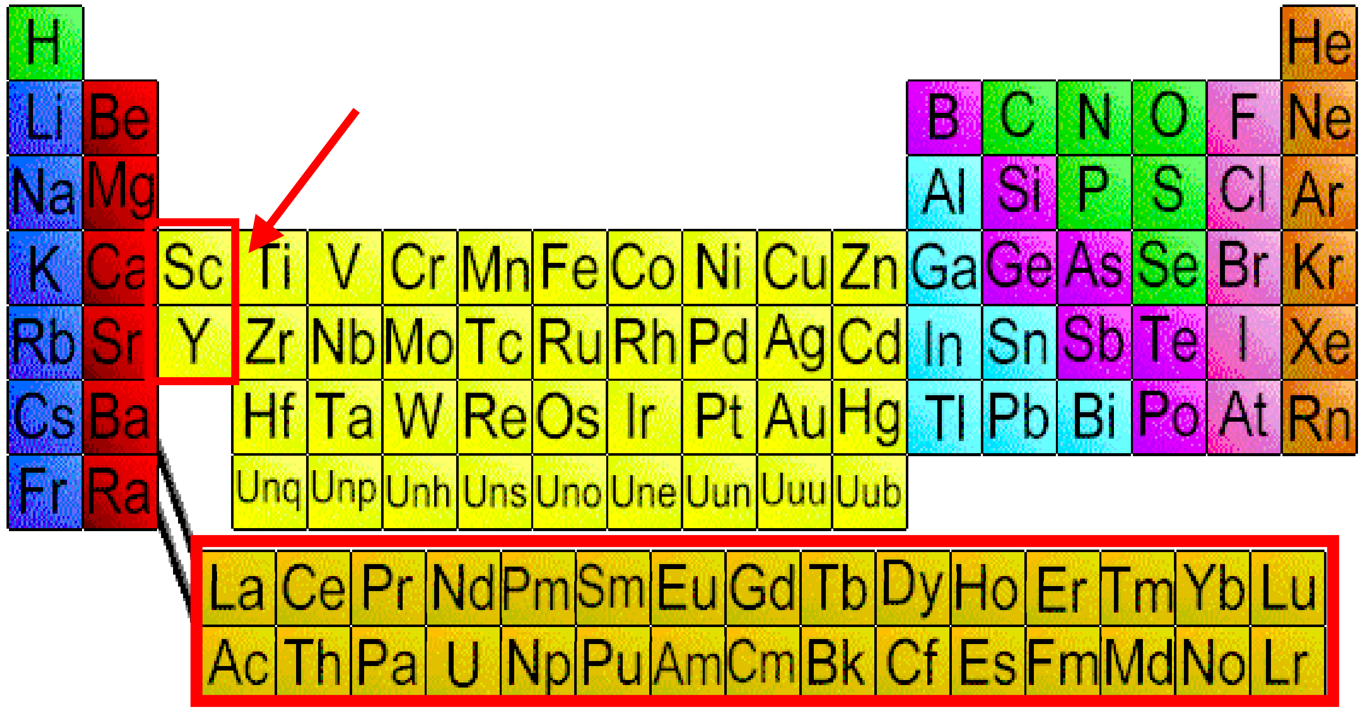
QUESTION:

IF I HAVE THE KINETICS GOING FOR ME
AND I KNOW THE THERMODYNAMICS

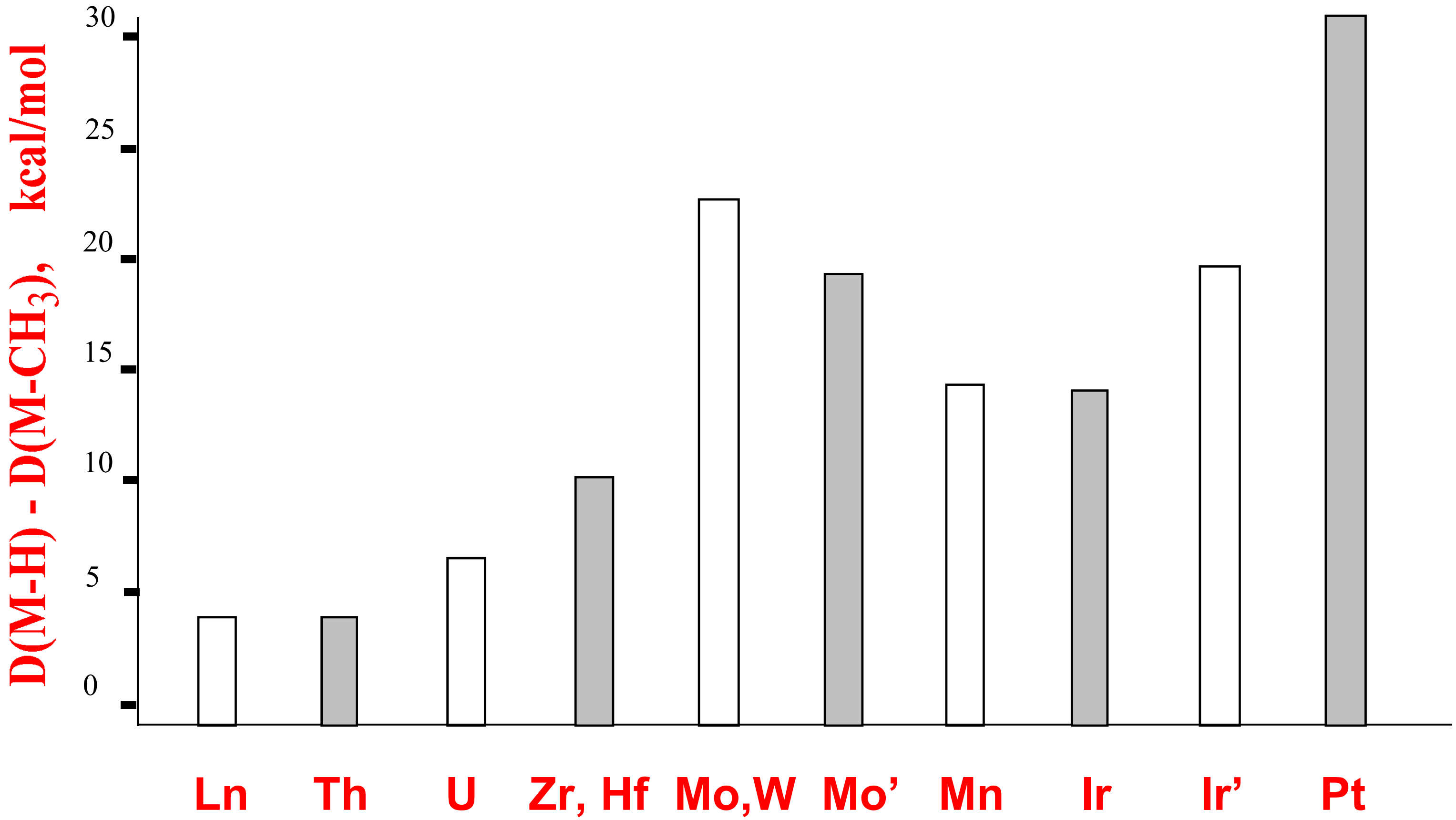
CAN I INVENT NEW CATALYTIC REACTIONS?

Lanthanides and Actinide Metals Are Unique



- Large, tunable metal ionic radii; potential for great coordinative unsaturation
- Well-defined formal oxidation states
- Polar metal-ligand bonding
- Kinetically very labile
- Distinctive metal-ligand bonding energetics
- Diamagnetic or paramagnetic
- Abundant

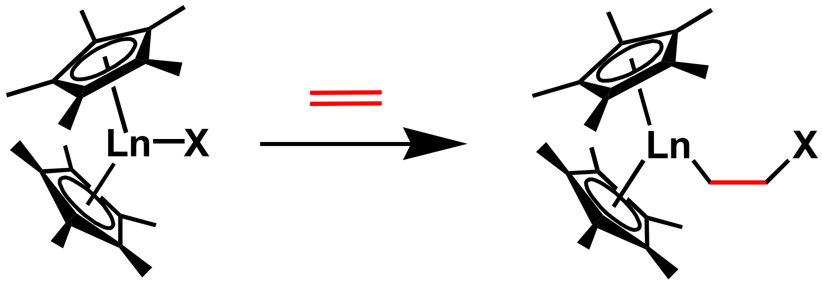
Bond Enthalpy Trends Across the Periodic Table: Hydrides vs. Alkyls. We Need Data!



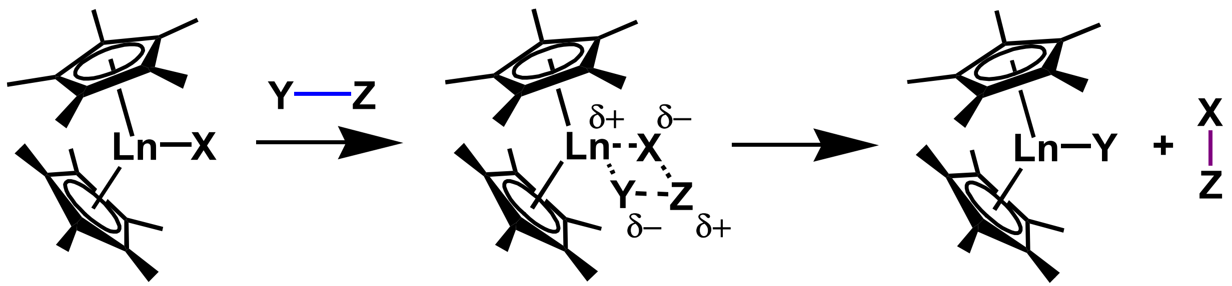
- Electronegativity, Orbital Overlap Basis
- Implications for β-H Elimination, C-H Activation

Distinctive Reactivity Patterns of Organolanthanide Centers

I. Olefin Insertion



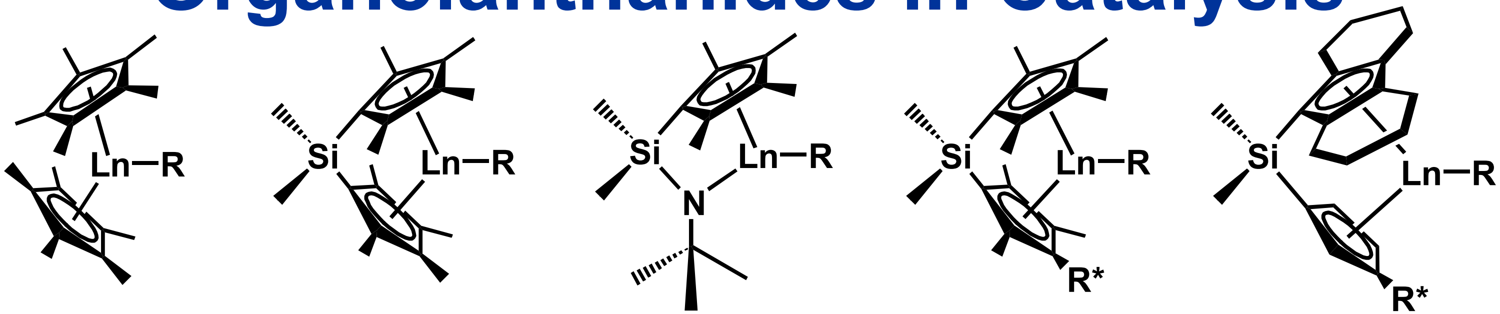
II. Sigma Bond Metathesis



I. NEW ISSUES

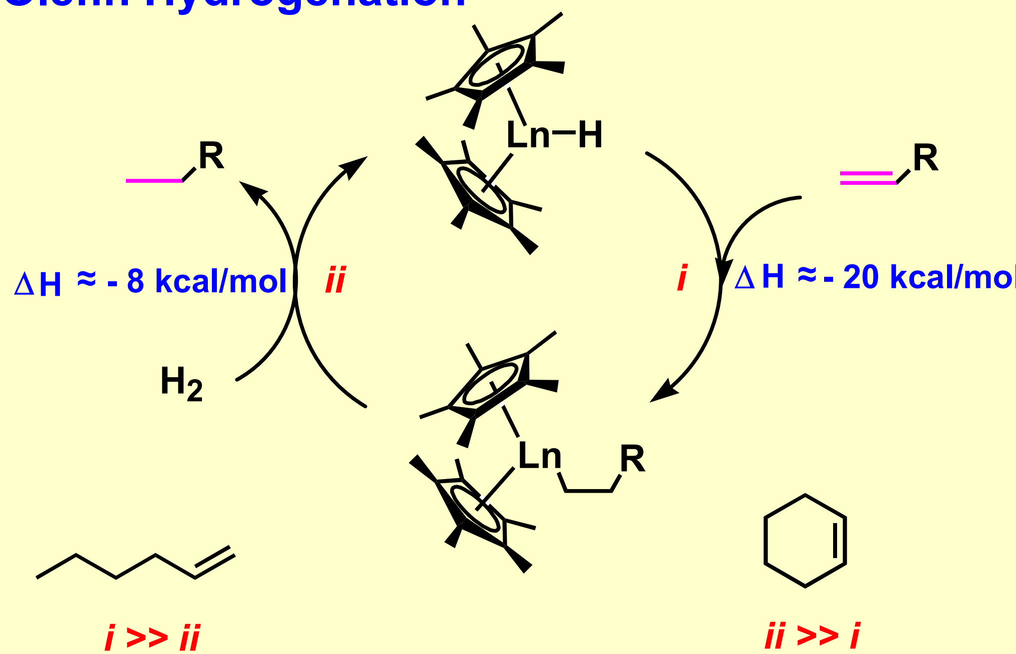
- X = Heteroatom
- Regioselectivity, Enantioselectivity, Diastereoselectivity
- Thermodynamic Control (Experimental Bond Energies)
- Mechanism
- Tandem Reactions

Organolanthanides in Catalysis



- Stable, Soluble, Crystalline
- Reactivity Tunable w/ Ionic Radius
- Efficient, Active Homogeneous Catalysts
- Different Mechanisms, Selectivities than Transition Metals

Olefin Hydrogenation



$\nu = [\text{Olefin}]^0[H_2][\text{Ln}]$

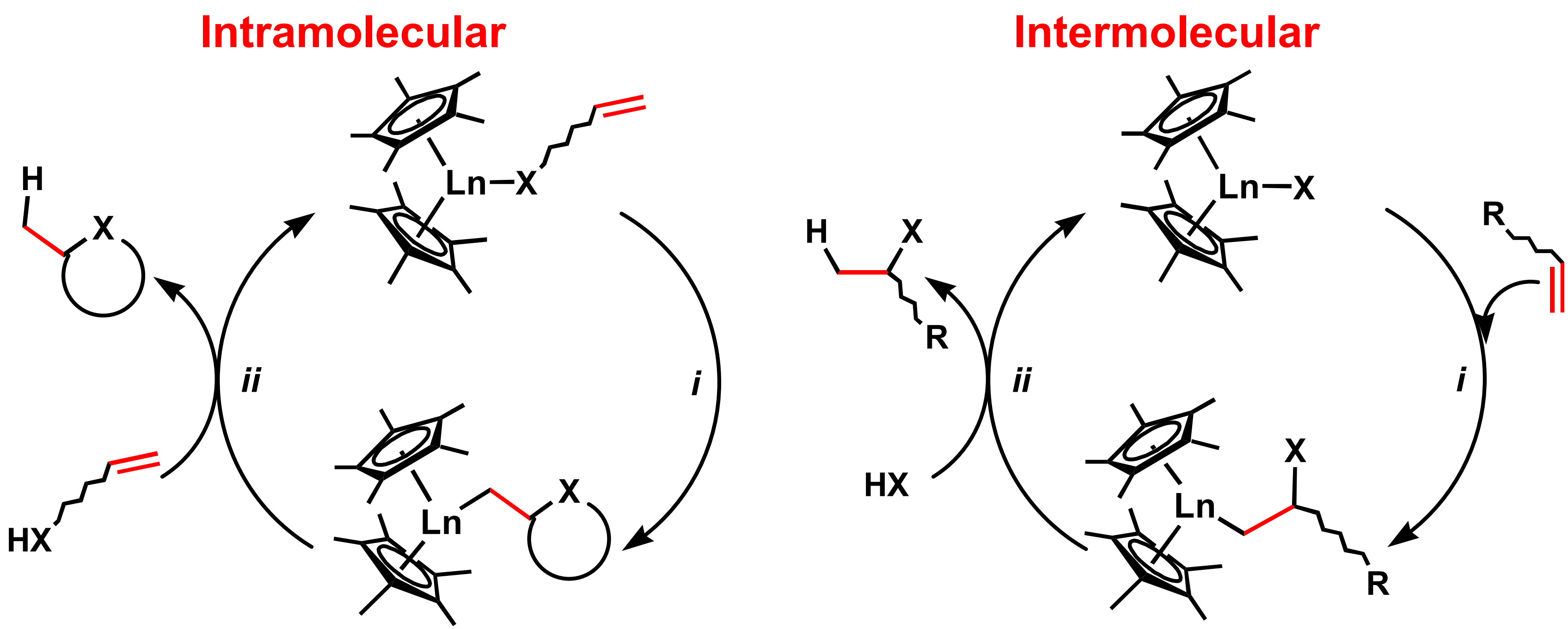
$\nu = [\text{Olefin}][H_2]^0[\text{Ln}]^{1/2}$

N_t = 20,000 – 120,000 h^{-1}!

Anwender, Bercaw, Carpentier, Evans, Hessen, Hultzsch, Livinghouse, Molander, Okuda, Roesky, Schumann, Scott, Teuben, Yasuda, Watson

CATALYSIS. *THERMODYNAMICALLY-BASED* STRATEGIES FOR CATALYTIC *HETEROATOM* ADDITION (HYDROELEMENTATION = X-H ADDITION TO C=C)

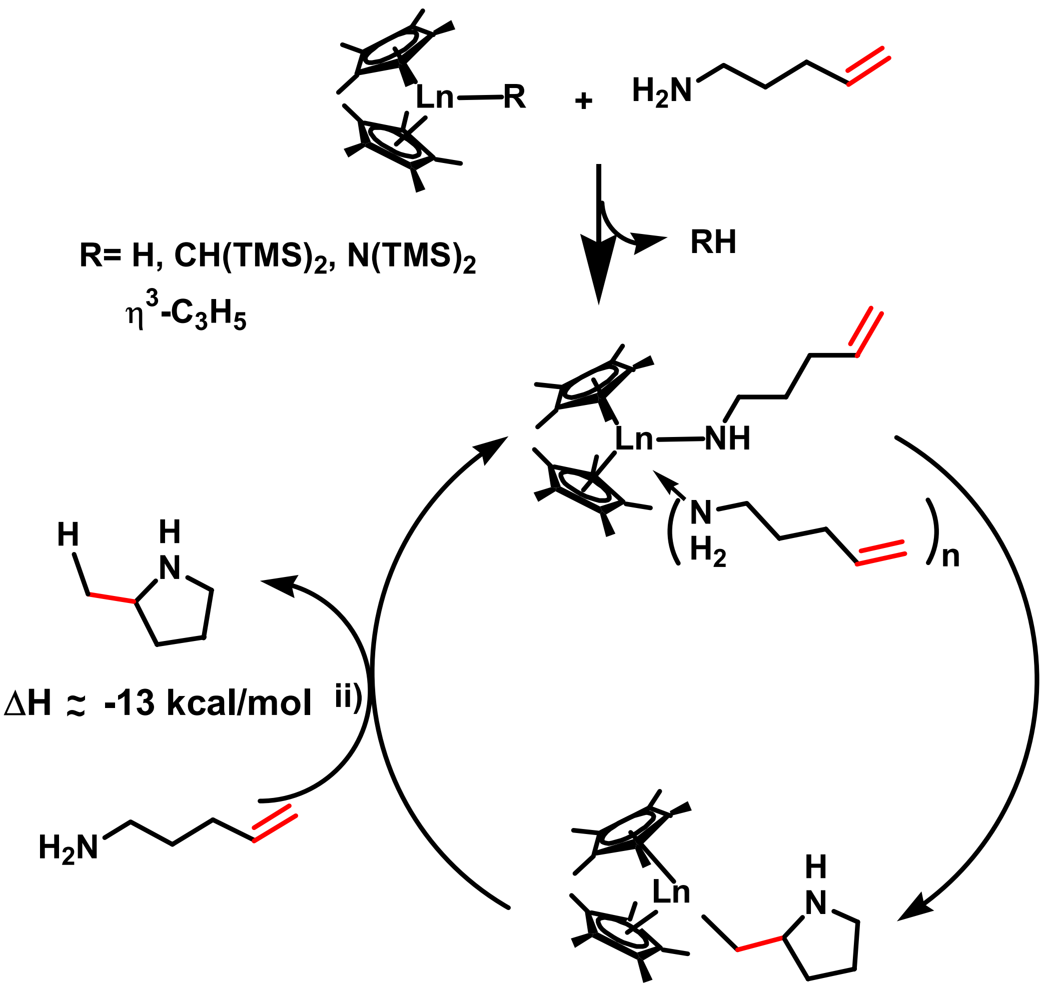
EXAMPLE: Olefinic Substrates **(X = Heteroatom Group)**



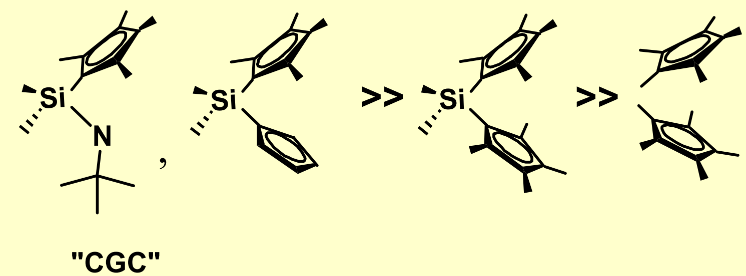
EXPECTATIONS

- $\Delta H_{ii} < \Delta H_{i}$
- ΔS, $\Delta S^{\ddagger}$ Favor Intramolecular Process
- $k_{ii} > k_{i}$
- ΔH_{i} (X): $CH_3 \leq H < Pr_2, NR_2 < SR, OR$

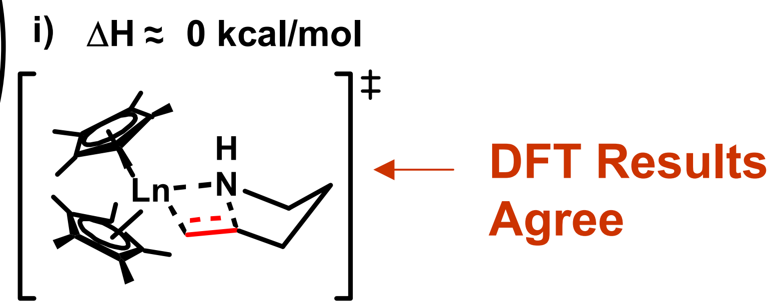
Beginning. Organolanthanide-Catalyzed Intramolecular Hydroamination / Cyclization of Aminoalkenes



- Rate = k [catalyst]^1[substrate]^0
- Sensitive to steric demand
  - Metal ionic radius: La > Sm > Lu
  - Ligand structure



- Aminoalkynes, -allenes

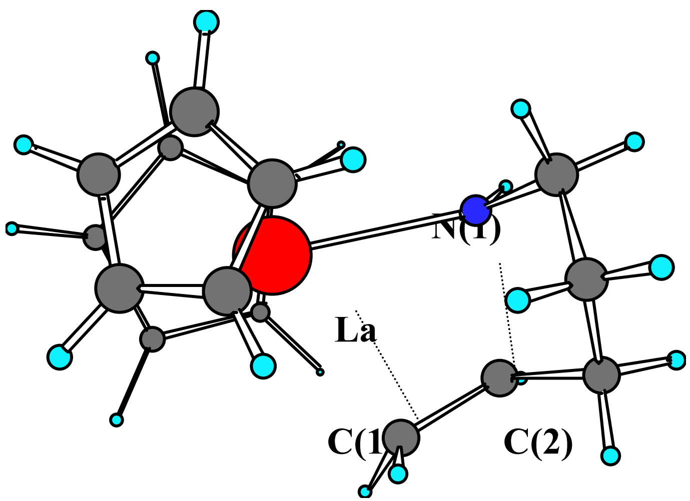


Turnover-limiting

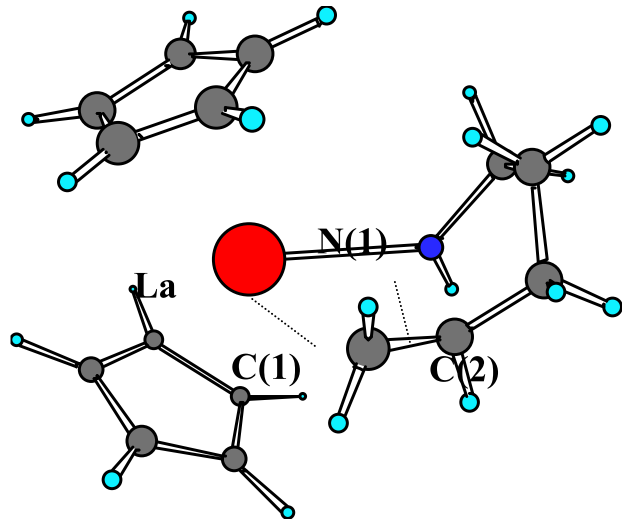
Limited to Terminal Aminoalkenes

Hong, S.; Marks, T. J. *Accts. Chem. Res.* **2004**, *37*, 673.

DFT Optimized Structure of Hydroamination/Cyclization Transition State



Top view



Side view

Bond Length (Å)		Δ
La-Cp_{centr}	2.64	(0.00)
La-N(1)	2.51	(+0.14)
C(1)-C(2)	1.43	(+0.08)
La-C(1)	2.68	(-0.40)
La-C(2)	3.09	(-0.13)
N-C(2)	2.00	(-0.98)

Values in parentheses refer to activated catalyst

I. Fragalà

CHALLENGES IN ORGANOLANTHANIDE-MEDIATED HYDROELEMENTATION CATALYSIS

- Utilize Sterically Encumbered Substrates
- Understand/Enhance Chemo-, Regio-, Enantioselectivity
- Understand Scope of Functional Group Tolerance
- Utilize Cascaded Bond-Forming Sequences (C-N + C-C; C-N + C-N; C-N + ?)
- Utilize Intermolecular Processes
- Develop New Stereodirecting, Non-Cp Ancillary Ligands
- Understand Electronic Structure Aspects of Mechanism
- Apply Understanding to Other Heteroatoms, Metal Centers

INVENTION OF NEW ORGANO-f-ELEMENT-CENTERED CATALYTIC TRANSFORMATIONS

I. Introduction

A. Distinctive d°/f-Element Reaction Patterns

B. Organolanthanides as Potential Catalysts

II. Hydroamination

A. Scope, Mechanism, Selectivity

B. Overcoming Steric Hindrance: Allenes, Dienes, Internal Olefins

C. Intermolecular

D. New Chiral Ancillary Ligands

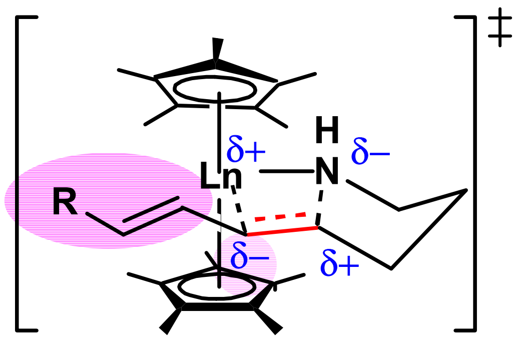
III. Hydrophosphination

A. Scope, Mechanism, Selectivity

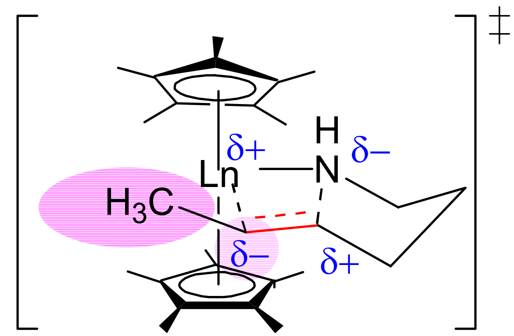
B. Coupling to Olefin Polymerization

V. Conclusions

Broadening Scope of Aminoalkene Hydroamination. *Conjugated Dienes*.

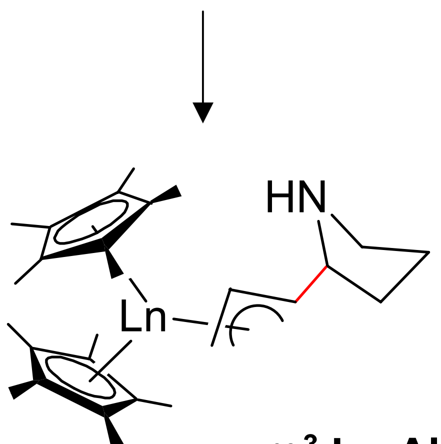


vs.



Electron-Withdrawing Vinyl

Electron-Donating Methyl

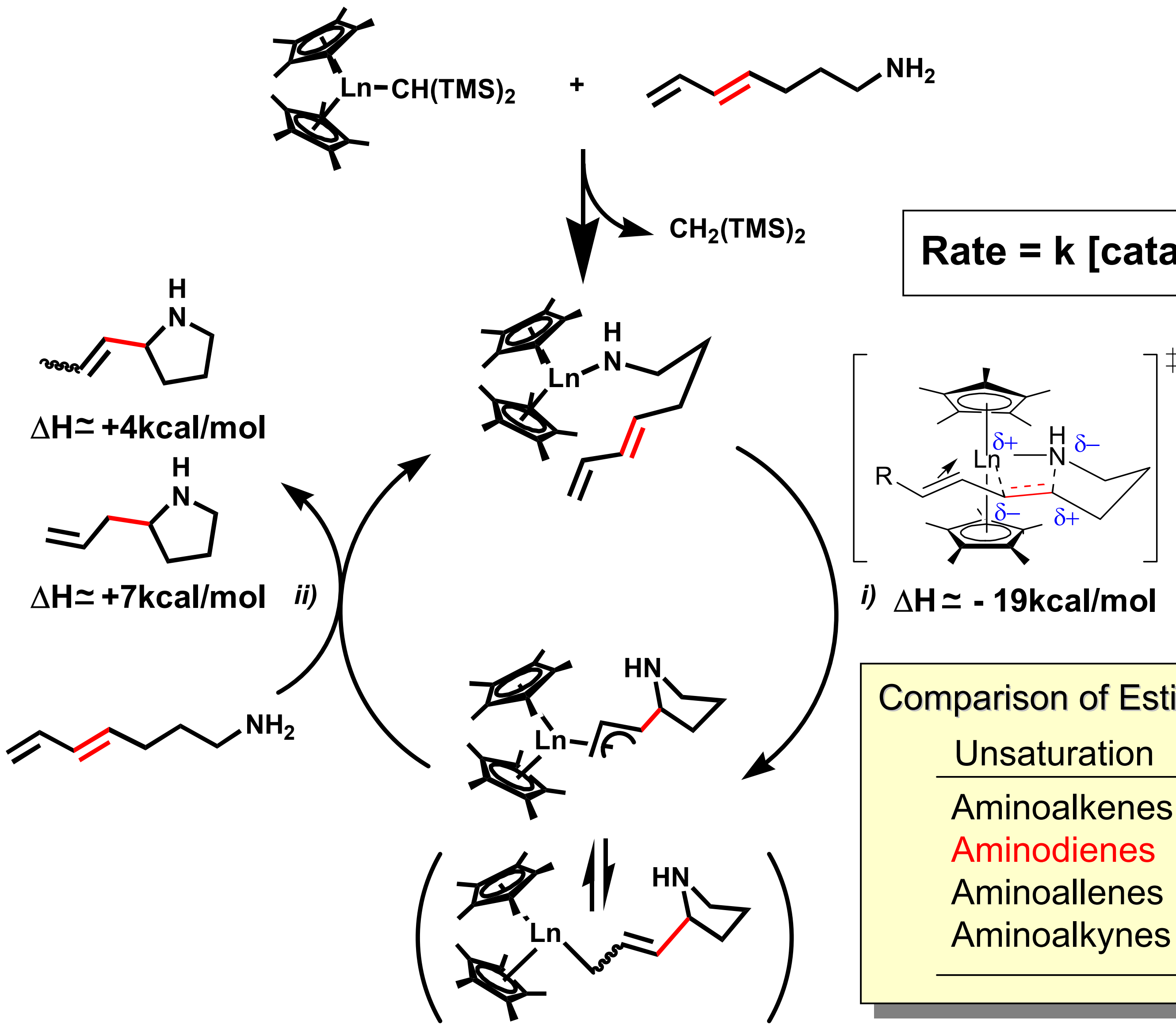


η^3 Ln-Allyl

- **Electronic effects**
  stabilize proposed partial charges developed in the transition state
- **Relief of steric crowding by isomerization ($\eta^3 \rightleftarrows \eta^1$)**
- **More sterically-demanding substrate**
  diastereo and enantioselectivity

Hong, S.; Marks, T. J. *Accts. Chem. Res*. **2004**,*37*, 673.

Proposed Catalytic Cycle and Thermodynamic Estimates

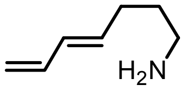
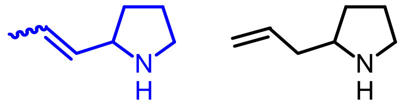
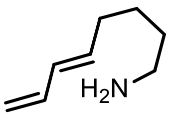
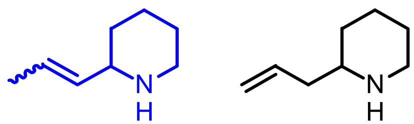
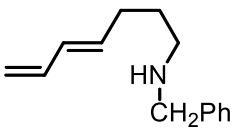
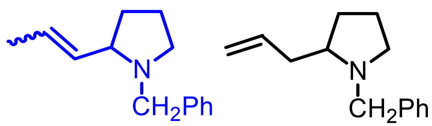
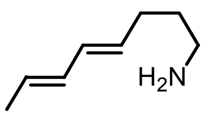
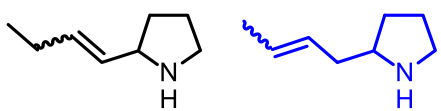
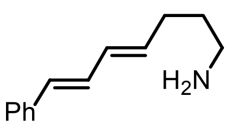
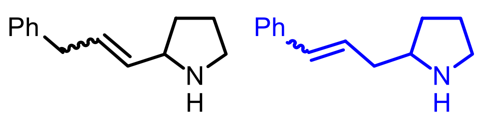


Rate = k [catalyst]^1[substrate]^0

Comparison of Estimated ΔH's (kcal/mol)

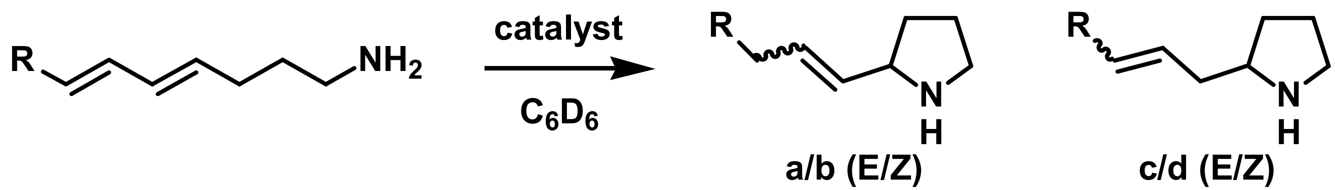
Unsaturation	Step i	Step ii
Aminoalkenes	0	-13
Aminodienes	-19	+4 ~ +7
Aminoallenes	-29	0
Aminoalkynes	-35	0

Diene Scope, Conversion, Turnover Frequencies

Entry	Subtsrate	Products	% Yield[a] (Isolated Yield)	Product Ratio[c] a : b : c : d	Pre-Catalyst	N_t, h^{-1c} (°C)[d]
1.		 a/b (E/Z) c	**> 95**	**84: 16: 0**	**$Cp'_2LaCH(TMS)_2$**	**40 (25)**
			> 95	72: 11: 17	$Cp'_2SmCH(TMS)_2$	0.79 (60)
			93	30: 19: 51	$Cp'_2YCH(TMS)_2$	0.05 (60)
			90	59: 41: 0	$CGCSmN(TMS)_2$	3.1 (25)
			> 95	93: 7: 0	$(OHF^*)SmN(TMS)_2$[e]	12 (25)
2.		 a/b (E/Z) c	**> 95**	**97 : 3: 0**	**$Cp'_2LaCH(TMS)_2$**	**3.0 (25)**
			> 95 (91[b])	97: 3: 0	$(OHF^*)SmN(TMS)_2$[e]	0.11 (25)
3.		 a/b (E/Z) c	**85 (71)**	**87: 7: 6**	**$CGCSmN(TMS)_2$**	**5.8 (60)**
4.		 a/b (E/Z) c/d (E/Z)	**94**	**38: 0: 47:15**	**$Cp'_2LaCH(TMS)_2$**	**1.8 (60)**
			93	23: 0: 72: 5	$Cp'_2SmCH(TMS)_2$	0.02 (60)
5.		 a/b (E/Z) c/d (E/Z)	**92**	**>94% c**	**$Cp'_2LaCH(TMS)_2$**	**89 (60)**
			90	>94% c	$Cp'_2SmCH(TMS)_2$	2.3 (60)

[a]Determined by ^{1}H-NMR. [b]Isolated yield of in-situ derivatized Cbz carbamate. [c]Determined by ^{1}H-NMR and/or GC-MS of Boc derivatives, [d] Turnover frequencies measured in C_6D_6 with 3 ~11 mol% precatalyst. [e]OHF* = (S)-Me_2Si-(η^5-octahydrofluorenyl)(CpR*), R*= (-)-menthyl.

Substituent Effects on Diene Hydroamination



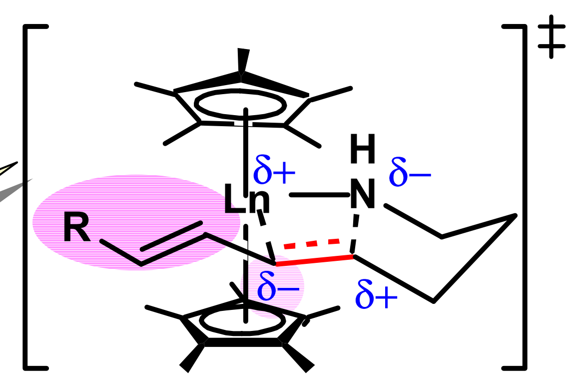
Entry	R	Pre-Catalyst	N_t, h^{-1} (°C)
1	Ph	$Cp'_2SmCH(TMS)_2$	2.3 (60)
2	H	$Cp'_2SmCH(TMS)_2$	0.79 (60)
3	Me	$Cp'_2SmCH(TMS)_2$	0.02 (60)
4	Ph	$Cp'_2LaCH(TMS)_2$	89 (60)
5	Me	$Cp'_2LaCH(TMS)_2$	1.8 (60)

Sm : Ph > H > Me

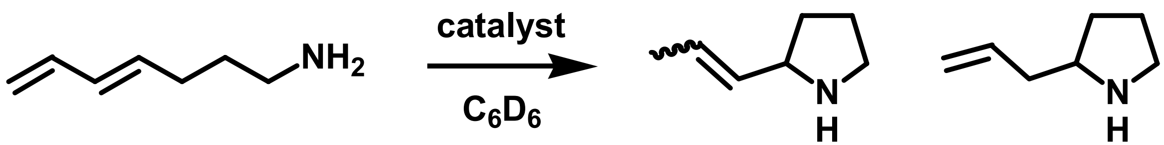
La : Ph > Me

Electronic Effects

In accord with proposed transition state electronic demands



Metal Ionic Radius and Ancillary Ligand Effects



a/b (E/Z)   c

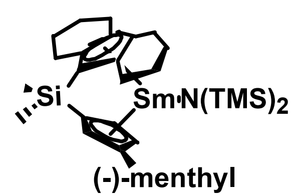
Metal Size Effect

Entry	Ln^{3+} radius (Å)	Pre-Catalyst	N_t, h^{-1} (°C)
1	1.160	$Cp'_2LaCH(TMS)_2$	40 (25)
2	1.079	$Cp'_2SmCH(TMS)_2$	0.79 (60)
3	1.019	$Cp'_2YCH(TMS)_2$	0.05 (60)
4	1.079	$CGCSmN(TMS)_2$	3.1 (25)
5	1.019	$CGCYN(TMS)_2$	~0.08 (25)

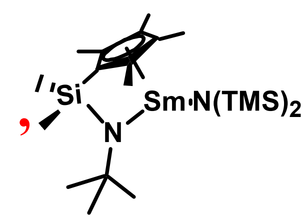
Ancillary Ligand Effect

Entry	Pre-Catalyst	N_t, h^{-1} (°C)
6	$Me_2Si(OHF)(Cp^*)SmN(TMS)_2$	12 (25)
7	$CGCSmN(TMS)_2$	3.1 (25)
8	$Cp'_2SmCH(TMS)_2$	0.79 (60)

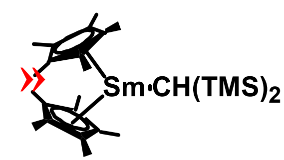
Increased rates with
- **Larger metal ionic radii**
- **More open ligand structures**



$Me_2Si(OHF)(Cp^*)SmN(TMS)_2$



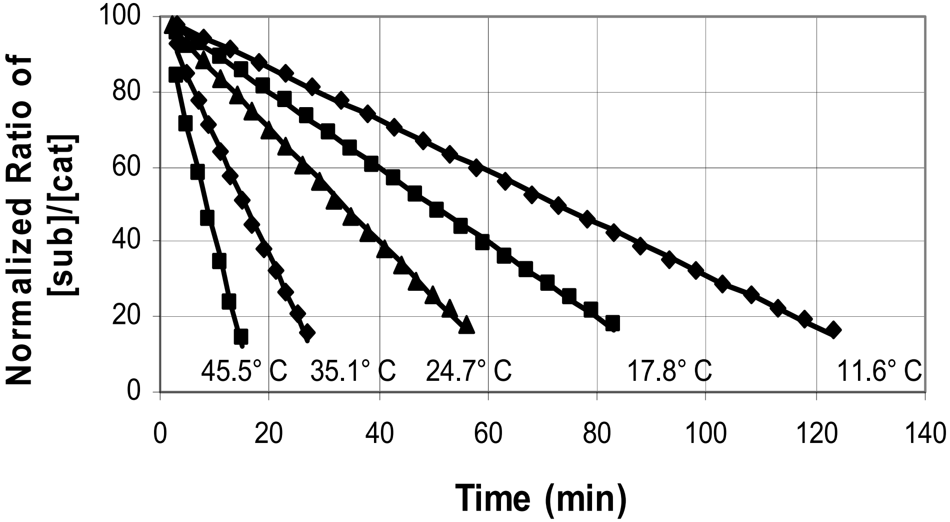
$CGCSmN(TMS)_2$



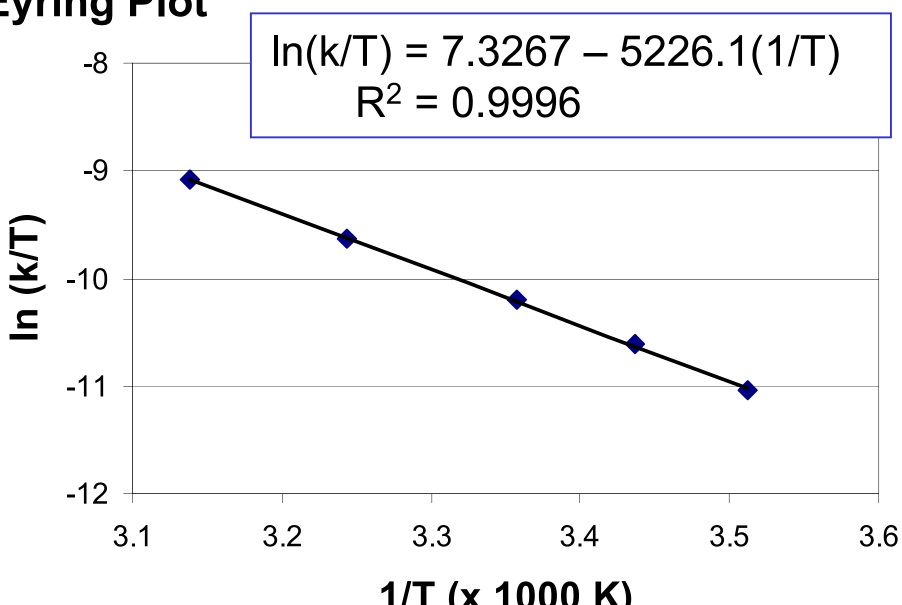
$Cp'_2SmCH(TMS)_2$

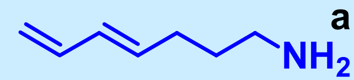
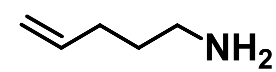
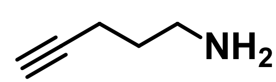
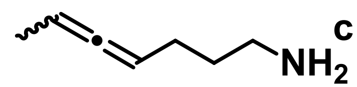
KINETICS, ACTIVATION PARAMETERS

Rate = k [catalyst] ^{1} [aminodiene] ^{0}



Eyring Plot

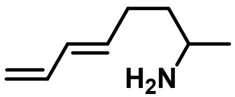
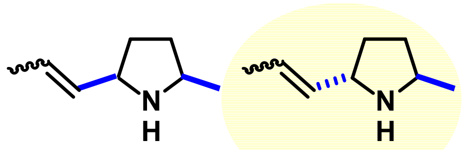
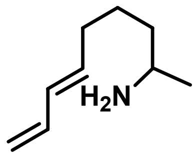
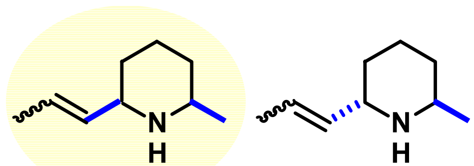


Substrate	$\Delta H^‡$, kcal/mol	$\Delta S^‡$, eu
 [a]	10.4 (0.4)	-32.7 (1.2)
 [b]	12.7 (1.4)	-27.0 (4.6)
 [b]	10.7 (8)	-27.4 (6)
 [c]	16.9 (1.3)	-16.5 (4.3)

[a] Determined using $Cp'_2LaCH(TMS)_2$ in benzene-d_6.
[b] Determined using $Cp'_2LaCH(TMS)_2$ in toluene-d_8.
[c] Determined using $Cp'_2SmCH(TMS)_2$ in toluene-d_8.

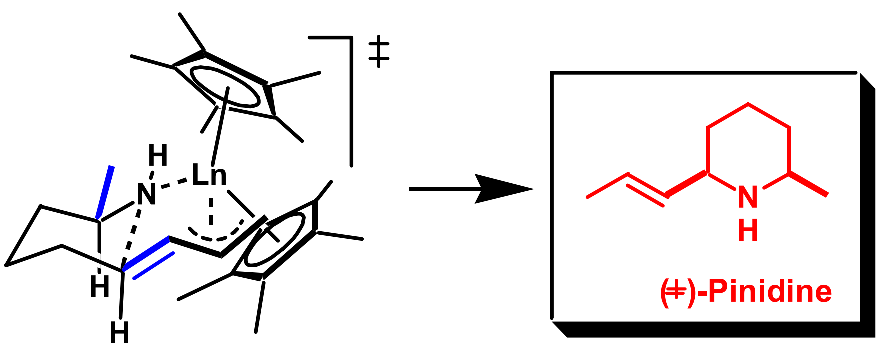
Highly organized, polar transition state

Diastereoselectivity in Aminodiene Cyclizations

Entry	Subtsrate	Products	Conversion[a] (%)	Product Ratio[b] *cis* : *trans*	Pre-Catalyst	N_t, h^{-1} (^oC)[c]
1.		 2,5-*cis* 2,5-*trans*	> 95	42 : 58	$Cp'_2LaCH(TMS)_2$	1.0 (25)
			> 95	**10 : 90**	**$CGCSmN(TMS)_2$**	**78 (25)**
2.		 2,6-*cis* 2,6-*trans*	**> 95**	**99.4 : 0.6[d]**	**$Cp'_2LaCH(TMS)_2$**	**3.7 (25)**
			> 95	78 : 22	$CGCSmN(TMS)_2$	4.0 (60)

[a]Determined by ^{1}H-NMR, [b]Determined by GC-MS ratio of the corresponding hydrogenated Boc derivatives, [c]Turnover frequencies measured in C_6D_6 with 6 mol% precatalyst, [d]*cis*: *trans* = 178:1; Alkene isomer ratio (E: Z: allyl)= 94: 1: 5

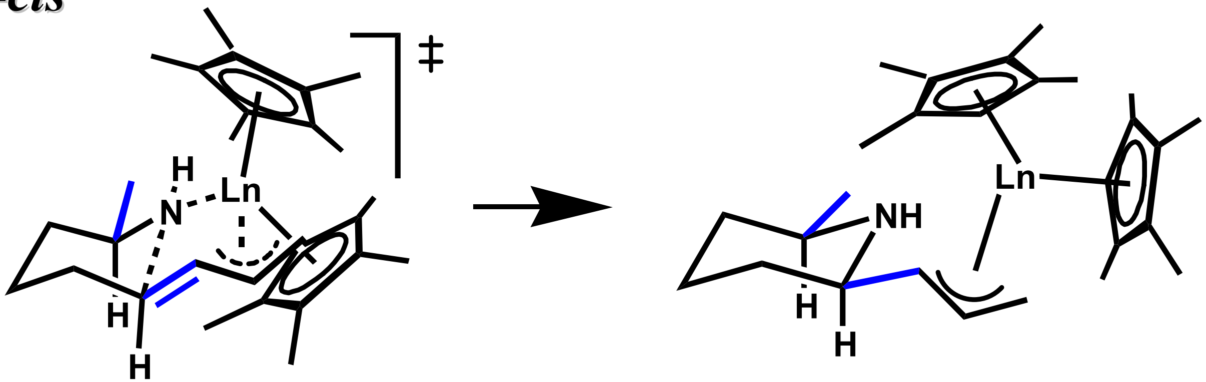
Good to excellent 2,5-*trans* (80% de), and 2,6-*cis* (99% de) diastereoselectivities



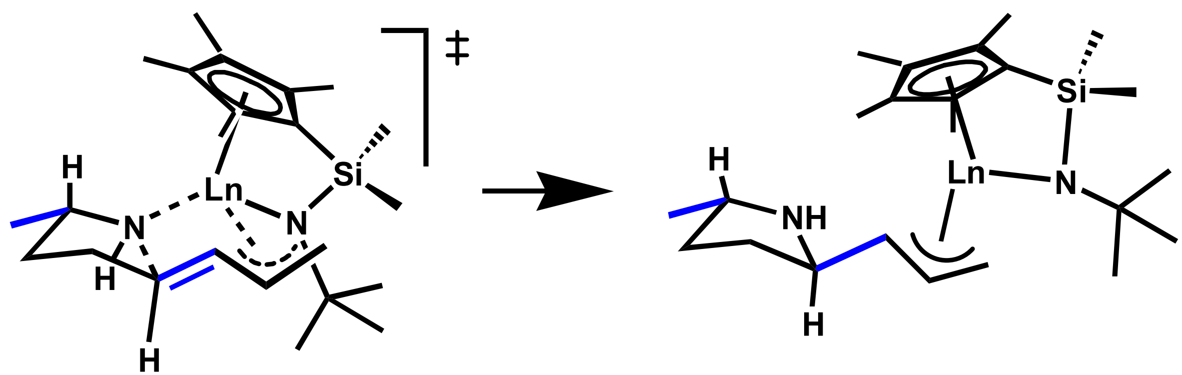
Concise synthesis of (±)-pinidine with excellent stereocontrols (2,6-*cis* and *trans*-alkene)

Plausible Diene Stereochemical Pathways

2,6-*cis*

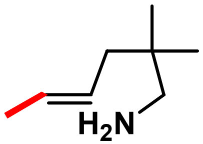
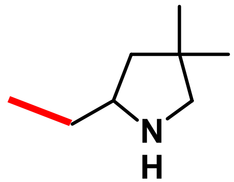
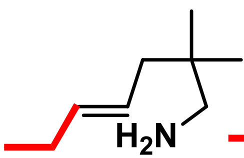
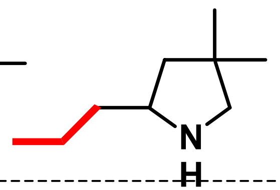
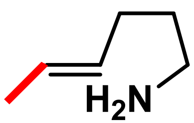
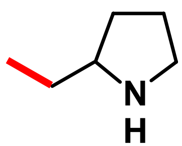


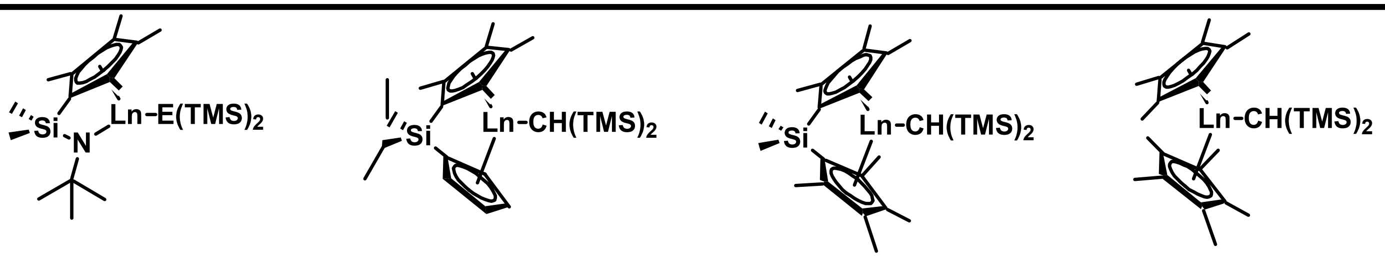
2,5-*trans*



Chair-like transition states in which methyl and diene units occupy equatorial positions

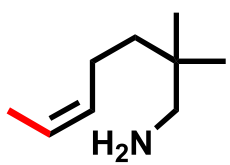
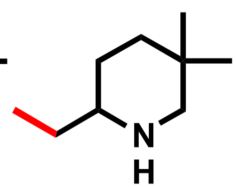
Internal Olefins. Hydroamination of Five-membered Rings at High Temperatures

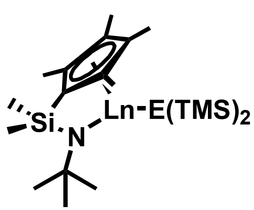
Substrate	Product	Precatalyst (mol %)	Time	Temp	Conversion
		(CGC)SmN(TMS)$_2$ (6.7)	19 h	125 ^{o}C	>95 %
		(CGC)YN(TMS)$_2$ (3.3)	19 h	125 ^{o}C	>95 %
		Me$_2$SiCp"$_2$NdCH(TMS)$_2$ (5.0)	19 h	125 ^{o}C	>95 %
		Cp'$_2$LaCH(TMS)$_2$ (4.8)	12 h	125 ^{o}C	>95 %
		Cp'$_2$SmCH(TMS)$_2$ (2.3)	65 h	120 ^{o}C	20 %
		(CGC)SmN(TMS)2 (4.5)	34 h	120 ^{o}C	93 %
		(CGC)YN(TMS)2 (6.9)	39 h	120 ^{o}C	98 %
		(CGC)LuCH(TMS)2 (4.3)	38 h	120 ^{o}C	95 %
		(CGC)SmN(TMS)$_2$ (7.2)	168 h	125 ^{o}C	42 %
		Et$_2$SiCp"CpNdCH(TMS)$_2$ (3.6)	240 h	120 ^{o}C	56 %
		Me$_2$SiCp"$_2$NdCH(TMS)$_2$ (3.3)	165 h	125 ^{o}C	56 %
		Cp'$_2$LaCH(TMS)$_2$ (3.3)	43 h	120 ^{o}C	>95 %
		Cp'$_2$SmCH(TMS)$_2$ (3.3)	100 h	120 ^{o}C	10 %



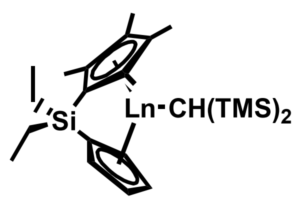
(CGC)LnE(TMS)$_2$ | Et$_2$SiCpCp"LnCH(TMS)$_2$ | Me$_2$SiCp"$_2$LnCH(TMS)$_2$ | Cp'$_2$LnCH(TMS)$_2$

Hydroamination of Internal Olefins; Six-membered Ring Closure

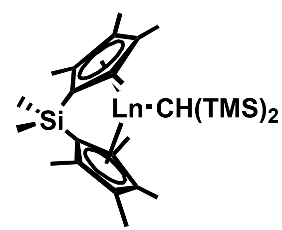
Substrate	Product	Precatalyst (mol %)	Time	Temp	Conversion
		**$(CGC)SmN(TMS)_2$ (4.7)**	116 h	120 ^oC	>95 %
		$(CGC)YN(TMS)_2$ (4.0)	107 h	120 ^oC	>95 %
		$(CGC)YbCH(TMS)_2$ (8.2)	25 h	120 ^oC	>95 %
		$(CGC)LuCH(TMS)_2$ (5.9)	46 h	120 ^oC	>95 %
		$Et_2SiCp''CpNdCH(TMS)_2$ (5.0)	137 h	125 ^oC	>95 %
		$Cp'_2LaCH(TMS)_2$ (6.1)	4 h	120 ^oC	>95 %



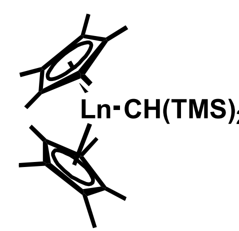
$(CGC)LnE(TMS)_2$



$Et_2SiCpCp''LnCH(TMS)_2$



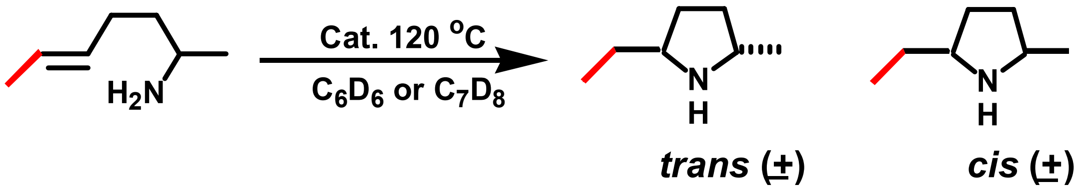
$Me_2SiCp''_2LnCH(TMS)_2$



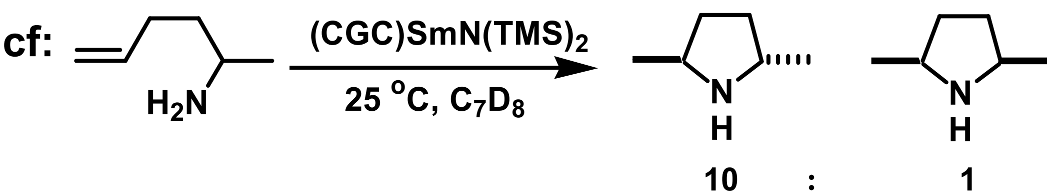
$Cp'_2LnCH(TMS)_2$

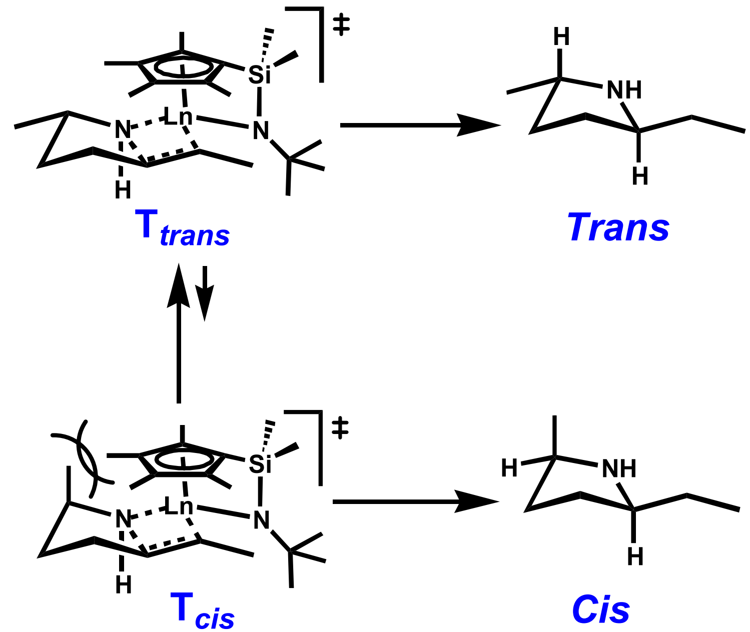
Ryu, J.-S.; Marks, T. J.; McDonald, F. E., *Org. Lett*. **2001**, *3*, 3091.
J. Org. Chem., **2004**, *69*, 1038.

Diastereoselectivity in Internal Olefin Hydroamination



Precatalysts	Mol%	Time	Conversion	[*trans*]:[*cis*]
(CGC)SmN(TMS)$_2$	10.2	40 h	95 %	11:1
(CGC)YN(TMS)$_2$	8.8	37 h	90 %	16:1
(CGC)LuCH(TMS)$_2$	3.7	92 h	77 %	15:1
Cp'$_2$LaCH(TMS)$_2$	6.0	148 h	32 %	-
Cp'$_2$SmCH(TMS)$_2$	4.4	-	N.R.	-

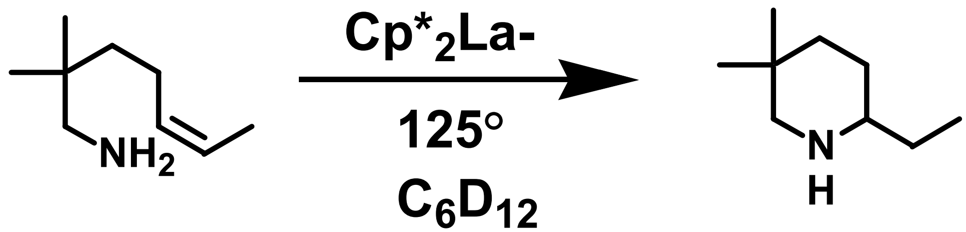


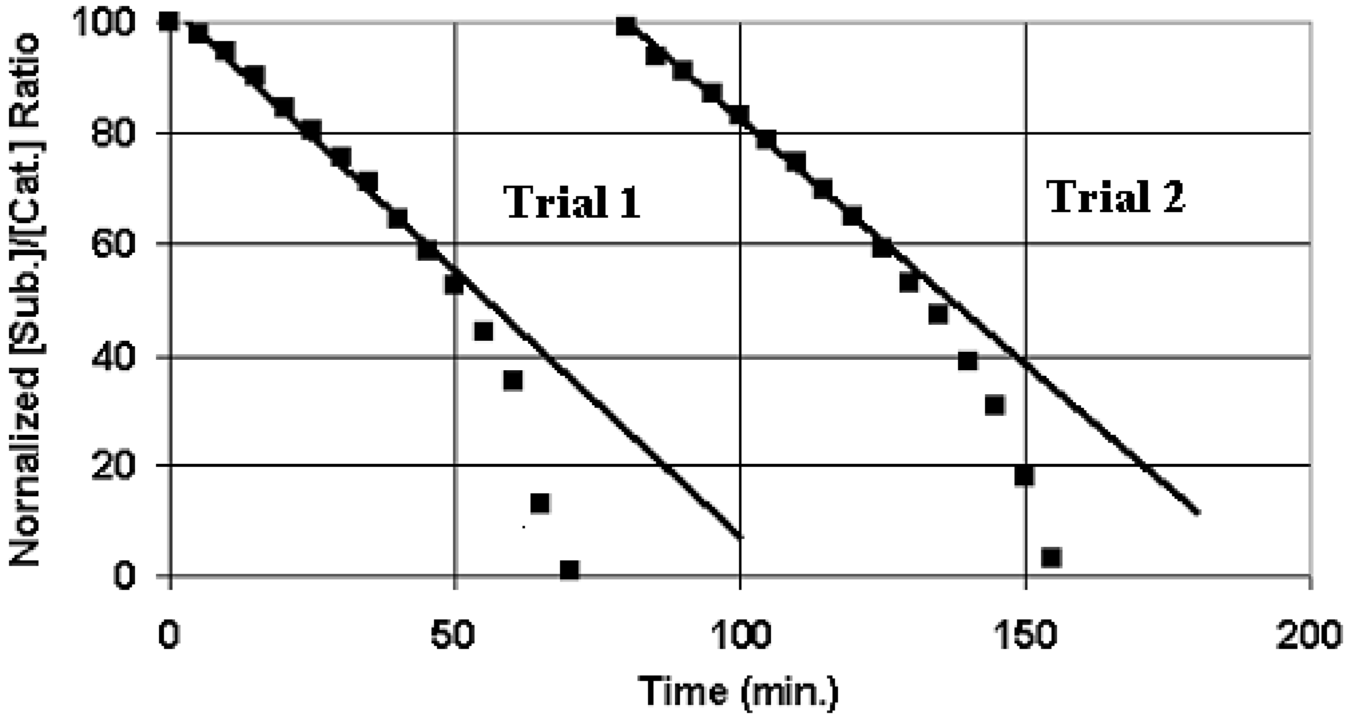


Diastereoselectivity depends on substrate conformation
Diastereoselectivity not sensitive to temperature

Ryu, J.-S.; Marks, T. J.; McDonald, F. E. *Org. Lett.* **2001**, *3*, 3091.
J. Org. Chem., **2004**, *69*, 1038.

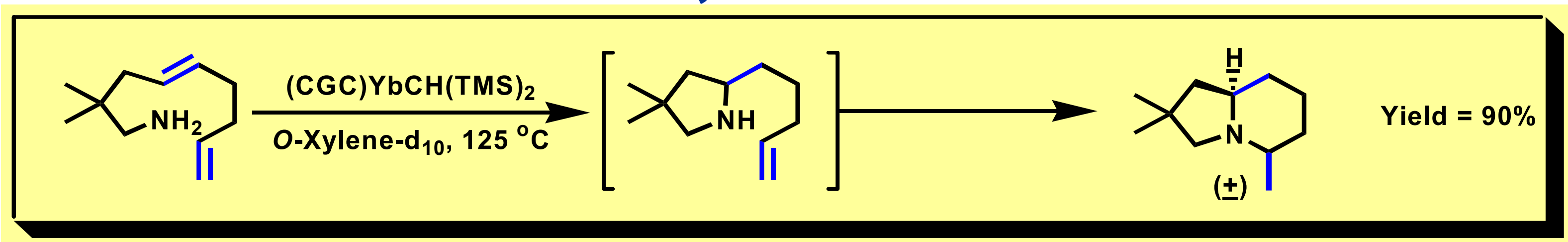
Impressive Catalyst Thermal Stability

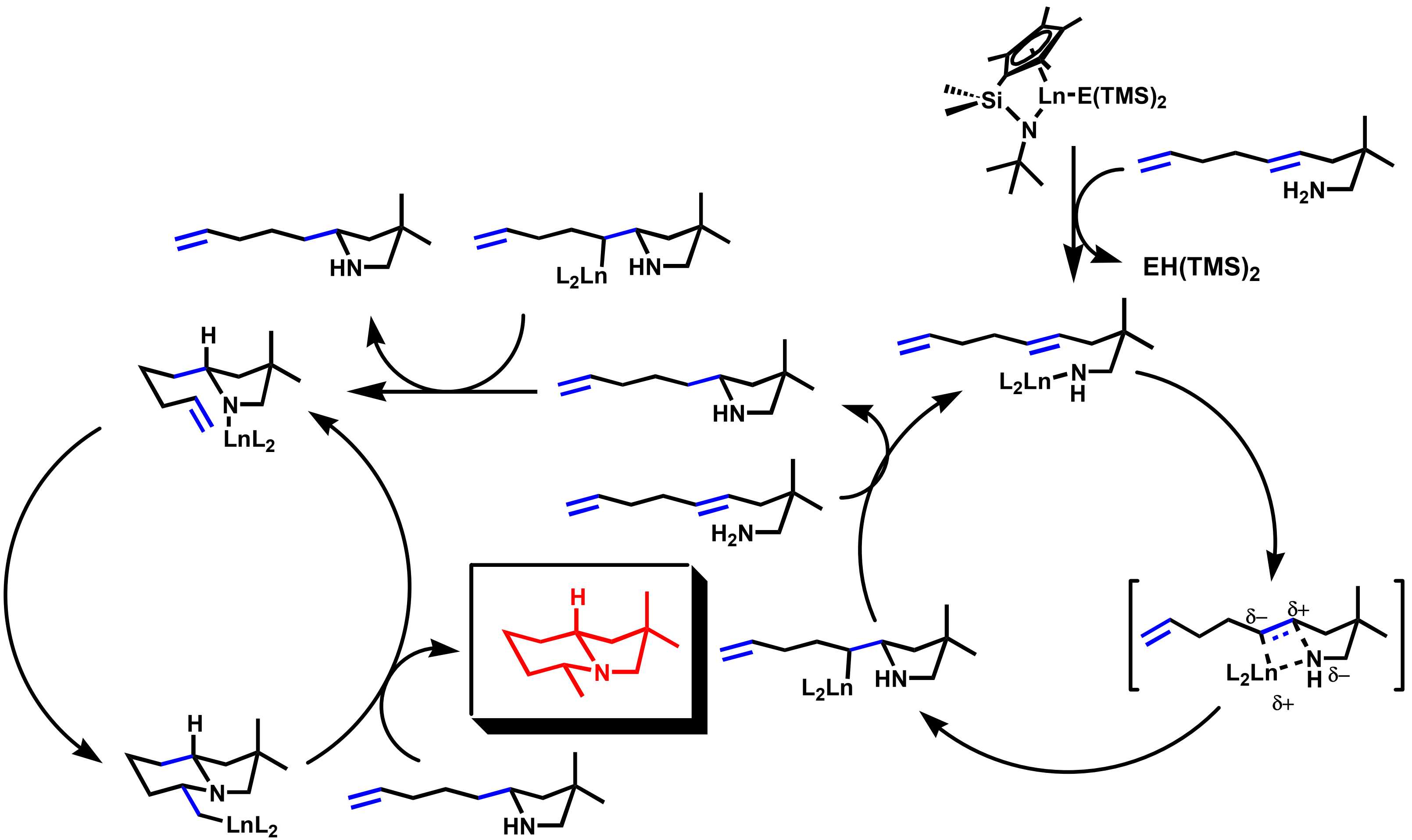




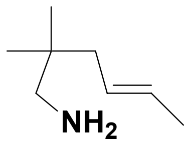
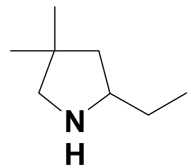
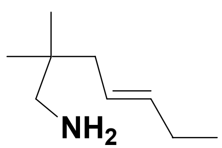
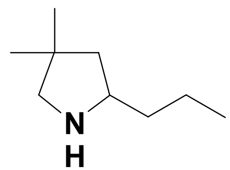
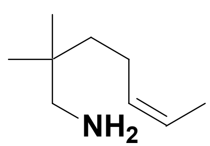
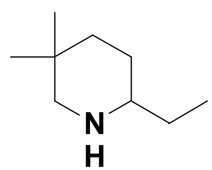
Add Second Substrate Aliquot ⇒ Negligible Catalyst Decomposition

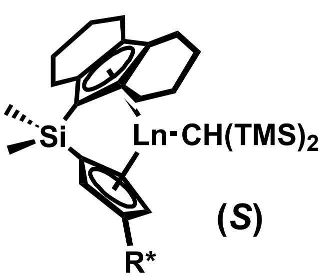
Organolanthanide-Catalyzed *Tandem Bicyclization* Amines Tethered to 1,2-Disubstituted Alkenes



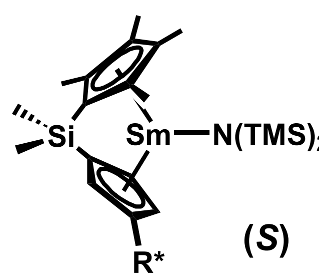


Enantioselectivity in Hydroamination of Internal Olefins

Entry	Substrates	Products	Precatalysts	N_t	ee
1.			$Me_2Si(OHF)Cp^*SmN(TMS)_2$	0.18 (80 °C)	23 %
			$Me_2Si(OHF)Cp^*YN(TMS)_2$	0.07 (100 °C)	26 %
			$Me_2SiCp''Cp^*SmN(TMS)_2$	0.26 (80 °C)	27 %
2.			$Me_2Si(OHF)Cp^*SmN(TMS)_2$	0.06 (80 °C)	21 %
			$Me_2Si(OHF)Cp^*YN(TMS)_2$	0.06 (100 °C)	28 %
			$Me_2SiCp''Cp^*SmN(TMS)_2$	0.15 (80 °C)	32 %
3.			$Me_2Si(OHF)Cp^*SmN(TMS)_2$	0.11 (80 °C)	16 %
			$Me_2Si(OHF)Cp^*YN(TMS)_2$	0.30 (100 °C)	57 %
			$Me_2Si(OHF)Cp^*YN(TMS)_2$	0.16 (80 °C)	65 %
			$Me_2Si(OHF)Cp^*YN(TMS)_2$	0.03 (60 °C)	68 %
			$Me_2SiCp''Cp^*SmN(TMS)_2$	0.16 (80 °C)	15 %

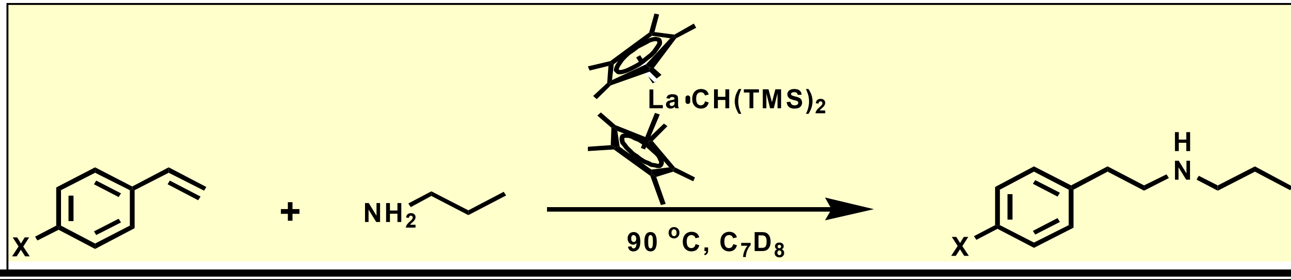


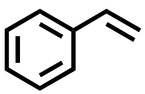
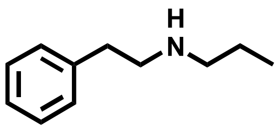
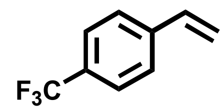
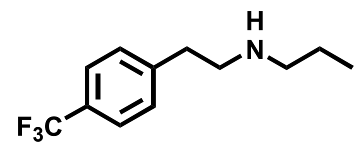
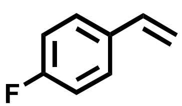
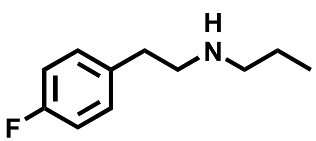
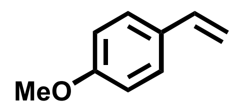
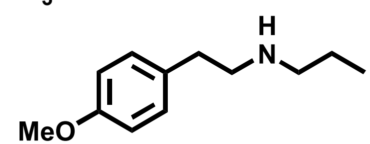
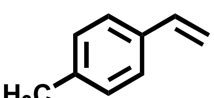
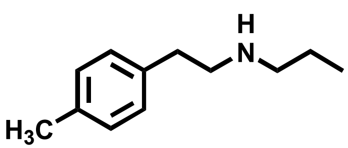
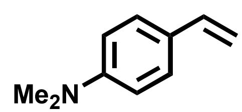
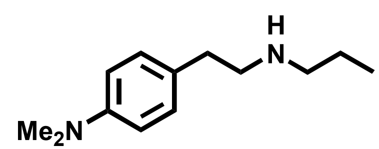
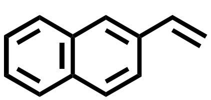
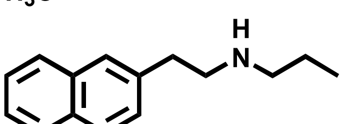
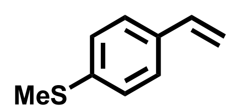
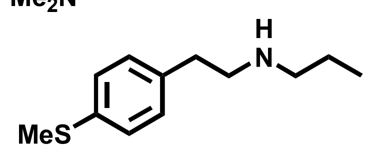
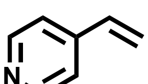
$Me_2Si(OHF)Cp^*LnCH(TMS)_2$
R * = (-)-Menthyl



$Me_2SiCp''Cp^*SmN(TMS)_2$

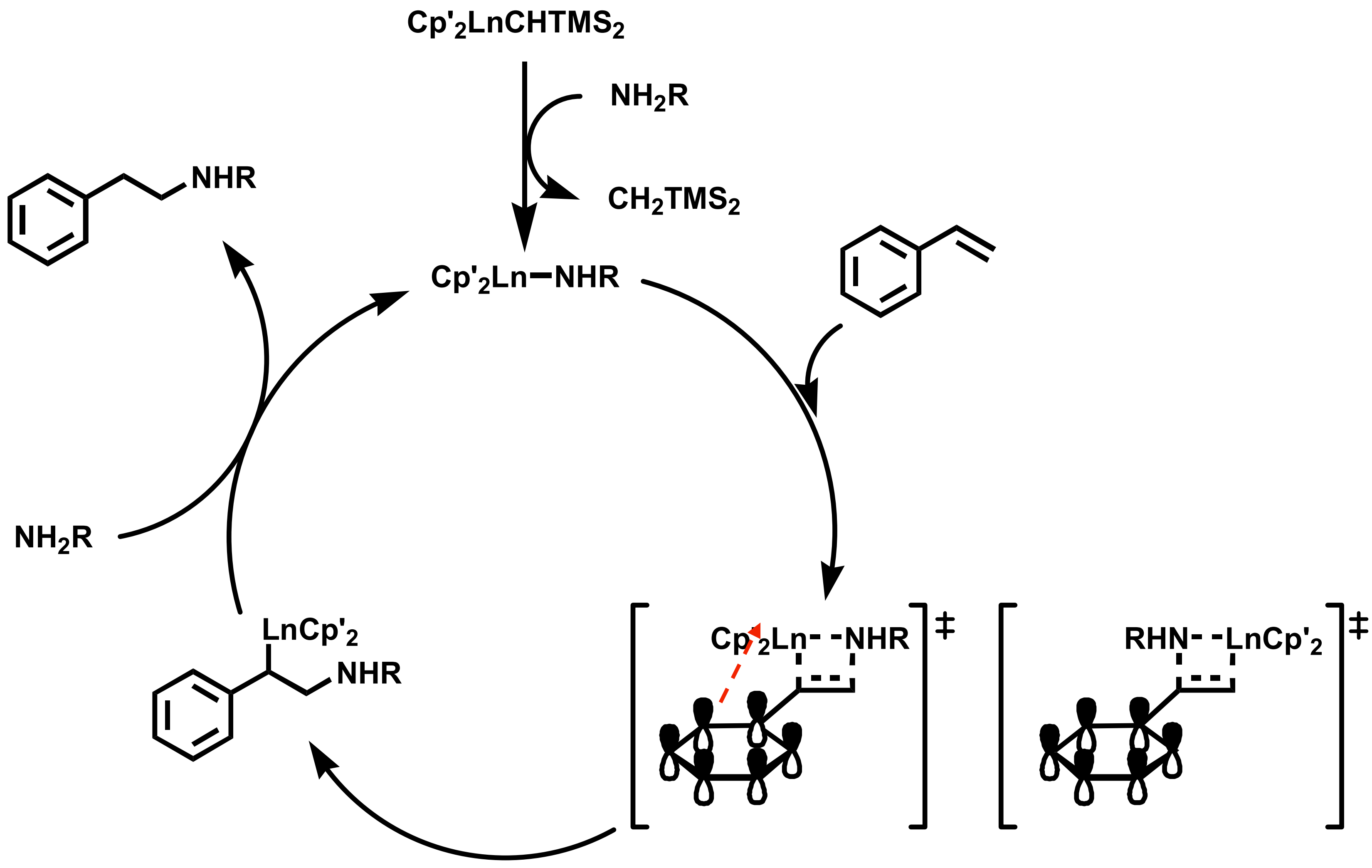
Intermolecular Hydroamination of Functionalized Styrenes



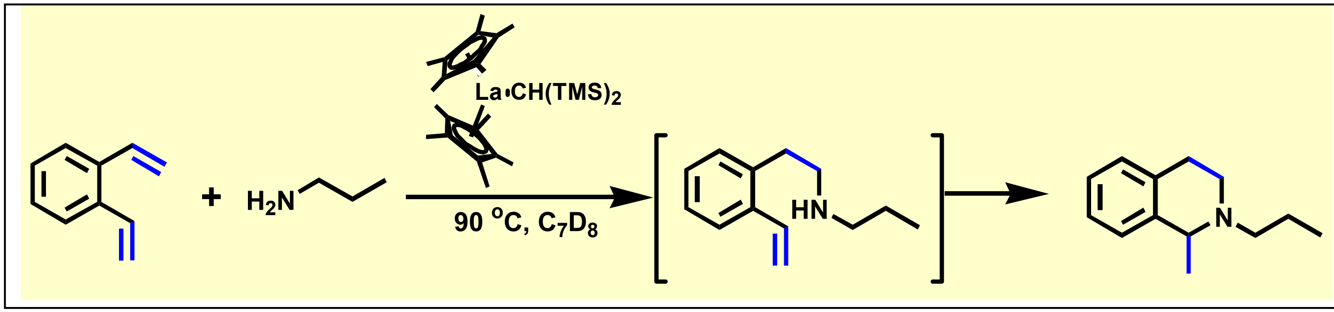
Styrene	Products	N_t (h^{-1})	Yield	Styrene	Products	N_t (h^{-1})	Yield
		2.0 (90 °C)	93%			3.4 (90 °C)	93%
		0.94 (120 °C)	94%			0.2 (90 °C)	89%
		0.15 (90 °C)	98%			0.05 (90 °C)	55%
		0.12 (90 °C)	98%			3.6 (90 °C)	85%
	—	No Reaction					

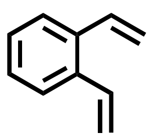
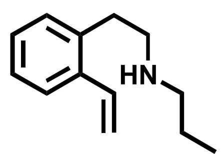
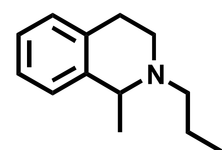
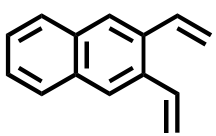
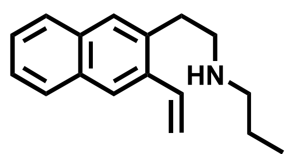
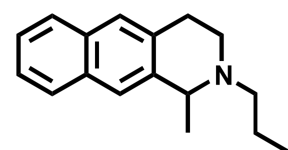
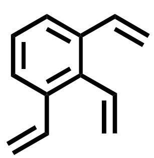
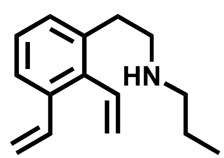
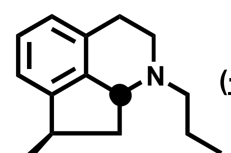
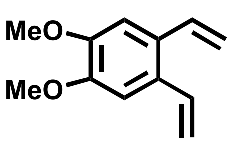
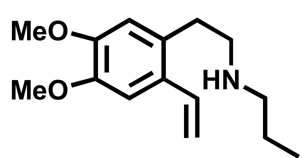
Anti-Markovnikov products, good functional group compatibility

Mechanism. Aryl-Directed Regioselectivity of Styrene Hydroamination

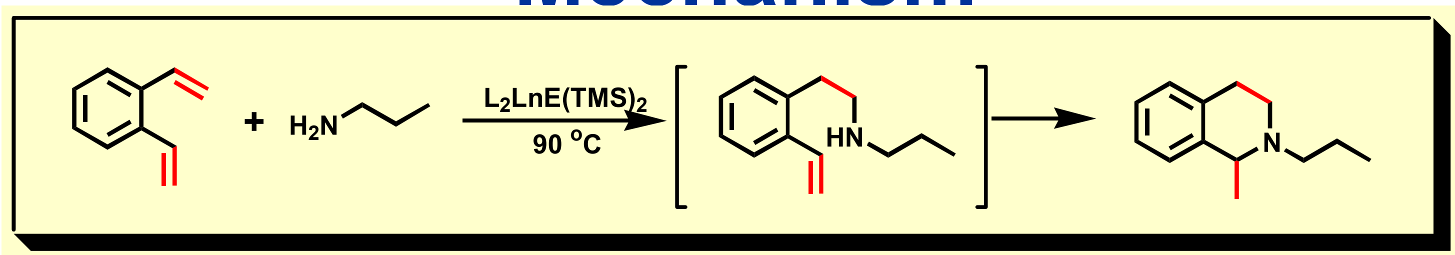


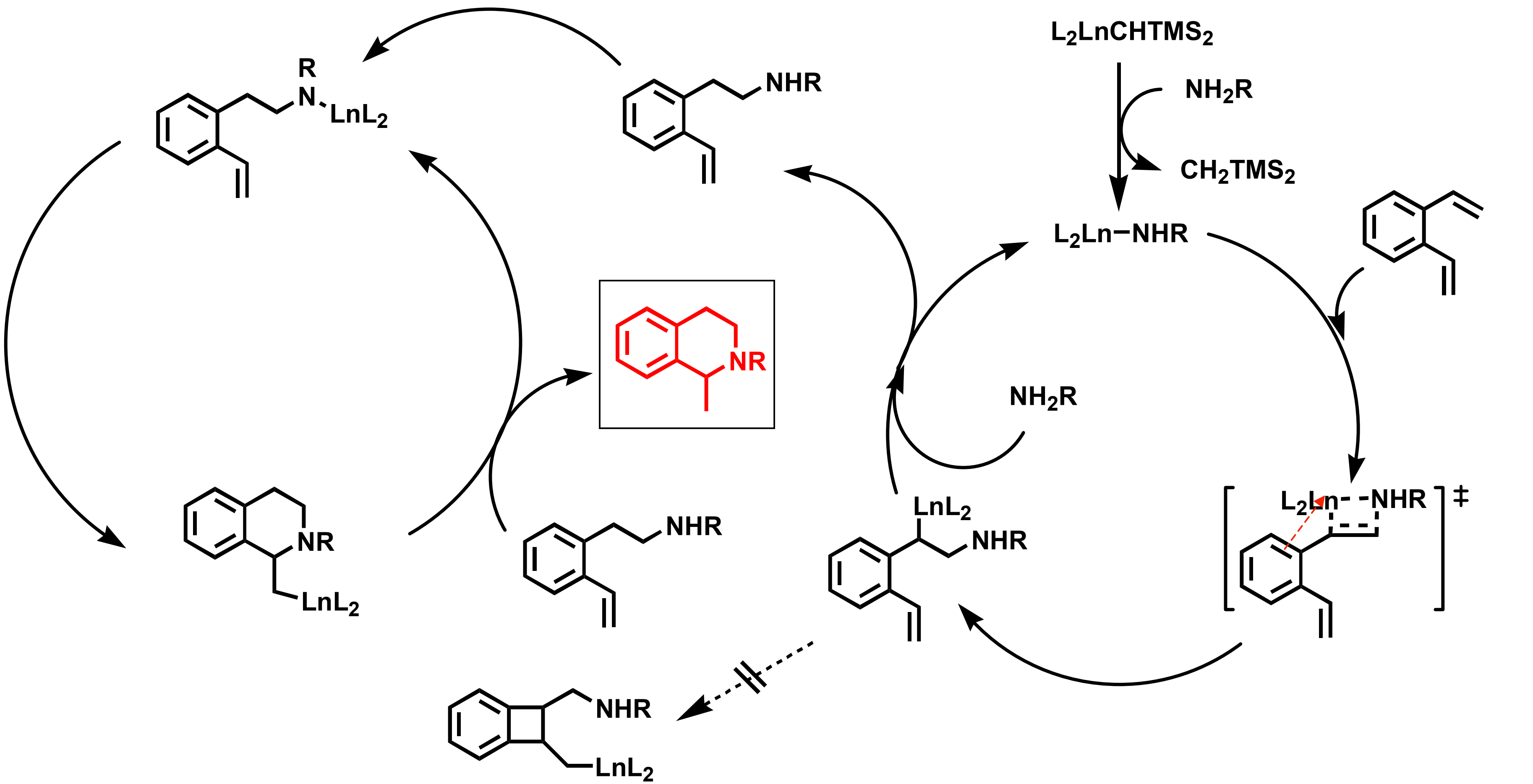
Intermolecular Hydroamination/Cyclization



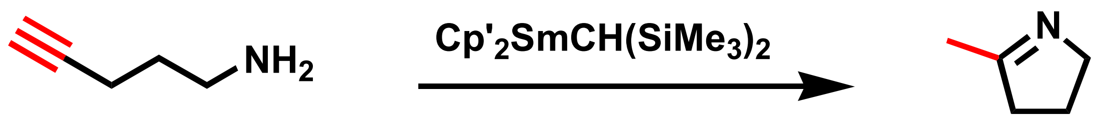
Substrates	Intermediates	N_t (h^{-1})	Products	N_t (h^{-1})	Yield
		2.1		1.1	97%
		9.6		6.0	98%
		6.0	 (±)	22.2	98%
		0.25	—		68%

Intermolecular Hydroamination/Cyclization Mechanism

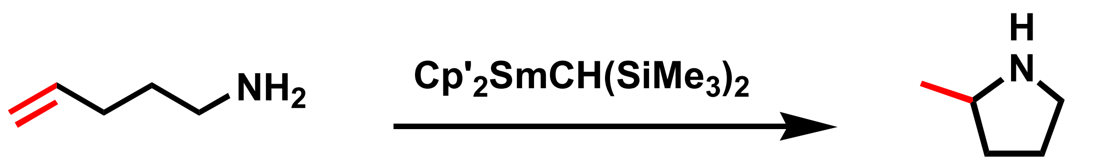




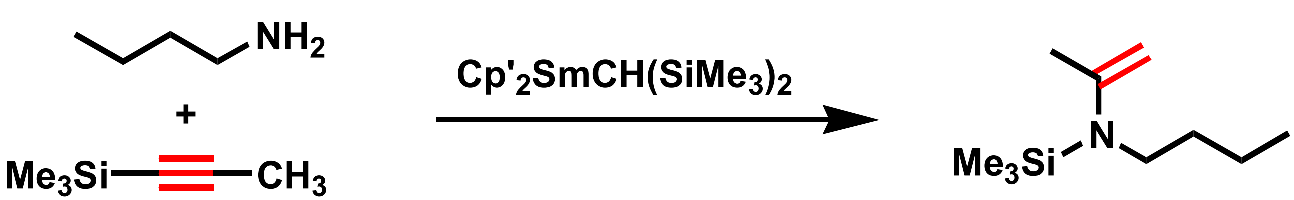
Intramolecular vs. Intermolecular. Comparative Activation Energies



$\Delta H^{\ddagger}$ = 10.7 (8) kcal/mol $\Delta S^{\ddagger}$ = -27.4 (1.0) eu



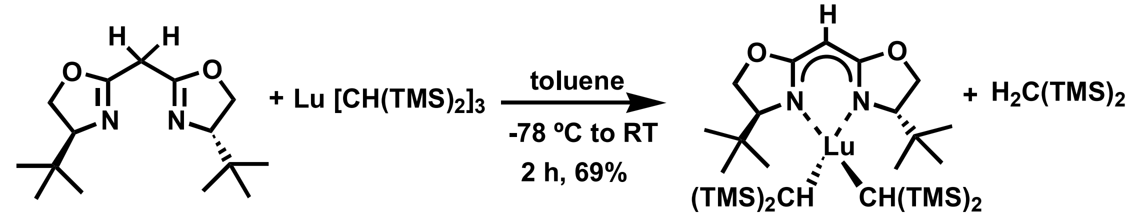
$\Delta H^{\ddagger}$ = 12.7 (1.4) kcal/mol $\Delta S^{\ddagger}$ = -27.0 (4.0) eu



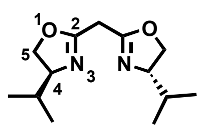
$\Delta H^{\ddagger}$ = 17.2 (1.1) kcal/mol $\Delta S^{\ddagger}$ = -25.9 (4.0) eu

Enantioselective Catalysts. Intrinsically Chiral BOX *C*$_2$-Symmetric Ligand Systems

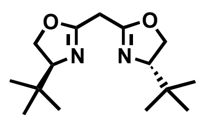
Synthesis (example)



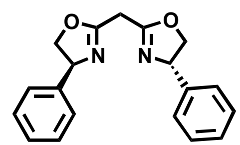
Ligand Library



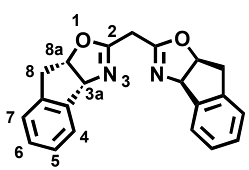
(4*S*)-^{i}PrBoxH (1)



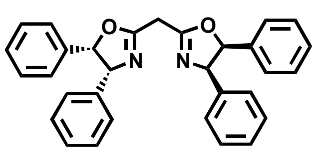
(4*S*)-^{t}BuBoxH (2)



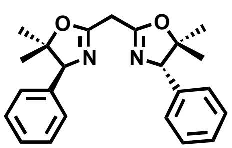
(4*S*)-PhBoxH (3)



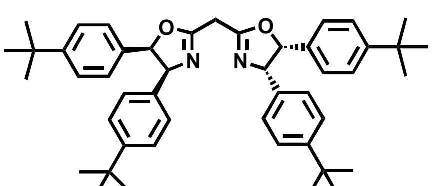
(3a*R*)-IndaBoxH (4)



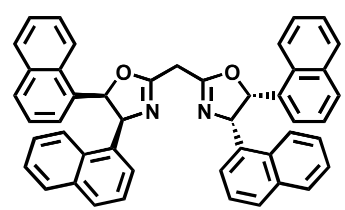
(4*R*,5*S*)-Ph$_2$BoxH (5)



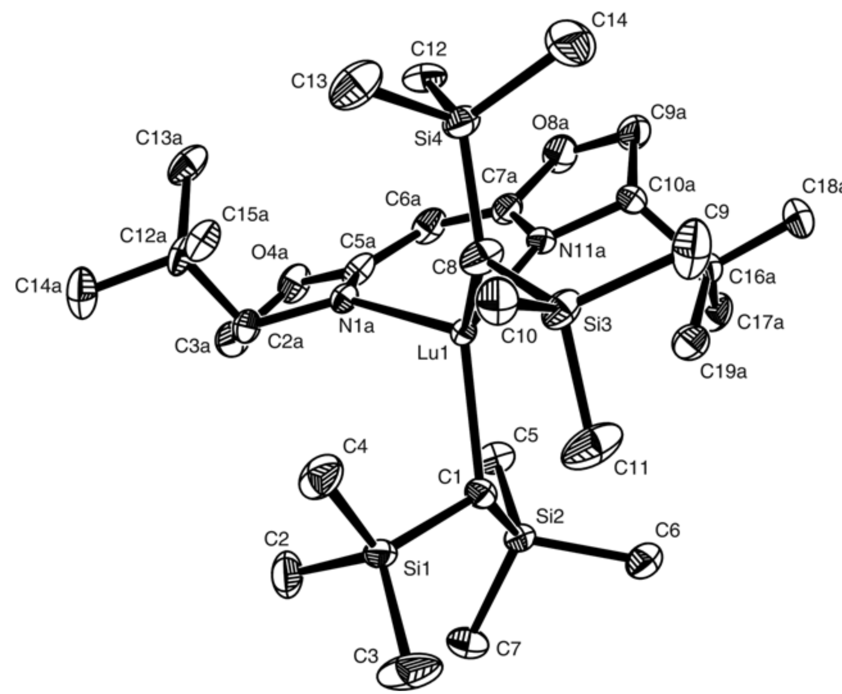
(4*S*)-Ph-5,5-Me$_2$BoxH (6)



(4*S*,5*R*)-(^{t}BuPh)$_2$BoxH (7)

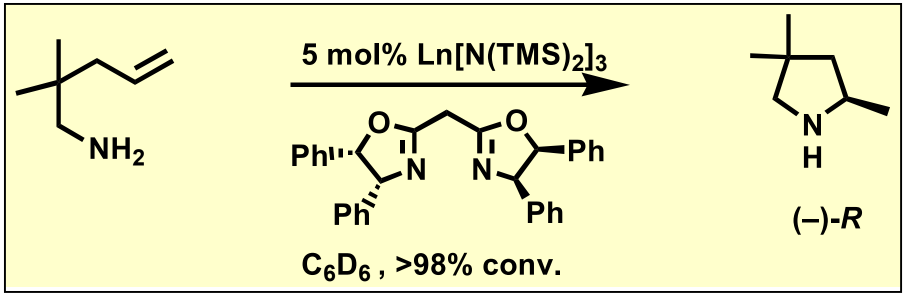


(4*S*,5*R*)-Naph$_2$BoxH (8)



Crystal Structure

Metal and Stoichiometry Effects on Enantioselectivity



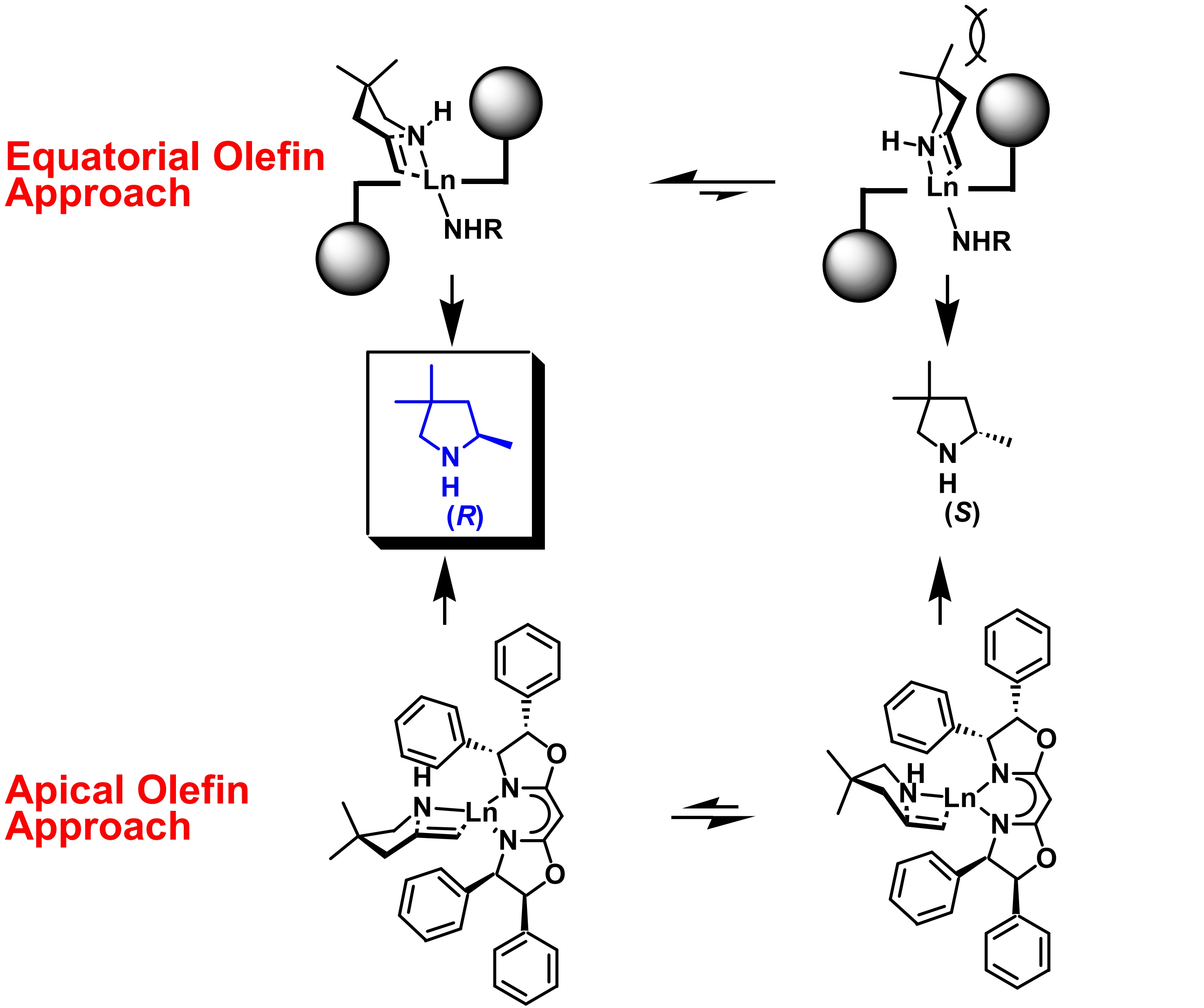
Entry	Ln	BoxH / Ln[N(TMS)$_2$]$_3$	Temp (°C)	N_t, (h^{-1})[a]	%ee[b] (config.)[c]
1	Sm	0	23	5.2[d]	Control exp
2	Sm	1.2	23	13	55 (R)
3	Sm	2.3	60	-	60 (R)
4	Nd	1.2	23	~10	61 (R)
5	La	0	23	7.7[d]	Control exp
6	La	1.2	23	25	67 (R)
7	La	2.3	23	10	63 (R)

Note uniformity of stereoinduction

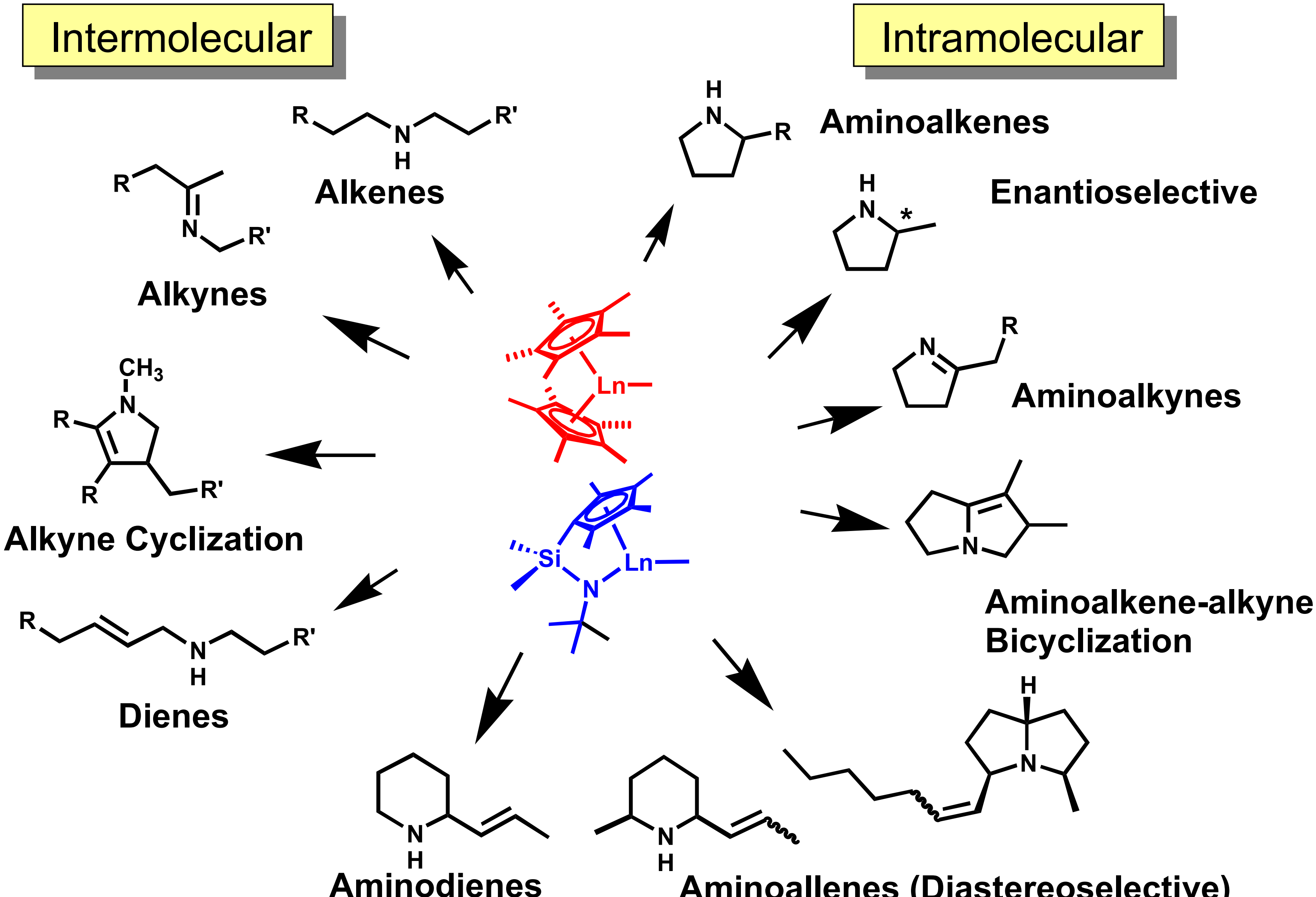
With greater ligand stereoenforcement: 80-85%ee

Many other examples

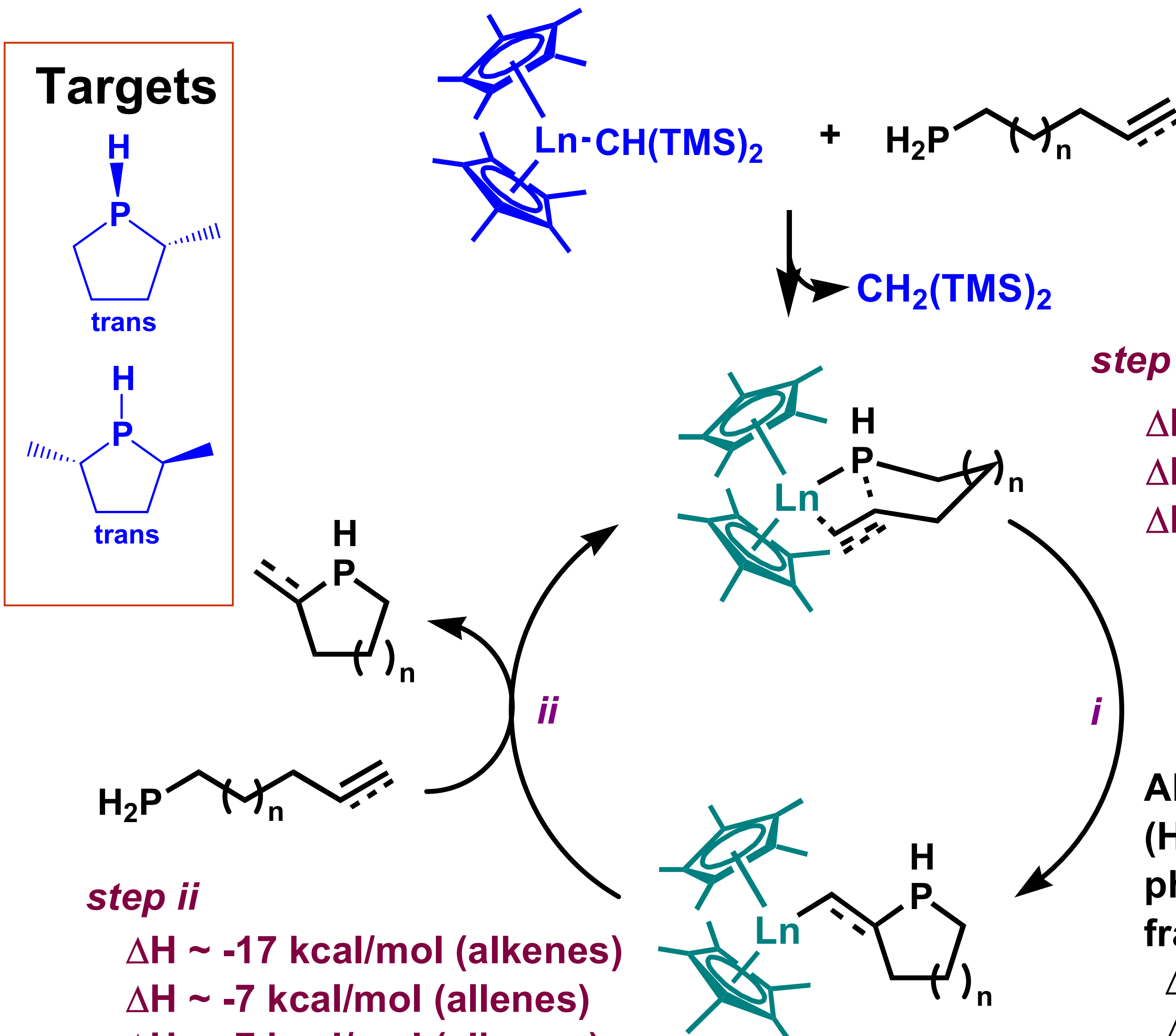
Working Model for BOX Enantioselection



Summary. Scope of Organolanthanide-Catalyzed Hydroamination



Is Hydrophosphination Analogous? Useful?



step i

ΔH ~ +2 kcal/mol (alkenes)
ΔH ~ -30 kcal/mol (allenes)
ΔH ~ -33 kcal/mol (alkynes)

AM-1 calculations:
(Heat of formation using methyl phosphine and carbon fragment)

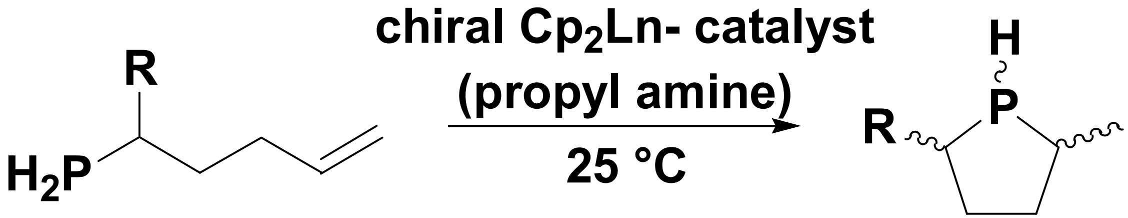
ΔH = -15 kcal/mol (alkenes)
ΔH = -38 kcal/mol (alkynes)
ΔH = -37 kcal/mol (allenes)

step ii

ΔH ~ -17 kcal/mol (alkenes)
ΔH ~ -7 kcal/mol (allenes)
ΔH ~ -7 kcal/mol (alkynes)

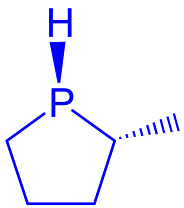
DFT: Step *ii* is Sometimes Turnover-Limiting

Hydrophosphination Diastereoselectivity

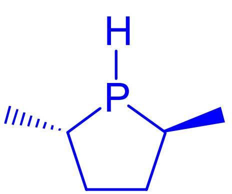


13: R = H
15: R = CH_3

Entry	Sub.	OHF Cat.	cis + trans	% de (Temp, °C)
1	13	Sm	81	89 (25)
2	13	Y	75	78 (25)
3	13	Lu	78	83 (25)
4	15	Sm	82	96 (0)
5	15	Sm	86	91 (25)
6	15	Y	68	77 (25)
7	15	Lu	72	90 (25)

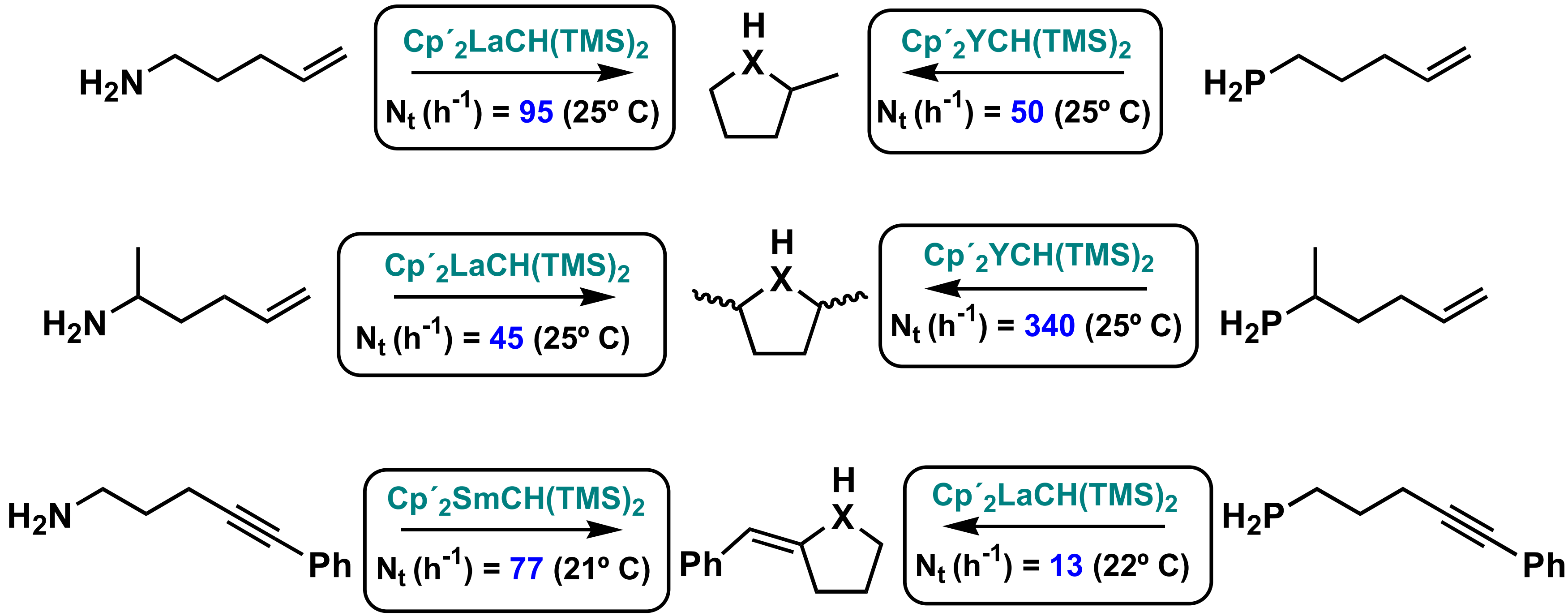


trans



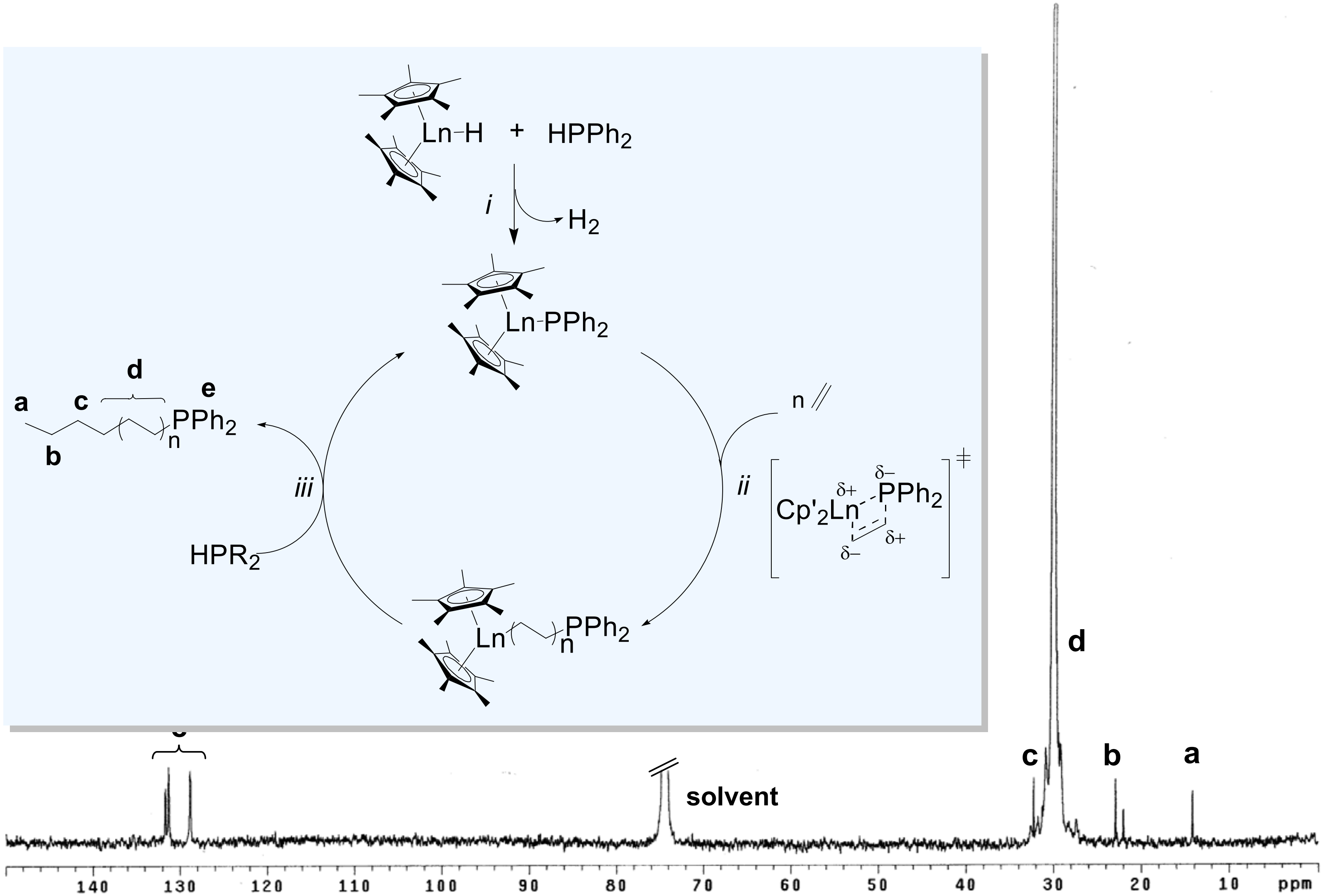
trans

Hydroamination vs Hydrophosphination



- Hydrophosphination generates analogous products
- Trends with catalyst variation differ, but overall process is similar
- DFT: Turnover-limiting steps insertion (N), protonolysis (P)

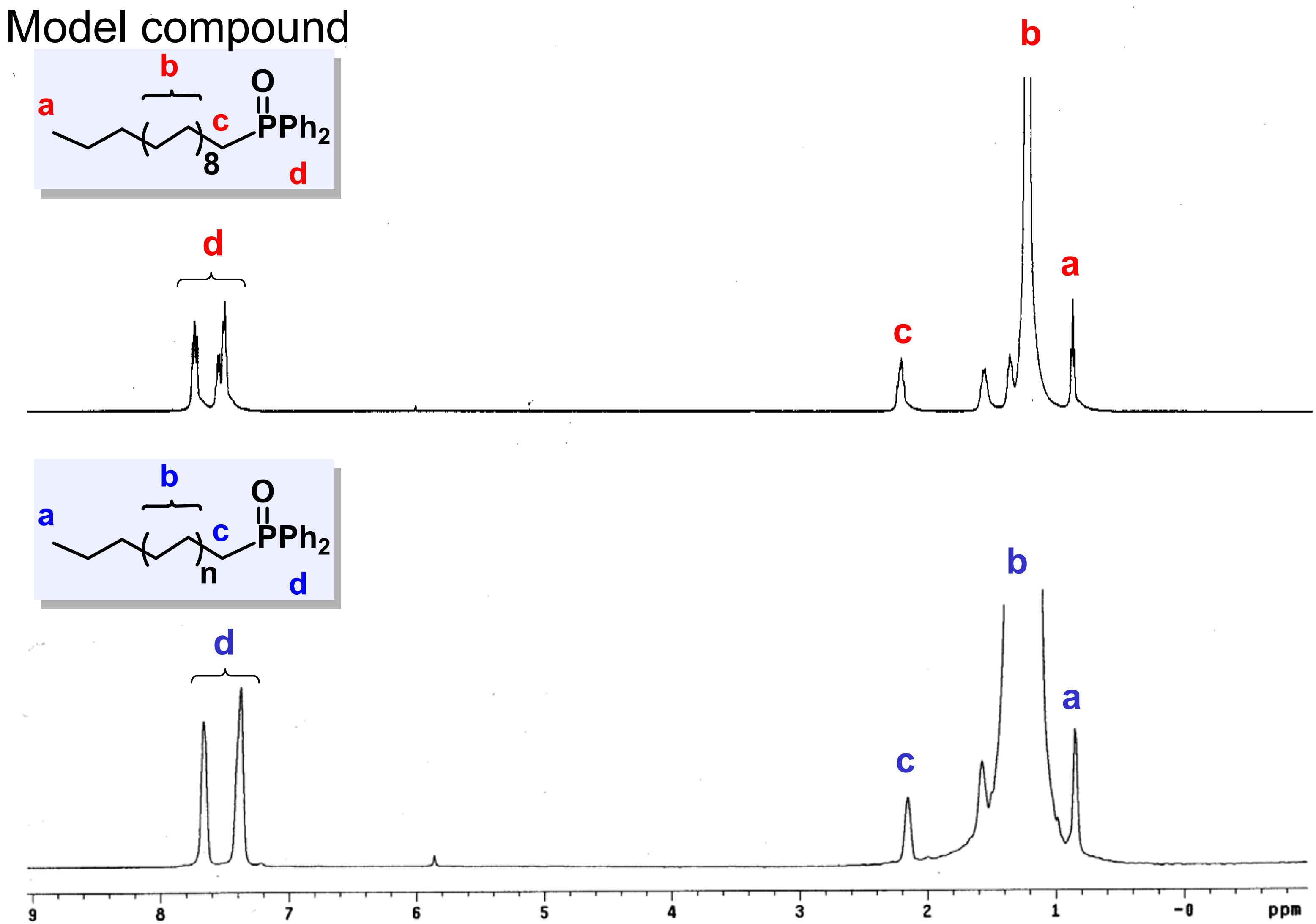
Could We Couple Hydrophosphination + Olefin Polymerization? Ethylene Polymerizationin Presence of Ph_2PH. ^{13}*C NMR*



^{13}C NMR of Polymer Sample at 125°C

A.M. Kawaoka, T.J. Marks, *J. Am. Chem. Soc.*, in press

Ethylene Polymerization in Presence of Ph_2PH.
^1H NMR



Phosphine-Capped Polyethylene!

CONCLUSIONS

ANALYSIS OF METAL-LIGAND BONDING ENERGETICS AFFORDS

- Better Understanding of Metal-Ligand Bonding
- Better Understanding of Known Reaction Patterns
- Aid in Inventing New Transformations

f-ELEMENT HOMOGENEOUS CATALYSTS OFFER

- Novel Reaction Patterns
- High Turnover Frequencies and Selectivities
- Tunable Redox and Steric Characteristics

CATALYSIS IS A SOURCE OF NEW MATERIALS

- New Polymers

ACKNOWLEDGEMENTS

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Kwangmo Koo
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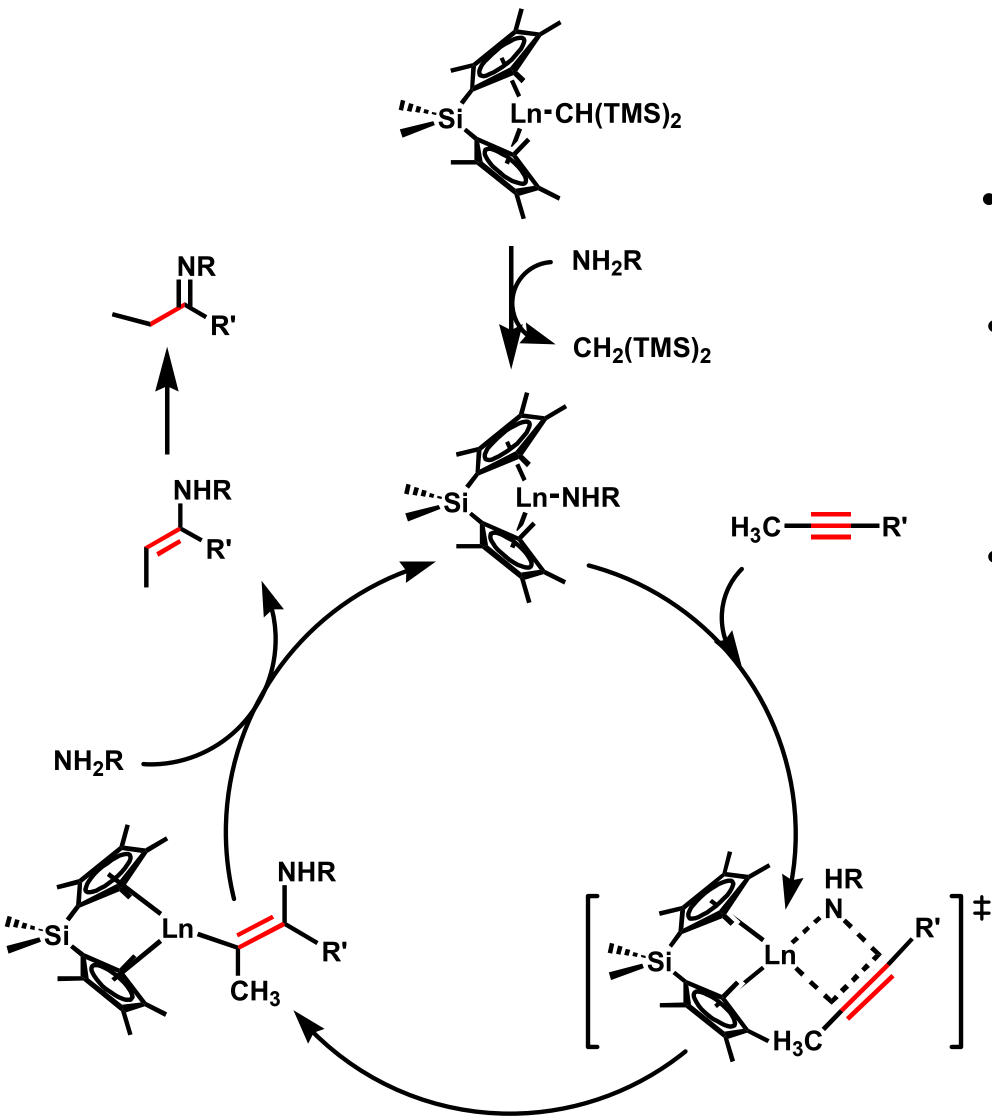
Jaesang Ryu
Charlotte Stern
Michael Salata
Shun Tian
Frank McDonald

NSF

Dow Corning

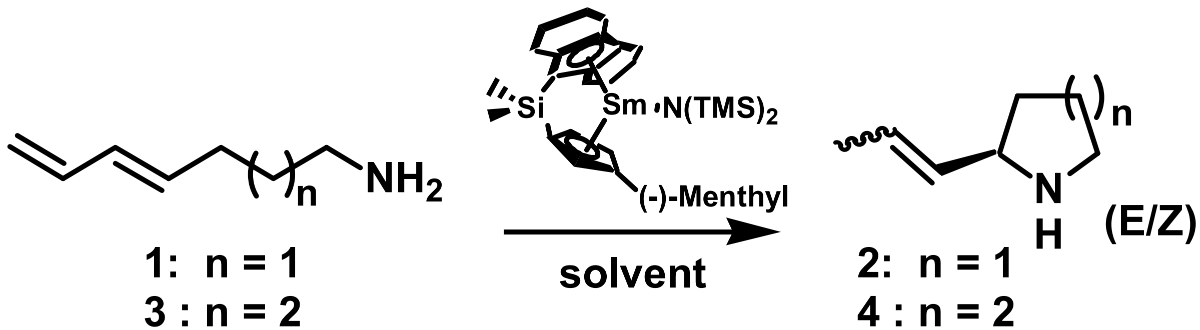
Intermolecular Hydroamination



- $\upsilon = k\ [\text{Amine}]^0[\text{Alkyne}]^1[\text{Cat}]^1$
- **Slower than Intramolecular hydroamination**
  Alkyne (~1/1400), Alkene(~1/350)
- **High kinetic barrier**
  e.g. $\Delta H^{\ddagger}$ = 17.2 (1.1) kcal/mol
  $\Delta S^{\ddagger}$ = -25.9 (4.0) eu
- **Importance:**
  Facile approach to complex alkaloid skeletons from commercially available substrates

Li, Y.; Marks, T. J. *Organometallics*, **1996**, *15*, 3770-3772

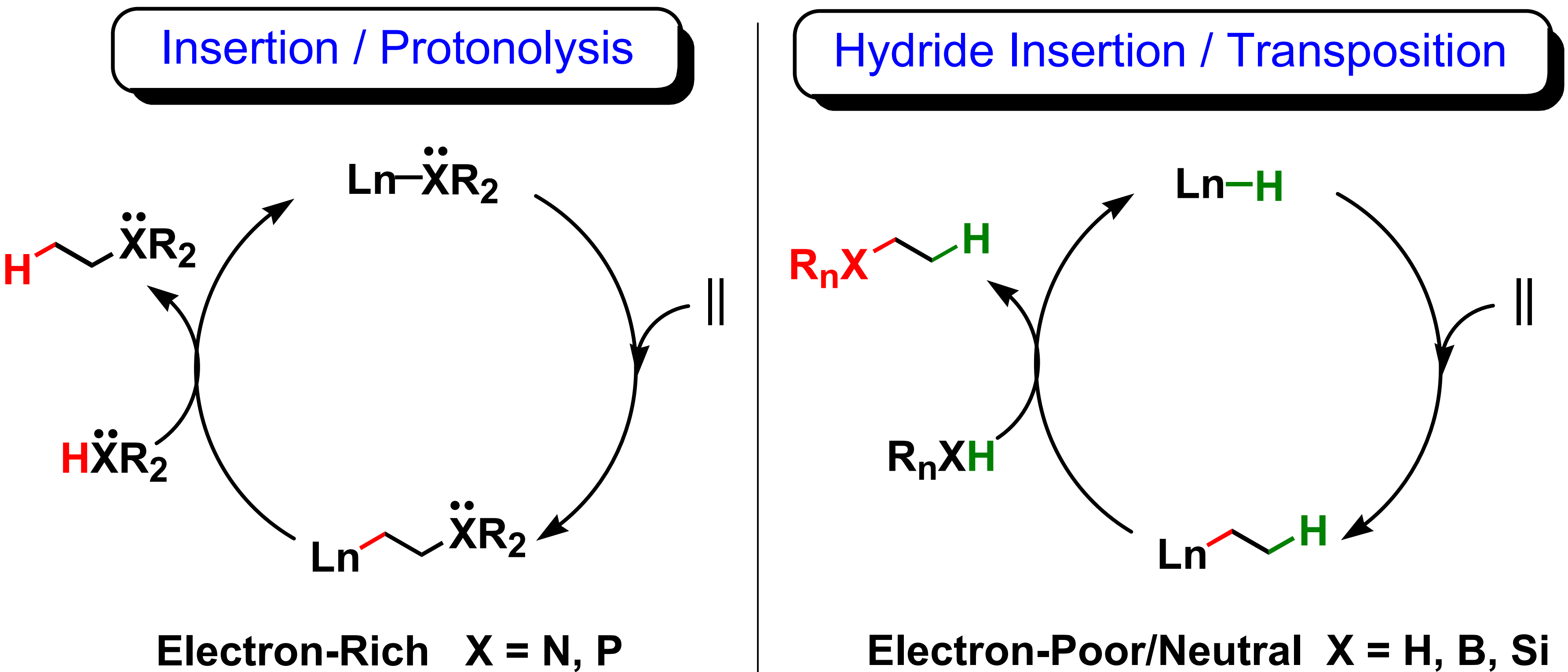
Enantioselective Cyclization of Aminodienes



entry	substrate	product(ratio)	solvent	temp (°C)	% ee[b] (config.)[c]
1	1	2a/b (93: 7)	C_6D_6	25	23
2	3	4a/b (97: 3)	C_6D_6	25	63 (R)
3	3	4a/b (96: 4)	C_6D_{12}	25	64 (R)
4	3	4a/b (95: 5)	C_6D_{12}	0	69 (R)

[a]Conditions: 7 mol% (entries 1, 2, 3) or 20 mol% (entry 4) (OHF*)SmN(TMS)$_2$ catalyst, ~ 0.6 ml solvent, [b]For the major isomer, determined by chiral HPLC analysis. Measured ee's vary only weakly with conversion. [c]Determined by optical rotation of HCl salt of hydrogenated product.

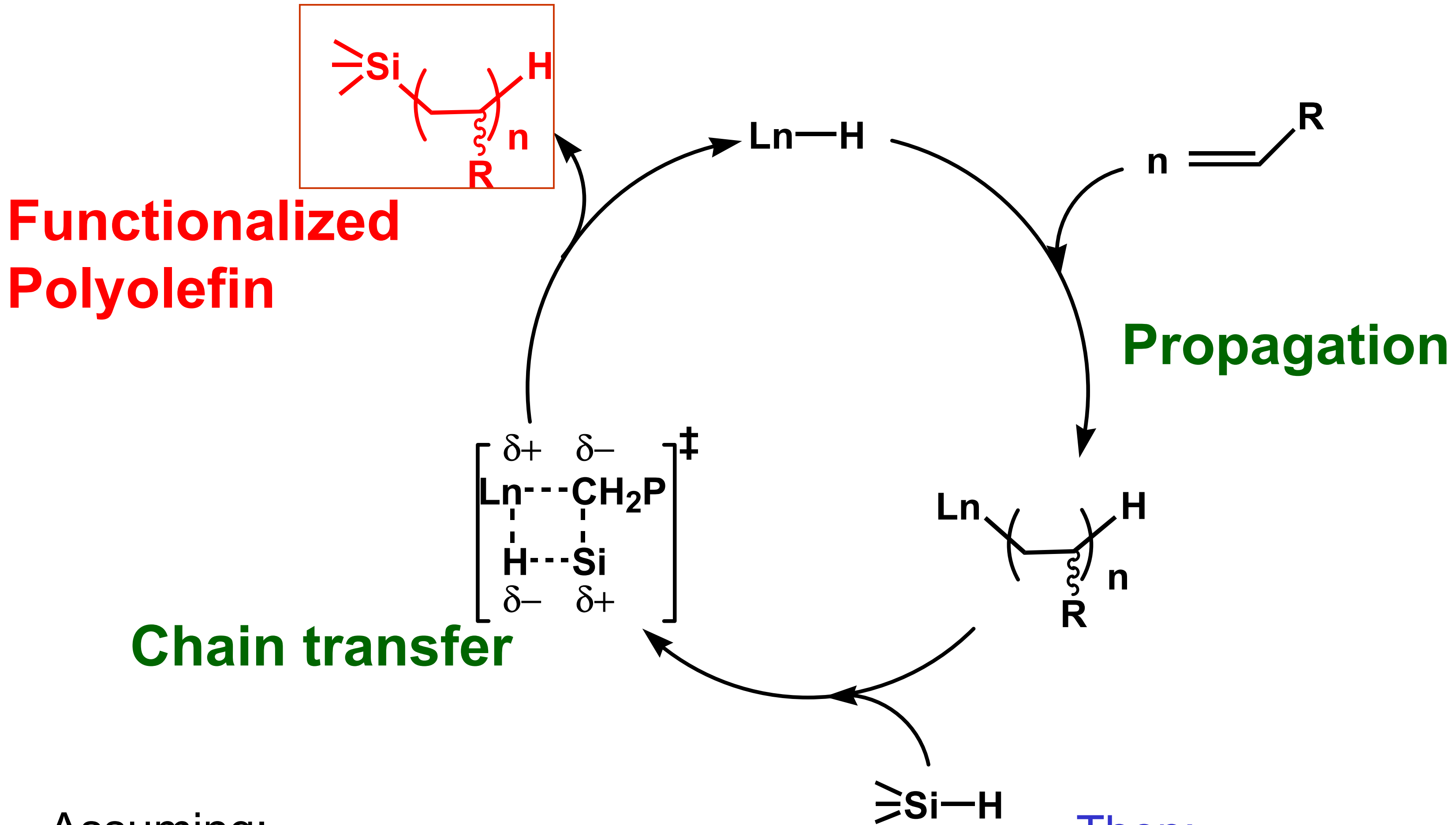
Two Catalytic Pathways for Organolanthanide-Mediated C-Heteroatom Bond Formation



Two Distinct Manifolds! What is Their Scope?

Can these Reactions Introduce Polar Heteroatoms in Polymers?

Polyolefin Functionalization with Silane Transfer Agents. Hydride Insertion / Transposition



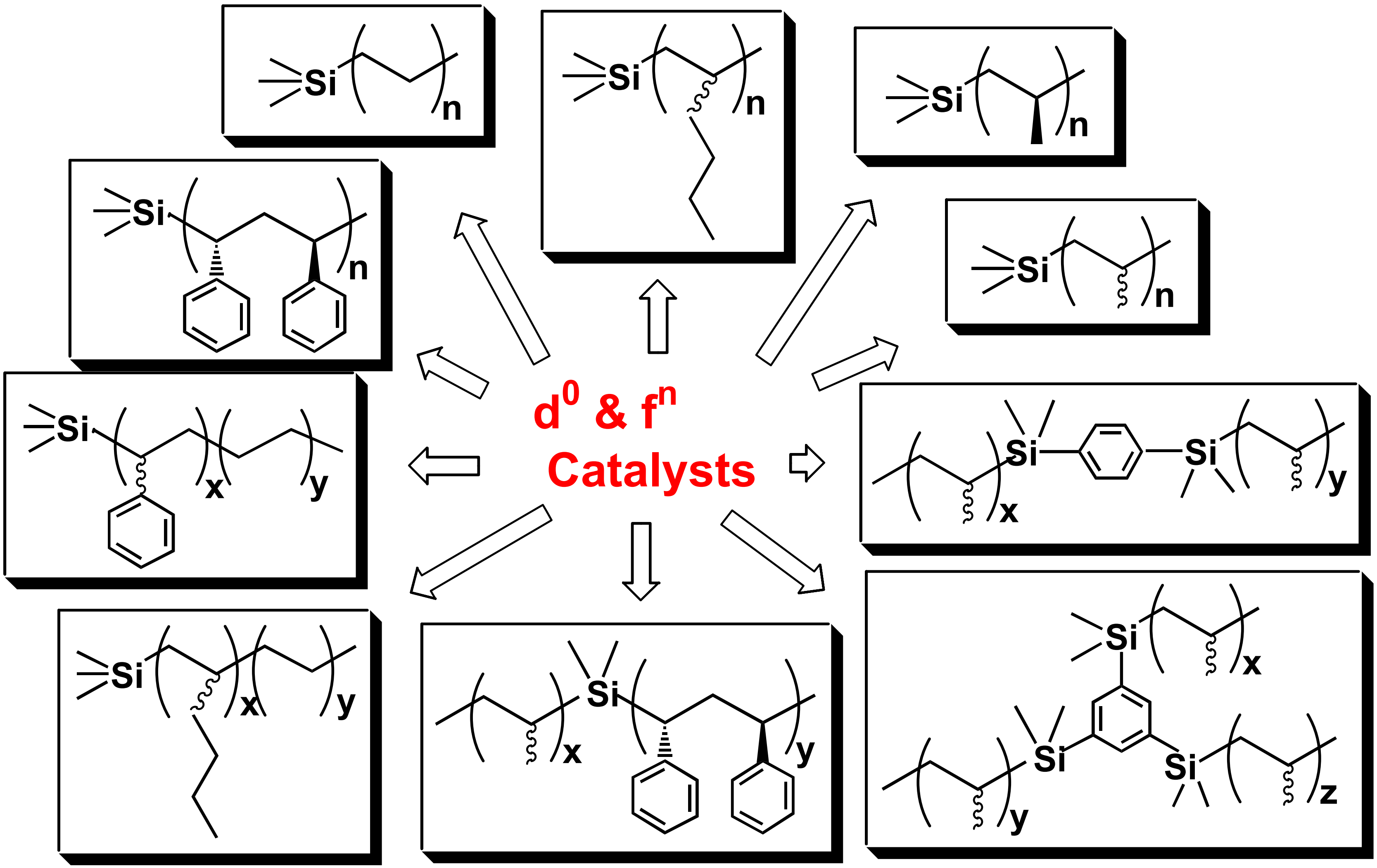
Assuming:

1. Constant [cat], [=], $[H_3SiPh]$
2. Rapid reinitiation after chain transfer
3. One dominant chain transfer mechanism

Then:

$$\overline{P_n} = \frac{k_p[=]}{k_{si}[H_3SiPh]}$$

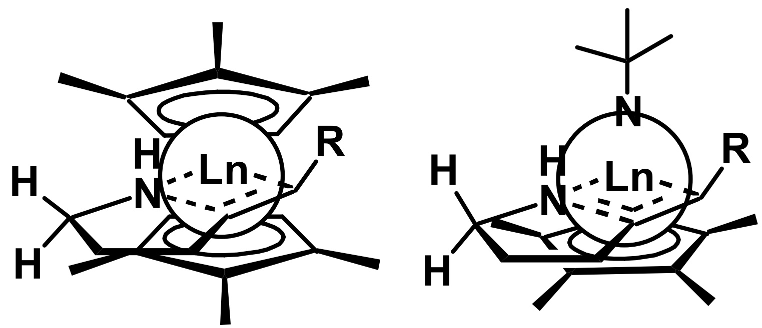
Scope of Silicon-Modified d^0/f^n-Mediated Polymerization Catalysis



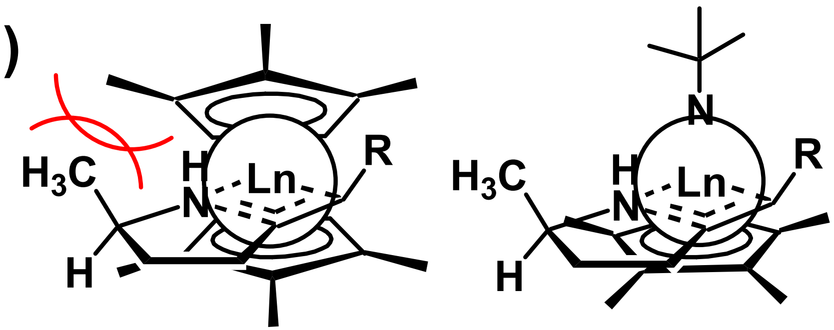
Also Works for Boranes

Hydroamination of α-Substituted Olefinic Substrates

(A)



(B)



<u>Sterically less hindered substrates</u>

- **$Cp'_2LaCH(TMS)_2$ having a large metal ionic radius and $(CGC)LnE(TMS)_2$ generally effective.**

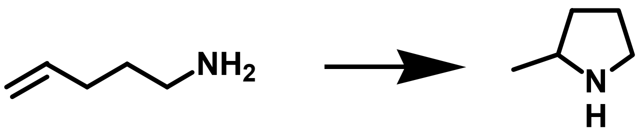
<u>Sterically demanding substrates</u>

- **$(CGC)LnE(TMS)_2$ which give more open coordination environments the most effective**

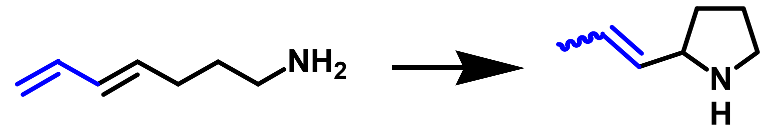
More open ancillary ligation reduces the steric congestion in transition state

Ryu, J.-S.; Marks, T. J.; McDonald, F. E. *Org. Lett*. **2001**, *3*, 3091.
J. Org. Chem., **2004**, *69*, 1038.

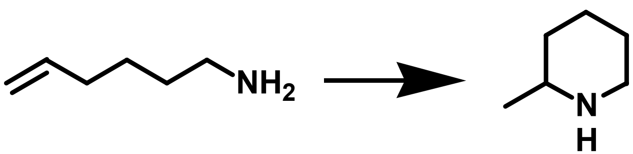
Enhanced Reaction Rates with Diene Units vs. Terminal Alkenes



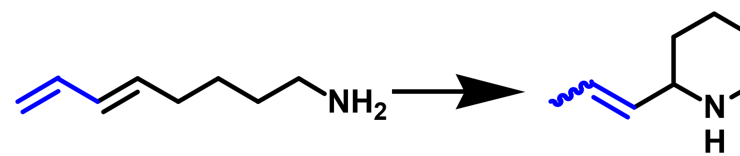
Pre-Catalyst	$N_t\ h^{-1}$ (°C)
$Cp'_2LaCH(TMS)_2$	13 (25)[a]
$Me_2Si(OHF)(Cp^*)SmN(TMS)_2$	5.5 (25)



Pre-Catalyst	$N_t\ h^{-1}$ (°C)
$Cp'_2LaCH(TMS)_2$	40 (25)
$Me_2Si(OHF)(Cp^*)SmN(TMS)_2$	12 (25)

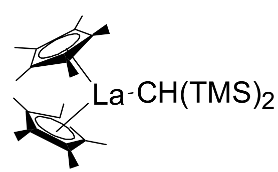


Pre-Catalyst	$N_t\ h^{-1}$ (°C)
$Cp'_2LaCH(TMS)_2$	5 (60)[a]

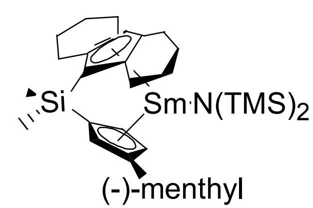


Pre-Catalyst	$N_t\ h^{-1}$ (°C)
$Cp'_2LaCH(TMS)_2$	3.0 (25)

[a] From the literature, Gagné, M. R.; Stern, C. L.; Marks, T. J. *J. Am.Chem. Soc.* **1992**, *114*, 275-294



$Cp'_2LaCH(TMS)_2$



$Me_2Si(OHF)(Cp^*)SmN(TMS)_2$

WHAT DRIVES ORGANOMETALLIC REACTIONS?

Understanding Bond Energies

M—R $\longrightarrow$ M• •R

$$D(M\text{—}R) = \Delta H^0_f(\bullet R) + \Delta H^0_f(M\bullet) - \Delta H^0_f(M\text{—}R)$$

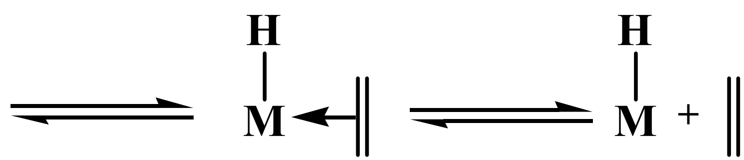
Consider the Reaction:

M—R + A—B $\longrightarrow$ M—A + R—B

$$\Delta H = D(M\text{—}R) + D(A\text{—}B) - D(M\text{—}A) - D(R\text{—}B)$$

Example:

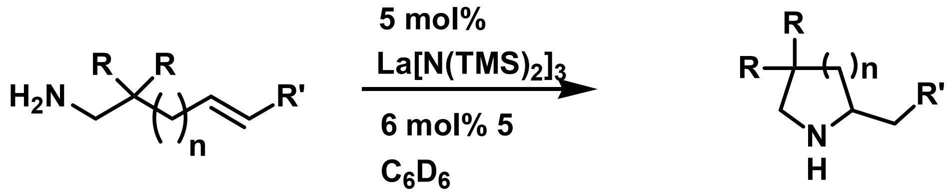
$M\text{—}CH_2CH_3$

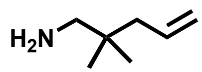
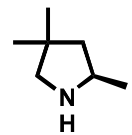
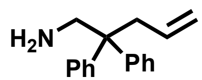
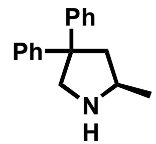
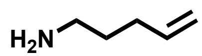
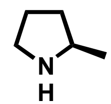
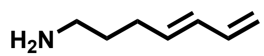
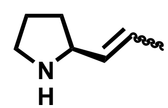
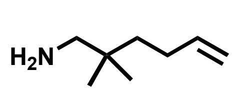
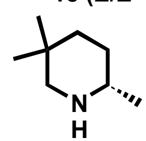
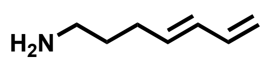
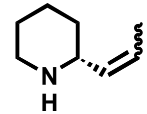
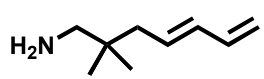
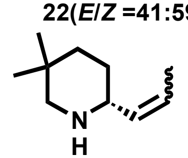


The crucial parameters are:

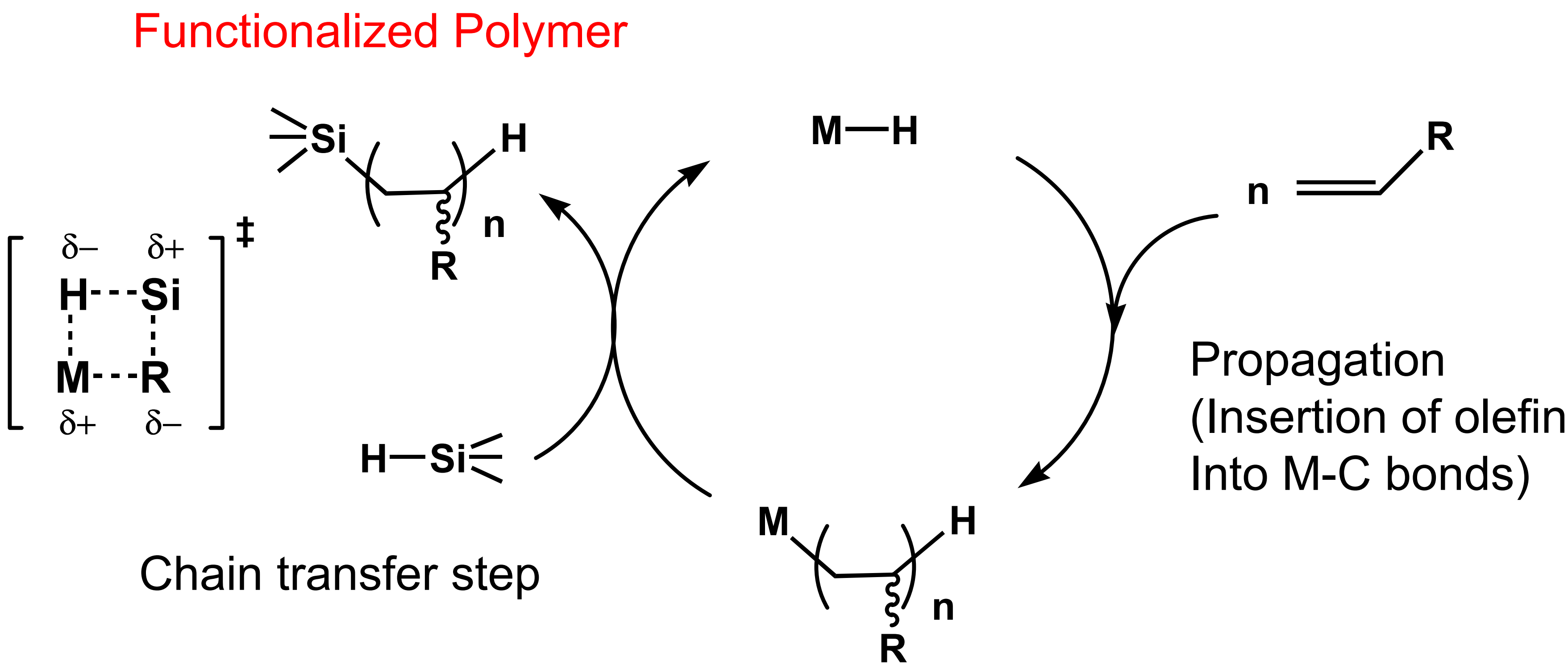
$D(M\text{—}C)$ **and** $D(M\text{-}H)$

Scope of BOX-Mediated Enantioselective Hydroamination



Entry	Subtsrate	Product[a]	N_t, (h^{-1})	Temp (ºC)	%ee[b] (config)[c]
1.			25	23	67 (*R*)
2.			660[d]	23	34 (*R*)
3.			0.09	23	40 (*R*)
4.		 18 (*E*/*Z* =63:37)	3.0	23	17 (*S*)
5.			4.0	60	56 (*S*)
6.		 22(*E*/*Z* =41:59)	0.6	60	54 (*R*)
7.		 24 (*E*/*Z*/allyl = 39:57:4)	1.4	23	45 (*R*)

Demonstrated Polymer MW Control by Silane Transfer Agents



Assuming:

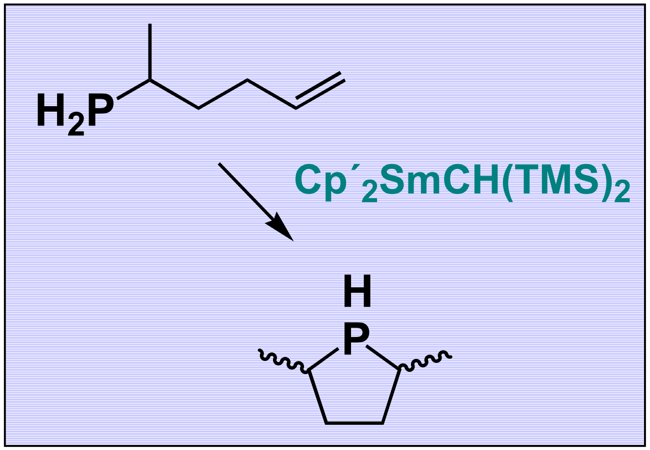
1. Constant [cat], [=], [H_3SiPh]
2. Rapid reinitiation after chain transfer
3. One dominant chain transfer mechanism

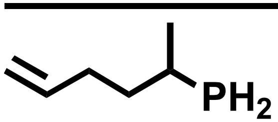
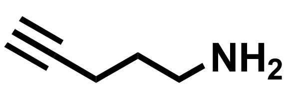
Then:

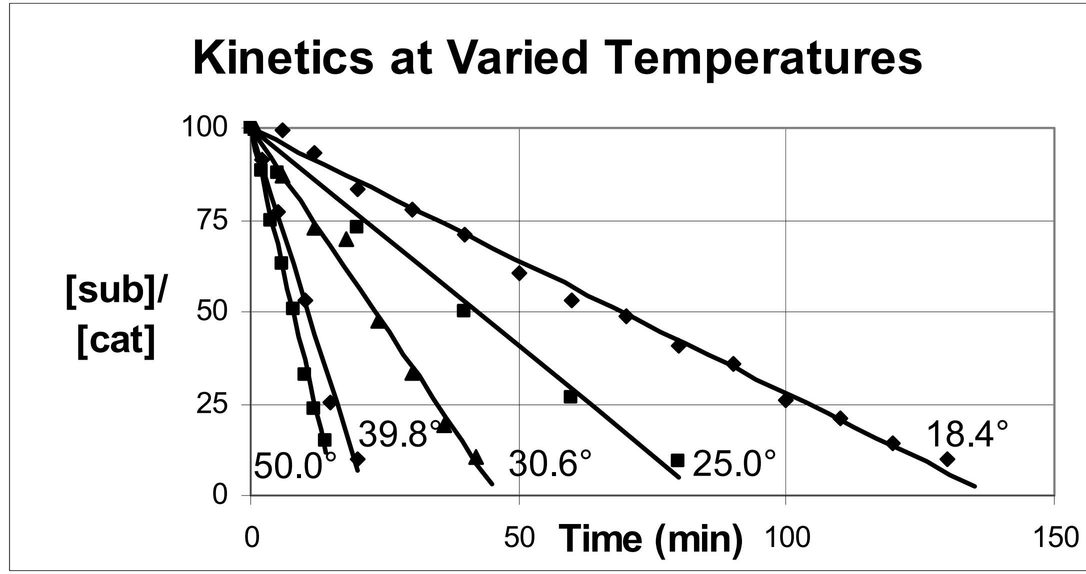
$$\overline{P_n} = \frac{k_p[=]}{k_{si}[H_3SiPh]}$$

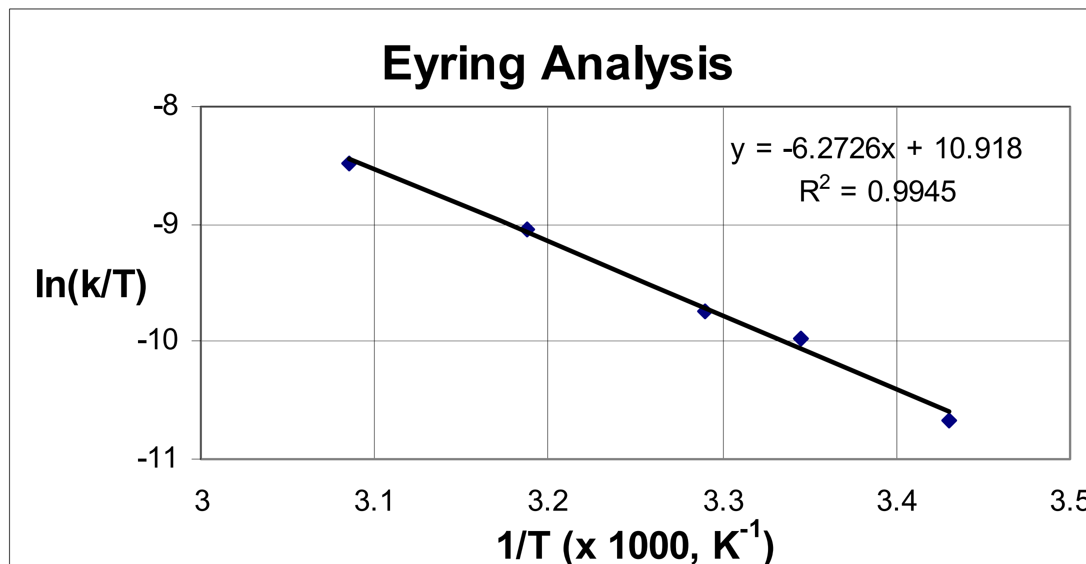
Activation Parameters

- Eyring and Arrhenius analysis carried out

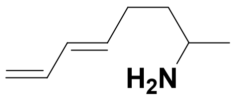
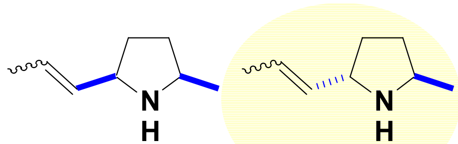
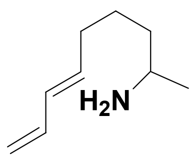
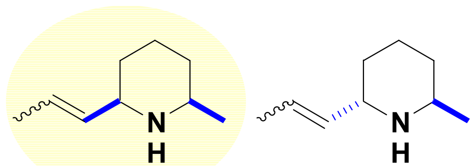


substrate	ΔH‡, kcal/mol	ΔS‡, eu
	12.3 (1.6)	-25.9 (5)
	12.7 (1.4)	-27.0 (5)
	10.7 (8)	-27.4 (6)



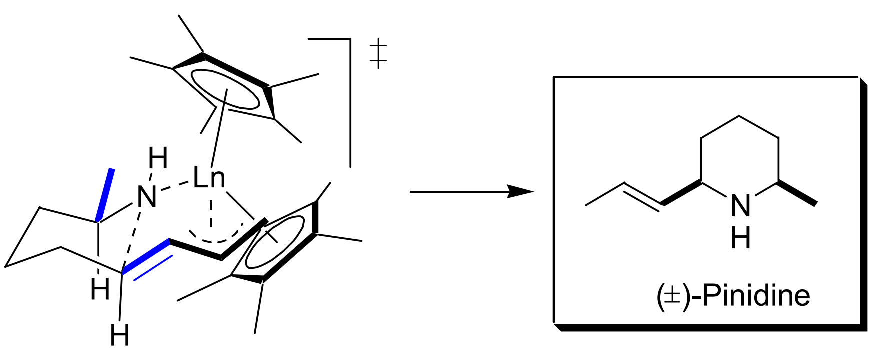


Diastereoselectivity in Aminodiene Cyclization

Entry	Subtsrate	Products	Conversion[a] (%)	Product Ratio[b] *cis* : *trans*	Pre-Catalyst	N_t, h^{-1} (^oC)[c]
1.		 2,5-*cis* 2,5-*trans*	> 95	42 : 58	$Cp'_2LaCH(TMS)_2$	1.0 (25)
			> 95	10 : 90	$CGCSmN(TMS)_2$	78 (25)
2.		 2,6-*cis* 2,6-*trans*	> 95	99.4 : 0.6[d]	$Cp'_2LaCH(TMS)_2$	3.7 (25)
			> 95	78 : 22	$CGCSmN(TMS)_2$	4.0 (60)

[a]Determined by ^{1}H-NMR, [b]Determined by GC-MS ratio of the corresponding hydrogenated Boc derivatives, [c]Turnover frequencies measured in C_6D_6 with 6 mol% precatalyst, [d]*cis*: *trans* = 178:1; Alkene isomer ratio (E: Z: allyl)= 94: 1: 5

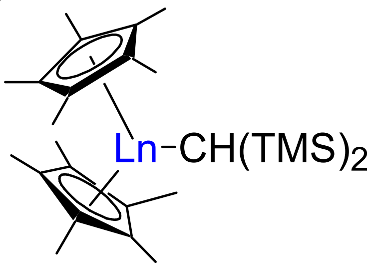
Good to excellent 2,5-*trans* (80% de), and 2,6-*cis* (99% de) diastereoselectivities



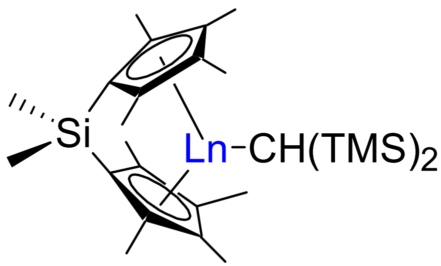
Concise synthesis of (±)-pinidine with excellent stereocontrols (2,6-*cis* and *trans*-alkene)

Organolanthanide Catalysts

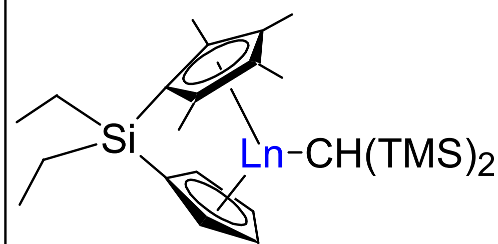
- Reactivity tunable by varying metal size or altering ligands
- Representative uses: olefin hydrogenation, polymerization, hydroamination, hydrophosphination, hydroboration



standard

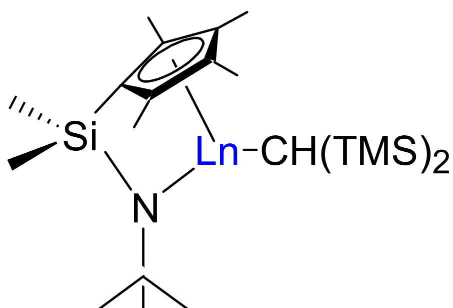


silicon bridged Cp's

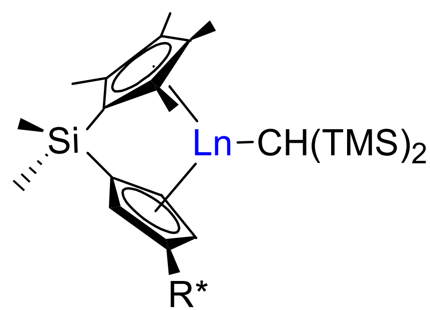


mixed Cp's

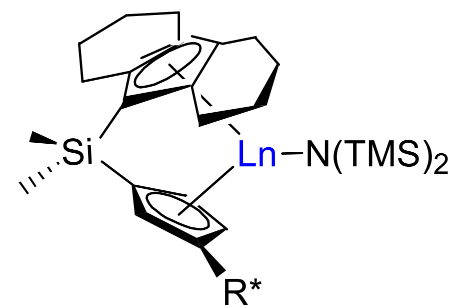
$LnE(TMS)_3$
(E = N, CH)
no-ring system



"CGC" catalyst



C_1-symmetric, chiral



chiral, OHF roof

(R^* = chiral moiety)

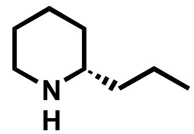
Molander, G. A.; Romero, J. A. C. *Chem. Rev.* **2002**, *102*, 2161-2185.

DISTINCTIVE CHARACTERISTICS OF LANTHANIDE AND ACTINIDE ORGANOMETALLICS

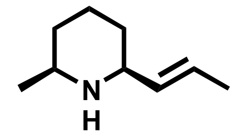
1. **Very Large Metal Ionic Radii**
   - Potential for high coordinative unsaturation
   - Tunable steric environment (lanthanide contraction)
2. **Well-Defined Formal Metal Oxidation States**
3. **Polar Metal-Ligand Bonding**
   (Electrophilic Metal Centers)
4. **Kinetically Very Labile**
5. **Distinctive Bonding Energetics**
   - Small D(M-H) – D(M-alkyl)
   - Large D(M-halide), D(M-OR), D(M-NR_2)

CHALLENGING HYDROELEMENTATION TARGETS

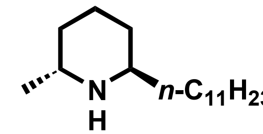
Alkaloid, Other Pharmacologically–Active Skeletons



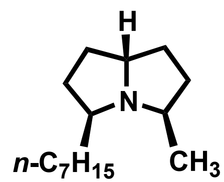
(+)-Coniine



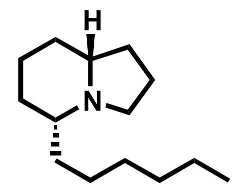
(+)-Pinidine



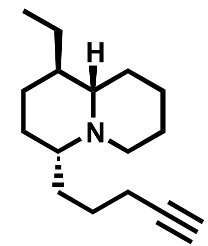
(-)-Solenopsin A



(+)-Xenovenine

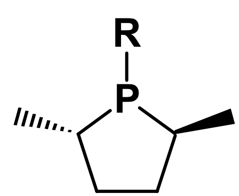


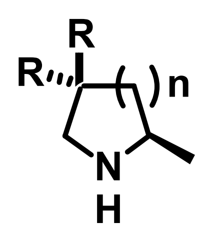
(-)- Indolizidine 209D



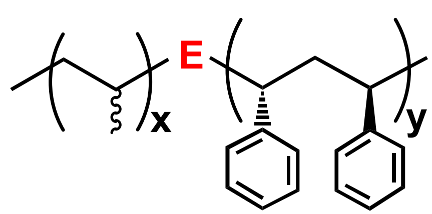
Quinolizidine 233A

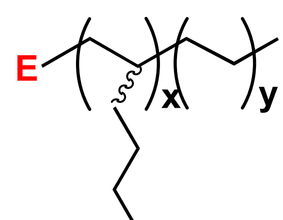
Chiral Structures

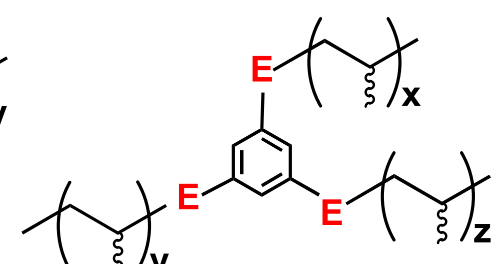




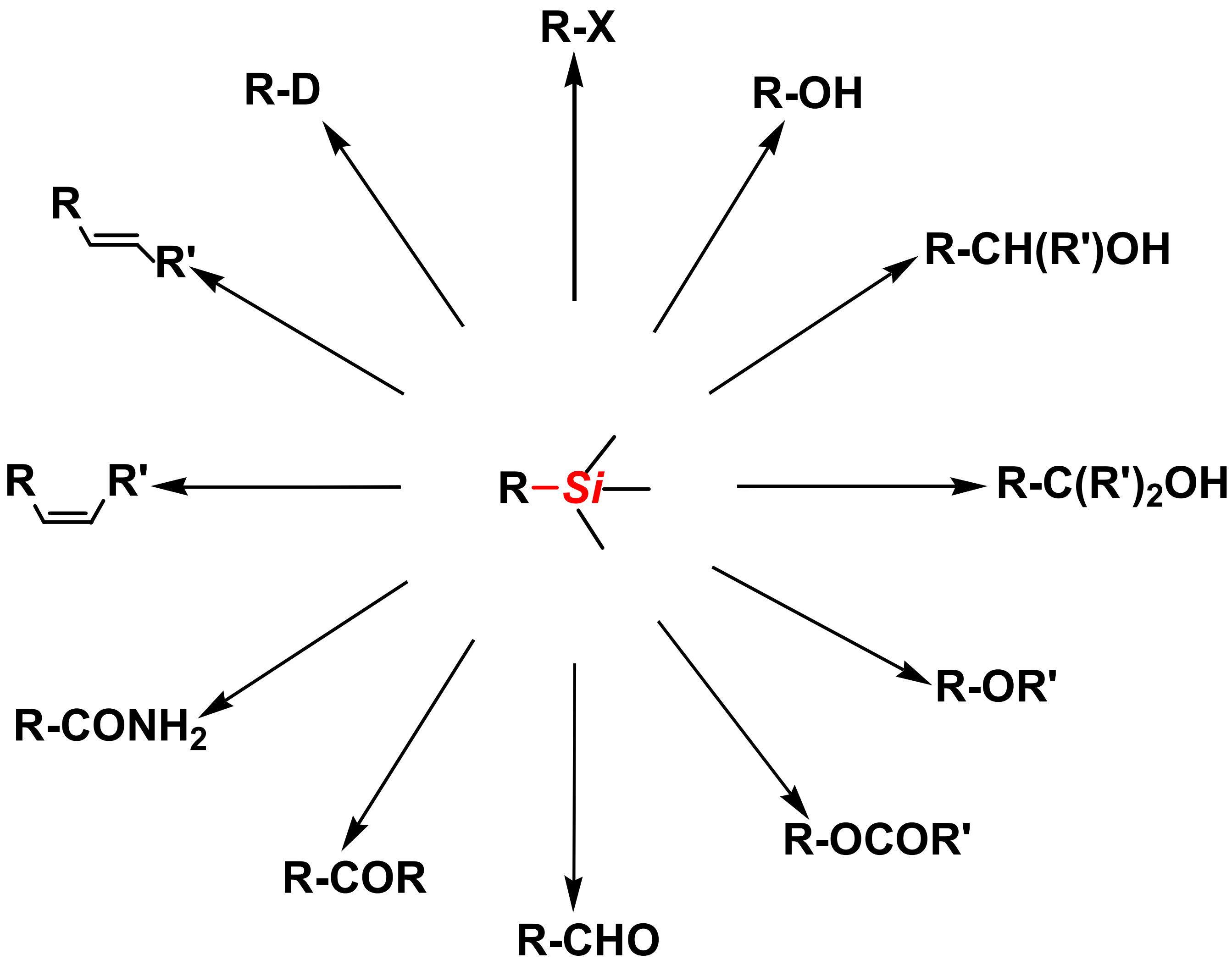
Novel Polymeric Materials



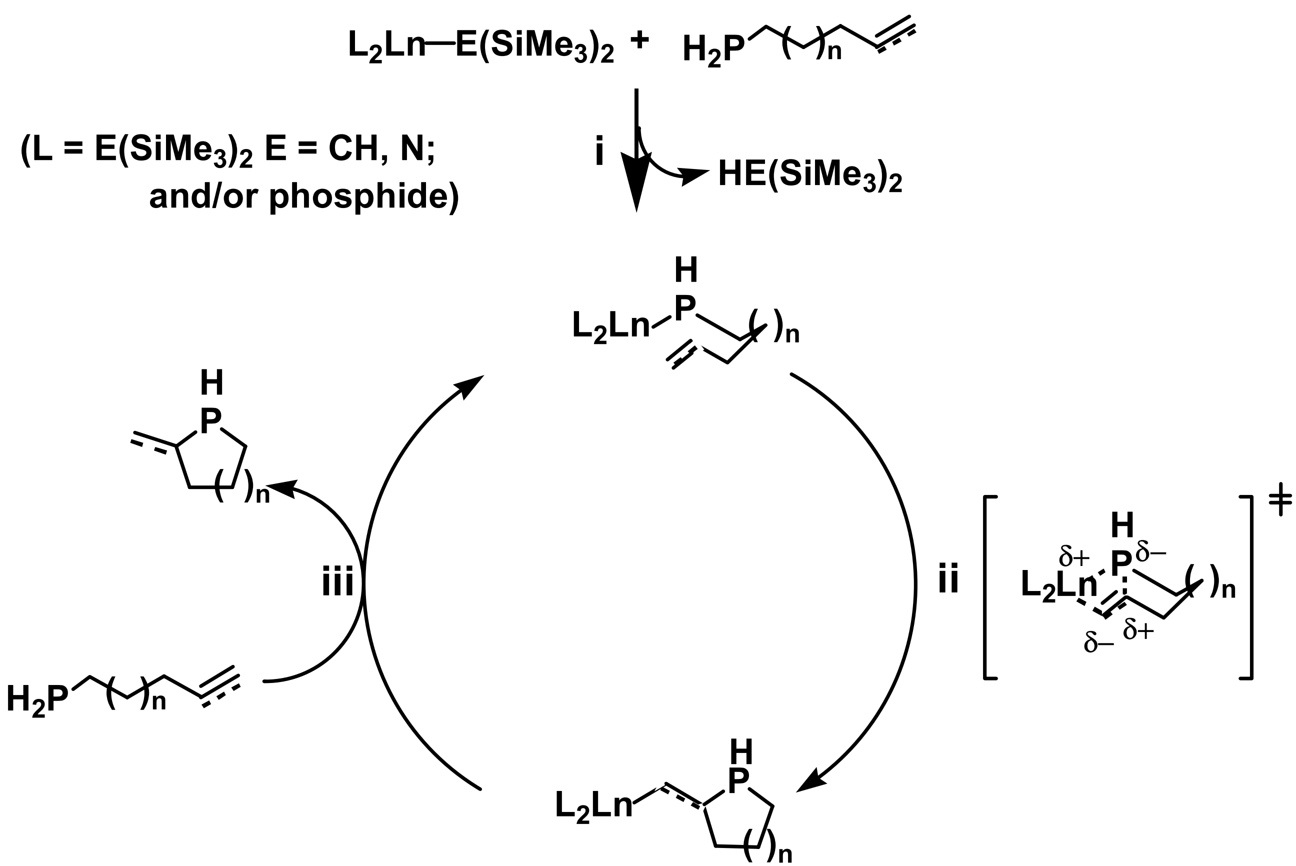




UTILITY OF ORGANOSILANES IN ORGANIC SYNTHESIS

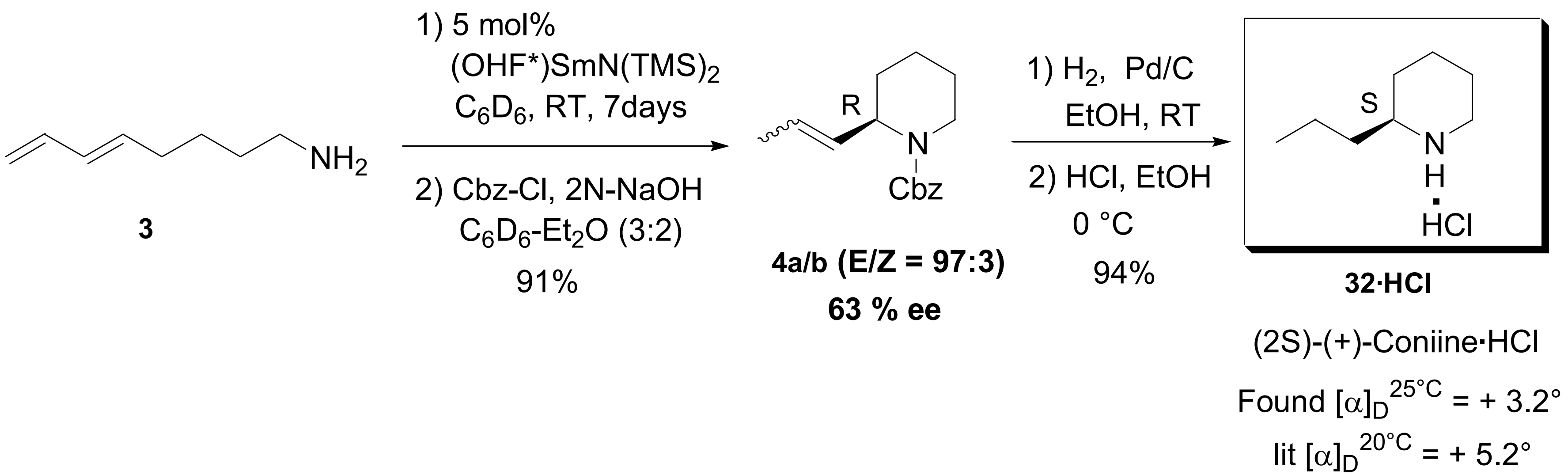


Hydrophosphination with Readily Accessible Homoleptic Lanthanide Catalysts



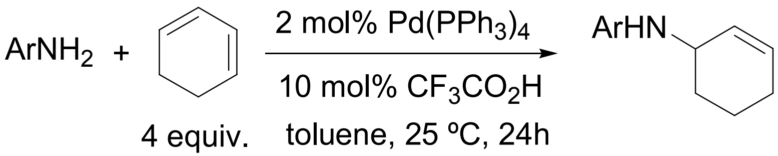
- Phosphinoalkenes and Phosphinoalkynes
- Turnover Frequencies, Scope Comparable to Lanthanocenes
- $\nu = k[\text{substrate}]^2[\text{Ln}]^1$
- Step i is slow

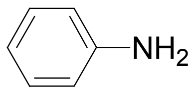
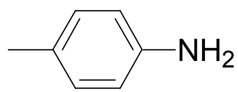
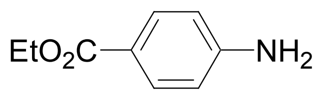
Synthesis of (2S)-(+)-Coniine·HCl, Determination of the Absolute Configuration of 4a



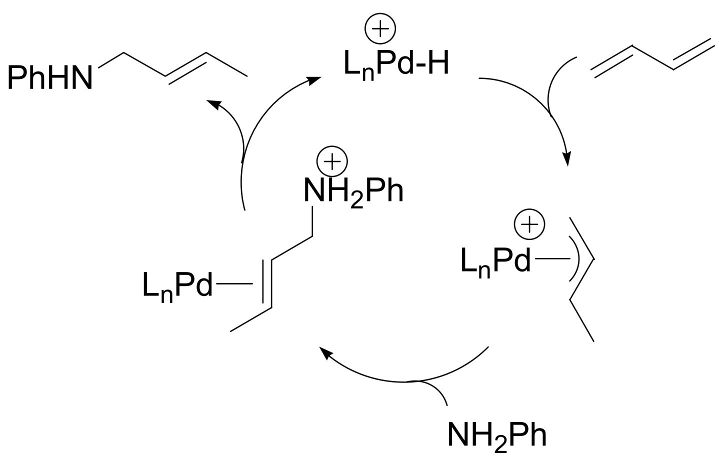
Reactivity and enantioselectivity improved for the intramolecular hydroamination/cyclization to 2-substituted piperidines

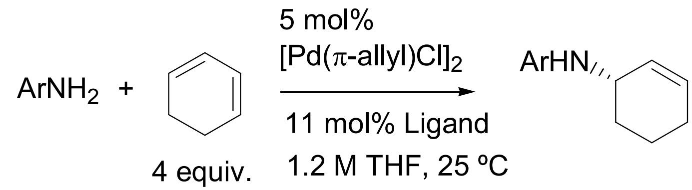
Palladium-Catalyzed Hydroamination of 1,3-Dienes

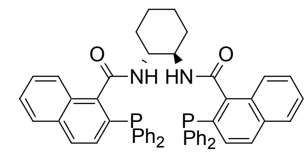


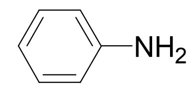
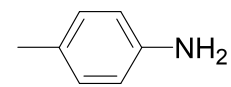
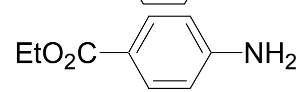
Entry	Amine	Yield(%)
1		99
2		85
3		96 (48 h)

Mechanism in the presence of acid

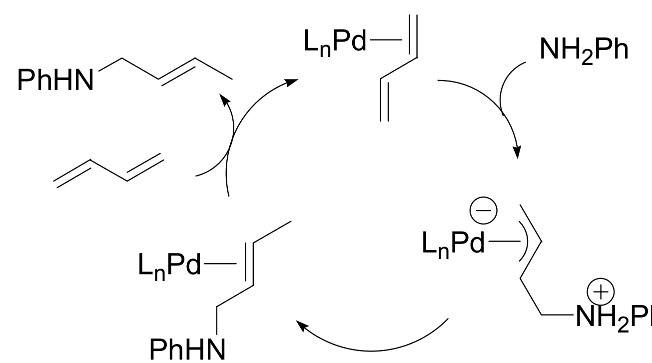




Ligand = 

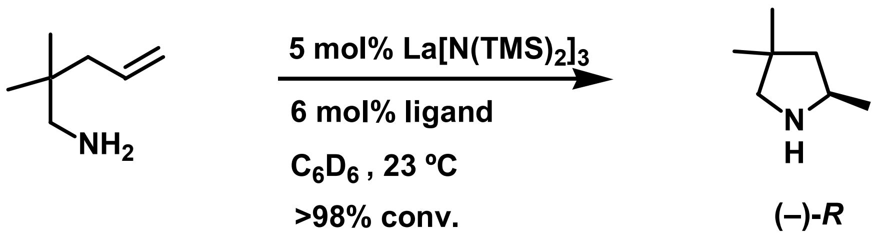
Entry	Amine	Time (h)	Yield (%)	ee (%)
1		120	87	89 (S)
2		120	78	86 (S)
3		120	83	95 (S)

Mechanism in the absence of acid



Löber, O; Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2001**, *123*, 4366-4367

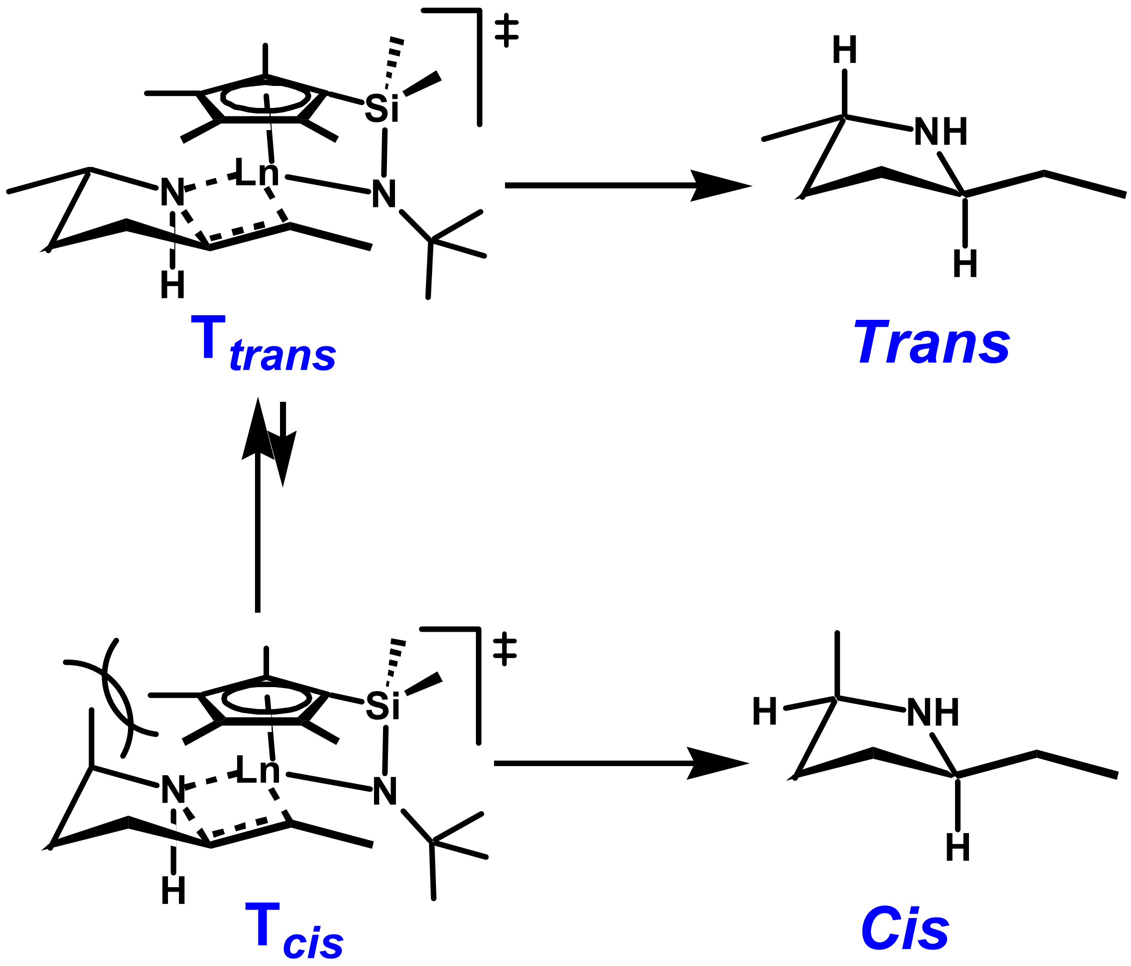
Ligand Effects on Enantioselectivity



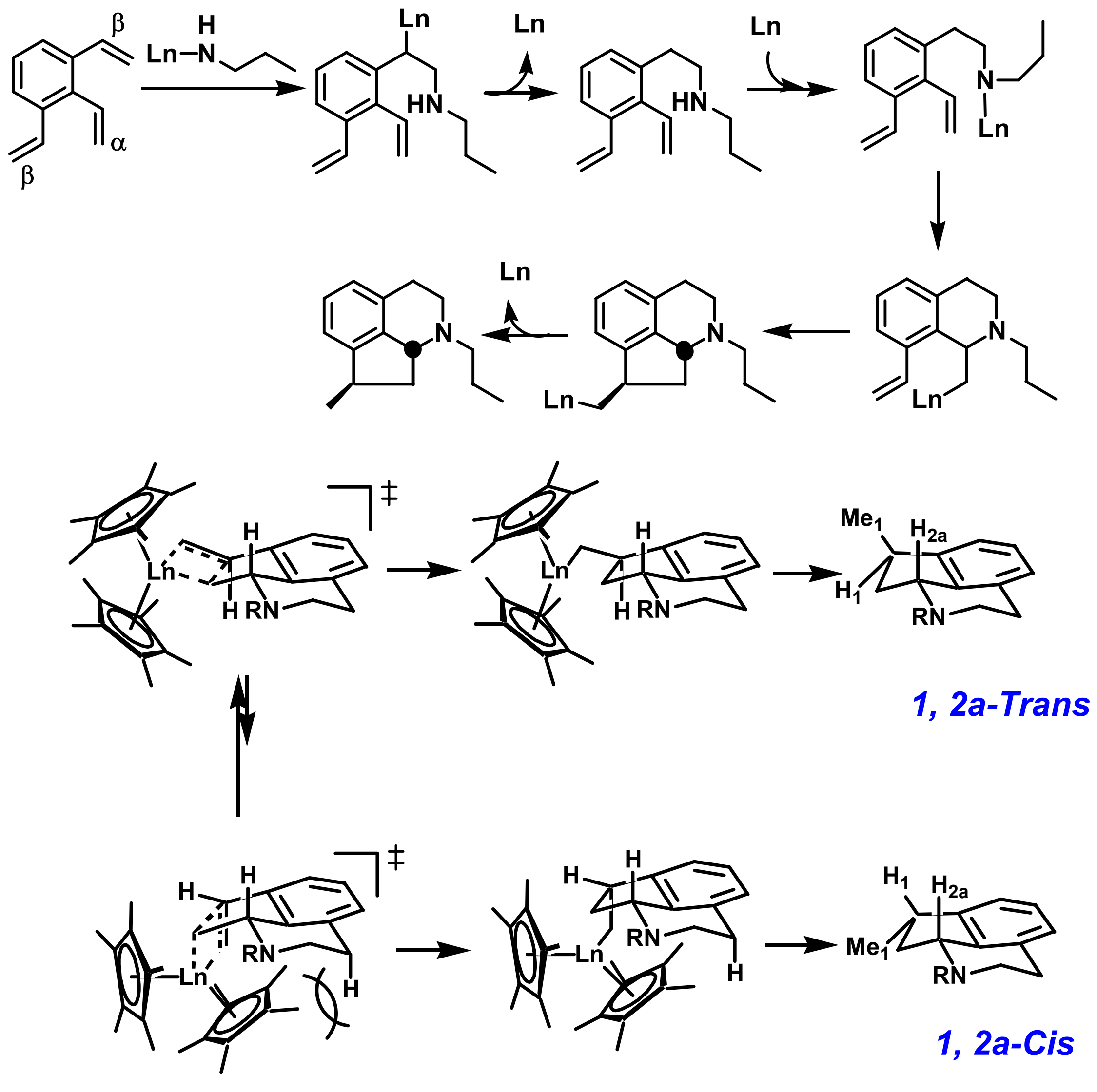
Entry	Ligand	N_t, (h^{-1})[a]	%ee[b] (config.)[c]
1	(4*S*)-^{i}PrBoxH (**1**)	3.2	6 (*R*)
2	(4*S*)-^{t}BuBoxH (**2**)	1.3	39 (*R*)
3	(4*S*)-PhBoxH (**3**)	7.1	56 (*S*)
4	(3a*R*)-IndaBoxH (**4**)	1.8	25 (*R*)
5	(4*R*,5*S*)-Ph_2BoxH (**5**)	25	67 (*R*)
6	(4*S*)-Ph-5,5-Me_2BoxH (**6**)	21	61 (*S*)
7	(4*S*,5*R*)-(^{t}BuPh)$_2$BoxH (**7**)	17	55 (*S*)
8	(4*S*,5*R*)-$Naph_2$BoxH (**8**)	17	59 (*S*)

Note uniformity of stereoinduction

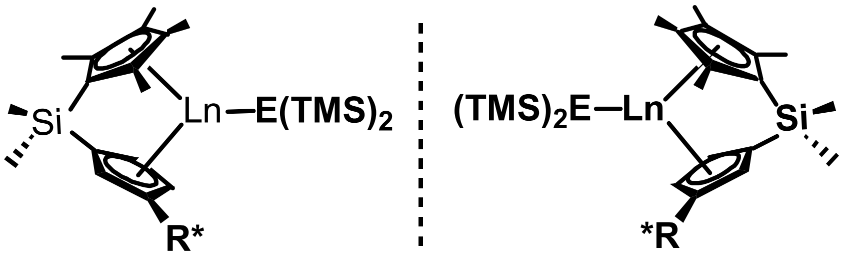
Stereochemical Pathways for Catalytic Intramolecular Hydroamination/Cyclization of Amine-Tethered 1,2-Disubstituted Alkenes to *trans*-Pyrrolidines.



Stereochemical Pathways for Intramolecular Hydroamination/Ensuing Cyclization of Trivinylbenzene + *n*-Propylamine to *Trans*-(±)-1-methyl-3-propyl-1,2,2a,3,4,5-hexahydro-3-aza-acenaphthylene



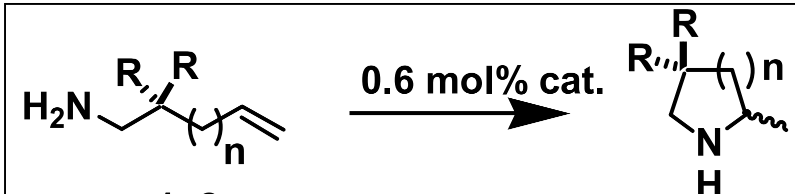
Enantioselective Hydroamination / Cyclization of Aminoalkenes



(*S*) (*R*)

E = CH, N

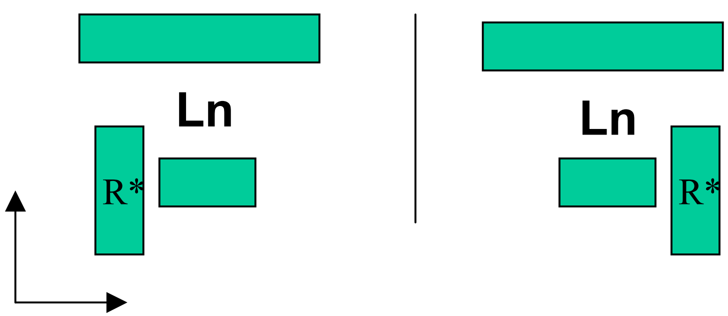
R* = (+)-neomenthyl, (-)-menthyl, (-)-phenylmenthyl



n = 1, 2
R = H, CH_3

Up to 74% ee

(n = 1, R = CH_3, -30°C)



C_1-Symmetric Catalyst

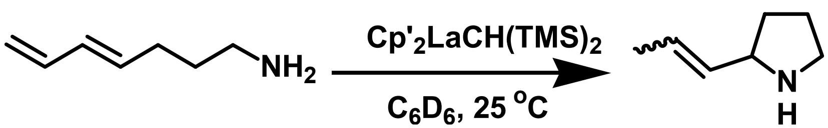
- **Use of a chiral moiety**
  - **Separable diastereomers**
- **C_5Me_4 vs C_5H_3 : transverse**
  Bulky R* : lateral discrimination

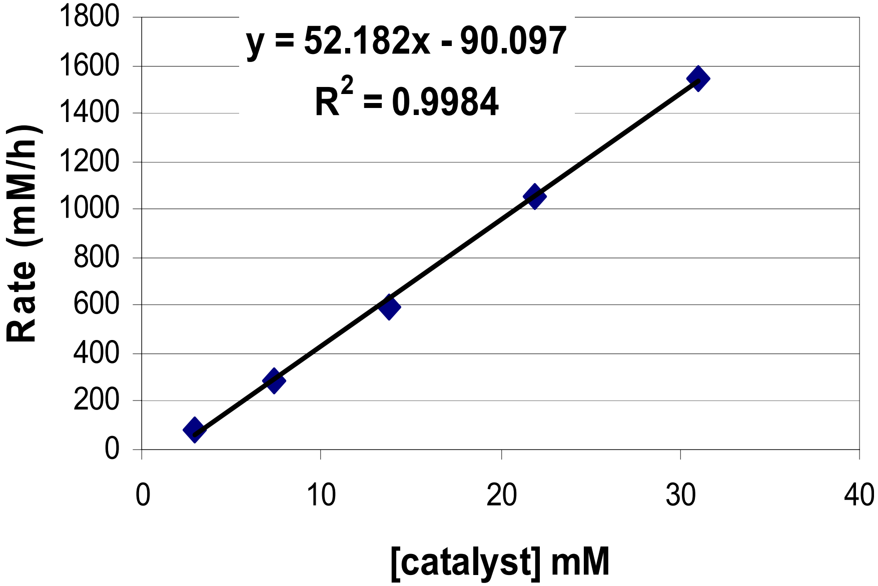
Marks, T. J. and coworkers, *J. Am.Chem. Soc.* **1994**, *116*, 10212-10240, 10241-10254

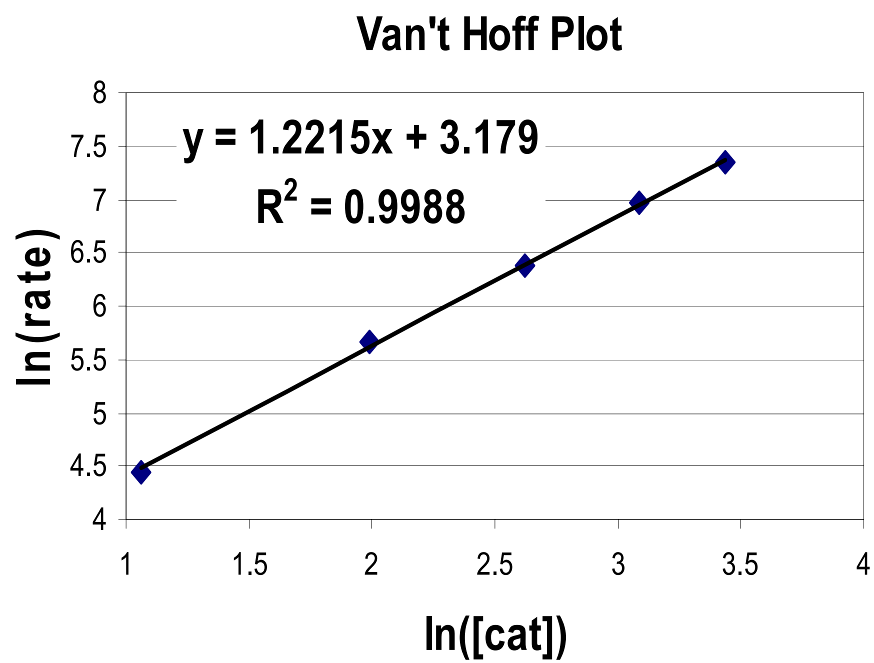
Giardello, M. A.; Yamamoto, Y.; Brard, L; Marks, T. J. *J. Am.Chem. Soc.* **1995**, *117*, 3276-3277

Fu, P.-F.; Brard, L; Li, Y.; Marks, T. J. *J. Am.Chem. Soc.* **1995**, *117*, 7157-7168

Kinetic Studies: Reaction Order in [catalyst]

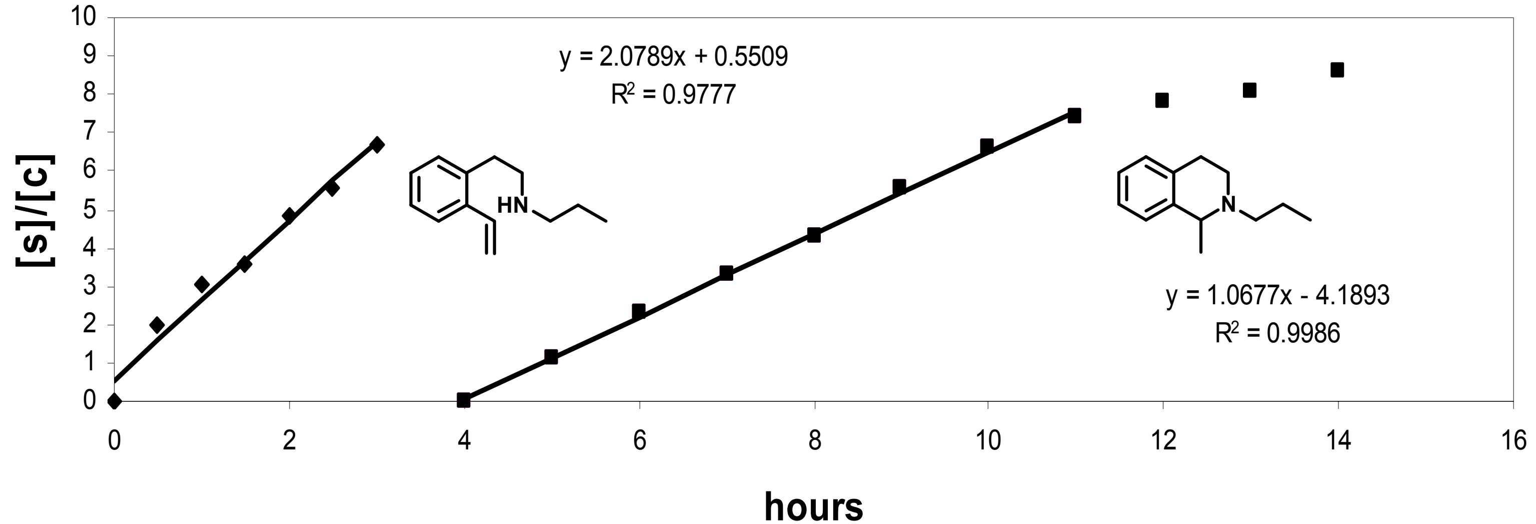


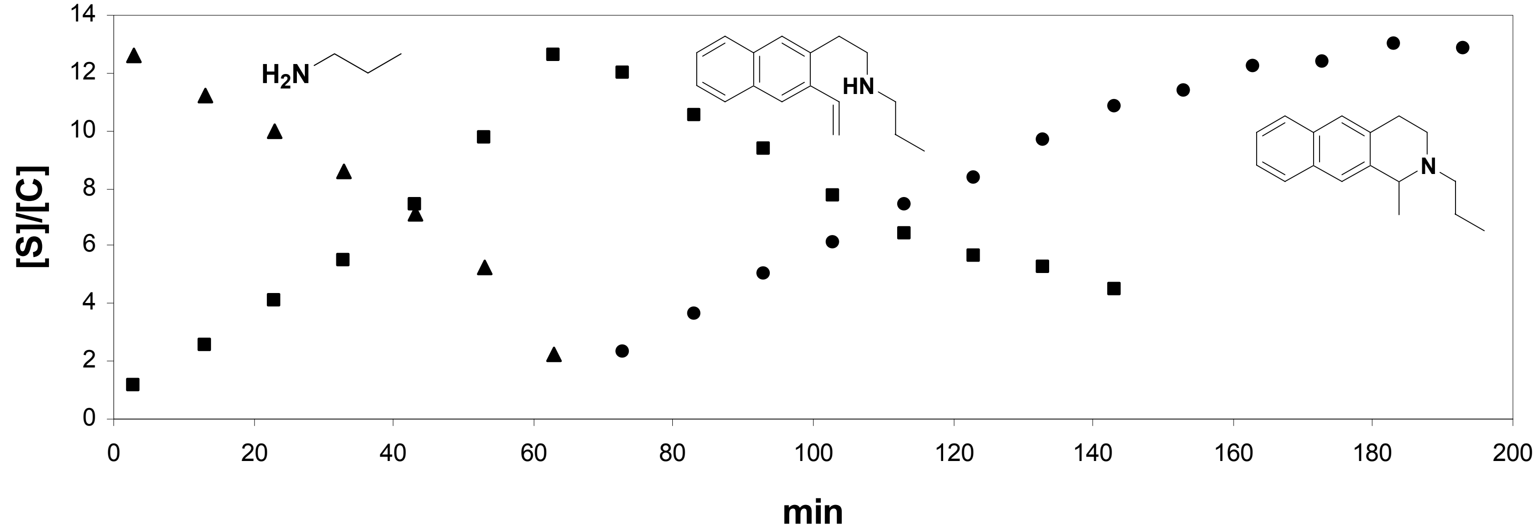




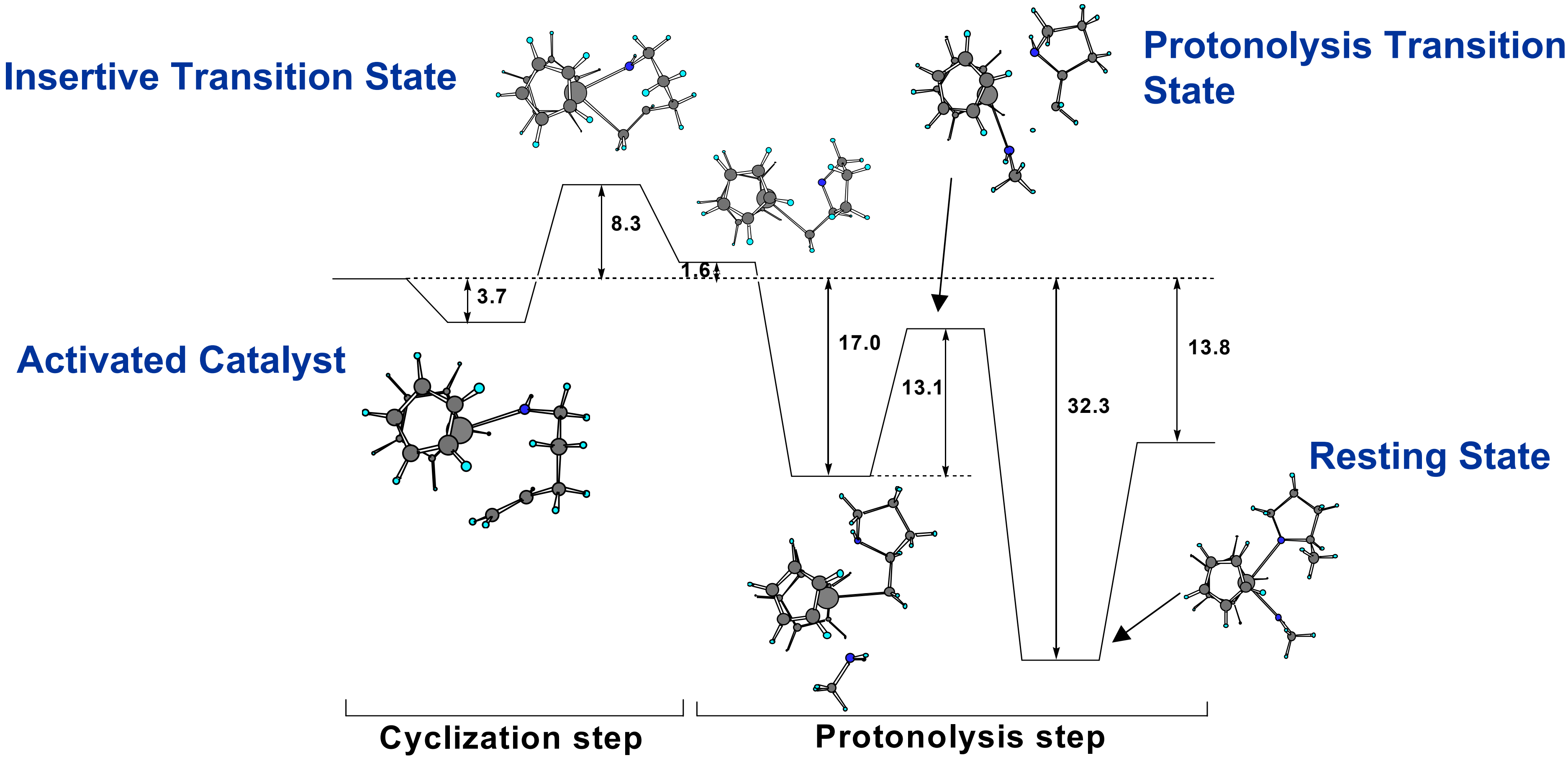
Rate = k [catalyst] ^{1} [aminodiene] ^{0}

Kinetics of Coupled Inter/Intramolecular C-N Bond Fusion





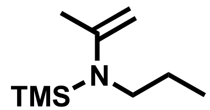
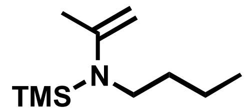
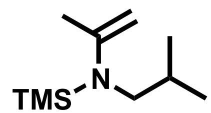
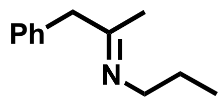
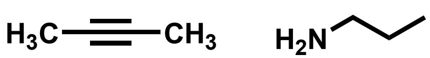
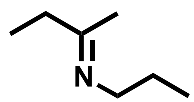
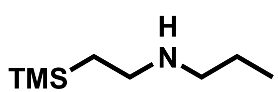
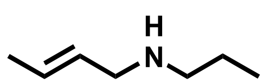
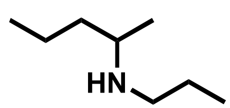
DFT Enthalpic Profile for Aminoalkene Hydroamination



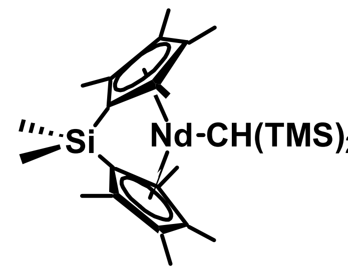
- Weak Olefin Complex
- Turnover-Limiting Olefin Insertion
- Exothermic Ln-C Bond Protonolysis
- Amine-Amido Catalyst Resting State

I. Fragalà

Intermolecular Hydroamination

Substrates	Products	Nt	Yield
		14 (60)	90
		13 (60)	62
		10 (60)	90
		2 (60)	85
		1 (60)	91
		2 (60)	93
		0.3 (21)	90
		0.4 (60)	90

Precatalyst



- **Alkynes and functionalized alkenes are reactive**
- **Regioselectivity & stereoselectivity**

Li, Y.; Marks, T. J. *Organometallics*, **1996**, *15*, 3770-3772
Ryu, J.: Li, Y.; Marks, T.J. *J. Am. Chem. Soc*. **2003**, *125*, 12584-12605.


SALUDA