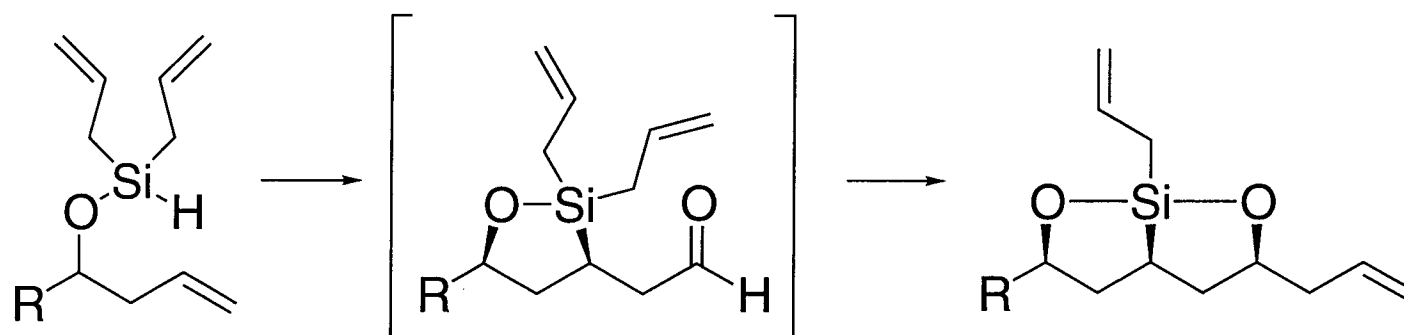


Rhodium Catalyzed Intramolecular Silylformylation



I) Introduction

II) Intramolecular silylformylation:

A) Of alkynes

B) Of ω -(dimethylsiloxy)alkynes

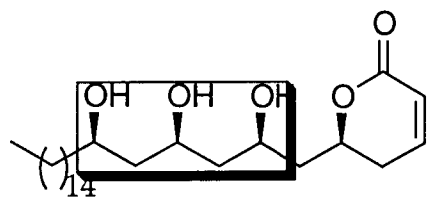
C) Of bis(silylamino)alkynes

D) Of alkenes

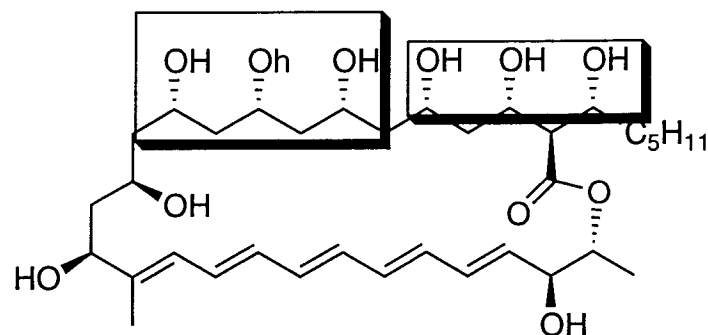
E) Tandem intramolecular silylformylation-allylsilylation

III) Conclusion

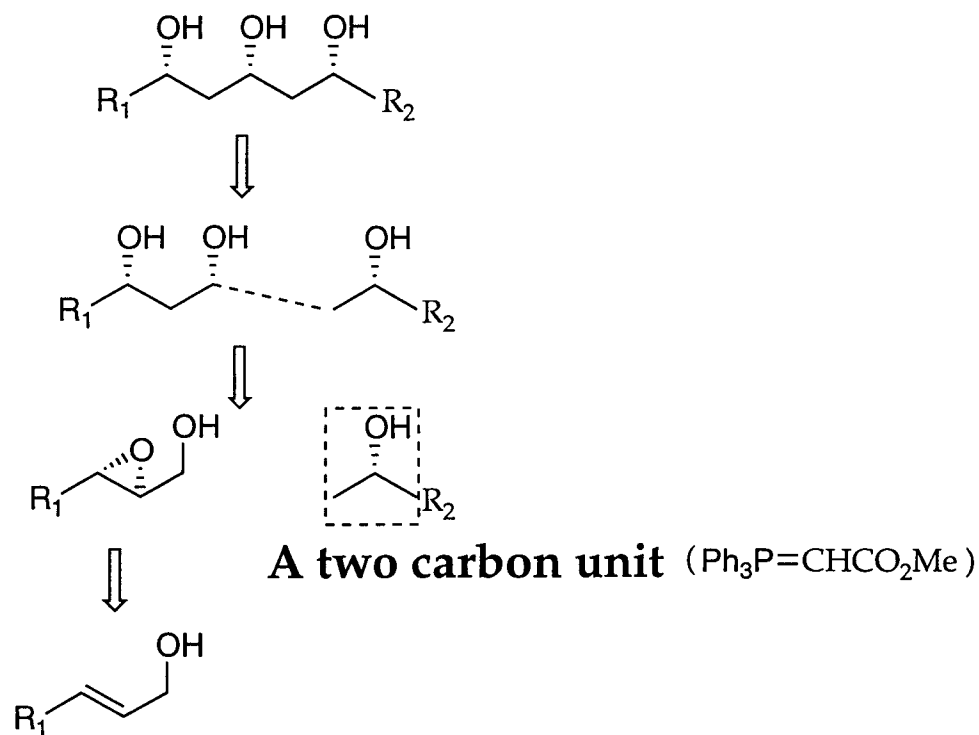
Natural Products with Polyol Structural Motif



Syn triol unit
Syn-tetraol derivative



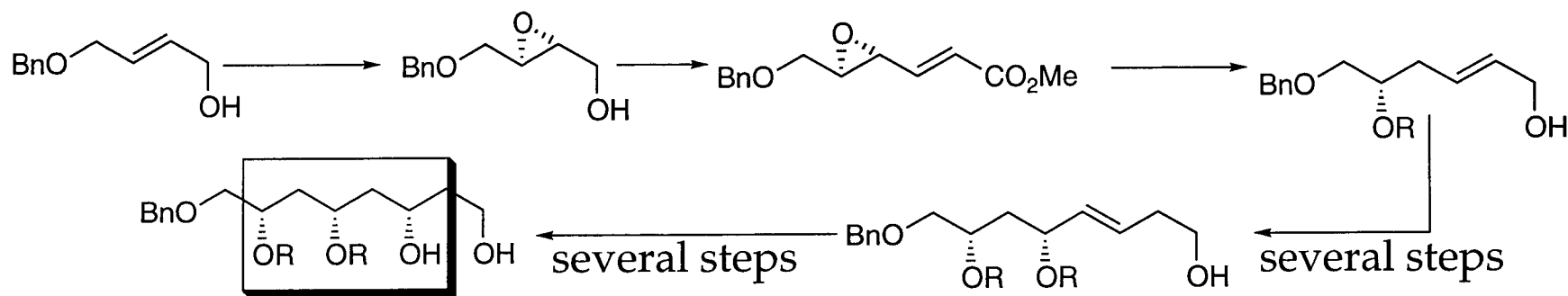
Filipin III



A Known Method for Constructing *Syn* triol Units

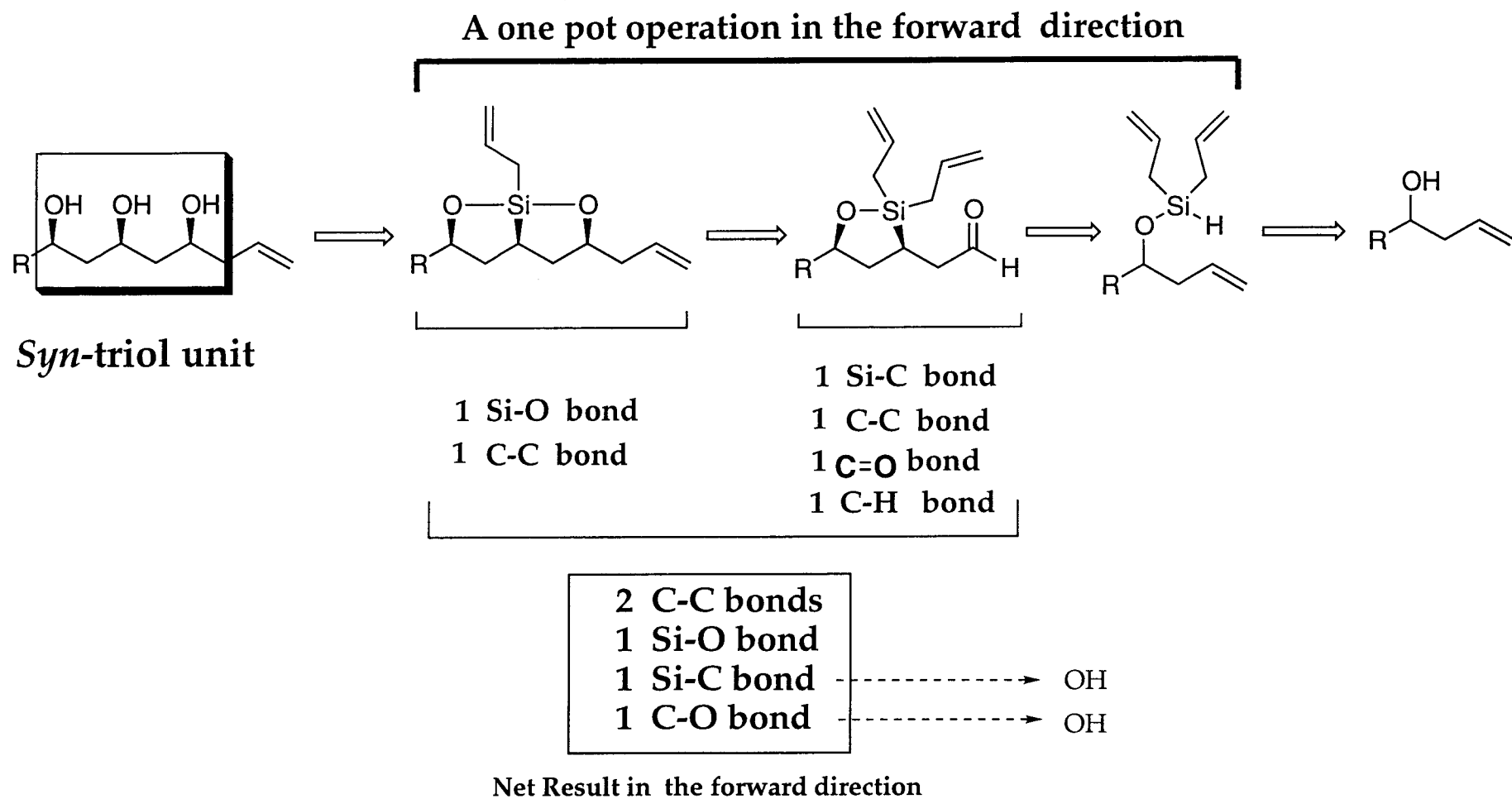
Strategy: Sharpless asymmetric epoxidation

Allylic alcohol \longrightarrow Epoxide \longrightarrow Oxidation/Wittig \longrightarrow Epoxide opening \longrightarrow Repeat

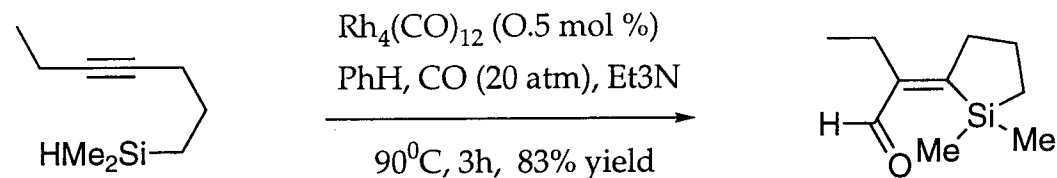


Nicolaou, K.C., J.Chem.Soc. Chem. Commun. 1982, 1292
Kishi, Y. Tetrahedron Lett. 1982, 23,2719

Intramolecular Silylformylation

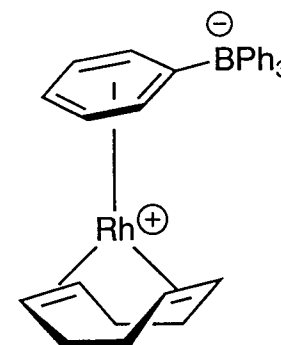


Intramolecular Silylformylation of Alkynes

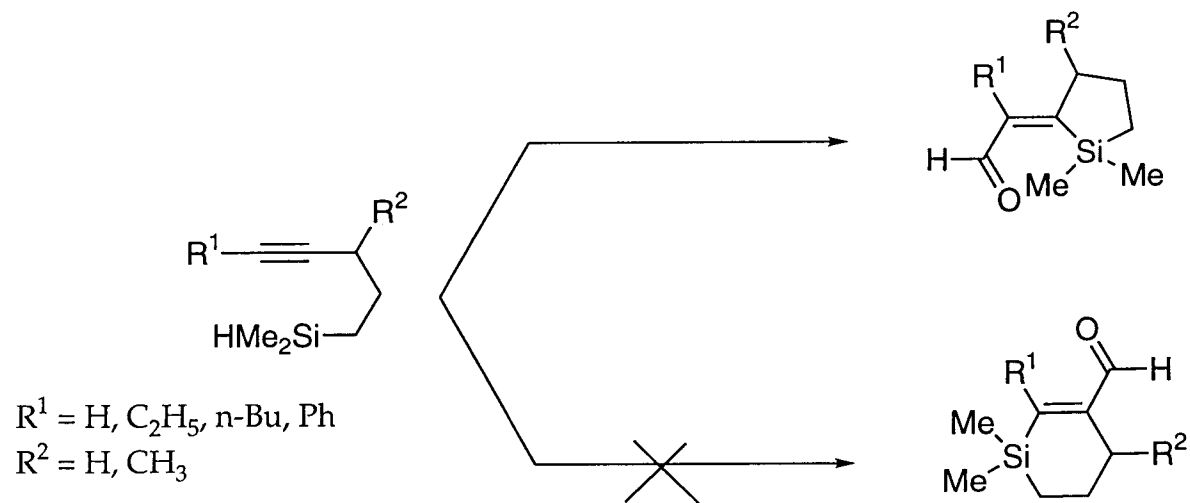


entry	alkynylsilane 4	catalyst ^a	product 6 ^b	yield (%) ^c
1		5		43
2		5		56
3		5		37
4		5		49
5		$\text{Rh}_4(\text{CO})_{12}$		83
6		$\text{Rh}_4(\text{CO})_{12}$		71
7		$\text{Rh}_4(\text{CO})_{12}$		79

Alternative catalyst (5)

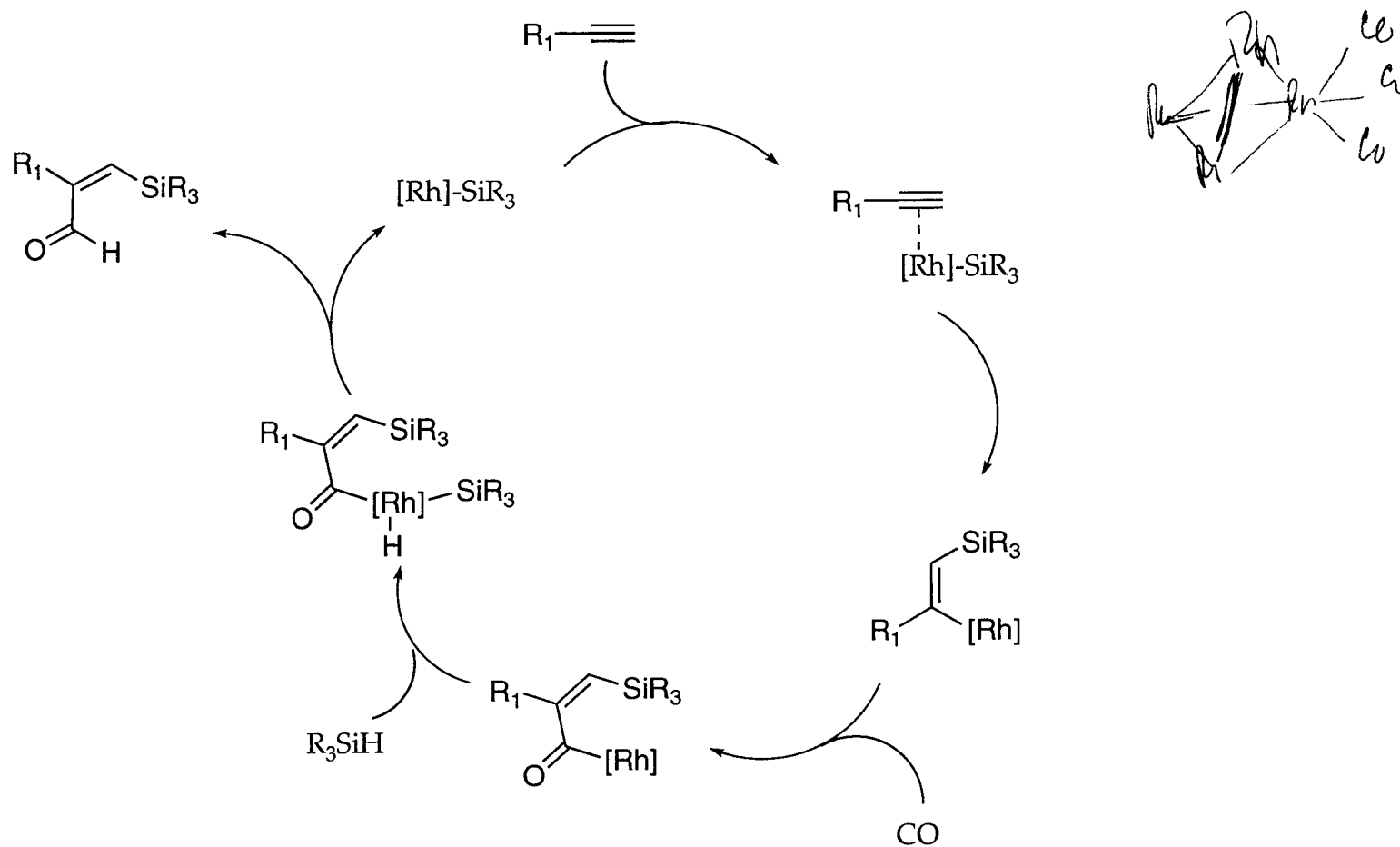


Regiochemistry

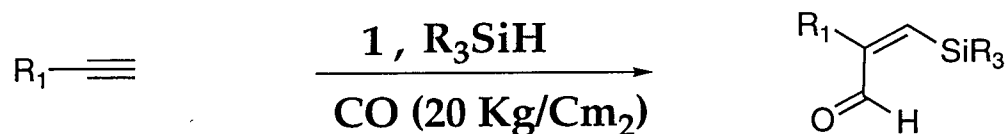
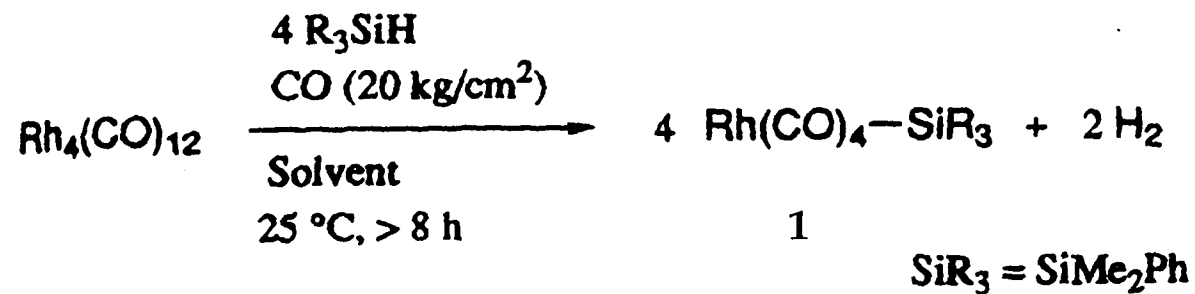


Alper, H., Matsuda, I. J. Am. Chem. Soc 1995, 117, 4419

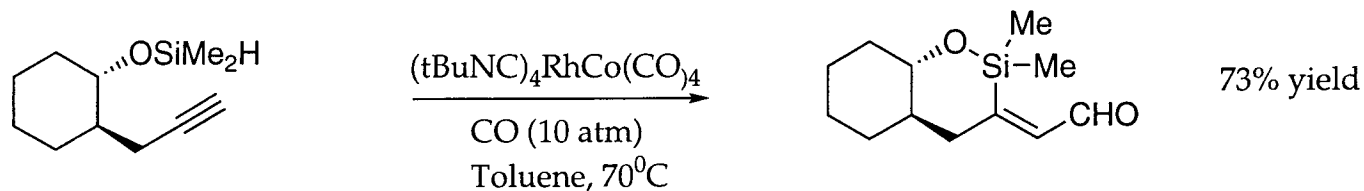
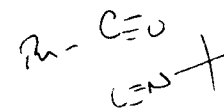
Mechanism for Silylformylation of Alkynes



Active Catalytic Species



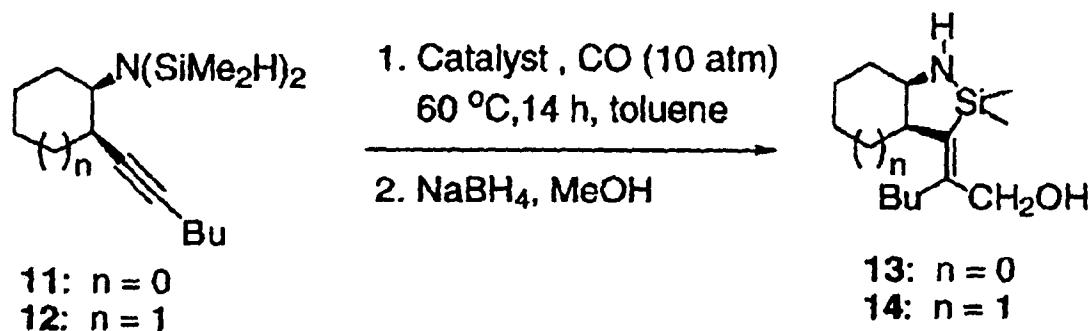
Dimethylsiloxy tethered Alkynes



Entry	ω -HSiMe ₂ O-alkyne	Catalyst	Temp. ($^\circ\text{C}$)	Time (h)	Product	Yield (%) ^b
1		$(t\text{BuNC})_4\text{RhCo}(\text{CO})_4$	70	14		89 (42)
2		$\text{Rh}_2\text{Co}_2(\text{CO})_{12}$	70	18		46
3		$\text{Rh}(\text{acac})(\text{CO})_2$	70	16		62
4		$(t\text{BuNC})_4\text{RhCo}(\text{CO})_4$	60	14		99 (66)
5		$\text{Rh}_2\text{Co}_2(\text{CO})_{12}$	60	3		84
5		$\text{Rh}(\text{acac})(\text{CO})_2$	60	3		93
7		$\text{Rh}_4(\text{CO})_{12}, \text{Et}_3\text{N}$	85 ^d	3.5		69
8		$(t\text{BuNC})_4\text{RhCo}(\text{CO})_4$	65	14		99 (73)
9		$\text{Rh}_2\text{Co}_2(\text{CO})_{12}$	65	3		80
10		$\text{Rh}(\text{acac})(\text{CO})_2$	65	3		96
11		$\text{Rh}_4(\text{CO})_{12}, \text{Et}_3\text{N}$	85 ^d	2		77 (51)

^a Reactions were run with ω -(dimethylsiloxy)alkyne (0.50 mmol) and a catalyst (2.5×10^{-3} mmol) in dry toluene (3.0 mL) in a 5 mL Pyrex reaction vessel under carbon monoxide (10 atm) using a 300 mL stainless steel autoclave unless otherwise noted. ^b GC yield. The value in parentheses is isolated yield after bulb-to-bulb distillation. ^c The reaction was performed in 15 mL of dry toluene under 50 atm of carbon monoxide. ^d The reaction was run using 2.76 mmol of ω -(dimethylsiloxy)alkyne, 7.3×10^{-3} mmol of catalyst, and 2.91 mmol of triethylamine in 13 mL of dry benzene under 20 atm of carbon monoxide.

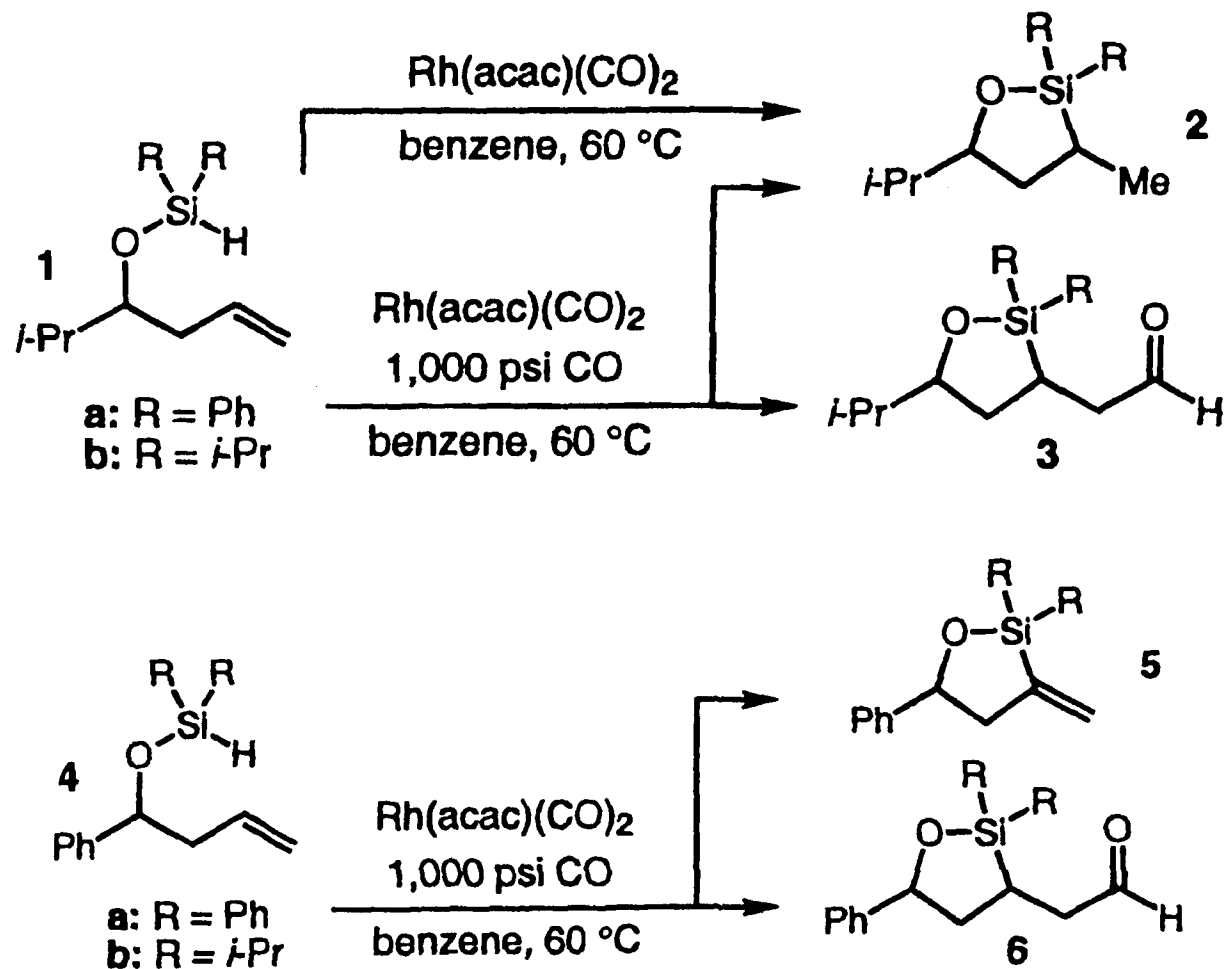
Bis(silylamino)Alkynes



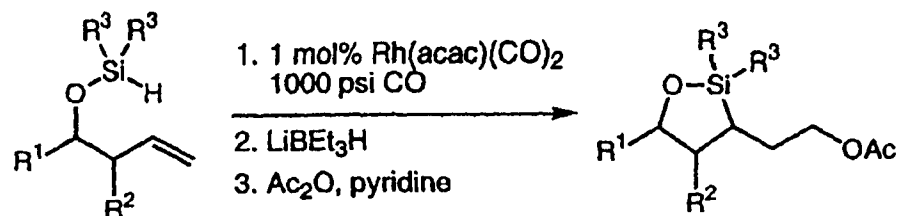
Catalyst: $(^t\text{BuNC})_4\text{RhCo}(\text{CO})_4$, $\text{Rh}(\text{acac})(\text{CO})_2$

Entry	Substrate	Catalyst	Product	Yield (%) ^a
		$\text{Rh}(\text{acac})(\text{CO})_2$		52
		$(^t\text{BuNC})_4\text{RhCo}(\text{CO})_4$		80
		$\text{Rh}(\text{acac})(\text{CO})_2$		71
		$(^t\text{BuNC})_4\text{RhCo}(\text{CO})_4$		87
		$\text{Rh}(\text{acac})(\text{CO})_2$		61
		$(^t\text{BuNC})_4\text{RhCo}(\text{CO})_4$		78
		$\text{Rh}(\text{acac})(\text{CO})_2$		84

Intramolecular Silylformylation of Alkenes

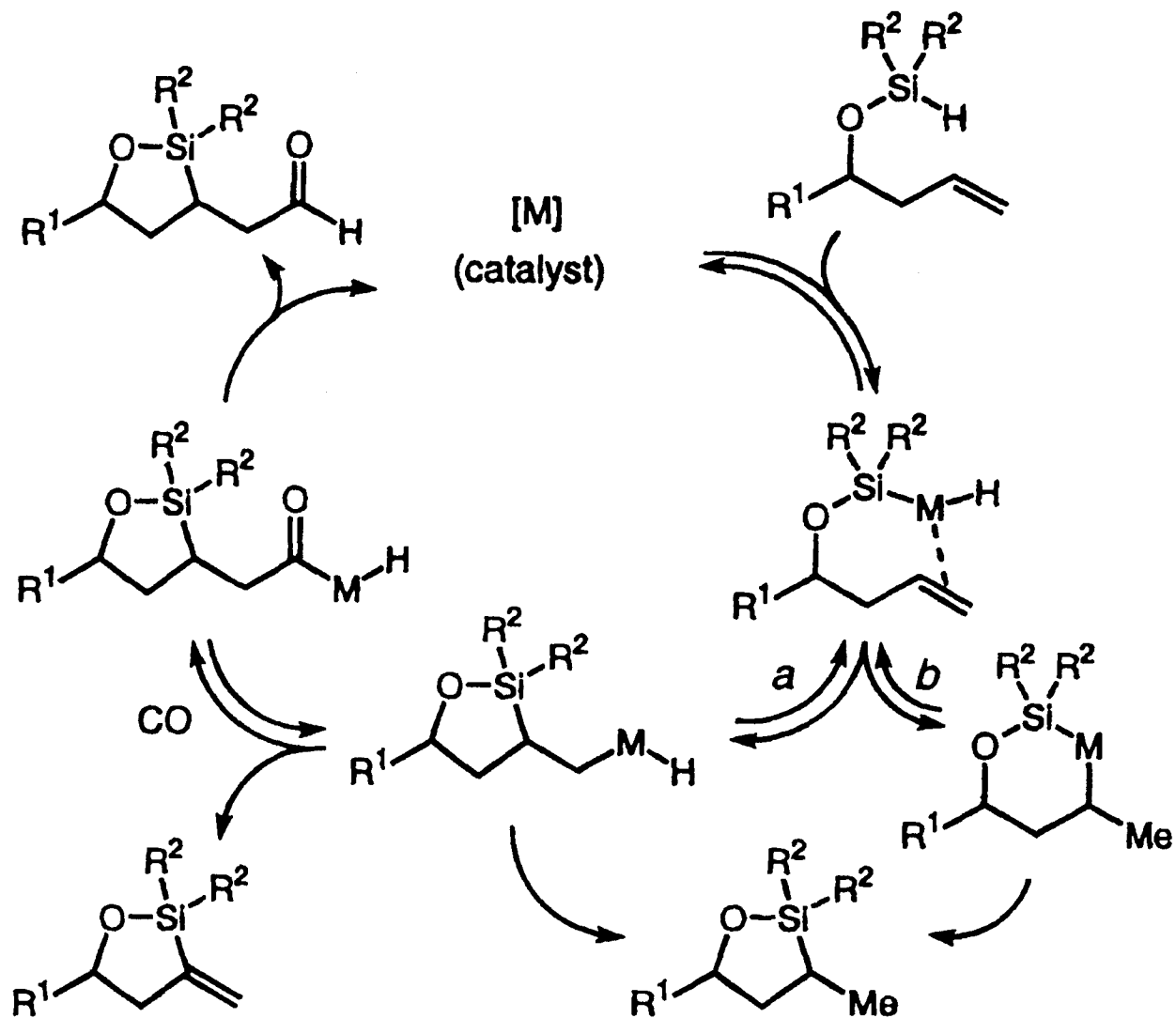


Scope of the Reaction

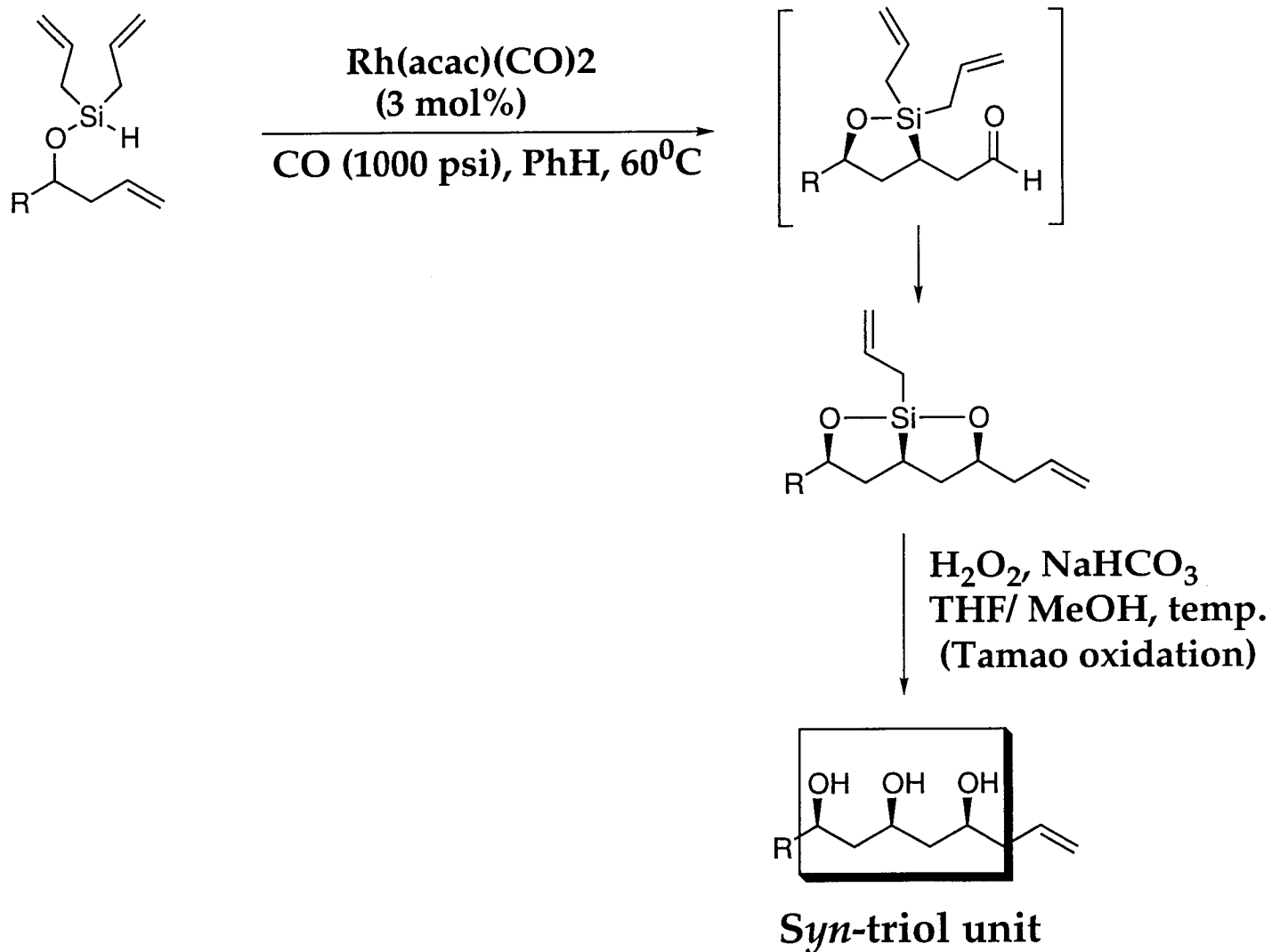


entry	R ¹	R ²	R ³	major product	ds ^b	y (%) ^c
1	Me	H	Ph		4.5:1	67
2	allyl	H	Ph		4:1	64
3	<i>i</i> Pr	H	Ph		6:1	79
4		H	Ph		4:1	60
5	Ph	H	<i>i</i> Pr		7:1	54
6	H	Me	Ph		11:1	10 ^d
7 ^e	<i>i</i> Pr	Me	Ph		10:1	71

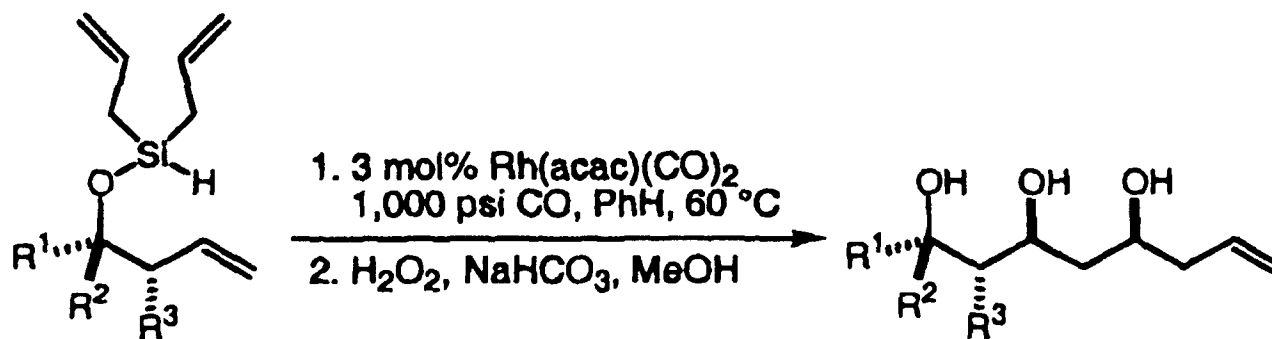
Reaction Mechanism



Tandem Intramolecular Silylformylation-Allylsilylation



Experimental Results

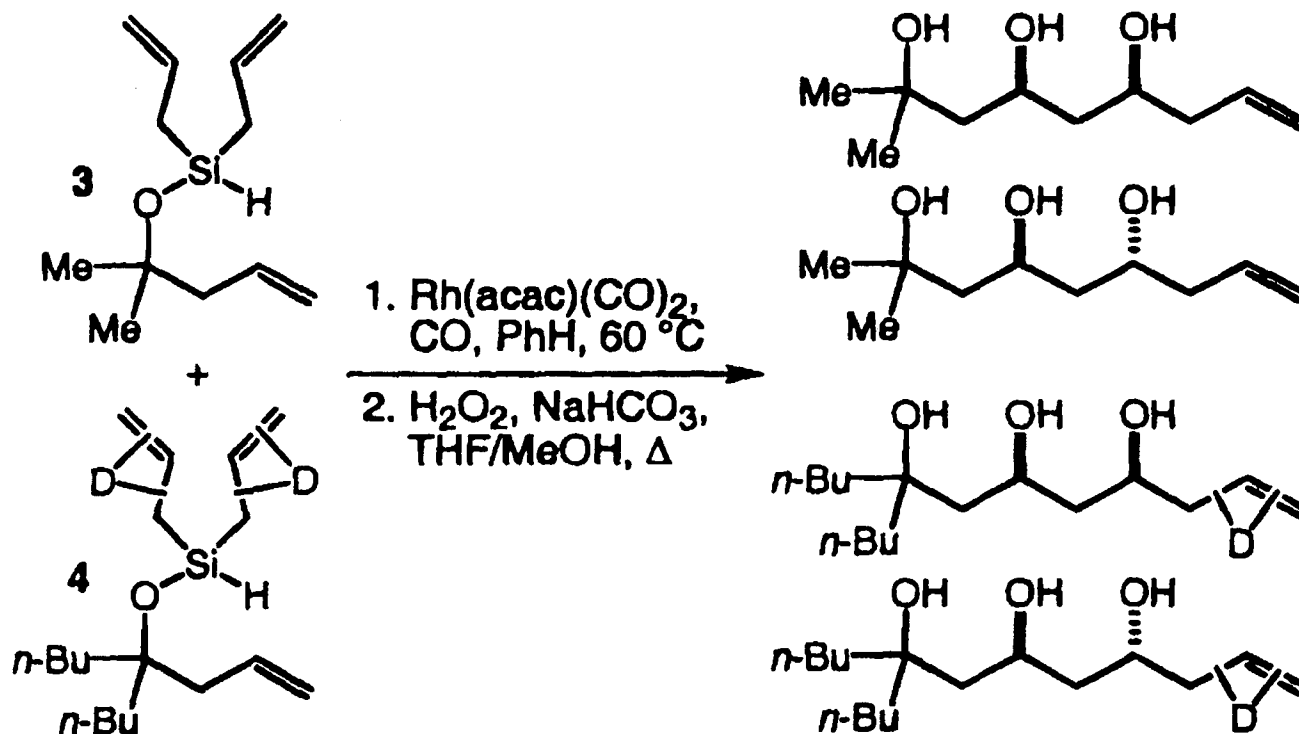


entry	R ¹	R ²	R ³	d.s. ^b	y (%) ^c
1	H	<i>i</i> -Pr	H	77:23	59
2	H	TBSOCH ₂ CH ₂	H	71:29	45
3	H	CH ₂ =CHCH ₂	H	69:31	50
4	H	<i>i</i> -Pr	Me	92:8	59
5	Me	Me	H	93:7	65

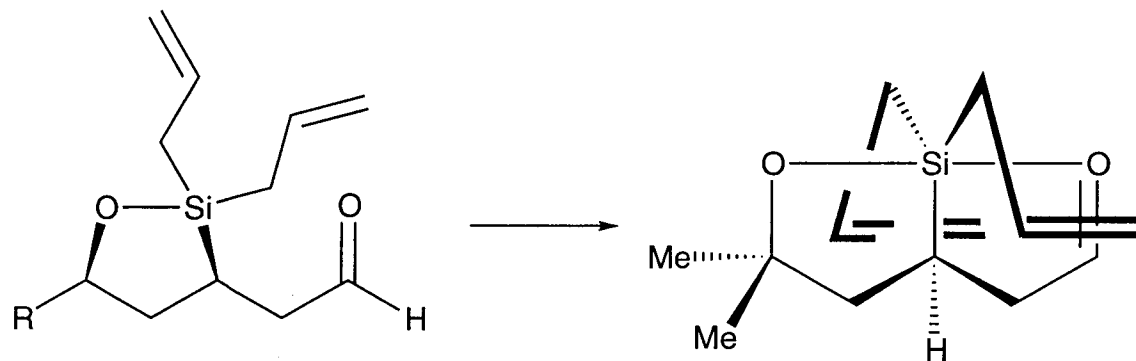
^a All reactions were conducted in a stainless steel pressure reactor equipped with a pressure gauge and a glass liner. ^b *Syn,syn* triol: sum of all other diastereomers. ^c Isolated yield of purified major product.

Is it an Inter or Intra ?

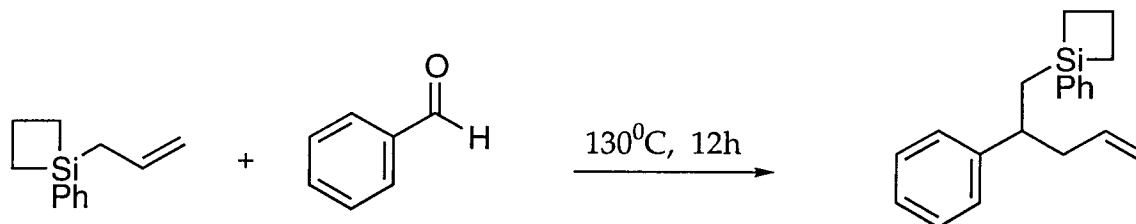
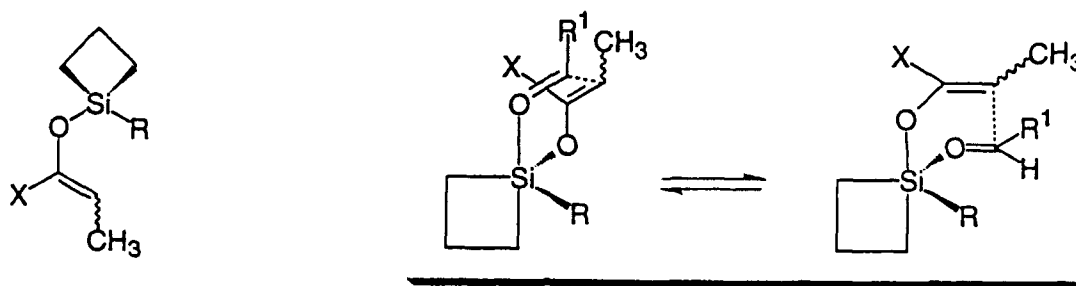
Deuterium Labeled Crossover Experiments:



Allylsilation Step: the Driving Force?

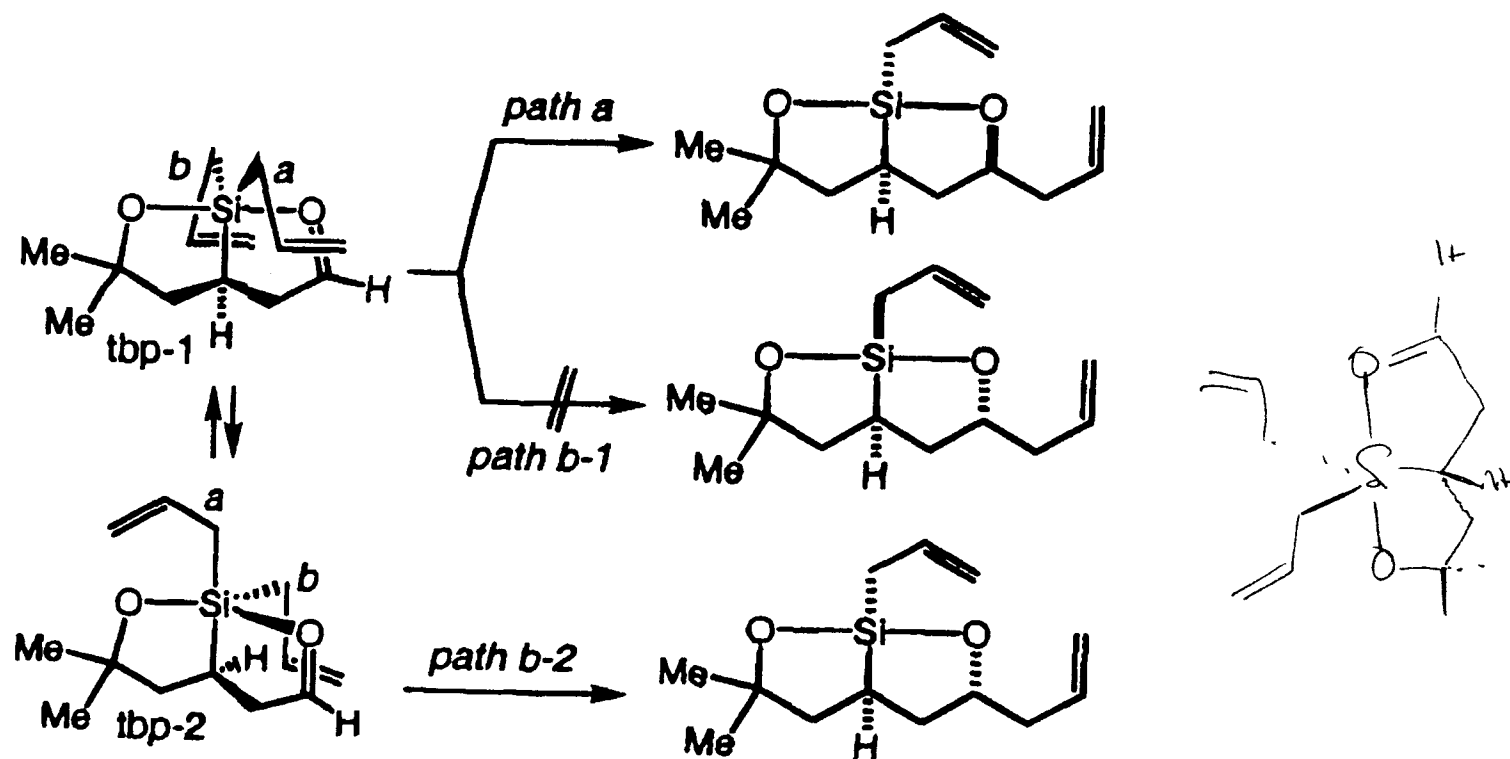


" Strain Release Lewis Acidity"



Denmark, S.E., *J. Am. Chem. Soc.*, 1994, 116, 7026
Myers, A. G., *J. Am. Chem. Soc.*, 1992, 114, 7922
Oshima, K. *J. Org. Chem.*, 1994, 59, 7152

Rationale for the Stereochemistry



Conclusion

Intramolecular silyformylation of alkynes and alkenes has been demonstrated

With this chemistry, a highly efficient method for generation of compounds with highly densed hydroxyl functionalites has been developed.

Still need to be improved

Rhodium (I) metal plays a remarkable role in these transformations