

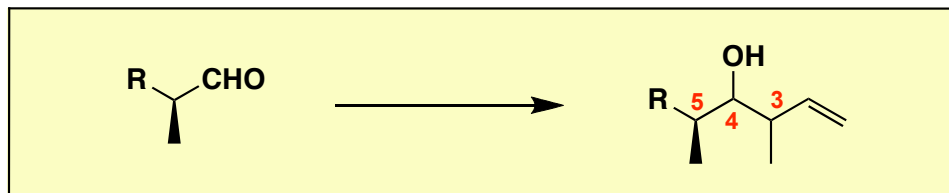
Massachusetts Institute of Technology

Organic Chemistry 5.511

November 30, 2007
Prof. Rick L. Danheiser

Lecture 17

Unit 5: Stereocontrolled Addition of Crotylmatal Compounds

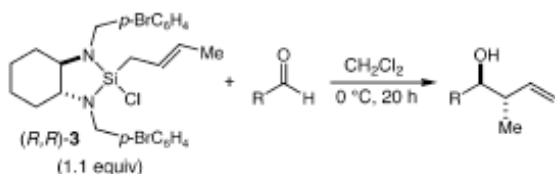


- ★ Substrate Control: Addition of Achiral Allylmets to α -Chiral Aldehydes
- ★ Reagent Control: Addition of Chiral Allylmets to Achiral Aldehydes
- ★ Reagent Control: Addition of Allylmets to Achiral Aldehydes (w/ Chiral Lewis Acids)
- ★ Addition of Chiral Allylmets to α -Chiral Aldehydes
- ★ Crotylmatal Additions: 3,4-Stereochemistry (Intrinsic Diastereoselection)
- ★ Crotylmatal Additions to α -Chiral Aldehydes

Crotylation with Leighton Reagents

Hackman, B. M.; Lombardi, P. J.; Leighton, J. L. *Org. Lett.* **2004**, 6, 4375

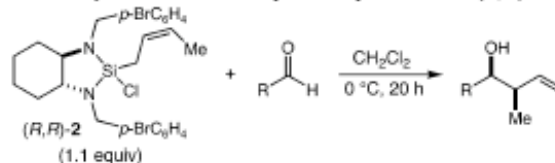
Table 2. *Anti*-Selective Aldehyde Crotylation with (*R,R*)-3



entry	R	yield (%)	ee ^a (%)
1	PhCH ₂ CH ₂	81	98
2	(CH ₃) ₂ CHCH ₂	71	97
3	Cy	68	97
4	BnOCH ₂	83	99
5	PMBOCH ₂ CH ₂	82	99
6	Ph	54	93
7	<i>p</i> -CF ₃ C ₆ H ₄	60	96
8	(<i>E</i>)-PhCH=CH	52	94

^a Enantiomeric excess determined by chiral GLC or HPLC.

Table 1. *Syn*-Selective Aldehyde Crotylation with (*R,R*)-2

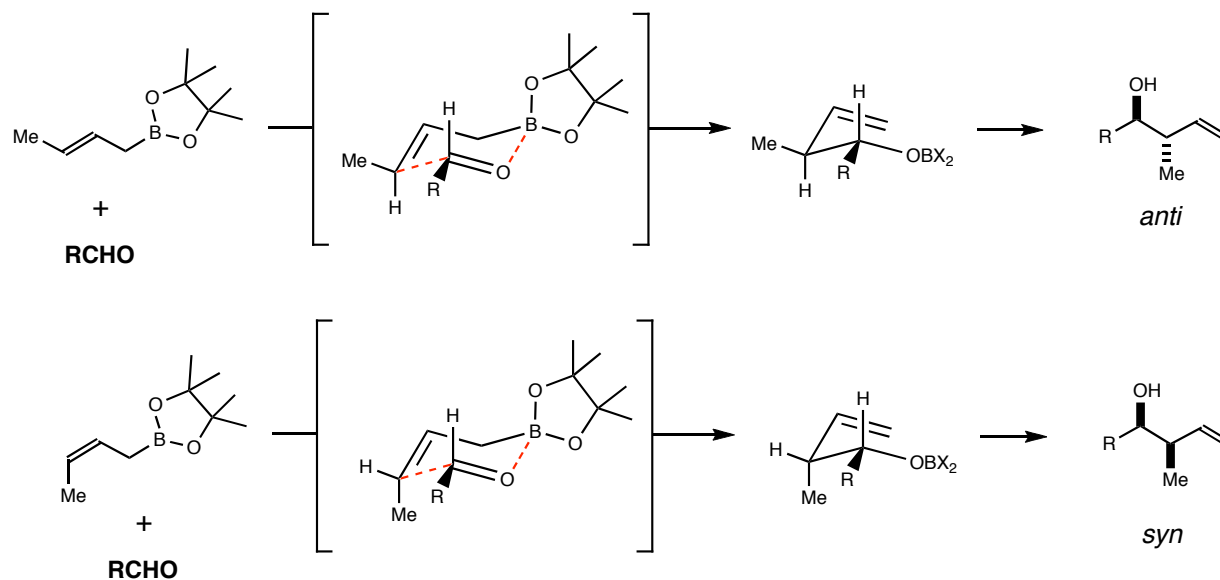


entry	R	yield (%)	ee ^a (%)
1	PhCH ₂ CH ₂	83	97
2	(CH ₃) ₂ CHCH ₂	70	96
3	Cy	67	97
4	BnOCH ₂	82	96
5	PMBOCH ₂ CH ₂	73	96
6	Ph	67	95
7	<i>p</i> -CF ₃ C ₆ H ₄	61	96
8	(<i>E</i>)-PhCH=CH	67	95

^a Enantiomeric excess determined by chiral GLC or HPLC.

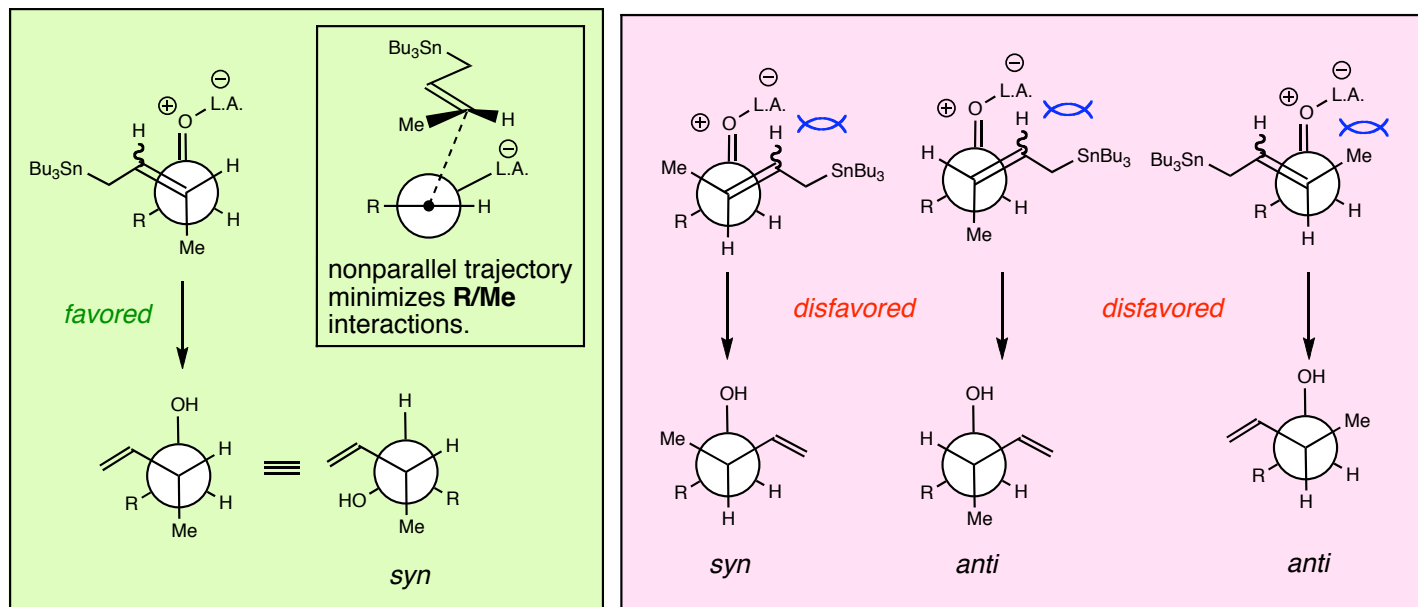
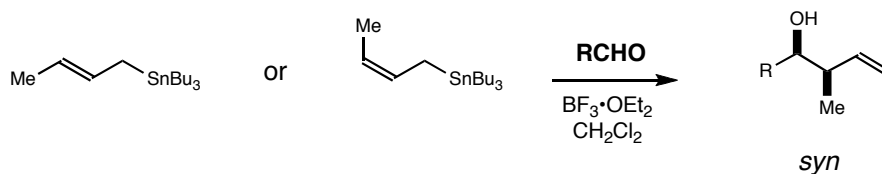
Type I Crotylmethyl Additions

The product *syn/anti* ratio reflects the (*Z*):(*E*) ratio in the crotyl moiety



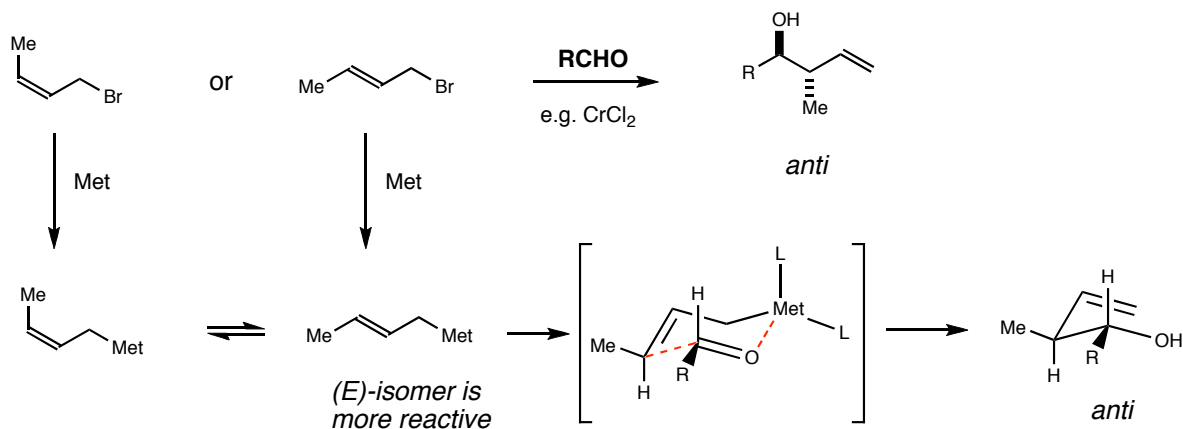
Type II Crotylmethyl Additions

Syn selective reactions with stereochemical outcome essentially independent of allyl geometry

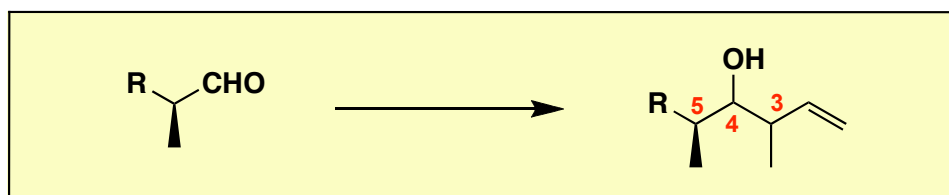


Type III Crotylmethyl Additions

Anti selective reactions independent of crotyl geometry



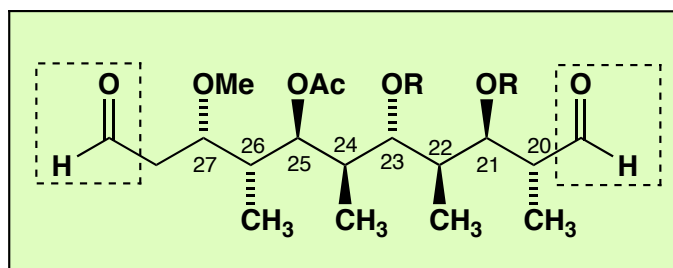
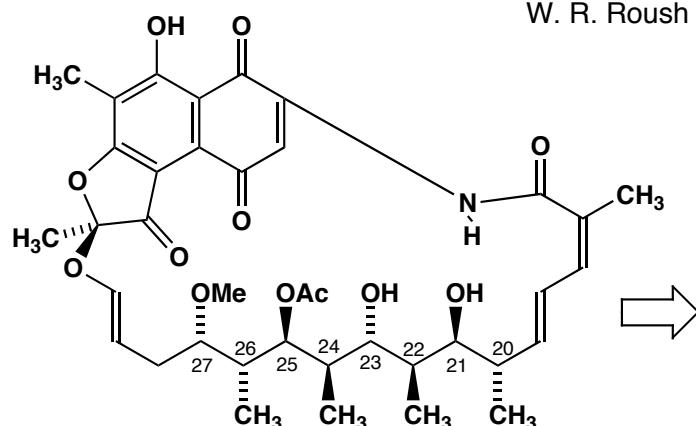
Construction of Stereotriads



Retron	C-3/C-4	C-4/C-5	C-3/C-5	Best Reagent
	Anti	Felkin	No Gauche Pentane	
	Anti	Anti-Felkin	Gauche Pentane	
	Syn	Anti-Felkin	No Gauche Pentane	
	Syn	Felkin	Gauche Pentane	

Case Study

W. R. Roush et al. *J. Am. Chem. Soc.* **1990**, *112*, 6348



Rifamycin S

