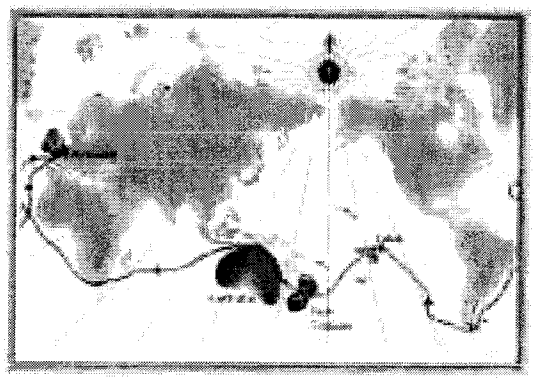
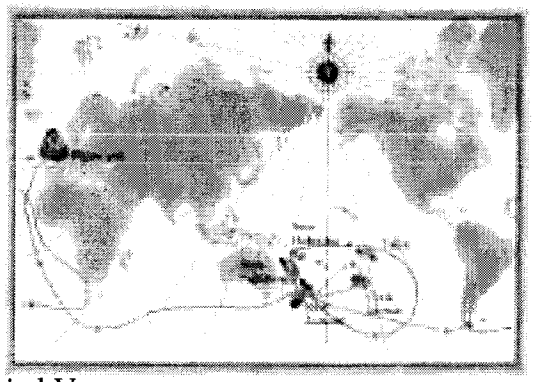
The Bounty

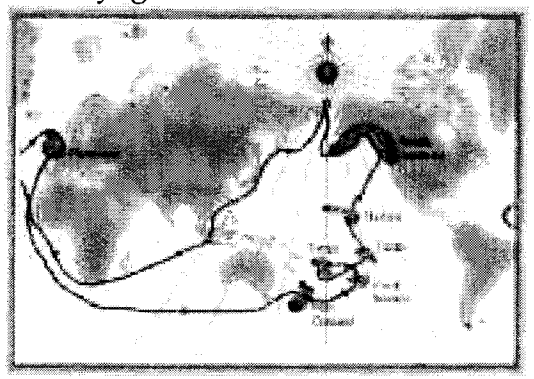
First Voyage:



Second Voyage:



Third Voyage:



Our bounty!!!!!

New Caledonia - Named by Captain James Cook (1774)because it remined him of the Scottish highland (called Caledonia by the Romans

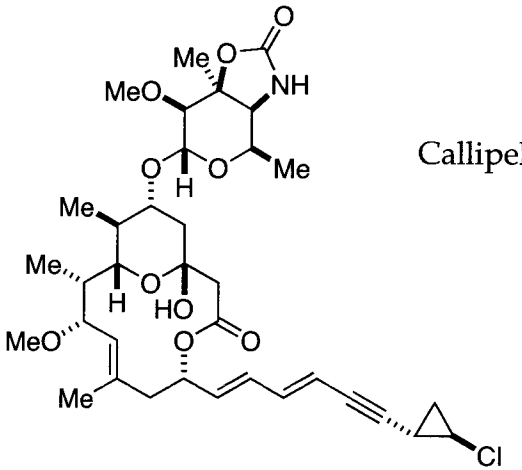
Both the French and the British claimed the island, but the French took control Under Napolean III in 1853

In 1864, the island was used as a prision, sending over 21,000 convicts.

The island is still a territory of France

Jeromy Cottell
Jan 21, 2003
(My last group mtg)

Callipeltoside A



Callipeltoside A

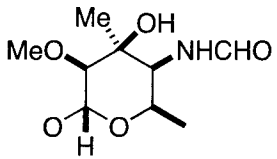
Collected between 1992-1994 off the coast of New Caledonia (5-10m depth)

-Out of 2.5 kg of the sponge *Callipelta*, 3.5 mg of macrolide was collected
-Extracted with Hex, CH_2Cl_2, and 8/2 CH_2Cl_2/MeOH

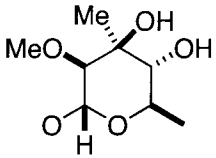
Mass spec showed $C_{35}H_{48}O_{10}NCl$
NMR corrolated and showed 12 degrees of unsaturation

Also isolated Callipeltoside B and C, as well as Callipeltin A, B, and C (cyclic polypeptides)

B) sugar =



C) sugar =



Activity: Callipeltoside A was found to inhibit the proliferation of:

Nonsmall-cell lung carcinoma (11.26 μg/mL)

P338 cells (15.26 μg/mL

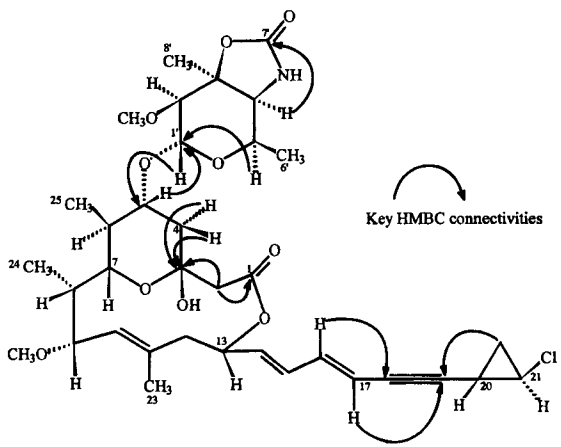
Protect *in vitro* cells infected by HIV virus

Minale *JACS*, **96**, *118*, 11085
Minale *Tet*, **97**, *53*, 3242

Stereostructure:

Structure Determination

Published structure was based on extensive NMR experiments



Callipeltoside A (1)

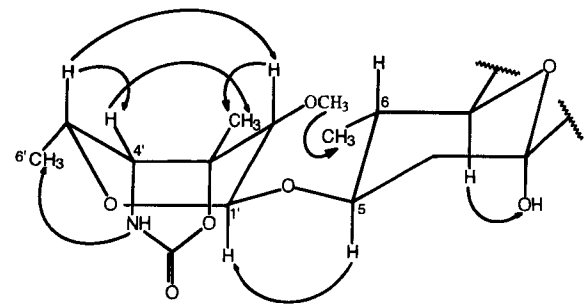


Figure 2. NOE enhancements observed for the sugar portion of callipeltoside A (**1**).

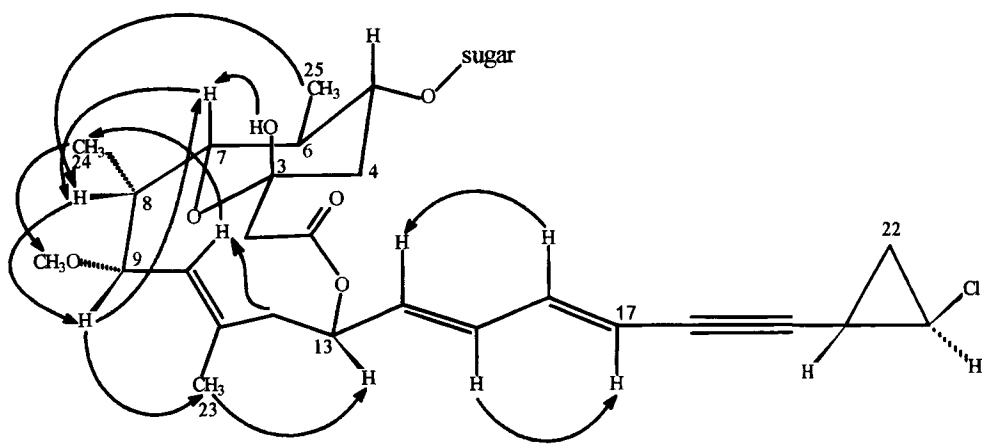
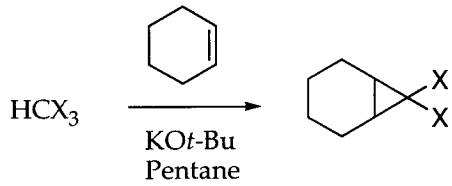


Figure 1. NOE enhancements observed in NOE difference experiments of callipeltoside A (**1**).

Preparation of Chlorocyclopropanes

Dihalocyclopropanes:



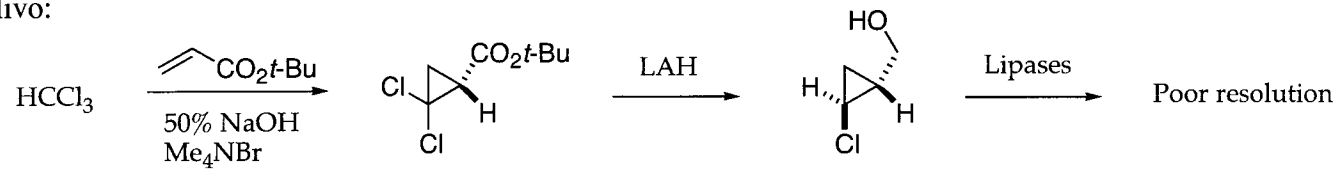
X = Cl 59%

X = Br 75%

Reaction was belived to proceed through a dihalocarbene.

Doering *JACS*, **54**, *76*, 6162.

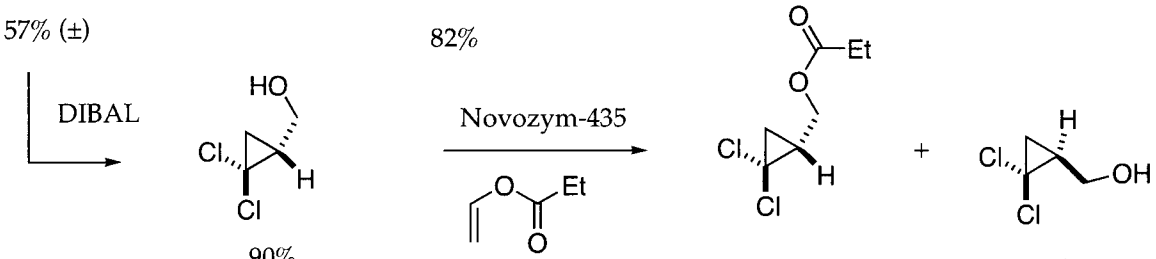
Olivo:



57% (±)

82%

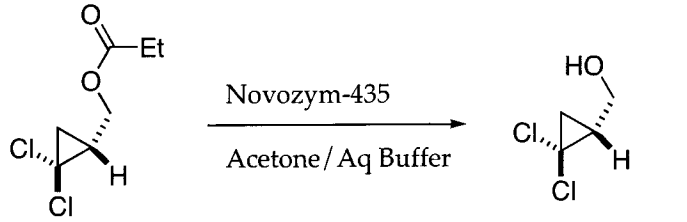
Jonczyk *JOC*, **93**, *58*, 6120



90%

57%
87/13 er

43%
> 98.5/1.5 er

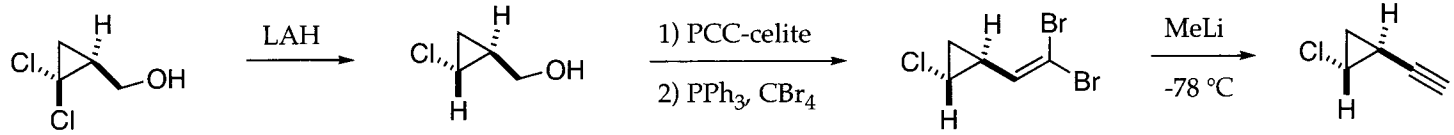


87/13 er

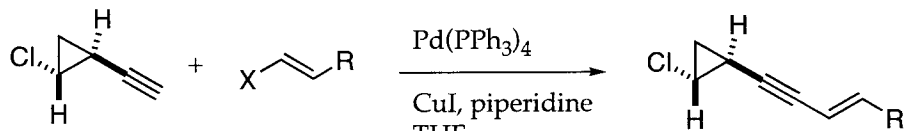
>98.5/1.5 er

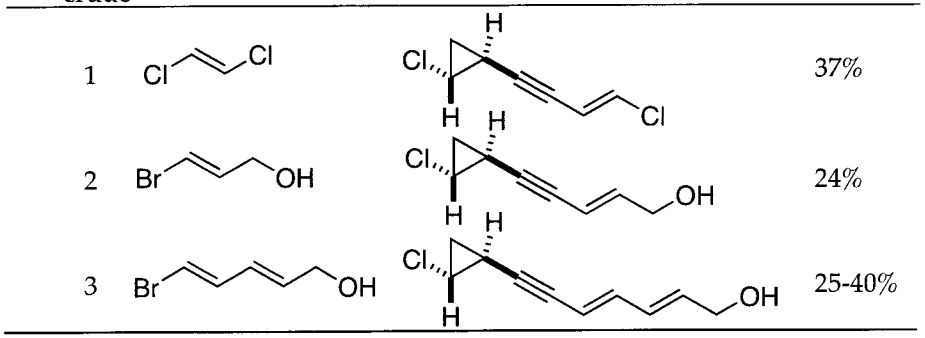
Olivo *OL*, **00**, 2, 4055

Conjugated Chlorocyclopropanes



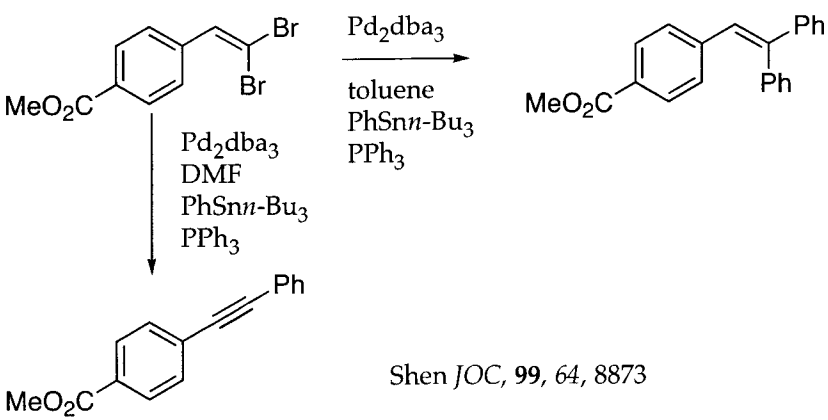
Compound was volatle and not easily purified



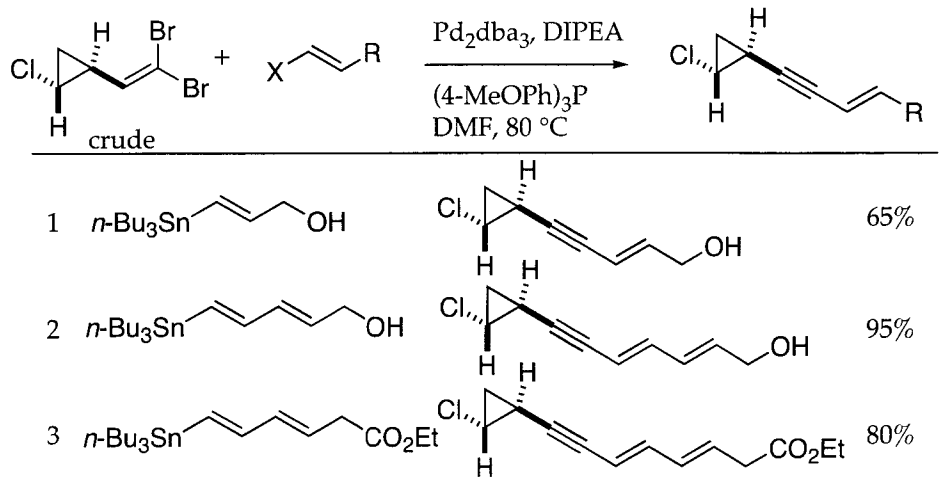


Typical Sonagashira coupling does not work well.

Shen:

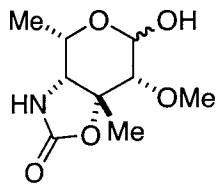


Shen *JOC*, **99**, *64*, 8873



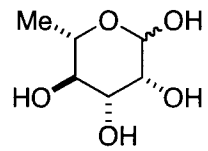
Carbohydrate synthesis

Giuliano

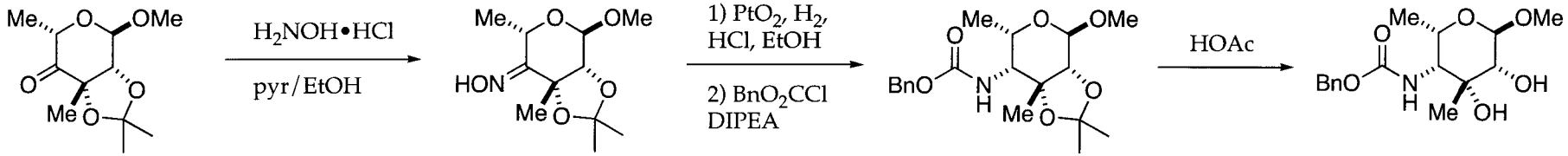


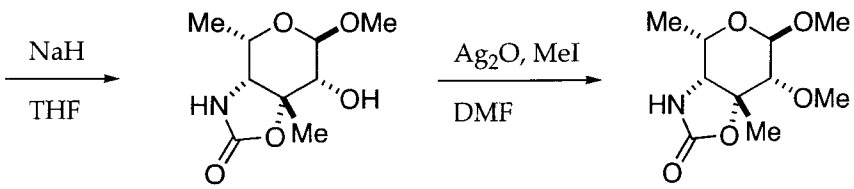
Callipeltose

Sugar is structurally related to *L*-rhamnose



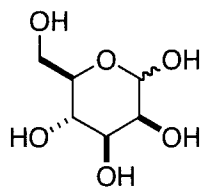
L-Rhamnose





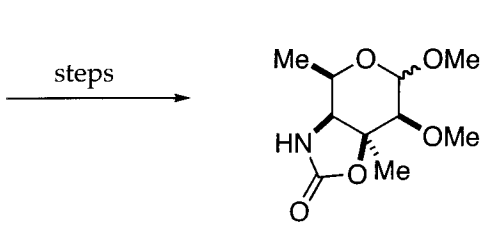
1H and 13C NMR spectroscopic data matched that of Callipeltose

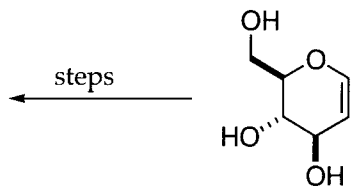
Giuliano *Carb. Res.*, **98**, *308*, 223



D-mannose

Reddy *Carb. Lett.*, **98**, *3*, 169



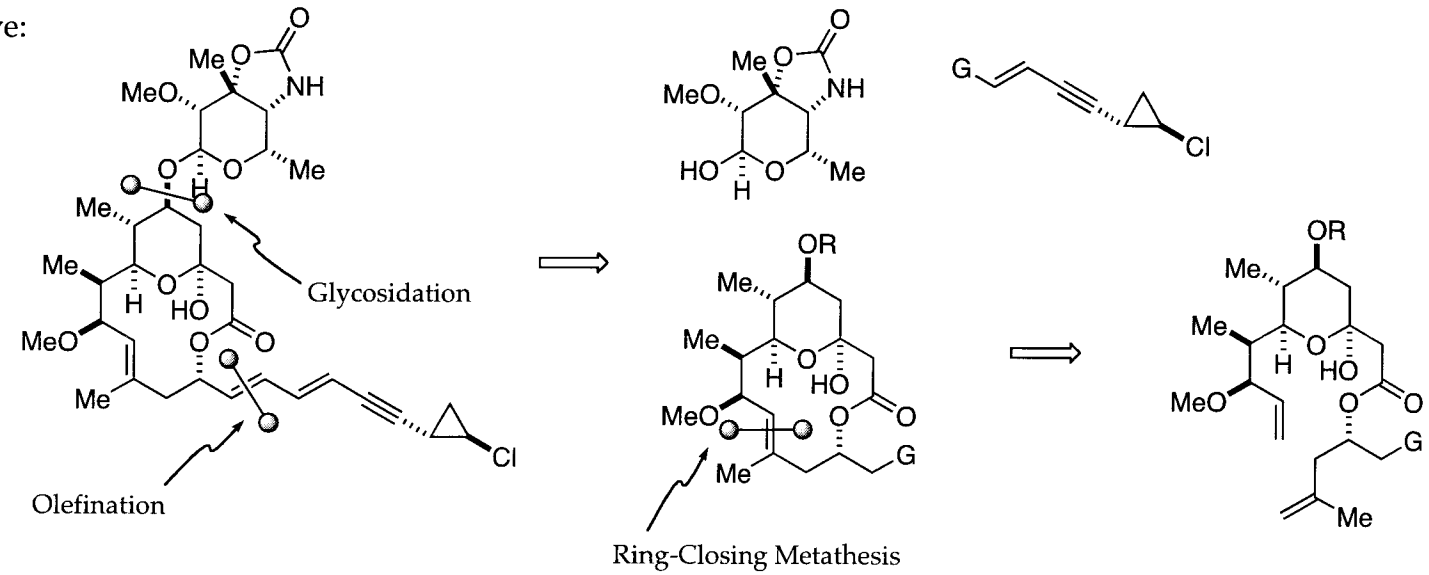


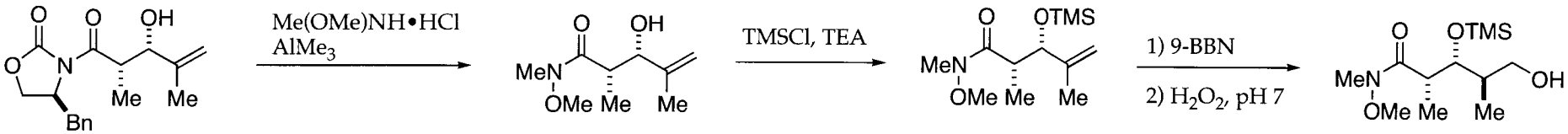
D-glucal

Nicolaou *Tet:Asym*, **01**, *12*, 937

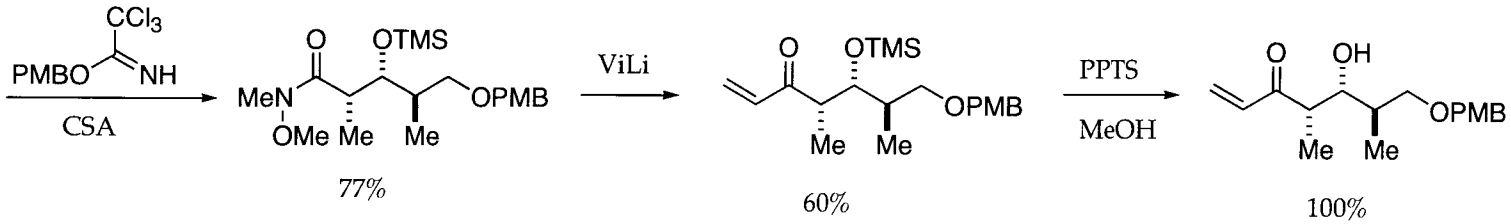
First Fragment Synthesis

Hoye:



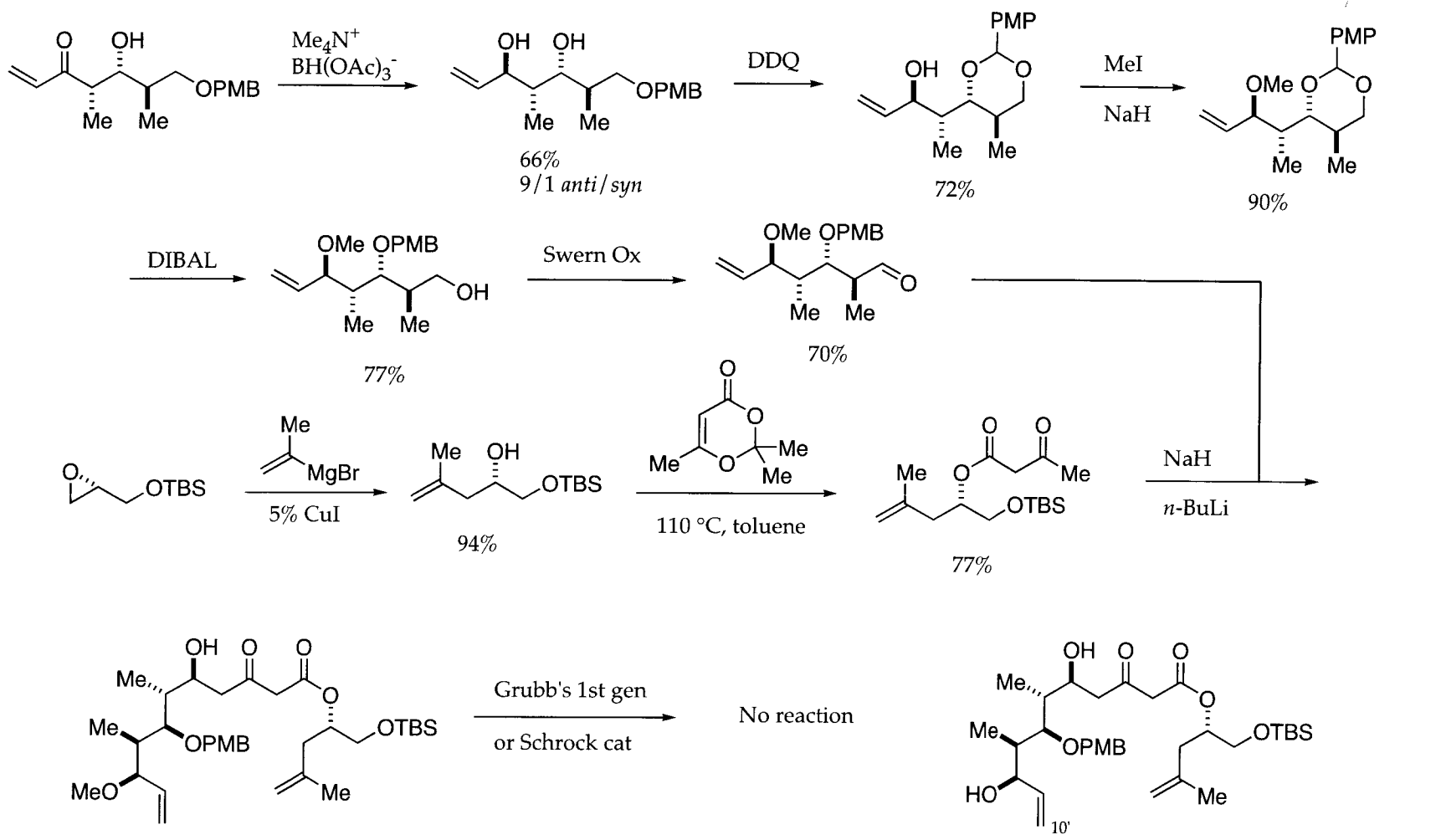


Evans *JOC*, **97**, *62*, 454



Hoye *OL*, **99**, *1*, 169

Ring Closing Metathesis



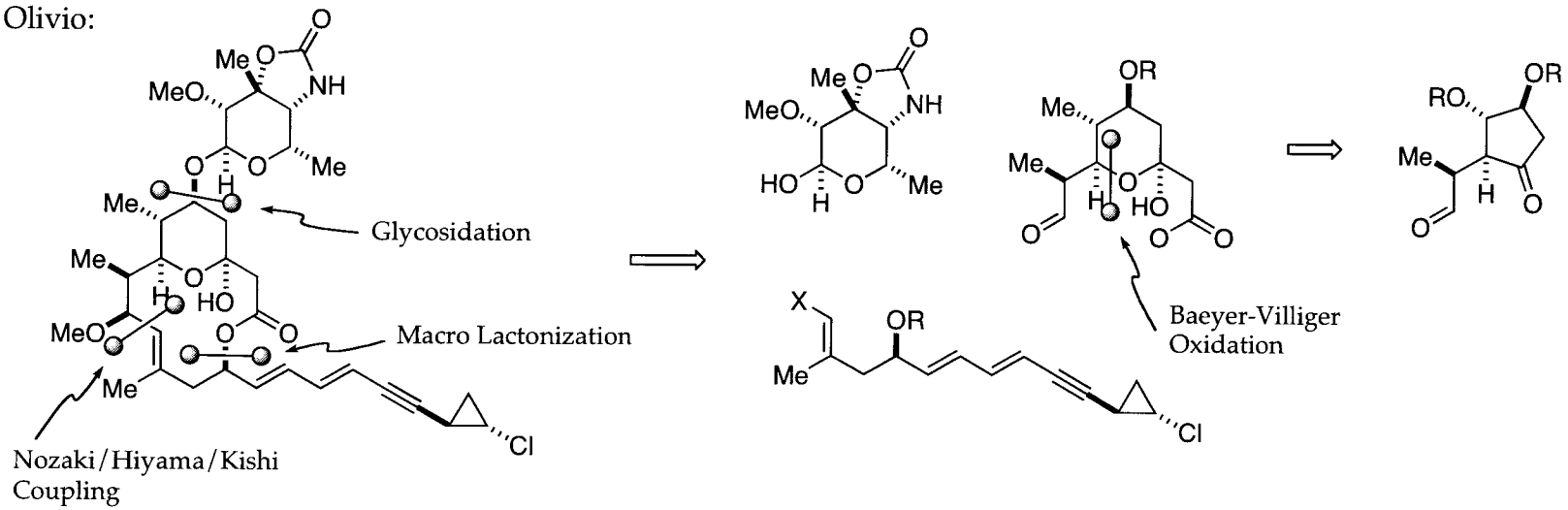
70%
2.5/1 dr

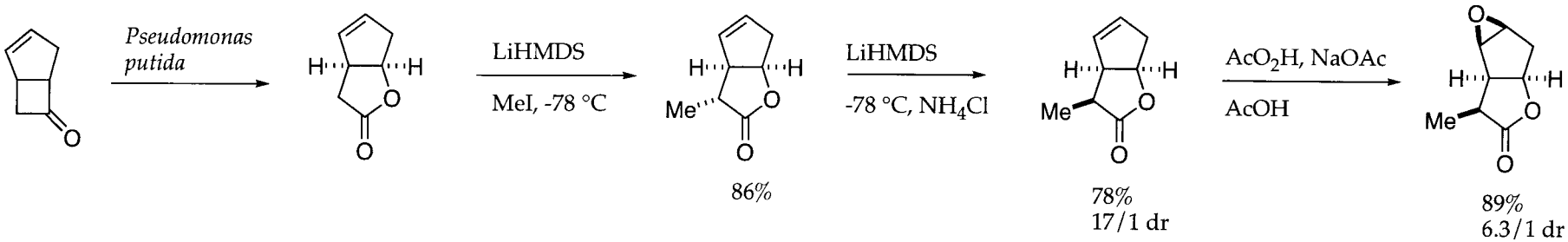
-established by oxidation of PMB to cyclic acetal

^{1}H NMR studies showed that the Ru cat initiates at C(10'), but does not close

Second Fragment Synthesis

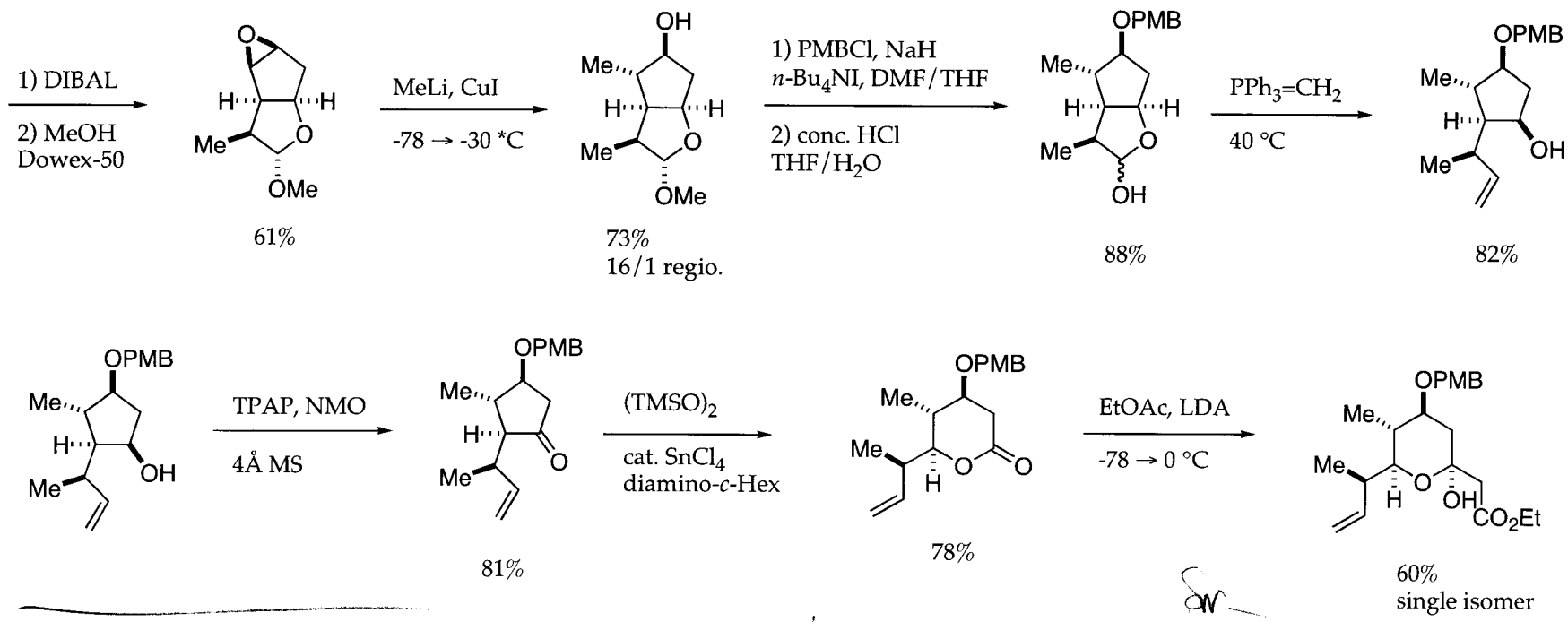
Olivio:

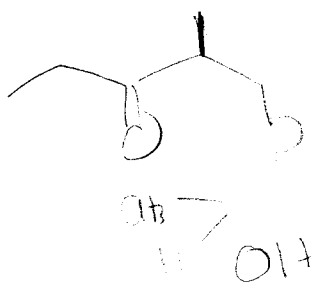


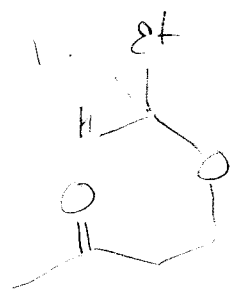


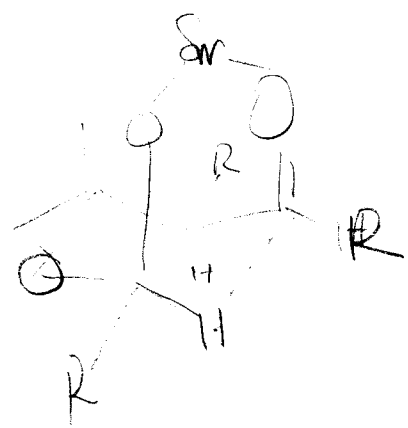
Olivio *OL*, **00**, 2, 1931

Baeyer-Villiger Oxidation



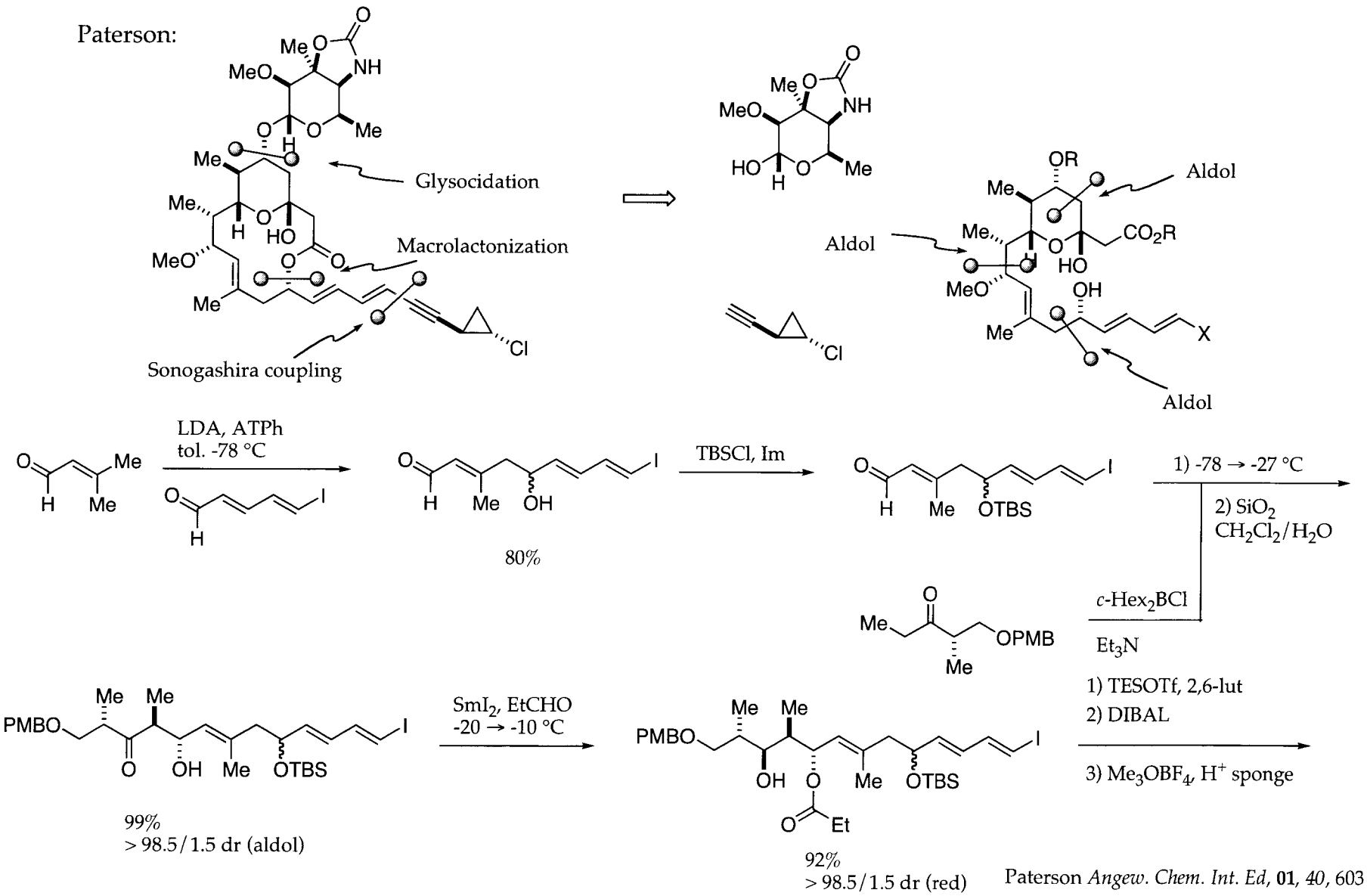






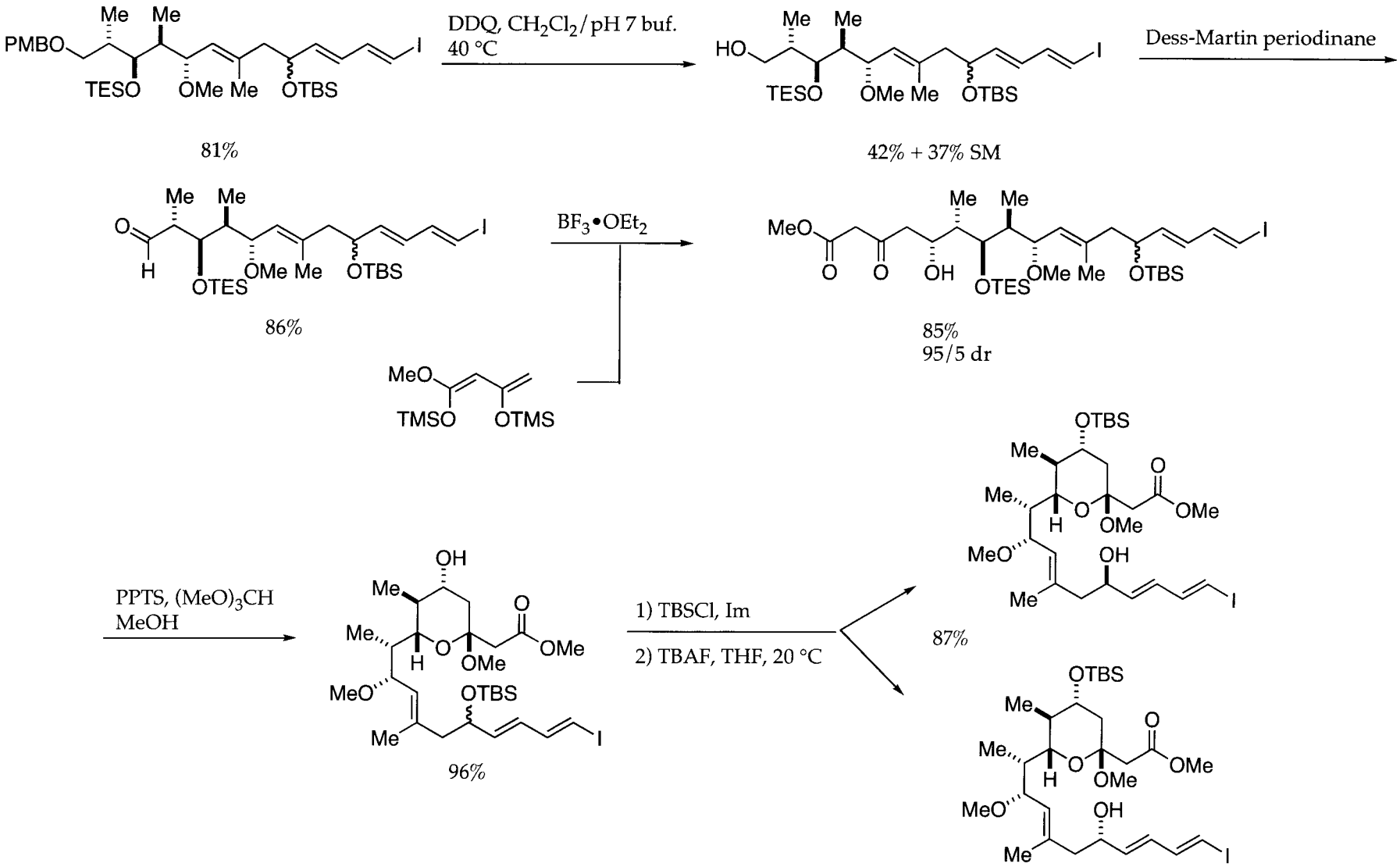
Aglycon synthesis

Paterson:

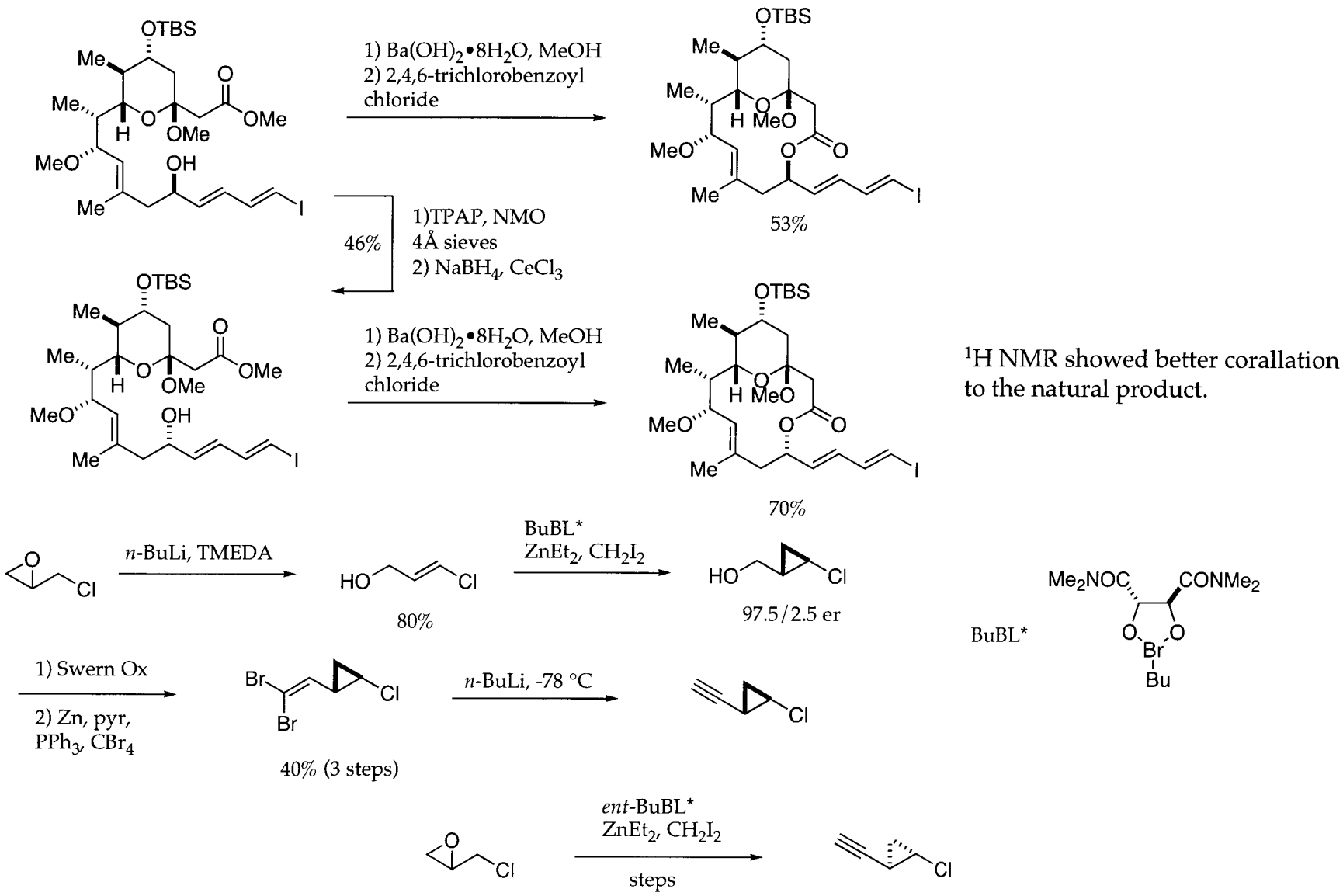


Paterson *Angew. Chem. Int. Ed*, **01**, *40*, 603

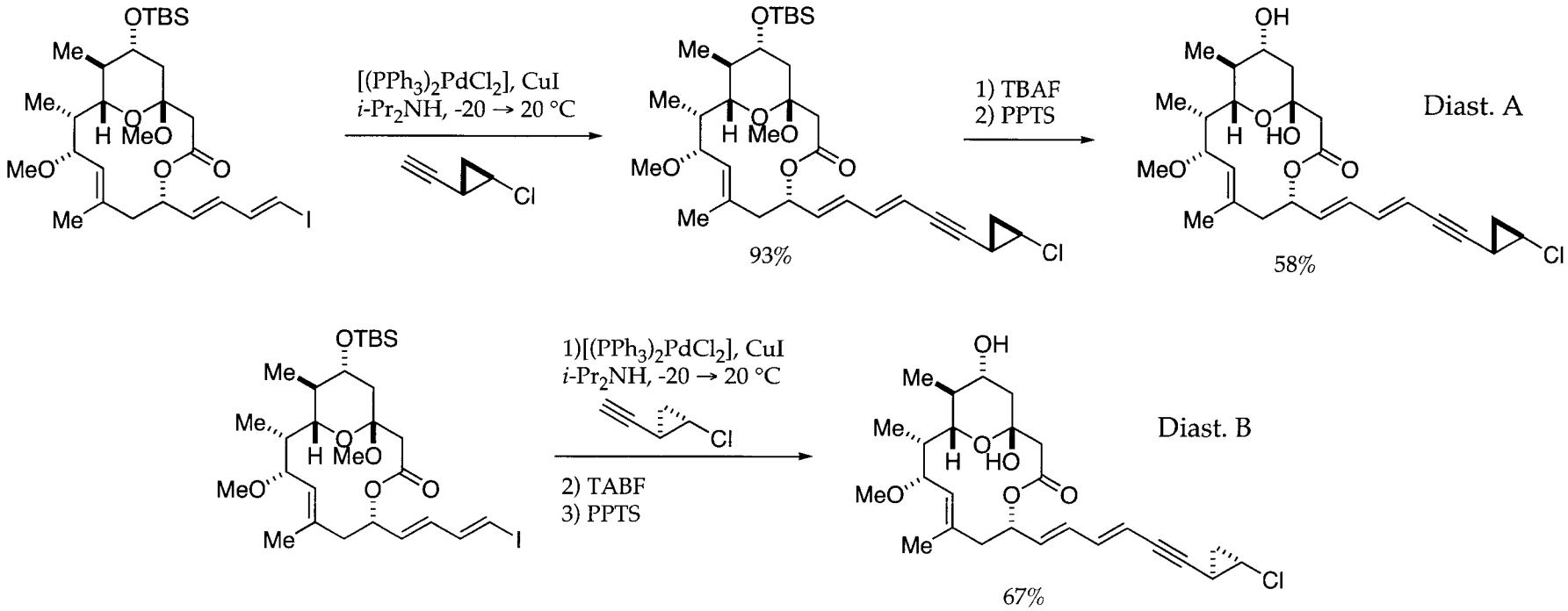
Aglycon continued



Aglycon continued 2



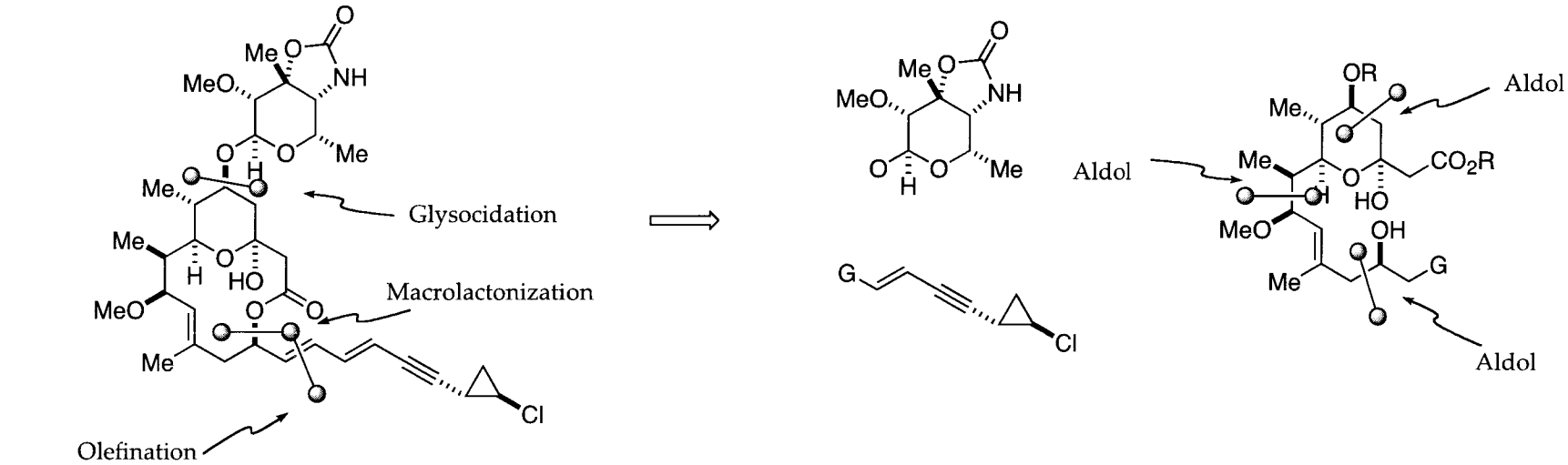
Aglycon continued 3

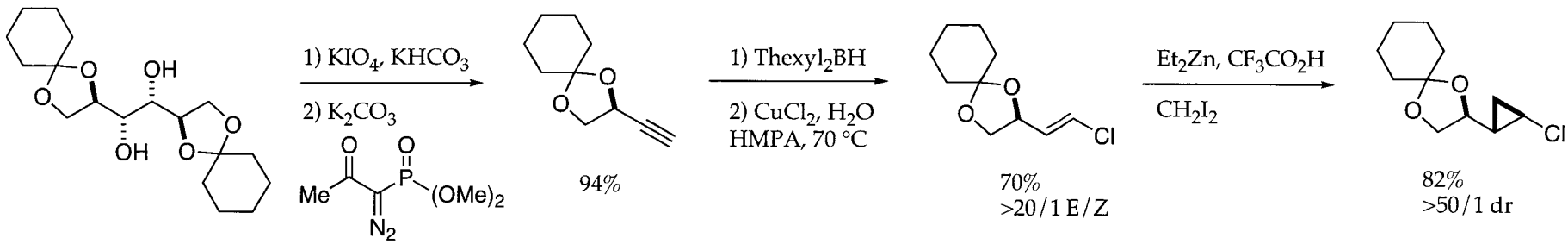


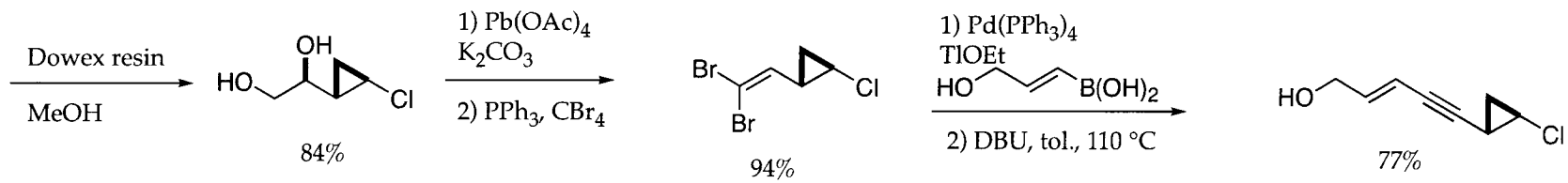
^{1}H NMR data for diast. A and B are almost identical to eachother and Callipeltoside A

Rotations:	Diast. A	-97.8° (c = 0.19, $CHCl_3$)
	Diast B	+45.8° (c = 0.28, $CHCl_3$)
	Call. A	-17.6° (c = 0.04, MeOH)

Total Synthesis - Evans

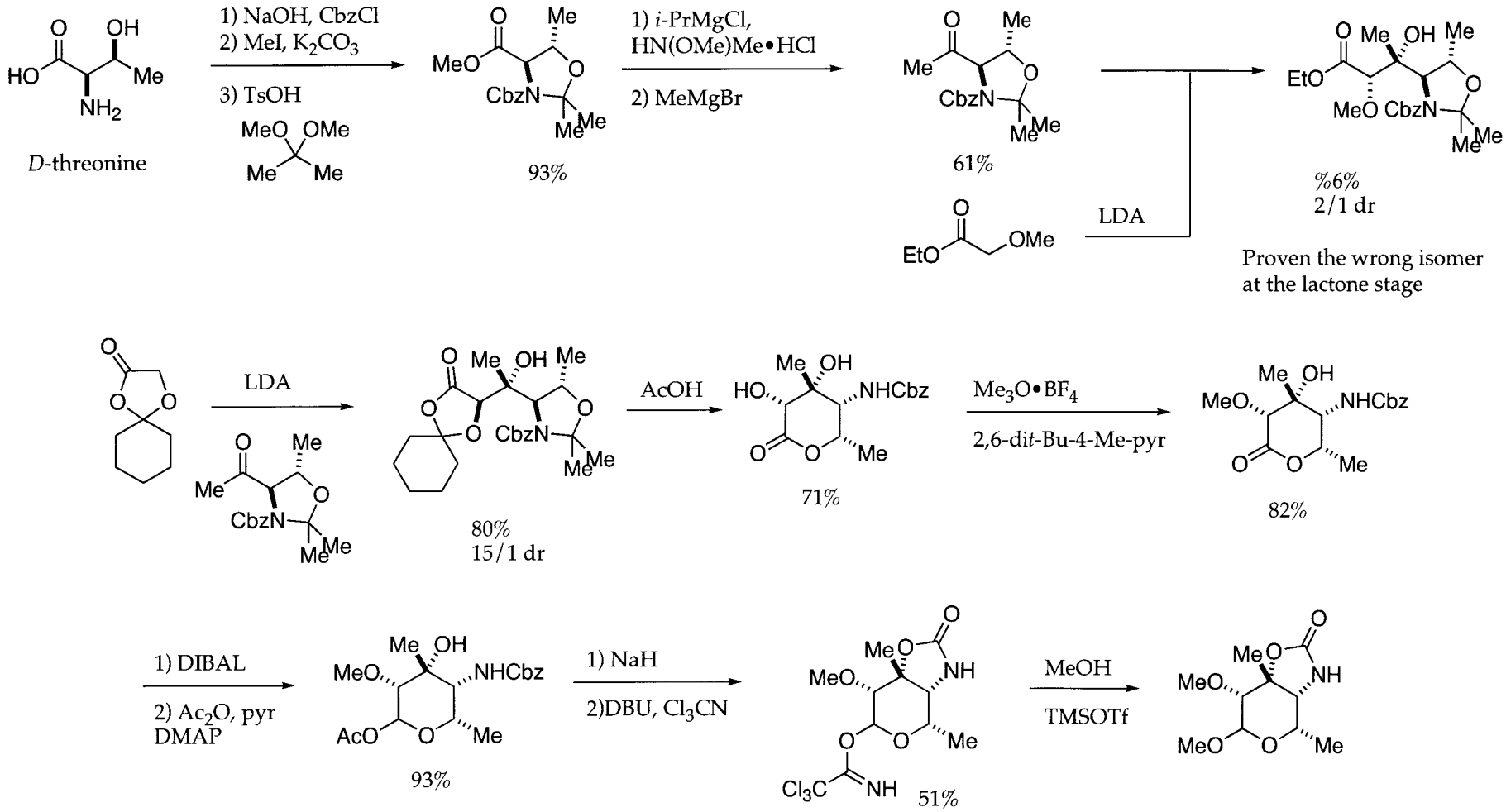






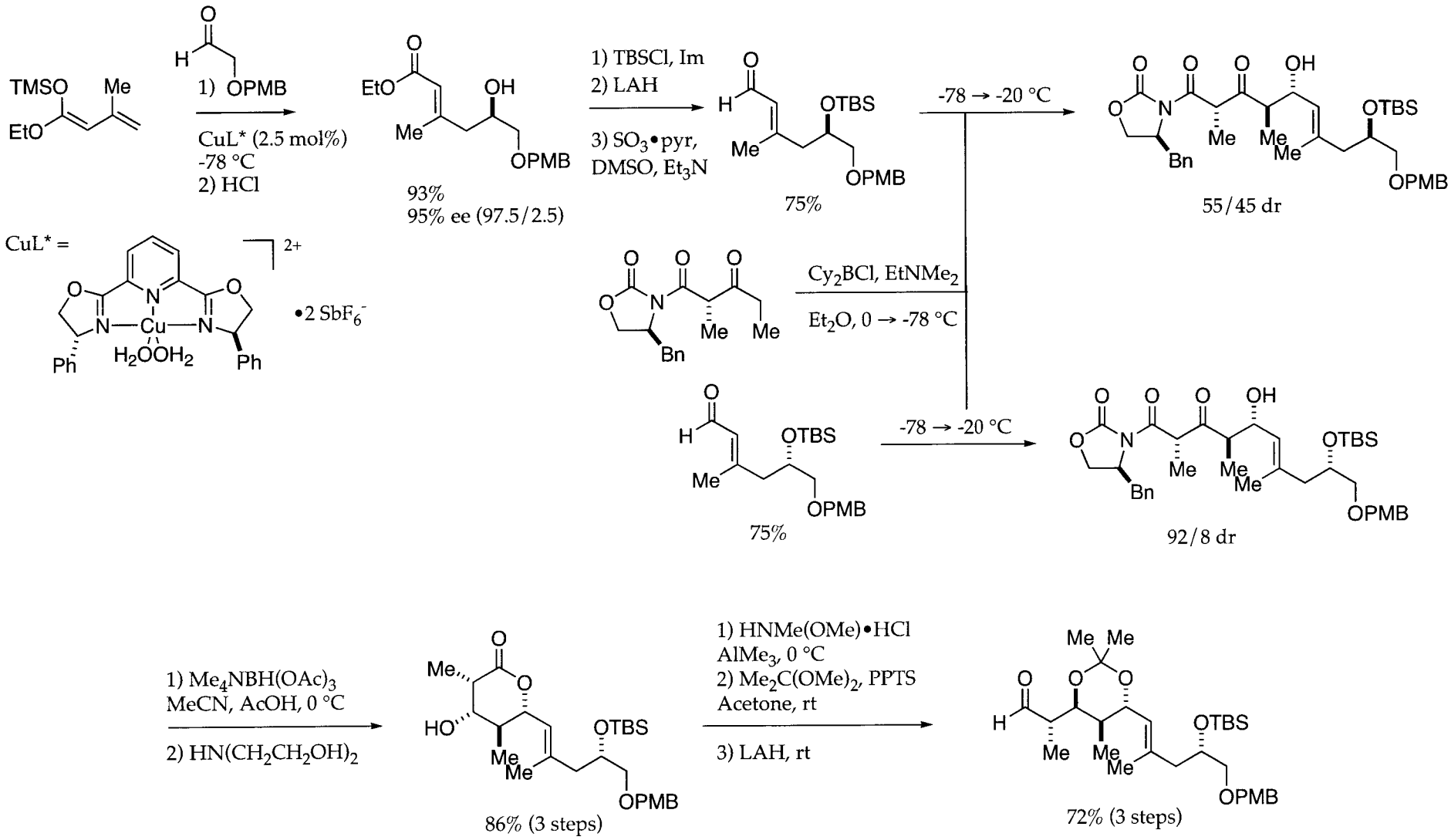
Evans *OL*, **01**, *3*, 503

Evans - Carbohydrate



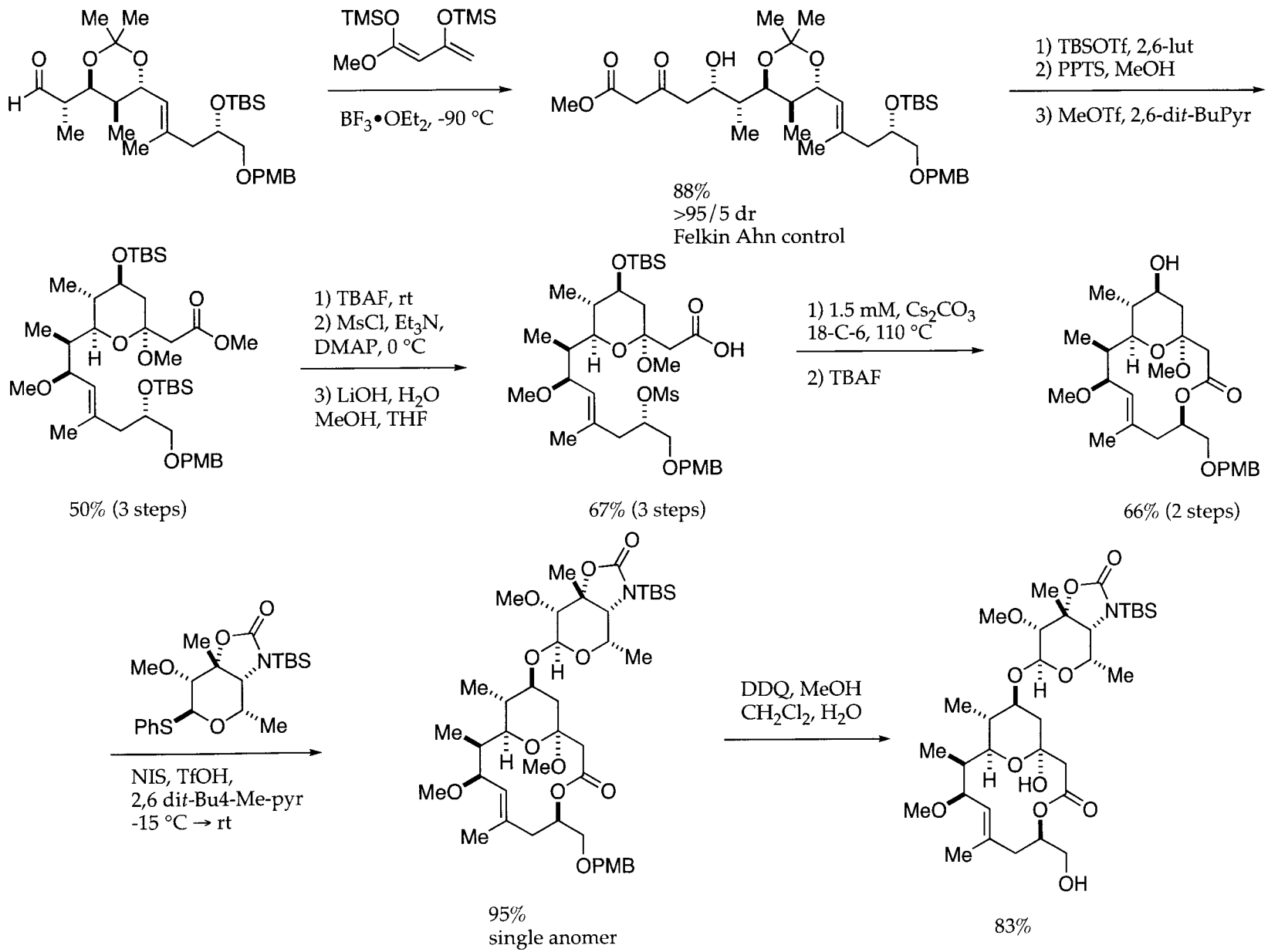
Evans *OL*, **01**, *3*, 3133

Evans - Core Structure

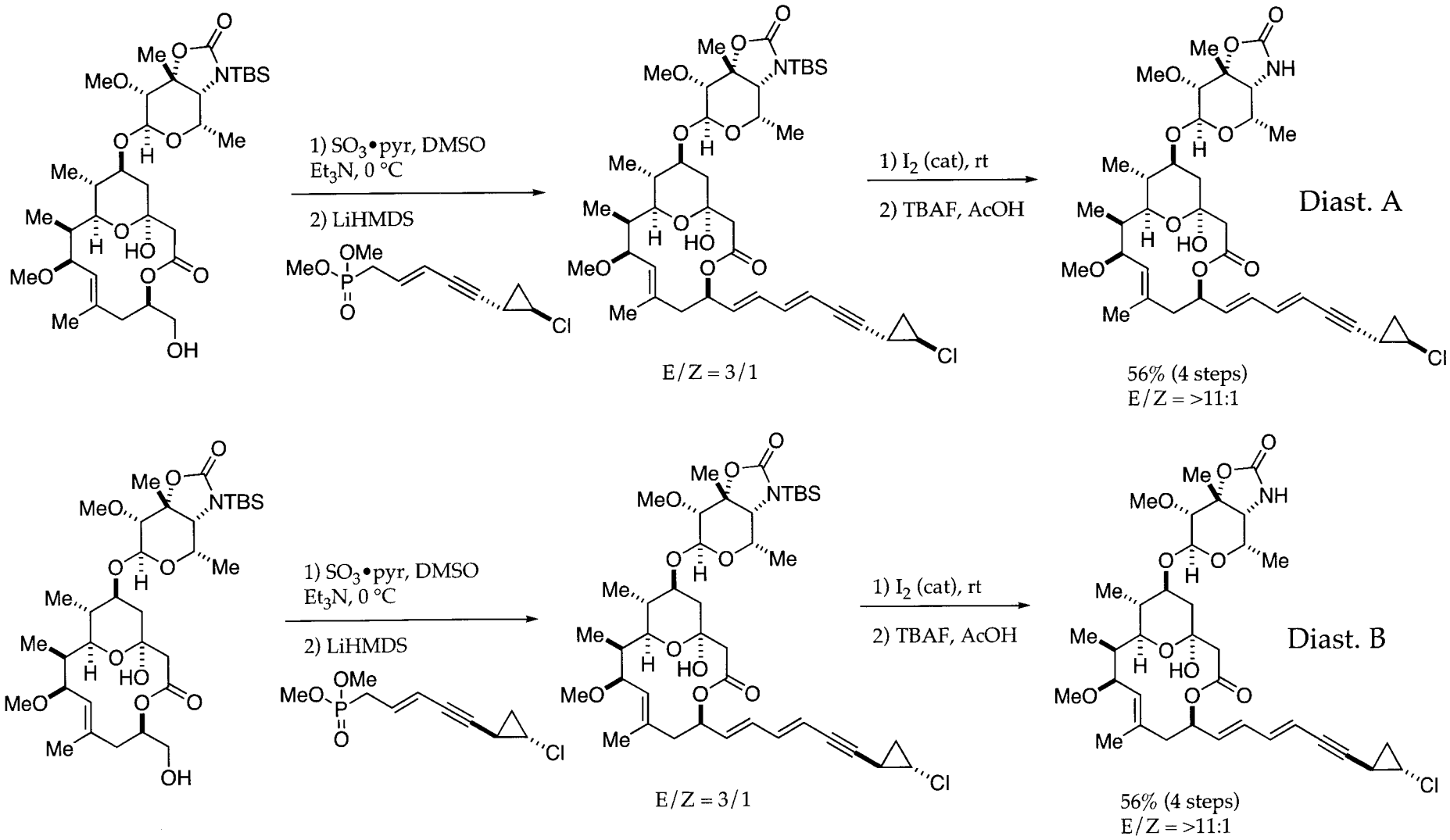


Evans *JACS*, **02**, *124*, 5654

Evans -Glycosidation

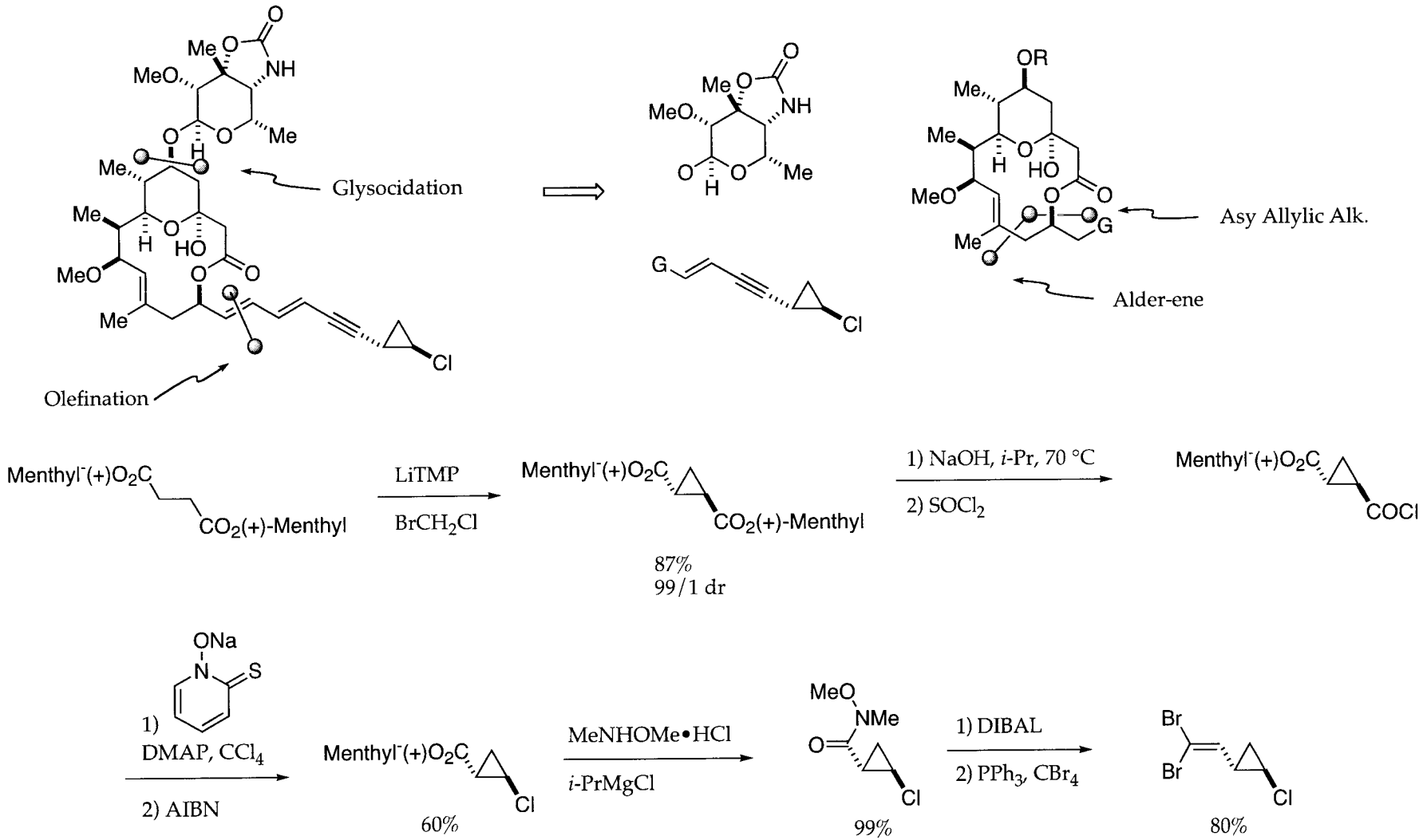


Evans - Coupling

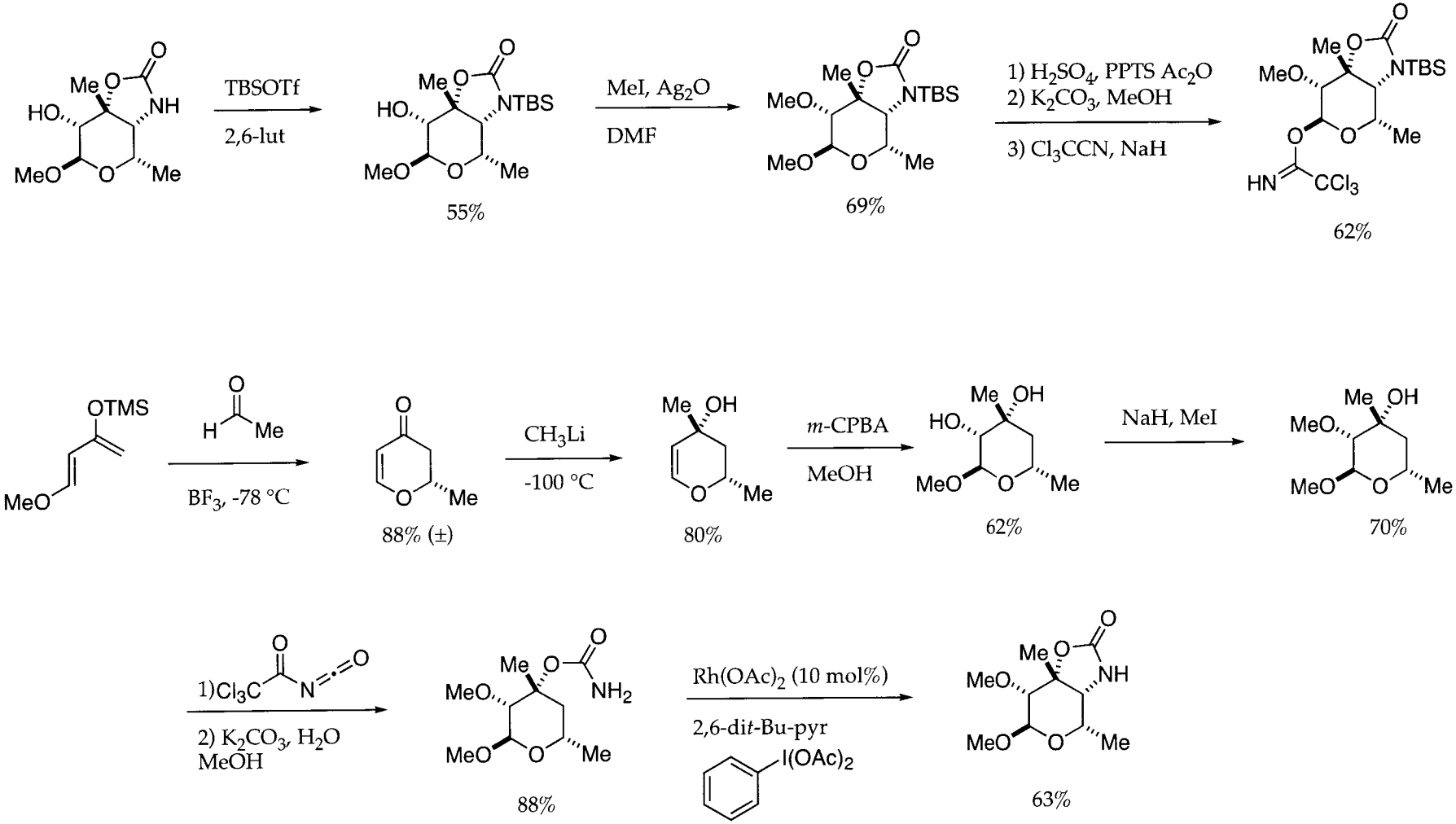


Diast. A -17.6° (c = 0.19, MeOH) Diast. B +140° (c = 0.05, MeOH)

Total Synthesis - Trost

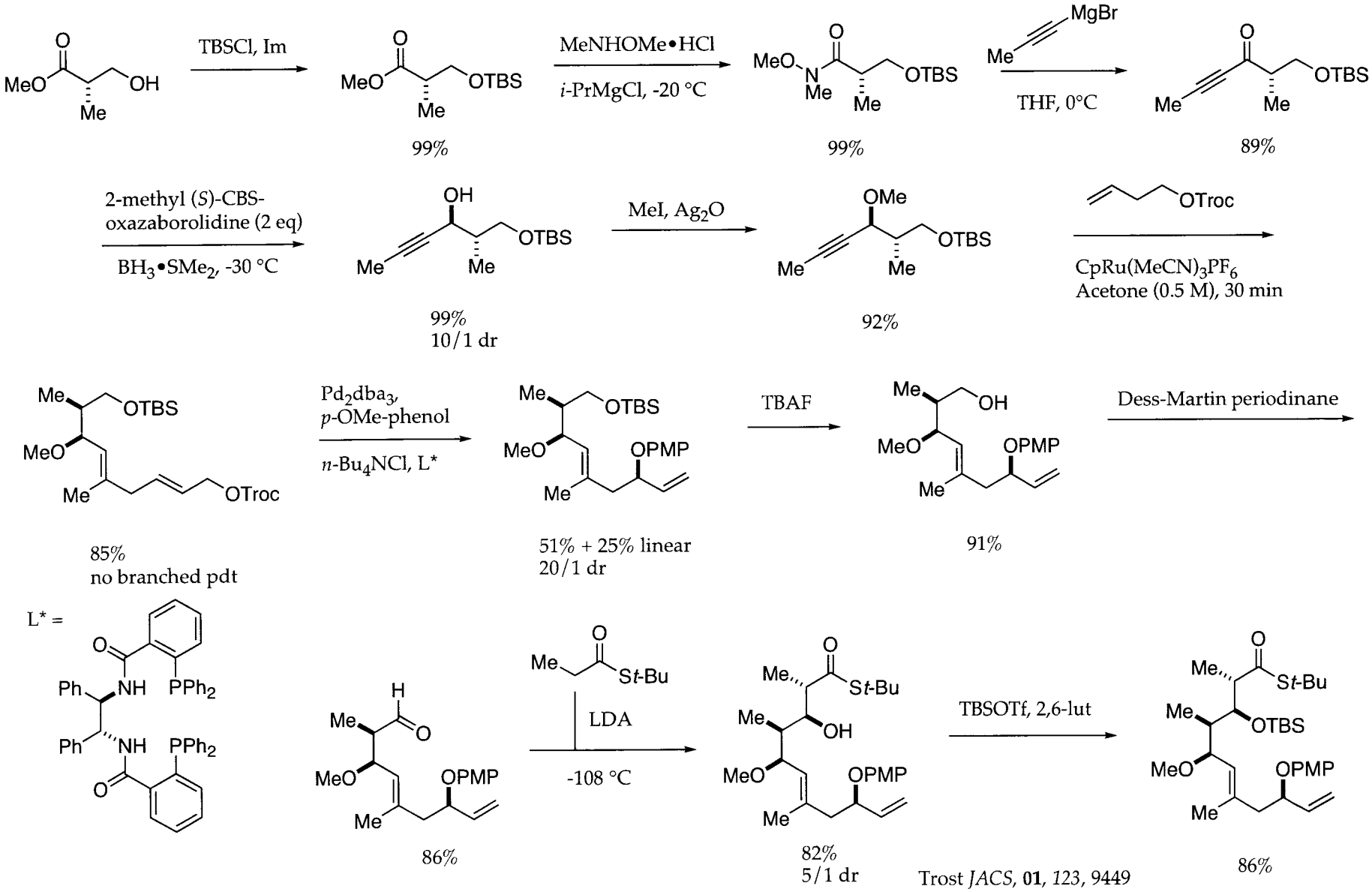


Trost - Carbohydrate



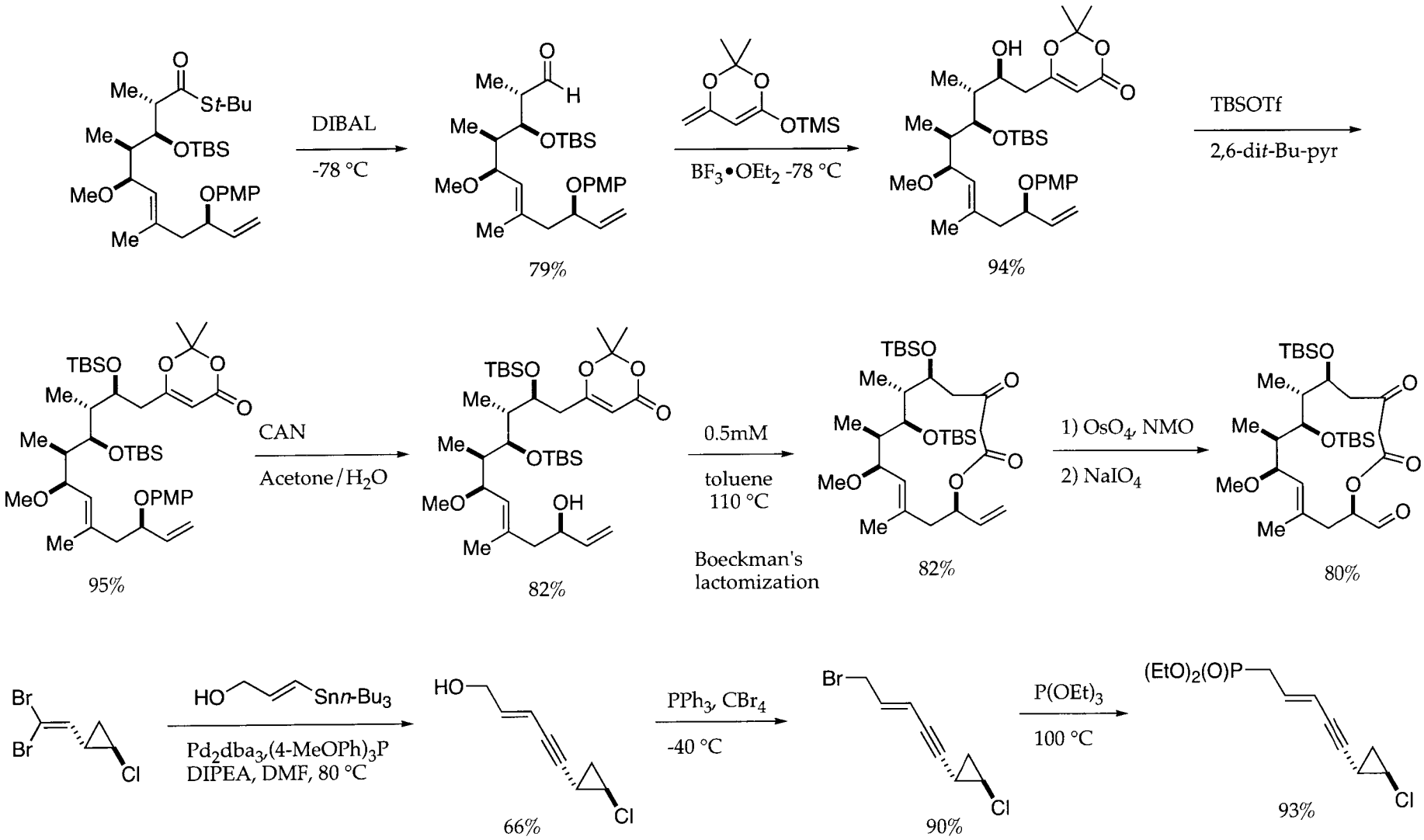
Trost *JACS*, **02**, *124*, 10396

Trost - Core Structure



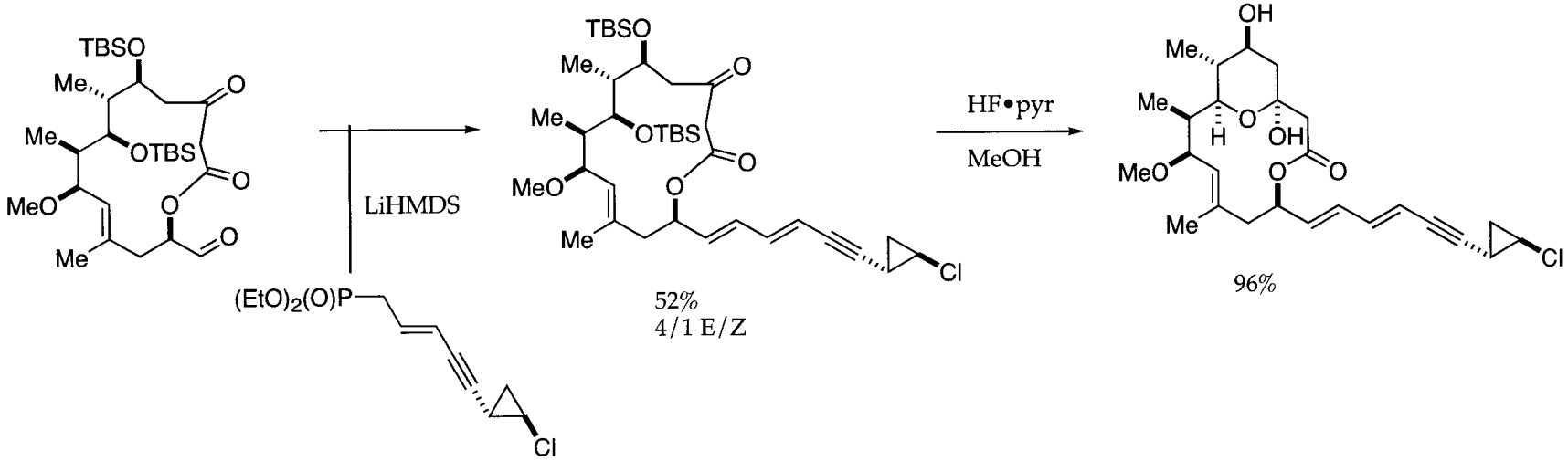
Trost *JACS*, **01**, *123*, 9449

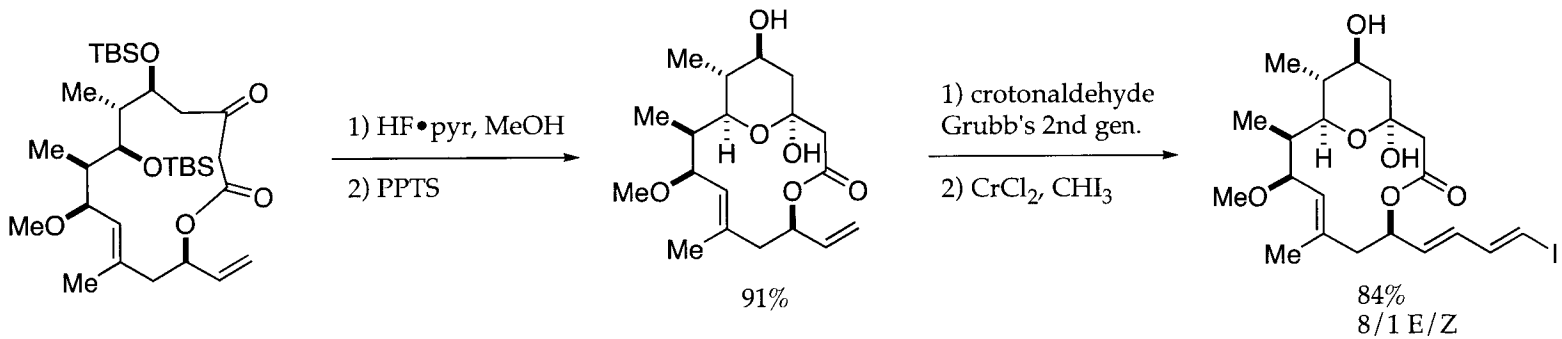
Trost - Cyclization

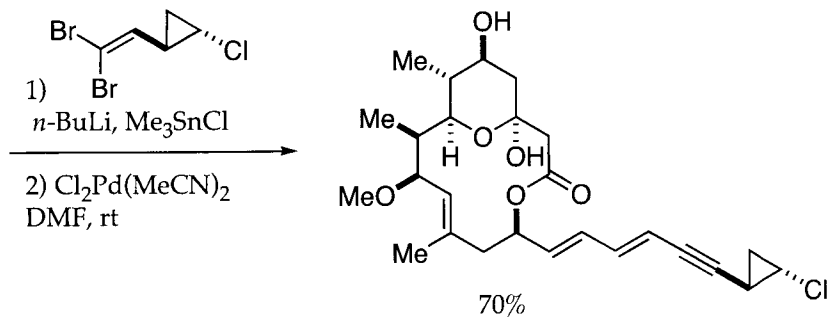


Trost *Angew. Chem Int. Ed.*, **02**, *41*, 841

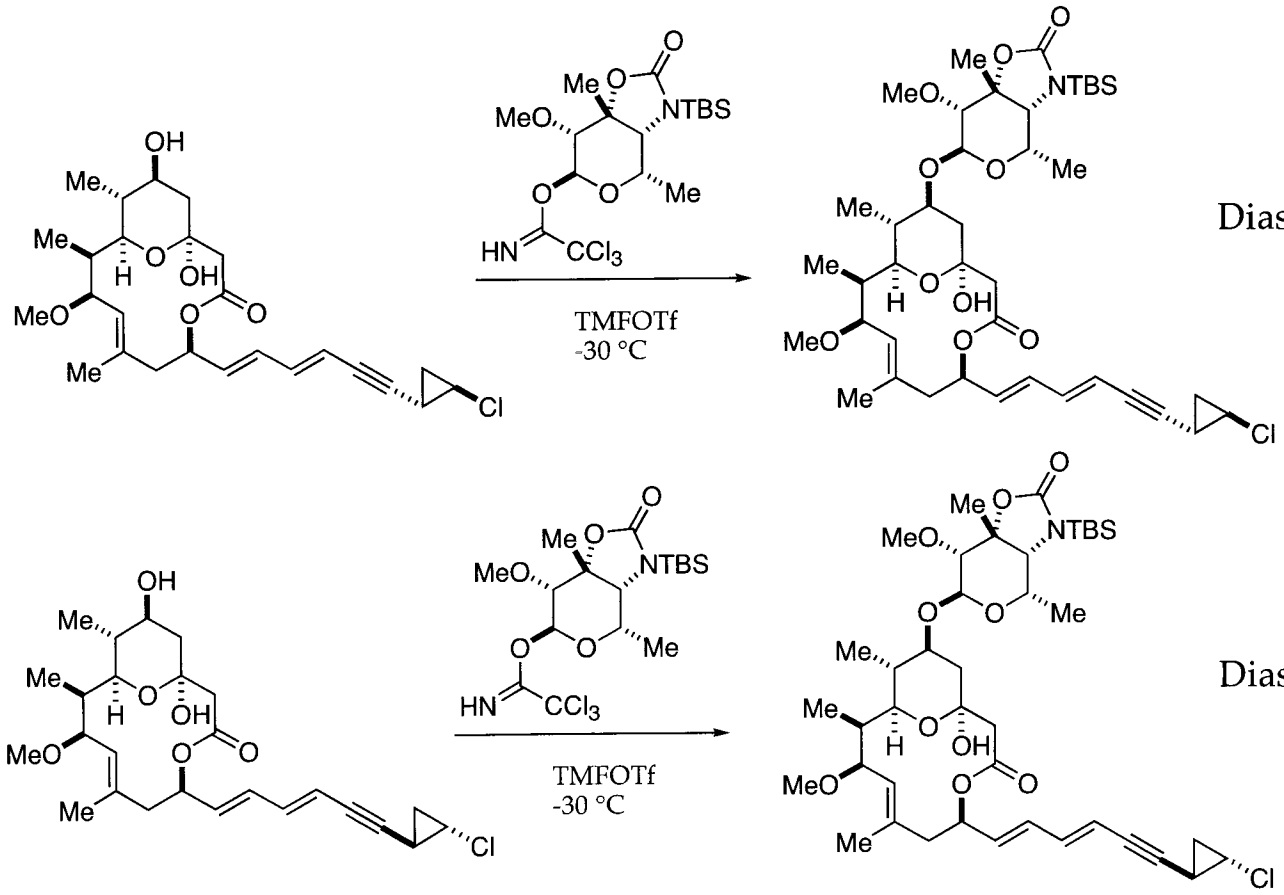
Trost - Coupling







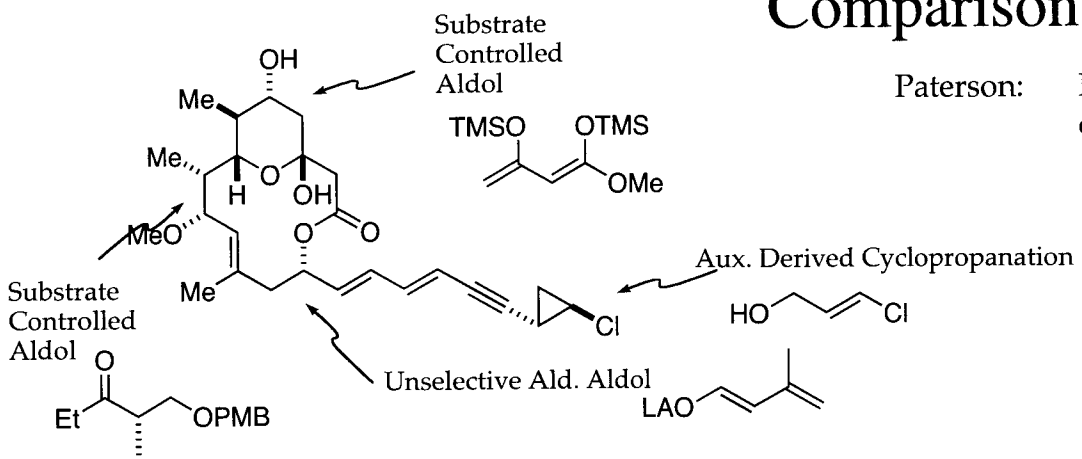
Trost - Glycosidation



Diast. A -19.2° (c = 1.0, MeOH)

Diast. B +156.3° (c = 1.0, MeOH)

Comparisons

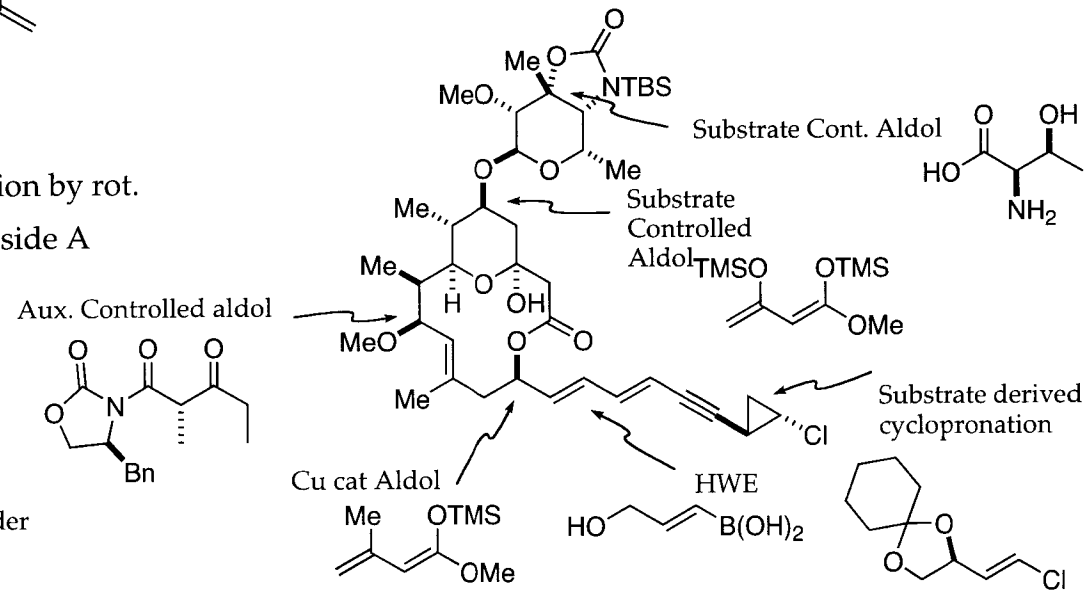


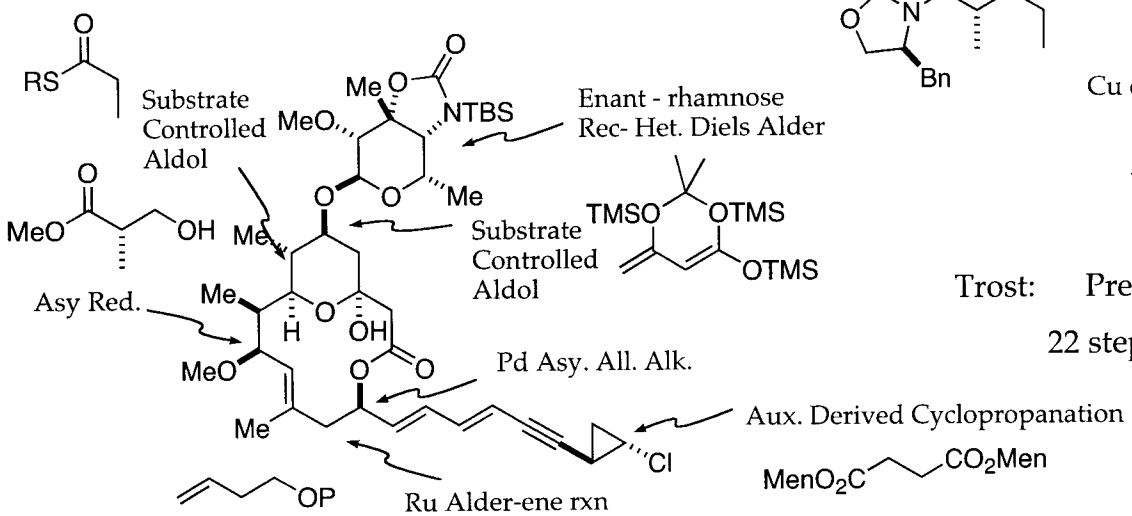
Paterson: Prepared both diastereomers - could not determine configuration in the natural product.

20 steps and 2.7% yield to the aglycon

Evans: Prepared Both diastereomers - configuration by rot.

15 steps (linear) and 3.0% yield to Callipeltoside A





Trost: Prepared Both diastereomers - configuration by rot.

22 steps (linear) and 3.8% yield to Callipeltoside A