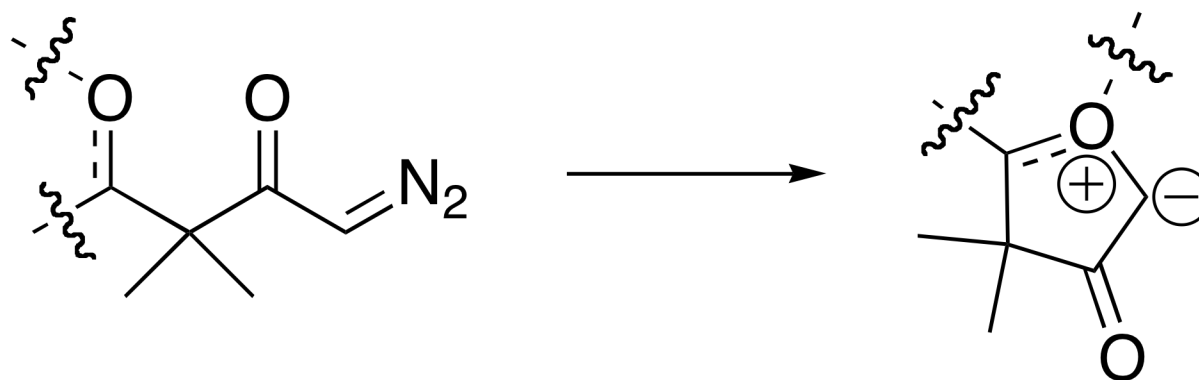# Multicomponent reactions involving tricyclooxonium ylide intermediate: diastereoselective synthesis of mono- and bisalkoxyoctahydro-1,4-benzodioxocin-6(5H)-one frameworks
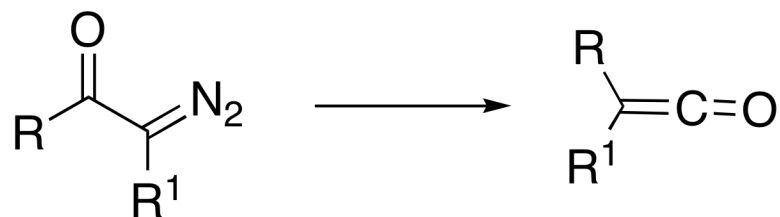
Presented by:

Cody Timmons

Wipf Group

University of Pittsburgh

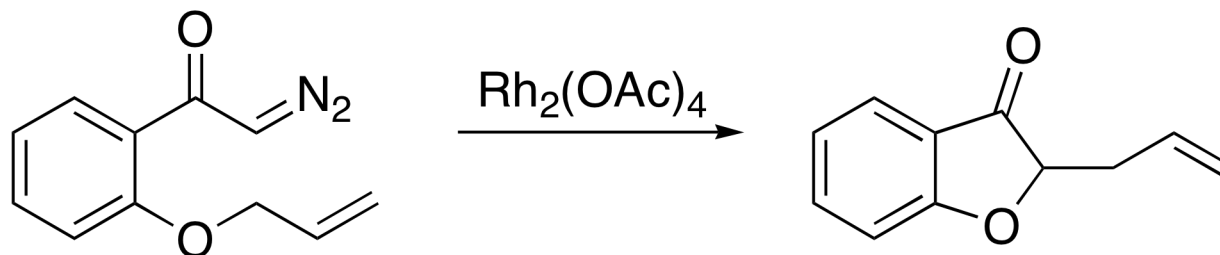October 28, 2006

Generation of *O*-ylides

Challenges: short lifetime -> high reactivity -> poor stereocontrol

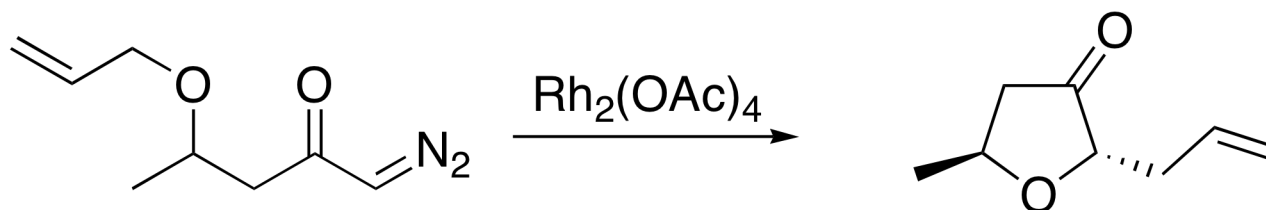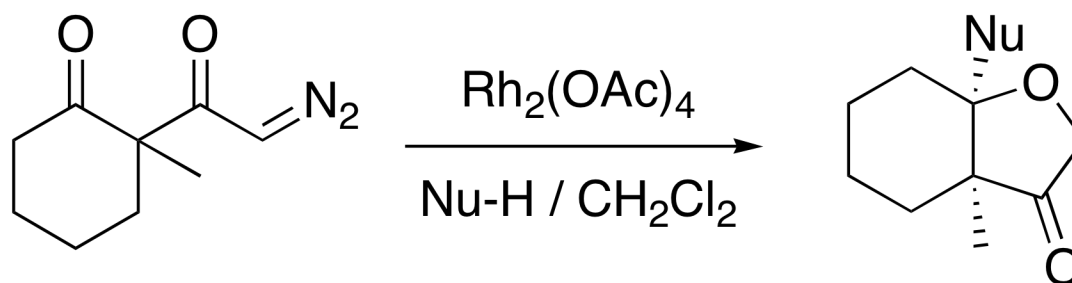Recall Wolff Rearrangement:

Background

Pirrung, *JACS*, **1986**, *108*, 6060

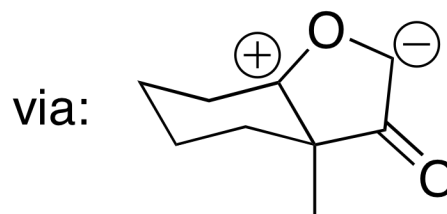Johnson, *JACS*, **1986**, *108*, 6062

Previous Work

Nu-H = H₂O, ROH, ArOH, ArNH₂, ArSH, etc

$Nu\text{-}H = H_2O, ROH, ArOH,$
$ArNH_2, ArSH, etc$

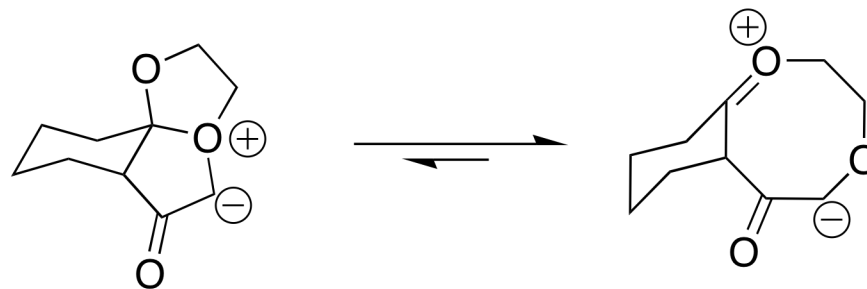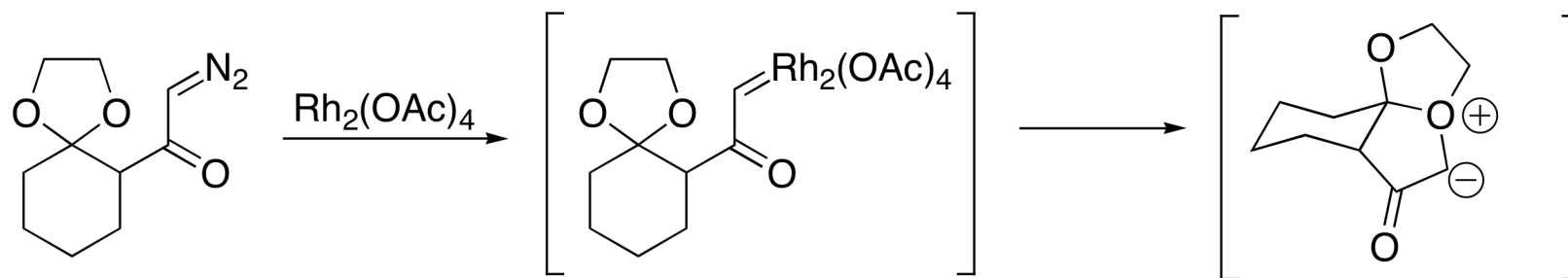Yield = 56-95%
dr = 100:0

via:

OL, **2005**, *7*, 4577

Previous Work
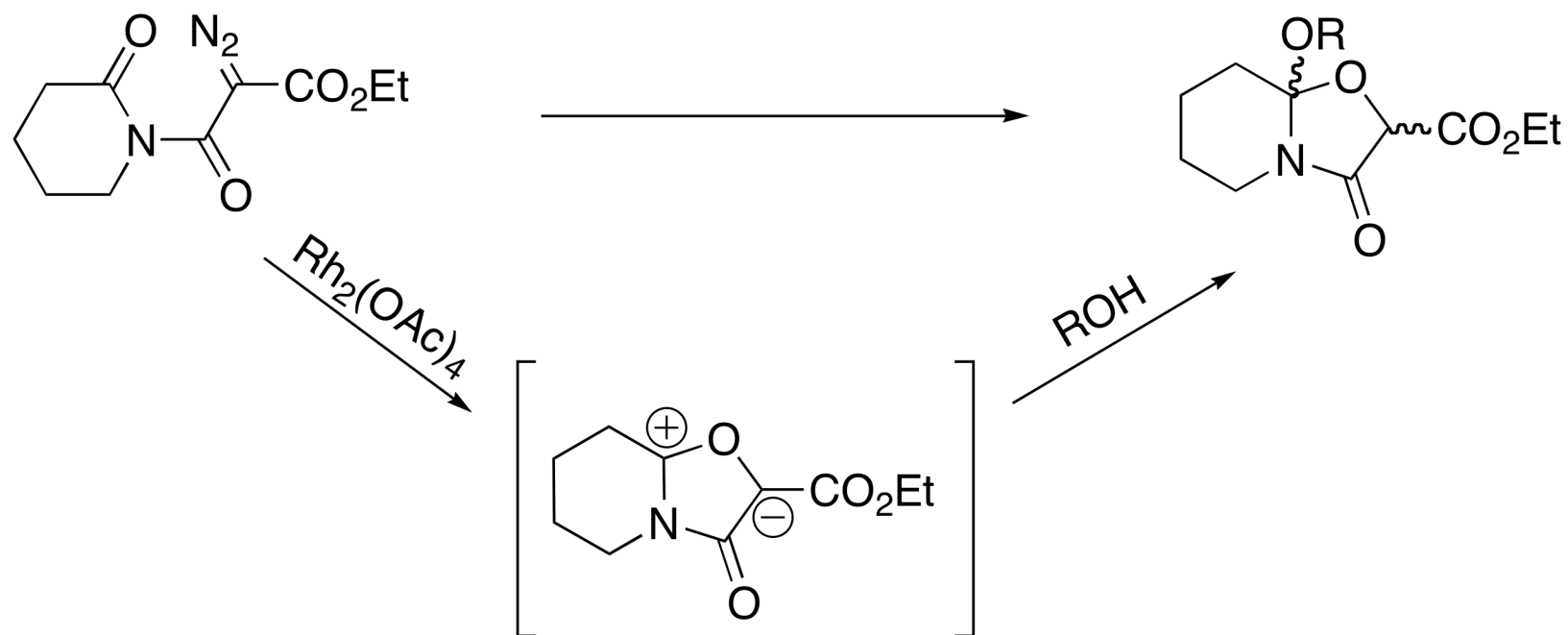
Chem. Commun., **2003**, 441
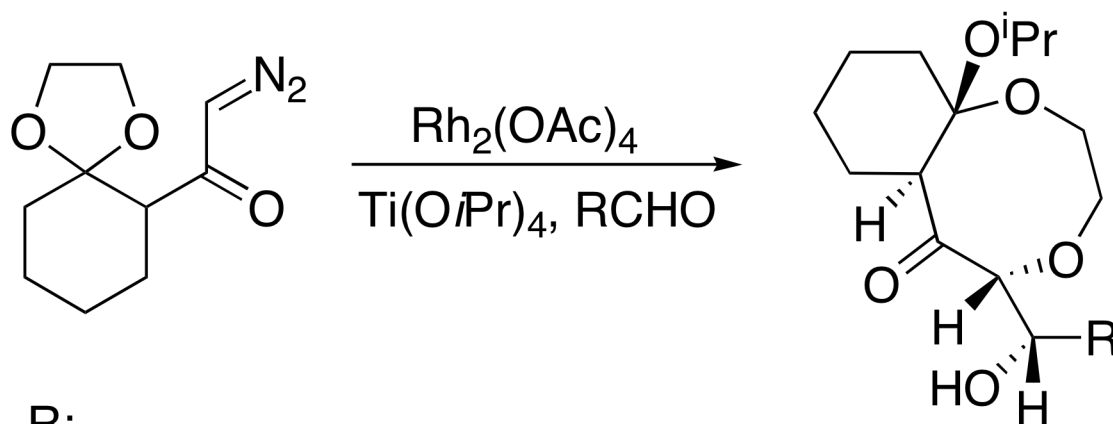
Current Work

Trapping with Nucleophiles

88%

Nu-H:

MeOH   85%
i-PrOH   70%
allyl-OH   74%
n-BuOH   72%
m-cresol   64%
4-tolyl-CO$_2$H 68%
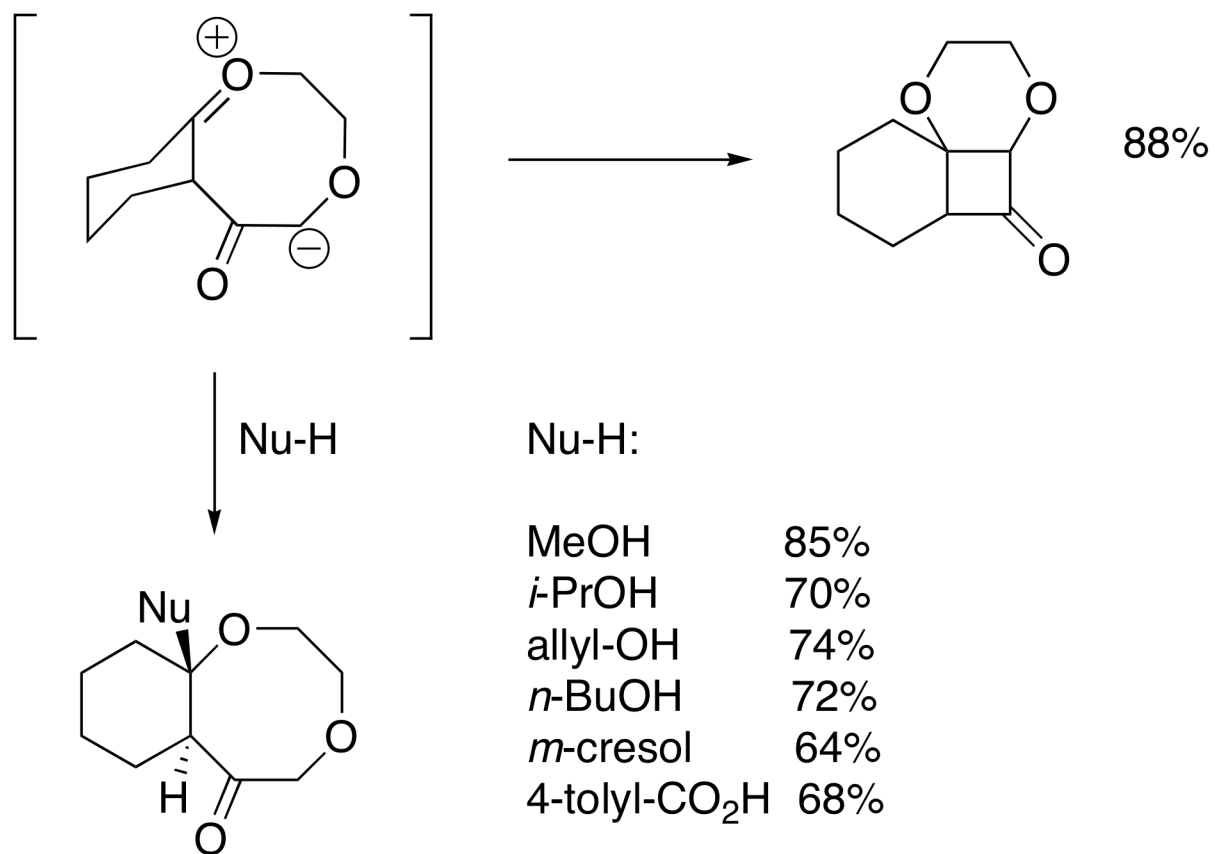
Trapping with Aldehydes

isolated as single diastereomers

R:

R	
Ph	79%
4-HOC$_6$H$_4$	87%
4-MeOC$_6$H$_4$	90%
4-CHOC$_6$H$_4$	78%
3-CHOC$_6$H$_4$	72%
4-BrC$_6$H$_4$	82%

Multicomponent Synthesis
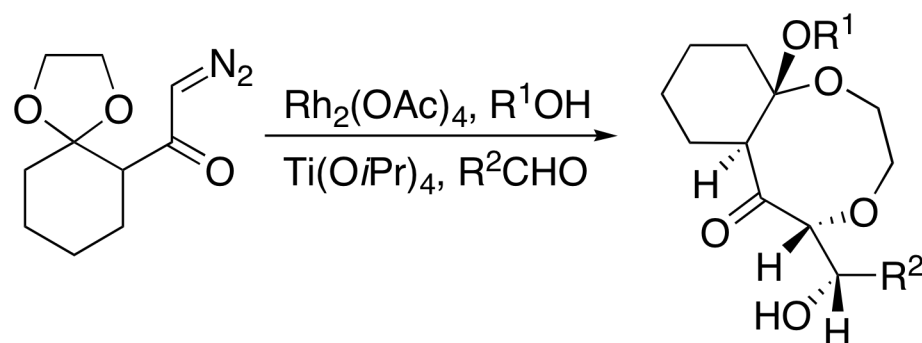
isolated as single diastereomers

R^1	R^2	
Me	Ph	81%
Et	Ph	77%
n-Bu	Ph	50%
Me	4-CHOC$_6$H$_4$	78%
Me	3-CHOC$_6$H$_4$	64%

crystal structure obtained

Trapping with Dialdehydes

2 eq.

isolated as single isomers
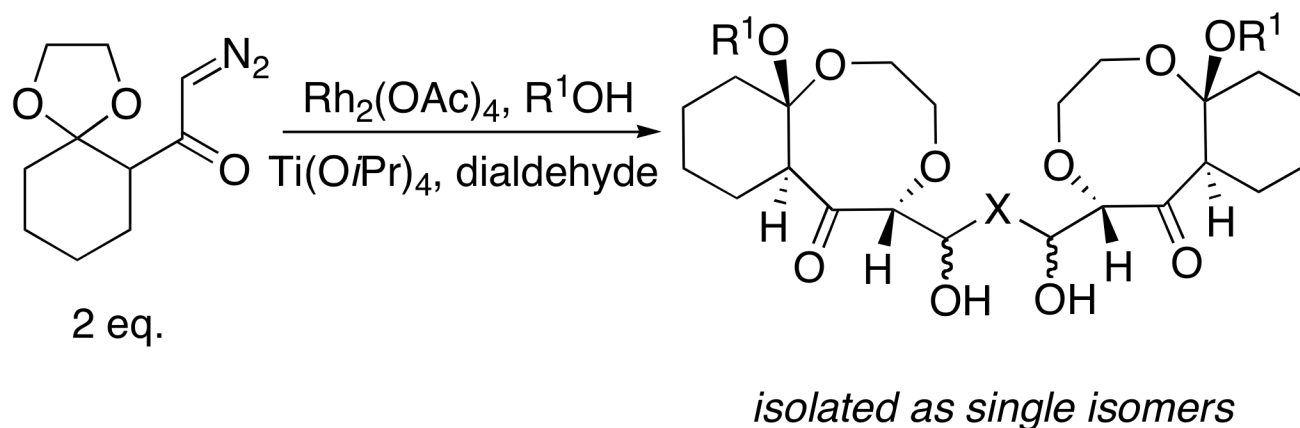
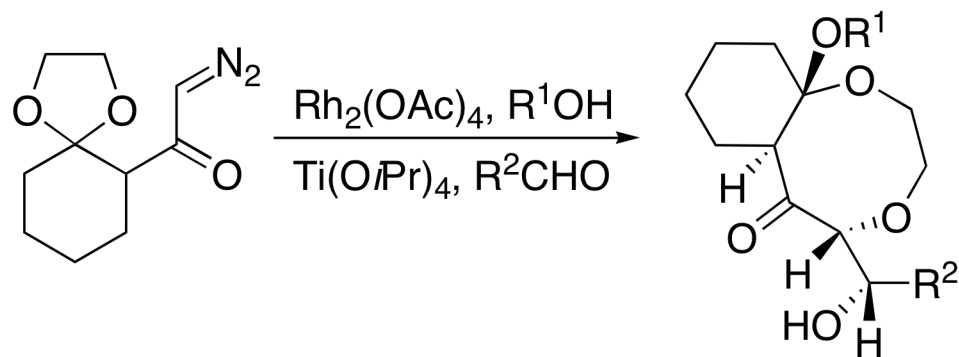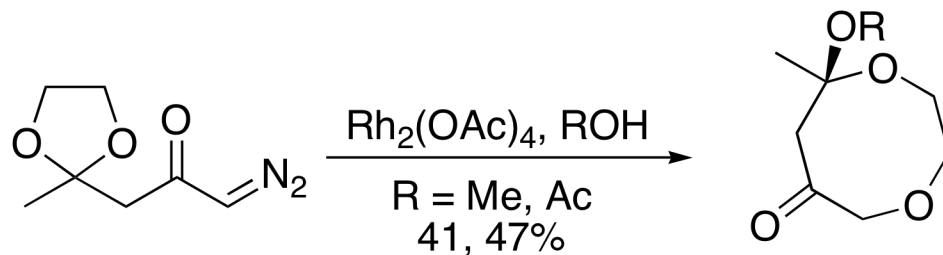| R^1	X	
i-Pr	1,4-C$_6$H$_4$	81%
i-Pr	1,3-C$_6$H$_4$	70%
Me	1,4-C$_6$H$_4$	63%
Me	1,3-C$_6$H$_4$	54%

Proposed Explanation for Stereoselectivity
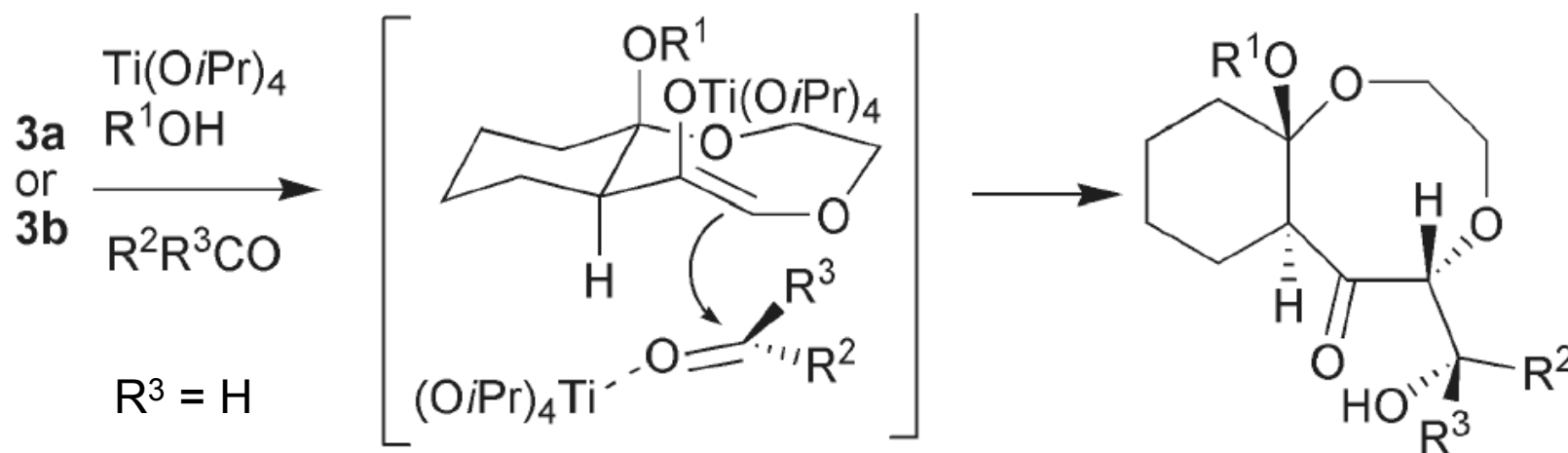
Note: bulkier R^2 pointed towards most of steric bulk; smaller R^3 pointed into free space…does this adequately explain the stereochemistry of the addition to the aldehyde?
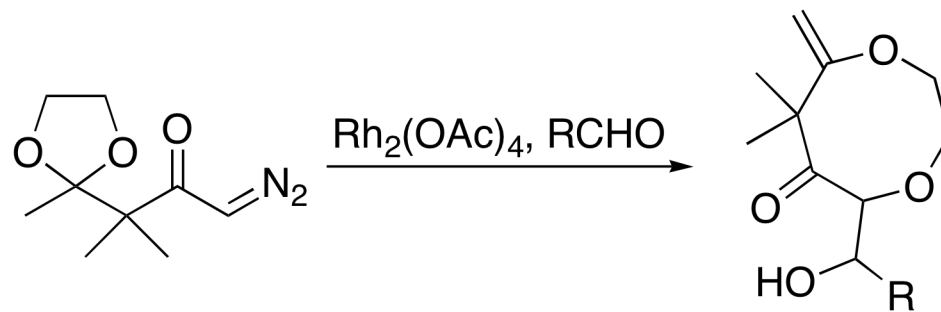
Novelty of Research

Current paper:

Oku, *JOC*, **1997**, *62*, 2123:

Oku, *Chem. Commun.*, **2001**, 1086:

Summary

- ## Strengths:
  - A tandem diazoketone decomposition / nucleophilic addition / electrophilic trapping was developed
  - Quick access to highly functionalized 8-membered rings with complete control of diastereoselectivity

- ## Weaknesses
  - Stereochemical outcome is not well explained
  - Novelty?
  - Enantiopure SM -> enantiopure product?