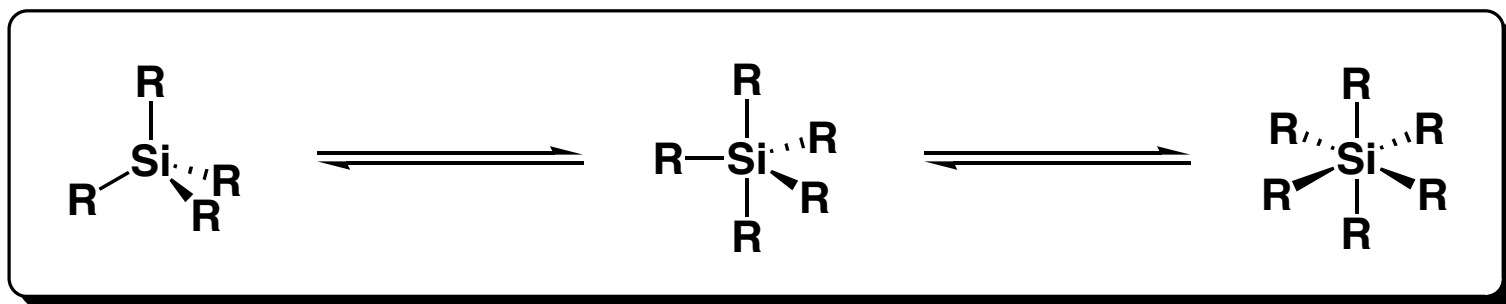


# ***Hypervalent Silicon: Bonding, Properties and Synthetic Utility***



*MacMillan Group Meeting  
Ian Storer  
20th July, 2005*

# Hypervalent Silicon: Reactivity and Application in C-C Bond Formation

*presentation outline*

## ■ Introduction to hypervalent silicon chemistry

- comparison of silicon with carbon – reactivity & coordination
- physical and chemical reactivity characteristics of hypervalent silicon complexes
- bonding considerations

## ■ Asymmetric C(sp<sup>3</sup>) – C(sp<sup>3</sup>) bond forming reactions – Organocatalytic Lewis base catalysis

- Conceptual origins – Sakurai allylation reaction (mid 1980s)
- Asymmetric addition of allyl silanes – Kobayashi, Denmark, Kocovsky (1994-present)
- Asymmetric synthesis of aldol products – Denmark (1994-present)

## ■ C(sp<sup>n</sup>) – C(sp<sup>2</sup>) bond forming reactions

- Pd cross-coupling – Denmark (1994-present)

### Useful Reviews:

- Hypervalent Silicon as a Reactive Site in Selective Bond-Forming Processes. Rendler, S., Oestreich, M., *Synthesis*. **2005**, *11*, 1727-1747.
- Carbon-Carbon Bond Forming Reactions Mediated by Silicon Lewis Acids. Dilman, A. D., Ioffe, S. L., *Chem. Rev.* **2003**, *103*, 733-772.
- Comparison of Phosphorus and Silicon: Hypervalency, Stereochemistry and Reactivity. Holmes, R. R., *Chem. Rev.* **1996**, *96*, 927-950.
- Reactivity of Penta- and Hexacoordinate Silicon Compounds and Their Role as Reaction Intermediates. Chult, C., Corriu, R. J. P., Réye, C., Young, J. C., *Chem. Rev.* **1993**, *93*, 1371-1448.
- Corriu, R. J. P.; Perz, R.; Réye, C. *Tetrahedron*, **1983**, *39*, 999.

# Introduction to Silicon Chemistry

## physical properties

### ■ Physical characteristics

- Silicon comes directly below carbon in periodic table – atomic no. = 14 ( $3s^2 3p^2$ )

Electronegativity (Allred-Rochow scale)		$\sigma$ -Bond strengths (kcal/mol)		Average Bond Lengths (Å)	
Si	1.7	C–C	83	C–C	1.54
		C–Si	76	C–Si	1.87
H	2.1	Si–Si	53		
		C–H	83	C–O	1.43
C	2.5	Si–H	76	Si–O	1.66
Cl	3.0				
		C–O	86		
N	3.0	Si–O	108		
		C–N	83		
O	3.5	Si–N	76		
F	4.0	C–F	116		
		Si–F	135		

- Silicon forms **very strong bonds to oxygen and fluorine**. Much of organosilicon chemistry is driven by the formation of these bonds at the expense of weaker bonds
- Silicon does not form very stable multiple bonds, as the large 3p orbital on Si does not overlap well with the 2p orbital on C, O or N

⇒ Si=C, Si=O and Si=N are generally not found

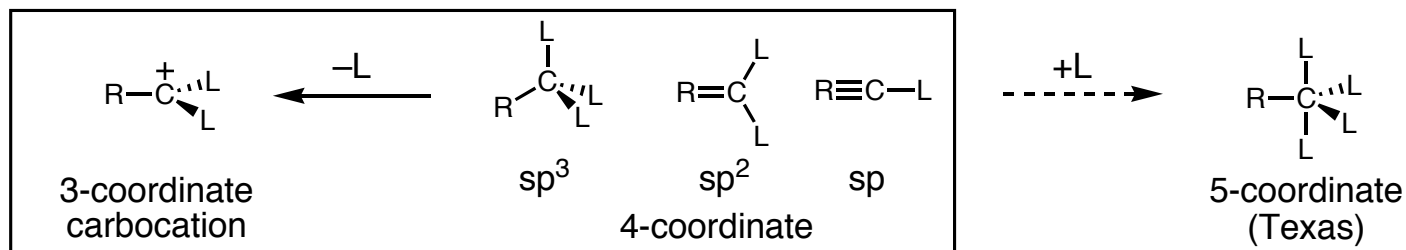
### $\pi$ -Bond strengths (kcal/mol)

C=C	65
C=Si	36

## Coordination of Silicon vs Carbon

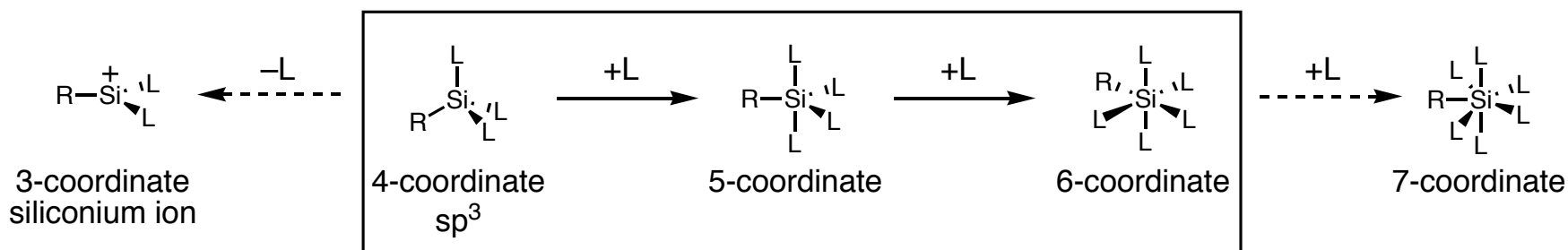
common coordinations

### Carbon ( $2s^2 2p^2$ ): adopts 3- and 4- coordinate complexes



- Carbon is unable to access hypervalent complexes
- Silicon is below carbon in the periodic table but is capable of very different bonding characteristics

### Silicon ( $3s^2 3p^2$ ): adopts 4-, 5- and 6- coordinate complexes



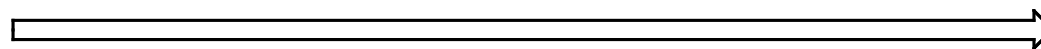
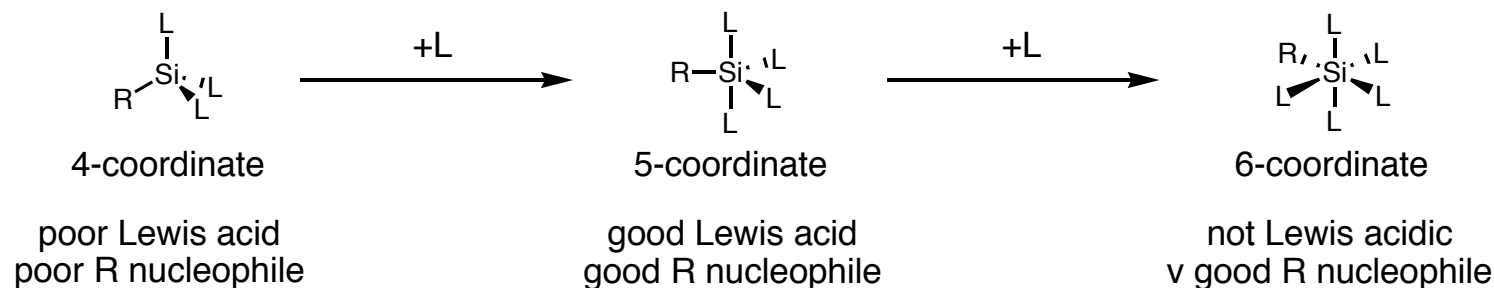
- How does silicon access these higher coordination complexes? – need to consider the bonding options available
- What are the reactivity profiles of the different coordination states?

# Hypervalent Silicon : Pentavalent and Hexavalent Complexes

## Chemical Reactivity

### ■ Silicon can adopt 4-, 5- and 6- coordinate complexes

- 4-coordinate = electrophile,
- 5-coordinate = electrophile & nucleophile,
- 6-coordinate = nucleophile



- Increasing  $\delta^+$  at silicon
- Increasing  $\delta^-$  at ligands L and R
- Increasing Lewis acidity

L = negatively charged or neutral silaphilic ligands such as  
F, Cl, O-alkyl, O-aryl (good Lewis bases)

R = H or C(sp<sup>n</sup>) (n = 1-3)

nucleophilicity of R = ability of R-transfer

■ Electron density at Si decreases with increased coordination, causing the electropositive character (Lewis acidity) of the Silicon centre to be increased

■ How does the extracoordination or hypervalency originate – vacant d-orbitals on Si combined with the effect of  $\sigma^*$  (Si-L) orbitals

# Bonding to Silicon - How are 5 or 6 Bonds Accommodated?

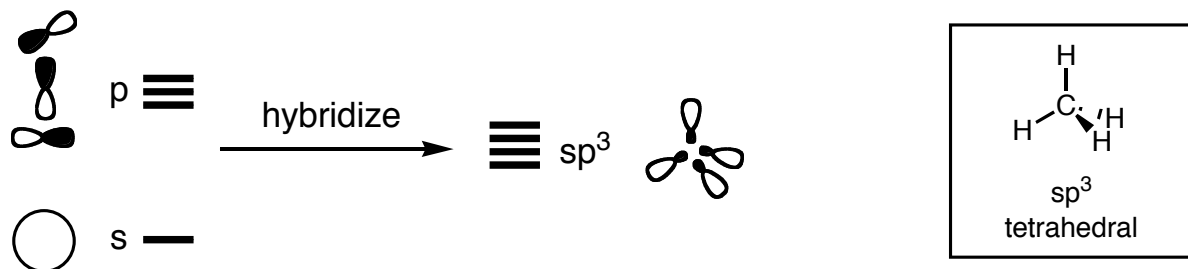
Valence Shell Electron Pair Repulsion Theory (VSEPR)

■ Theory to account for molecular bond geometries

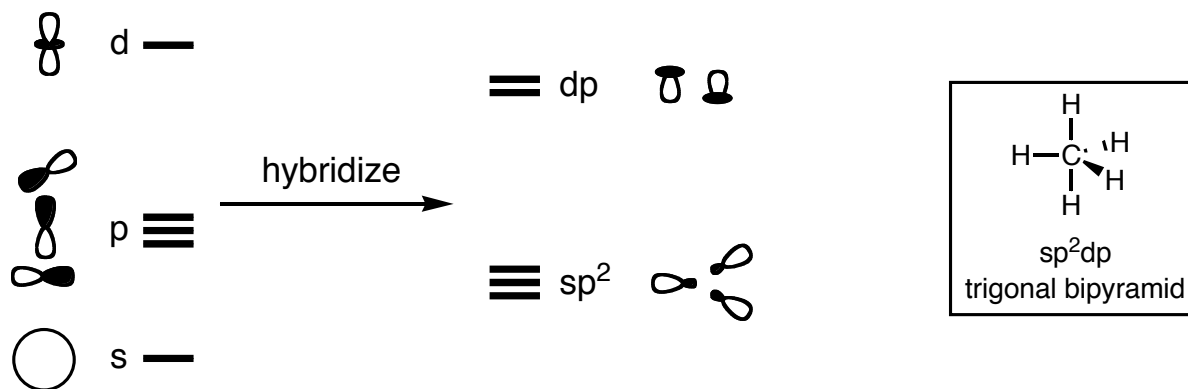
■ Predicted hybrid orbitals for 2–6 coordinate compounds



■ Tetrahedral coordination – sp<sup>3</sup> rehybridization



■ Trigonal bipyramidal 5-coordinate – sp<sup>3d</sup> rehybridization?



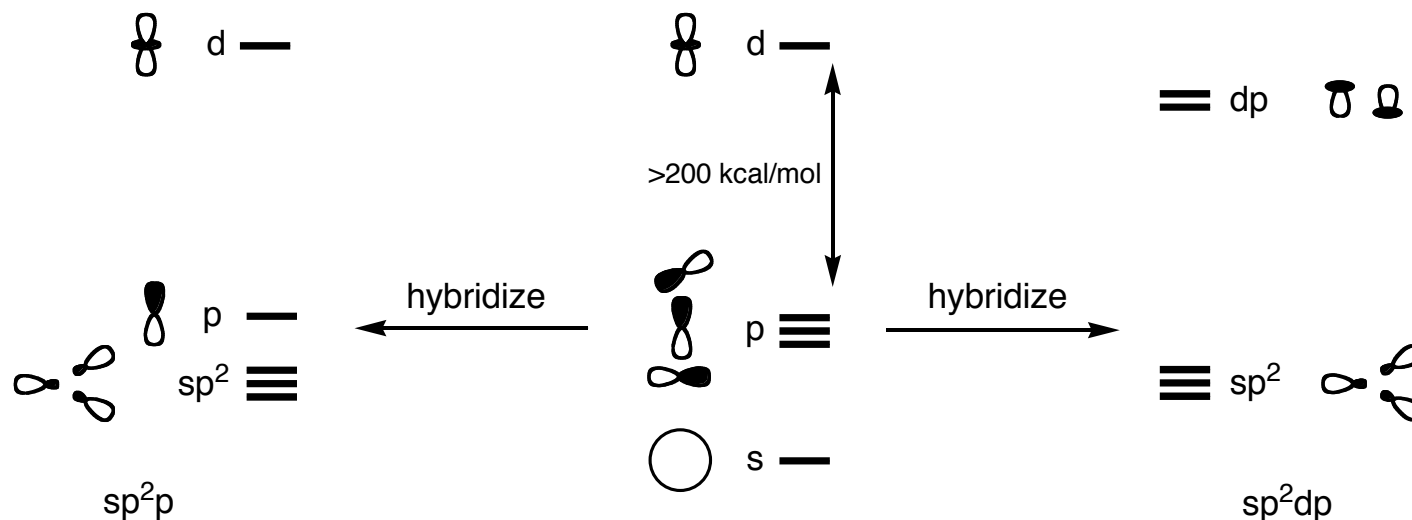
Gillespie, R. J. *Chem. Soc. Rev.*, **1992**, 21, 59.

Michael, F. *Evans Group Seminar: Hypercoordinate Main Group Compounds*, **1999**.

# The Role of d-Orbitals in Main-Group Compounds

*pentavalent compounds*

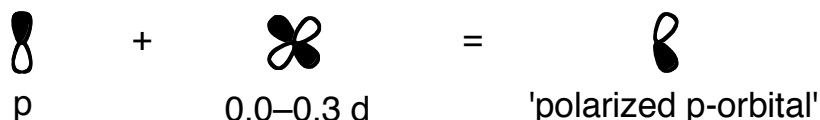
## How do 3s, 3p and 3d orbitals really hybridize to permit pentavalency?



- The d-orbitals must be close enough in energy to the s and p orbitals to mix favourably
- The  $3sp^2dp$  hybridization would come at a massive energetic cost of  $>200$  kcal/mol rendering this unlikely to ever occur –  $sp^2p$  hybridization is likely to occur preferentially

## 3d orbitals are still involved to a limited extent

- The d-orbitals have been essential for complete computation of all main group compounds
- Their role appears to be confined to that of polarization of the p-orbitals – d-orbital occupation of  $<0.3e$

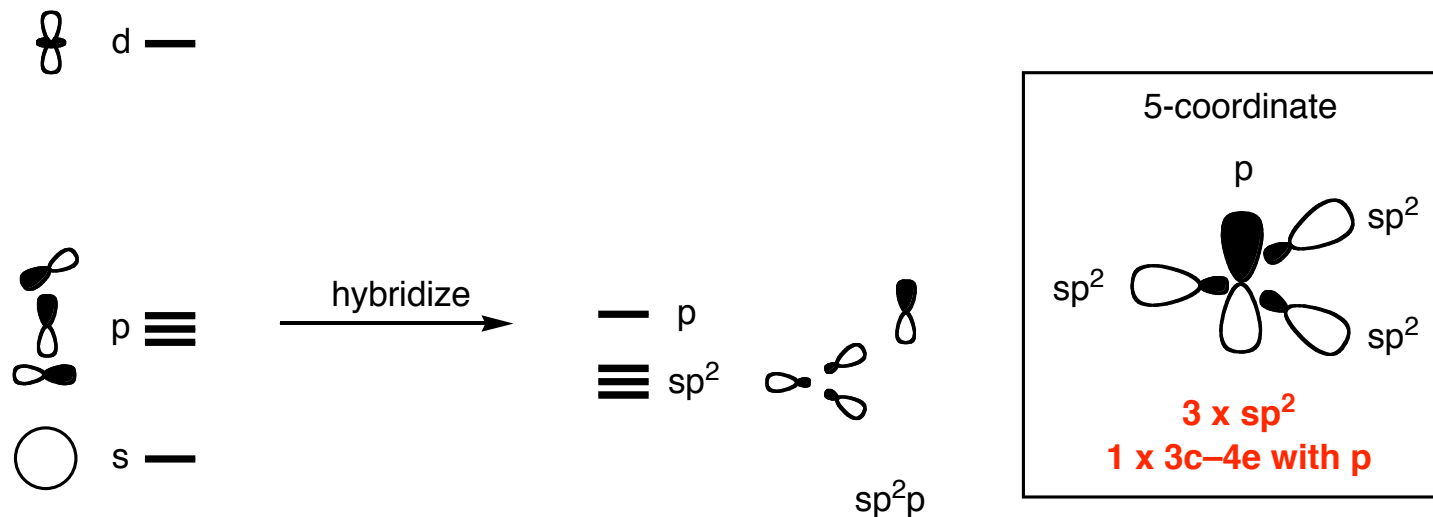


Michael, F. *Evans Group Seminar: Hypercoordinate Main Group Compounds*, 1999.

# Hypervalent Main Group Complexes

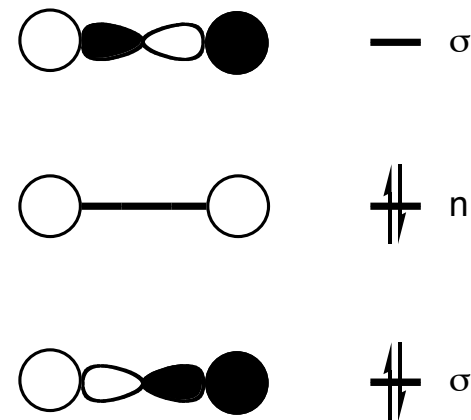
## The Existence of 3c-4e Bonds

### How do 3s, 3p and 3d orbitals really hybridize to permit pentavalency?



### The 3c-4e bond – MO consideration

- The filled non-bonding MO has all of the electron density on the ligand atoms
- Consequently ligands/atoms that stabilize electron density (electronegative) promote 3c-4e bonding.
- This is why virtually all hypervalent compounds bond F, Cl, OR!
- Bent's rule: Electronegative elements prefer bonds with more p-character
- Result: Hypervalent compounds are more d+ at the central atom (Si) - more Lewis acidic

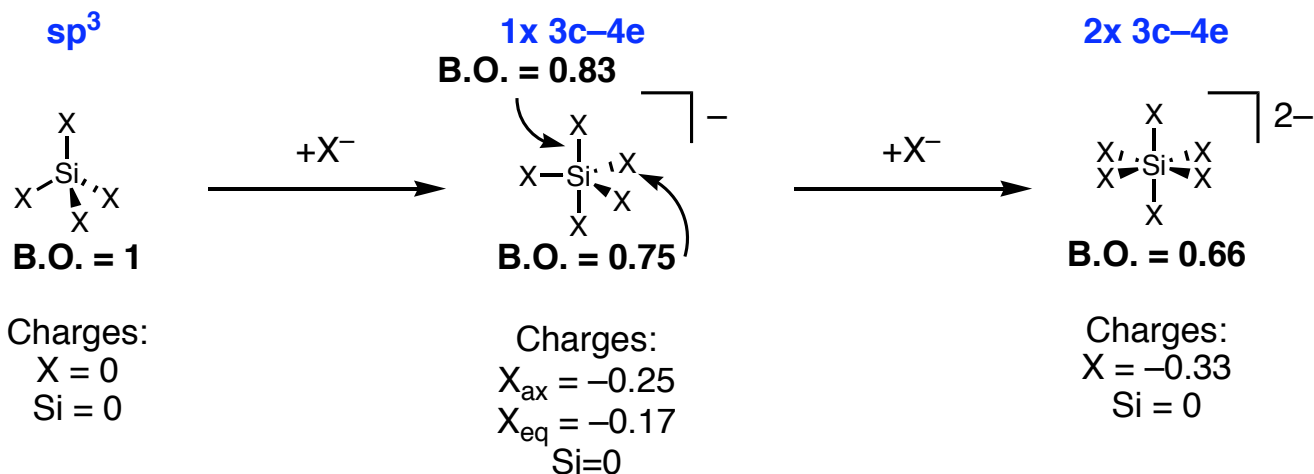




# Hypervalent Silicon

bond order and charge distribution

## ■ Consider Bond Order and charge distribution



## ■ Study of charge distribution

Complex	Coordination	Si charge	Ligand charge
SiH <sub>4</sub>	4	+0.63	-0.16
SiH <sub>5</sub> <sup>-</sup>	5	+0.84	-0.29(eq), -0.49(ax)
SiH <sub>3</sub> F	4	+1.10	-0.15(H), -0.67(F)
SiH <sub>3</sub> F <sub>2</sub> <sup>-</sup>	5	+1.26	-0.26(H), -0.74(F)
SiF <sub>4</sub>	4	+1.434	-0.358
SiF <sub>4</sub> .NH <sub>3</sub>	5	+1.470	-0.397(F, eq), -0.385(F, ax), +0.084(NH <sub>3</sub> )
SiF <sub>4</sub> .2NH <sub>3</sub>	6	+1.463	-0.463(F), +0.196(NH <sub>3</sub> )

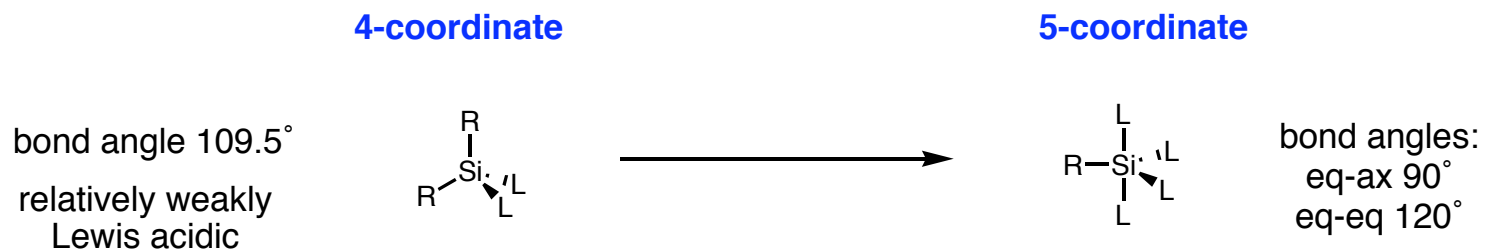
Voronkov, M. *Top. Curr. Chem.* **1986**, 131, 99.

Corriu, R. *Chem. Rev.* **1993**, 93, 1371.

# Reactivity at Silicon - Parameters

## Lewis acidity of Tetracoordinate Si

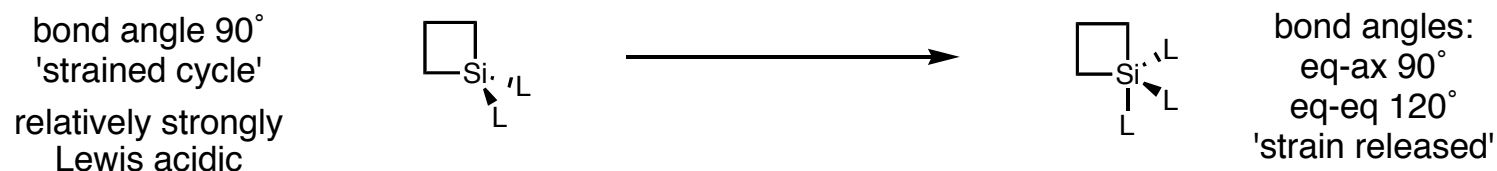
### ■ Activation by Lewis bases



- limited to electronegative ligands on Si and/or strongly Lewis basic Nu
- Lewis base catalyzed activation- Denmark

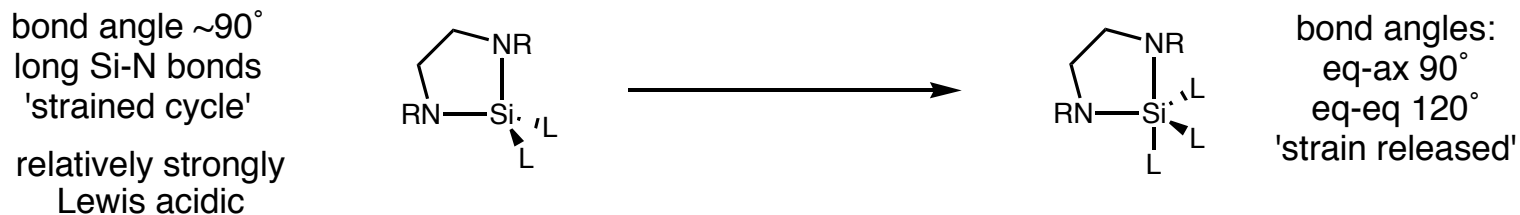
### ■ Activation driven by 'strain release Lewis acidity'

#### ■ Cyclobutane 'strained' silacycles – Myers (1992), Denmark (1993)



- Reactive driving force = release of ring strain

#### ■ Cyclocycles 'strained' with diamine ligands – Leighton (late 1990s–present)

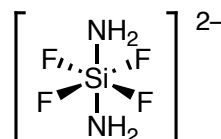
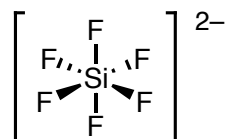


- Long Si–N bonds distort the 5-membered ring – strained cycle

# Hypervalent Silicon

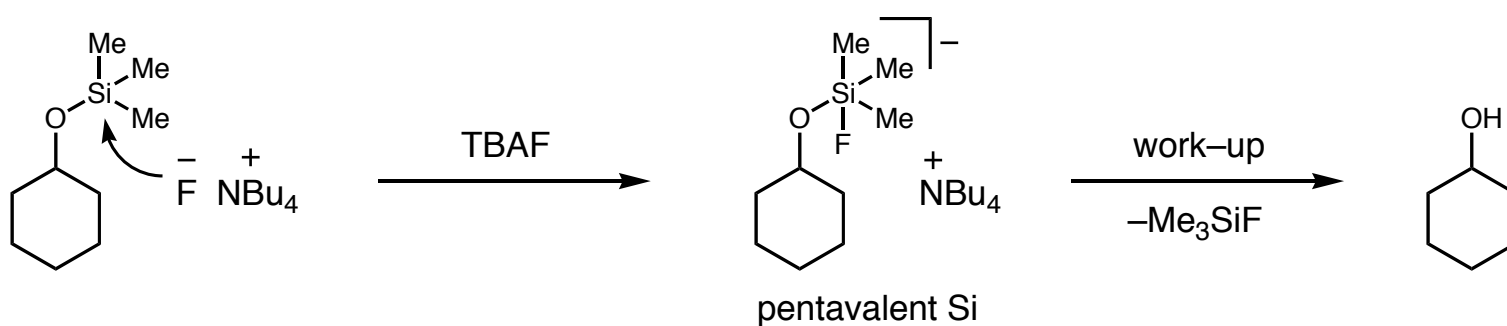
historical perspective

- Silicon compounds with a coordination number higher than four have been known since the early 19th century



Gay-Lussac, J. L.; Thenard, L. J. *Mémoires de Physique et de Chimie de la Société d'Arcueil*, **1809**, 2, 317.  
Davy, J. *Phil. Trans. Roy. London*, **1812**, 102, 352.

- Mechanism of fluoride deprotection of silyl ethers

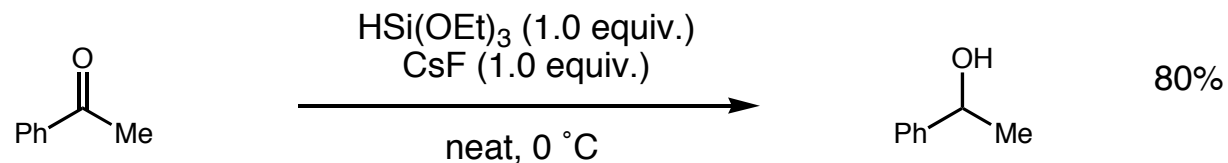


- Driving force: the strength of Si-F bond (135 kcal/mol)

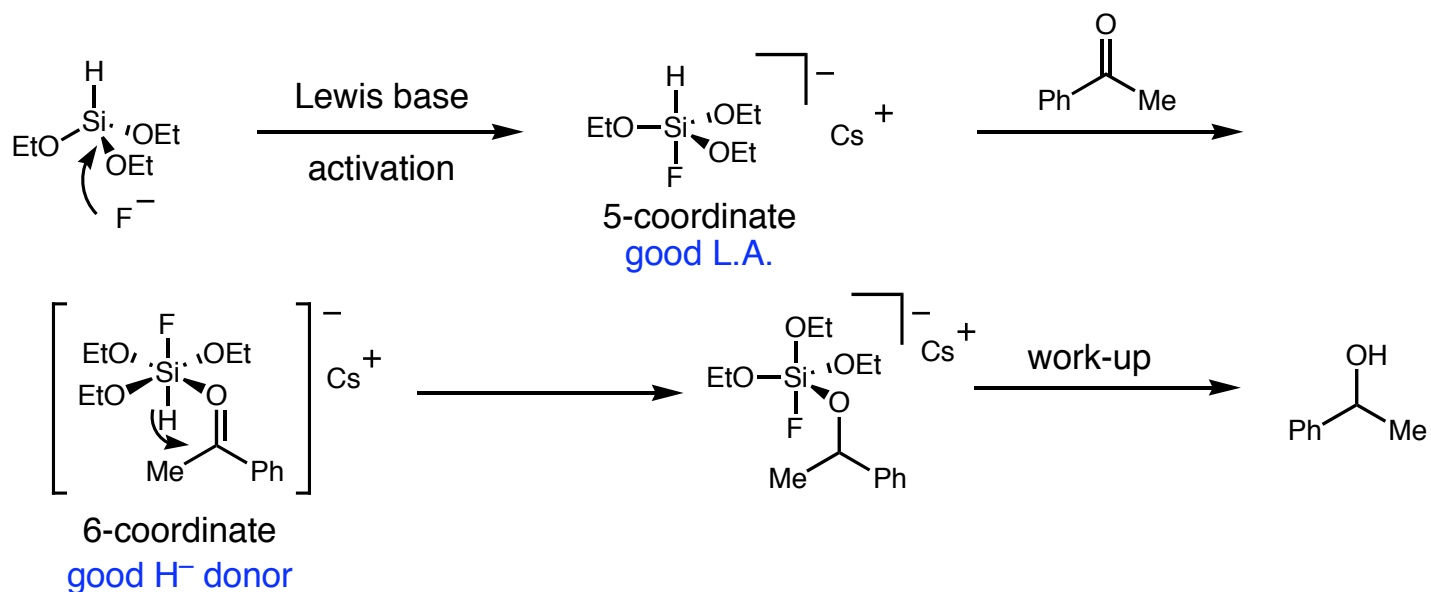
## Lewis Base Activation : Hydride Transfer

*racemic hydrosilation*

### ■ Hydrosilation – Corriu (1981)



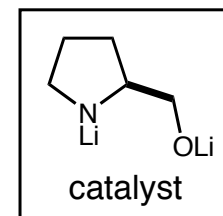
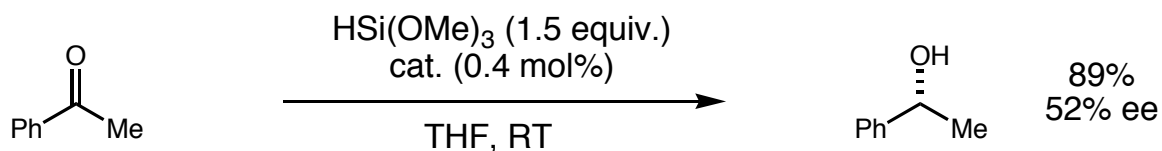
### ■ Probable mechanism



Boyer, J.; Corriu, R. J. P.; Perz, R.; Reye, C. *Tetrahedron*, **1981**, 37, 2165.  
Corriu, R. J. P.; Perz, R.; Reye, C. *Tetrahedron*, **1983**, 39, 999.

## Hypervalent Silicon : Hydride Transfer asymmetric hydrosilation

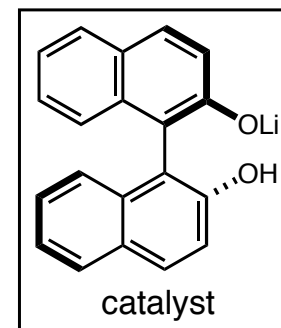
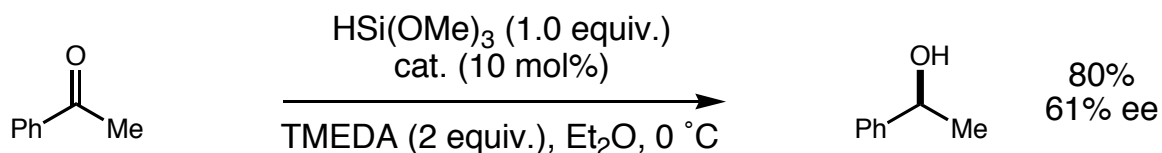
### ■ Hosomi (1988)



Kohra, S; Hayashida, H.; Tominaga, Y.; Hosomi, A. *Tetrahedron Lett.*, **1988**, 29, 89.

- Hosomi discovered that lithium alkoxides can act as reversible binding Lewis bases
- Development of highly catalytic processes (0.4 mol%)

### ■ Kagan (1997)



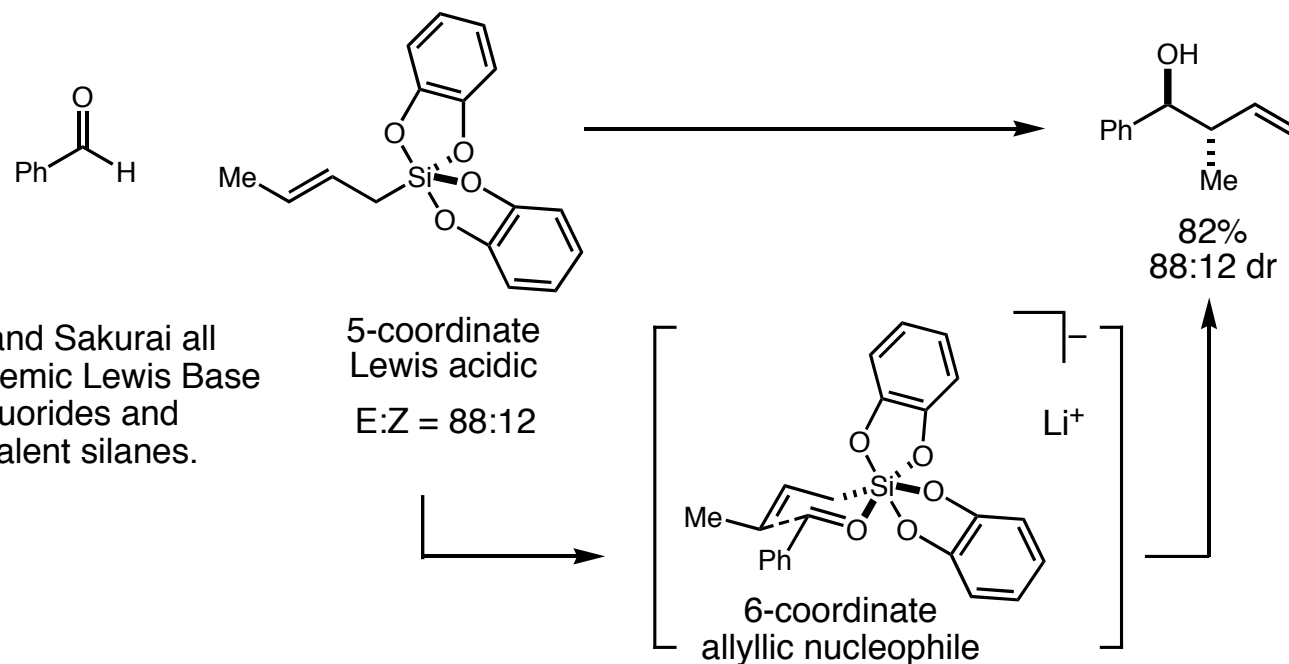
Schiffers, R.; Kagan, H. B. *Synlett.*, **1997**, 1175.

- Problem: Product alkoxide can also act as a Lewis base catalyst – alternative low ee reaction

# Hypervalent Silicon : Lewis Base Catalyzed Allylation

## Seminal Contributions

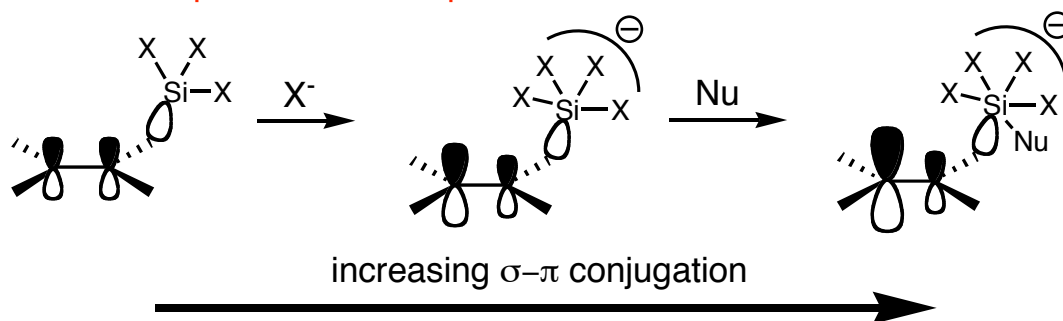
### ■ Sakurai (1988)



- In 1987 Corriu, Hosomi and Sakurai all independently reported racemic Lewis Base promoted allylation using fluorides and alkoxides to activate tetravalent silanes.

Kira, M.; Kobayashi, M.; Sakurai, H. *Tetrahedron Lett.*, **1987**, 28, 4081.  
Kira, M.; Sato, K.; Sakurai, H. *J. Am. Chem. Soc.*, **1988**, 110, 4599.

### ■ Dual activation of both electrophile and nucleophile via a 6-membered closed TS.



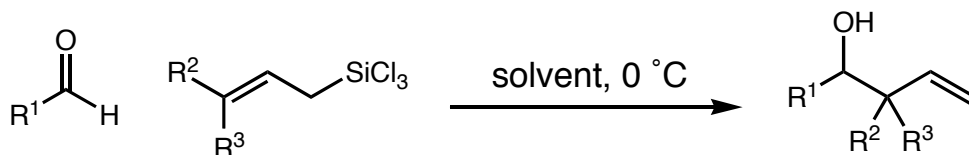
- Coordination of electron rich ligands increases the  $\sigma$ - $\pi$  conjugation. (<sup>13</sup>C NMR evidence)

Sakurai, H. *Synlett*, **1989**, 1.

# Kobayashi's Observation: DMF Promotes Allylations

## Seminal Contributions

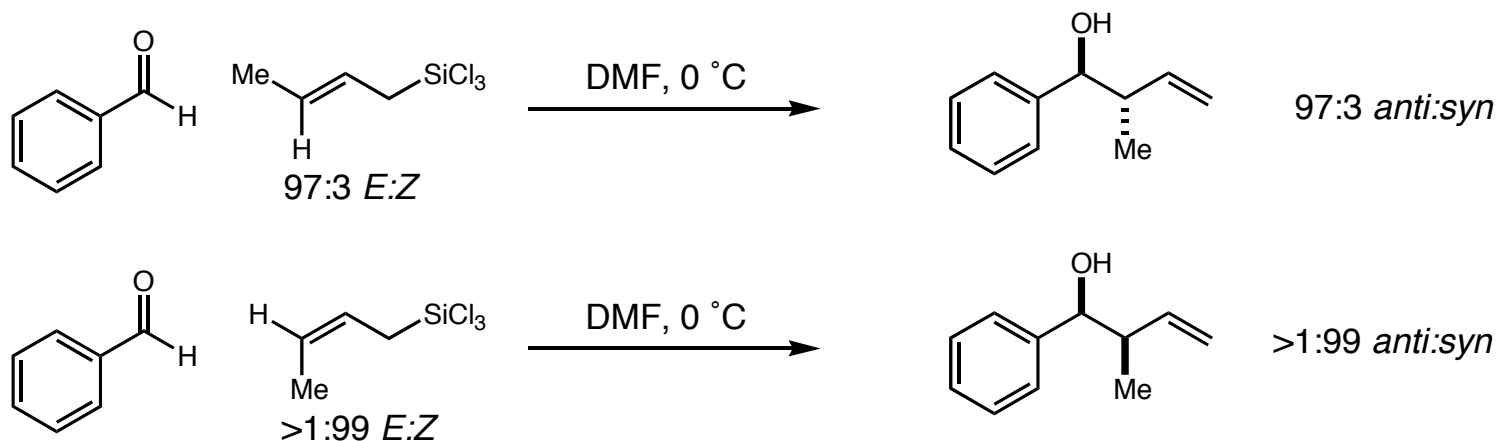
### ■ Dramatic solvent effect!



Solvent	Yield
$CH_2Cl_2$	trace
$Et_2O$	trace
benzene	trace
THF	trace
DMF	90%
$CH_2Cl_2$ + 1 equiv DMF	68%

- Important discovery: Neutral Lewis bases such as DMF can activate trichlorosilanes!!

### ■ Reaction is stereospecific



- High diastereoselectivity indicative of a rigid closed transition state

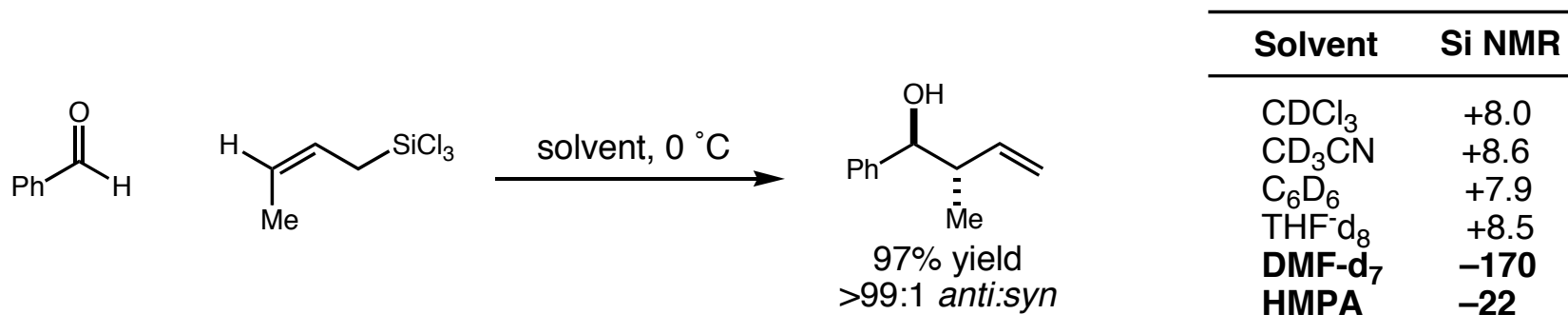
Kobayashi, S.; Nishio, K. *Tetrahedron Lett.* **1993**, *34*, 3453-3456.

Kobayashi, S.; Nishio, K. *J. Org. Chem.* **1994**, *59*, 6620-6628.

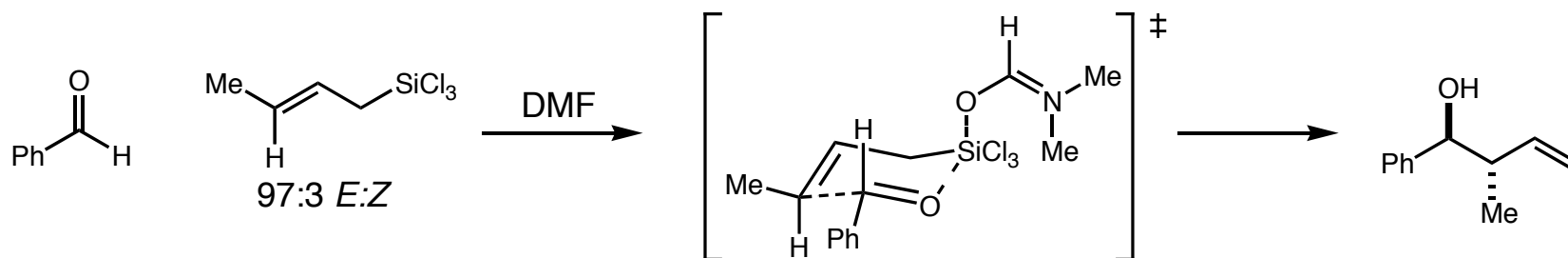
## Rationale Behind the Kobayashi Allylation

*diastereoselective closed transition state*

### ■ <sup>29</sup>Si NMR Chemical Shifts of (Z)-crotyltrichloro silane in various solvents



### ■ Kobayashi proposes a 6-coordinate Si, closed transition state



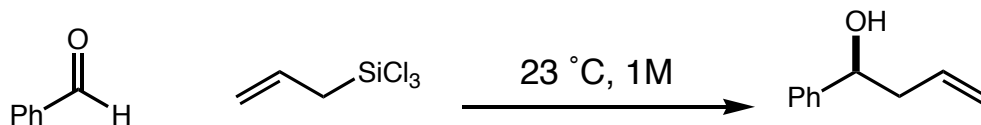
- Dual activation of both electrophile and nucleophile via a 6-membered closed TS.

Kobayashi, S.; Nishio, K. *Tetrahedron Lett.* **1993**, *34*, 3453-3456.  
Kobayashi, S.; Nishio, K. *J. Org. Chem.* **1994**, *59*, 6620-6628.

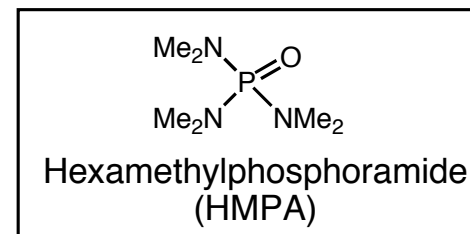


## Denmark Expands the Potential Phosphoramides

### ■ Re-examined common Lewis Base additives



Lewis base	solvent	conversion	time	yield
DMF (1 eq)	benzene - d6	83	70 h	n/a
HMPA (1 eq)	benzene - d6	n/a	n/a	77%
<b>HMPA (1 eq)</b>	<b>CDCl<sub>3</sub></b>	63	<b>4 min</b>	<b>85%</b>
<b>HMPA (1 eq)</b>	<b>acetonitrile - d3</b>	63	<b>4 min</b>	<b>86%</b>
HMPA (0.1 eq)	benzene - d6	60	46 h	n/a
HMPA (0.1 eq)	THF - d8	80	124 h	n/a



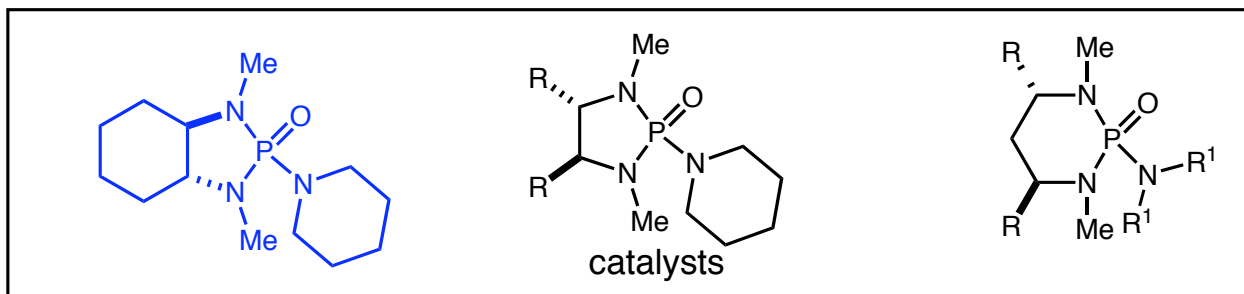
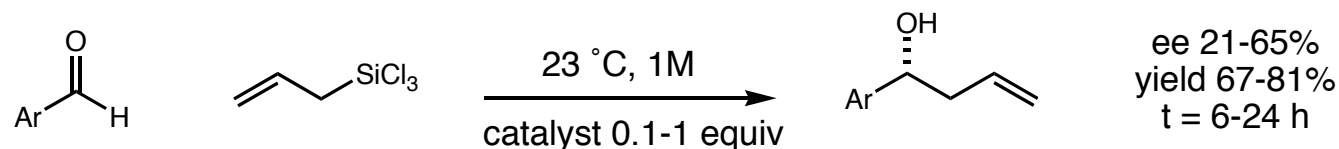
- In contrast to Kobayashi, Denmark found that HMPA gave superior results to DMF
- Reaction rate solvent dependent
- DMSO (sulfoxide) and pyridine N-oxide were tried, but were not compatible with the reaction

### ■ Can an asymmetric HMPA analogue be developed to catalyze the enantioselective variant?

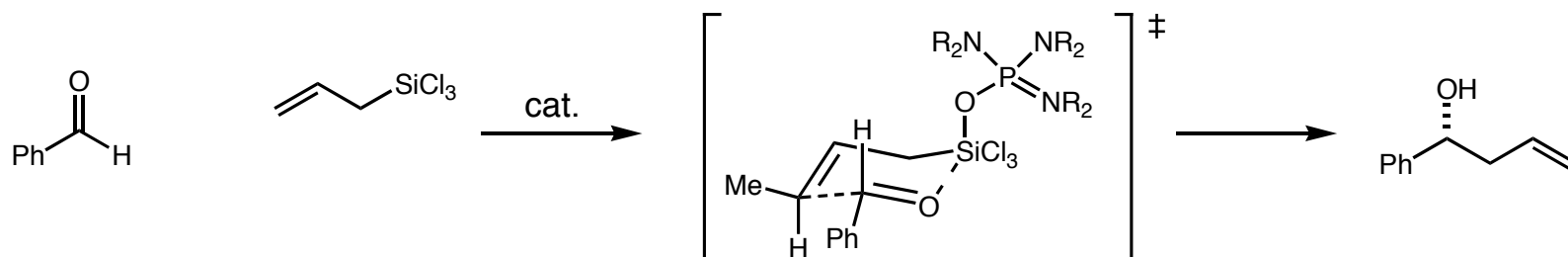
Denmark, S. E.; Coe, D. M.; Pratt, N. E.; Griedel, B. D. *J. Org. Chem.* **1994**, *59*, 6161-6163.

## Early Lewis Base Catalyzed Asymmetric Allylations

### Denmark - chiral phosphoramides



- Assumed a similar associative mechanism of action to DMF



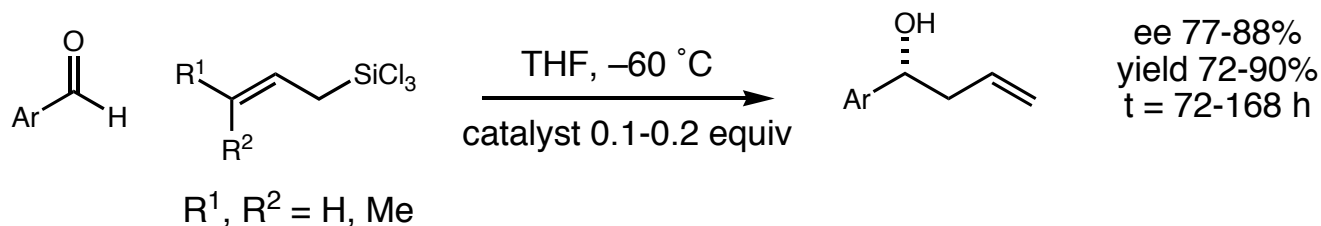
- Low enantioselectivities, generally high loadings of catalyst only aromatic aldehydes tolerated – but a huge leap in the right direction

Denmark, S. E.; Coe, D. M.; Pratt, N. E.; Griedel, B. D. *J. Org. Chem.* **1994**, *59*, 6161-6163.

## Early Lewis Base Catalyzed Asymmetric Allylations

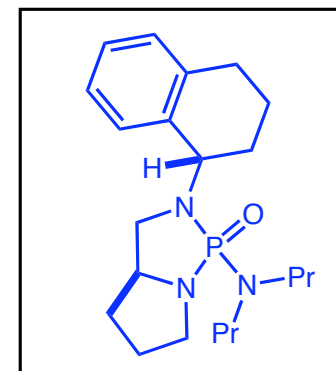
Iseki also tried chiral HMPA and DMF

### ■ Iseki (1996) - chiral phosphoramides

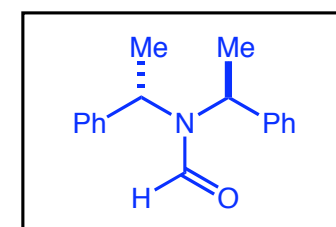
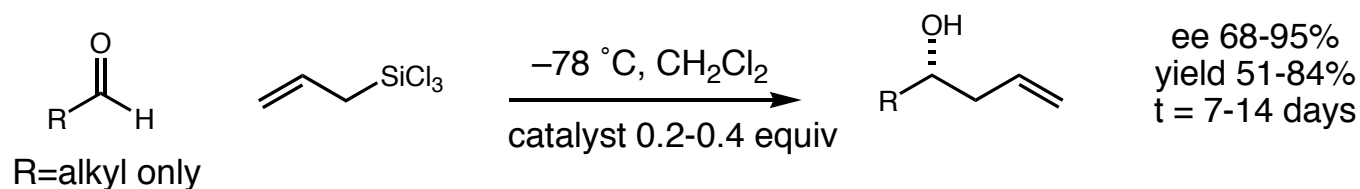


- Low enantioselectivities, generally high loadings of catalyst and only aromatic aldehydes were tolerated

Iseki, K. *Tetrahedron Lett.* **1996**, *37*, 5149-5150.  
Iseki, K. *Tetrahedron.* **1997**, *53*, 3513-3526.



### ■ Iseki (1998) - chiral formamides



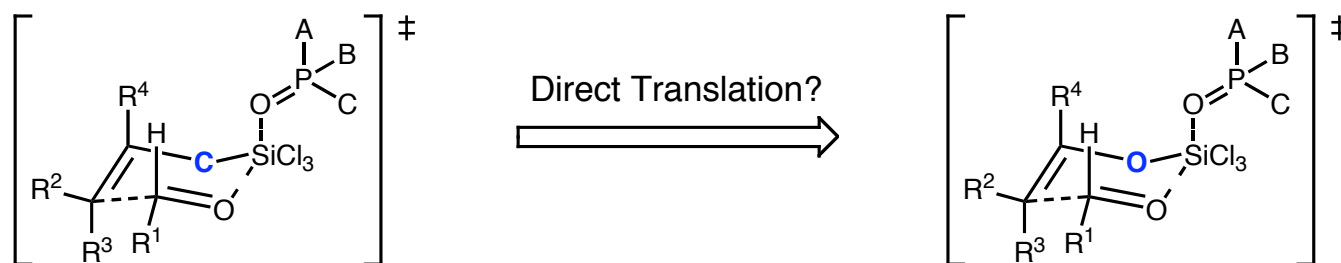
- good to excellent enantioselectivities, only aliphatic aldehydes tolerated

Iseki, K.; Mizuno, S.; Kuroki, Y.; Kobayashi, Y. *Tetrahedron Lett.* **1998**, *39*, 2767-2770.  
Iseki, K.; Mizuno, S.; Kuroki, Y.; Kobayashi, Y. *Tetrahedron* **1999**, *55*, 977-988.

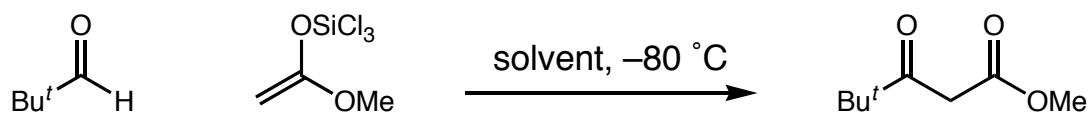
# Denmark – Could the Allylation Strategy be Applied to Aldol Reactions?

*aldol of trichloro silylketene acetals*

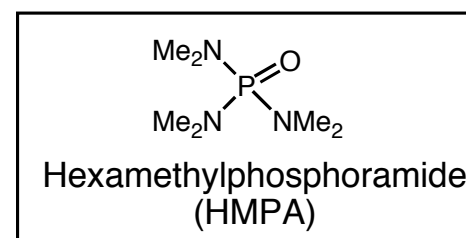
## ■ Transferring the concept



## ■ Investigated HMPA as a reaction additive



Lewis base	solvent	conversion	time
none	toluene - d8	18	120 min
none	CD <sub>2</sub> Cl <sub>2</sub>	50	120 min
none	THF - d8	69	120 min
HMPA (0.1 eq)	CD <sub>2</sub> Cl <sub>2</sub>	100	<3 min

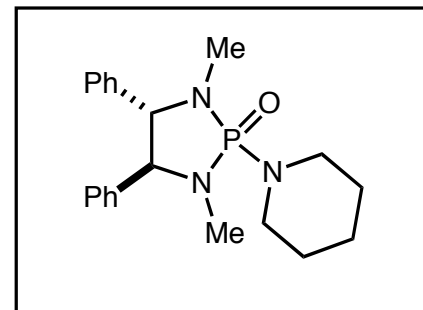


- HMPA catalyzed the trial reactions, but a potential background reaction was evident

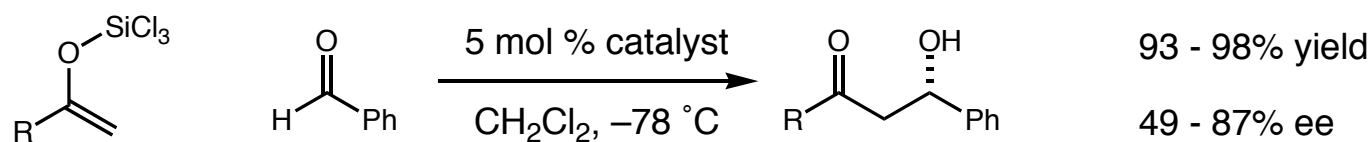
Denmark, S. E.; Winter, S. B. D.; Su, X.; Wong, K. -T. *J. Am. Chem. Soc.* **1996**, *118*, 7404-7405.

# Enantioselective Catalysis by Phosphoramides

*aldol reactions*

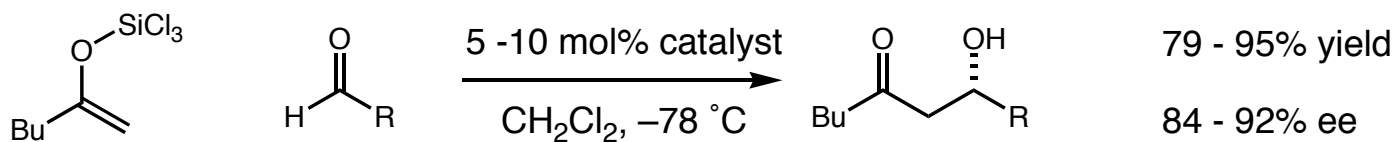


## Variation in the trichlorosilyl enol ether component



R = Me, *n*Bu, *i*Bu, *i*Pr, *t*Bu, Ph, CH<sub>2</sub>OSiMe<sub>3</sub>*t*Bu

## Variation in the aldehyde component



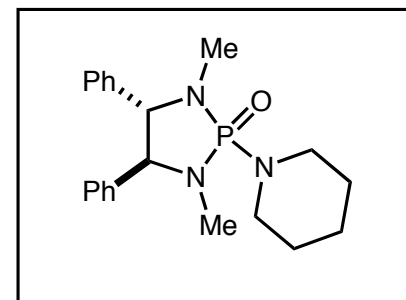
R = cinnamyl,  $\alpha$ -methylcinnamyl, naphthyl, 4-phenyl-phenyl, cyclohexyl, *t*Bu

- Trichlorosilyl enol ethers are prepared from the corresponding trimethylsilyl enol ethers by treatment with SiCl<sub>4</sub> and catalytic Hg(OAc)<sub>2</sub>

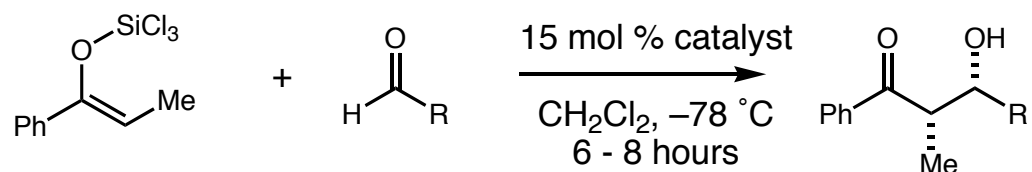
Denmark, S. E., et al., J. Org. Chem., 1998, 63, 918.

## Enantioselective Catalysis by Phosphoramides

*syn* and *anti* aldol reactions



### ■ Propionate aldol with various aldehydes

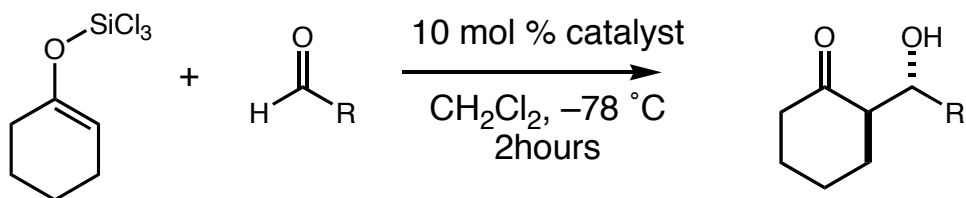


89 - 97% yield  
3:1 - 18:1 *syn:anti*  
84 - 96% ee

R = cinnamyl, naphthyl, phenyl, tolyl, crotyl

The uncatalyzed reaction at 0° C is slightly *anti* selective (2:1)

### ■ Enforced E-enol silane aldol reaction: *anti* selective



94 - 98% yield  
61:1 - 99:1 *anti:syn*  
94 - 98% ee

R = cinnamyl,  $\alpha$ -methylcinnamyl, naphthyl, phenyl

- The uncatalyzed reaction at 0 °C is highly *syn* selective (5:1 - 49:1)

Denmark, S. E., et al., *J. Am. Chem. Soc.*, **1996**, *118*, 7404-7406.

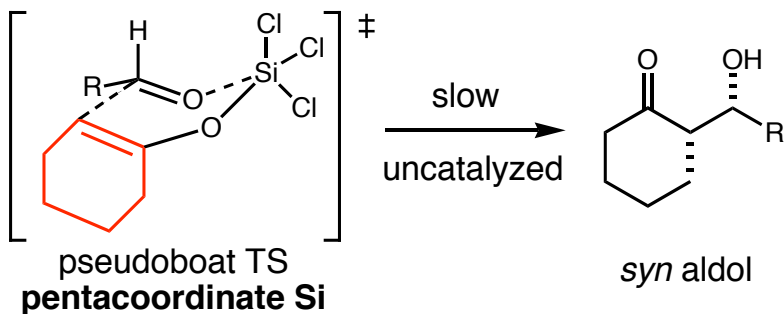
Denmark, S. E., et al., *J. Am. Chem. Soc.*, **1997**, *119*, 2333-2334.

# Enantioselective Catalysis by Phosphoramides

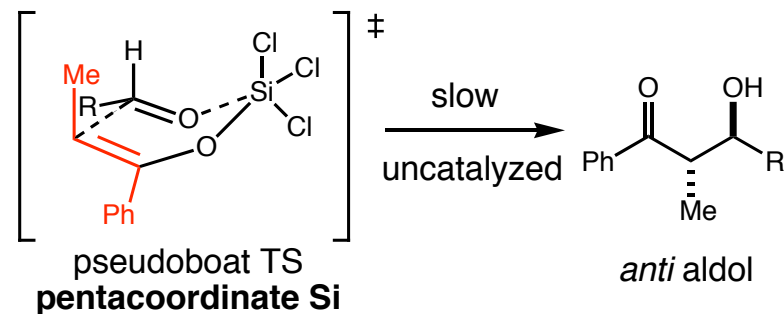
preliminary rational for the aldol stereochemistry

## ■ Uncatalyzed Reactions

### ■ E-enolsilane

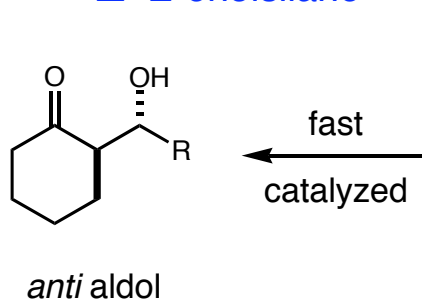


### ■ Z-enolsilane

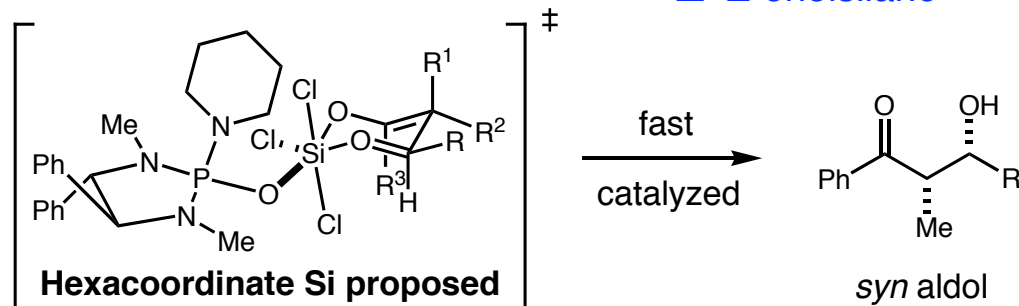


## ■ Catalyzed Reactions - An initial proposal

### ■ E-enolsilane



### ■ Z-enolsilane



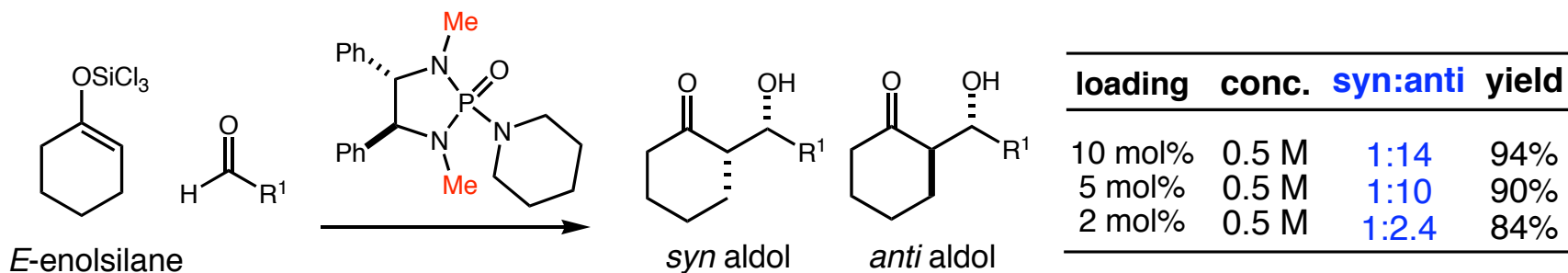
- Chair-like transition state accounts for observed diastereo- and enantioselectivities
- Precise coordination geometry was not known at this stage

Denmark *J. Am. Chem. Soc.* **1997**, *119*, 2333-2334.

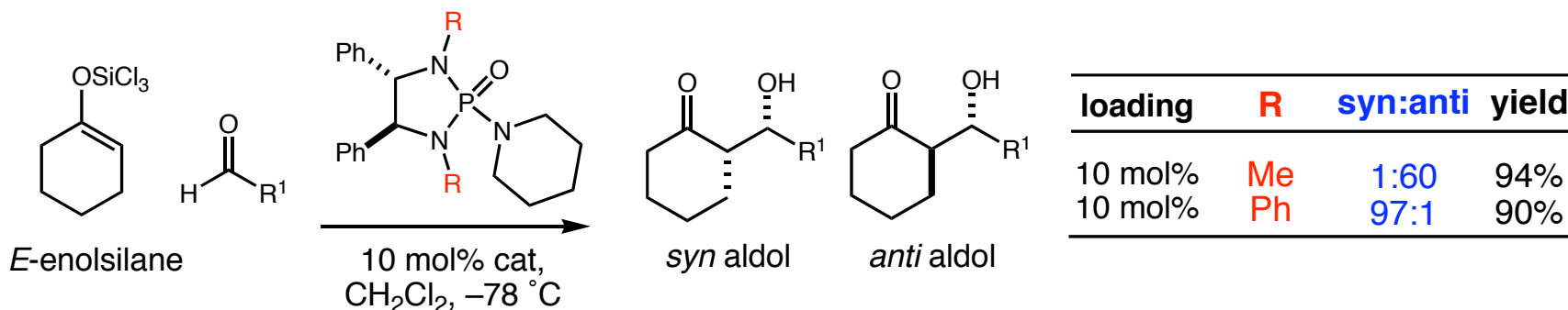
# Enantioselective Catalysis by Phosphoramides

Intriguing Observations - New TS Required!

## ■ Diastereoselectivity dependent on catalyst loading



## ■ Catalyst change give a complete switch in diastereoselectivity



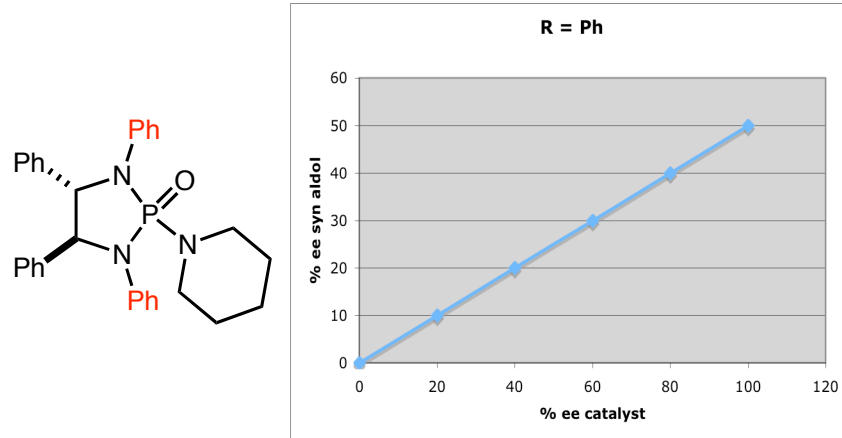
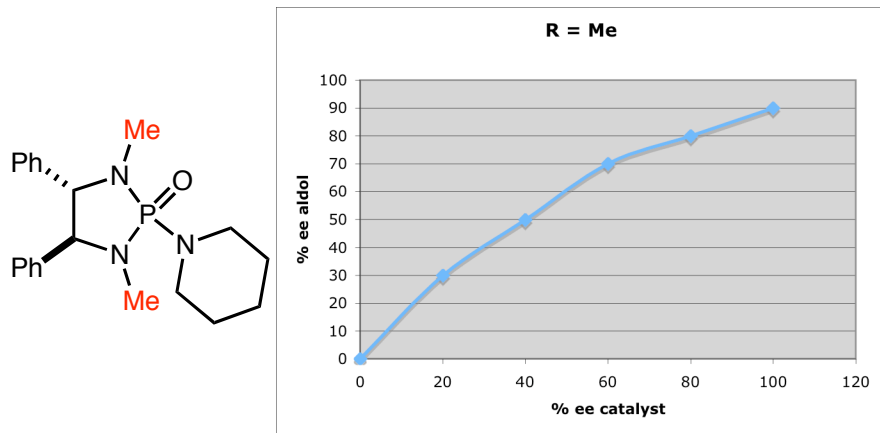
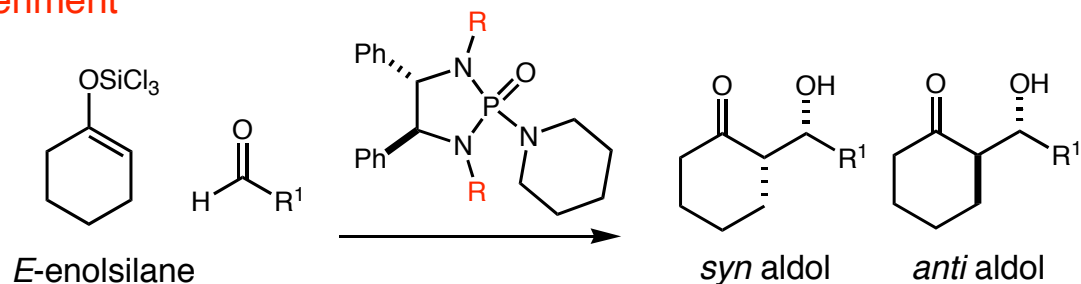
- *Anti*-diastereoisomer dominates with less bulky ligands and high concentrations
- *Syn*-diastereoisomer dominates with more bulky ligands and low concentrations



# Enantioselective Catalysis by Phosphoramides

Intriguing Observations - New TS Required!

## ■ A productive experiment



## ■ Positive non-linear effect using less bulky catalyst

- A new mechanistic postulate is needed

■ Conclusion: 2 pathways operating (a) TS contains 1 molecule of catalyst - *syn* product  
(b) TS contains 2 molecules of catalyst - *anti* product

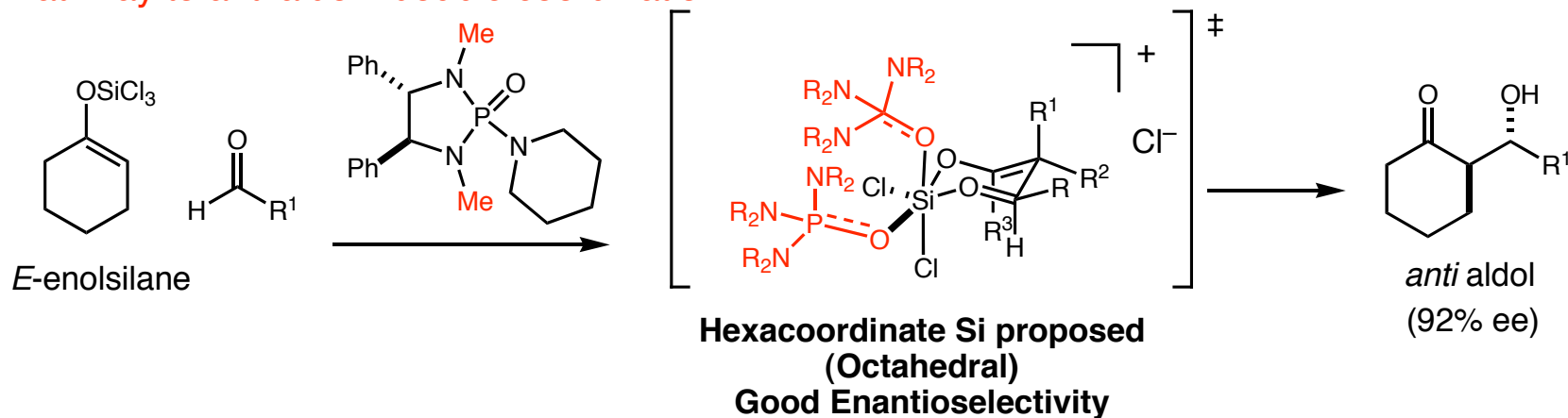
- R=Me catalyst operates via mix of (a) and (b).
- R=Ph catalyst operates via mostly (a)

Denmark *J. Am. Chem. Soc.* **1998**, *120*, 12990.

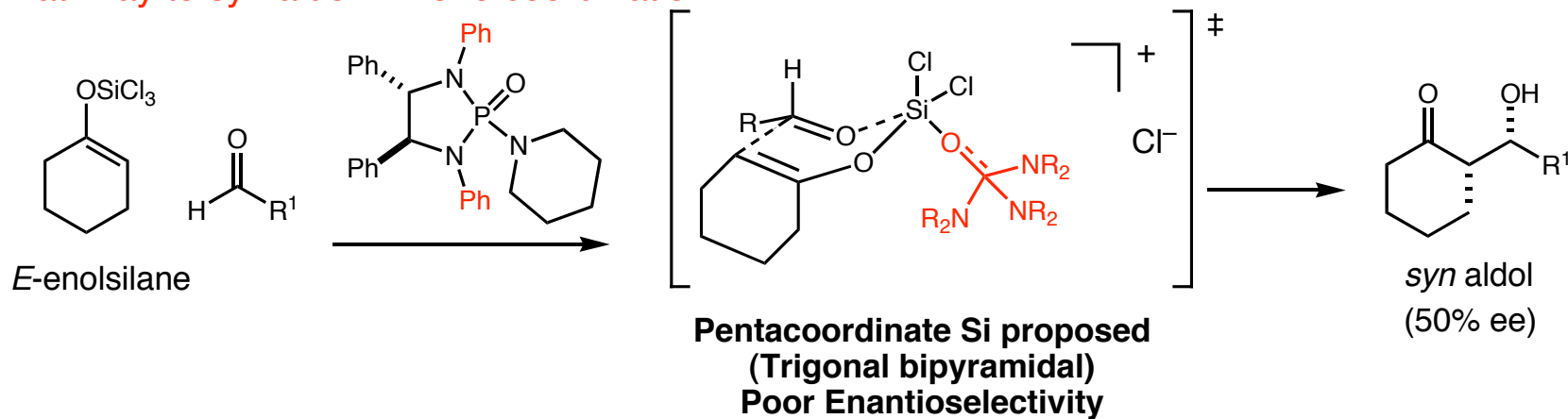
# Denmark: Asymmetric Lewis Base Catalyzed Aldol Reaction

Refined Mechanism: *Dissociative*

## ■ Pathway to anti aldol - double coordination



## ■ Pathway to syn aldol – mono coordination



## ■ Ligand binding forces Cl<sup>-</sup> dissociation. Experimental evidence:

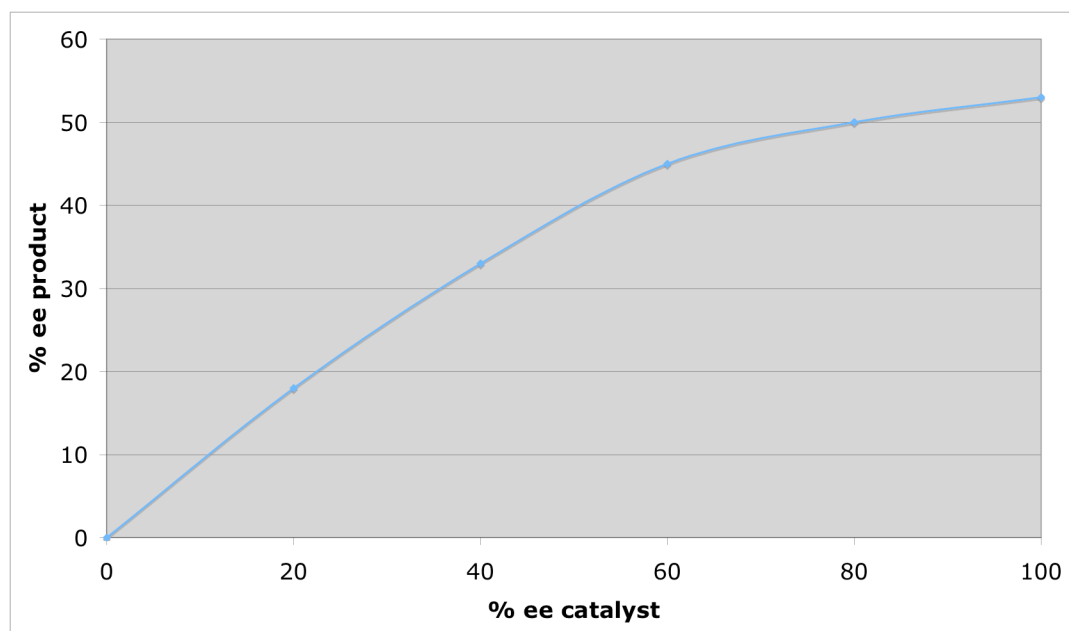
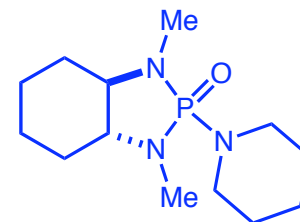
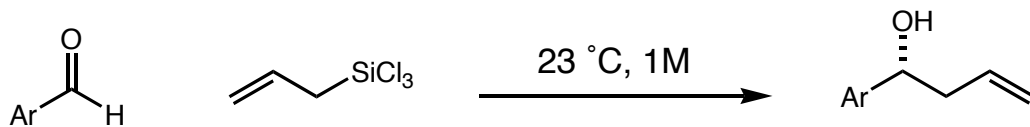
- Bu<sub>4</sub>NCl retards the reaction rate - common ion effect
- Bu<sub>4</sub>NOTf and Bu<sub>4</sub>NI accelerate the rate by increasing ionic strength

Denmark *J. Am. Chem. Soc.* **1998**, *120*, 12990.

# Revisiting the Phosphoramidate Asymmetric Allylations

## Kinetic Study

- Do multiple mechanisms operate here?

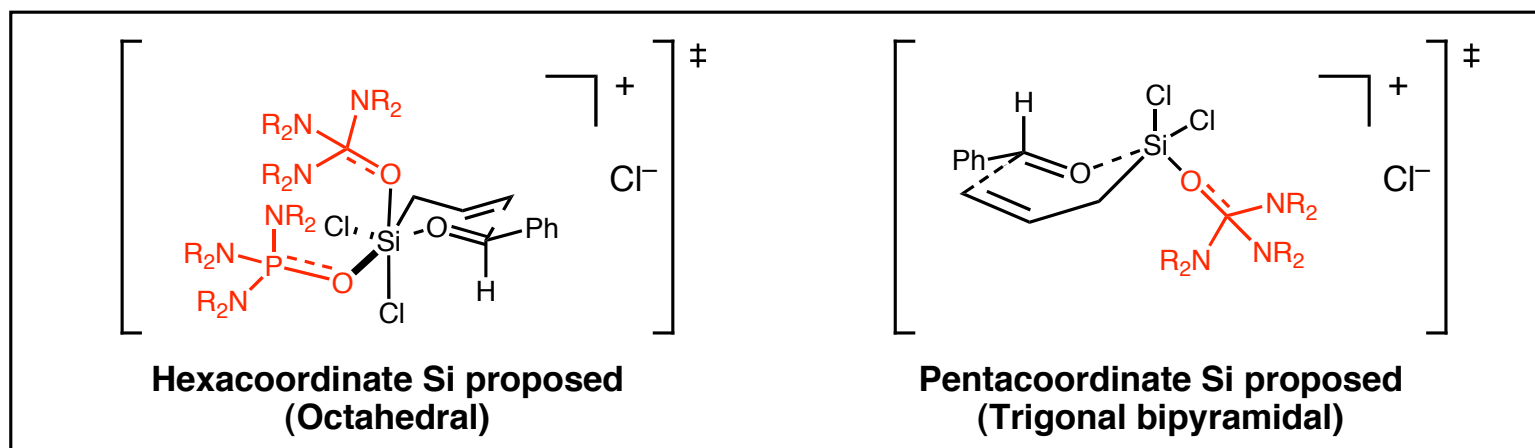
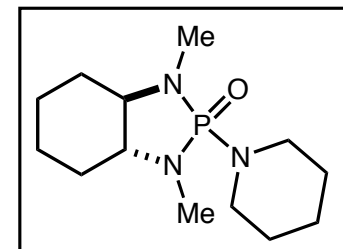
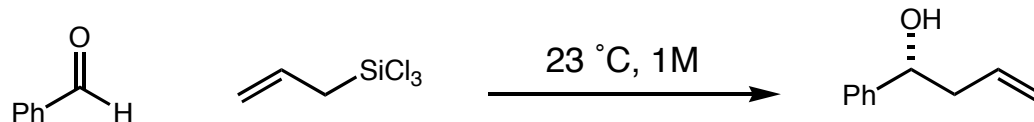


- Positive non-linear relationship with catalyst ee - seen similar indicators in the aldol work!
- Proposal: The 1.77th order in catalyst is due to competing mechanisms involving 1 or 2 phosphoramidates on silicon

# Enantioselective Allylation Mechanism

## Dissociative Mechanism

### Two competing transition states

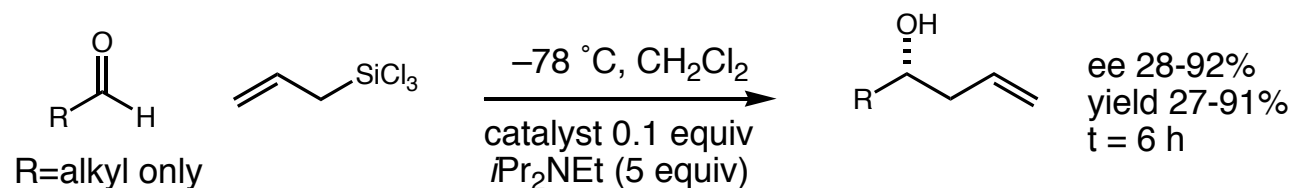


- Enantioselectivity is likely lower because the cationic octahedral TS gives the opposite facial selectivity to the cationic trigonal bipyramidal TS.
- Would a new bidentate phosphoramidate avoid the problem of mono-coordination in allylations?

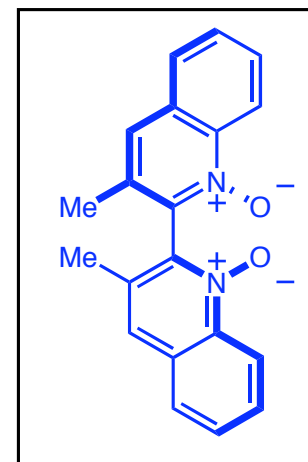
# Lewis Base Catalyzed Asymmetric Allylations

pyridine N-oxides

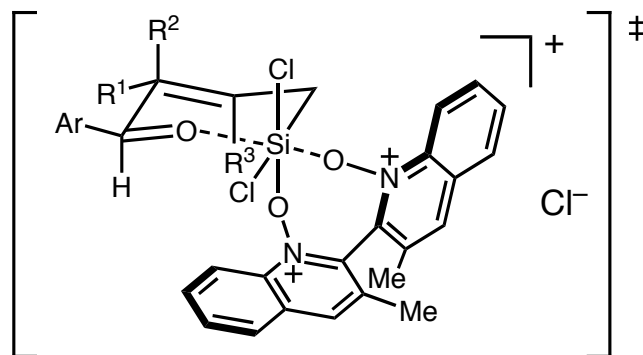
## ■ Nakajima - chiral N-oxides



- good to excellent enantioselectivities, only aliphatic aldehydes tolerated



## ■ Proposed transition state model - cationic hexacoordinate



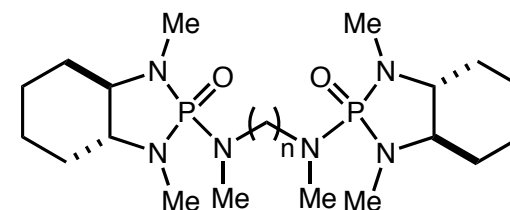
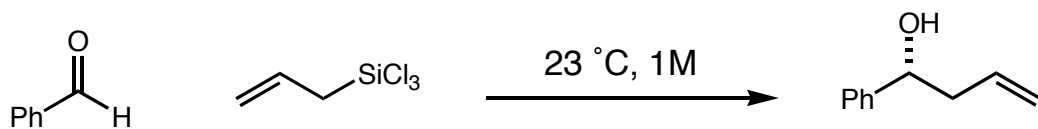
- Bidentate chelation to give a 6-coordinate octahedral silicon
- Kocovsky later made a library of related catalysts and optimized this reaction further

Nakajima, M.; Saito, M.; Shiro, M.; Hashimoto, S.-I. *J. Am. Chem. Soc.* **1998**, *120*, 6419-6420

# Allylation: Solving the Dual Mechanism Problem

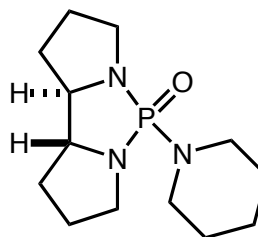
bidentate catalysts

## Testing a range of asymmetric bisphosphonamides

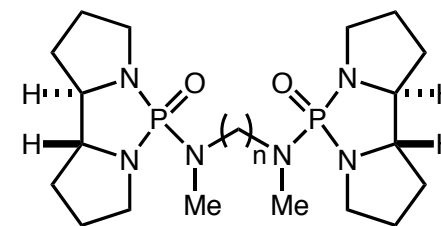


a: n=2    b: n=3  
c: n=4    d: n=5  
e: n=6

catalyst	ee	catalyst	ee
a	0%	f	56%
b	35%	g	18%
c	17%	h	87%
d	65%	i	67%
e	46%		

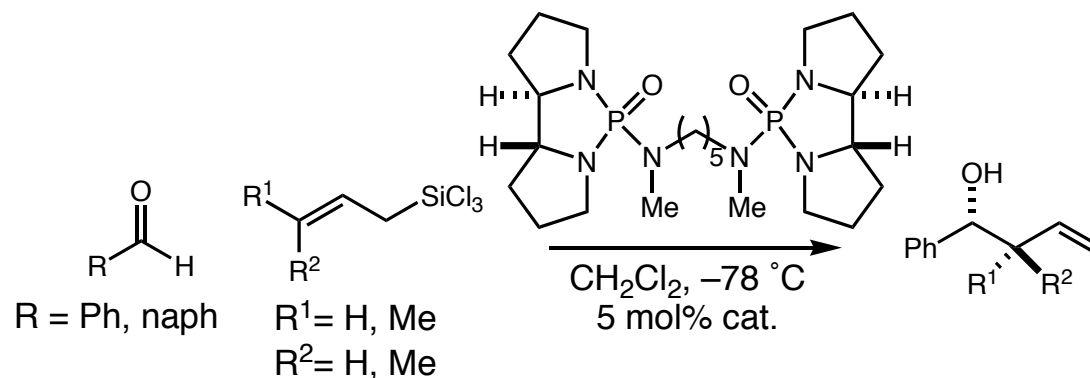


f:



g: n=4    h: n=5  
i: n=6

## Using the new bisphosphonamide



R = Ph, naph

R<sup>1</sup> = H, Me

R<sup>2</sup> = H, Me

57-92% yield

80-94% ee

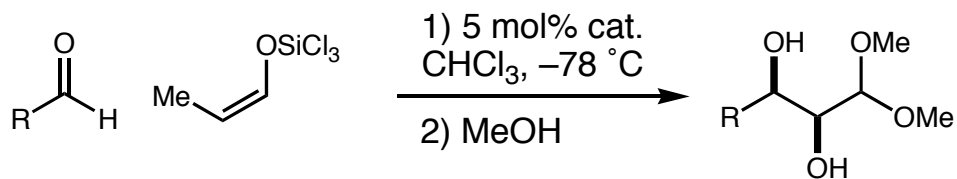
>99:1 diastereomers

Denmark *J. Am. Chem. Soc.* **2000**, *122*, 12021.  
Denmark *J. Am. Chem. Soc.* **2001**, *122*, 9488.

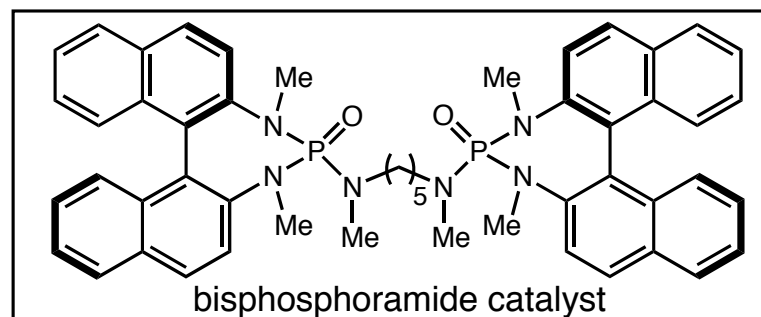
## Crossed-Aldol Reactions of Aldehydes

application of the bidentate catalyst

### Z-enolsilane - syn products

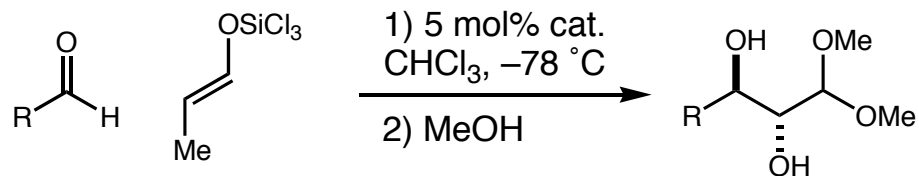


R	ee	anti:syn	yield
Ph	81%	2:98	95%
cinnamyl	42%	1:99	86%
crotyl	5%	1:99	85%
phenyl propargyl	7%	2:98	98%
dihydrocinnamyl	8%	5:95	47%



- High levels of diastereoselectivity
- Generally poor ee

### E-enolsilane - anti products

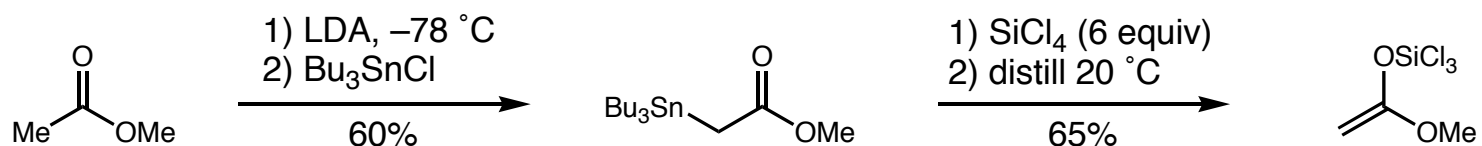


R	ee	anti:syn	yield
Ph	59%	99:1	97%
cinnamyl	26%	99:1	88%
crotyl	52%	98:2	91%
phenyl propargyl	76%	98:2	99%
dihydrocinnamyl	66%	99:1	79%

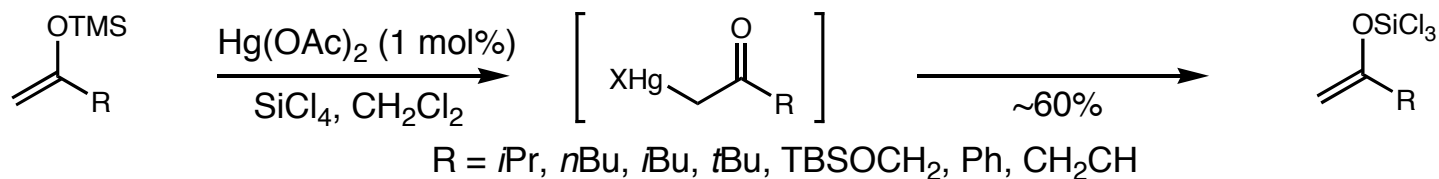
- High levels of diastereoselectivity
- Low ee

## Limitations of Aldol Methodology to This Point

- Trichlorosilanes are difficult to prepare and handle

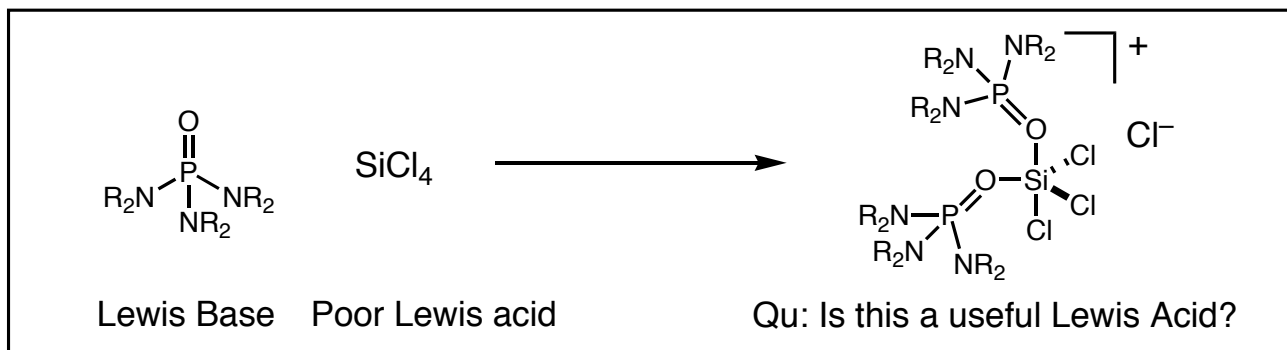


Denmark, S. E.; Winter, S. B. D.; Su, X.; Wong, K.-T. *J. Am. Chem. Soc.* **1996**, *118*, 7404-7405.



Denmark, S. E.; Winter, S. B. D.; Su, X.; Wong, K.-T. *J. Org. Chem.* **1998**, *63*, 9517-9523.

- Possible solution to this problem?

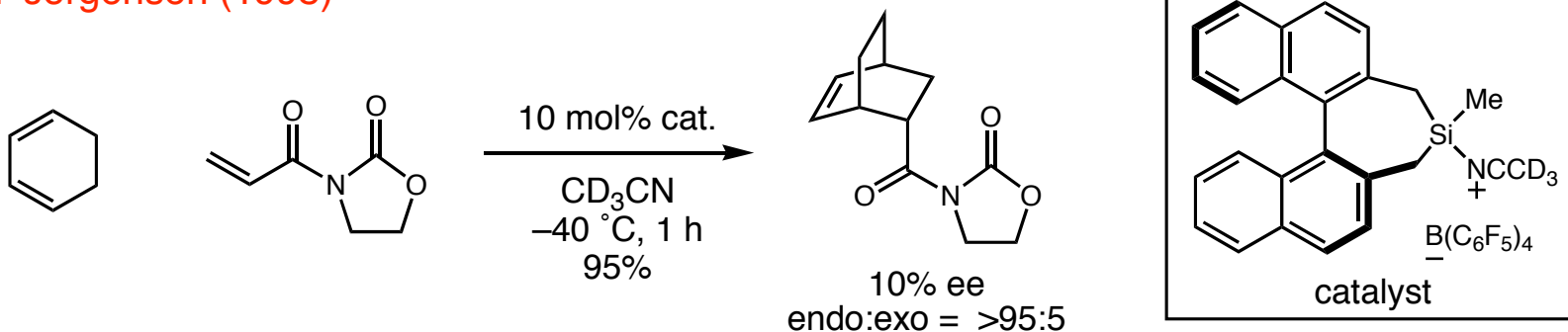




## Hypervalent Silicon : Chiral Lewis Acids

covalently bonded chiral backbones

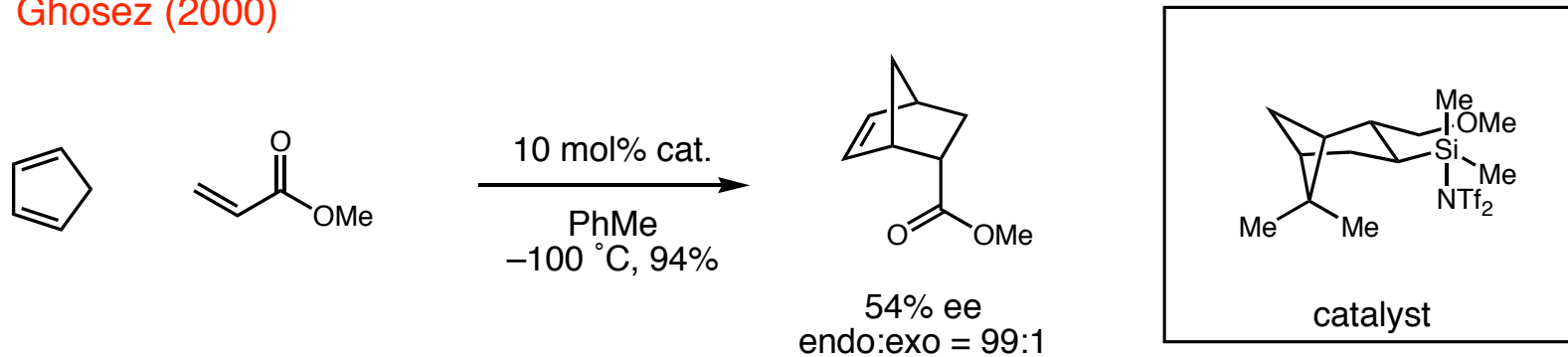
### ■ Jorgensen (1998)



First example of an asymmetric silicon-based Lewis Acid

Johannsen, M.; Jorgensen, K. A.; Helmchen, G. *J. Am. Chem. Soc.* **1998**, *120*, 7636.

### ■ Ghosez (2000)

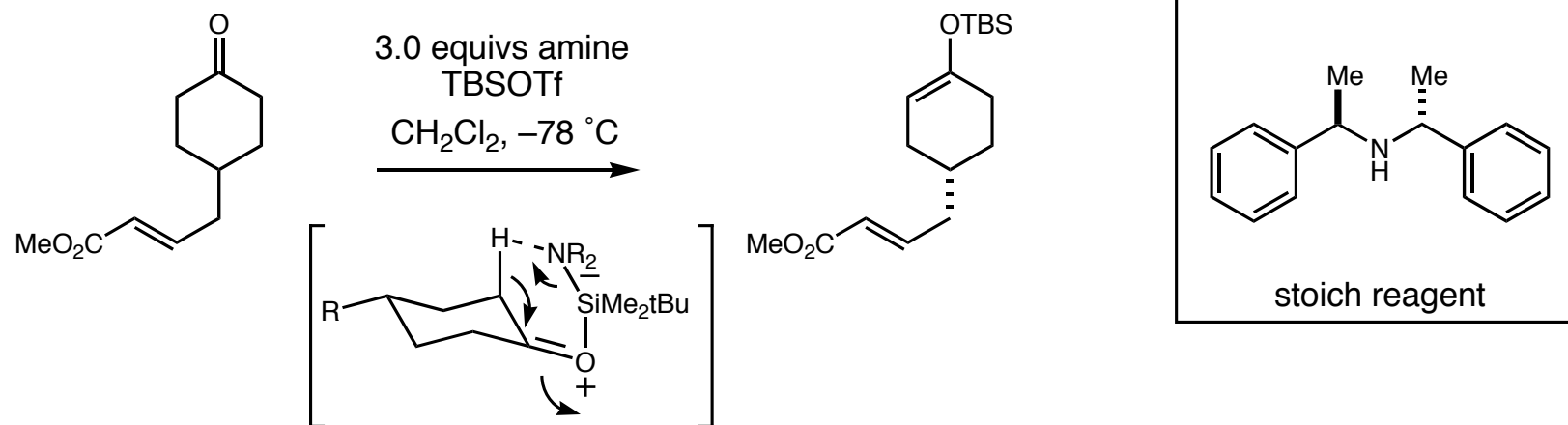


Mathieu, B.; de Fays, L.; Ghosez, L. *Tetrahedron Lett.*, **2000**, *41*, 9561.

## Hypervalent Silicon : Chiral Lewis Acids

non-covalently bonded chiral backbones

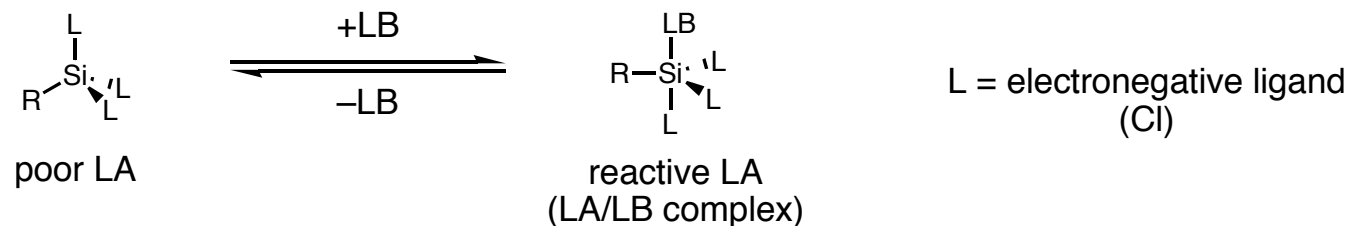
### Ihara (2000) - resolution



Amine needed in stoichiometric quantities due to protonation

Ihara, L. et al. *Chem. Commun.*, **2000**, 1739.

### Chiral Lewis Base activation

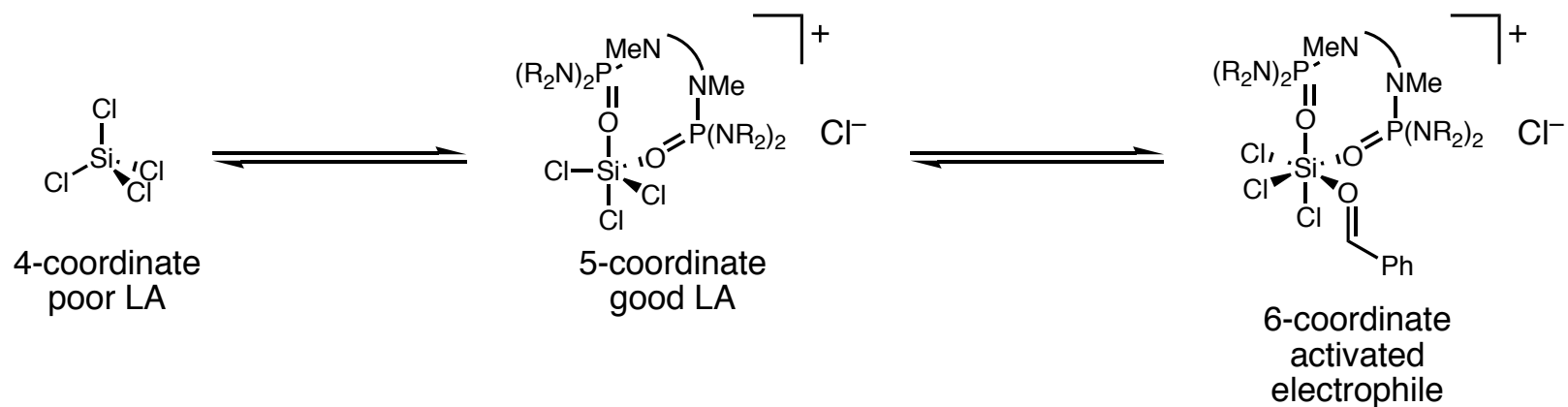
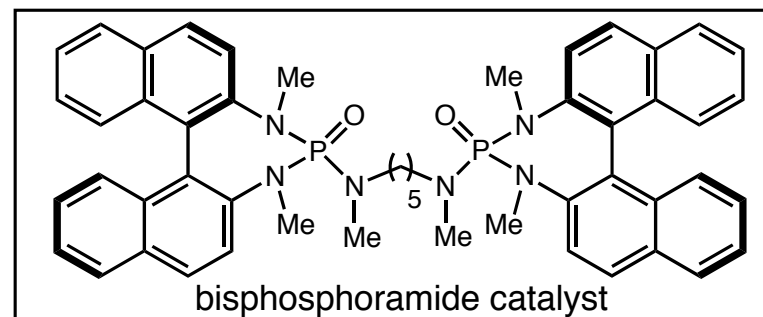
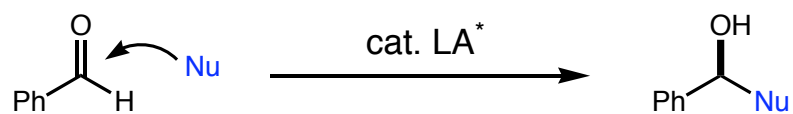


Stoichiometric in Si, but catalytic in chiral Lewis base

# Hypervalent Silicon : Chiral Lewis Acids

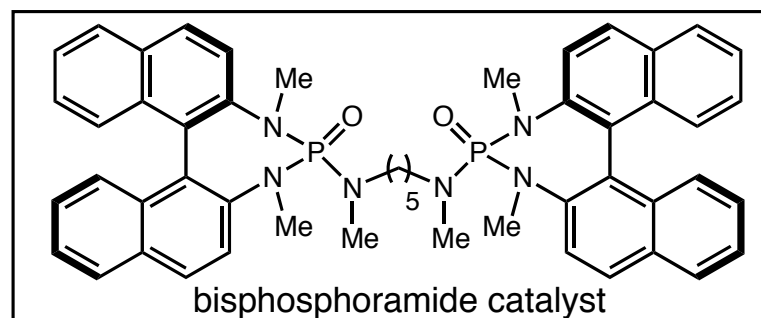
Chiral Lewis Base activated Lewis Acids

## ■ Denmark (2001–2005)

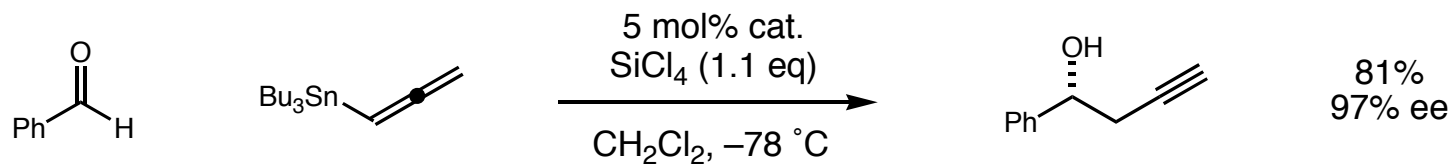


## Hypervalent Silicon : Chiral Lewis Acids

Denmark's bisphosphoramidate complex

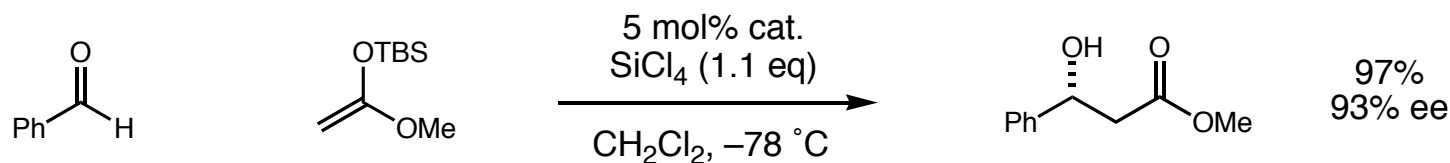


### ■ Denmark (2001) – Asymmetric propargylation

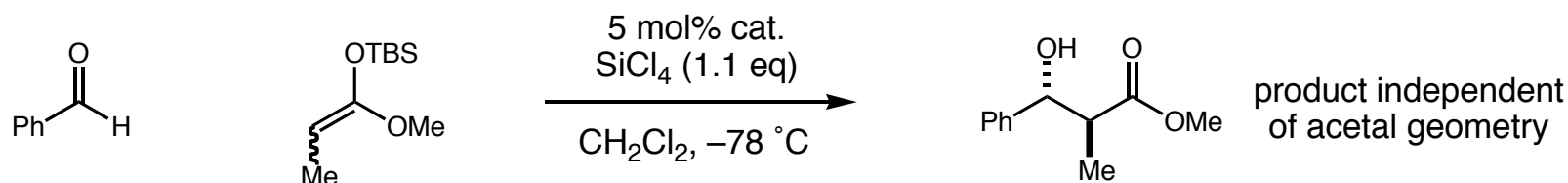


Denmark, S. E.; Wynn, T. *J. Am. Chem. Soc.* **2001**, *123*, 6199.

### ■ Denmark (2002) – Addition of silyl ketene acetals



### ■ Diastereoselective addition of silyl ketene acetals



<i>E</i> : <i>Z</i> = 95:5	93% yield	<b>dr = 99:1</b>	ee = 99%
<i>E</i> : <i>Z</i> = 12:88	73% yield	<b>dr = 99:1</b>	ee = 99%

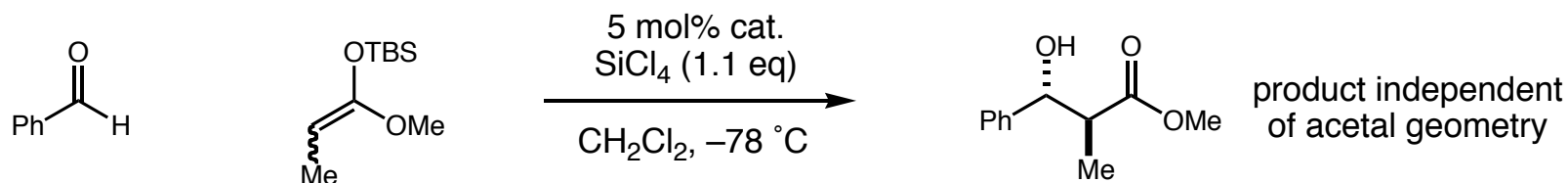
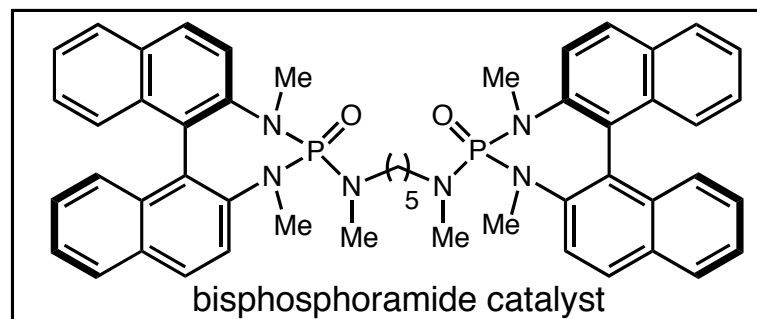
Indicative of the expected open (acyclic) transition state

Denmark, S. E.; Wynn, T., Beutner, G. L. *J. Am. Chem. Soc.* **2002**, *124*, 13405.

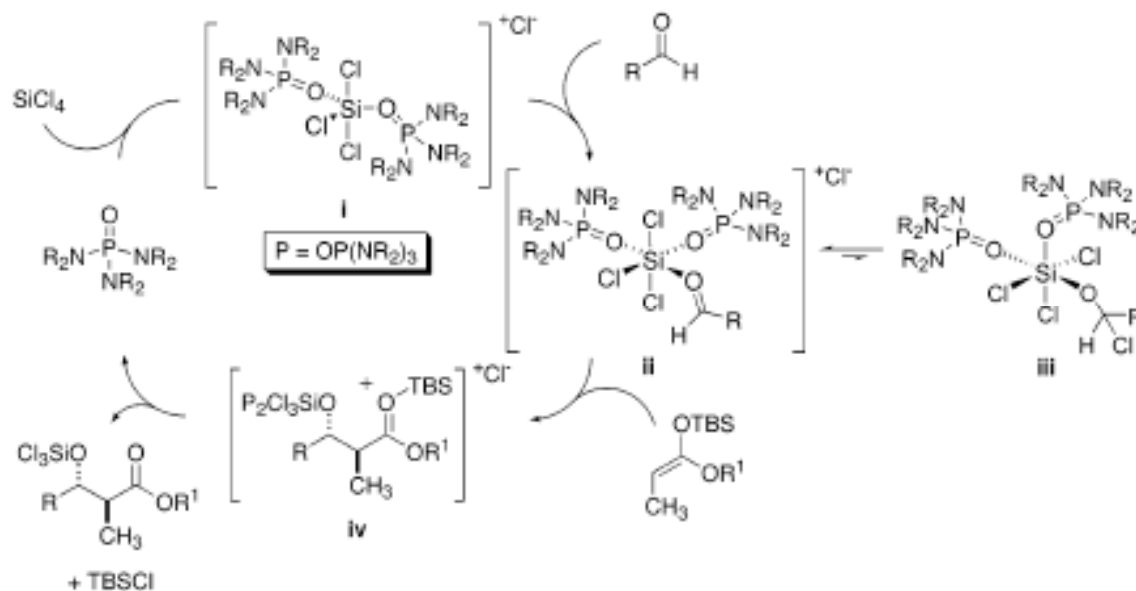
# Hypervalent Silicon : Chiral Lewis Acids

Aldol diastereoselectivity

## Denmark (2005) – Diastereoconvergent aldol



$E:Z = 95:5$	93% yield	<b>dr = 99:1</b>	ee = 99%
$E:Z = 12:88$	73% yield	<b>dr = 99:1</b>	ee = 99%

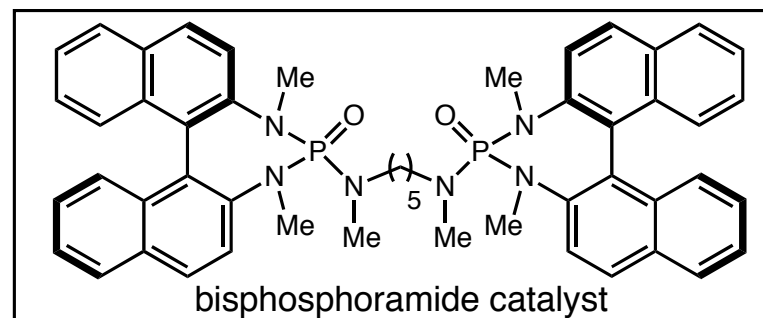


- Stoichiometric in Lewis acid: Ligand acceleration by catalytic Lewis base

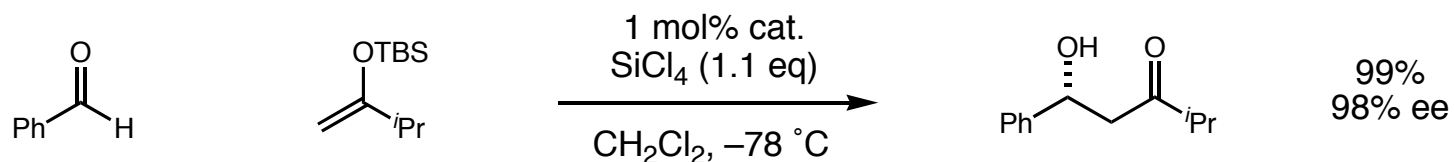
Denmark, S. E.; Beutner, G. L.; Wynn, T.; Eastgate, M. D. *J. Am. Chem. Soc.*, **2005**, 127, 3774-3789.

## Hypervalent Silicon : Chiral Lewis Acids

Denmark's bisphosphoramidate complex

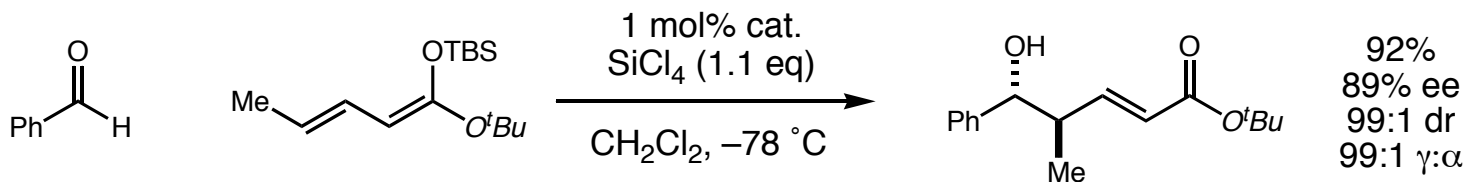


### ■ Denmark (2003) – Addition of silyl enol ethers



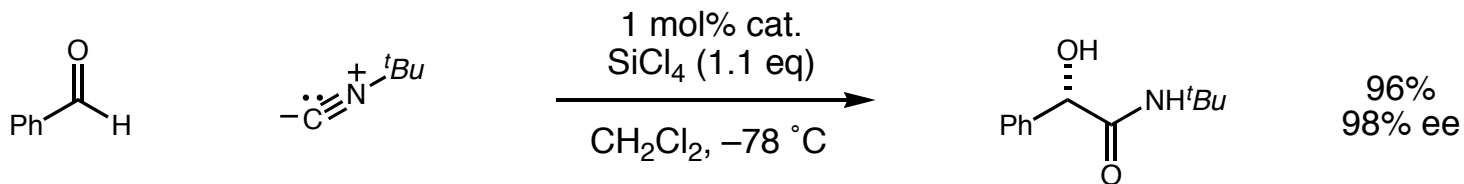
Denmark, S. E.; Heemstra J. R. jr. *Org. Lett.*, **2003**, 5, 2303.

### ■ Denmark (2003) – Addition of vinylogous enol ether



Denmark, S. E.; Beutner, G. L. *J. Am. Chem. Soc.*, **2003**, 125, 7800.

### ■ Denmark (2003) – Addition of isocyanides

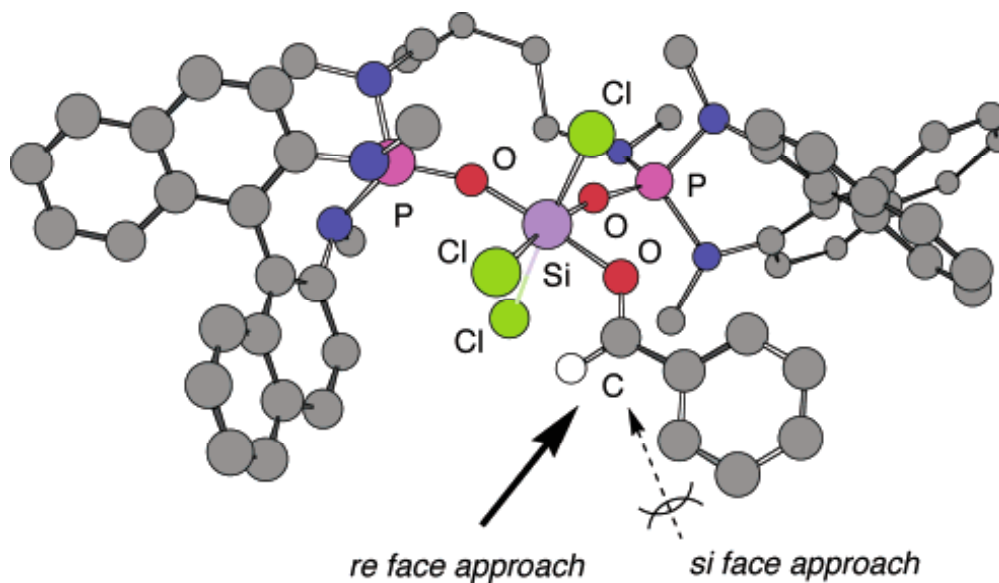
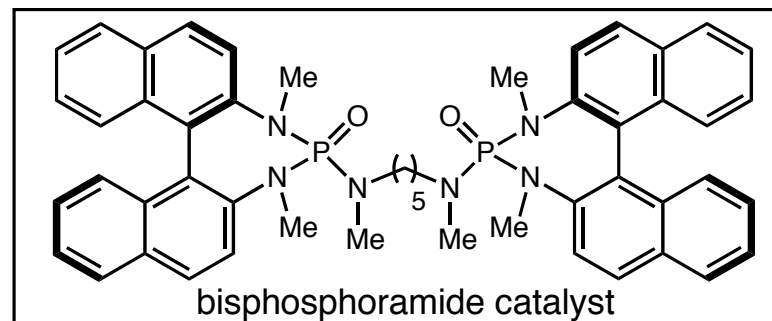


Denmark, S. E.; Fan, Y. *J. Am. Chem. Soc.*, **2003**, 125, 7825.

## Hypervalent Silicon : Chiral Lewis Acids

Denmark's bisphosphoramidate complex

■ Denmark (2005) – Calculated structure



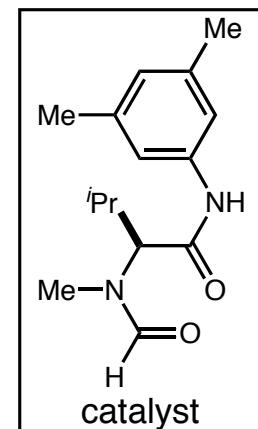
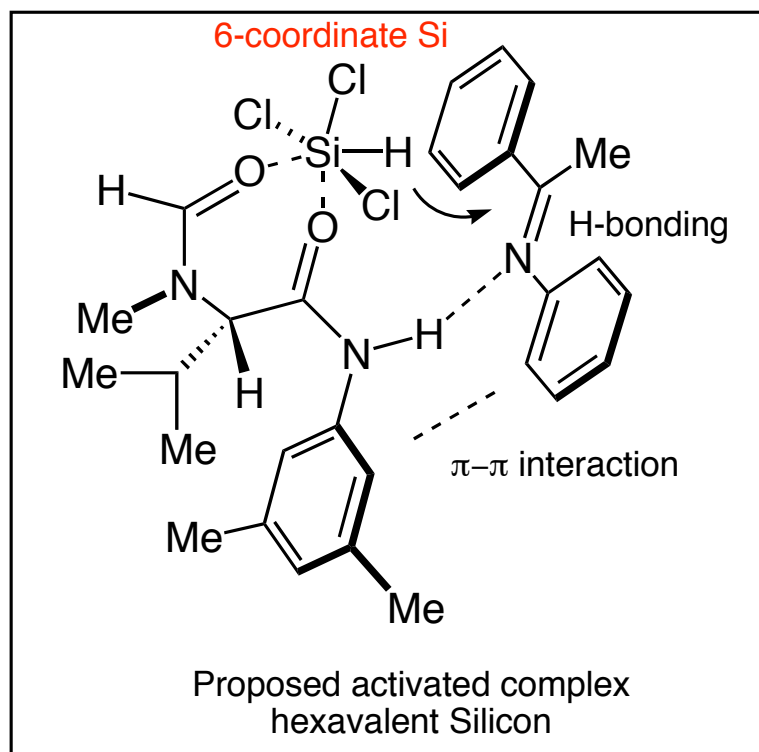
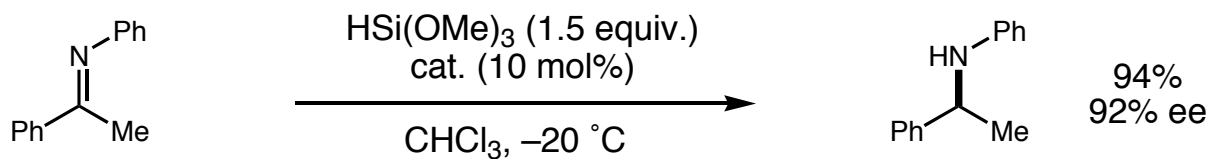
benzaldehyde-silyl cation complex optimized in GAMESS (US) at PM3 level

Denmark, S. E.; Beutner, G. L.; Wynn, T.; Eastgate, M. D. *J. Am. Chem. Soc.*, **2005**, 127, 3774-3789.

# Hypervalent Silicon : Hydride Transfer

asymmetric hydrosilation

■ Kocovsky (2004)



- Works well for limited range of methyl ketones
- TS postulated to involve a 6-coordinate Si

Malkov, A. V. Mariani, A.; MacDougall, K. N.; Kocovsky, P.; . *Org. Lett.*, **2004**, *6*, 2253.



## *Summary and Conclusions*

- Over the past 10 years the power of hypervalent silanes has begun to be harnessed
- Denmark in particular had made a large contribution to the development of this field both in terms of reaction development and mechanistic rationale
- Problem: Difficult to accurately assess the precise nature, coordination and conformation of the active catalyst and transition state orientation