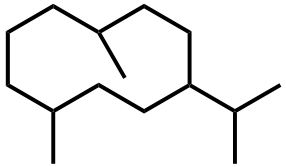
Germacranes

Ippei Usui

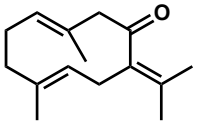
Germacrane Skelton



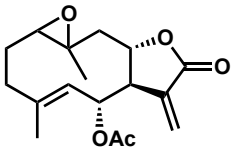
Scifinder Hit: 6801 hits (journal) till 09.2011
only 1 hit in 1963, 676 hits in 2009, 729 hits in 2010

Review: "Sesquiterpenes with Ten-Membered Carbon Rings. A Review"
Sorm, F. *J. Agr. Food. Chem.* **1971**, *19*, 1081.
"Sesquiterpenoids"
Roberts. J. S.; Bryson. I. *Nat. Prod. Rep.* **1984**, 105.
"Natural Sesquiterpenoids"
Fraga, B. M. *Nat. Prod. Rep.* 1985-2007 (ref Adio's review)
"The Synthesis of Germacranes Sesquiterpenes and Related Compounds"
Minnard, A. J.; Wijnberg, J. B. P. A.; de Groot, A. *Tetrahedron*, **1999**, *55*, 2115.
"Germacrene A-E and related compounds: thermal, photochemical and acid induced transannular cyclizations" Adio, A. M. *Tetrahedron*, **2009**, *65*, 1533.

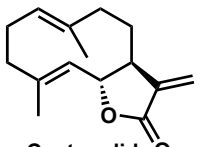
Structural establishment: **Germacrone** (Sorm, 1957). **Pyrethrosine** (Barton,1957), **Costunolide** (Sorm, 1959, X-ray)



Germacrone

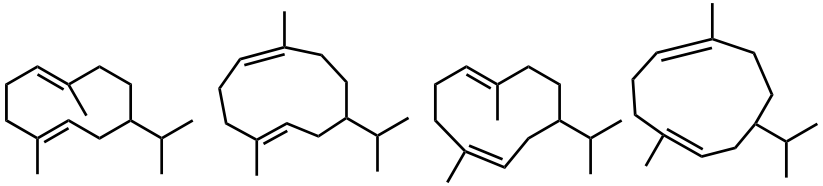


Pyrethrosine



Costunolide

Structure:
- Two endocyclic double bond
- Two methyl group and a isopropyl group
- Ccyclodecadiene consists of two isoprene
- The double bond geometry trend of natural occurrence
  (EE) > (EZ) ~ (ZE) > (ZZ)



EE **EZ** **ZE** **ZZ**

Feverfew

Herb root

American Cockroach

Aphid

Marine Interbrate

Bioactivity:

sex pheromones, alarm pheromone, anti-inflammatory activities, anti-cancer agents, antiplasmodial activity, antibacterial and antifungal activities, antifeedant, tubulin inhibitor, phytotoxic activity, inhibitor of tumour necrosis and interleukin-6, PTP1B inhibitor, NF-κB inhibitors, inhibitors of preadipocyte differentiation, inhibitors of germination and seedling growth in plant species, moth antennal receptor neuron activator, nematicidal activity, cytotoxic activity, tyrosinase inhibitory activities and other various biological activities.

Germacranes

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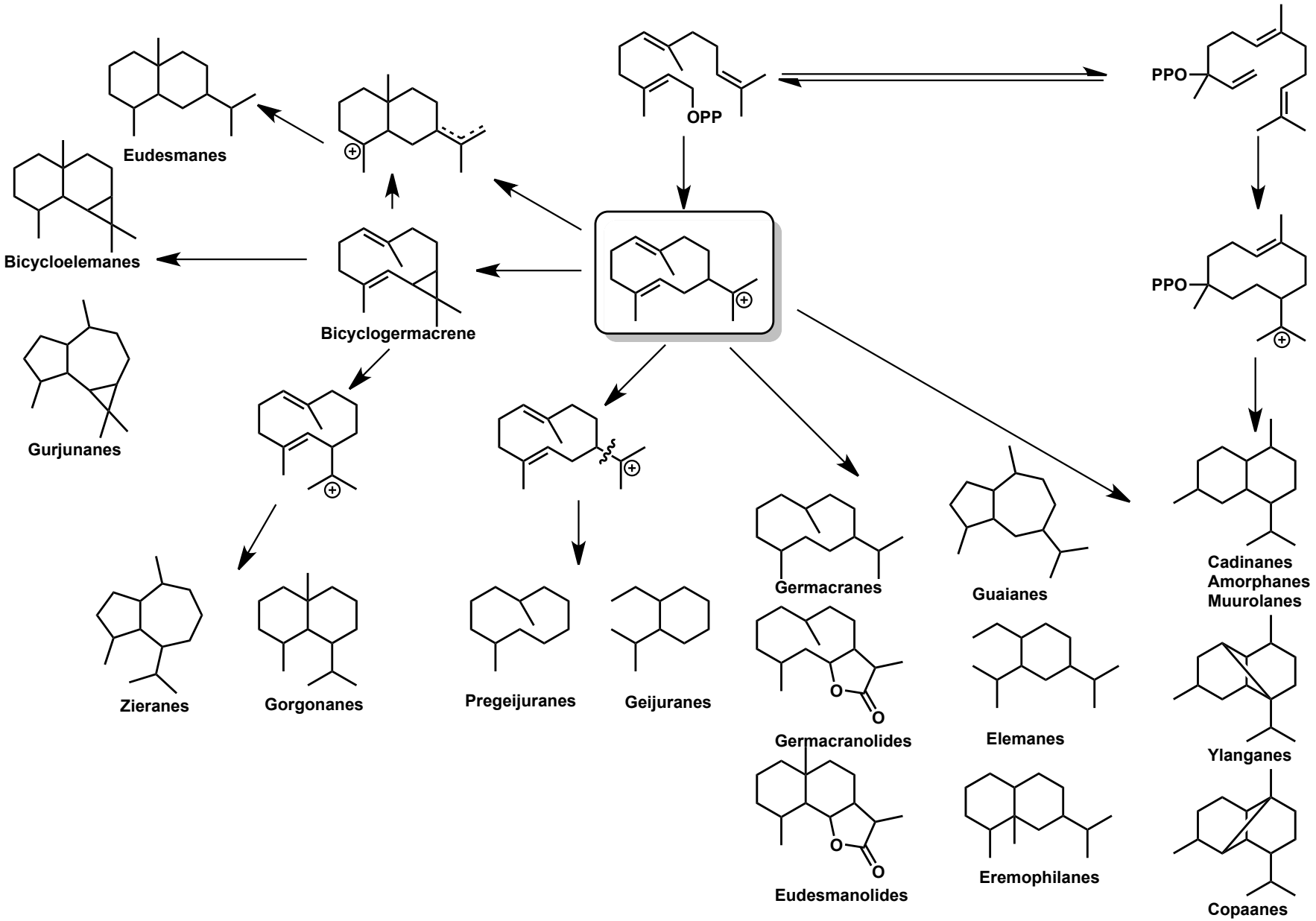

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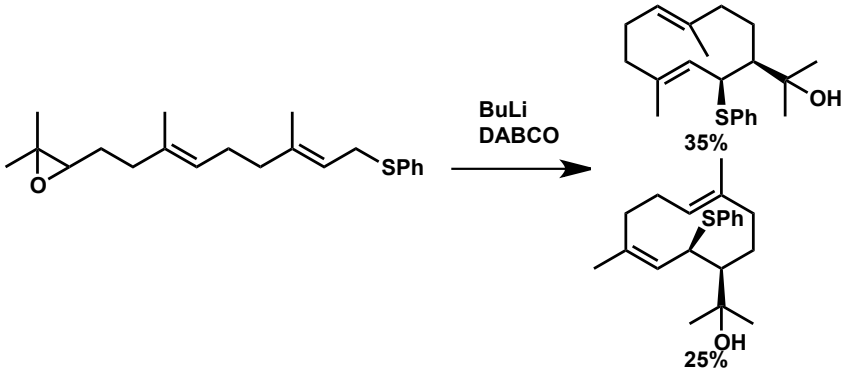
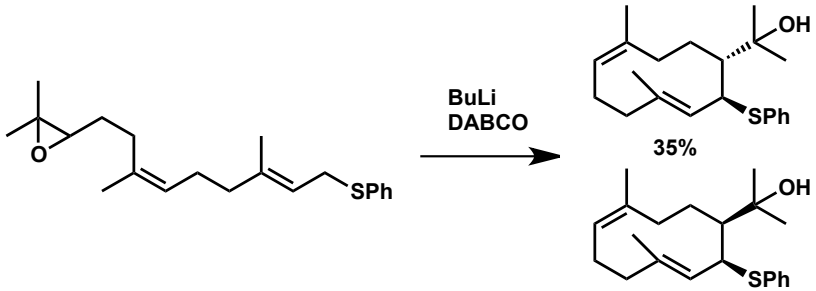
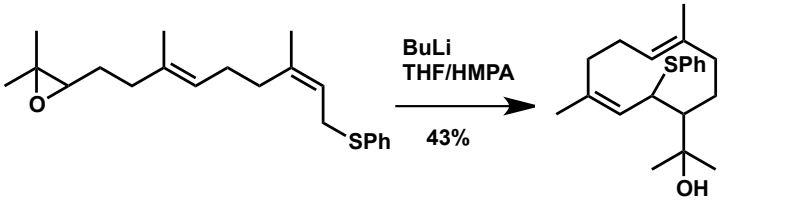


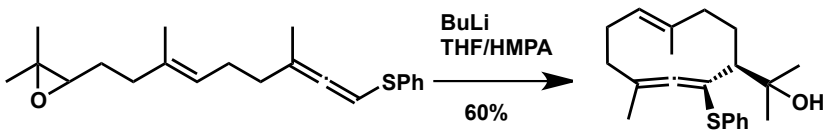
Ito, S. Tet. Lett. 1976, 14, 1121.



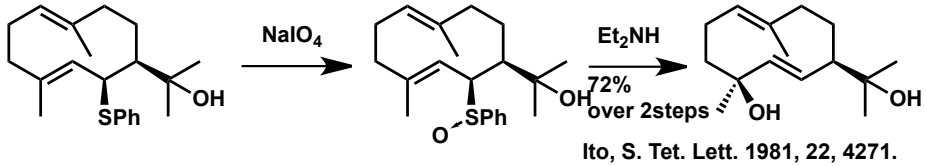
Ito, S. Tet. Lett. 1978, 34, 3121.



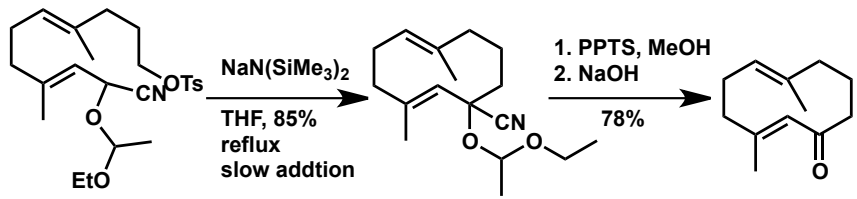
Winter, R. E. K. JOC, 1980, 45, 4786.



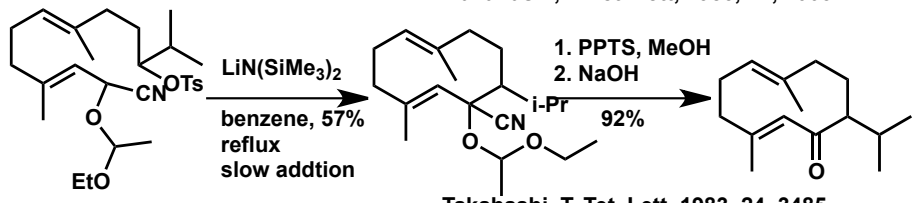
Winter, R. E. K. Tet. Lett, 1992, 33, 2941.



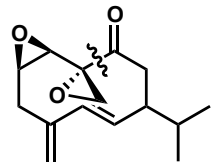
Ito, S. Tet. Lett. 1981, 22, 4271.



Takahashi, T. Tet. Lett, 1983, 24, 2005.

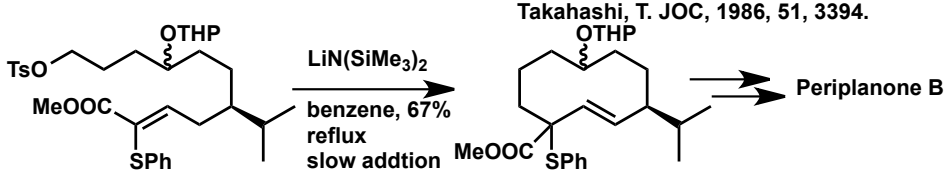


Takahashi, T. Tet. Lett, 1983, 24, 3485.

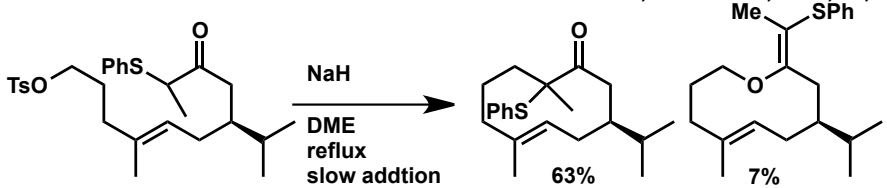


Periplanone B

Takahashi, T. JOC, 1986, 51, 3394.



Kitahara, T. Tet. Lett., 1986, 27, 1343.



Caine, D. Tetrahedron, 1992, 48, 33.

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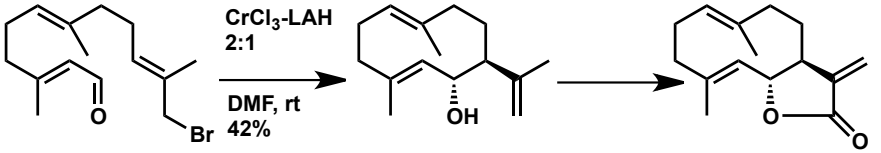
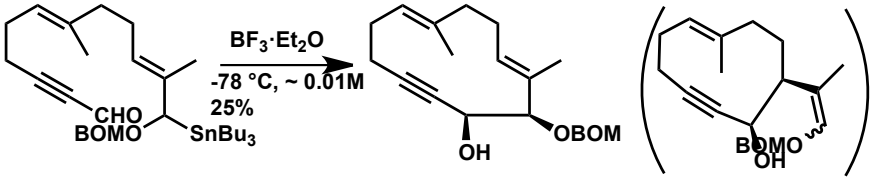
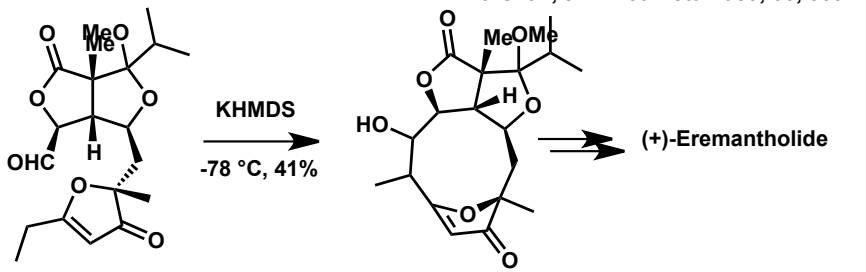


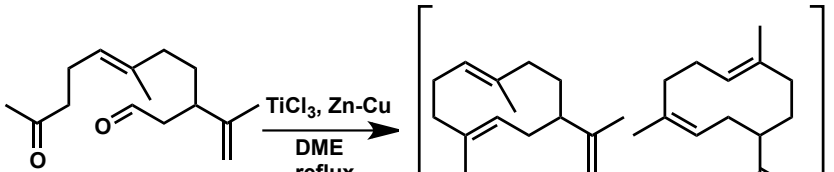
Costunolide: Kitagawa, I. Chem. Lett. 1986, 85.



Marshall, J. A. Tet. Lett. 1989, 30, 309.



Takao, K. Tet. Lett. 1995, 36, 1487.



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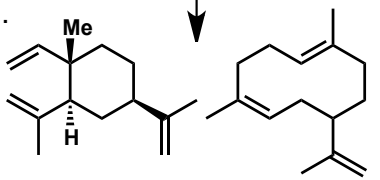

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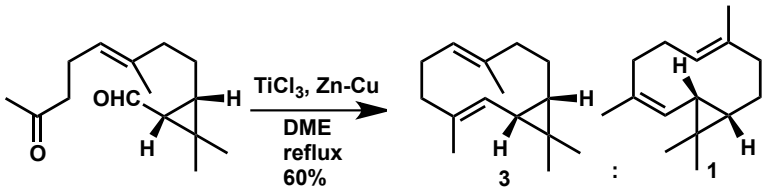

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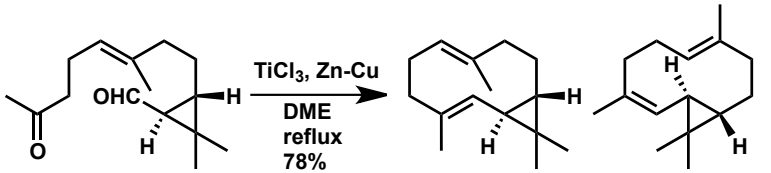
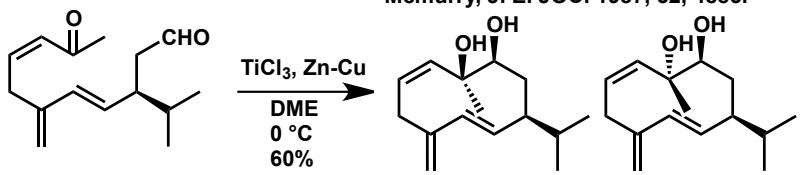


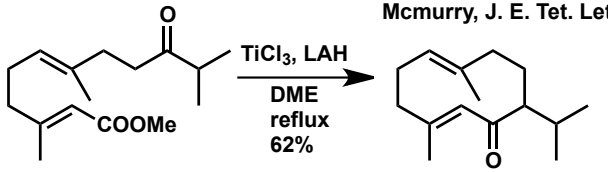
2 : 3

Mcmurry, J. E. JOC. 1987, 52, 4885.



1 : 2

Mcmurry, J. E. Tet. Lett 1994, 35, 4505.



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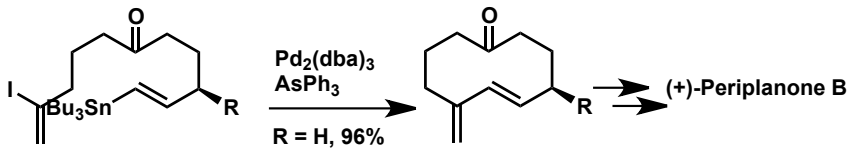

Hodgson, D. M. Synlett 1995, 267.
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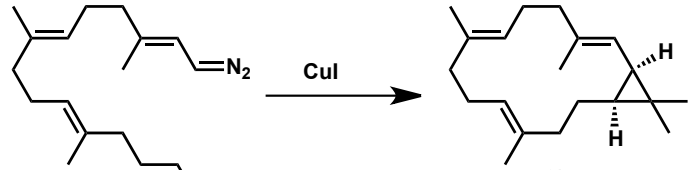

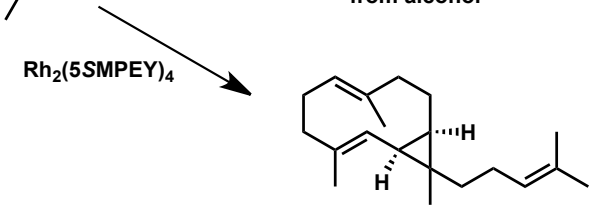

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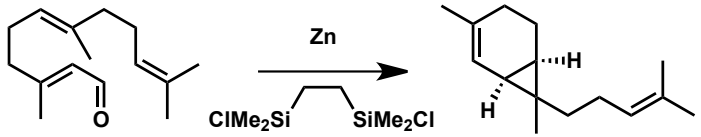
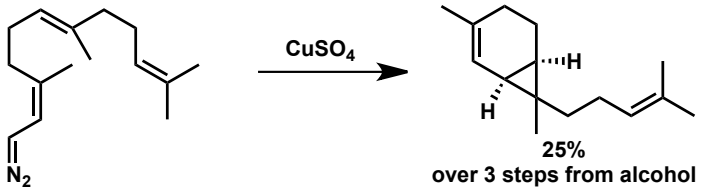
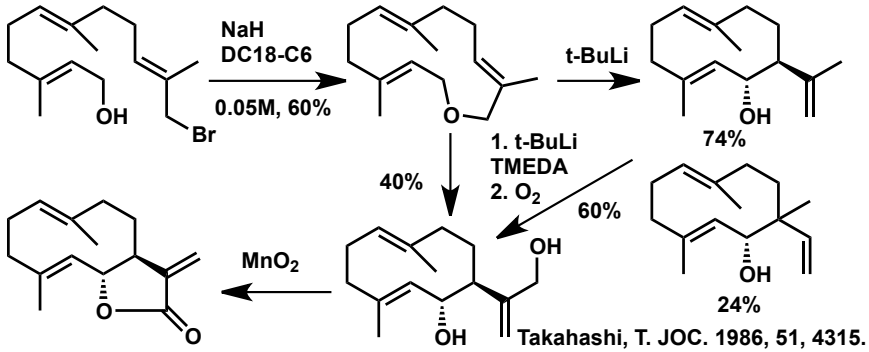


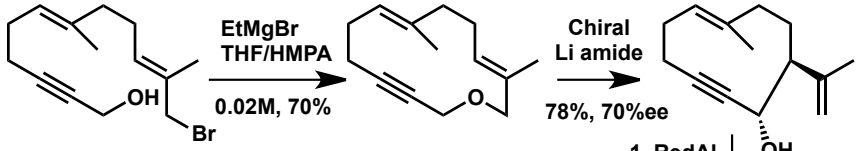
Motherwell, J. A. Tet. Lett. 1995, 36, 1121

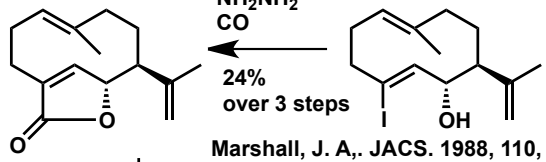


Corey, E. J. Tet. Lett. 1969, 38, 3257

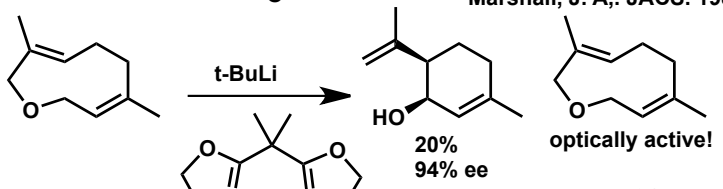


Takahashi, T. JOC. 1986, 51, 4315.





Marshall, J. A,. JACS. 1988, 110, 2925.



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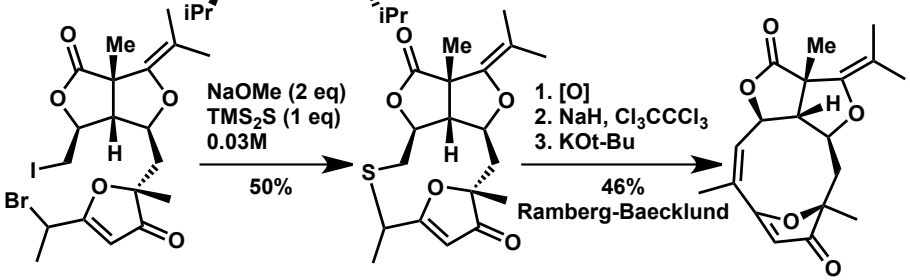

Boeckman, Jr. R. K. JACS. 1991, 113, 9682.

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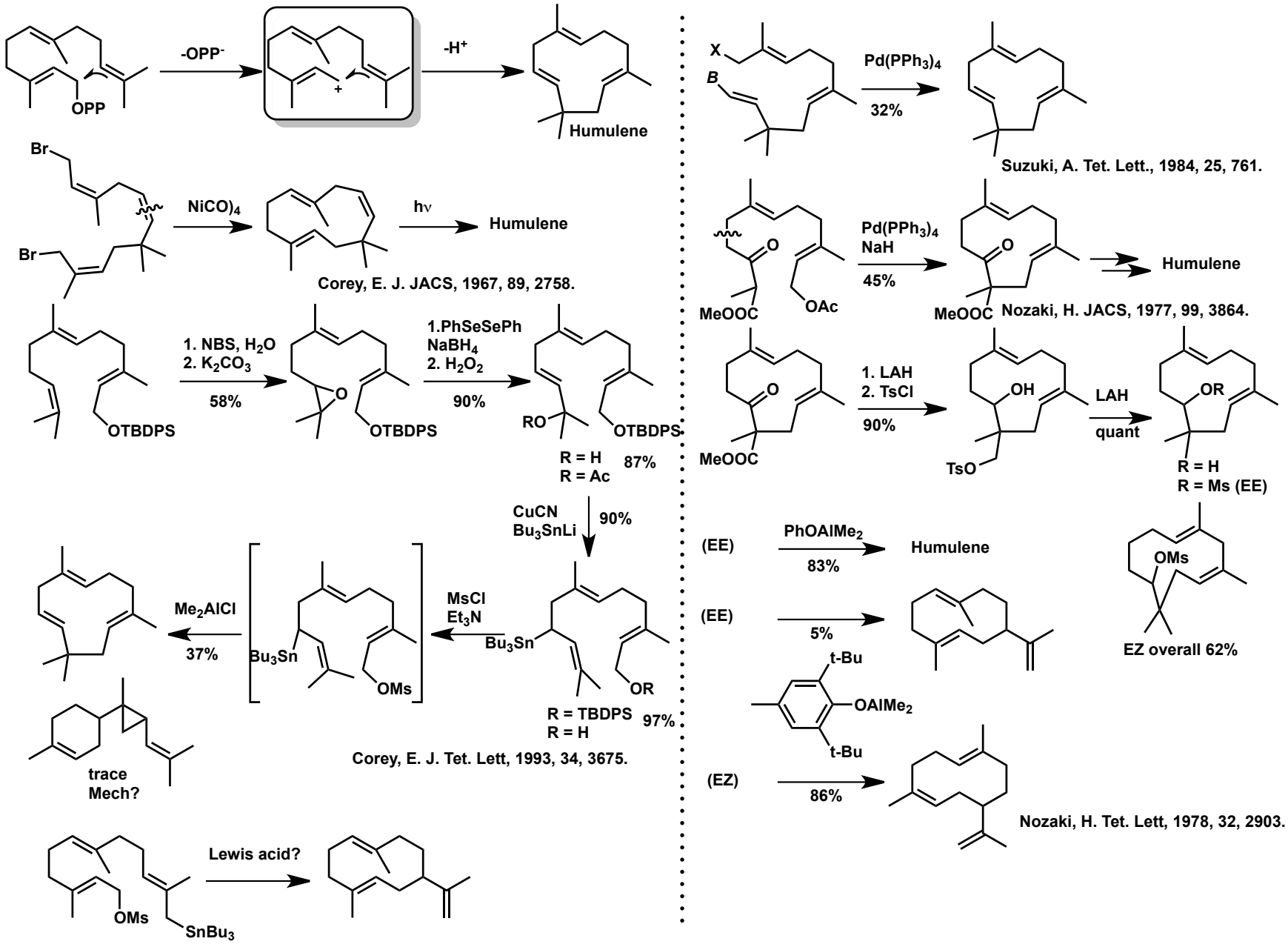

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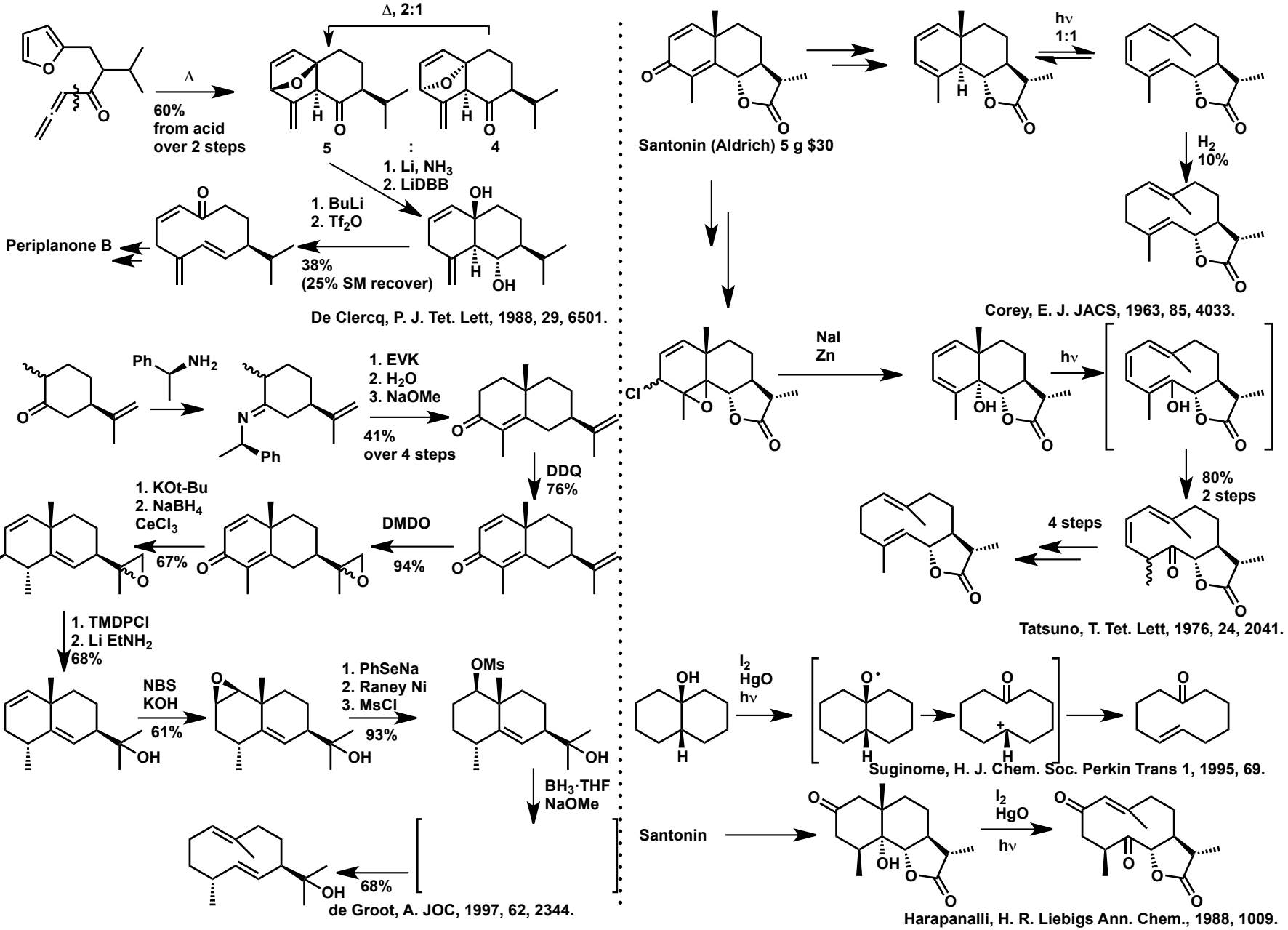

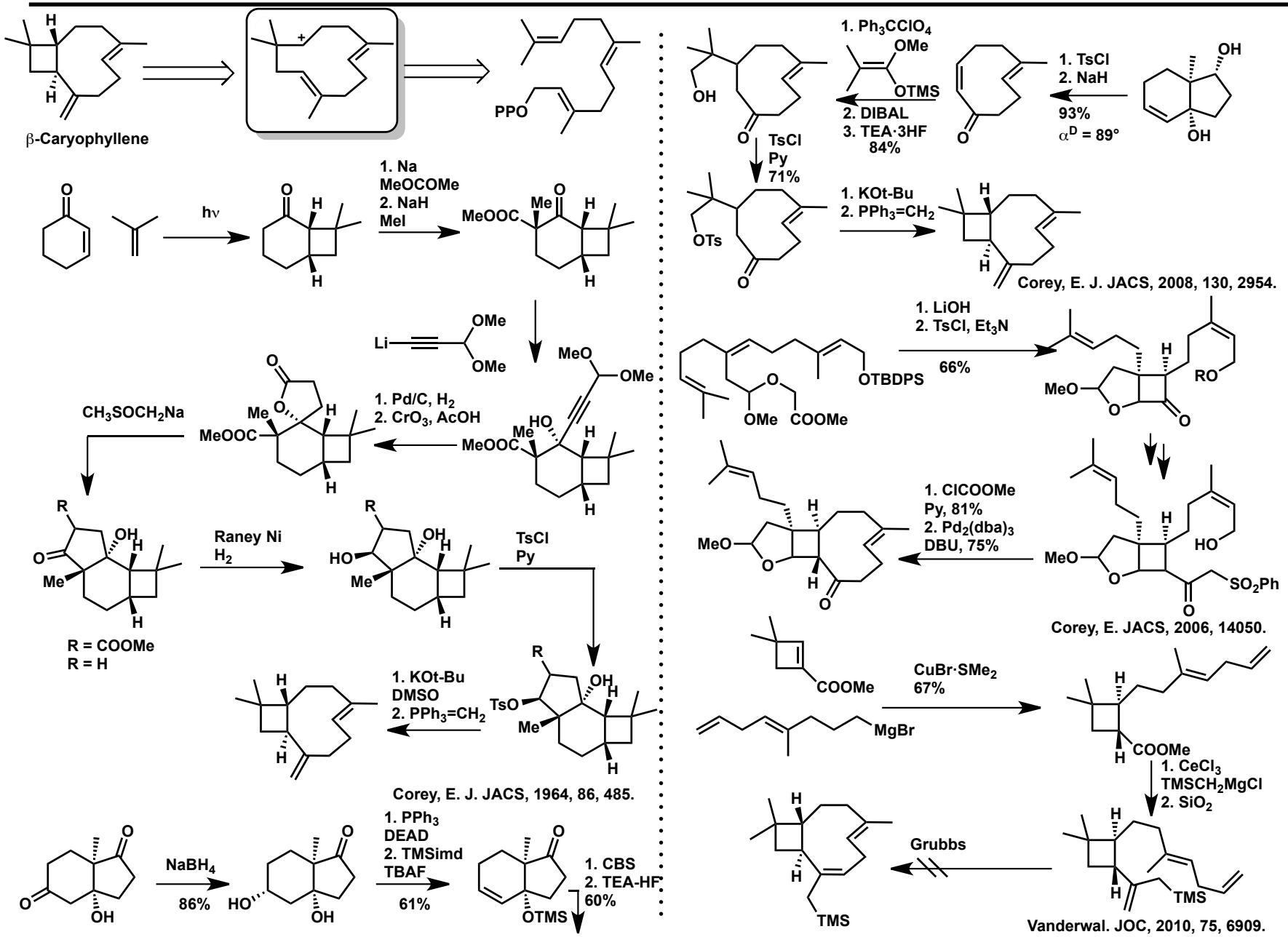
β-Caryophyllene
PPO
hν
1. Na
MeOCOMe
2. NaH
MeI
Li
OMe
OMe
1. Pd/C, H2
2. CrO3, AcOH
CH3SOCH2Na
R = COOMe
R = H
Raney Ni
H2
TsCl
Py
1. KOt-Bu
DMSO
2. PPh3=CH2
Corey, E. J. JACS, 1964, 86, 485.
NaBH4
86%
1. PPh3
DEAD
2. TMSimd
TBAF
61%
1. CBS
2. TEA-HF
60%
1. Ph3CClO4
2. DIBAL
3. TEA·3HF
84%
1. TsCl
2. NaH
93%
αD = 89°
TsCl
Py
71%
1. KOt-Bu
2. PPh3=CH2
Corey, E. J. JACS, 2008, 130, 2954.
1. LiOH
2. TsCl, Et3N
66%
OTBDPS
OMe COOMe
1. ClCOOMe
Py, 81%
2. Pd2(dba)3
DBU, 75%
Corey, E. JACS, 2006, 14050.
CuBr·SMe2
67%
MgBr
1. CeCl3
TMSCH2MgCl
2. SiO2
Grubbs
TMS
Vanderwal. JOC, 2010, 75, 6909.

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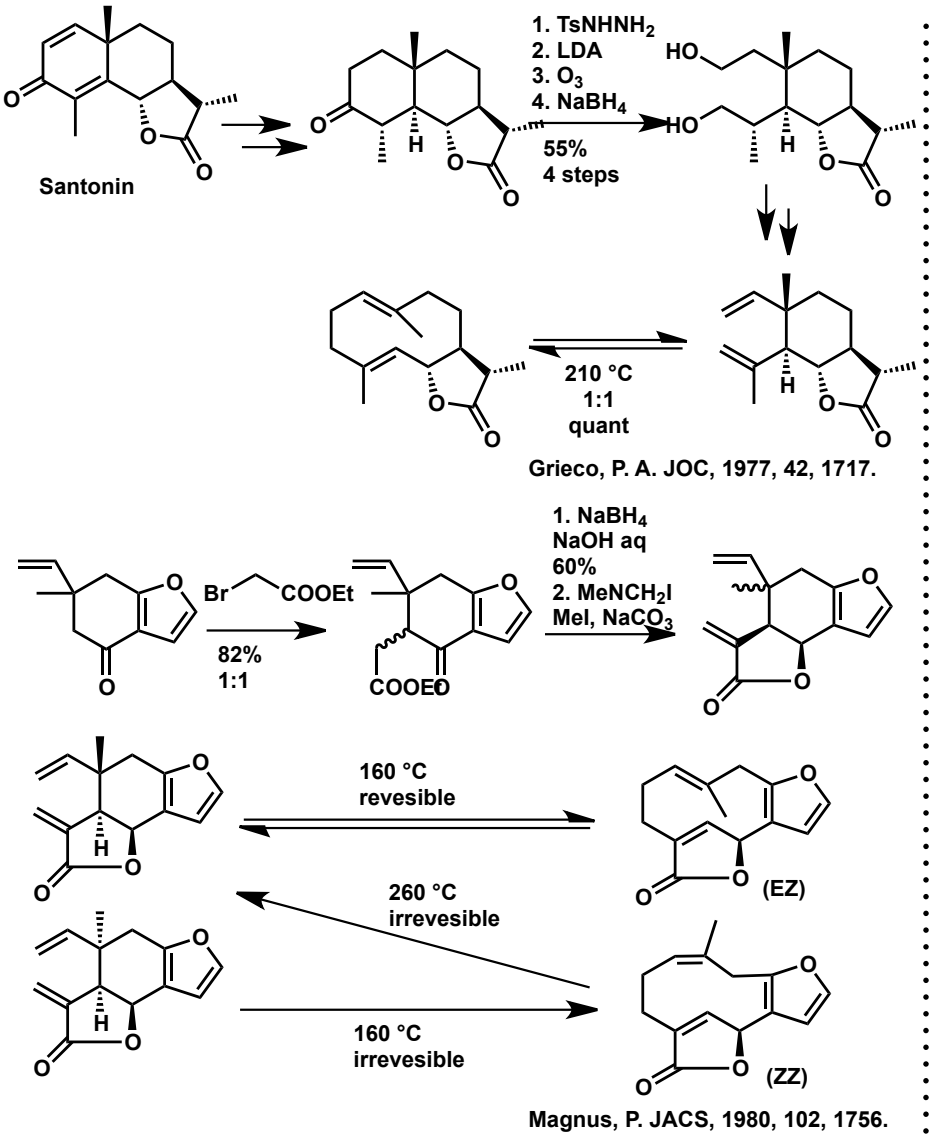

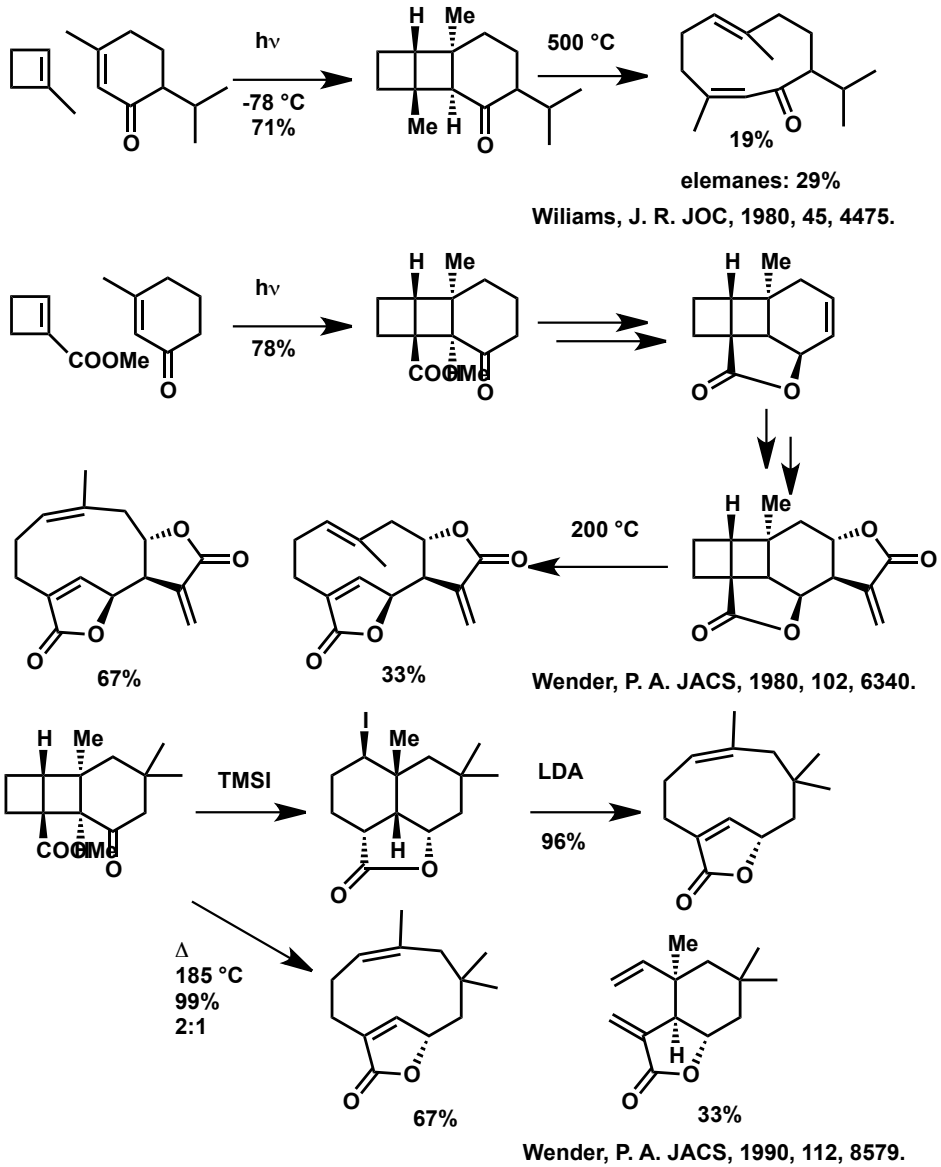

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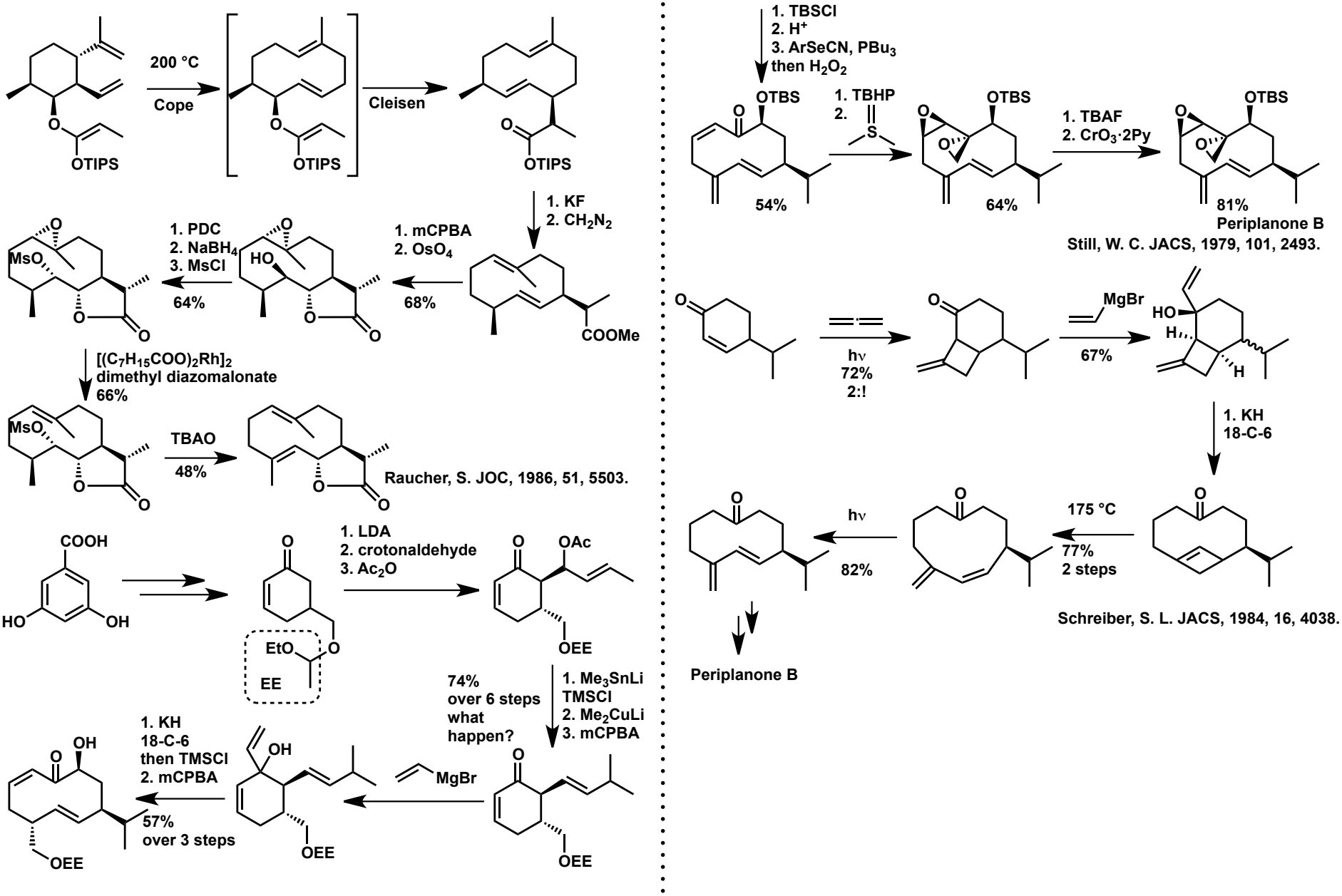
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