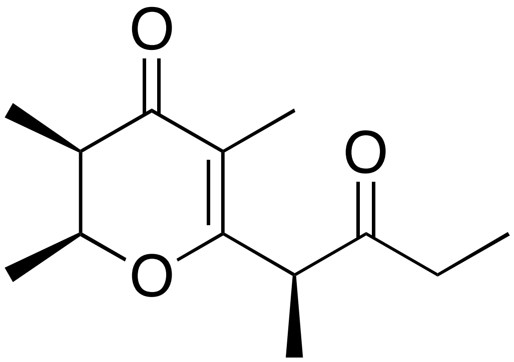
Synthesis of (±)-*epi*-Stegobinone Utilizing Silacyclopropanes as Synthetic Intermediates

Calad, S. A.; Cirakovic J.; Woerpel, K.A. ***J. Org. Chem.*** **2007,** ***72*****, 1027-1030.**



Presented by Melissa Sprachman, 1/29/07

Presentation Overview

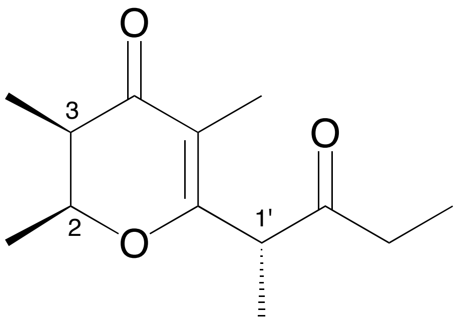
*Background and Significance

*Brief Insight into Woerpel's Silacyclopropane Methodology

*Woerpel Group Synthesis of (±)-*Epi*-Stegobinone

*Brief Comparison to Another Stegobinone Synthesis

Stegobinone Background



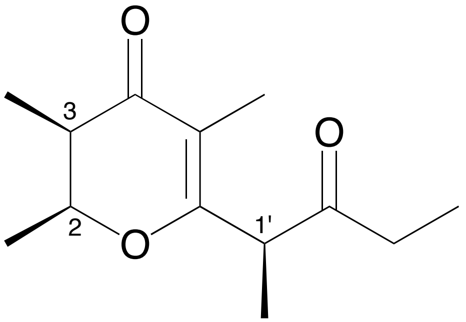
(2*S*, 3*R*, 1'*R*)-Stegobinone

-Sex pheremone produced by the female drugstore beetle

-Absolute configuration determined by stereocontrolled synthesis (Hoffmann, 1979: *Tetrahedron Lett.* **1979**, 4653-4656).

Image © Degesch

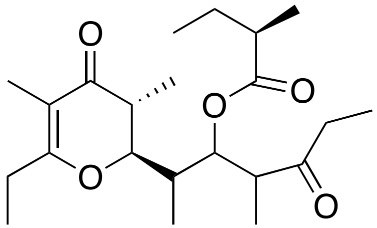
Stegobium paniceum (Linnaeus)



(2*S*, 3*R*, 1'*S*)-Stegobinone

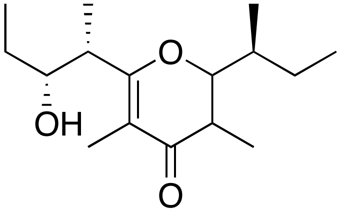
-Epimer of Stegobinone; repellent to the male of the species

Polypropionate Natural Products



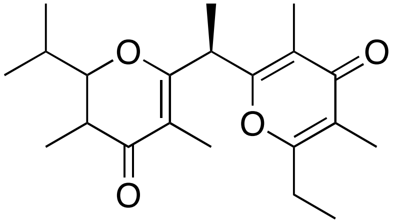
Membrenone-A
isolated from
Pleurobranchus Membranaceus

Tetrahedron Lett. **1993**, *34*, 6791-6794



(-)-Maurenone
Isolated from
Siphonaria maura

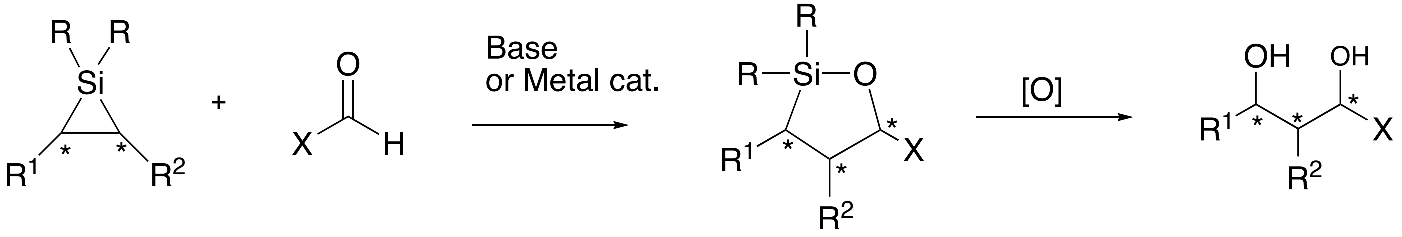
Recent synthesis reported by Perkins:
J. Org. Chem. **2006**, *71*, 117-124.



Vallartanone A
Isolated from
Siphonaria maura

J. Org. Chem. **1989**, *54*, 5374-5377

Silacyclopropane Insertion Methodology



-Takes advantage of strain energy release:

$SE_{silacyclopropane}$ = 40.5 kcałmol [*J. Phys. Chem.* **1989**, *93*, 1584-1585]

-Stereoselective: stereochemistry of the initial silacyclopropane species is retained

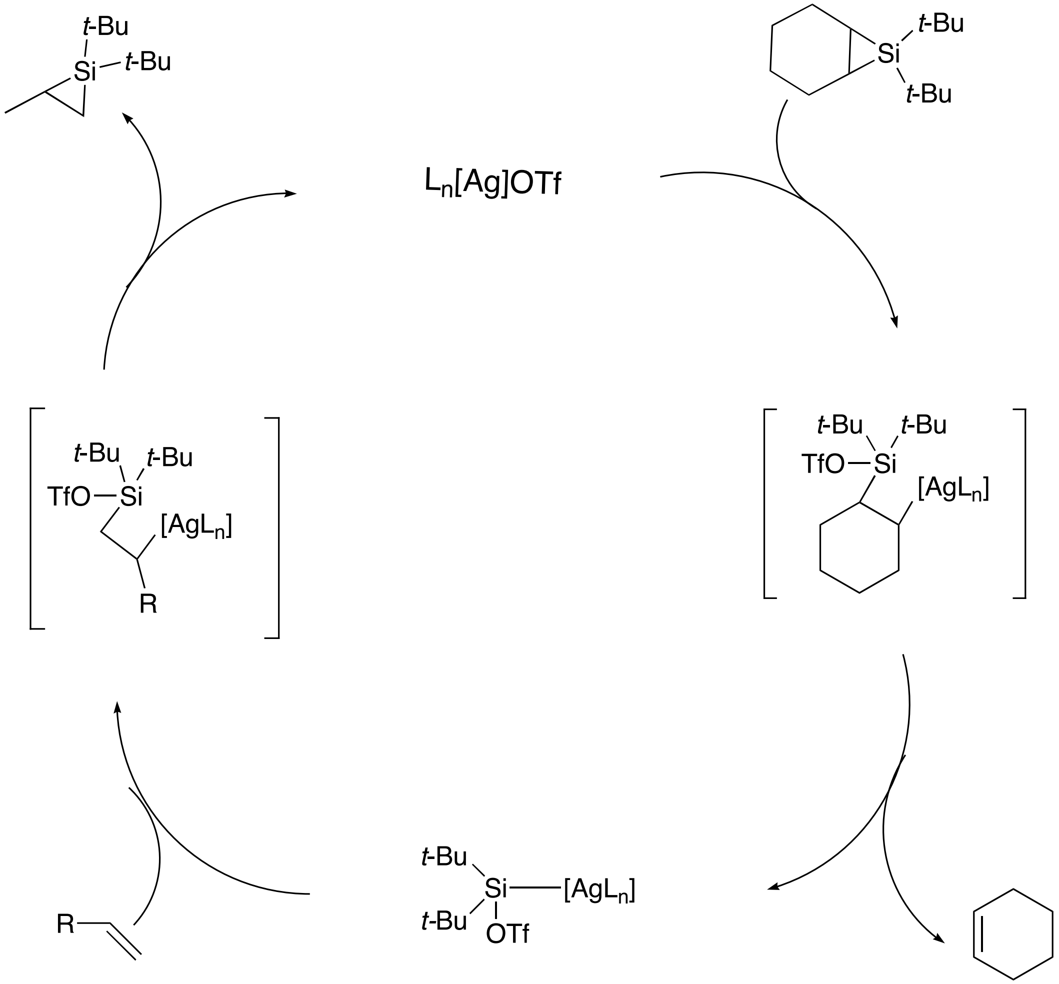
-Regioselective: dependent on metal catalyst

-Copper salts --> insertion at the more substituted carbon

-Zinc salts --> insertion at the less substituted carbon

Acc. Chem. Res. **2000**, *33*, 813-820.

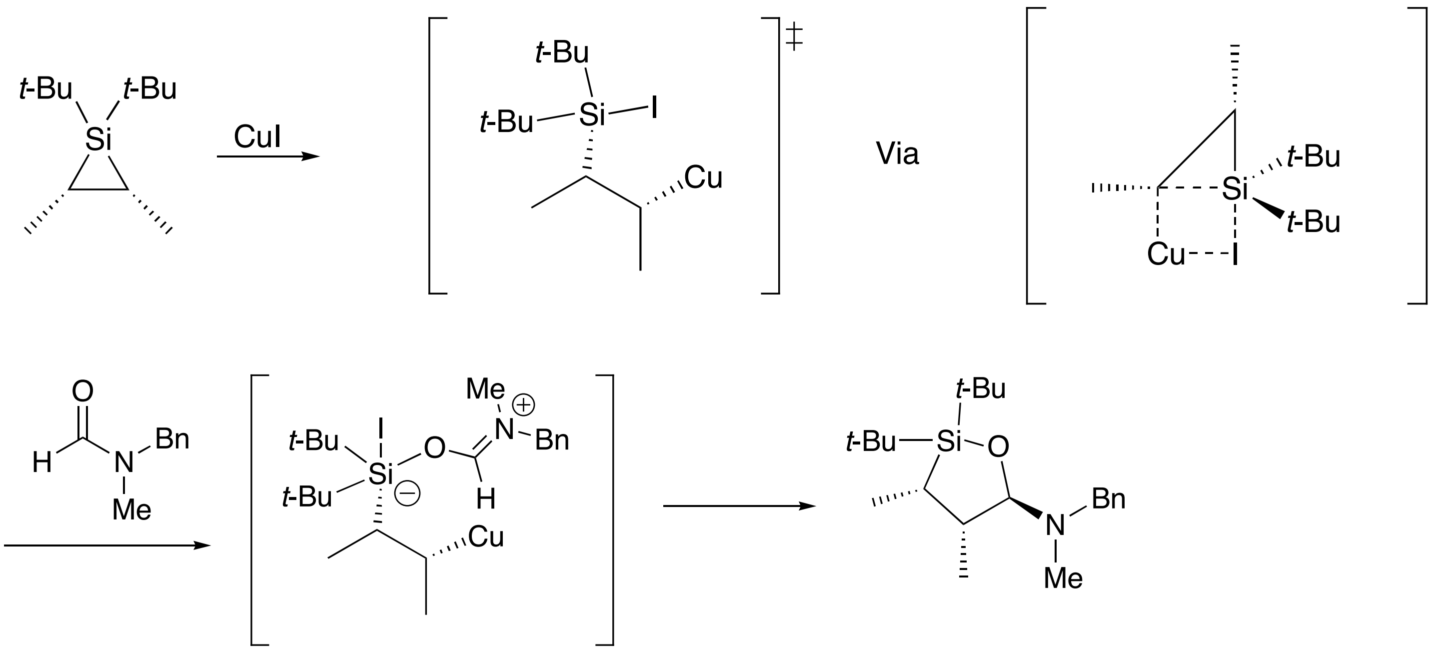
Silylene Extrusion Pathway



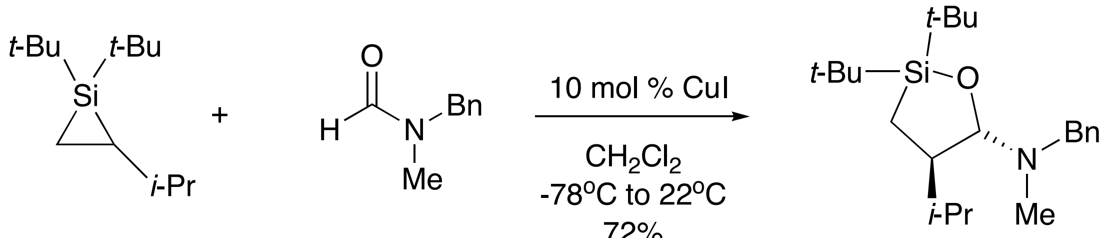
J. Org. Chem. **2004**, *69*, 4007-4012

J. Am. Chem. Soc. **2004,** *126*, 9993-10002

Copper Catalyzed Carbonyl Insertion



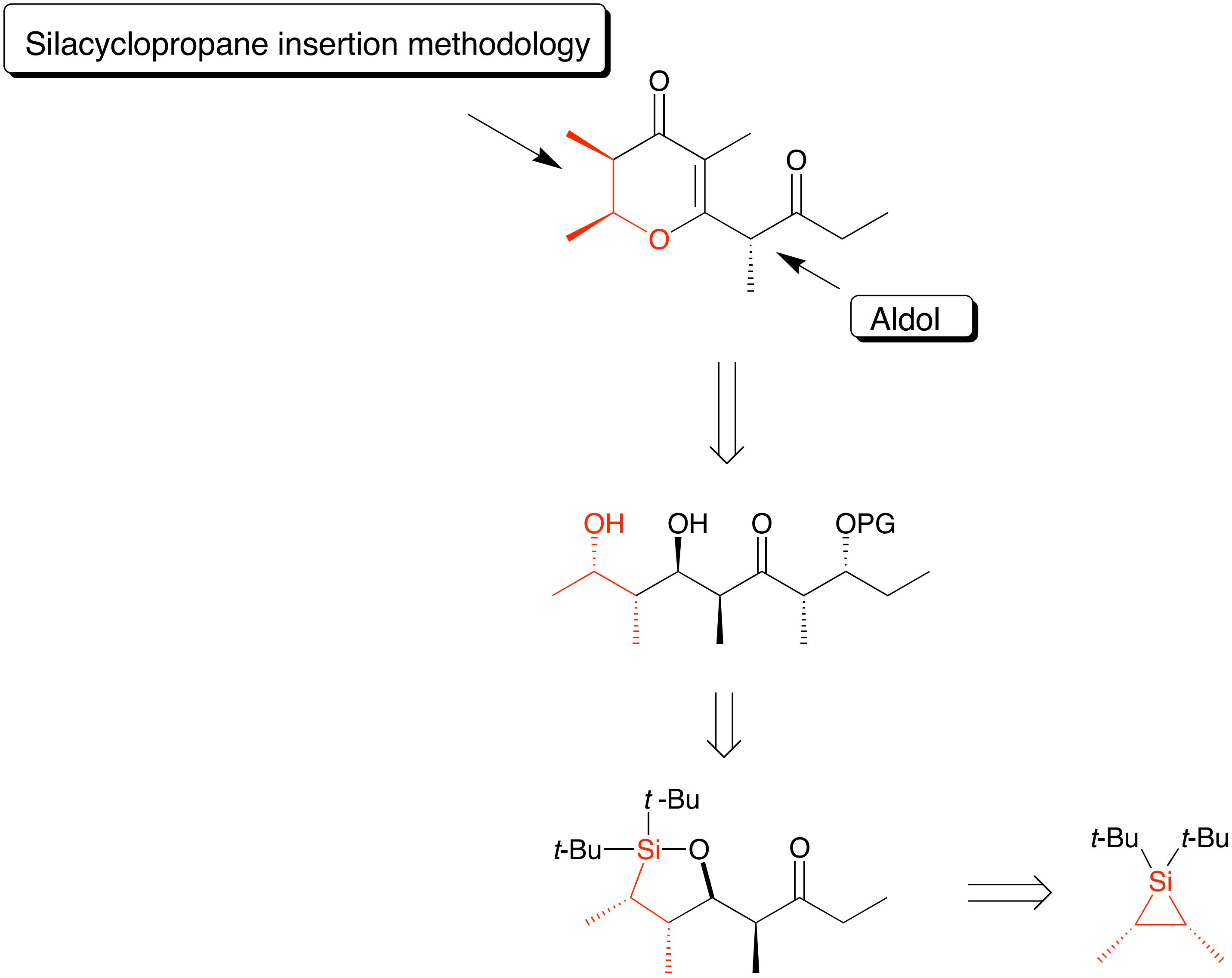
Example of Regioselectivity:



one stereoisomer
> 99:1 regioselectivity

Acc. Chem. Res. **2000**, *33*, 813-820

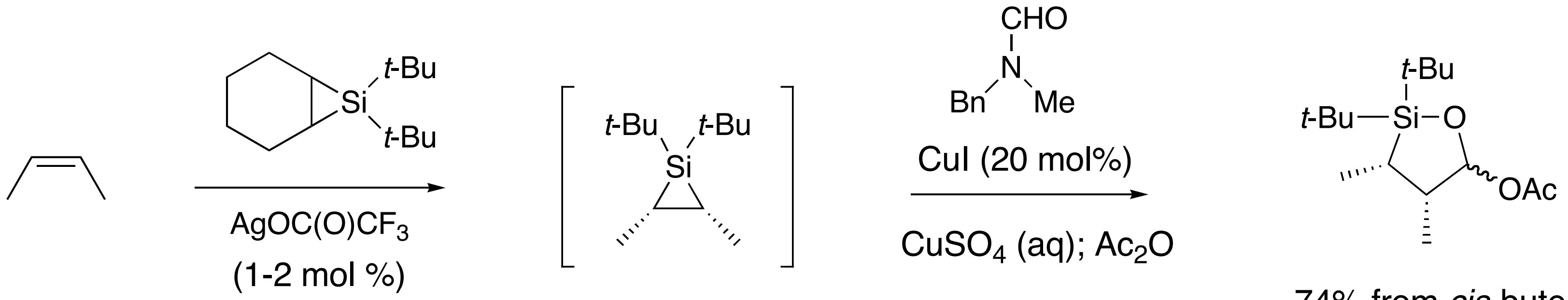
Retrosynthetic Analysis



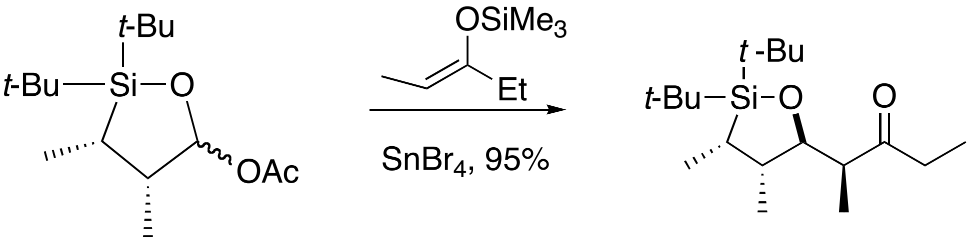
Silacyclopropane insertion methodology

Aldol

Synthesis of (±)-*Epi*-Stegobinone by Woerpel and Coworkers

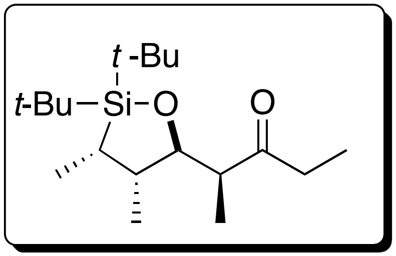


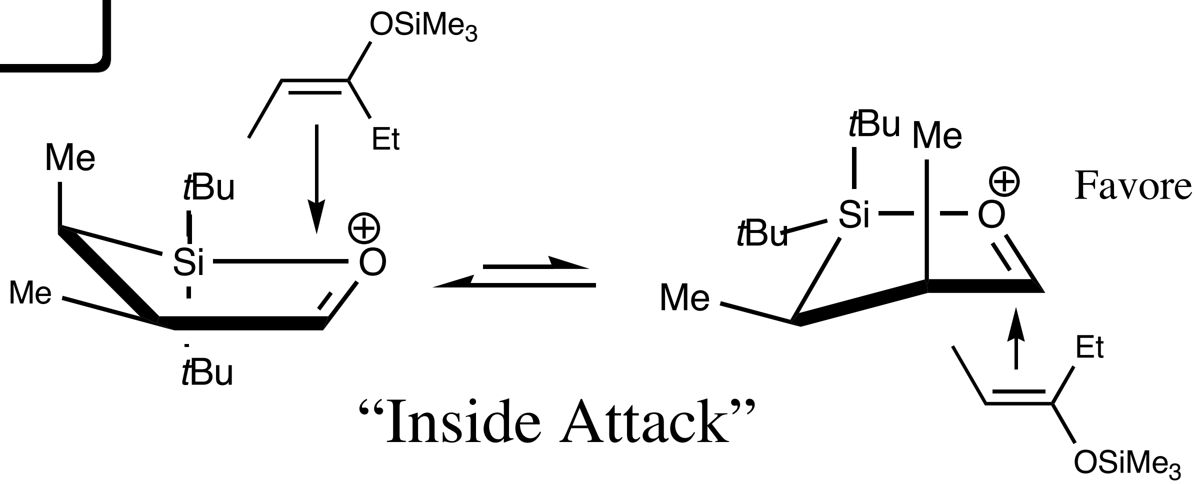
74% from *cis*-butene



97:2:1 dr

Explanation of Selectivity of the Enol Silane Addition

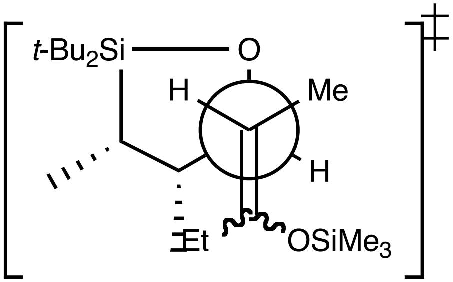




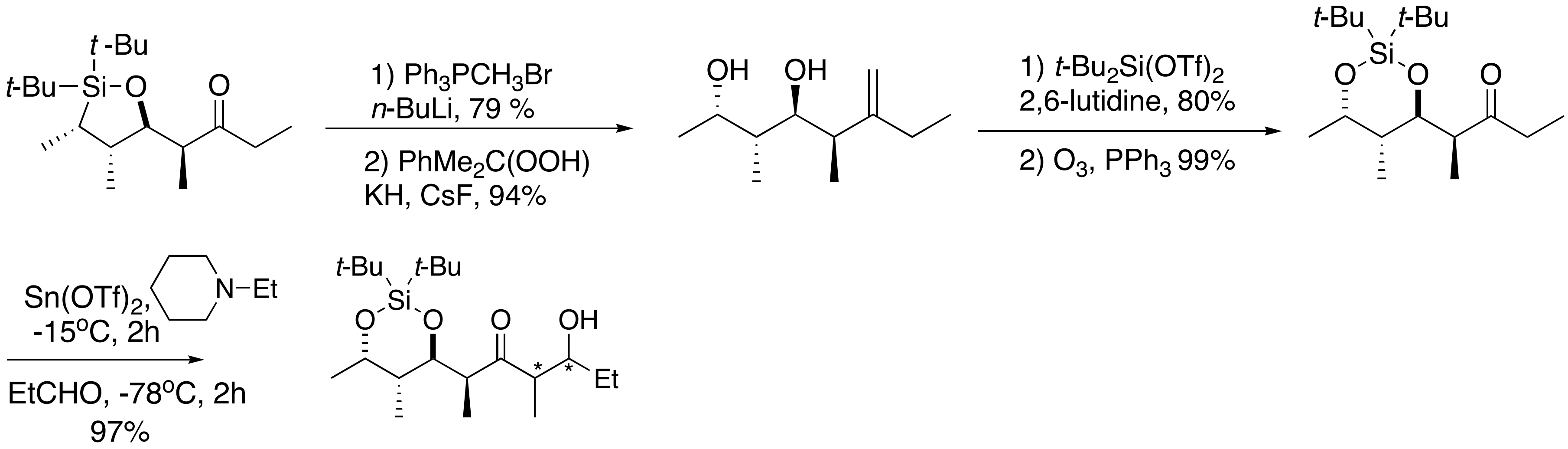
Favored TS

"Inside Attack"

Nucleophilic approach through an antiperiplaner TS

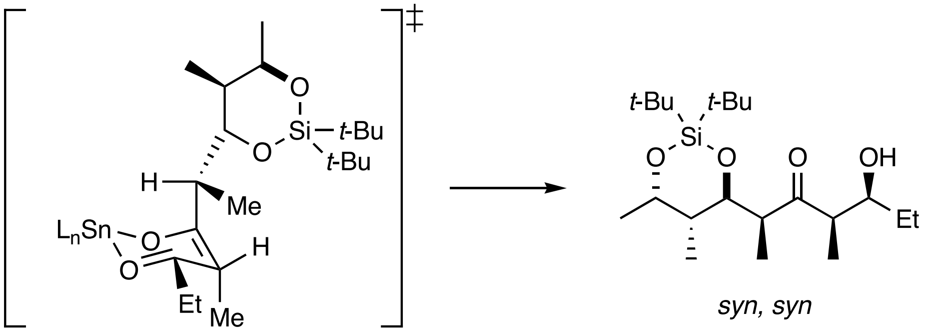


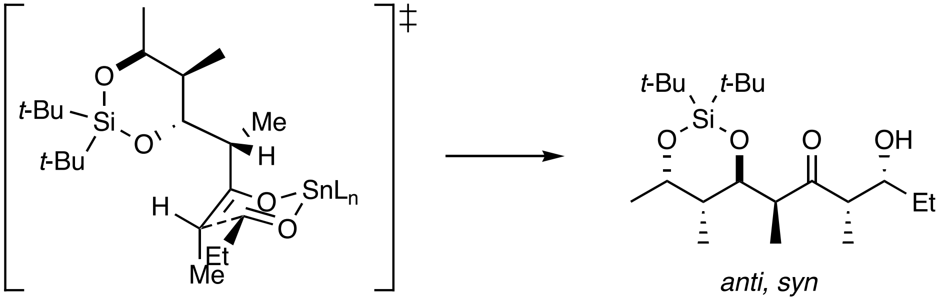
J. Org. Chem. **2002**, *67*, 2056-2064.



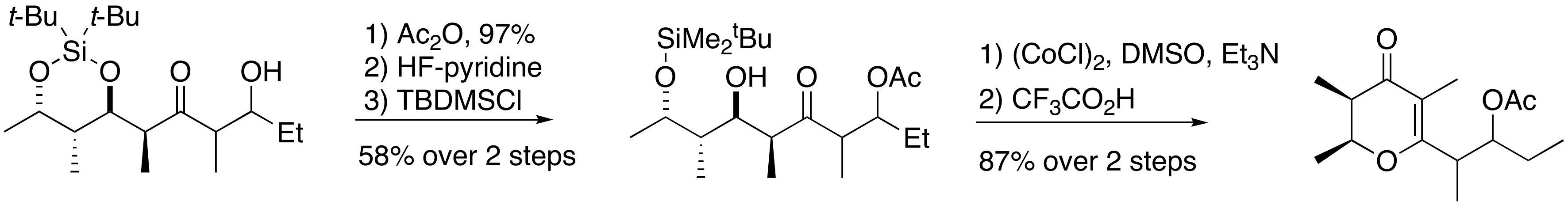
85:15 dr

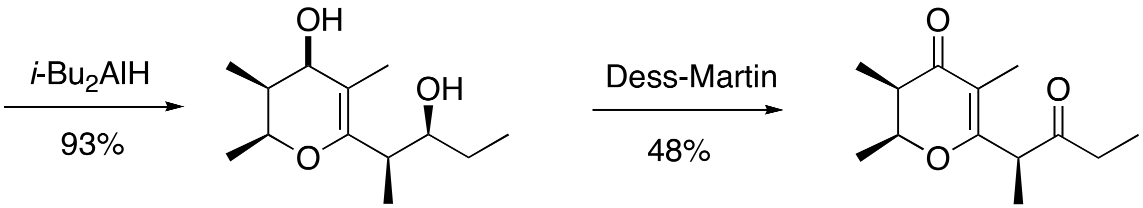
Proposed Aldol Transition States :





Completion of Synthesis and Stereochemical Determination





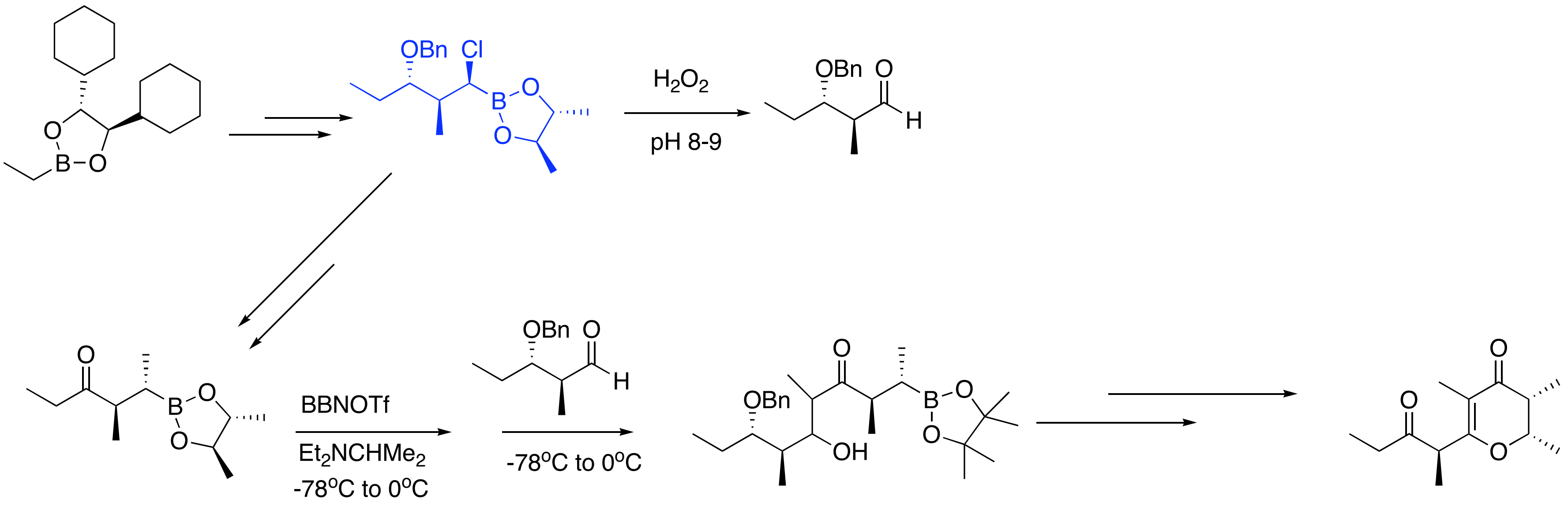
X-Ray Crystal Structure Confirmed the Indicated Stereochemical Relationship

17 Steps, 8.8% Overall Yield

Brief Overview of Another Stegobonine Synthesis

Matteson et al. *J. Am. Chem. Soc.* **1996**, *118 4560-4566*

-Achieved asymmetric synthesis of the natural epimer Stegobinone, deriving all stereocenters from a chloro boronic ester intermediate species:



18 steps, 12.5% overall yield (no ee's listed)

Conclusions

*Woerpel and Co-workers synthesized the epimer of their target molecule in 17 steps and 8.8% yield.

*Diastereoselectivity within the synthesis was accomplished via Woerpel's silacyclopropane methodology.

*This initial success indicates that the silacyclopranes may be used as synthetic intermediates in other natural product syntheses.

*Problems involved in using the silacyclpropane methodology were revealed, namely functional group tolerance under Si-C bond oxidation conditions.