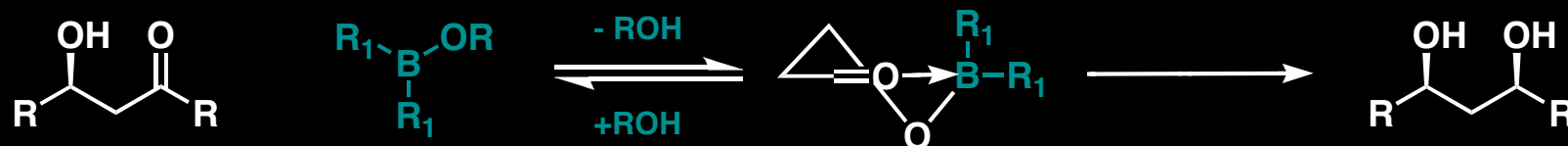

Diastereoselective 1,3-Syn Reduction of β -Hydroxyketones: The Prasad Reduction



Seminal Publication:

Prasad, *Tet. Lett.* (1987), 28, 155.

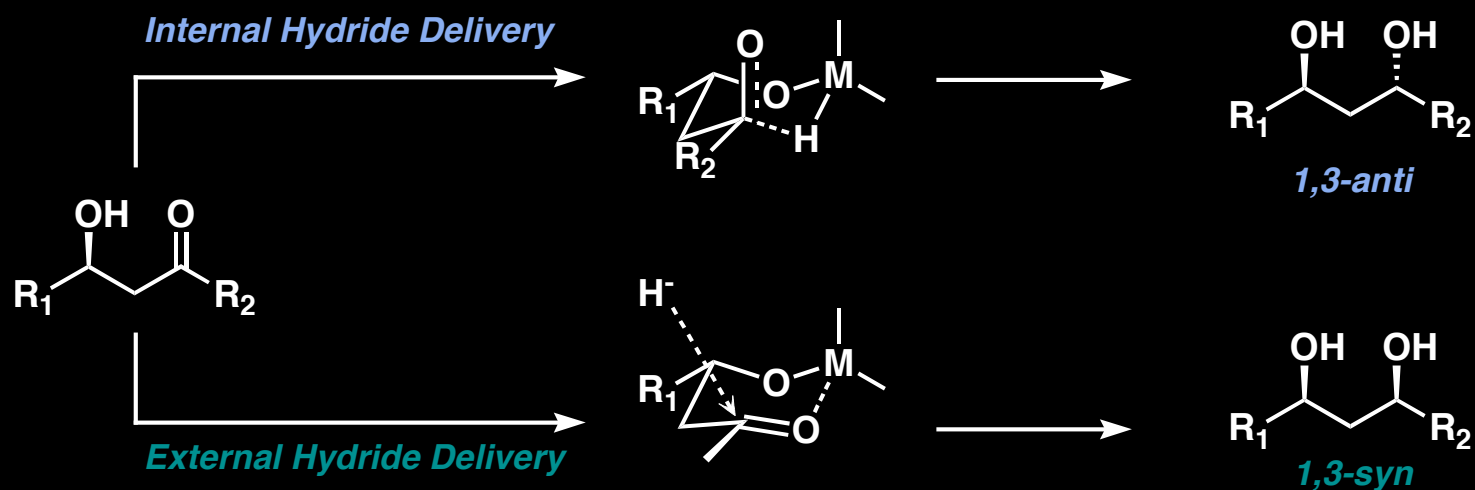
Adel ElSohly
Columbia Literature Seminar Series
June 6, 2008



The General Idea

Chelation control of β -hydroxyketones can lead to selective formation of 1,3-syn or 1,3-anti products

Intramolecular delivery gives 1,3-anti while external hydride delivery leads to 1,3-syn

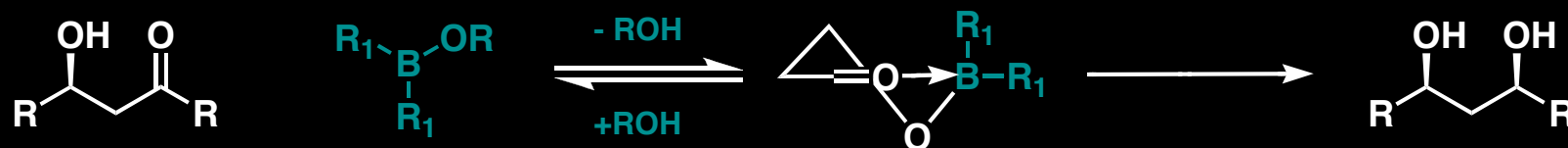


The Prasad Reduction

First example of a diastereoselective 1,3-syn reduction of aldol products using boron alkoxides as chelating agents

Advantages include high substrate scope/tolerance and high selectivity for reduction of β -hydroxyketones

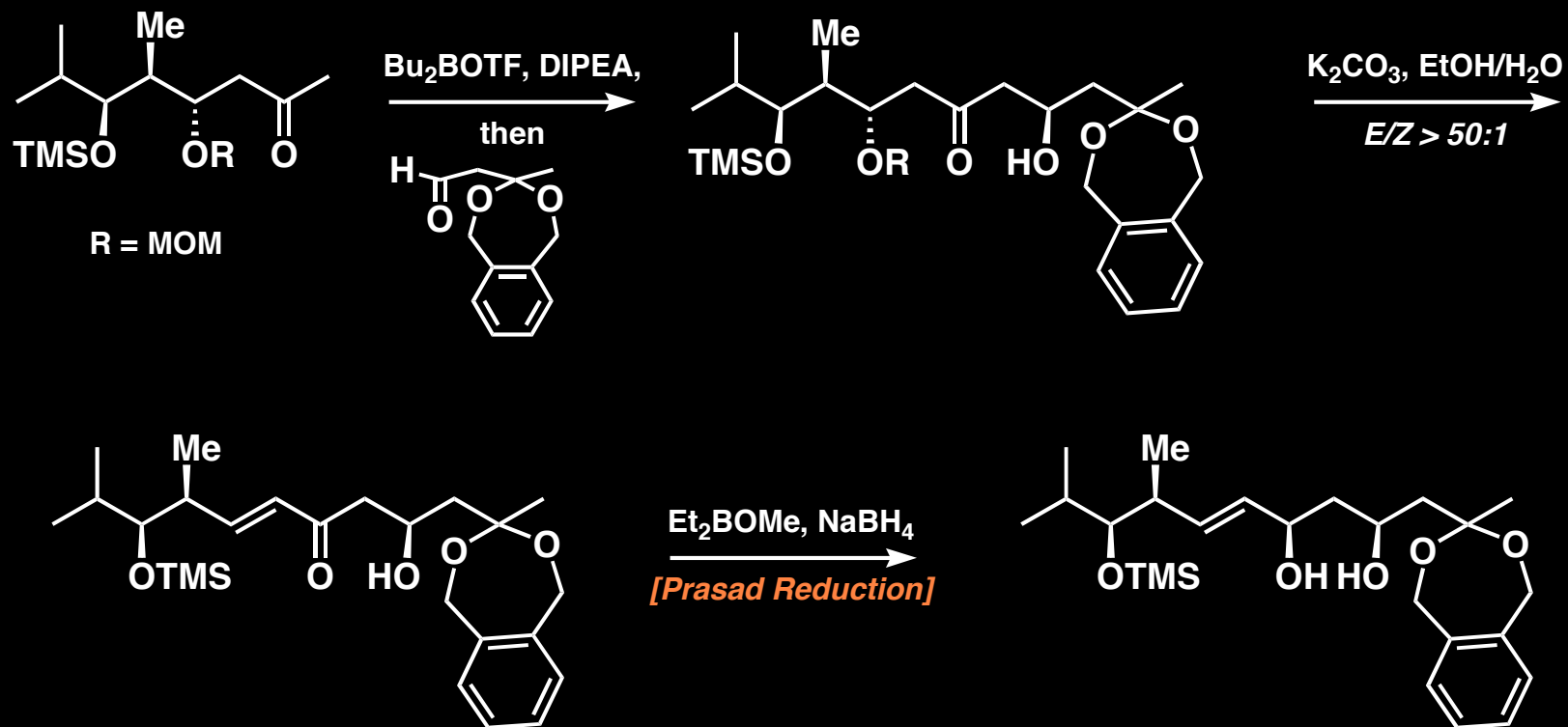
General Reaction:



Scope includes aliphatic, benzylic, and allylic alcohols along with aliphatic or conjugated ketones

Examples from Synthesis

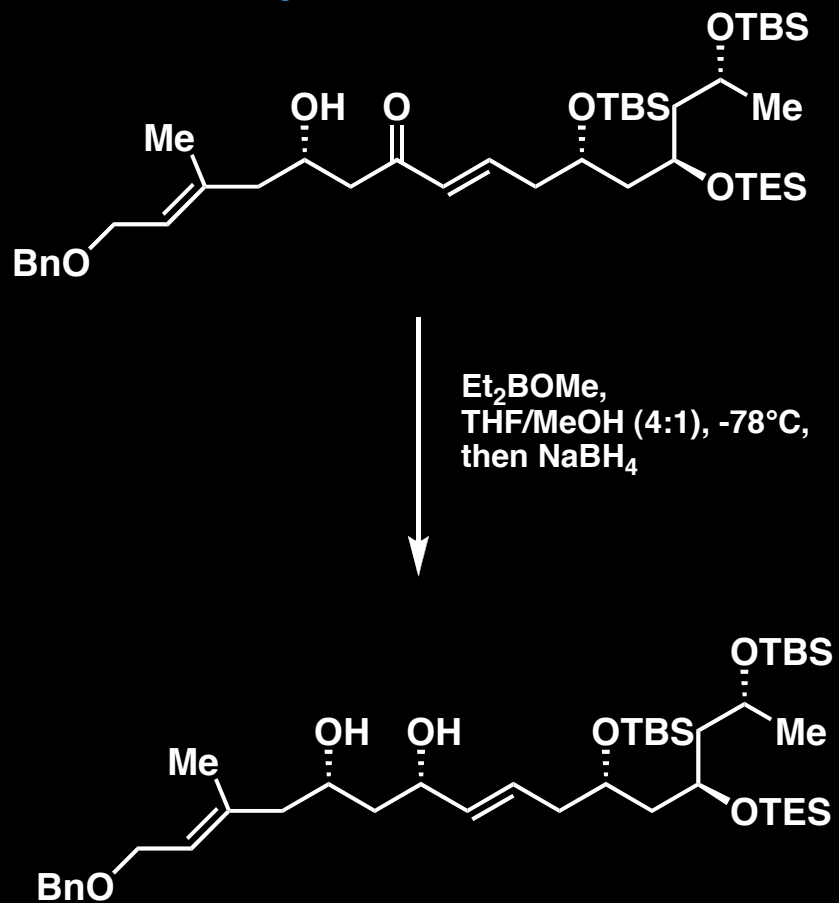
From Sammakia's Synthesis of RK-397



Sammakia, *ACIEE* (2007), 46, 1066.

Examples from Synthesis

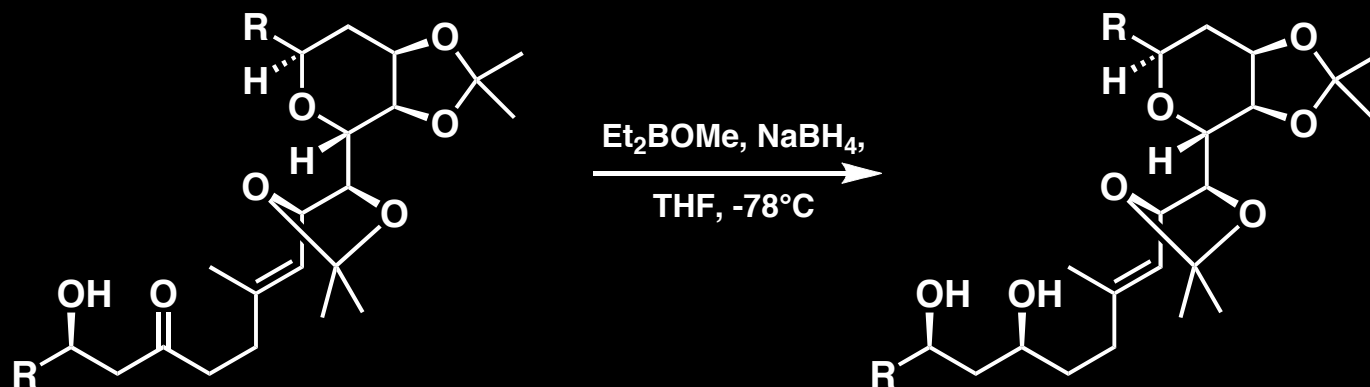
From Nicolaou's Synthesis of Marinomycins A-C



Nicolaou, *JACS* (2007), 129, 1760.

Examples from Synthesis

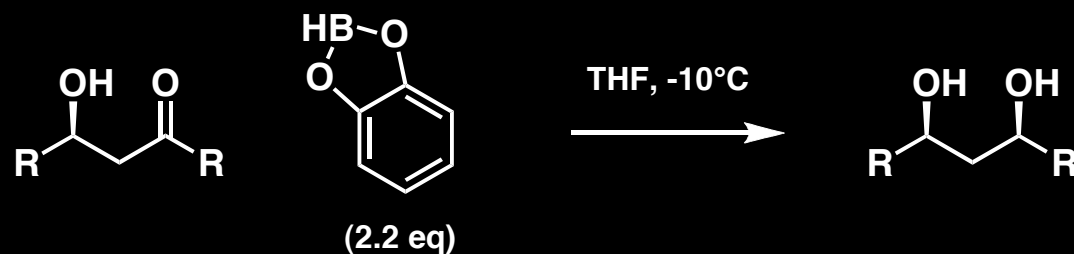
From Rychnovsky's Synthesis of C1-C52 Fragment of Amphidinol 3



Rychnovsky, *OL* (2007), 9, 4757.

A Related Procedure

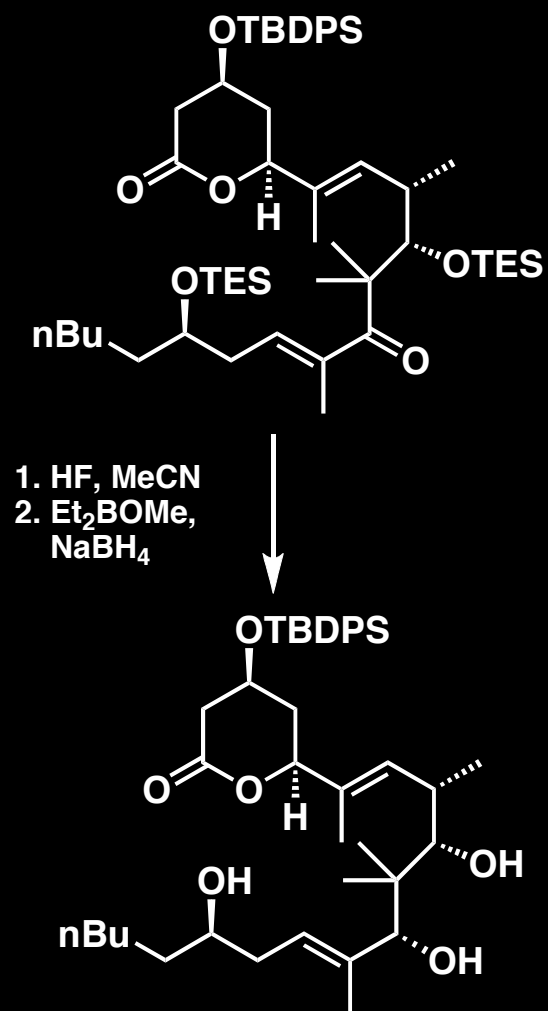
Evans and Hoveyda found that treatment of aldol products with 2.2 equiv. of catechol borane resulted in the diastereoselective formation of 1,3-syn diols through a boron-aldolate complex



Scope includes aliphatic and conjugated ketones

Evans and Hoveyda, JOC (1990), 55, 5190.

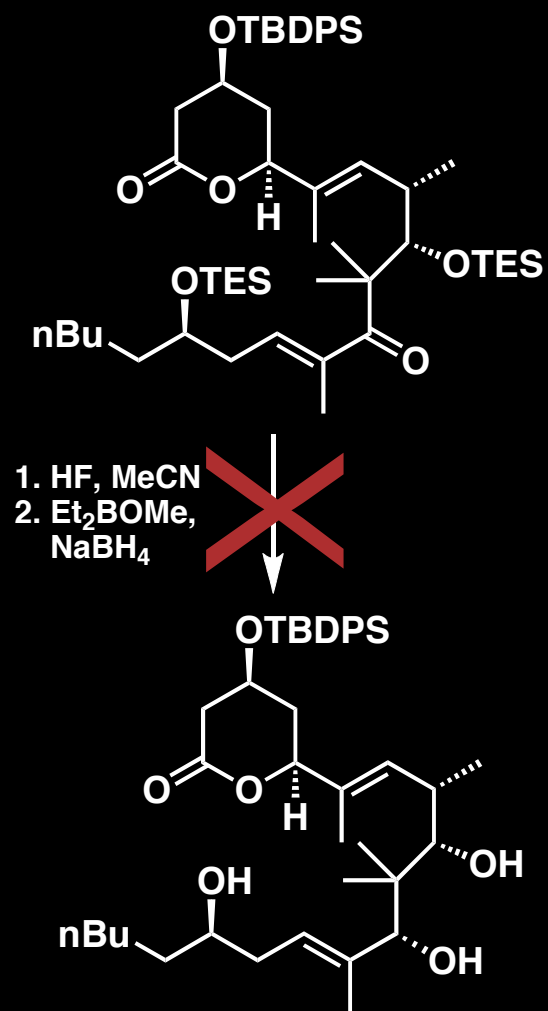
Examples from Synthesis



From Jamison's Synthesis of Acutiphycin

Jamison, *JOC* (2007), 72, 9736.

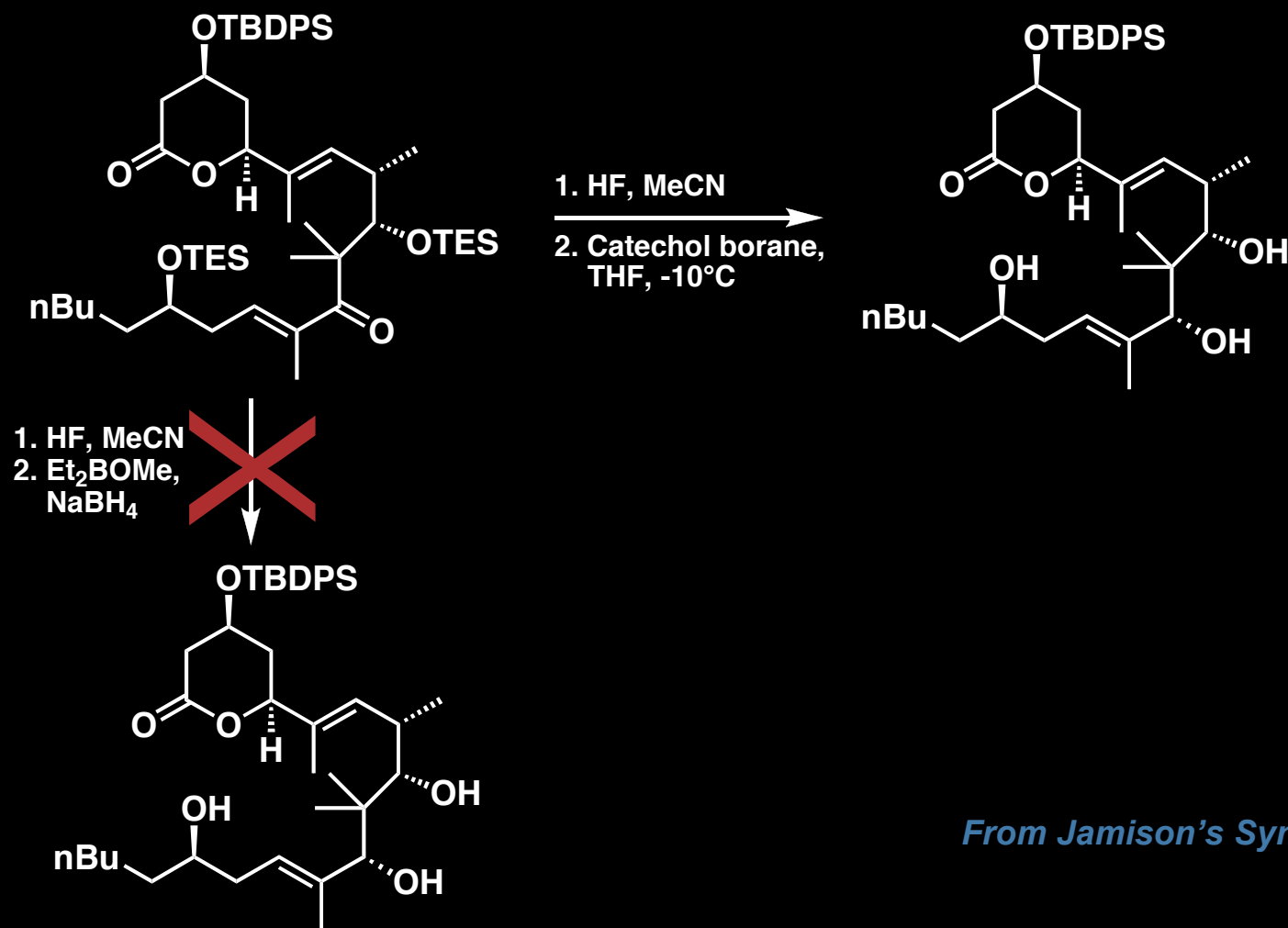
Examples from Synthesis



From Jamison's Synthesis of Acutiphycin

Jamison, *JOC* (2007), 72, 9736.

Examples from Synthesis

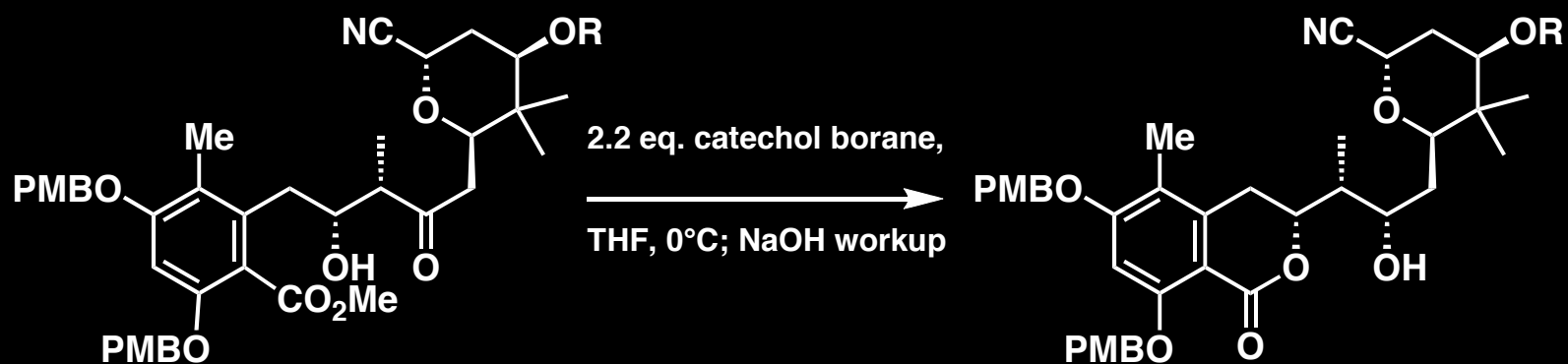


From Jamison's Synthesis of Acutiphycin

Jamison, *JOC* (2007), 72, 9736.

Examples from Synthesis

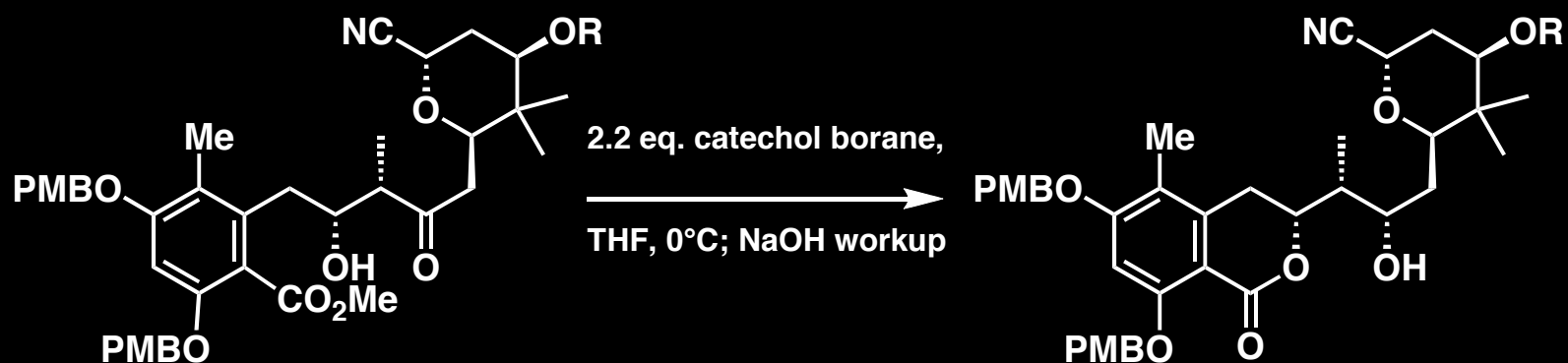
From De Brabander's Synthesis of Irciniastatin A



De Brabander, *JACS* (2005), 127, 11254.

Examples from Synthesis

From De Brabander's Synthesis of Irciniastatin A

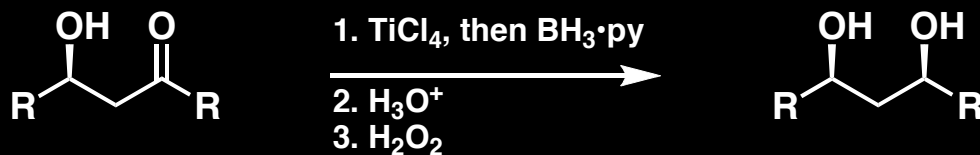


Note: This synthesis also utilizes Leighton's pseudoephedrine-derived allylsilane

De Brabander, *JACS* (2005), 127, 11254.

Another Related Procedure

Related procedure by Bartoli that incorporates TiCl_4 as the Lewis acid and borane as the external hydride source



Low substrate tolerability due to TiCl_4 and H_2O_2

No examples of this reduction used in complex molecule synthesis
