porco Jr., J. and co. *ACIE* **2007**, *46*, 7831; *JACS* **2004**, *126*, 13620; *JACS* **2006**, *128*, 7754.

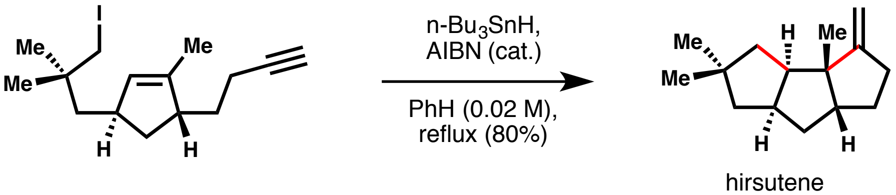
[5+2] cycloadditions can be used to form 5-membered rings



Green, J.C.; Pettus, T.R.R. *JACS* **2011**, *133*, 1603.

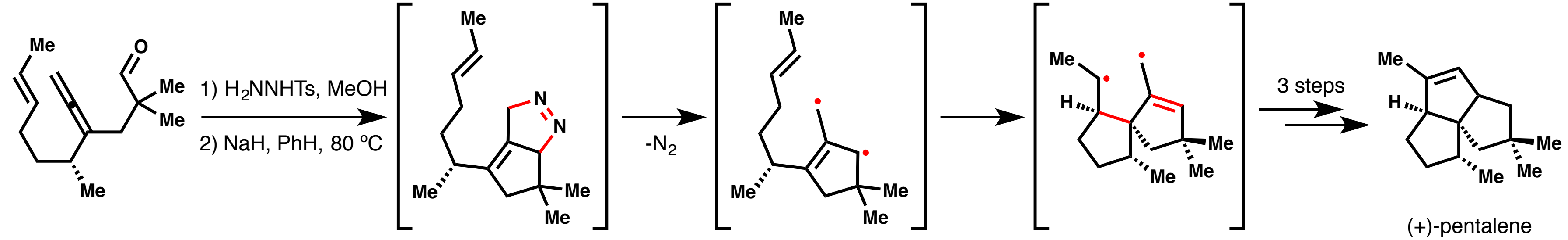
Make 2 bonds

Radical cascades



Curran and co. JACS **1985**, *107*, 1448; Tetrahedron **1985**, *41*, 3843.

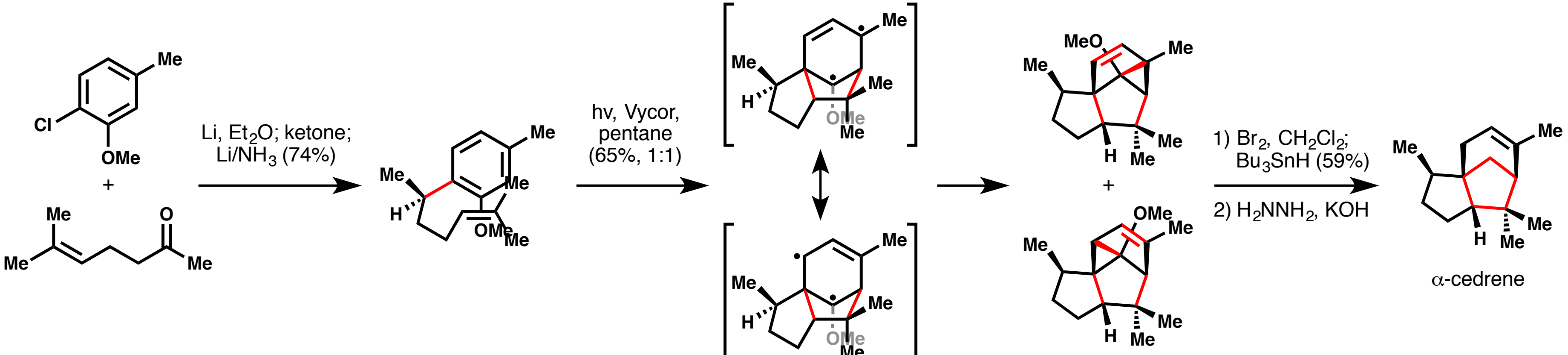
Trimethylenemethane and equivalents



Lee and co. *Tetrahedron* **2013**, *69*, 7810; See also Trost, B.M. *JACS* **1986**, *25*(1), 1.

Alkene-arene *meta* photocycloaddition. *The alkene-arene meta-photocycloaddition is one of the most powerful reactions for building up complexity (3 bonds and up to 6 stereocenters formed), but has numerous subtleties which make it difficult to modulate. The reaction has generally been used to rapidly construct triquinane (linear, angular and propellane) containing natural products. See Belstein J. Org. Chem.* ***2011****, 7, 525; Chem. Rev.* ***2016****, 116(7), 9816 for details.*

Paul Wender has shown the utility of this reaction in the synthesis of numerous natural products, including this seminal synthesis of α-cedrene. Through use of an intramolecular tether and judicious selection of aromatic substituents, Wender is able to effect the desired meta cycloaddition with the desired regiochemistry over competing ortho- and para- cycloaddition pathways.

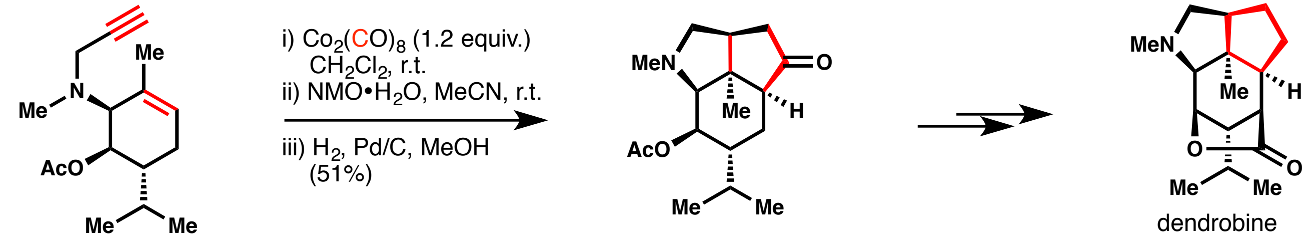


Wender and co. *JACS* **1981**, *103*, 688.

Make 3 bonds

Pauson-Khand reaction, a [2+2+1] annulation

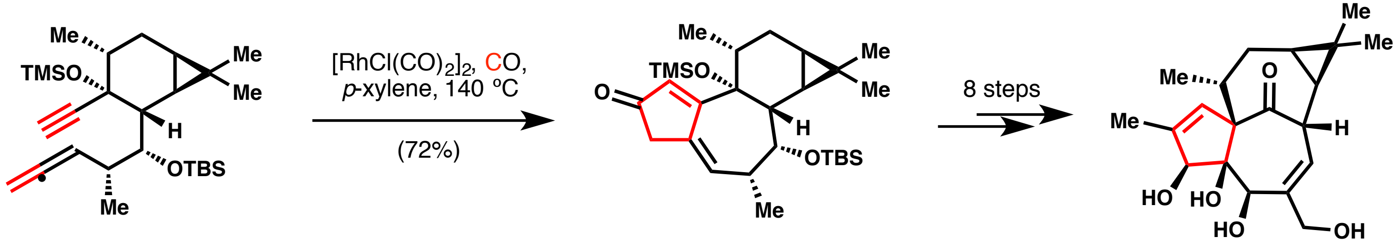
- *this reaction results in the formation of two ring systems when employed intramolecularly*



i) $Co_2(CO)_8$ (1.2 equiv.)
CH_2Cl_2, r.t.
ii) $NMO \bullet H_2O$, MeCN, r.t.
iii) H_2, Pd/C, MeOH
(51%)

dendrobine

Zard and co. *JACS* **1999**, *121*, 6072.

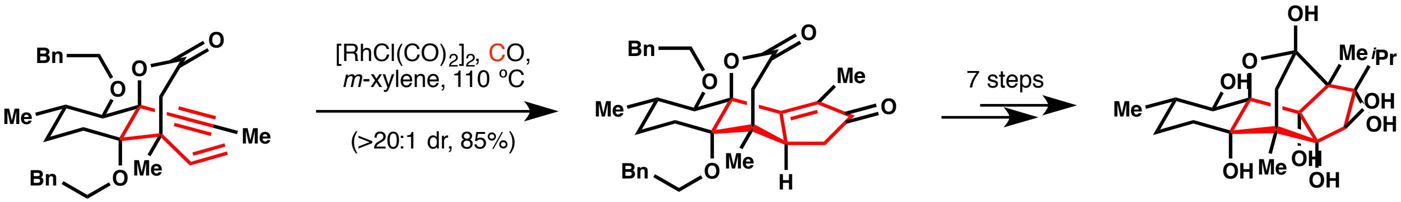


$[RhCl(CO)_2]_2$, CO,
p-xylene, 140 °C
(72%)

8 steps

ingenol

Baran and co. *Science* **2013**, *341*(6148), 878; *JACS* **2014**, *136*(15), 5799.



$[RhCl(CO)_2]_2$, CO,
m-xylene, 110 °C
(>20:1 dr, 85%)

7 steps

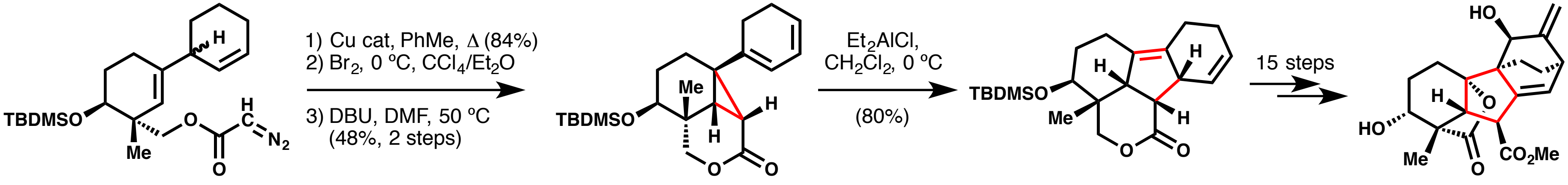
ryanodol

Reisman and co. *Science* **2016**, *353*(6302), 912; *ACS Cen. Sci.* **2017**, *3*(4), 278.

Rearrangements

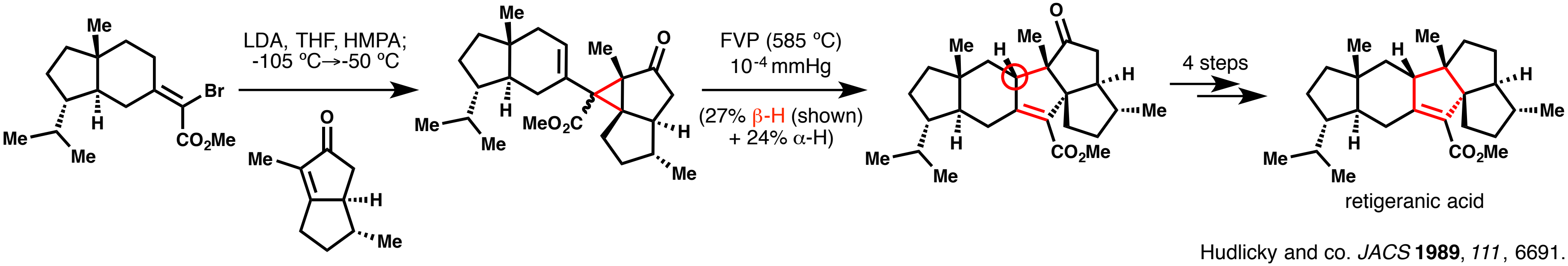
A) 3→5 ring expansion

vinyl-cyclopropane rearrangement. Normally required T > 300 ºC, but can occur under lewis acidic conditions if there are charge stabilizing functional groups.



antheridic acid

A. Myers' graduate work with E.J. Corey. Corey and co. *J. Am. Chem. Soc.* **1985**, *107*, 5574; *Tetrahedron Lett.* **1986**, *27*, 5083.



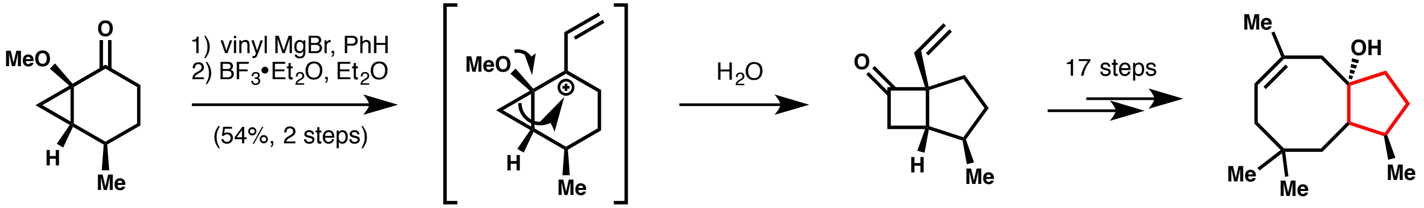
retigeranic acid

Hudlicky and co. *JACS* **1989**, *111*, 6691.

B) 4→5 ring expansion

Often effected from a [2+2] cycloaddition adduct by generation of cation or similarly activated leaving group.

pinacol



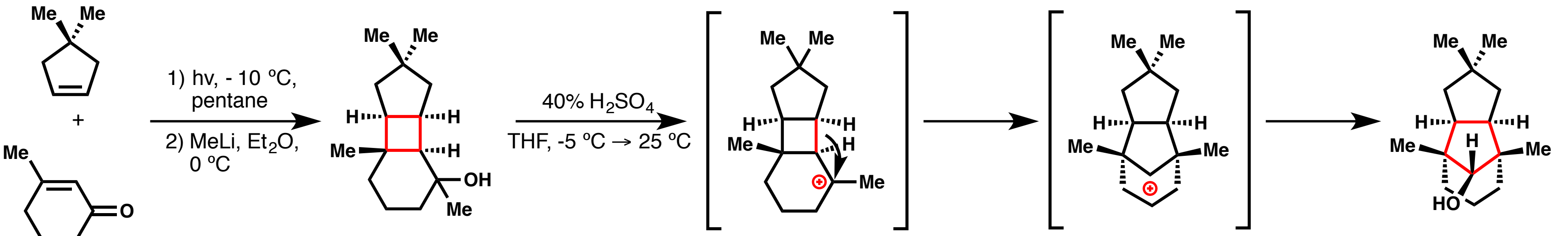
dactylol

Gadwood, R.C. and co. *JACS* **1986**, *108*, 6343.

Rearrangements

S. Crossley

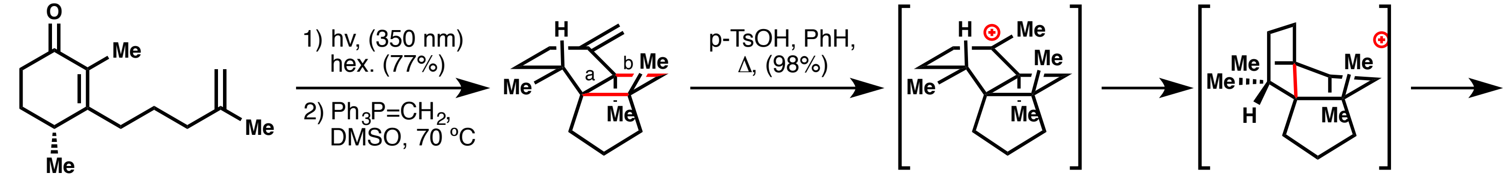
semi-pinacol rearrangement



α-caryophyllene alcohol

Corey and co. *JACS* **1964**, *86*, 1652.; *JACS* **1965**, *87*, 5733.

acid-induced ionization

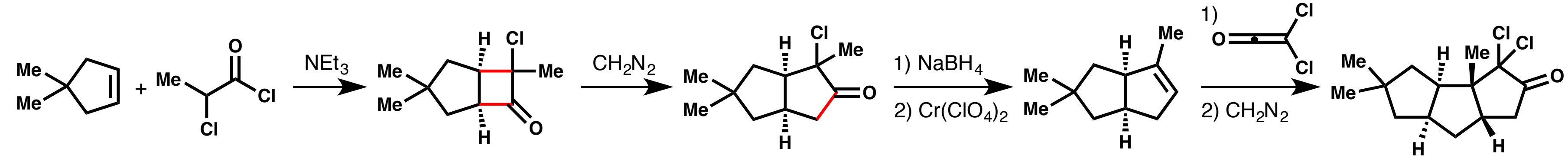


isocomene

Isocomene can also be obtained by a mechanism involving an initial shift of the b bond and a second Wagner-Meerwein shift. see Ch. 14 of Classics in Total Synthesis.

Pirrung, M.C. *JACS* **1979**, *101*, 7130; **1981**, *103*, 82.

Tiffeneau-Demjanov ring expansion



another
4 steps gives
hirsutene

Greene, A.E. *Tetrahedron Lett.* **1980**, *21*, 3059; **1981**.

Rearrangements

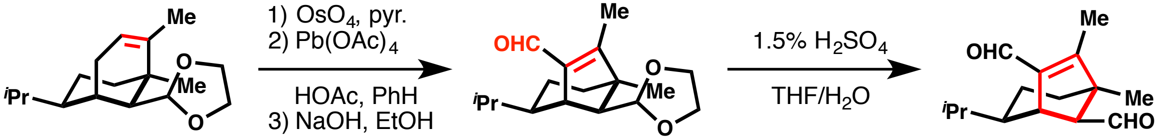
C) 6→5 ring contraction

Oxidative cleavage of alkenes, followed by aldol condensation is the classic way in which to effect a 6→5 ring contraction. This tactic is useful for several reasons:

a) Stereocontrolled formation of highly subsituted cyclohexenes is well studied, and oxidative cleavage/aldol addition/condensation is robust and hightly FG tolerant.

b) Allows one to use the chiral centers found in the numerous and cheap chiral pool 6-membered terpenes and terpenoids.

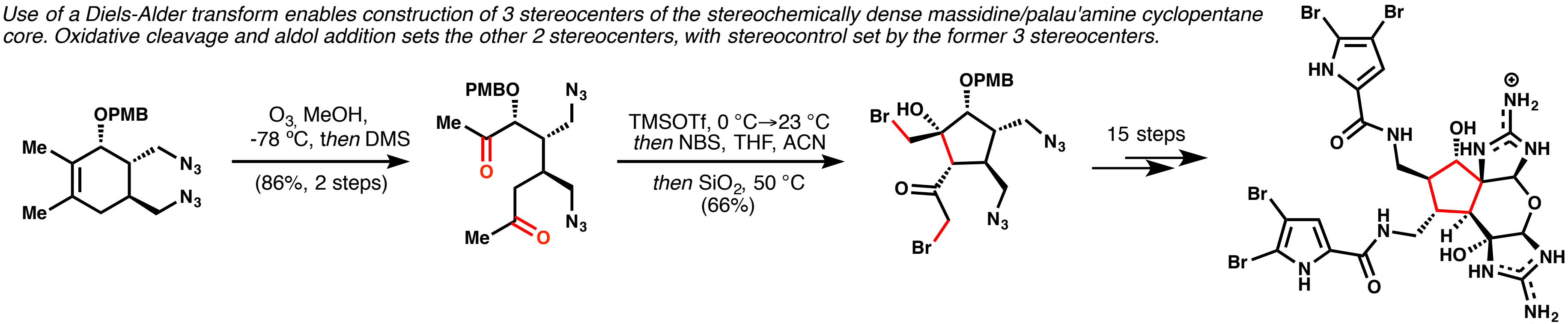
c) The transformation retains the olefin and adds an exocyclic carbonyl handle, both of which may be utilized for subsequent transformations.



Helminthosporal

Corey, E.J.; Nozoe, S. *JACS* **1965**, *87*(24), 5728.

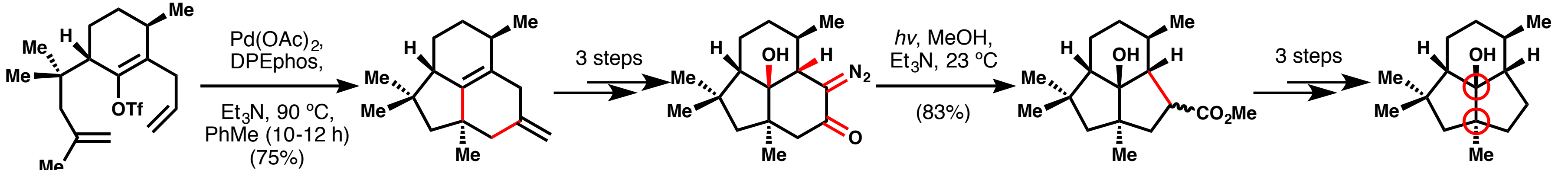
Use of a Diels-Alder transform enables construction of 3 stereocenters of the stereochemically dense massidine/palau'amine cyclopentane core. Oxidative cleavage and aldol addition sets the other 2 stereocenters, with stereocontrol set by the former 3 stereocenters.



Baran and co. *JACS* **2008**, *130*, 16490; **2011**, *133*, 14710; *ACIE* **2008**, *47*, 3578

(–)-massadine

In Hu and Synder's synthesis of (–)-presilphiperfolan-8-ol, a Wolff rearrangement proved optimal to effect the 6→5 ring contraction. Like epoxydictymene, palau'amine and the funebrenes, (syntheses of which are all featured in this group meeting) presilphiperifolan-8-ol contains a strained 1,2-trans ring fusion. In cases like these, direct formation of the 5-membered ring directly is often avoided in favor of the more facile 6-membered ring formation, followed by a ring contraction.

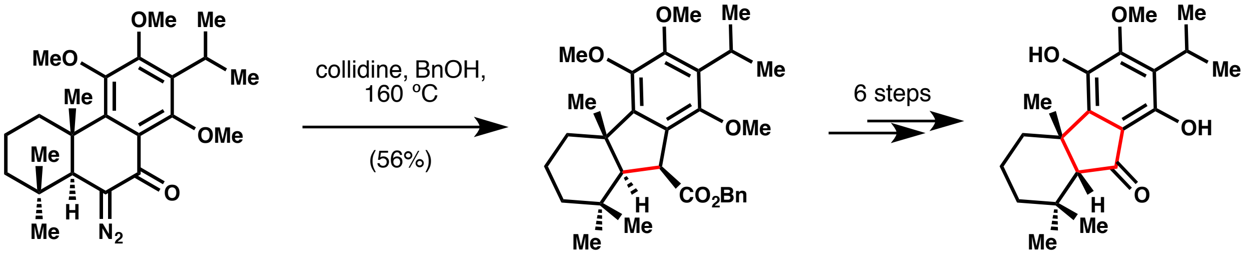


(–)-presilphiperfolan-8-ol
trans fused 5-5 ring junction highlighted

Hu, P. and Snyder, S.A. *JACS* **2017**, *139*, 5007.

Rearrangements

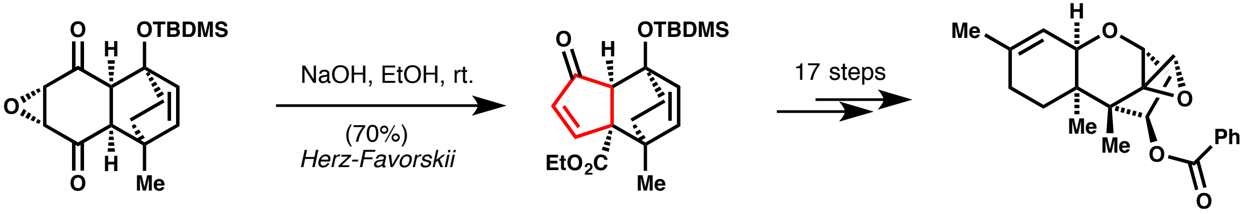
Wolff rearrangement



taiwaniaquinol B

Li, A. and co. *Org. Lett.* **2013**, *15*(8), 2022.

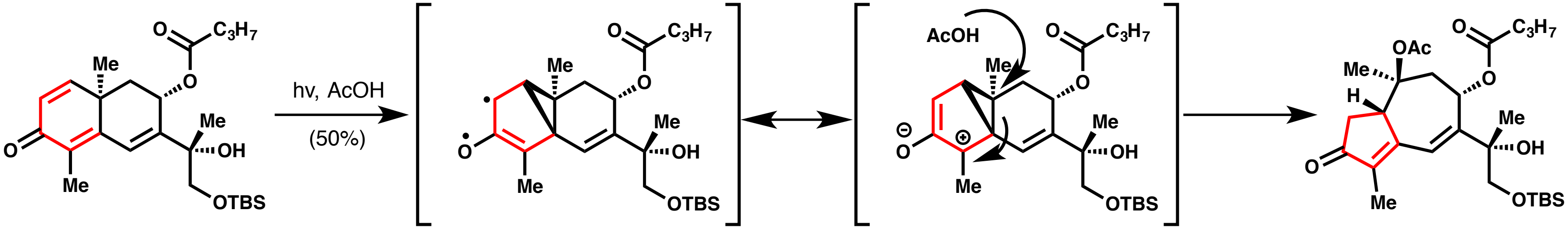
Favorskii rearrangement



trichodermol

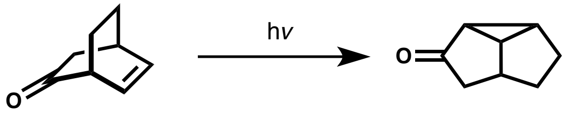
Still and co. *JACS* **1980**, *102*, 3654; For Herz-Favorskii, see: *JOC* **1980**, *40*(24), 3519.

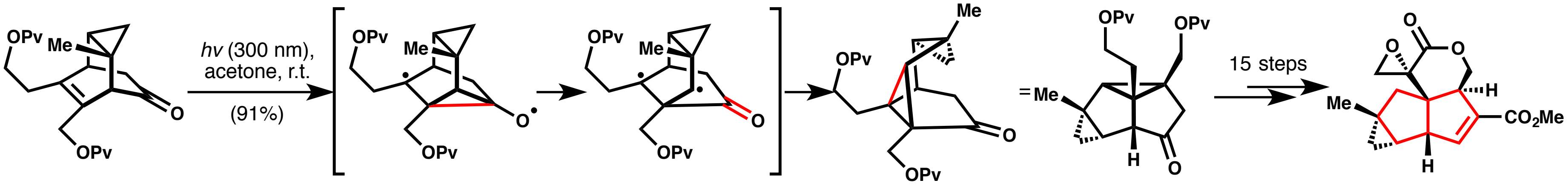
α-santonin rearrangement



Baran and co. *ACS Cent. Sci.* **2017**, *3*, 47.

di–π-methane and oxo-di-π-methane rearrangments can convert [2.2.2] (bridged) bicycles to [3.3.0] (fused) tricycles:

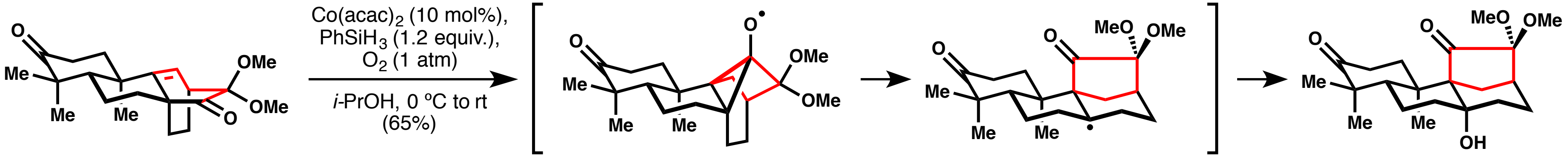




pentaleneolatone P methyl ester

Paquette, L.A. and co. *JACS* **1991**, *113*, 9384. For more details: see *Chem. Rev.* **2016**, *116* (17), 9683; *Chem. Rev.* **1973**, *73*(5), 531.

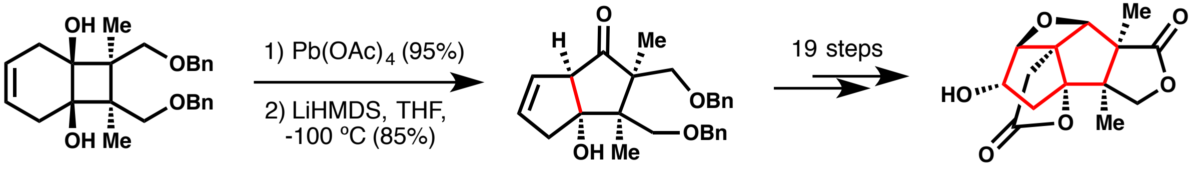
di-π-methane-like rearrangement



Song, L.; Zhu, G.; Liu, Y.; Liu, B.; Qin, S. *J. Am. Chem. Soc.* **2015**, *137*, 13706.

D) Other

5-membered ring formation from 8 membered macrocycle

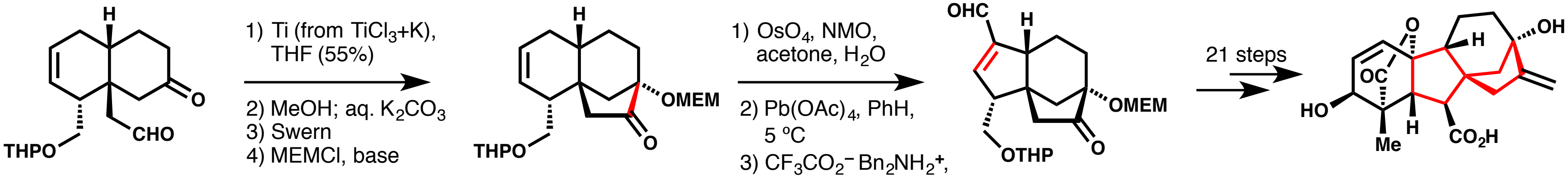


merrilactone A

Inoue and co. *JACS* **2003**, *125*, 10772.

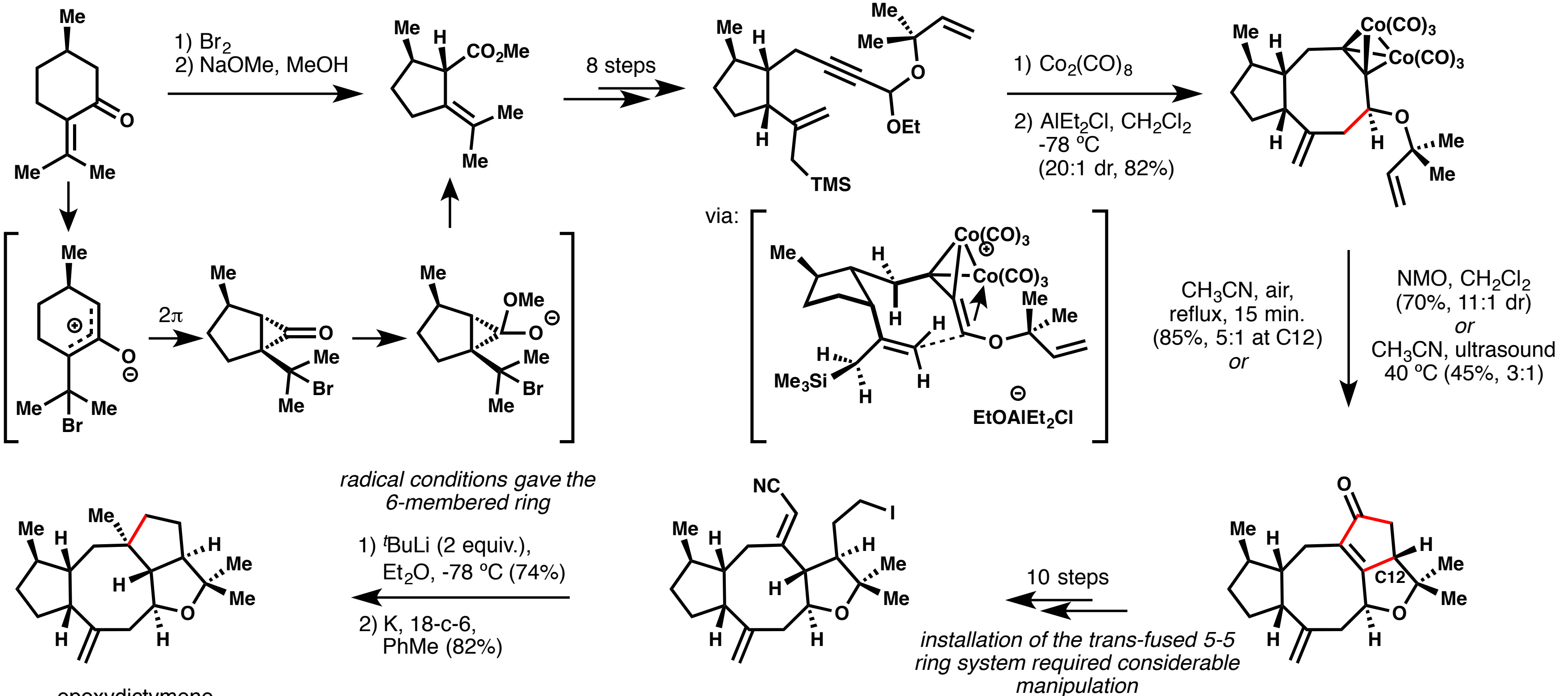
Multiple Strategies

Pinacol coupling, followed by a 6→5 ring-contraction



giberellic acid

Favorskii, Nicholas/Prins/Prins/Sakurai, Pauson-Khand, conjugate addition

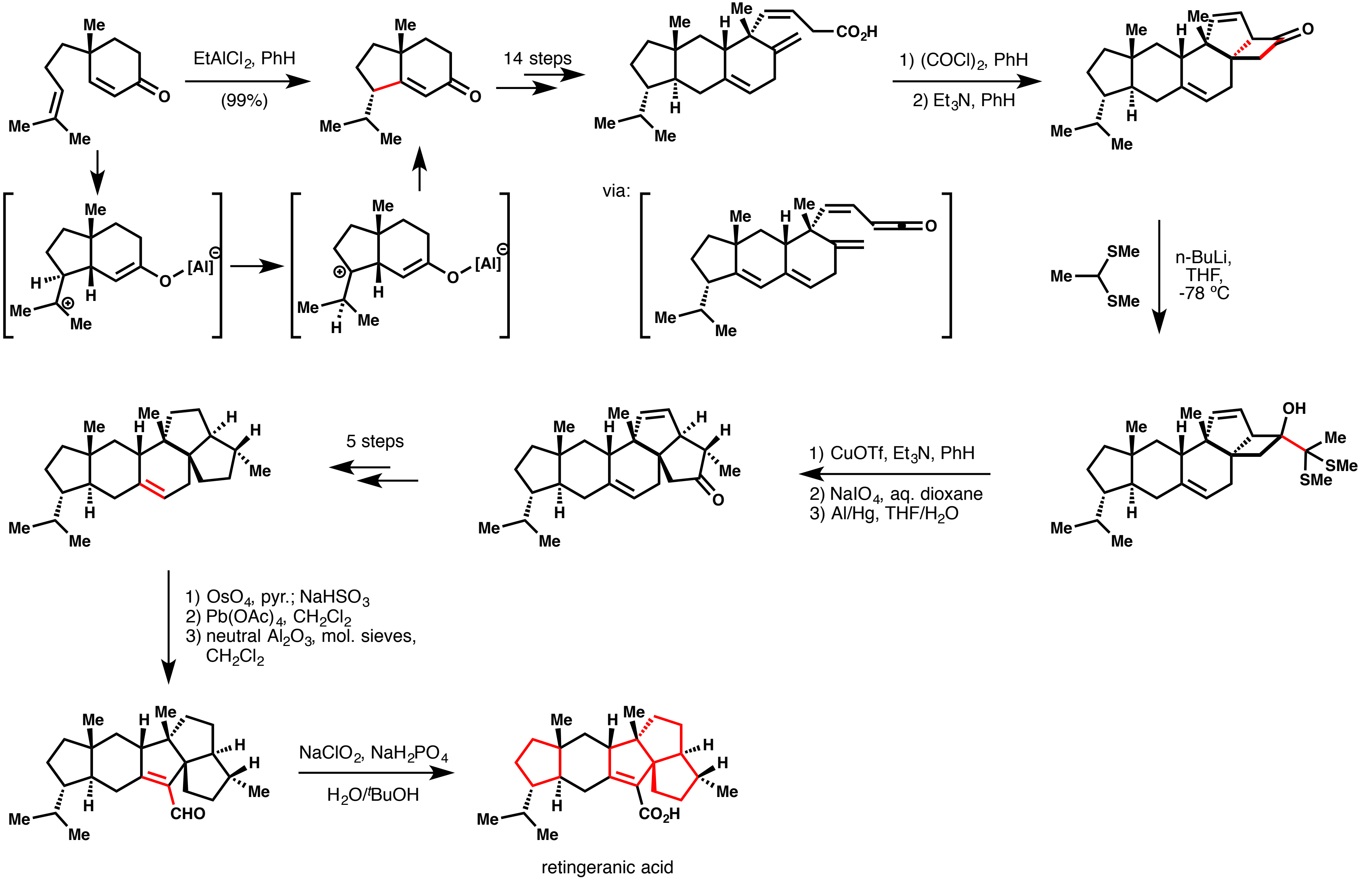


epoxydictymene

T. Jamison's graduate work with Schreiber. *JACS* **1994**, *116*, 5505; *JACS* **1997**, *119*, 4353; Wolinsky *et al.* *Tetrahedron* **1965**, *21*, 1247.

Multiple Strategies

Prins, 4→5 ring expansion, 6→5 ring contraction



Snider and co. *JACS* **1980**, *102*, 5872; Corey and co. *JACS* **1985**, *172*, 4339; *Tetrahedron Lett.* **1983**, *24*, 5571.