Cyclopropanes in Synthesis

J. Gallagher

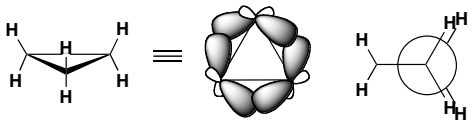
Wednesday, February 18, 2004

An Brief History of Cyclopropanes-

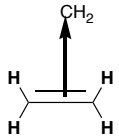
1884 First synthesis of a cyclopropane derivative by William Henry Perkin with Adolf von Baeyer's.
1896 Vinylcyclopropane synthesized by Gustavson.
1922 Existence of vinylcyclopropane secured, yet faces despite residual disbelief.
1931 Pauling describes the banana bonding model of cyclopropane
1942 Cyclopropanol synthesize by Cottle.
1947 Walsh describes cyclopropane as a coordinate bond between ethylene and :CH_2
1952 Hexafluorocyclopropane generated by TFE photolysis.
1954 Doering et al. find dichlorocarbene adds into alkenes to generate *gem*-dichlorocyclopropane.
1957 Triphenyl cyclopropenylium perchlorate synthesized byr Breslow, constituting the smallest aromatic species possible.
1958 Simmons and Smith determine that iodoalkylzinc species are capable of cyclopropanation.
1964 Wittig elaborates diazoalkanes as an alternative to iodoalkane precursors oforganozinc species.

Physical Descriptions of Cyclopropane-

-Pauling's sp^3, "banana" bonded cyclopropane: This model suggests that sp^3 hybridized carbons give rise to a stable, trigonal planar arrangement. Further instability is inferred as all hydrogens are eclipsed.

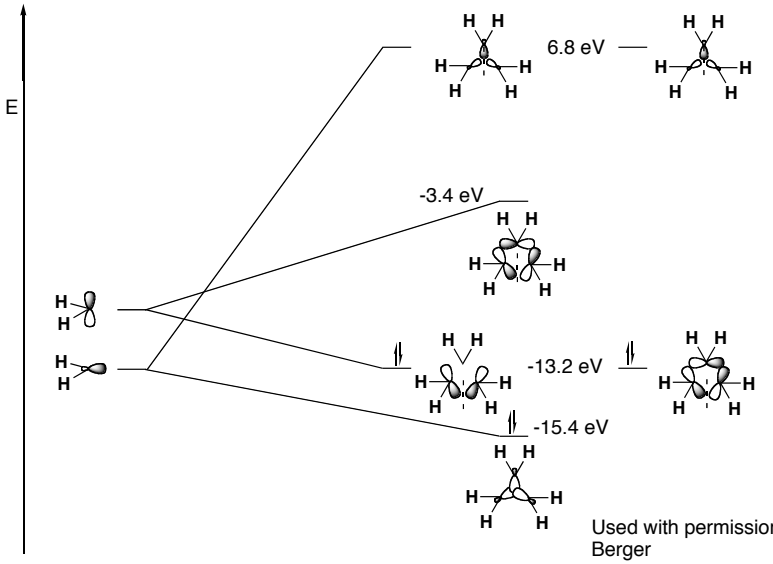


-Walsh cyclopropane description: In an analogy to epoxides, A.D. Walsh proposed that cyclopropanes be considered as an insertion of methylene into ethylene, ultimately giving rise to the D_{3h} symmetric product.



Thus, Walsh cyclopropane has significant sp^2 character and should react in analogy to olefins; further, as reactivity is generally governed by HOMO-LUMO chemistry, one can also see why Walsh cyclopropane has a propensity to open, yet while it is also a stable compound. The dative bond suggestion was immediately hated by the British chemical community, with Sir. R. Robinson leading the criticism. Walsh's suggestions had been picked apart due to his suggestion of subtle similiarities between ethylene oxide/cyclopropane and N-oxide species, ethylene, and the relationship between chemical character and depiction. Experimental support, however, was presented a year later for cyclopropane's olefinic character, strengthening Walsh's hypothesis.

Walsh Oribital Energies



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Outline of Cyclopropanes in Synthesis:

- Stereocontrol via cyclopropanation:
- Corey's syntheses of (±)-Atractyligenin and (±)-Cafestol
- Smith's synthesis of (±)-MycorrhizinA and (±)-Dechloromychorrhizin A

- Cyclopropanes as equivalents or masked groups:
- Danishefsky's synthesis of Epothilone A
- Carreira's synthesis of (–)-Spirotryptostatin and (±)-Horsfilin

- Synthesis of unusual cyclopropanated natural products:
- Barrett's synthesis of FR-900848
- Falck's synthesis of FR-900848

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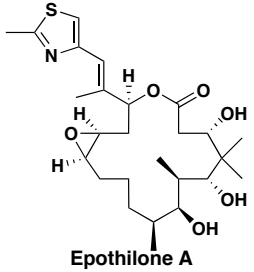
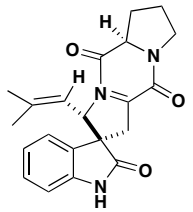
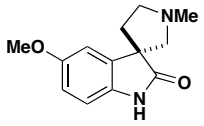
Cyclopropanes in Selected Total Syntheses:



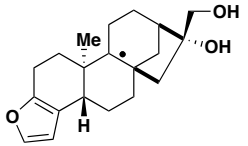
Epothilone A



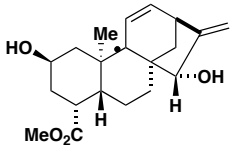
(-)-Spirotryptostatin B



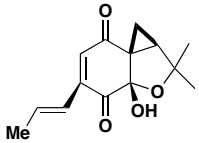
(±)-Horsfiline



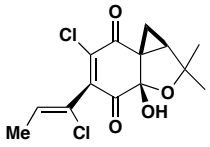
(±)-Cafestol



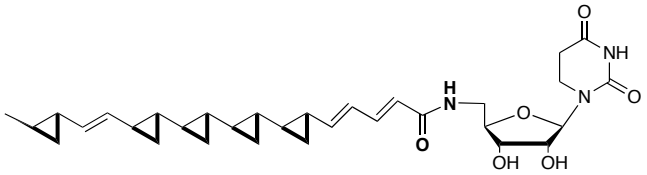
(±)-Atractyligenin



(-)-Dechloromycorrhizin

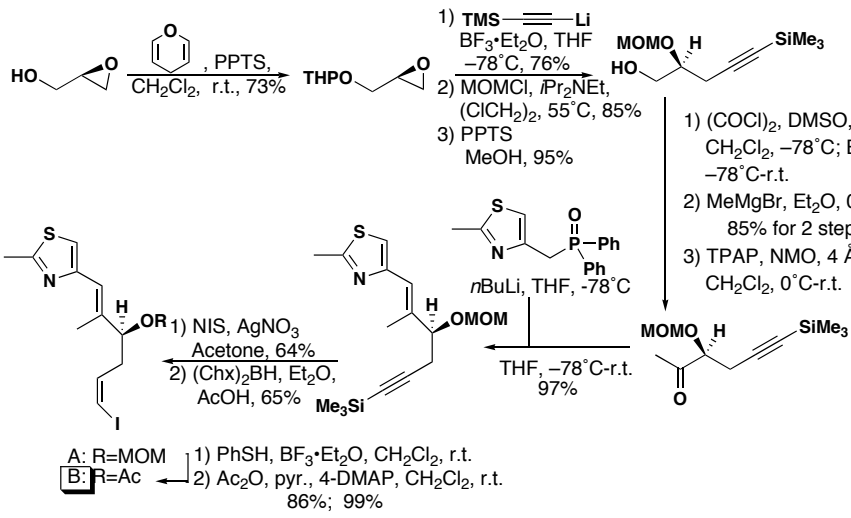


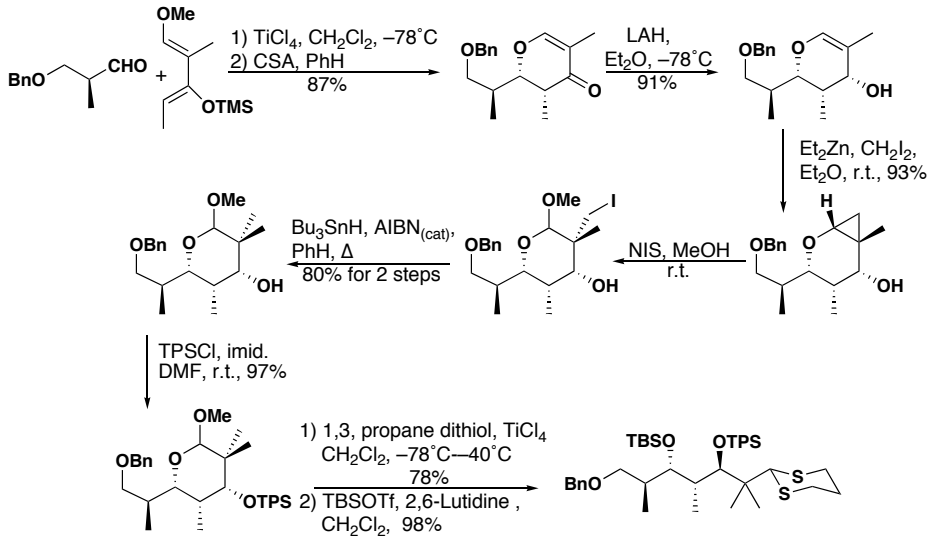
(-)-Mycorrhizin



FR-900848

Epothilone A: Danishefsky et al., JACS, **1997**, 10073





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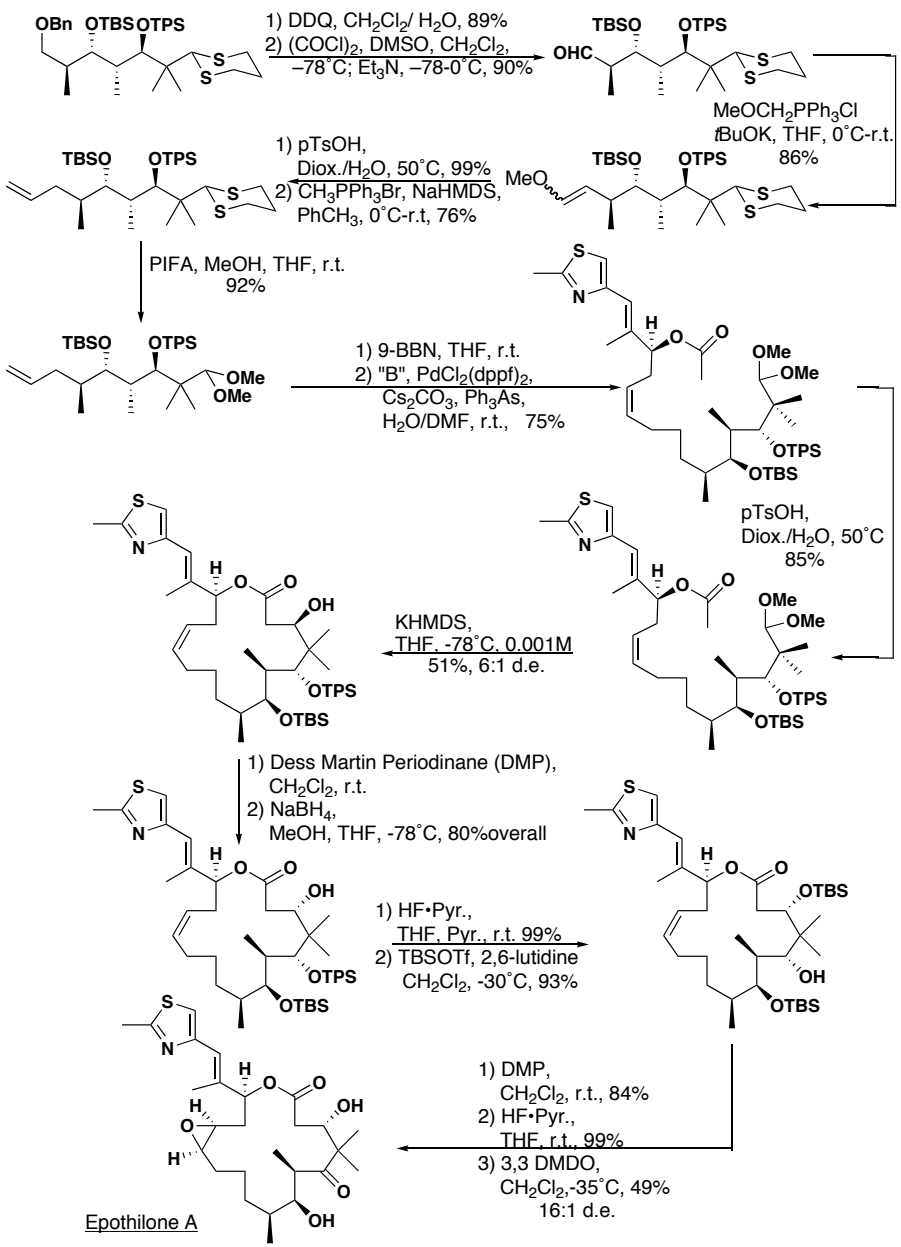
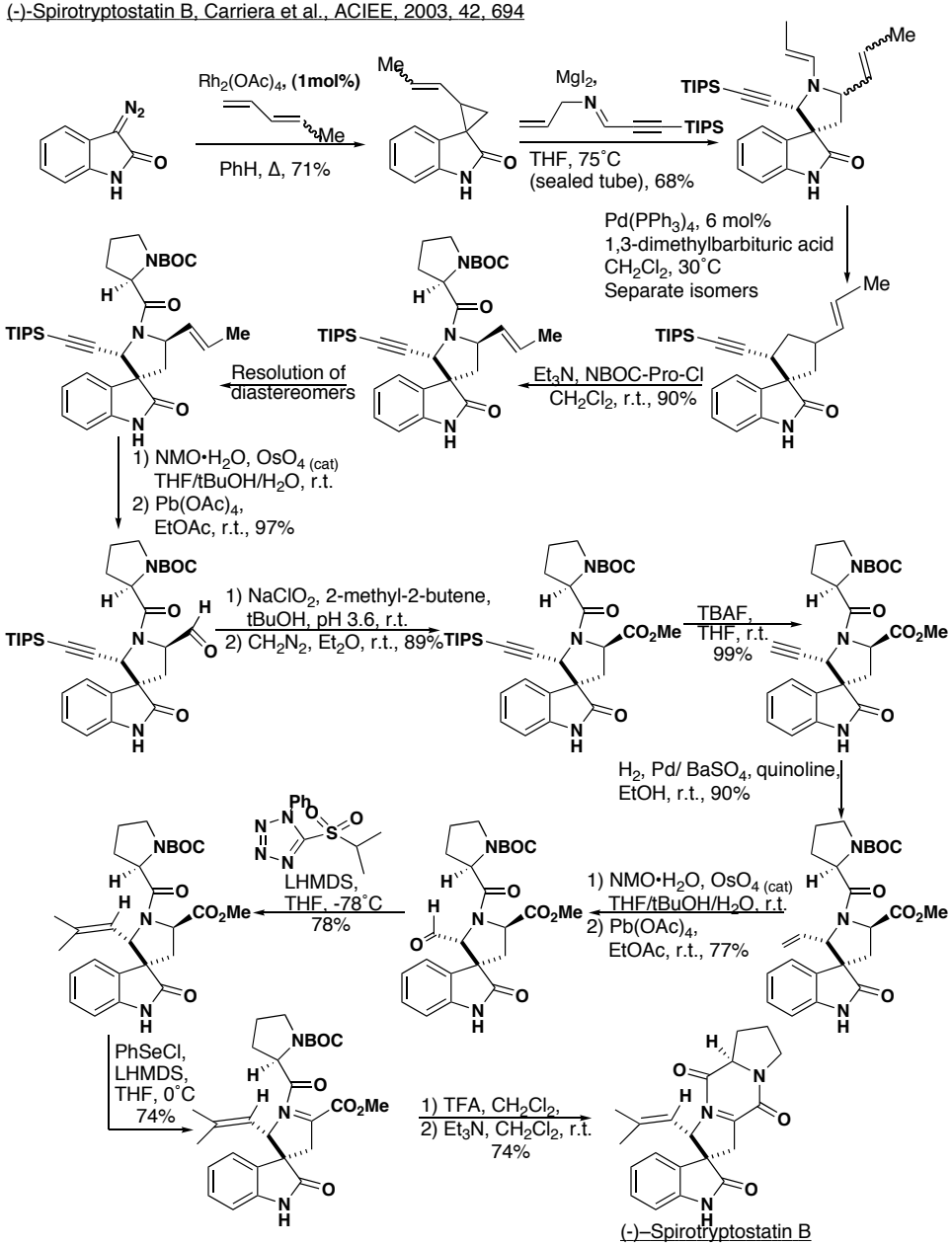


(-)-Spirotryptostatin B, Carriera et al., ACIEE, 2003, 42, 694



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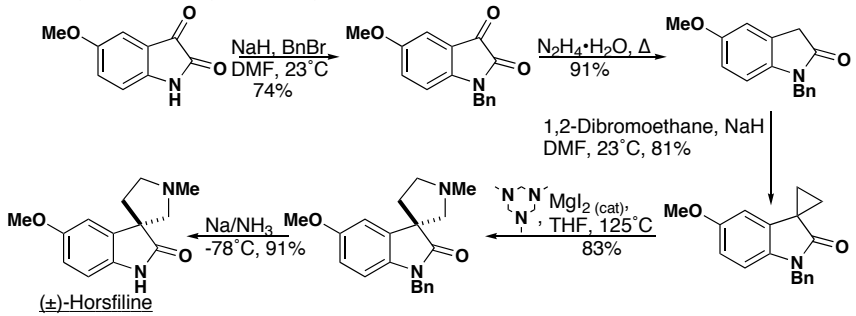
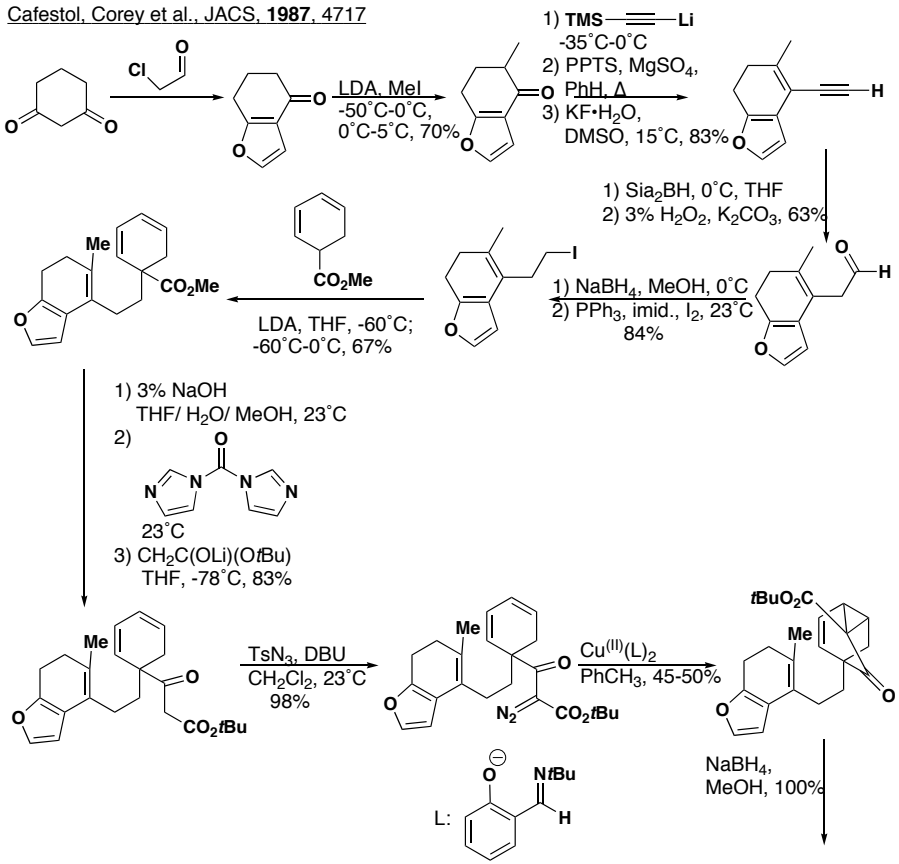
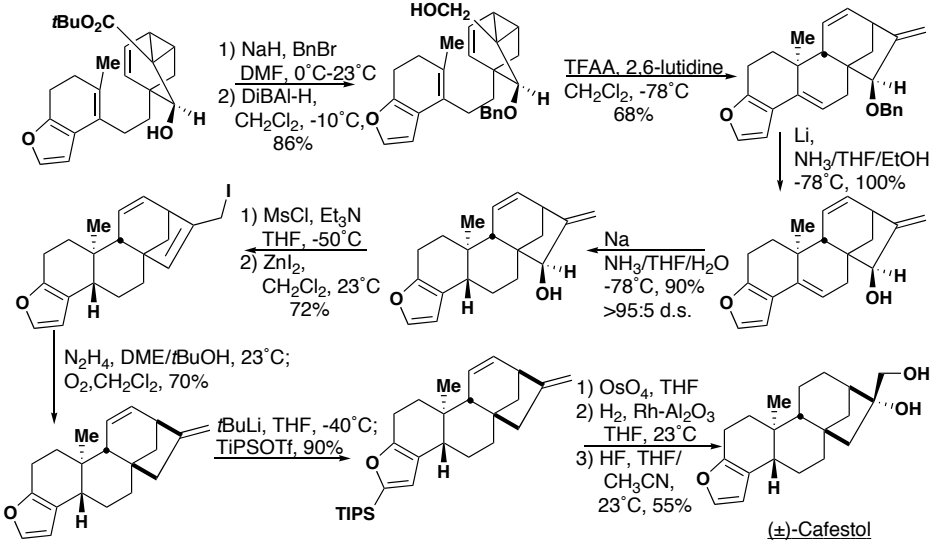
Horsfiline, Carriera et al., HCA 2000, 1175

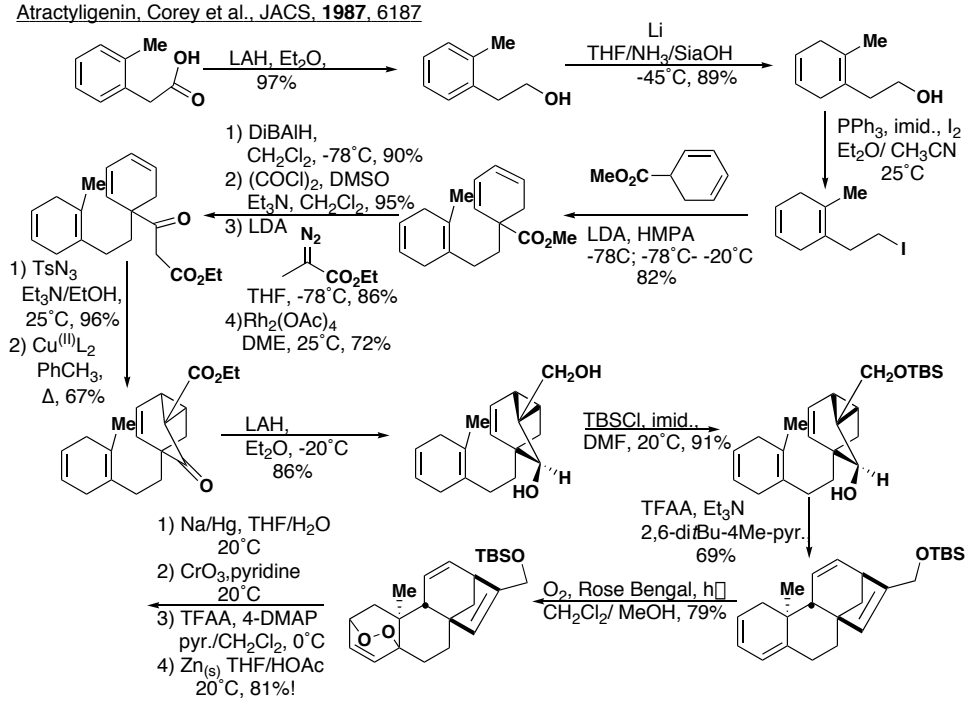


Cafestol, Corey et al., JACS, **1987**, 4717





Atractyligenin, Corey et al., JACS, **1987**, 6187



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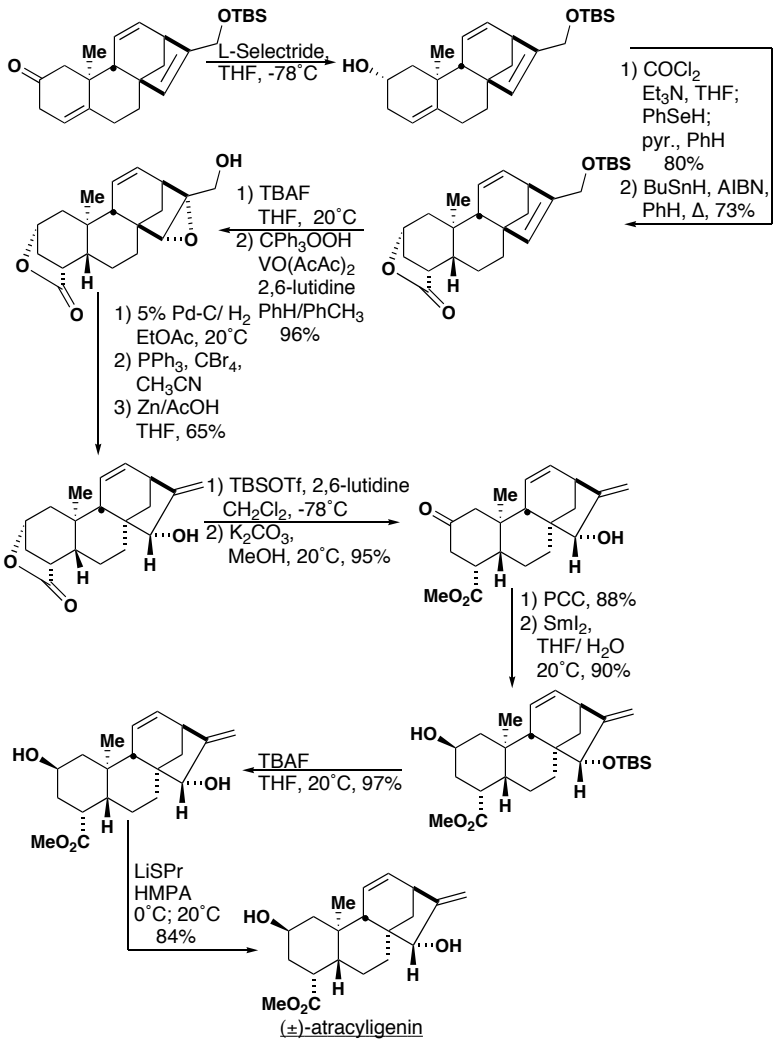
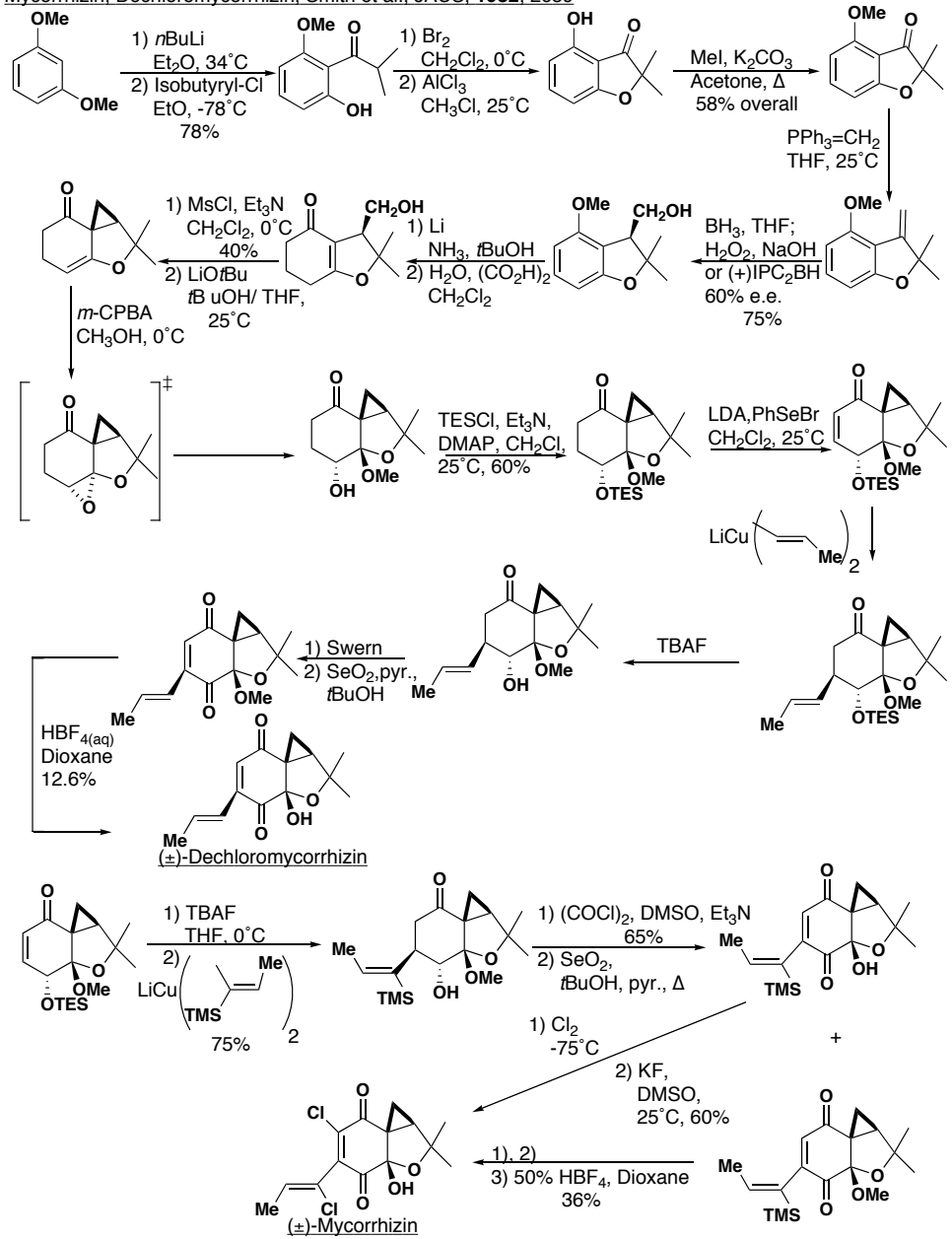


Mycorrhizin, Dechloromycorrhizin, Smith et al., JACS, **1982**, 2659



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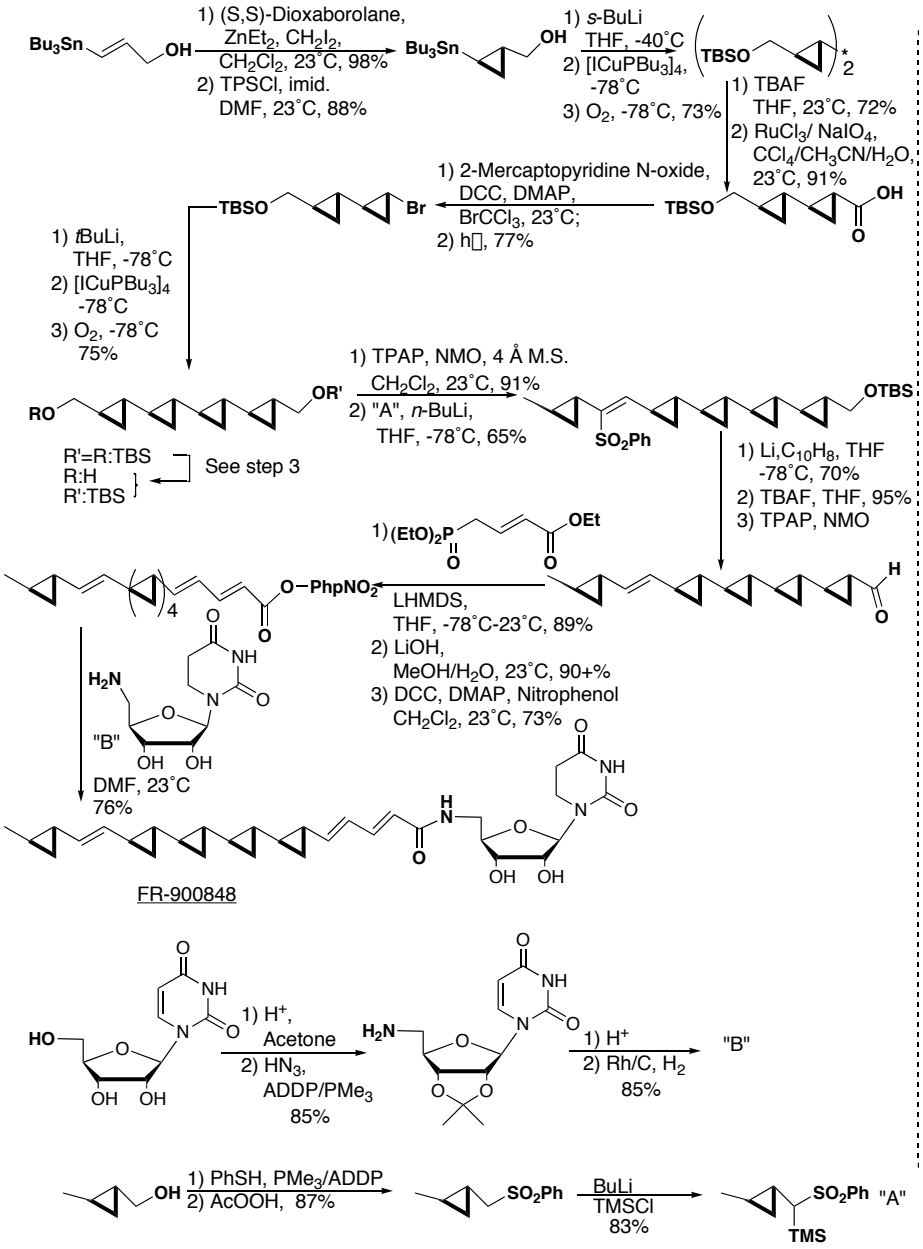
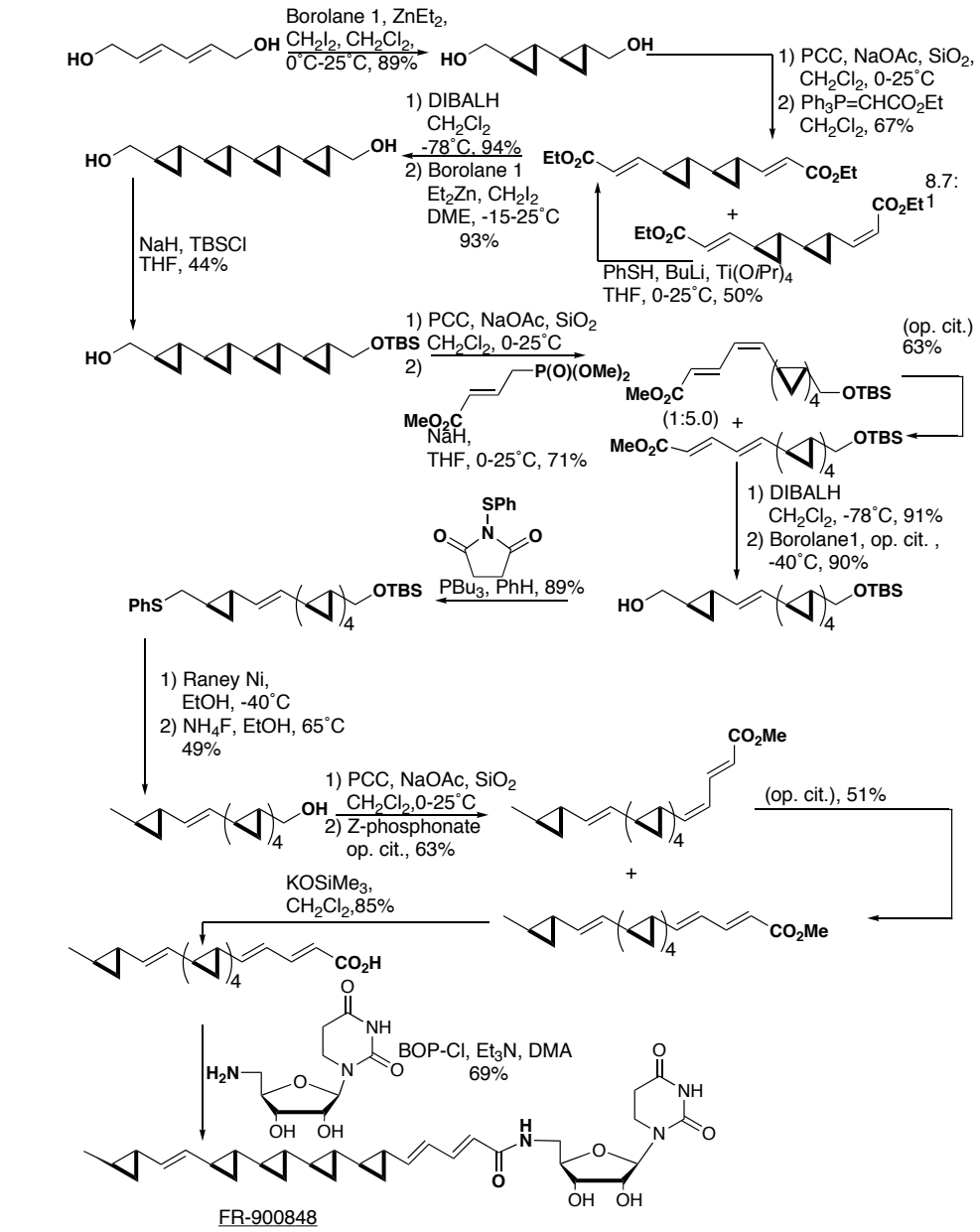
FR-900848, Falck et al. JACS **1996**, 6096



FR-900848, Barrett et al., CC, 1997, 1693