sp³ C-H Alkylation with Olefins

,

Yan Xu

Dec. 3, 2014

1) sp^3 C-H Alkylation via Directed C-H activation
2) Hydroaminoalkylation (still via C-H activation)
3) Hydrohydroxyalkylation (via radical chemistry)
4) Hydrohydroxyalkylation (via transfer hydrogenation chemistry)

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   - *Rare-earch-metal-philic DG*
   - *Allylic C-H bond alkylation (double bond as DG)*
   - *Pyridine type DG*

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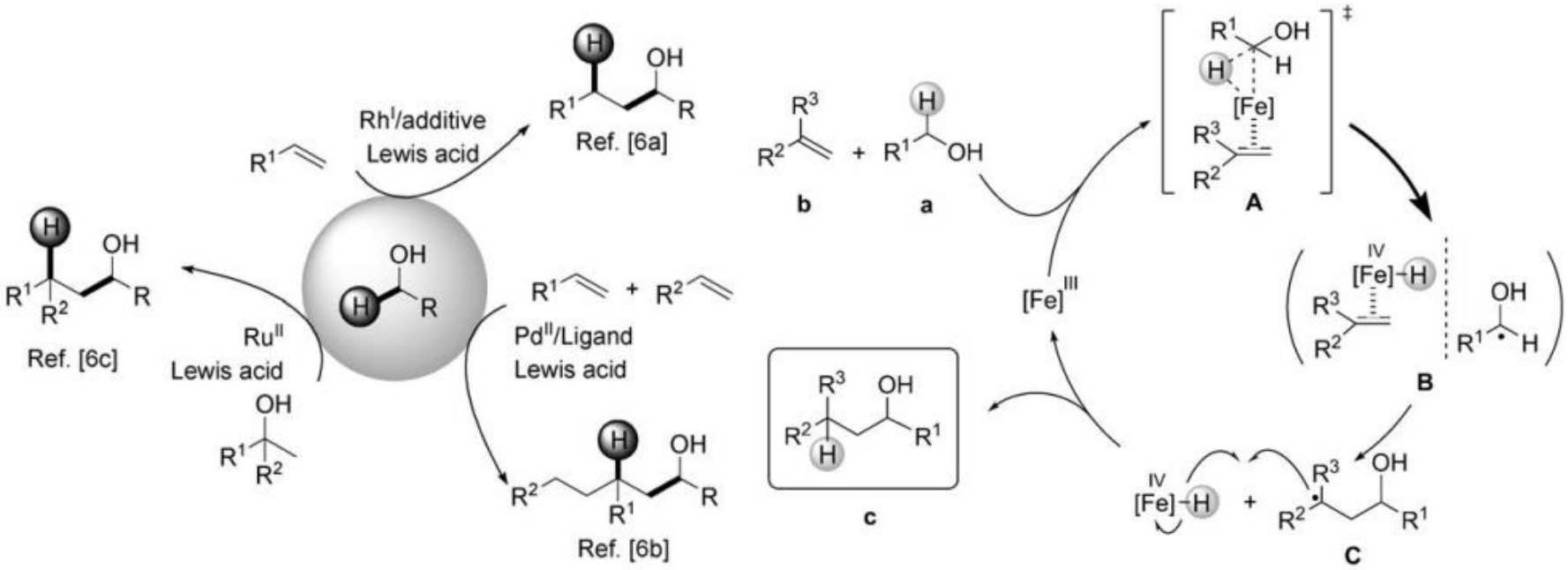

Yong-Qiang Tu, *Angew. Chem. Int. Ed*. **2009**, *48*, 8761

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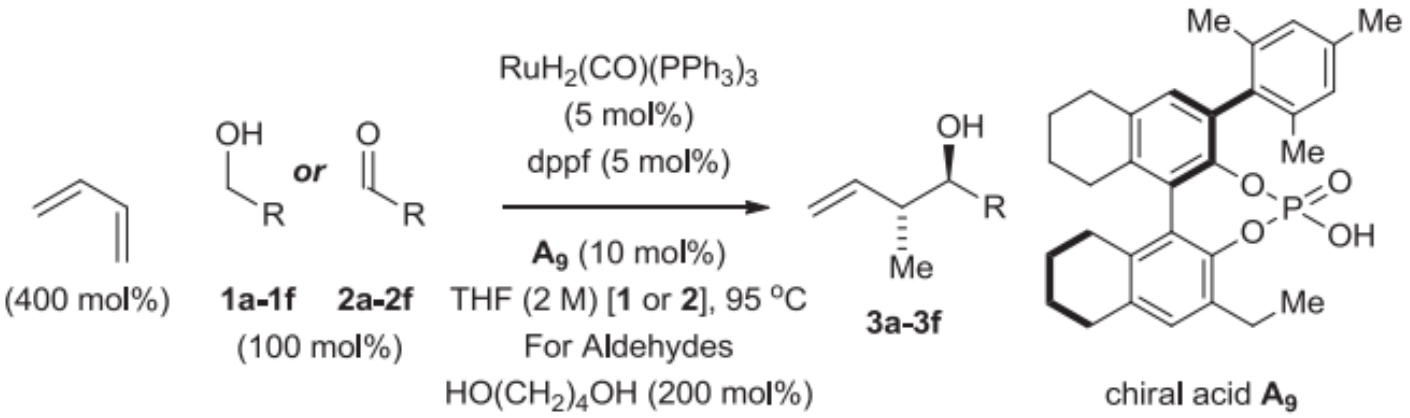

Michael J. Krische, *Science*. **2012**, *336*, 324

sp^3 C-H Alkylation with Olefins Through C-H activation

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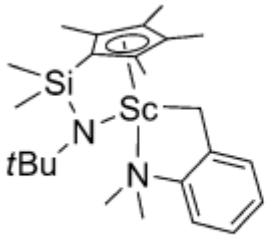

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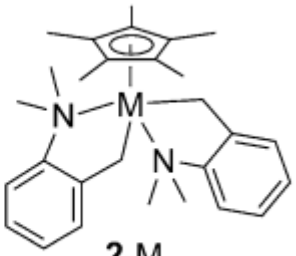
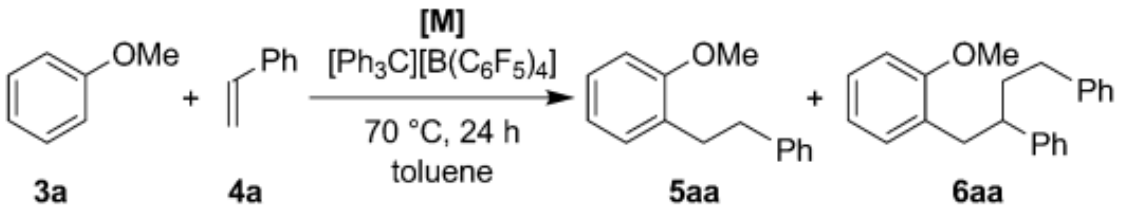


2-M
(M = Sc, Y, Sm, Gd, Lu)

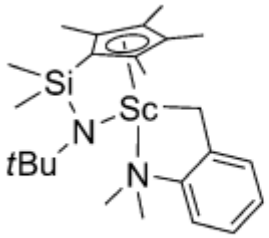
Rare-earth metal:

- Strong oxophilicity
- High activity of rare-earth alkyl species toward olefin



3a **4a** **5aa** **6aa**

Zhaomin Hou, *ACIE*. *2012*, **51**, 12828 –12832



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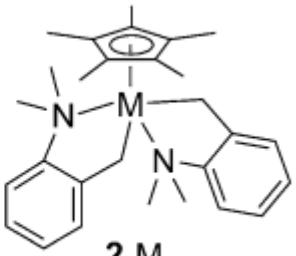

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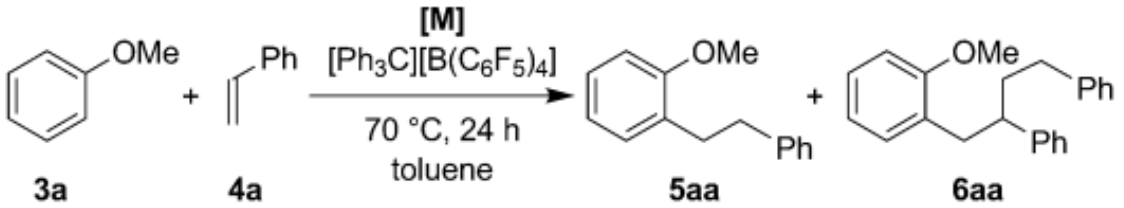
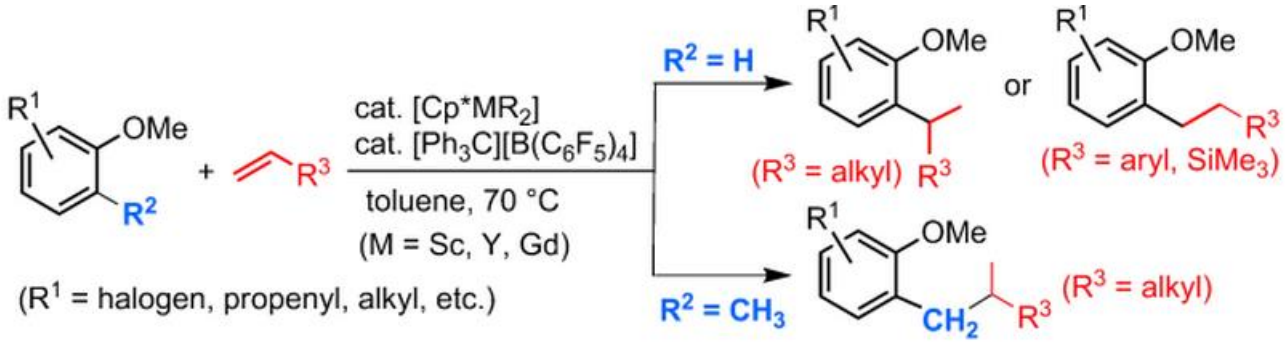


3a **4a** **5aa** **6aa**

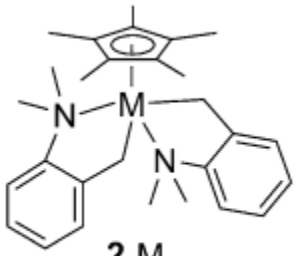
Entry	[M]	Yield of **5aa** [%][b]	Yield of **6aa** [%][b]
1[c]	**1**	0	0
2	**2**-Sc	60	15
3	**2**-Sc[d]	58	12
4	**2**-Y	94 (91)	2
5	**2**-Gd	91	1
6	**2**-Sm	1	0
7	**2**-Lu	17	0

[a] Reaction conditions: **[M]** (0.025 mmol), $[Ph_3C][B(C_6F_5)_4]$ (0.025 mmol), **3a** (1 mmol), **4a** (1.5 mmol), toluene (3 mL), 70 °C, 24 h, unless otherwise noted. [b] Yield (based on **3a**) measured by GC analysis. Yield of isolated product is given in parentheses. [c] With or without $[Ph_3C][B(C_6F_5)_4]$. [d] **4a** (1 mmol).

Zhaomin Hou, *ACIE*. *2012*, **51**, 12828 –12832



Olefin: must be terminal
Ethylene: oligomer



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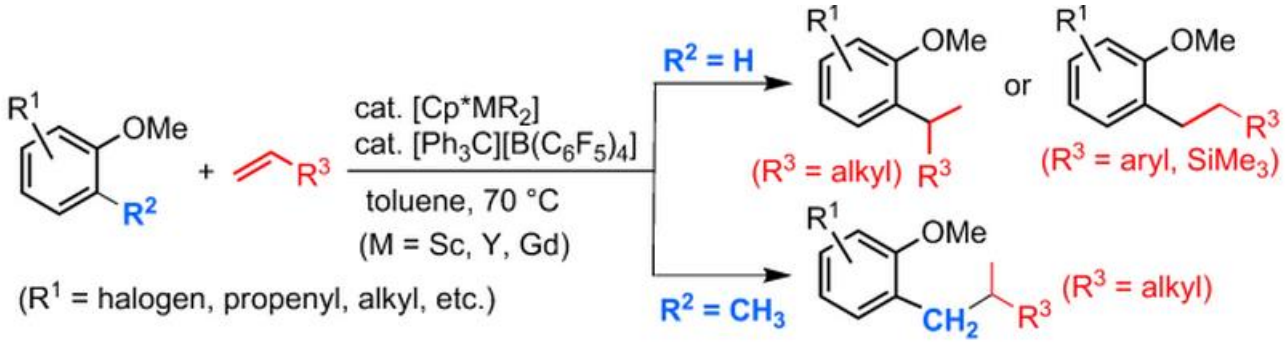

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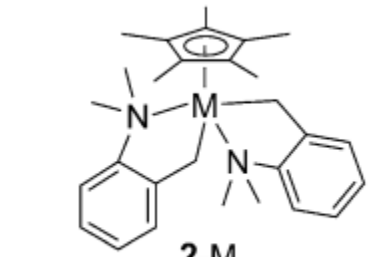

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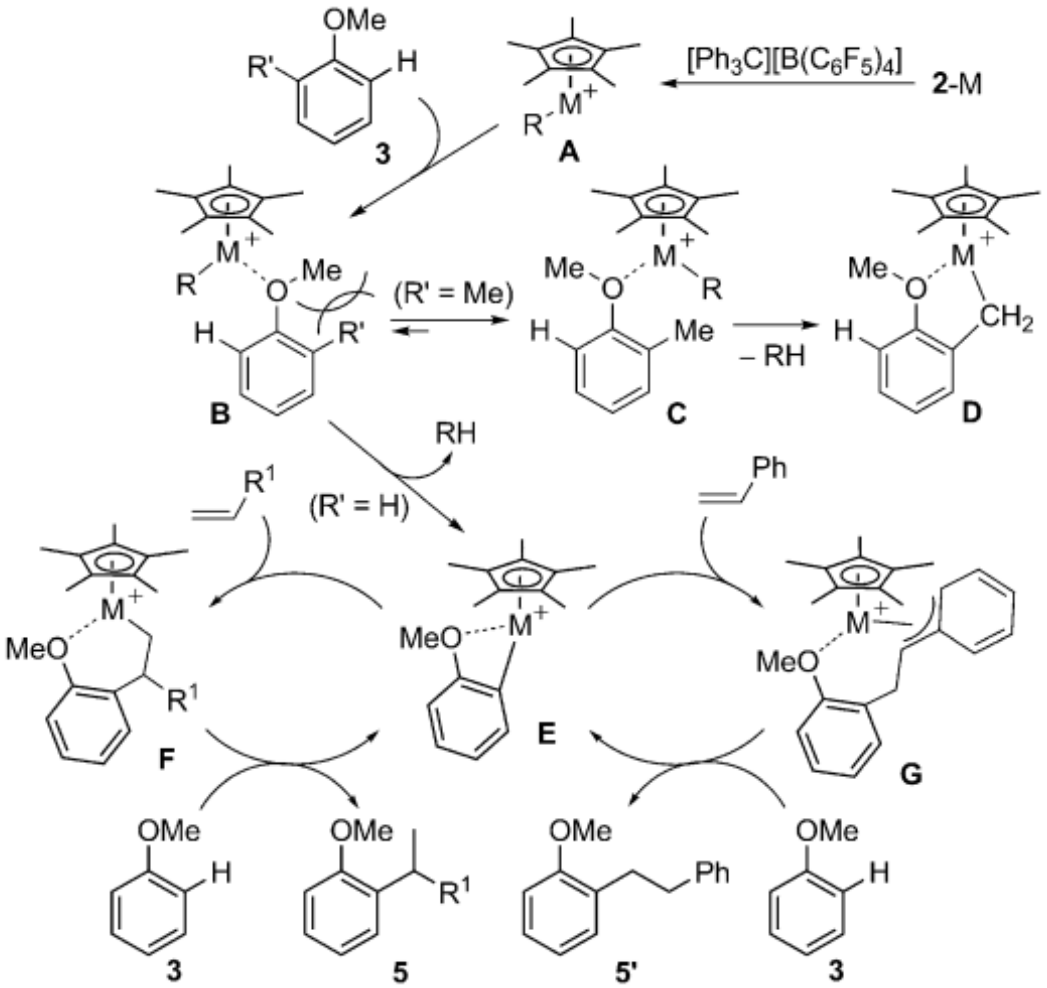

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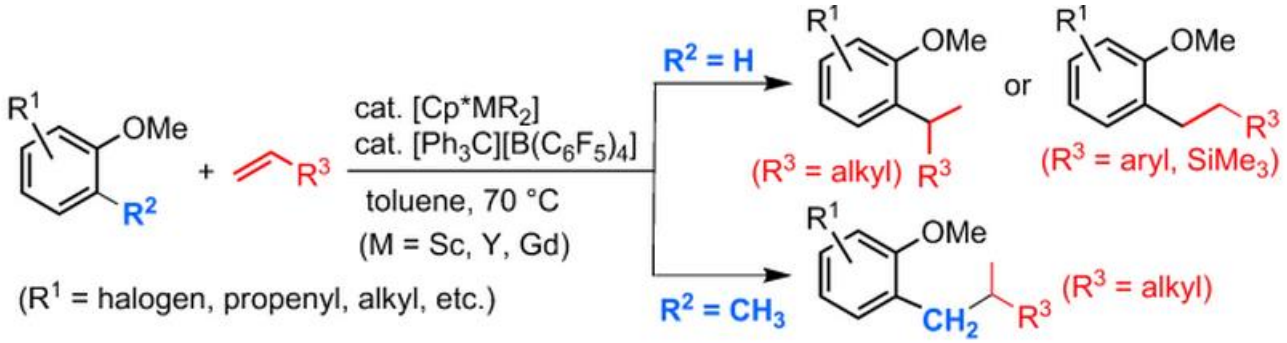

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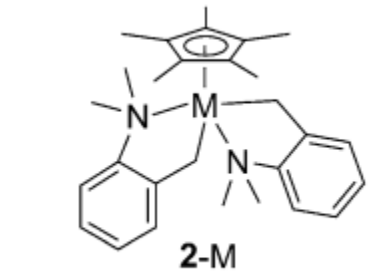

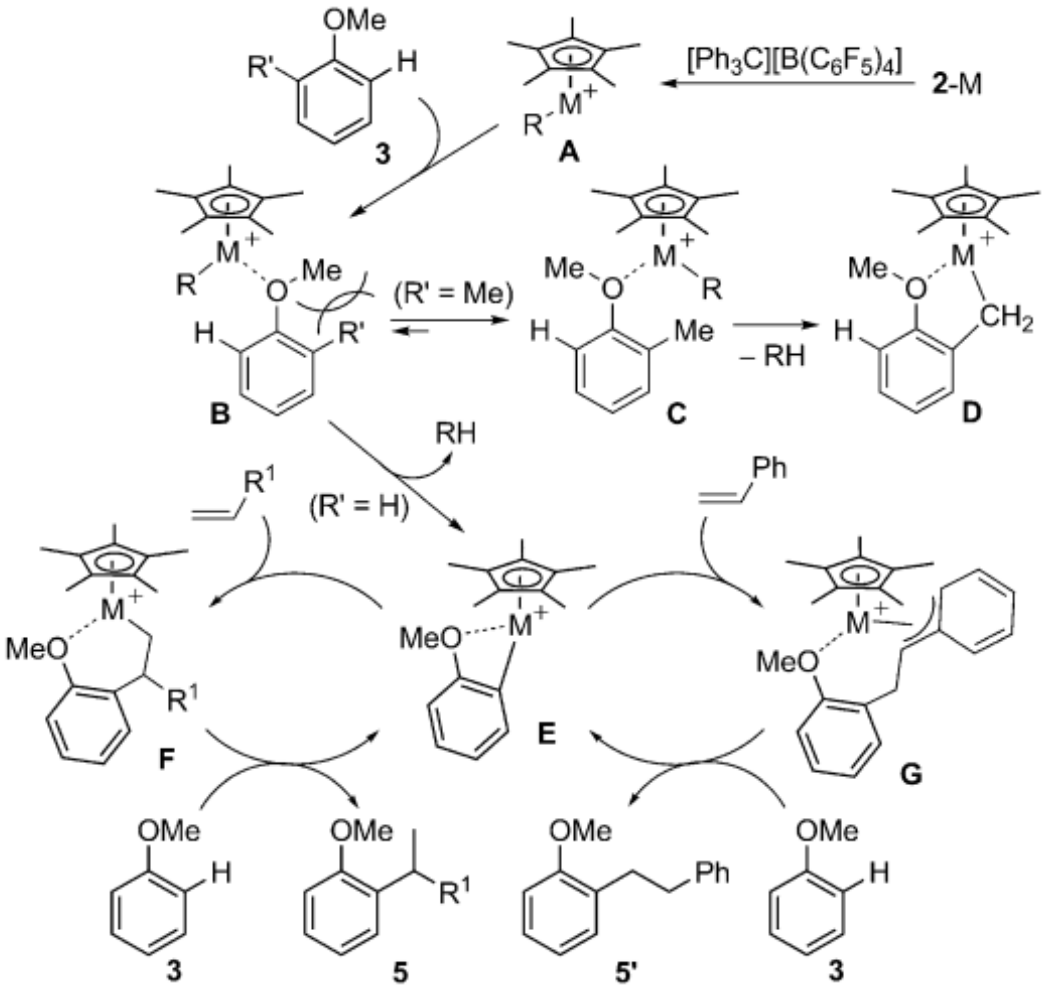

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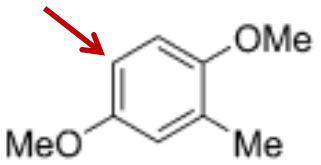

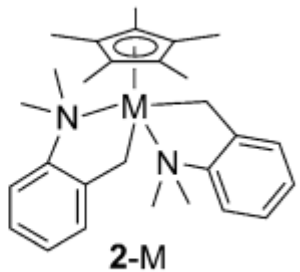

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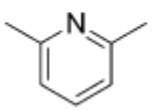
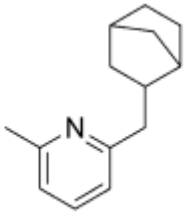


1

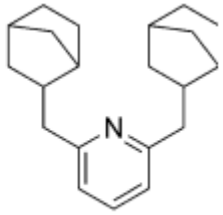
+

2

[Ln] (4.0 mol %)
[B] (4.0 mol %)
toluene, 70 °C

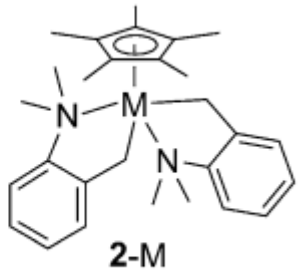


3a



3b

Zhaomin Hou, *ACIE*. *2013*, **52**, 4418



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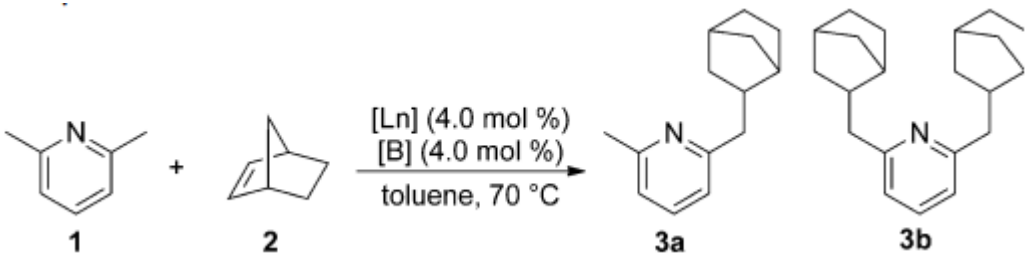
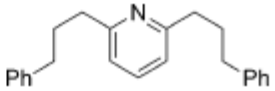
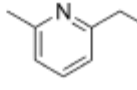
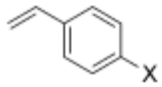
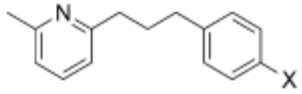
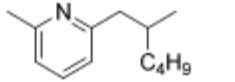
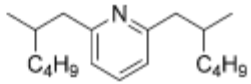
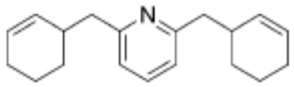
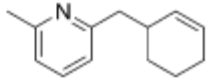
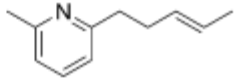
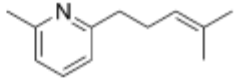


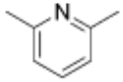
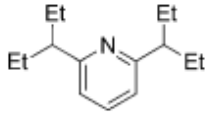
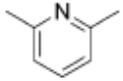
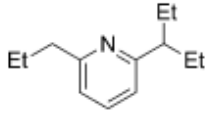
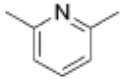
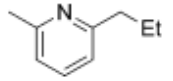
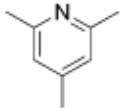
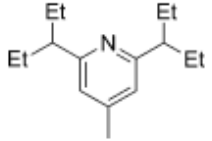
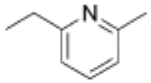
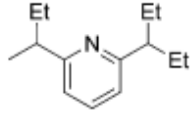
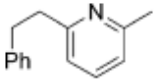
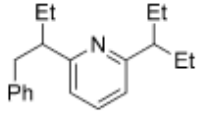
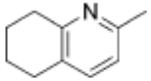
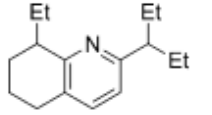
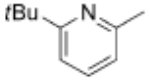
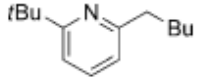
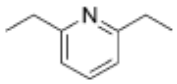
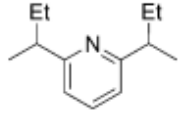
1 **2** **3a** **3b**

Entry	[Ln][b]	[B]	*t* [h]	Yield **3a** [%][c]	Yield **3b** [%]
1	$[C_5Me_5ScR_2]$	$B(C_6F_5)_3$	24	5	–
2	$[C_5Me_5YR_2]$	$B(C_6F_5)_3$	24	0	–
3	$[C_5Me_5ScR_2]$	$[Ph_3C][B(C_6F_5)_4]$	24	5	–
4	$[C_5Me_5YR_2]$	$[Ph_3C][B(C_6F_5)_4]$	24	40	–
→ 5	$[C_5Me_5YR_2]$	$[Ph_3C][B(C_6F_5)_4]$	48	65	–
6	$[C_5Me_5YR_2]$	–	24	0	–
7	–	$[Ph_3C][B(C_6F_5)_4]$	24	0	–
8	$[C_5Me_5LaR_2]$	$[Ph_3C][B(C_6F_5)_4]$	24	0	–
9	$[C_5Me_5SmR_2]$	$[Ph_3C][B(C_6F_5)_4]$	24	10	–
10	$[C_5Me_5GdR_2]$	$[Ph_3C][B(C_6F_5)_4]$	24	23	–
11	$[C_5Me_5LuR_2]$	$[Ph_3C][B(C_6F_5)_4]$	24	8	–
12[d]	$[C_5Me_5YR_2]$	$[Ph_3C][B(C_6F_5)_4]$	24	25	–
13	$[C_5Me_5SiMe_3YR_2]$	$[Ph_3C][B(C_6F_5)_4]$	24	31	–
14	$[C_5Me_4HYR_2]$	$[Ph_3C][B(C_6F_5)_4]$	24	49	–
→ 15	$[C_5H_5YR_2]$	$[Ph_3C][B(C_6F_5)_4]$	24	89 (85)[e]	–
16[f]	$[C_5H_5YR_2]$	$[Ph_3C][B(C_6F_5)_4]$	24	–	99

[a] Reactions were carried out with 0.75 mmol of 2,6-lutidine and 0.5 mmol of norbornene in 2 mL of toluene at 70 °C, unless otherwise noted. [b] [Ln] = Half-sandwich rare-earth dialkyl complex; R = Me_2N-2-$CH_2C_6H_4$. [c] Yields of **3a** were determined by GC with tridecane as an internal standard. [d] Reaction was carried out at 50 °C. [e] Yield of the isolated product in parentheses. [f] Reaction was carried out with 0.5 mmol of 2,6-lutidine and 2 mmol of norbornene.

Zhaomin Hou, *ACIE*. *2013*, **52**, 4418

Entry	Olefin	[Y]	t [h]	Product	Yield [%][b]
1		$[C_5H_5YR_2]$	24		79
2		$[C_5Me_5YR_2]$	24		70
					
3	X = Me	$[C_5Me_5YR_2]$	24	X = Me	67
4	X = *t*Bu	$[C_5Me_5YR_2]$	24	X = *t*Bu	67
5	X = F	$[C_5Me_5YR_2]$	24	X = F	63
6	X = Cl	$[C_5Me_5YR_2]$	24	X = Cl	74
7[c]		$[C_5Me_5YR_2]$	24		69
8[c]		$[C_5Me_5YR_2]$	72		92
9		$[C_5H_5YR_2]$	24		97
10[d]		$[C_5H_5YR_2]$	24		65
11[d]		$[C_5H_5YR_2]$	24		41
12[d]		$[C_5H_5YR_2]$	24		51

Entry	Alkyl Pyridine	[Y]	t [h]	Product	Yield [%][b]
1		$[C_5H_5YR_2]$	6		97
2		$[C_5Me_5YR_2]$	4		92
3[c]		$[C_5Me_5YR_2]$	24		68
4		$[C_5H_5YR_2]$	6		98
5		$[C_5H_5YR_2]$	3		99
6		$[C_5H_5YR_2]$	12		95
7		$[C_5H_5YR_2]$	12		95
8		$[C_5Me_5YR_2]$	12		58
9		$[C_5H_5YR_2]$	2		93

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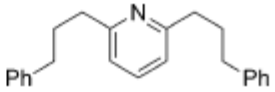
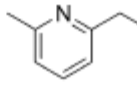
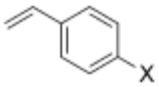
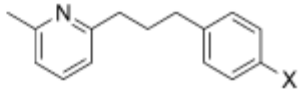
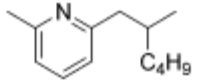
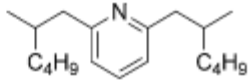
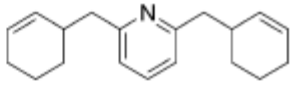
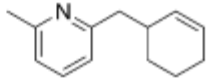
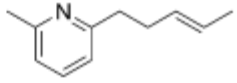
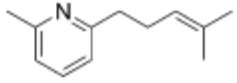
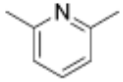
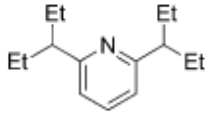
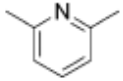
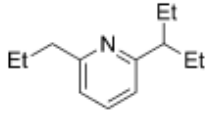
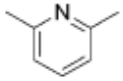
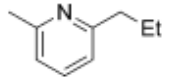
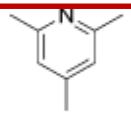
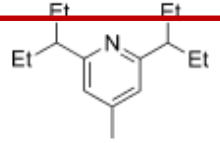
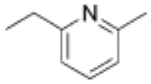
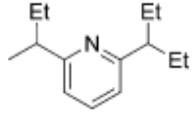
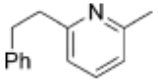
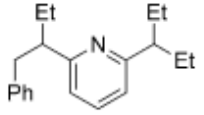
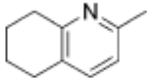
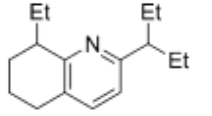
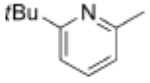
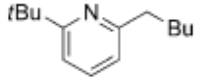
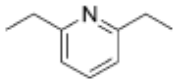
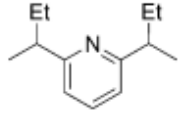
Entry	Olefin	[Y]	t [h]	Product	Yield [%][b]
1		$[C_5H_5YR_2]$	24		79
2		$[C_5Me_5YR_2]$	24		70
					
3	X = Me	$[C_5Me_5YR_2]$	24	X = Me	67
4	X = *t*Bu	$[C_5Me_5YR_2]$	24	X = *t*Bu	67
5	X = F	$[C_5Me_5YR_2]$	24	X = F	63
6	X = Cl	$[C_5Me_5YR_2]$	24	X = Cl	74
7[c]		$[C_5Me_5YR_2]$	24		69
8[c]		$[C_5Me_5YR_2]$	72		92
9		$[C_5H_5YR_2]$	24		97
10[d]		$[C_5H_5YR_2]$	24		65
11[d]		$[C_5H_5YR_2]$	24		41
12[d]		$[C_5H_5YR_2]$	24		51

Entry	Alkyl Pyridine	[Y]	t [h]	Product	Yield [%][b]
1		$[C_5H_5YR_2]$	6		97
2		$[C_5Me_5YR_2]$	4		92
3[c]		$[C_5Me_5YR_2]$	24		68
4		$[C_5H_5YR_2]$	6		98
5		$[C_5H_5YR_2]$	3		99
6		$[C_5H_5YR_2]$	12		95
7		$[C_5H_5YR_2]$	12		95
8		$[C_5Me_5YR_2]$	12		58
9		$[C_5H_5YR_2]$	2		93

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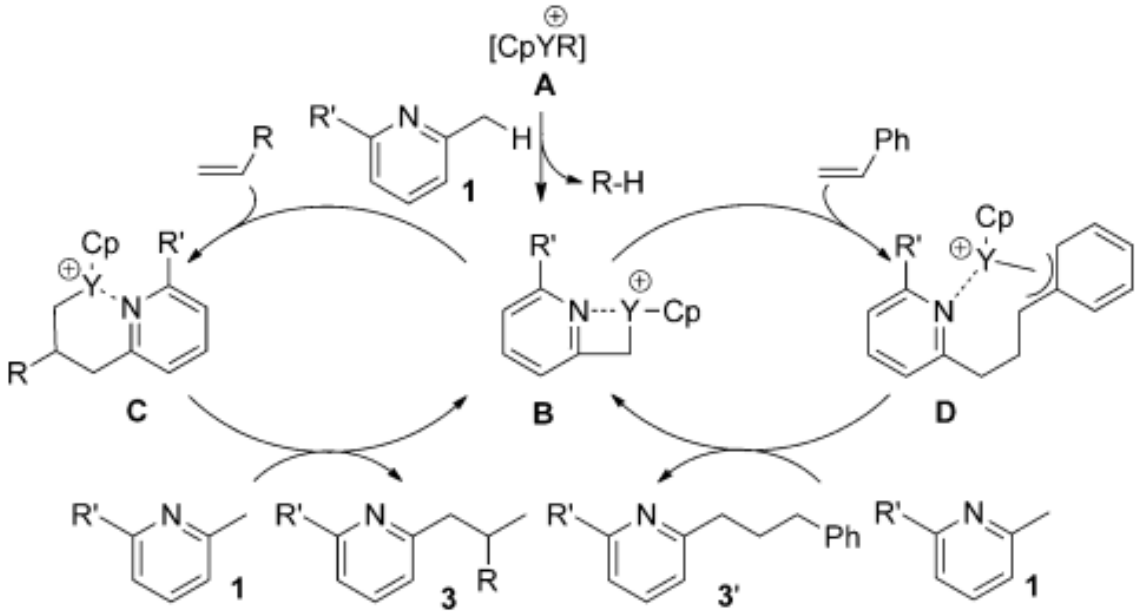
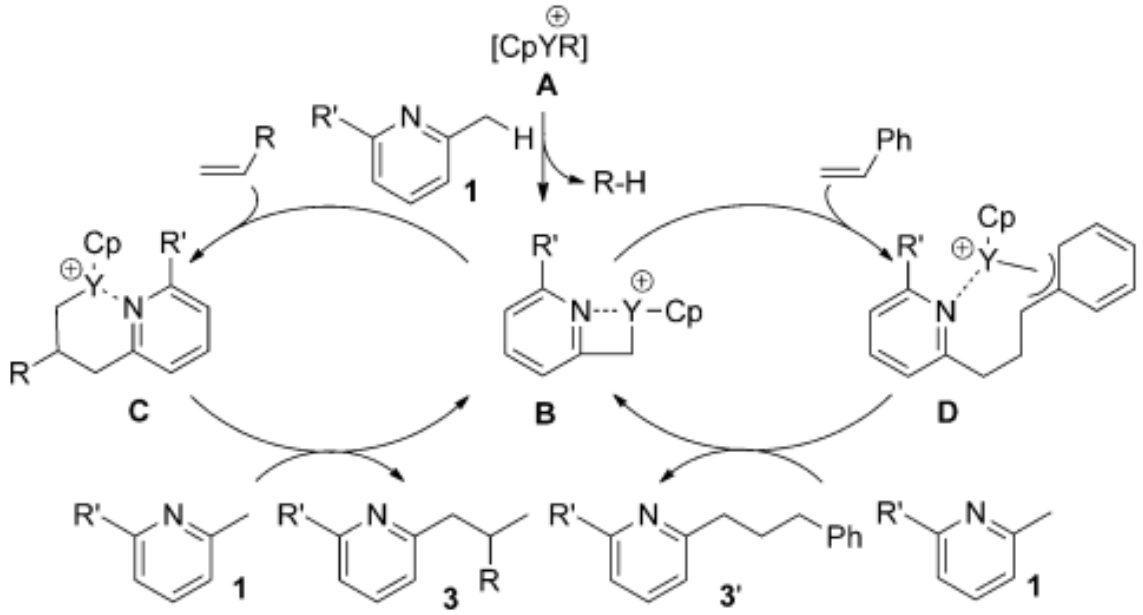
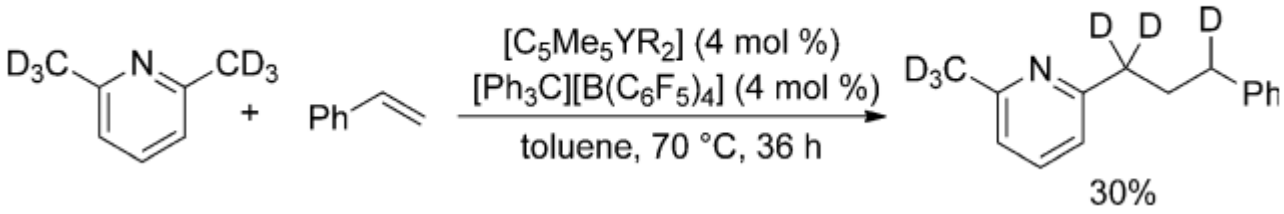
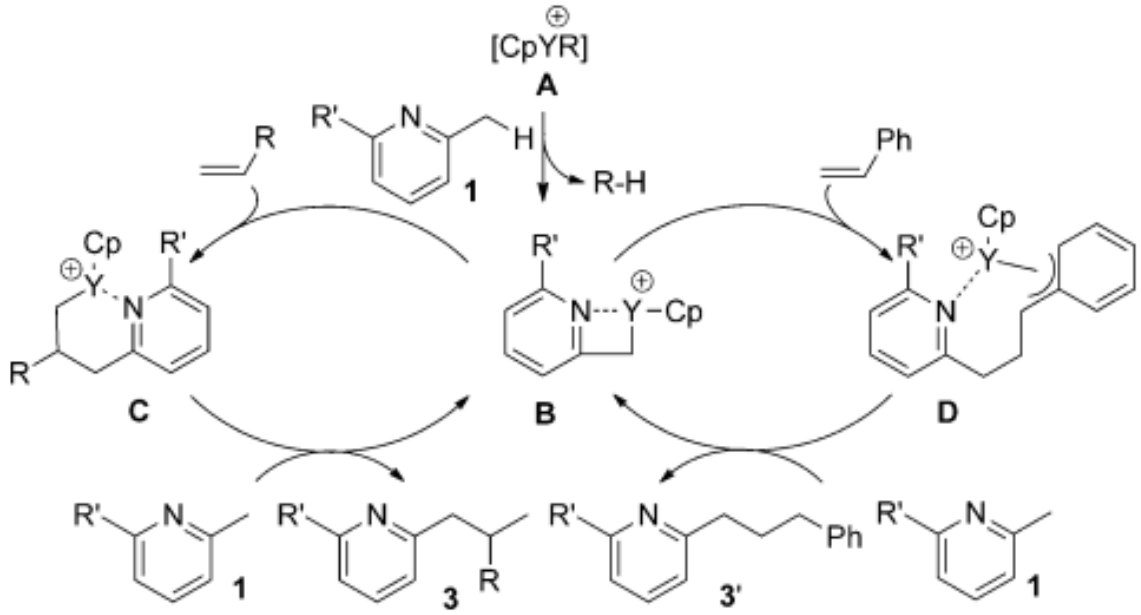
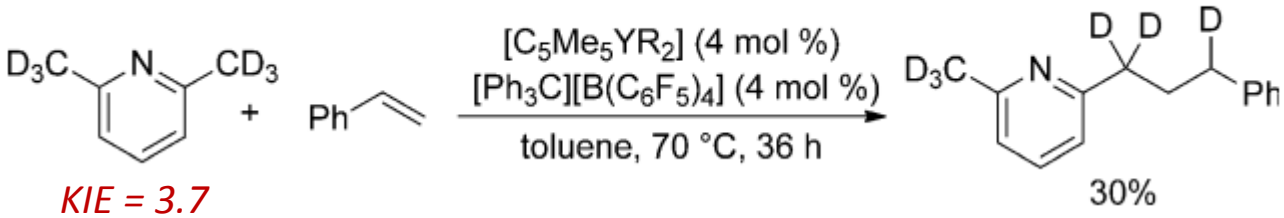

[CpYR]
A
R'
N
H
R-H
1
R
Ph
Cp
Y
C
B
D
3
3'

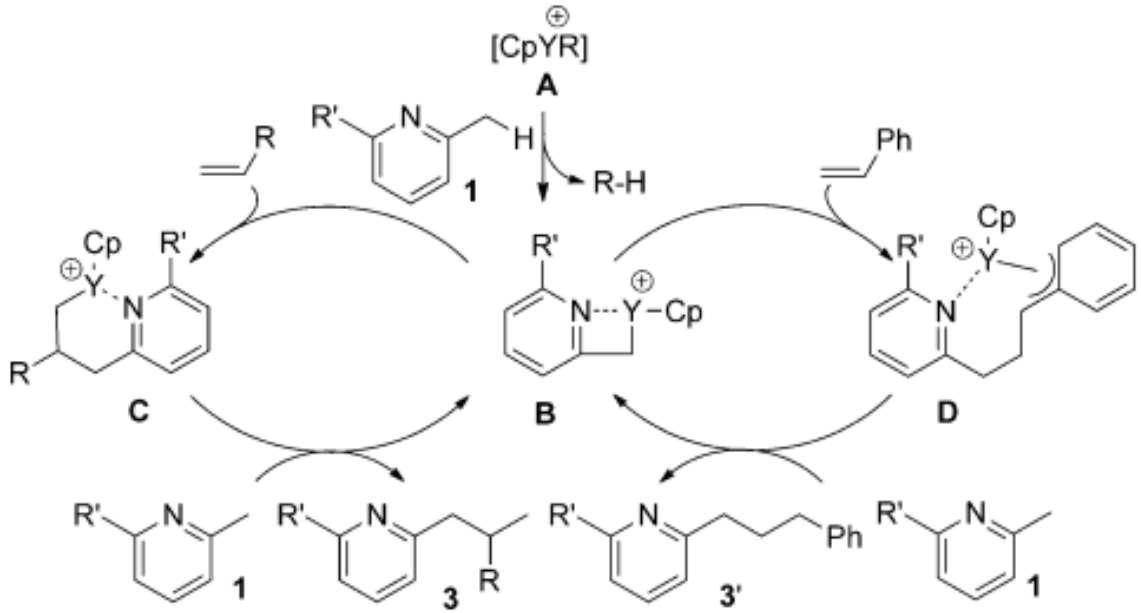

[CpYR]
A
R-H
1
C
B
D
3
3'

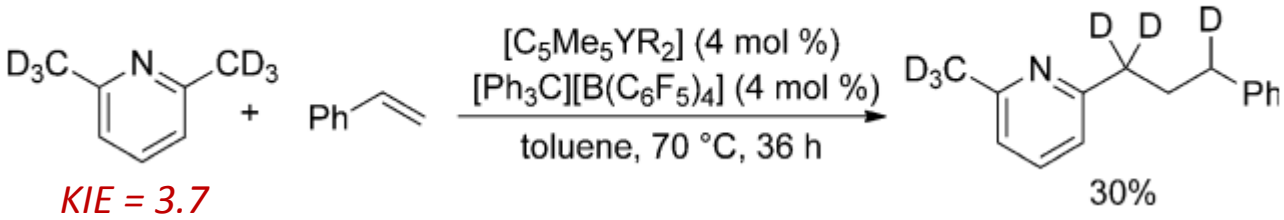

[C5Me5YR2] (4 mol %)
[Ph3C][B(C6F5)4] (4 mol %)
toluene, 70 °C, 36 h
30%


[CpYR]
A
R'
N
H
R
1
R-H
Ph
Cp
R'
Y
N
R
C
B
D
1
3
R
3'
Ph
1

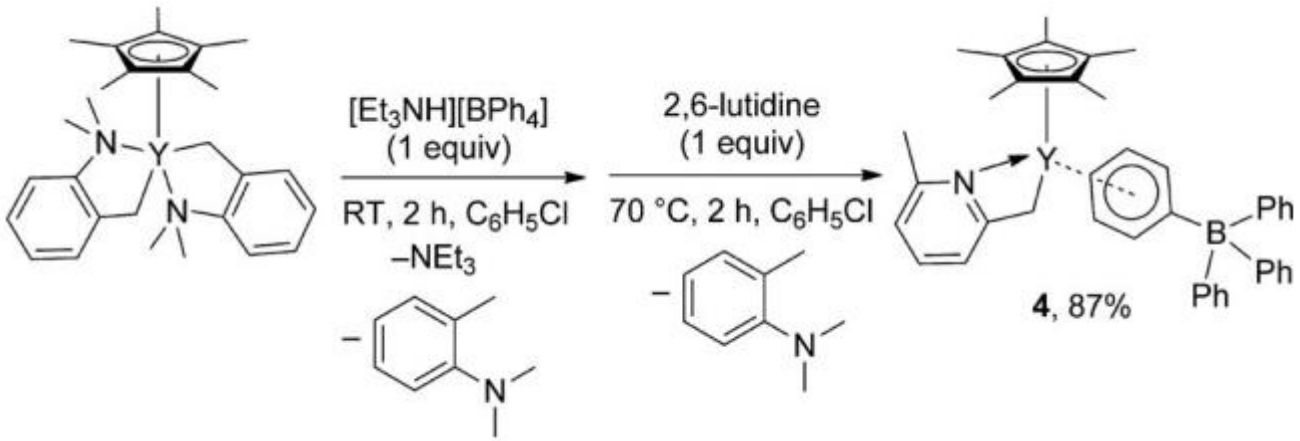

D3C
N
CD3
+
Ph
[C5Me5YR2] (4 mol %)
[Ph3C][B(C6F5)4] (4 mol %)
toluene, 70 °C, 36 h
D
D
D
D3C
N
Ph
30%

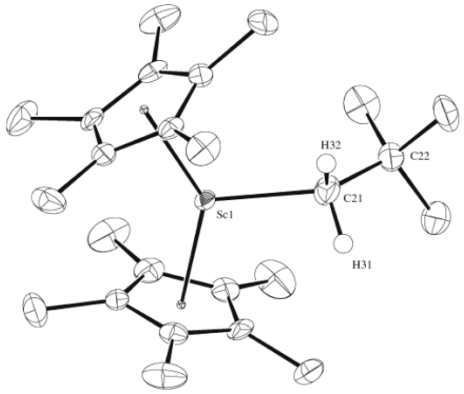
KIE = 3.7

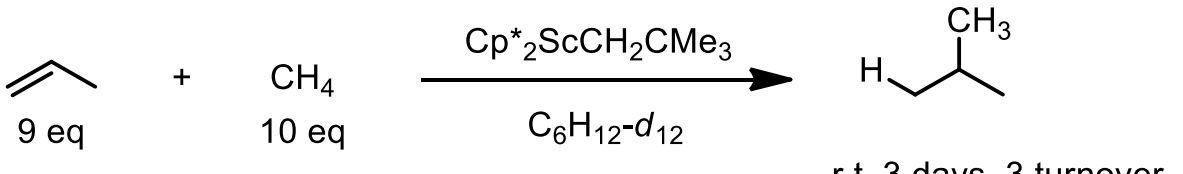

[CpYR]
A
R-H
1
B
C
D
3
3'


[C5Me5YR2] (4 mol %)
[Ph3C][B(C6F5)4] (4 mol %)
toluene, 70 °C, 36 h
30%

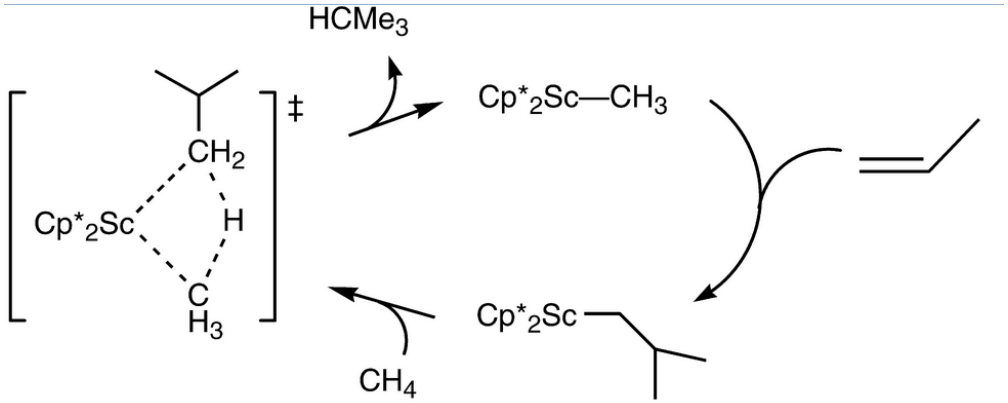
KIE = 3.7


[Et3NH][BPh4]
(1 equiv)
RT, 2 h, C6H5Cl
–NEt3
2,6-lutidine
(1 equiv)
70 °C, 2 h, C6H5Cl
4, 87%



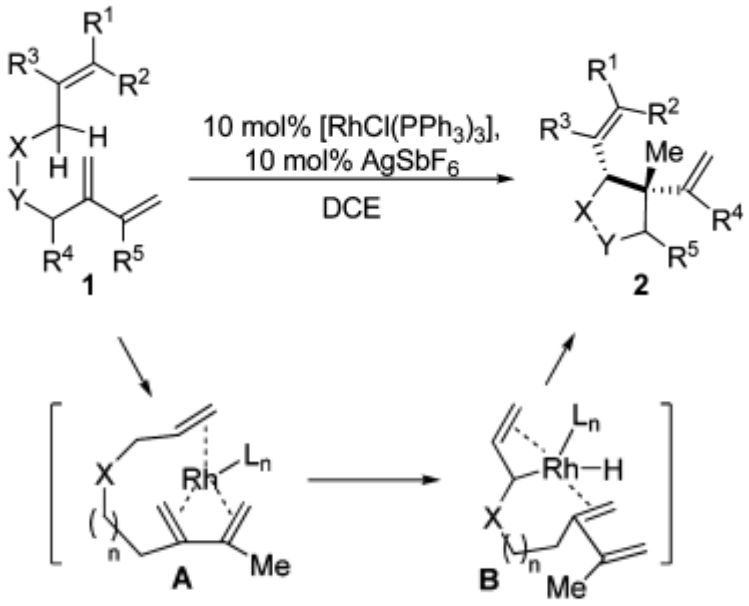


r.t, 3 days, 3 turnover
80 ^{o}C, O/N, 4 turnover

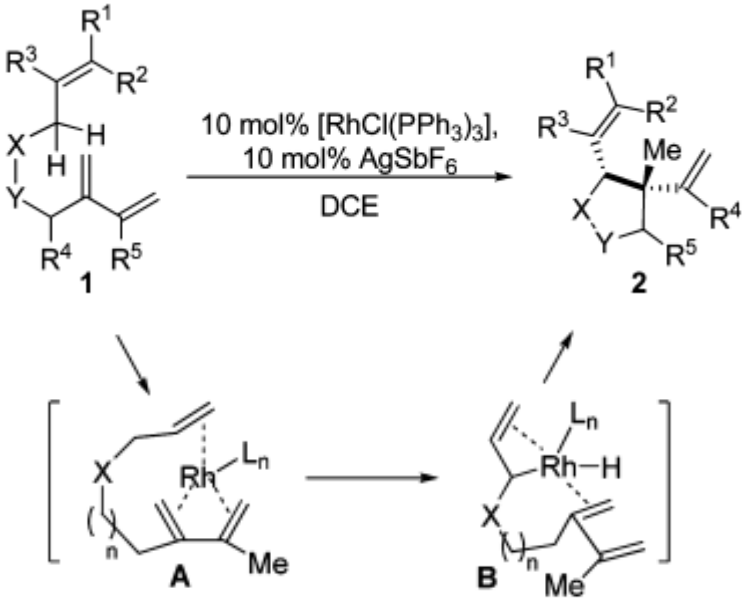


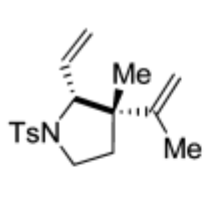
non-reactive substrates:
cis/trans-2-butene, 1-hexene, 1-butene, 2-methylpropene, norbornylene, and 2-butyne

T. Don Tilley *J. Am. Chem. Soc.*, **2003**, *125*, 7971

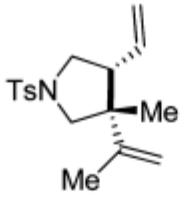


Zhi-Xiang Yu, *JACS*. *2010*, **132**, 4542

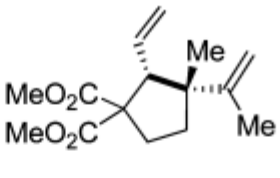




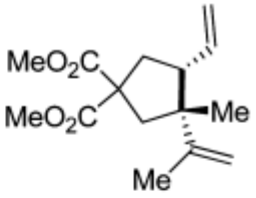
2a
65 °C, 2 h, 90%



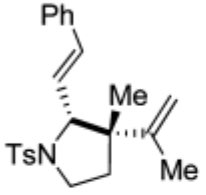
2b
70 °C, 2 h, 76%



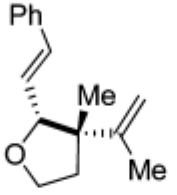
2c
80 °C, 2 h, 75%



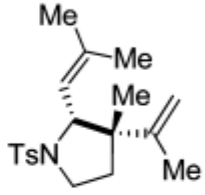
2d
70 °C, 2 h, 82%



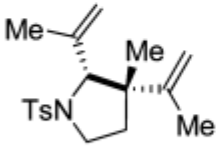
2e
80 °C, 24 h, 69%



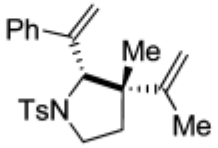
2f
60 °C, 3 h, 62%,
dr = 5:1



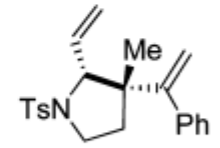
2g
80 °C, 30 h, 45%,
dr = 11:1



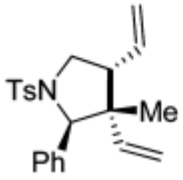
2h
80 °C, 12 h, 81%



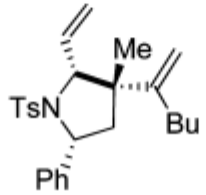
2i
80 °C, 20 h, 81%



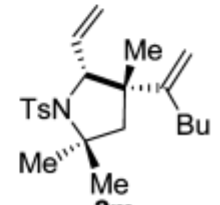
2j
65 °C, 2 h, 64%, dr = 7:1



2k
65 °C, 2 h, 70%

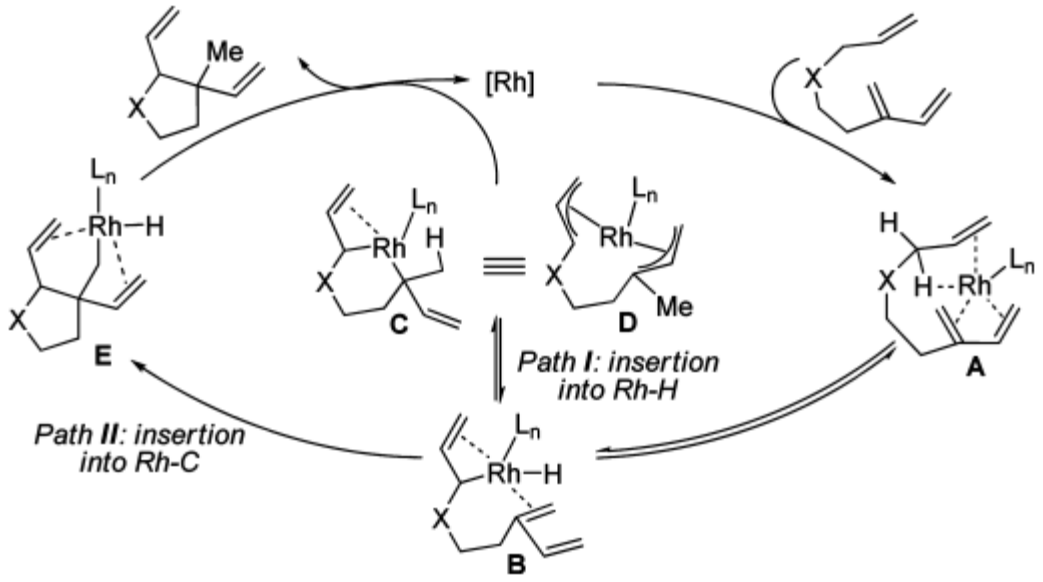


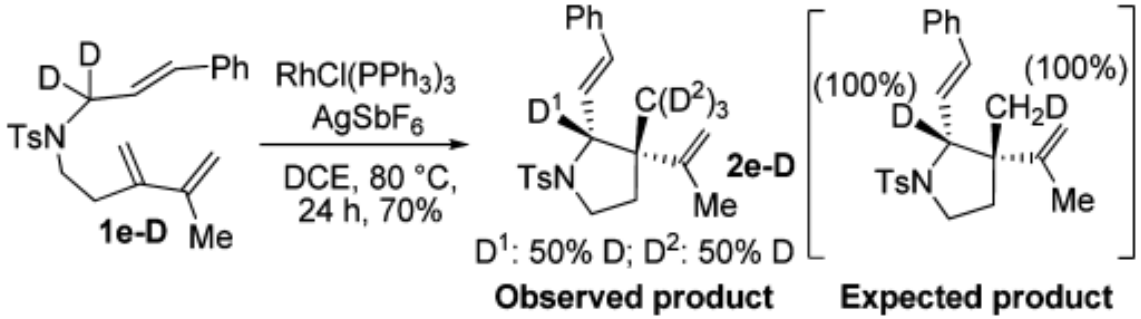
2l
60 °C, 2 h, 59%, dr = 15:1



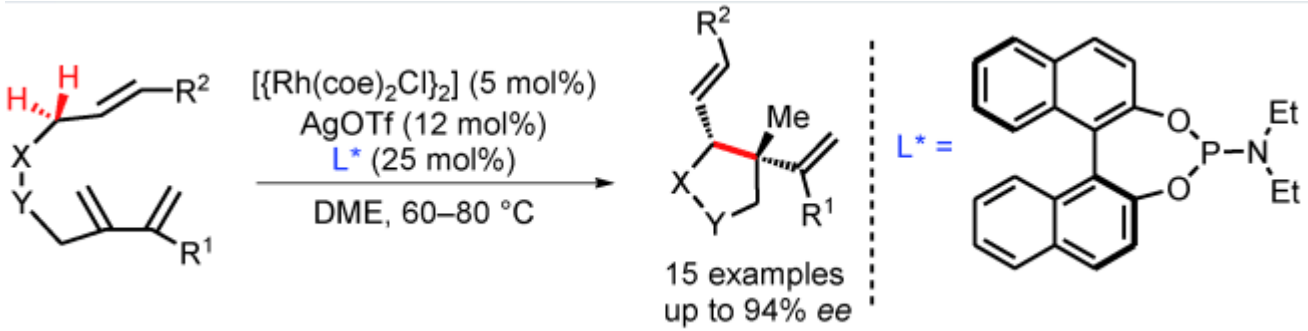
2m
60 °C, 2 h, 76%, dr = 8:1

Zhi-Xiang Yu, *JACS*. *2010*, **132**, 4542

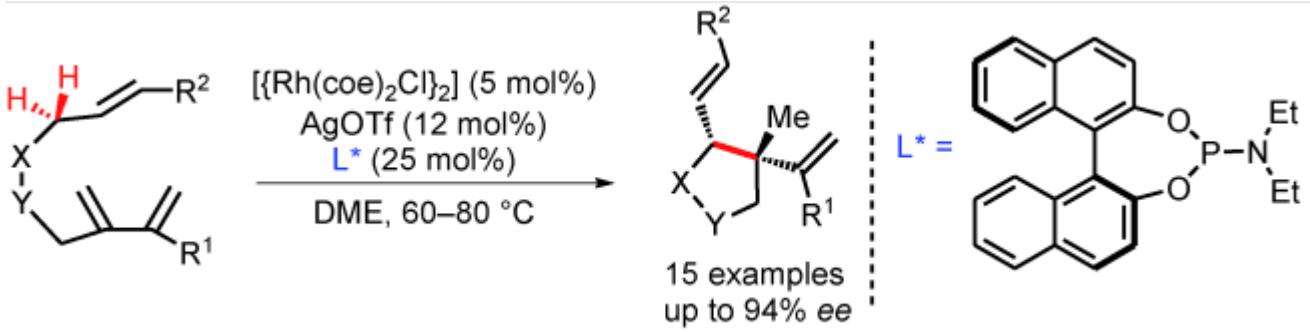




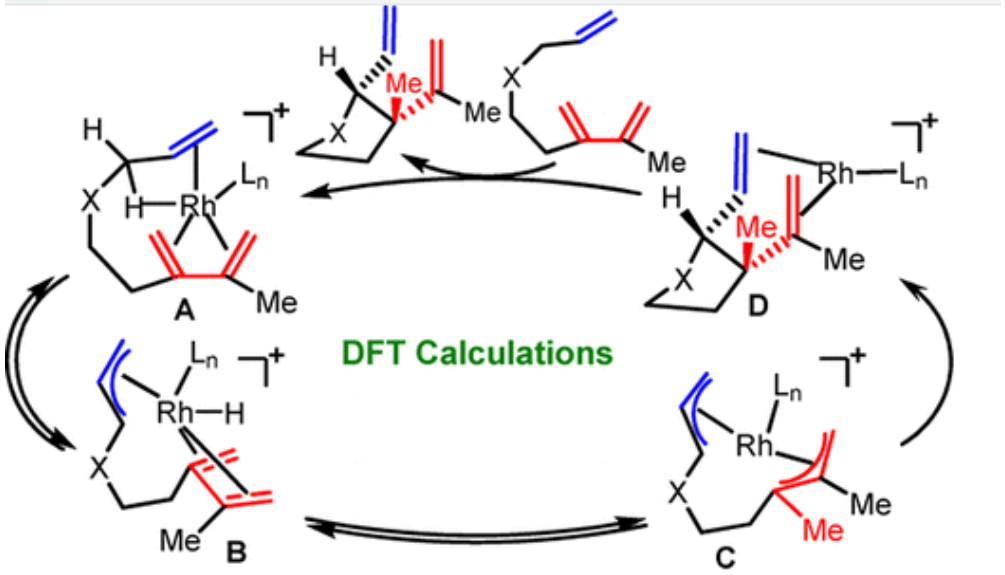
Zhi-Xiang Yu, *JACS*. *2010*, **132**, 4542



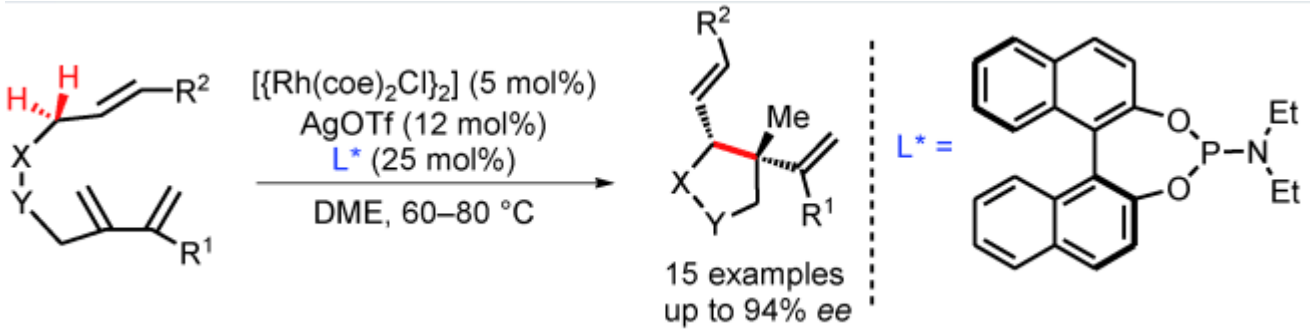
Zhi-Xiang Yu, *ACIE*. *2011*, **50**, 2144



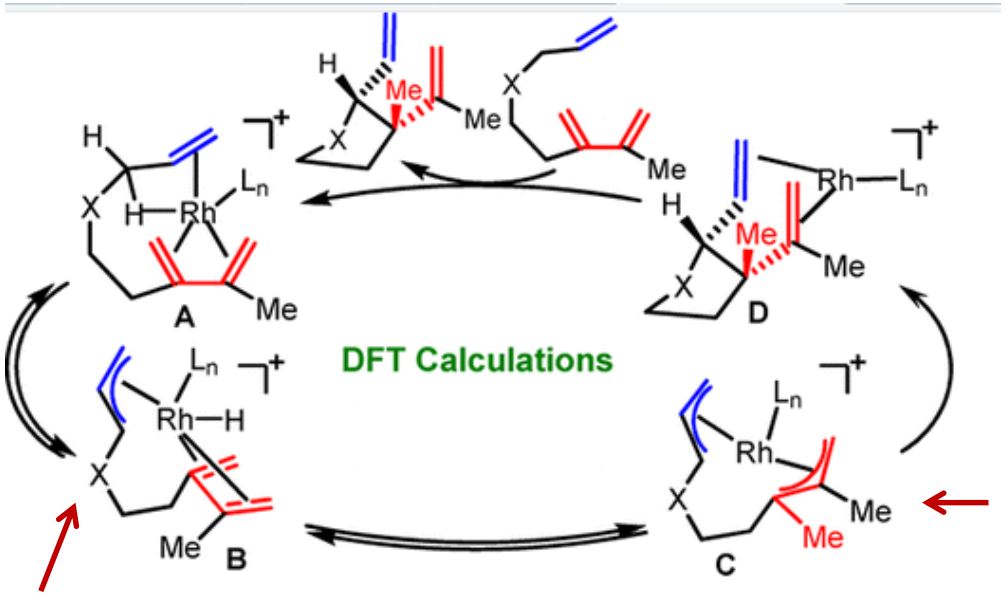
Zhi-Xiang Yu, *ACIE*. *2011*, **50**, 2144



Zhi-Xiang Yu, *Organometallics*, **2012**, *31*, 5185



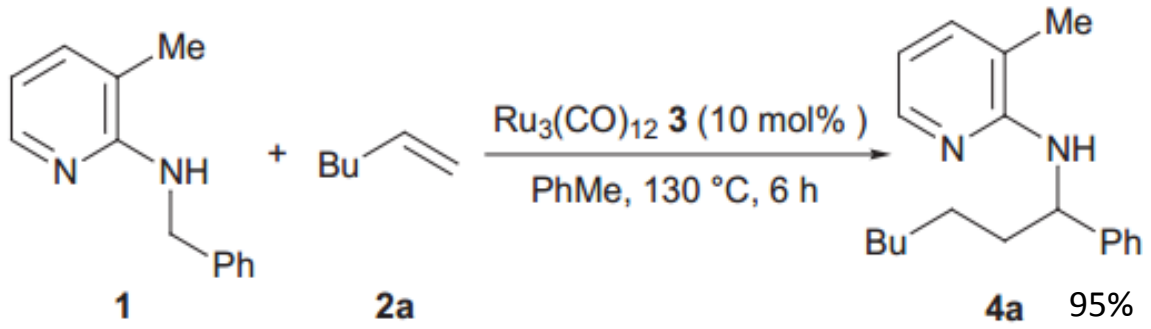
Zhi-Xiang Yu, *ACIE*. *2011*, **50**, 2144



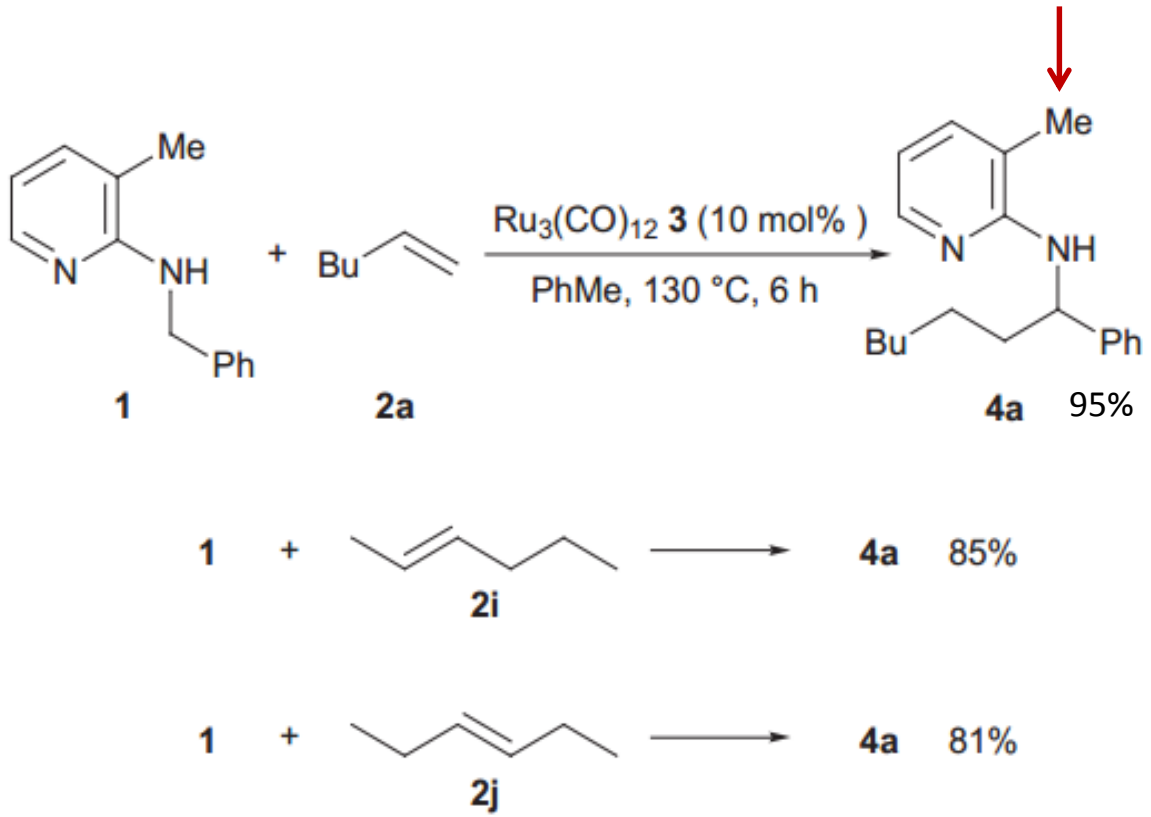
Bis-allylic Rh complex facilitate the reductive elimination

Diene coordination disfavored the double-bond isomerization

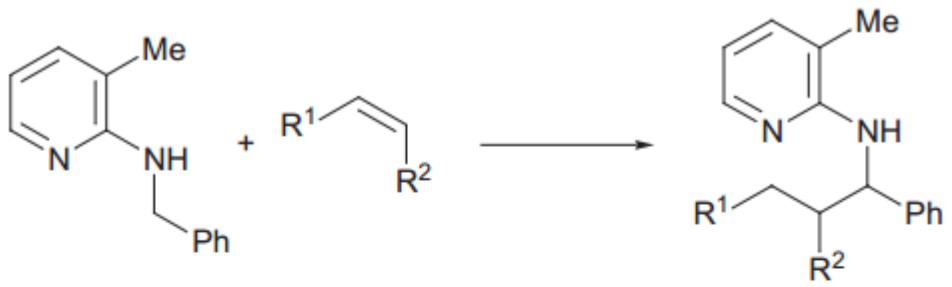
Zhi-Xiang Yu, *Organometallics*, **2012**, *31*, 5185



Chul-Ho Jun *Chem. Commun.*, **1998**, 1405



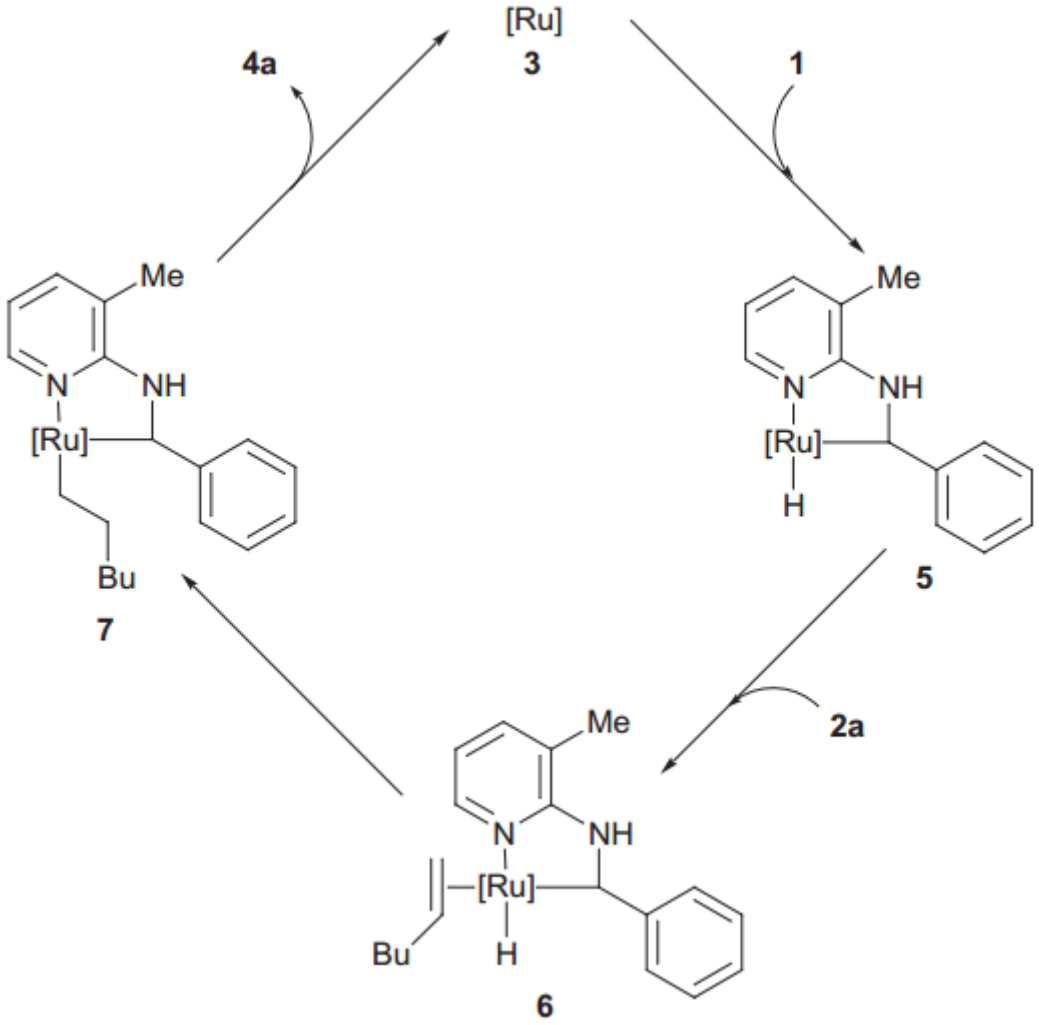
Chul-Ho Jun *Chem. Commun.*, **1998**, 1405

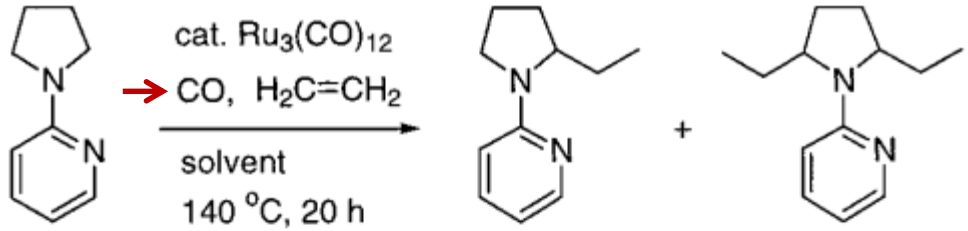


1 **2** **4**

Entry	Alkene	R^1	R^2	Product	Isolated yield (%)
1	**2a**	Bu	H	**4a**	95
2	**2b**	C_8H_{17}	H	**4b**	93
3	**2c**	Bu^t	H	**4c**	72
4	**2d**	Cyclohexyl	H	**4d**	75
5	**2e**	Ph	H	**4e**	70
6	**2f**	Bn	H	**4f**	85
7	**2g**	$-(CH_2)_3-$		**4g**	70
8	**2h**	$-(CH_2)_4$		**4h**	60

Chul-Ho Jun *Chem. Commun.*, **1998**, 1405


[Ru]
3
1
4a
2a
Me
N
NH
[Ru]
H
Bu
5
6
7

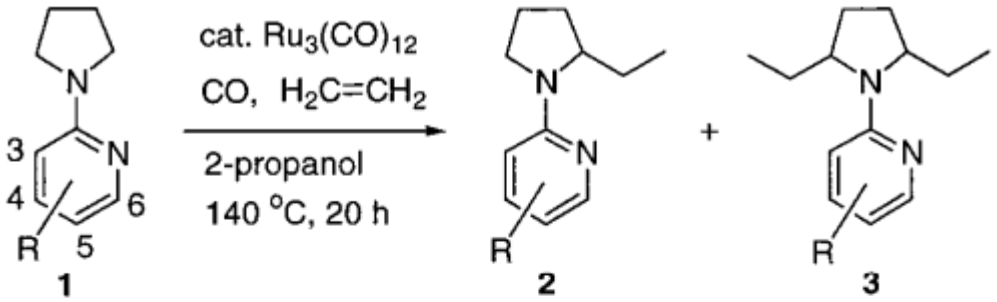


1a **2a** **3a**

entry	solvent	yields, %[b] **2a**	**3a**	recovery of **1a**
1	toluene	22	12	25
2	CH_3CN	27	0	55
3	THF	10	0	86
4	dioxane	0	0	nd[c]
5	DMF	0	0	nd[c]
6	DMSO	0	0	nd[c]
7	MeOH	14	31	9
8	EtOH	8	86	0
9	^{i}PrOH	0	92	0

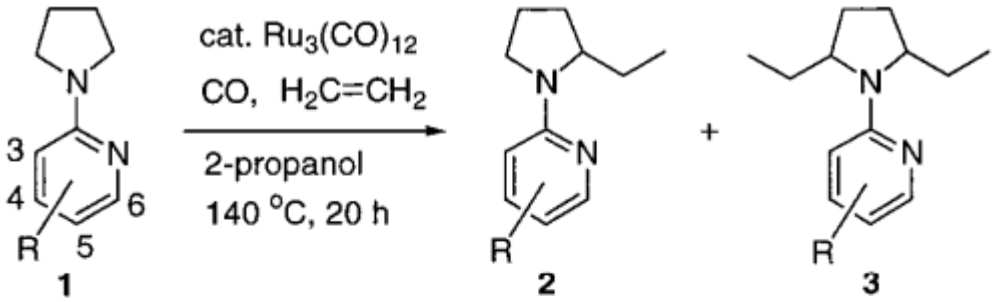
[a] Reaction conditions: **1a** (1 mmol), $Ru_3(CO)_{12}$ (0.08 mmol), ethylene (initial pressure 10 atm at 25 °C in a 50 mL stainless autoclave), CO (1 atm), solvent (2 mL) at 140 °C for 20 h. [b] Isolated yields based on **1a**. [c] **1a** was recovered, but the amount was not determined.

Shinji Murai *J. Am. Chem. Soc.*, **2001**, *123*, 10935



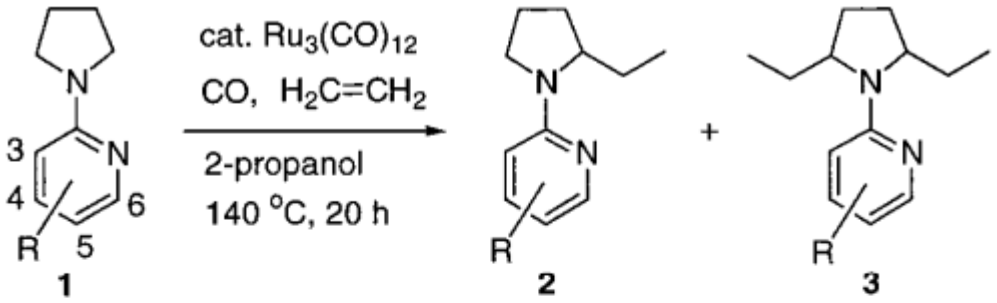
R	yields, %[b,c] 2	3	recovery of **1**
H (**1a**)	0	92 (54:46)	0
3-Me (**1b**)	0	76 (70:30)	0
4-Me (**1c**)	0	90 (66:34)	0
5-Me (**1d**)	0	93 (61:39)	0
6-Me (**1e**)	39	11 (52:48)	35
3-OMe (**1f**)	0	86 (52:48)	0
6-OMe (**1g**)	11	0	77
5-CF_3 (**1h**)	0	94 (63:37)	0
4-COOMe (**1i**)	no reaction		nd

Shinji Murai *J. Am. Chem. Soc.*, **2001**, *123*, 10935

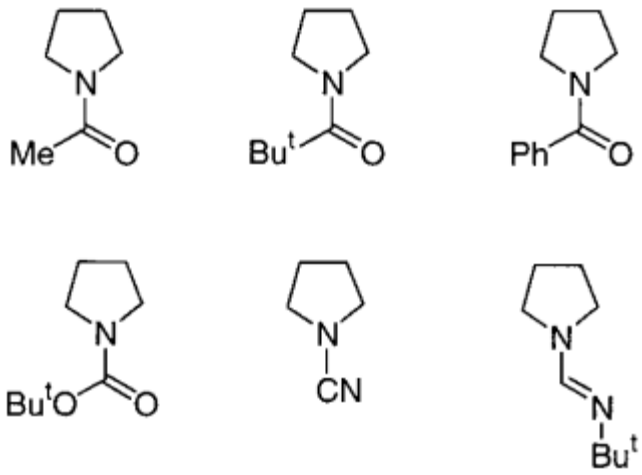


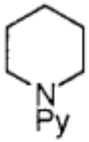
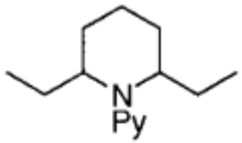
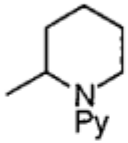
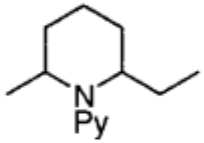
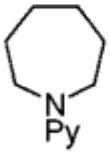
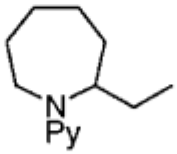
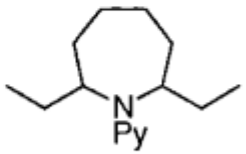
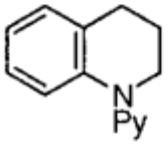
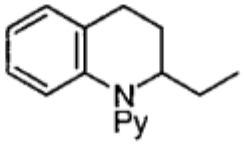
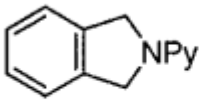
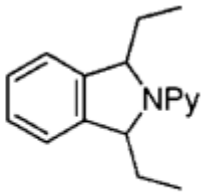
R	yields, %[b,c] 2	3	recovery of 1
H (**1a**)	0	92 (54:46)	0
3-Me (**1b**)	0	76 (70:30)	0
4-Me (**1c**)	0	90 (66:34)	0
5-Me (**1d**)	0	93 (61:39)	0
6-Me (**1e**)	39	11 (52:48)	35
3-OMe (**1f**)	0	86 (52:48)	0
6-OMe (**1g**)	11	0	77
5-CF_3 (**1h**)	0	94 (63:37)	0
4-COOMe (**1i**)	no reaction		nd

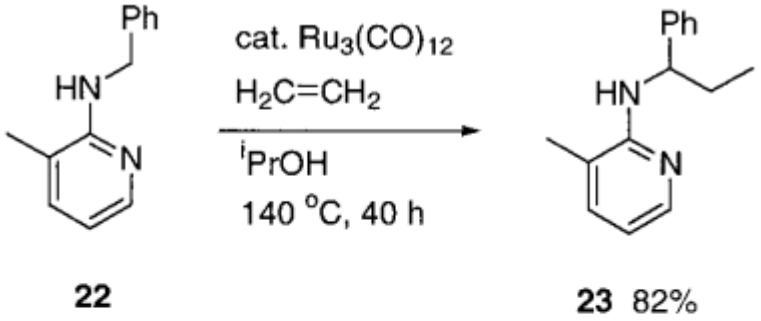
Shinji Murai *J. Am. Chem. Soc.*, **2001**, *123*, 10935



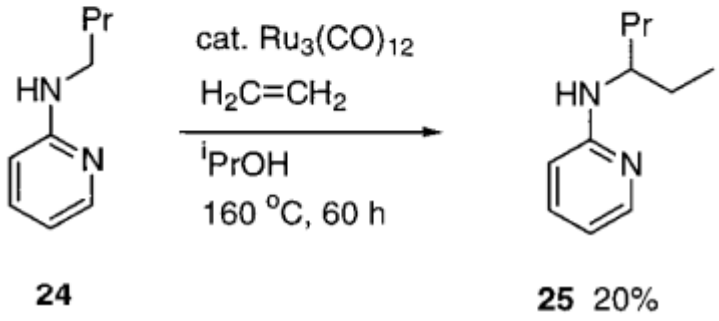
R	yields, %[b,c] 2	3	recovery of 1
H (**1a**)	0	92 (54:46)	0
3-Me (**1b**)	0	76 (70:30)	0
4-Me (**1c**)	0	90 (66:34)	0
5-Me (**1d**)	0	93 (61:39)	0
6-Me (**1e**)	39	11 (52:48)	35
3-OMe (**1f**)	0	86 (52:48)	0
6-OMe (**1g**)	11	0	77
5-CF_3 (**1h**)	0	94 (63:37)	0
4-COOMe (**1i**)	no reaction		nd



entry	substrate	products [b,c]		
1	 **4**	 **5** 73% (60/40)		
2	 **6**	 **7** 75% (63/37)		
3	 **8**	 **9** 47%	 **10** 14% (52:48)	
4	 **11**	 **12** 73%		
5	 **13**		 **14** 90% (80:20)	



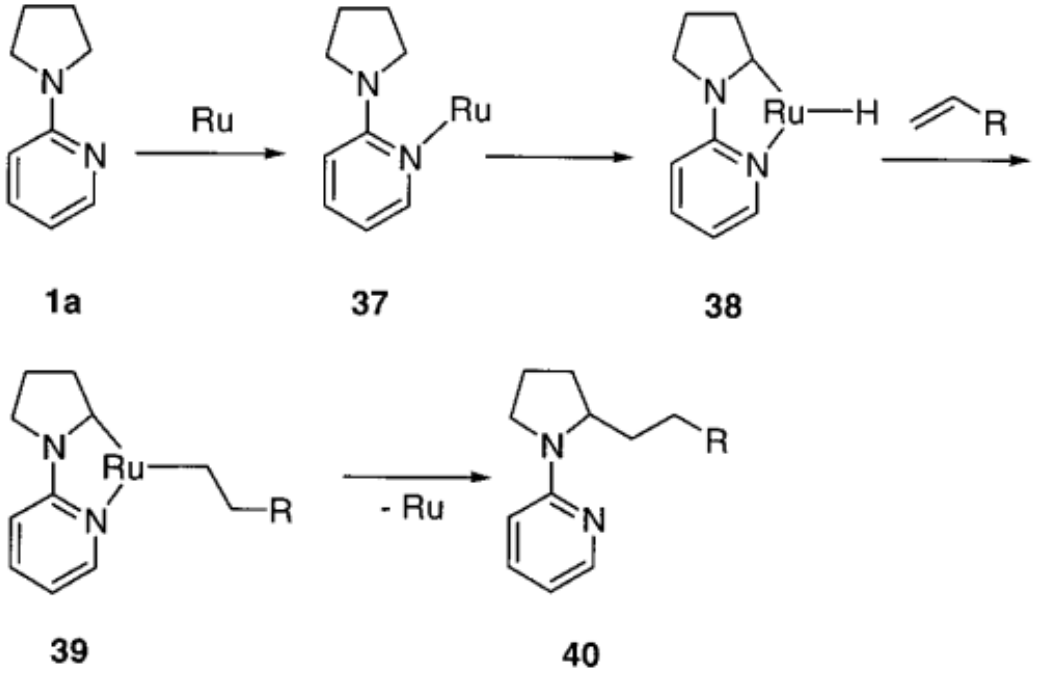
22 **23** 82%



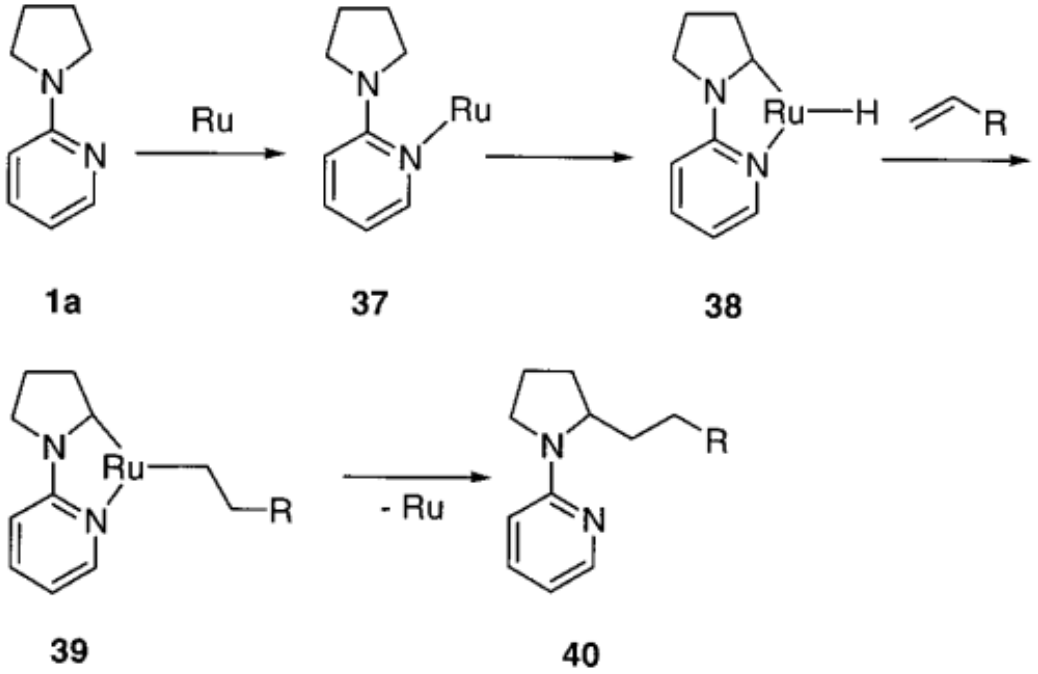
24 **25** 20%

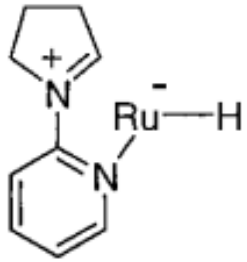
Olefin part substrate scope is similar as Jun's

Shinji Murai *J. Am. Chem. Soc.*, **2001**, *123*, 10935

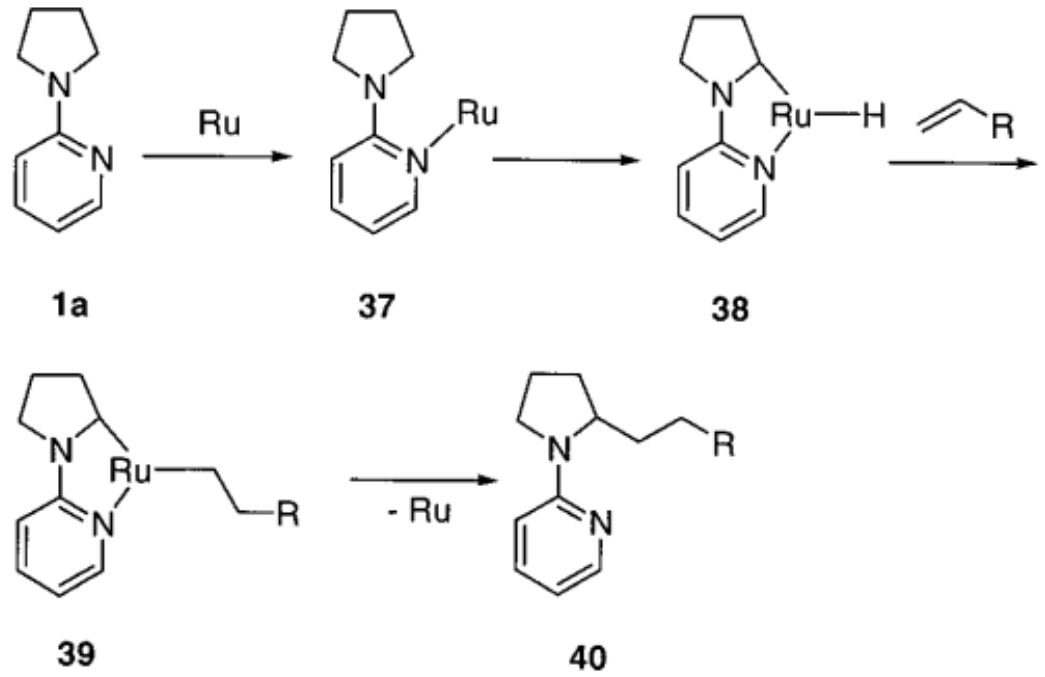


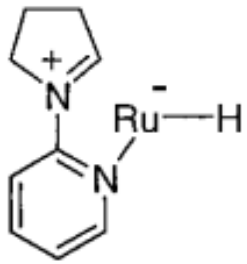
Shinji Murai *J. Am. Chem. Soc.*, **2001**, *123*, 10935





Shinji Murai *J. Am. Chem. Soc.*, **2001**, *123*, 10935

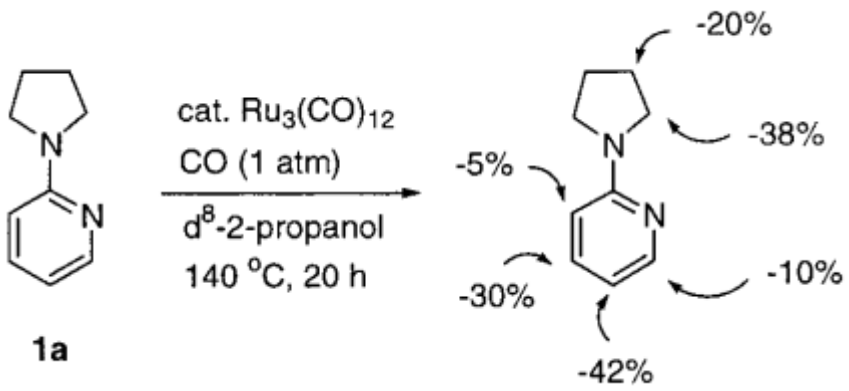




1) H/D exchange experiment

" provided good evidence for the reversibility of C-H bonds between substrates and reactants (alkenes), indicating that the cleavage of C-H bonds is not the rate-determining step"

2)



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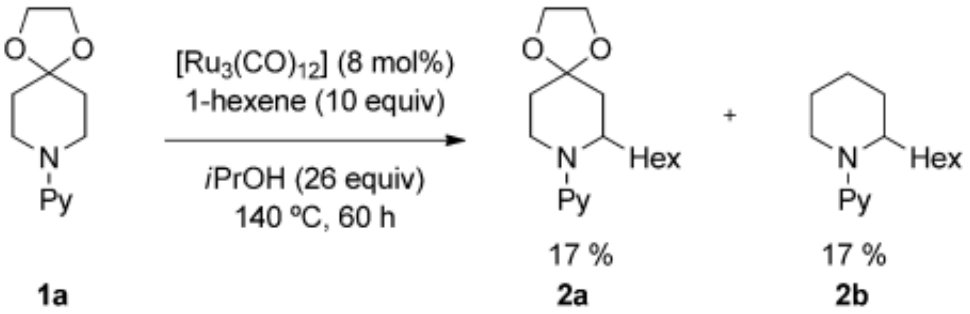


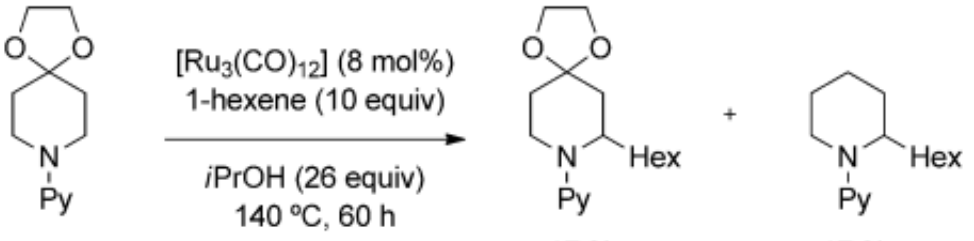
1a

2a

2b

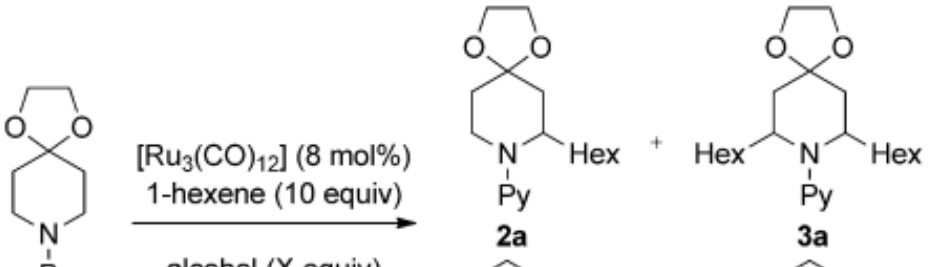
Py = pyridin-2-yl

Bert U. W. Maes *Chem. Eur. J.* **2012**, *18*, 10393



1a **2a** **2b**

Py = pyridin-2-yl



1a **2a** **3a** **1b** **2b**

Py = pyridin-2-yl

Entry	Alcohol	X	**1a**[a]	**2a**[a]	**3a**[a,b]	**1b**[a]	**2b**[a]
1	*n*BuOH	26	53	40	0	2	5
2	*i*PrOH	26	61	23	0	7	9
3	2,4-dimethyl-3-pentanol	26	57	39	4	0	0
4	*t*BuOH	26	90	10	0	0	0
5	2,4-dimethyl-3-pentanol[c]	10	71	27	2	0	0
6	2,4-dimethyl-3-pentanol	10	45	49	6	0	0
7	2,4-dimethyl-3-pentanol	5	38	54	8	0	0
8	2,4-dimethyl-3-pentanol	2.5	50	45	5	0	0

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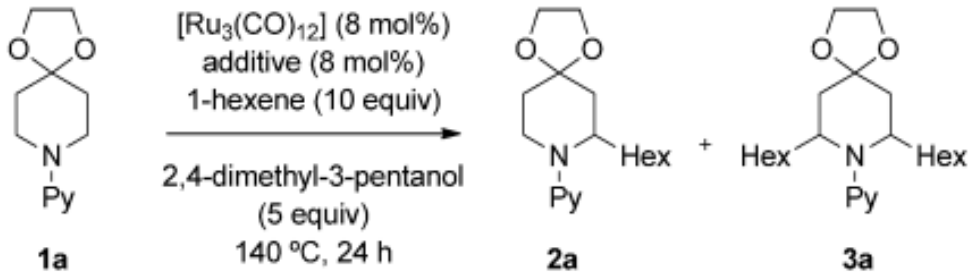
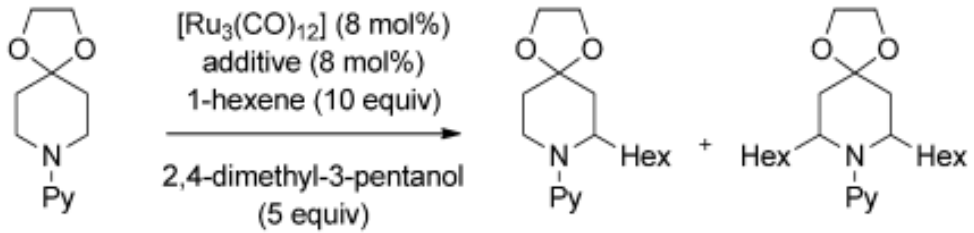


Py = pyridin-2-yl

Entry	Additive	pK_a	**1a**[a]	**2a**[a]	**3a**[a,b]
1	–	–	38	54	8
2	AcOH	3.58	18	63	19
3	PivOH	5.01	26	60	14
4[c,d]	*trans*-1,2-Cy(COOH)$_2$	4.18, 5.93	7	65	28
5	*cis*-1,2-Cy(COOH)$_2$	4.34, 6.76	17	64	19
6	(4-MeO)C$_6$H$_4$COOH	4.53	25	60	15
7	PhCOOH	4.20	23	61	16
8	(4-F)C$_6$H$_4$COOH	4.14	17	62	21
9	(3,4,5-tri-F)C$_6$H$_2$COOH	3.46	11	59	30
10	C$_6$F$_5$COOH	1.60	25	60	15
11	phthalic acid	2.98, 5.28	90	10	0
12	*p*-TsOH	1.99	57	40	3
13	Py·HCl	5.21	46	47	7
14	Et$_3$N·HCl	10.75	48	46	6
15	AcOK	–	62	35	3
16	(3,4,5-tri-F)C$_6$H$_2$COOK	–	83	16	1

Bert U. W. Maes *Chem. Eur. J.* **2012**, *18*, 10393



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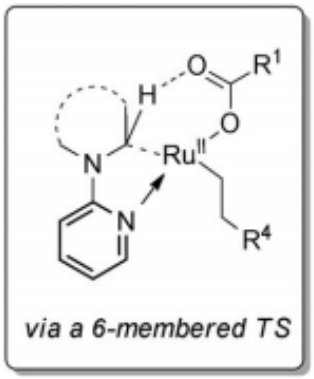
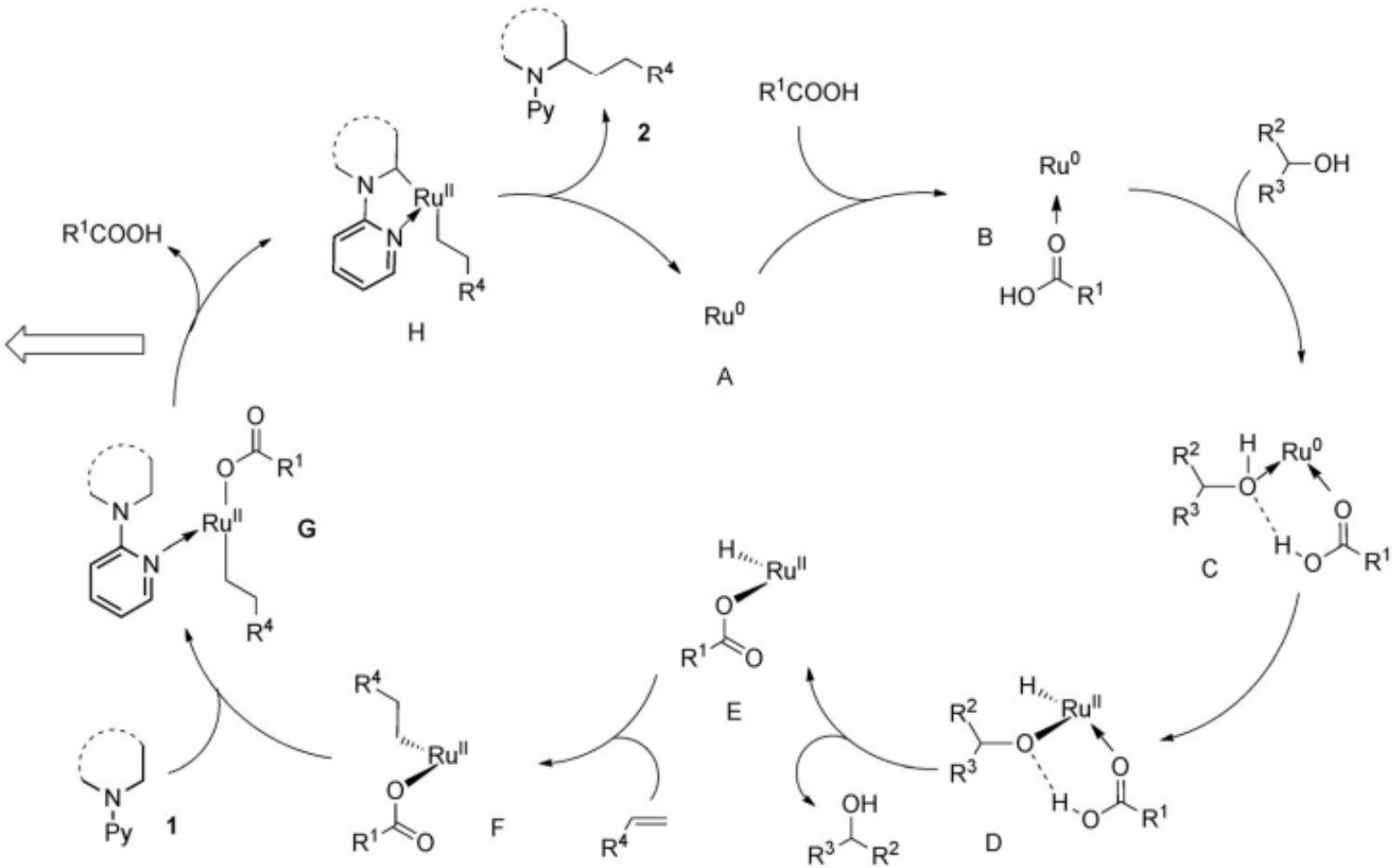
13	Py·HCl	5.21	46	47	7
14	Et$_3$N·HCl	10.75	48	46	6
15	AcOK	–	62	35	3
16	(3,4,5-tri-F)C$_6$H$_2$COOK	–	83	16	1

Bert U. W. Maes *Chem. Eur. J.* **2012**, *18*, 10393

“ carboxylic acid / alcohol has a significant effect on catalyst initiation ”





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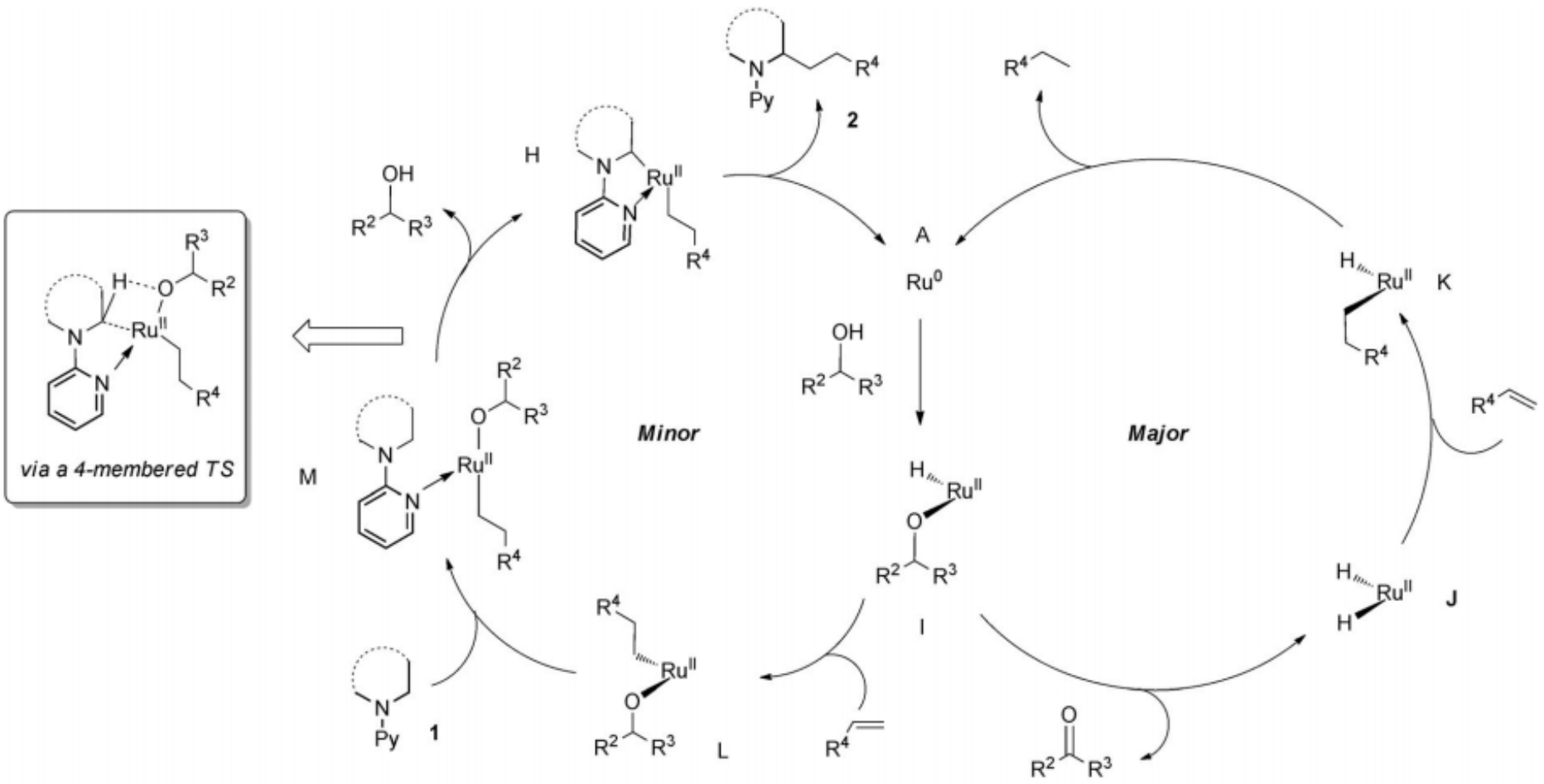

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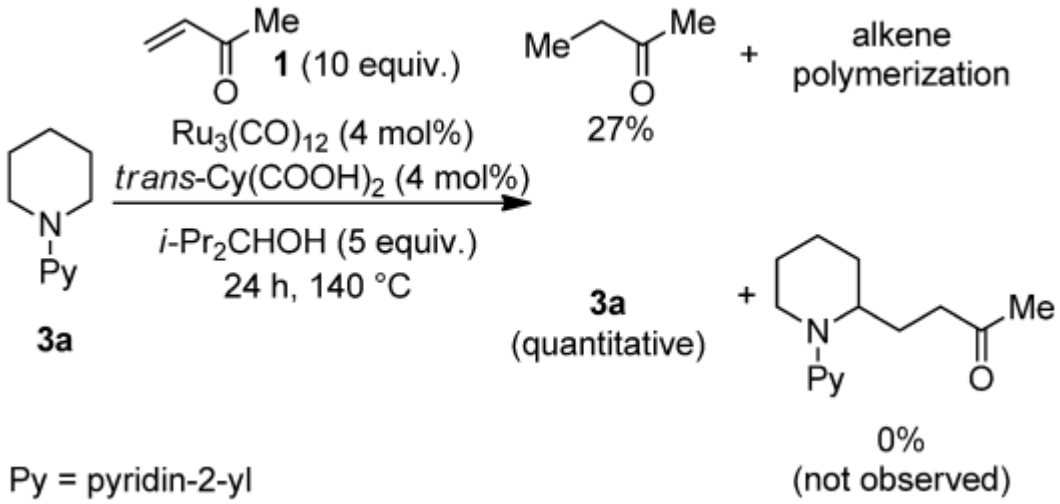

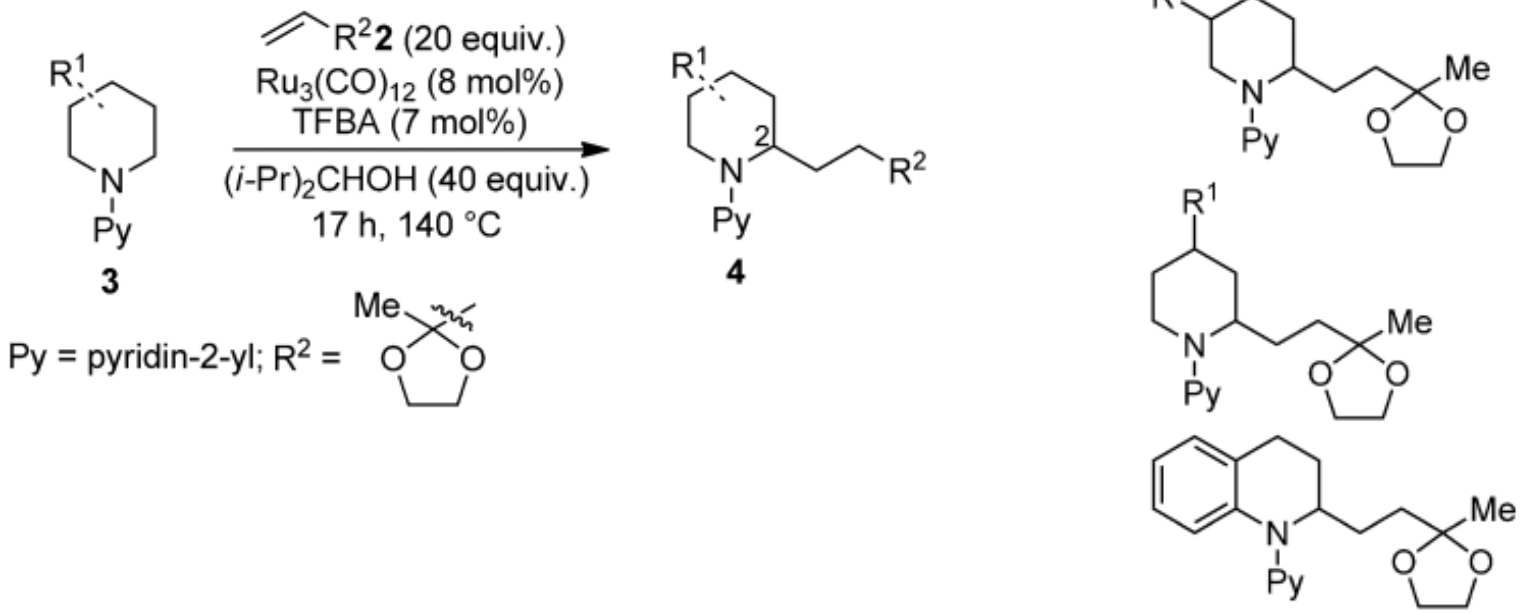

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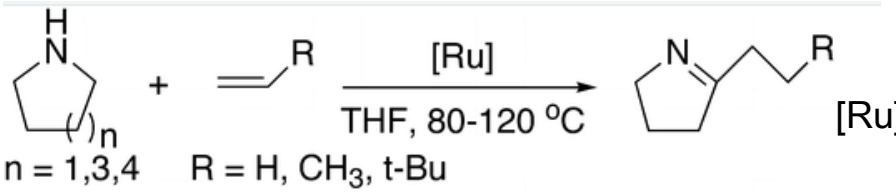
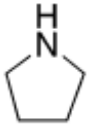
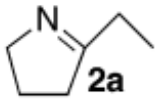
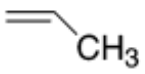
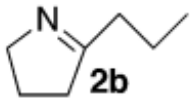
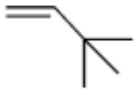
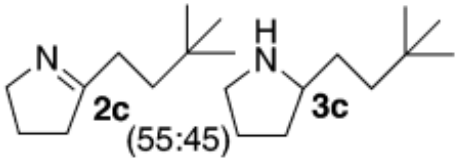
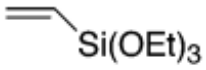
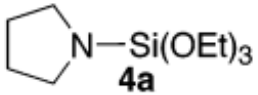
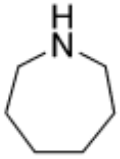
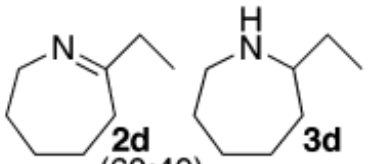
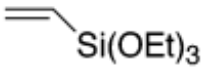
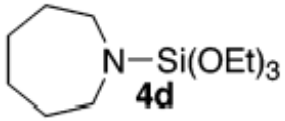
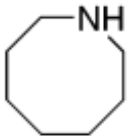
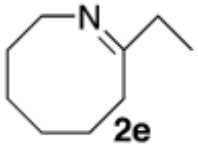


n = 1,3,4 R = H, CH_3, t-Bu

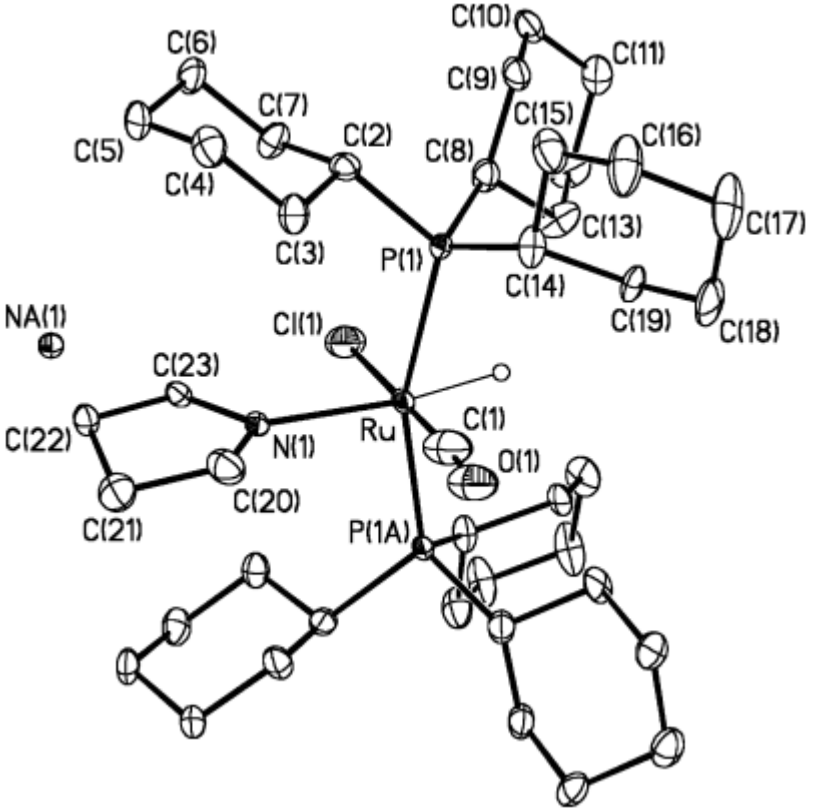
[Ru] = $(PCy_3)_2(CO)RuHCl$

entry	amine	alkene	product (s)	**1** (mol %)	temp (°C)	t (h)	yield (%)[b]
1		$H_2C{=}CH_2$	 **2a**	5	80	24	86 (61)
2			 **2b**	10	120	24	51
3			 **2c** (55:45) **3c**	10	120	24	29
4			 **4a**	5	120	20	88 (82)
5		$H_2C{=}CH_2$	 **2d** (60:40) **3d**	15	80	24	87 (51)
6			 **4d**	5	120	20	88
7		$H_2C{=}CH_2$	 **2e**	3	70	16	76

Chae S. Yi *Organometallics* **2004**, *23*, 5392

1 = $(PCy_3)_2(CO)RuHCl$

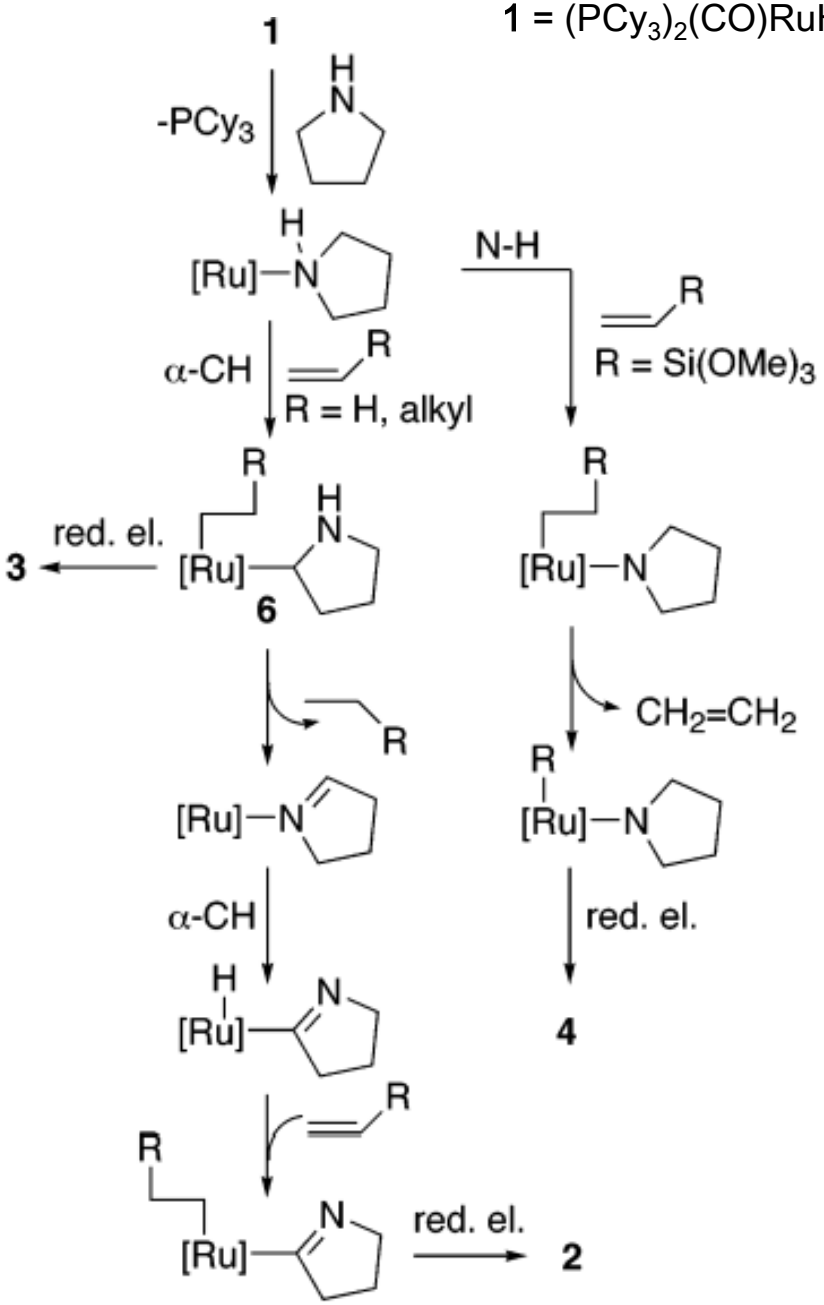
1)



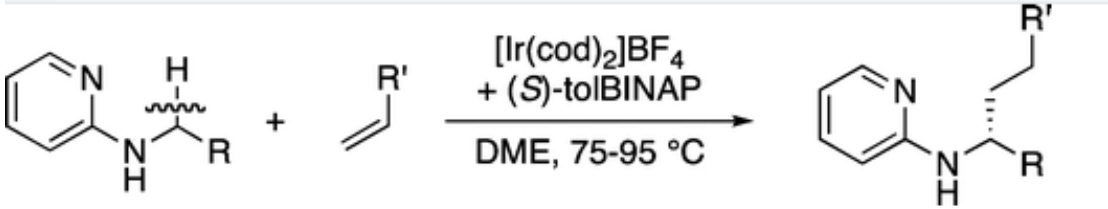
catalytic active

2) $k_{NH}/k_{ND} = 1.9$

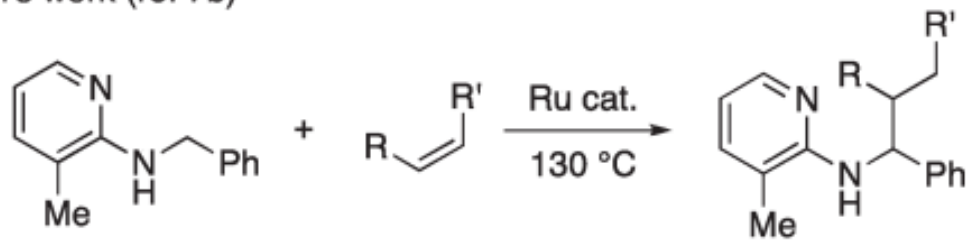
(consistent with a rate-limiting N-H bond activation step)



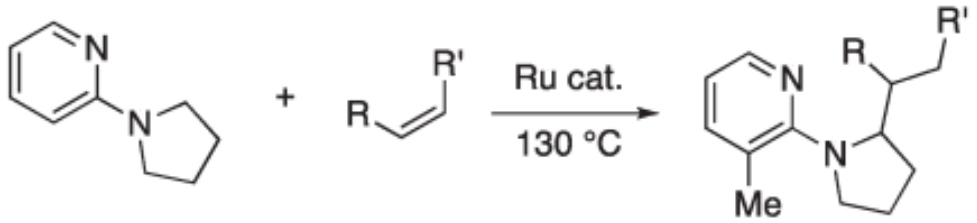
Chae S. Yi *Organometallics* **2004**, *23*, 5392



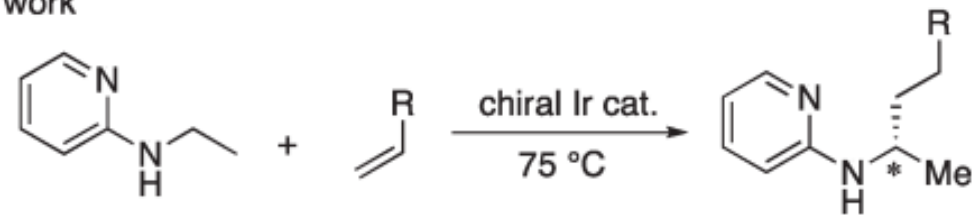
Jun's work (ref 7b)



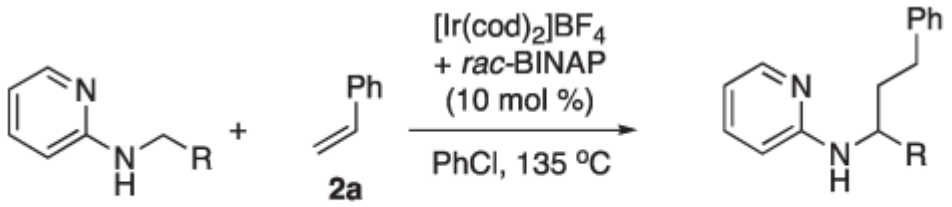
Chatani's work (ref 7c)



This work



Takanori Shibata *Org. Lett.*, **2011**, *13*, 4692



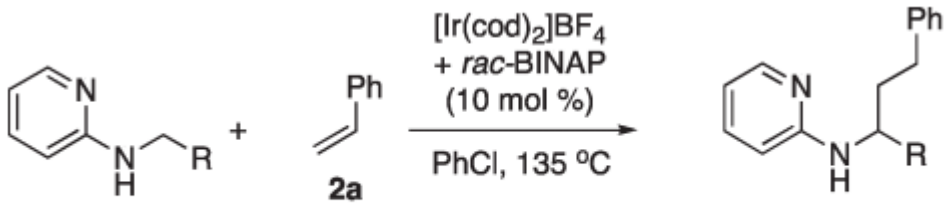
entry	X	chiral ligand	yield (%)[b]	*ee* (%)
1	BF_4	(*S*)-BINAP	37	70
2	BF_4	(*S*)-tolBINAP	62	80
3	BF_4	(*S*)-xylylBINAP	75	10
4	BF_4	(*S*)-H_8–BINAP	81	56
5	BF_4	(*R*)-DM-H_8–BINAP	84	–37
6	OTf	(*S*)-tolBINAP	48	81
7	PF_6	(*S*)-tolBINAP	24	74
8	BARF	(*S*)-tolBINAP	9	40
9[c]	BF_4	(*S*)-tolBINAP	76	88
10[d]	BF_4	(*S*)-tolBINAP	75	86

[a] Conditions: 2-(ethylamino)pyridine (**1**) (0.1 mmol), styrene (0.8 mmol), PhCl (0.2 mL), unless otherwise noted. [b] Isolated yield. [c] DME was used as a solvent at 75 °C for 48 h. [d] Less amount of styrene (0.3 mmol) was used, and DME was used as a solvent at 85 °C for 72 h.

For substrate scope:
R = Me, Et
Olefin = styrene, diene,

ee = 61-90%
terminal olefin's yield is low

Takanori Shibata *Org. Lett.*, **2011**, *13*, 4692



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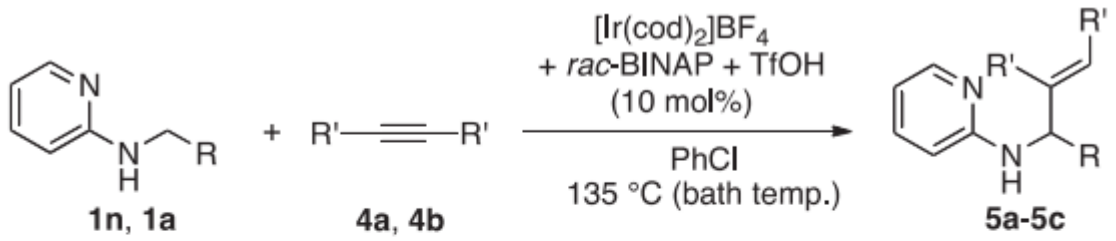
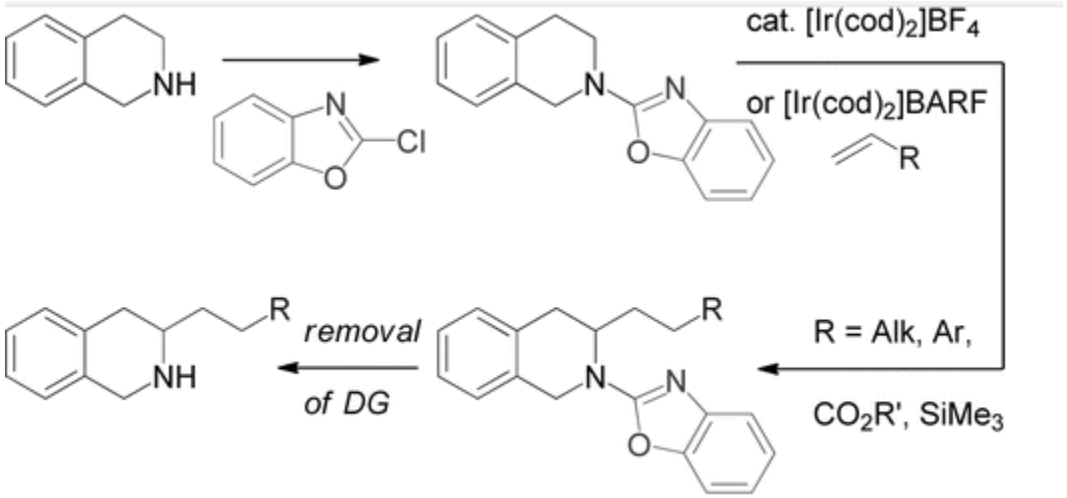
Takanori Shibata *Org. Lett.*, **2011**, *13*, 4692

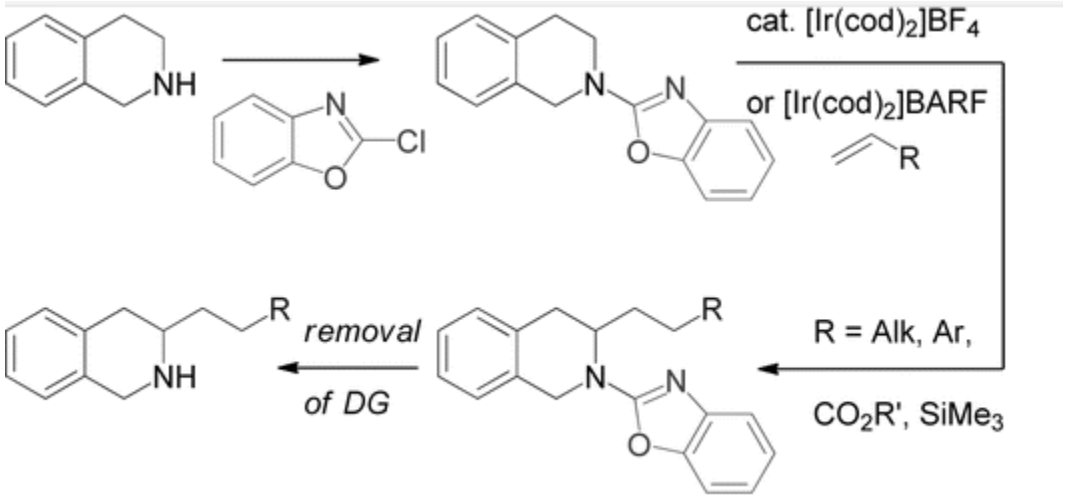


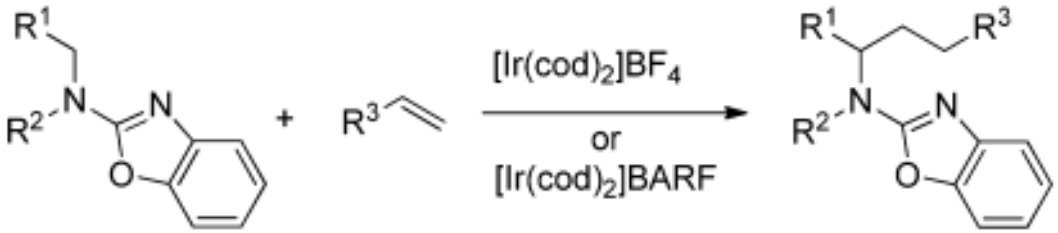
Entry[a]	R	R′	Time (h)	Yield (%), ee (%)
1	H (**1n**)	Ph (**4a**)	8	82 (**5a**)
2[b]	H (**1n**)	Ph (**4a**)	24	59 (**5a**)
3	H (**1n**)	*n*-C_4H_9 (**4b**)	24	42 (**5b**)
4[b,c]	Me (**1a**)	*n*-C_4H_9 (**4b**)	18.5	32 (**5c**), 89%

Takanori Shibata *Tetrahedron* 68 (**2012**) 9009



Till Opatz Org. Lett., **2014**, *16*, 4201



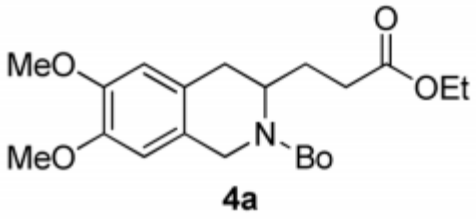


Reaction condition:

Acrylate, Vinylsilane (DME, 85 ℃)

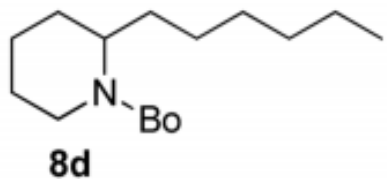
Styrene, vinylboronic ester, 1-hexene (DME, 140 ℃)

better substrate scope



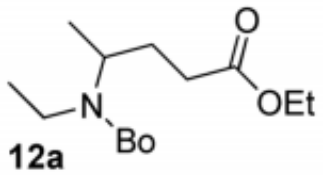
4a

63%



8d

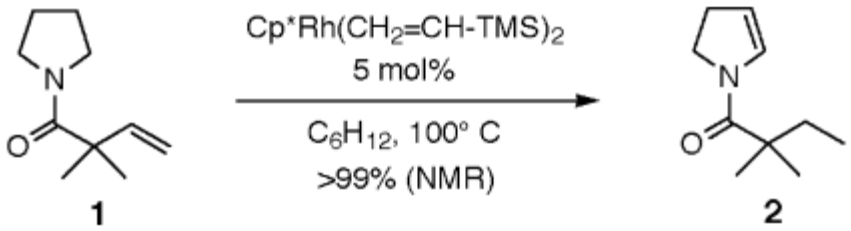
42%



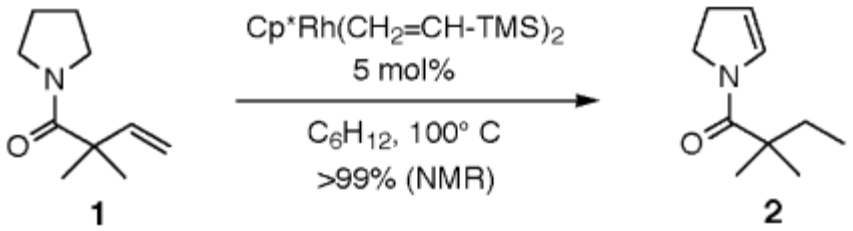
12a

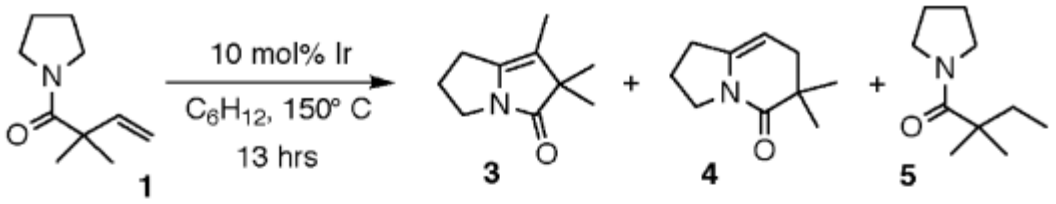
64%

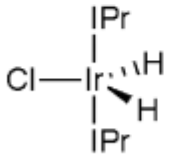
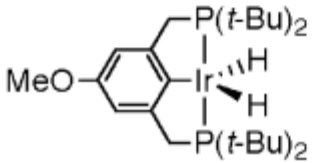
Till Opatz Org. Lett., **2014**, *16*, 4201



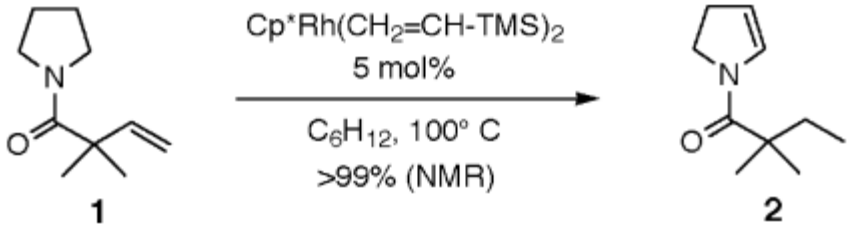
Dalibor Sames *J. Am. Chem. Soc.*, **2004**, *126*, 6556

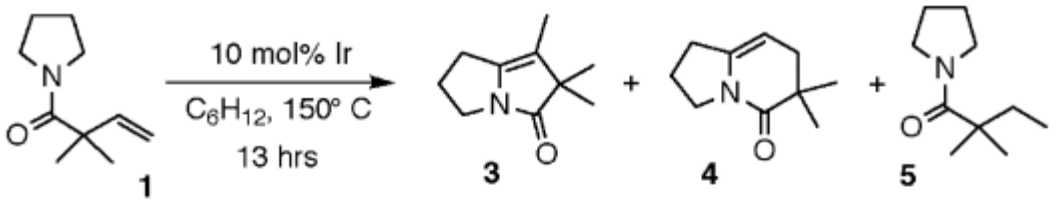




entry	complex	NMR yields[a]		
1	$[Ir(COE)_2Cl]_2$ / PCy_3 (2 eq)	26	11	25
2	$[Ir(COE)_2Cl]_2$ / IPr (2 eq)	41	4	41
3	**$[Ir(COE)_2Cl]_2$ / IPr (2 eq) + 4 eq NBE**	**66**	**17**	**10**
4	$(Cy_3P)_2Ir(Cl)H_2$, **6**	9	0	20
5	$(Cy_3P)_2Ir(CF_3CO_2)H_2$, **7**	0	0	24
6	 **8**	trace	0	trace
7	 **9**	0	0	0

Dalibor Sames *J. Am. Chem. Soc.*, **2004**, *126*, 6556





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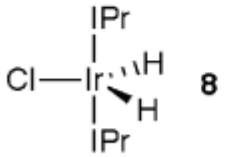
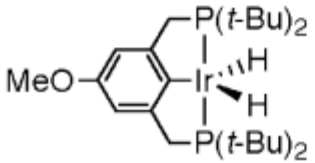
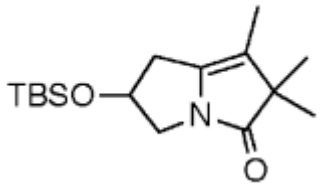
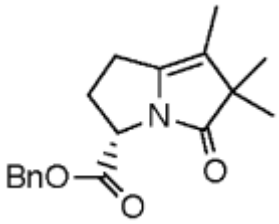
6	 **8**	trace	0	trace
7	 **9**	0	0	0

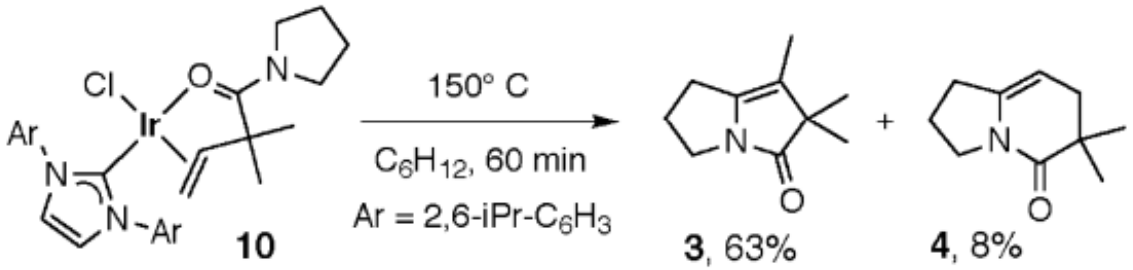


60 %

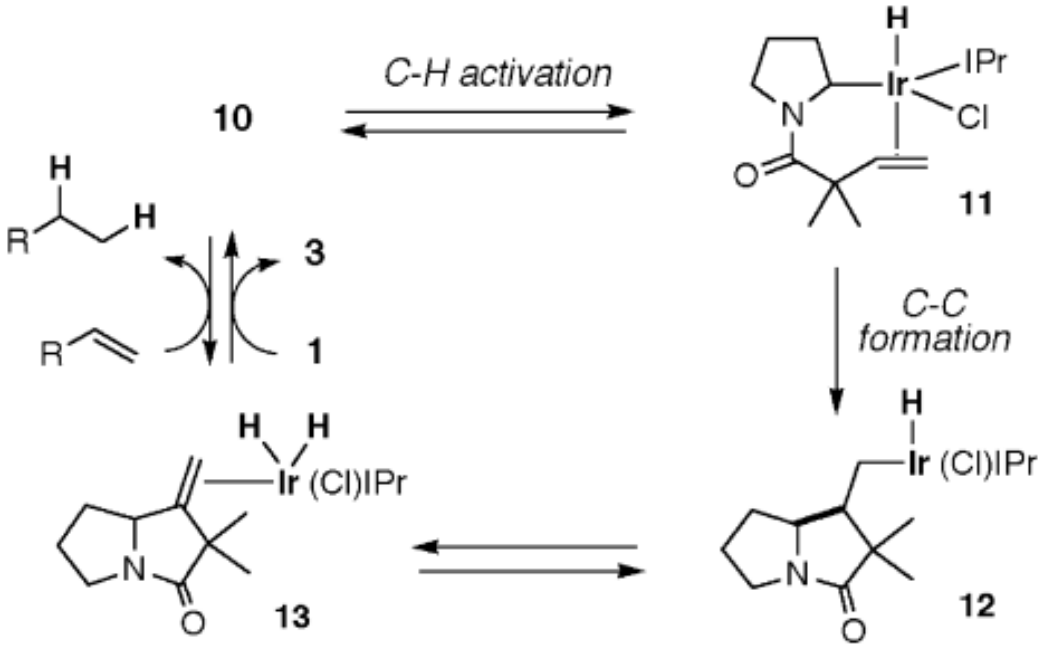


46 %

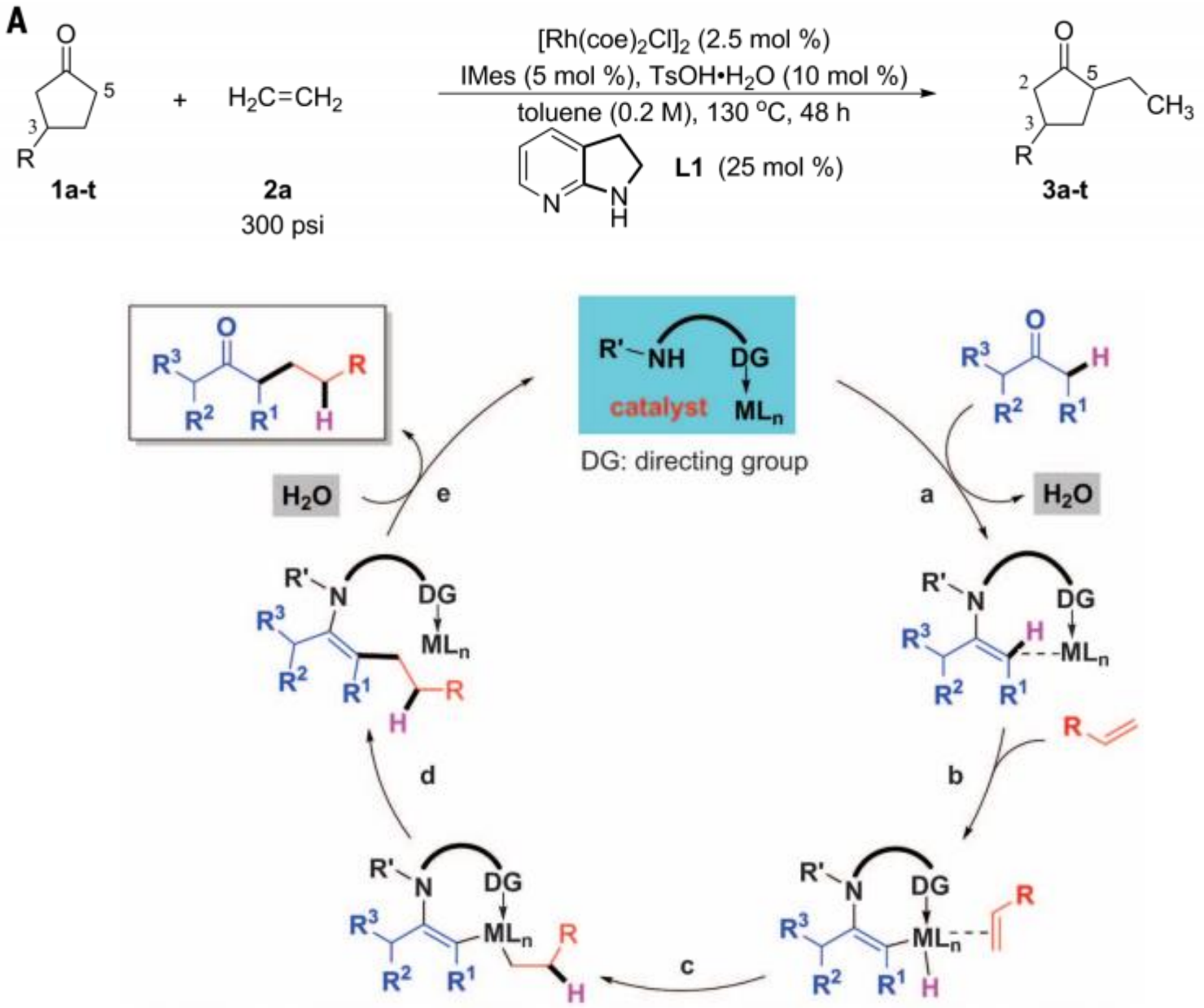
Dalibor Sames *J. Am. Chem. Soc.*, **2004**, *126*, 6556



Kinetic competent and chemical competent catalyst



Dalibor Sames *J. Am. Chem. Soc.*, **2004**, *126*, 6556



Guangbin Dong, *Science* **2014**, *345*, 68

1) sp^3 C-H Alkylation via Directed C-H activation

   - *Rare-earch-metal-philic DG*
   - *Allylic C-H bond alkylation (double bond as DG)*
   - *Pyridine type DG*

2) Hydroaminoalkylation (still via C-H activation)

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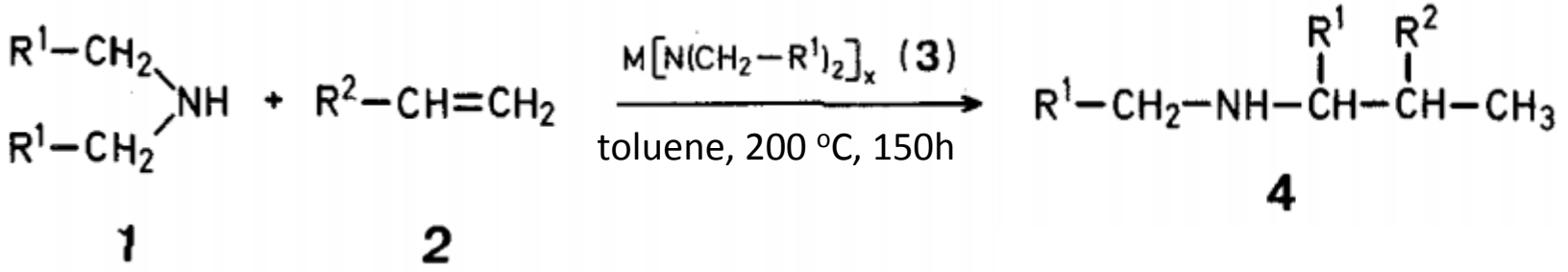


R¹ in 1 and 3	R² in 2	M in 3	Yield [%][b] of 4
H	*n*-C_4H_9	Nb	10
			12
H	*n*-C_4H_9	Ta	20[d]
			38[d]
H	*n*-C_4H_9	Zr	18
H	H	Nb	28[e]
H	CH_3	Nb	21
CH_3	H	Nb	13[e]

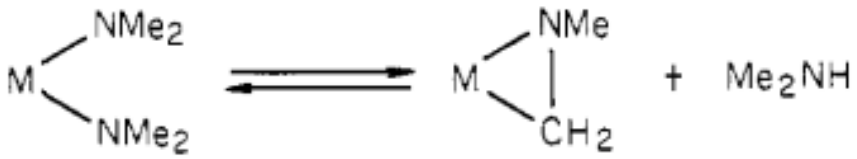
* Isolated by distillation

Maspero, F. *Synthesis* **1980**, 305.

$$(CH_3)_2ND \xrightleftharpoons{M(NMe_2)_n} (CH_3)(CH_2D)NH$$

catalyst	% H–D exchange[c]	insertn (turnovers)[d]
$Ti(NMe_2)_4$	0[e]	0.0
$Zr(NMe_2)_4$	37	0.0
$Hf(NMe_2)_4$	0[e]	
$Nb(NMe_2)_5$	67	4.5
$Ta(NMe_2)_5$	26	0.3
$W(NMe_2)_n$[b]	57	7.0
$Sn(NMe_2)_4$	0[e]	0.0

[a] All runs in evacuated sealed tubes 14 h at 160 °C.



Nugent, W. A *Organometallics* **1983**, *2*, 161

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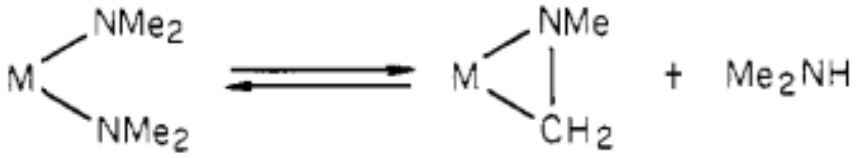
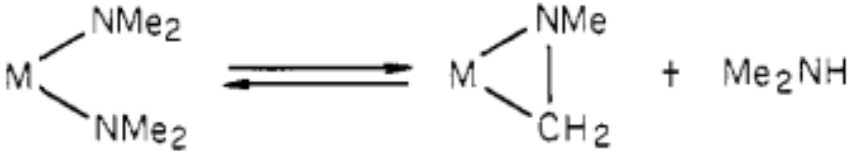


$$Me_2NH + CH_2{=}CHC_3H_7 \xrightarrow{\text{cat.}} MeHNCH_2C(CH_3)HC_3H_7$$

yield not given

“ **The activity of the various metal amides for this reaction roughly parallels their efficacy for H-D exchange”**

Nugent, W. A *Organometallics* **1983**, *2*, 161

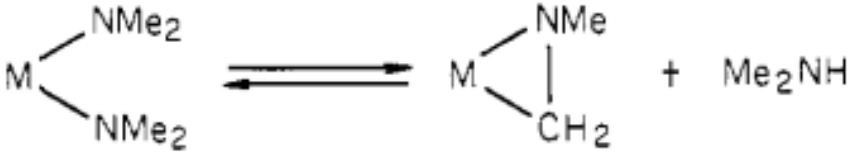


Nugent, W. A *Organometallics* **1983**, *2*, 161

zirconocene-η^2-imine complexes was formed faster from **N-alkyl arylamido** complexes than from **dialkylamido** complexes.

Organometallics **1994**, *13*, 190

John Hartwig *J. Am. Chem. Soc.*, **2007**, *129,* 6690



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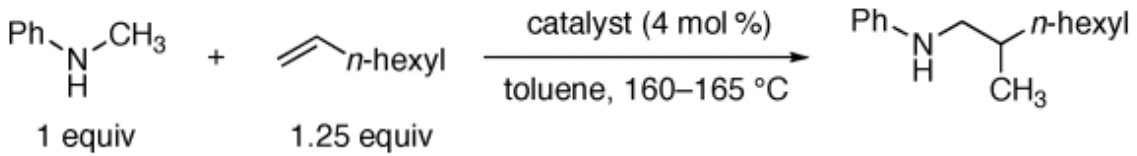
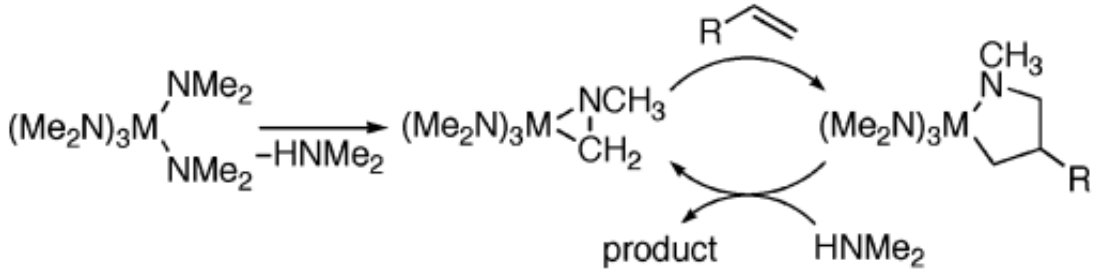
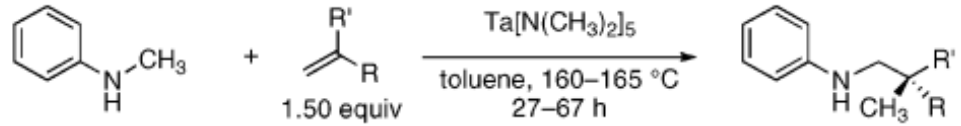


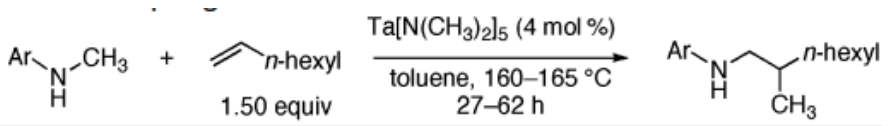
		% yield[a]		
entry	catalyst precursor	1.3 h	5.1 h	24 h
1	$Ta[N(CH_3)_2]_5$	32	60	96
2	$Ta[N(CH_2CH_3)_2]_5$	23	41	66
3	$Nb[N(CH_3)_2]_5$	20	29	35
4	$Cp_2Zr[N(CH_3)_2]_2$	0.6	1.2	3.0
5	$Zr[N(CH_3)_2]_4$	0[b]	0[b]	0.1
6	none	0[b]	0[b]	0[b]



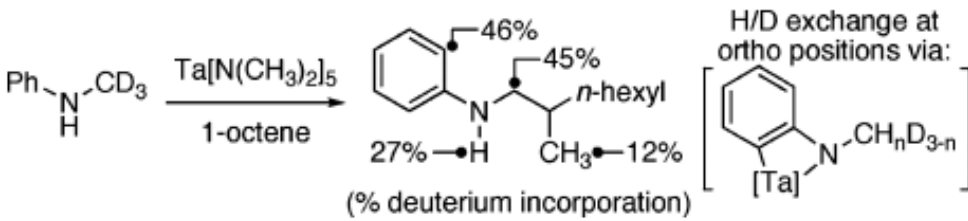
John Hartwig *J. Am. Chem. Soc.*, **2007**, *129,* 6690



entry	olefin	mol% Ta	products(s)	yield[a]
1	*n*-hexyl	4	Ph, N, H, *n*-hexyl, CH_3	88%
2	$SiPh(CH_3)_2$	4	Ph, N, H, $SiPh(CH_3)_2$, CH_3 + Ph, N, H, $SiPh(CH_3)_2$	50% 28%
3	Ph	4	Ph, N, H, Ph, CH_3	77%
4[b]	CH_3, *n*-pentyl	8	Ph, N, H, *n*-pentyl, CH_3, CH_3	76%
5[b]		4	Ph, N, H, CH_3	71%
6[b]	TMS	8	Ph, N, H, TMS, CH_3	66%
7		4	Ph, N, H (3:1 dr)	96%



entry	arylamine	product	yield[a]
1	Ar = *m*-$(CH_3)_2$-C_6H_3	Ar, N, H, *n*-hexyl, CH_3	88%
2	Ar = *m*-*t*-Bu_2-C_6H_3		93%
3	Ar = *m*-F_2-C_6H_3		84%
4	Ar = *p*-(CH_3O)-C_6H_4		90%
5	Ar = *p*-F-C_6H_4		78%
6	N, H	N, H, H, *n*-hexyl, CH_3 (single diastereomer)	72%[b]
7	N, H	N, H, CH_3 (1:1 dr)	88%[c]



Cannot use styrene and 1,2-disubstituted olefin

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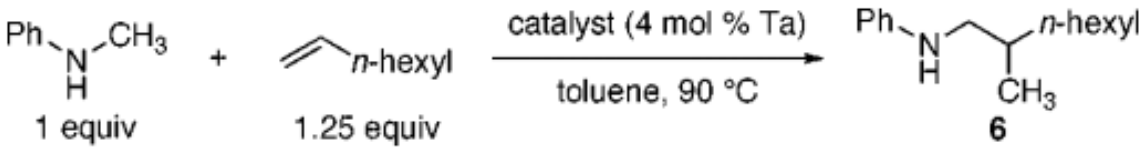

		% yield **6**[a]		
entry	catalyst precursor	2.3 h	5.1 h	24 h
1	$[Cl_3Ta(NMePh)_2]_2$ (**4**)	34[b]	53[b]	72[b]
2	$Ta(NMe_2)_5$ (**1**)	0[c]	0[c]	0[c]
3	$[Cl_4Ta(NMePh)]\bullet OEt_2$ (**5**)	2.1	3.8	14

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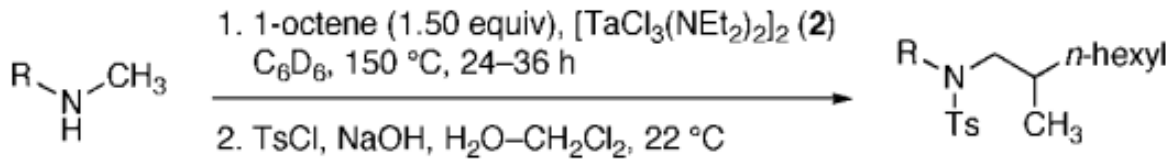
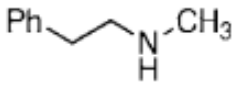
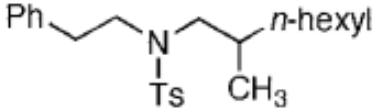
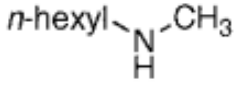
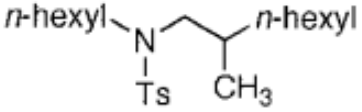
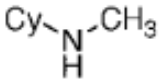
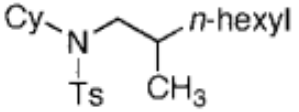
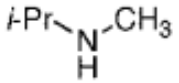
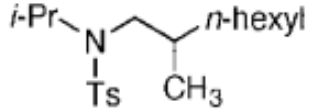
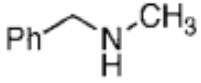
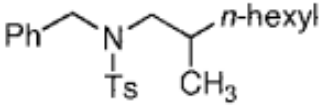
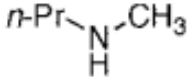
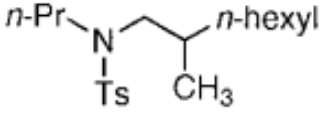
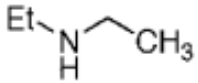
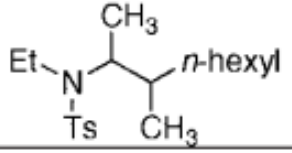


entry	alkylamine	mol% **2**	sulfonamide	yield amine[a]	yield sulfonamide[b]
1		2		93%[c]	85%
2		2		91%	81%
3		2		96%	91%
4		3		94%	89%
5		4		47%	41%
6		3		78%	72%
7		2		91%	86%[d]

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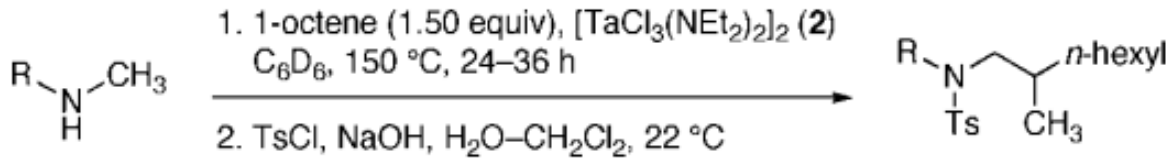
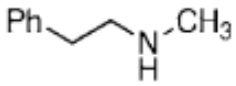
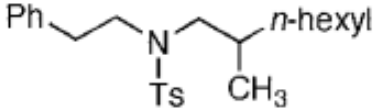
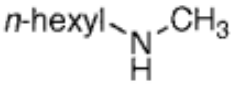
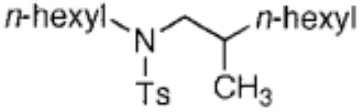
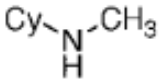
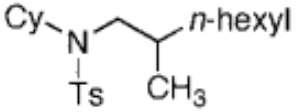
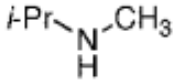
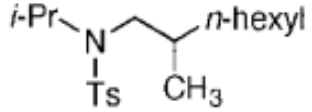
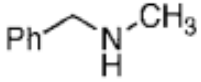
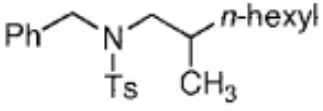
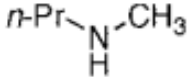
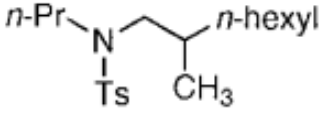
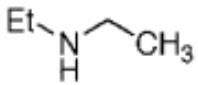
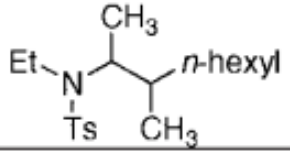


entry	alkylamine	mol% **2**	sulfonamide	yield amine[a]	yield sulfonamide[b]
1		2		93%[c]	85%
2		2		91%	81%
3		2		96%	91%
4		3		94%	89%
→ 5		4		47%	41%
6		3		78%	72%
→ 7		2		91%	86%[d]

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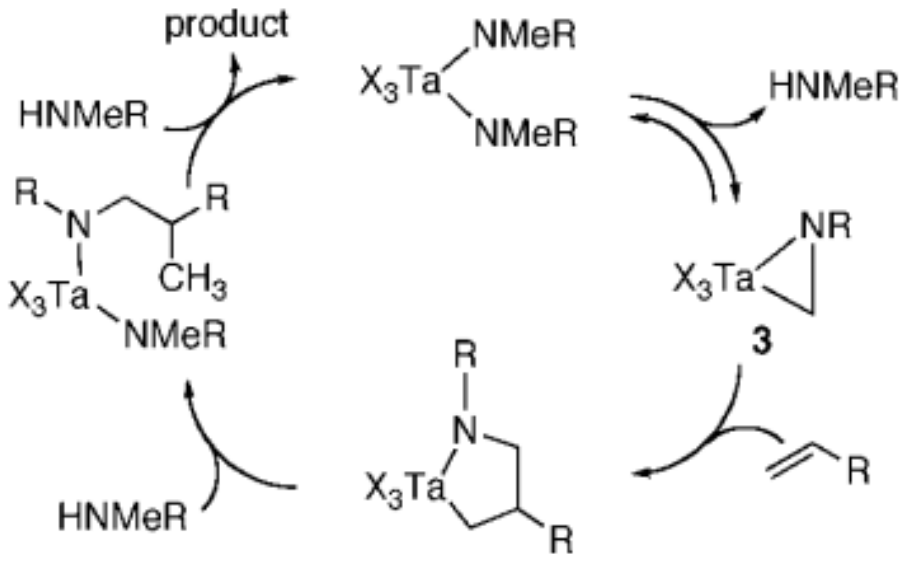

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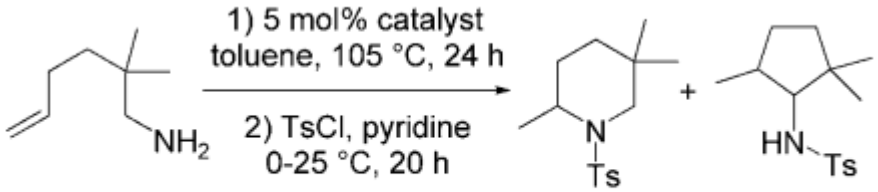

catalyst:	$[Ti(NMe_2)_4]$	72 %	26 %[a]
	$[Ind_2TiMe_2]$	71 %	28 %[a]

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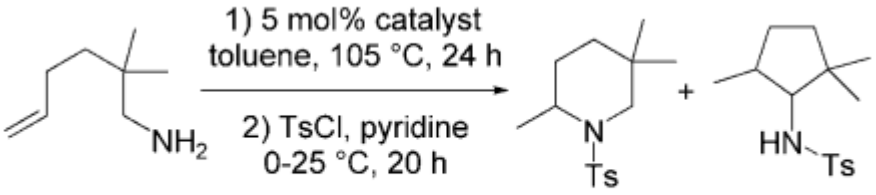
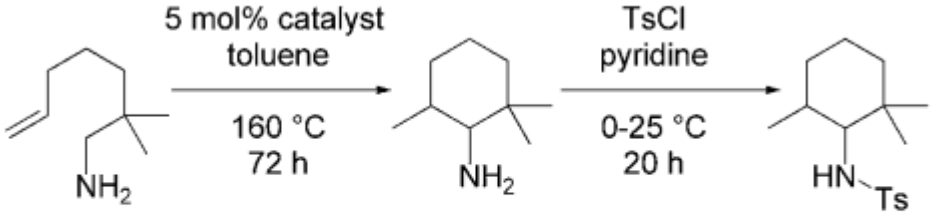


catalyst:			
	$[Ti(NMe_2)_4]$	72 %	26 %[a]
	$[Ind_2TiMe_2]$	71 %	28 %[a]



1 **2** **3**

catalyst:		
$[Ti(NMe_2)_4]$	46 %[a]
$[Ind_2TiMe_2]$	0 %

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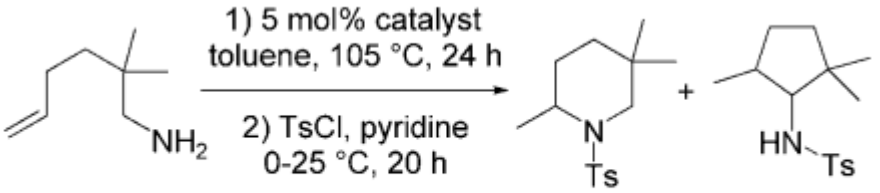
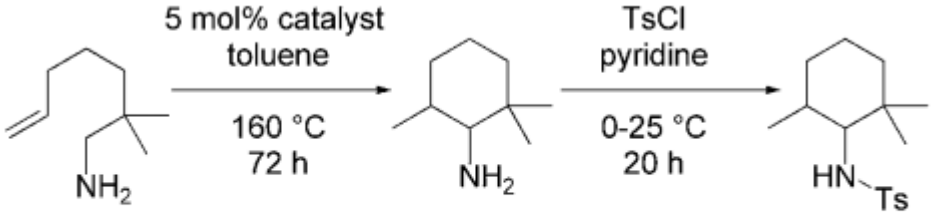
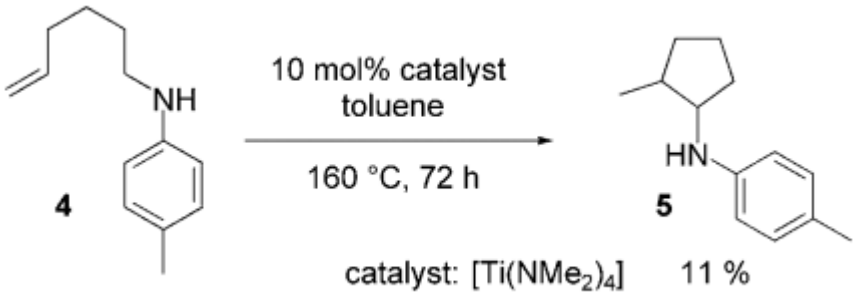


catalyst:			
	$[Ti(NMe_2)_4]$	72 %	26 %[a]
	$[Ind_2TiMe_2]$	71 %	28 %[a]



1 **2** **3**

catalyst:		
$[Ti(NMe_2)_4]$	46 %[a]
$[Ind_2TiMe_2]$	0 %



4 **5**

catalyst:		
$[Ti(NMe_2)_4]$	11 %
$[Ind_2TiMe_2]$	0 %

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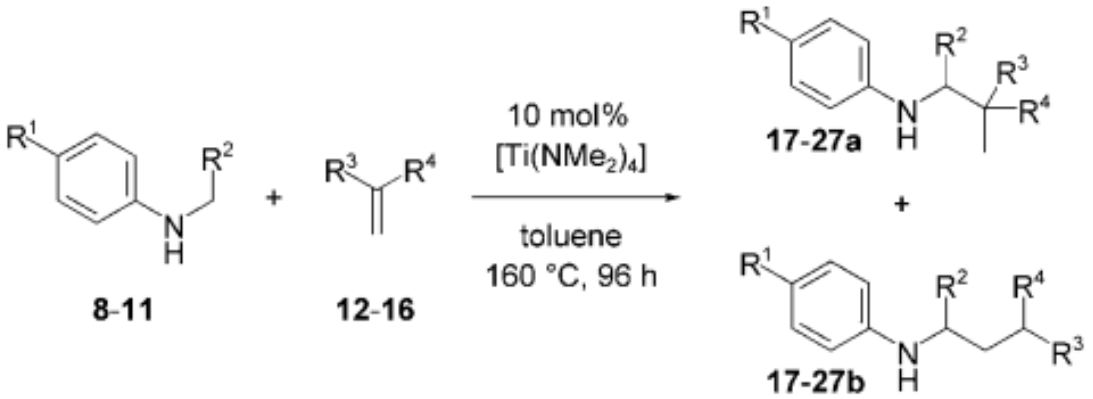

Entry	Amine	R^1	R^2	Alkene	R^3	R^4	Product	Yield **a** + **b** [%][b]	Selectivity **a**/**b**[c]
1	**8**	H	H	**12**	*n*-C_6H_{13}	H	**17a/b**	32	90:10
2	**8**	H	H	**12**	*n*-C_6H_{13}	H	**17a/b**	62[d]	90:10
3	**8**	H	H	**13**	Bn	H	**18a/b**	94	90:10
4	**8**	H	H	**14**	-$(CH_2)_5$-		**19a/b**	–	–
5	**8**	H	H	**15**	Ph	H	**20a/b**	–	–
6	**8**	H	H	norbornene (**16**)			**21**	78	–
7	**9**	Me	H	**12**	*n*-C_6H_{13}	H	**22a/b**	20	95:5
8	**9**	Me	H	**13**	Bn	H	**23a/b**	80	95:5
9	**10**	Me	Et	**12**	*n*-C_6H_{13}	H	**24a/b**	–	–
10	**10**	Me	Et	**13**	Bn	H	**25a/b**	–	–
11	**11**	H	Ph	**12**	*n*-C_6H_{13}	H	**26a/b**	75	1:1
12	**11**	H	Ph	**13**	Bn	H	**27a/b**	84	1:1

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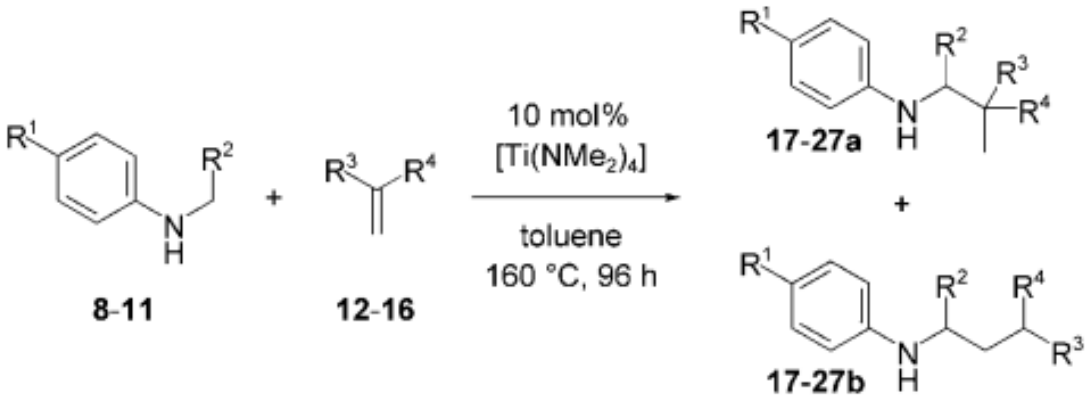

Entry	Amine	R^1	R^2	Alkene	R^3	R^4	Product	Yield **a** + **b** [%][b]	Selectivity **a**/**b**[c]
1	**8**	H	H	**12**	*n*-C_6H_{13}	H	**17a/b**	32	90:10
2	**8**	H	H	**12**	*n*-C_6H_{13}	H	**17a/b**	62[d]	90:10
3	**8**	H	H	**13**	Bn	H	**18a/b**	94	90:10
4	**8**	H	H	**14**	-$(CH_2)_5$-		**19a/b**	–	–
5	**8**	H	H	**15**	Ph	H	**20a/b**	–	–
6	**8**	H	H	norbornene (**16**)			**21**	78	–
7	**9**	Me	H	**12**	*n*-C_6H_{13}	H	**22a/b**	20	95:5
8	**9**	Me	H	**13**	Bn	H	**23a/b**	80	95:5
9	**10**	Me	Et	**12**	*n*-C_6H_{13}	H	**24a/b**	–	–
10	**10**	Me	Et	**13**	Bn	H	**25a/b**	–	–
11	**11**	H	Ph	**12**	*n*-C_6H_{13}	H	**26a/b**	75	1:1
12	**11**	H	Ph	**13**	Bn	H	**27a/b**	84	1:1

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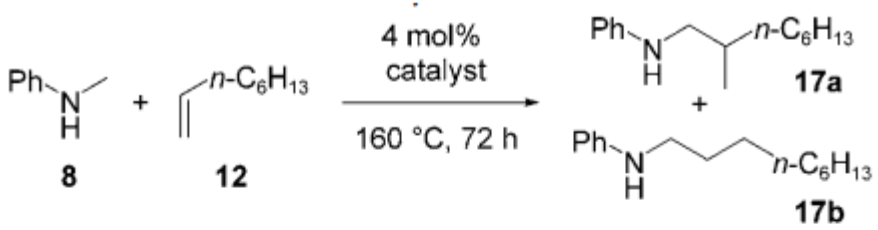
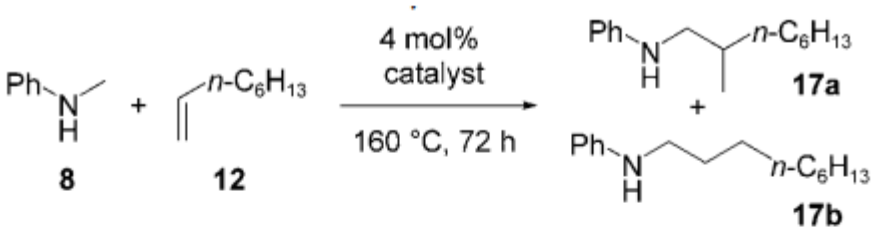


Entry	Catalyst	Yield **17a** + **17b** [%][b]	Selectivity **17a**/**17b**[c]
1	$[Ti(NMe_2)_4]$	62	90:10
2	$[Cp_2TiMe_2]$	3	n.d.[d]
3	$[Ind_2TiMe_2]$	16	n.d.[d]
4	$[\{(\eta^5\text{-}C_5H_4)(Me_2Si)NtBu\}Ti(NMe_2)_2]$	77	>99:1
5	$[\{(\eta^5\text{-}C_5H_4)(Me_2Si)NtBu\}TiMe_2]$	75	>99:1
6	[(ebthi)$TiMe_2$]	–	–

Sven Doye *Angew. Chem. Int. Ed*. **2009**, *48*, 1153



Entry	Catalyst	Yield **17a** + **17b** [%][b]	Selectivity **17a**/**17b**[c]
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5	$[\{(\eta^5\text{-}C_5H_4)(Me_2Si)NtBu\}TiMe_2]$	75	> 99:1
6	$[(ebthi)TiMe_2]$	–	–

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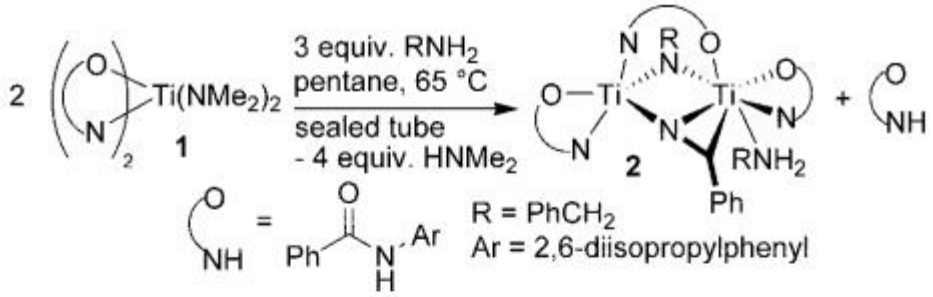
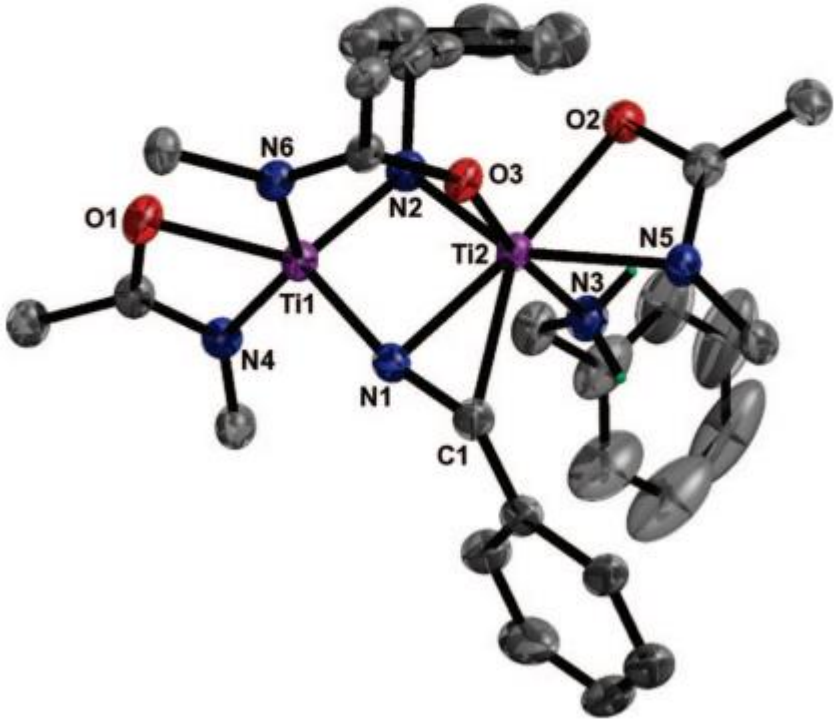
$[Ti(Bn)_4]$

- Slightly enhanced activity
- First addition to styrene: 30% yield, 1:1 branch:linear

Sven Doye *ChemCatChem* **2009**, *1*, 162





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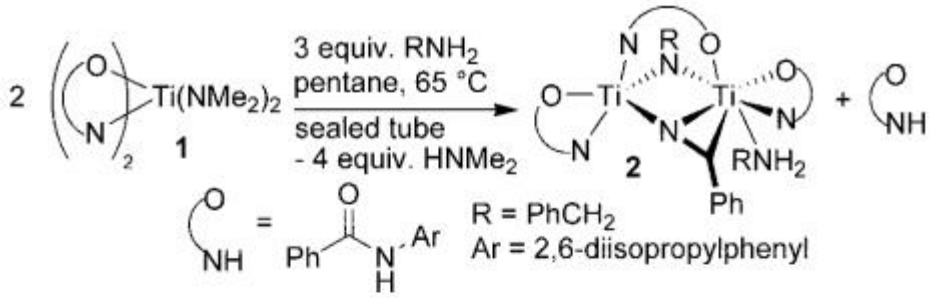
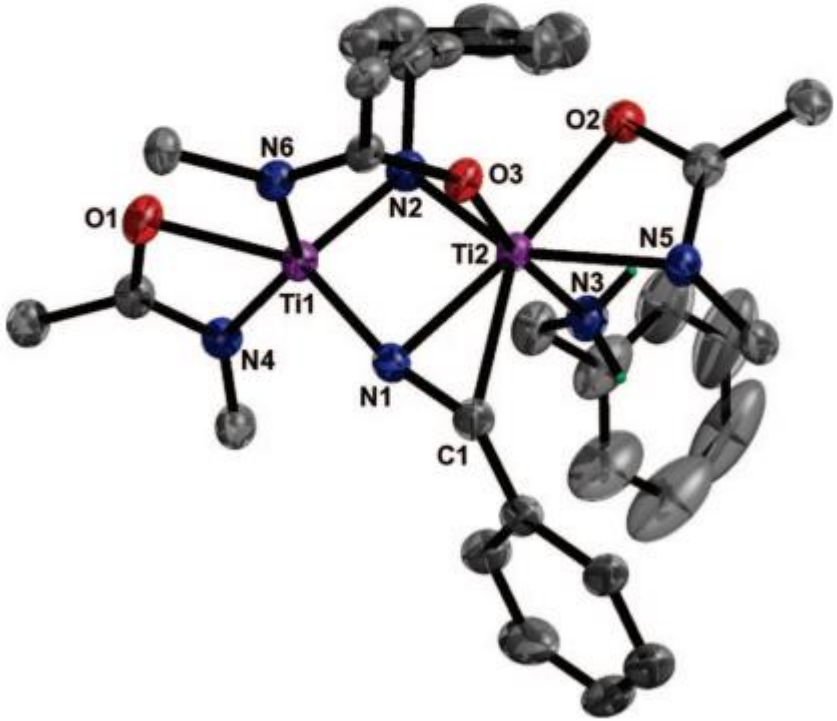
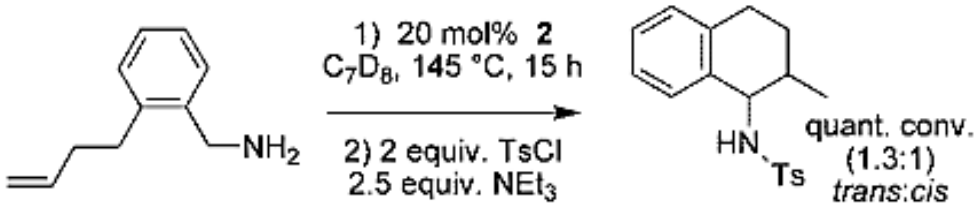
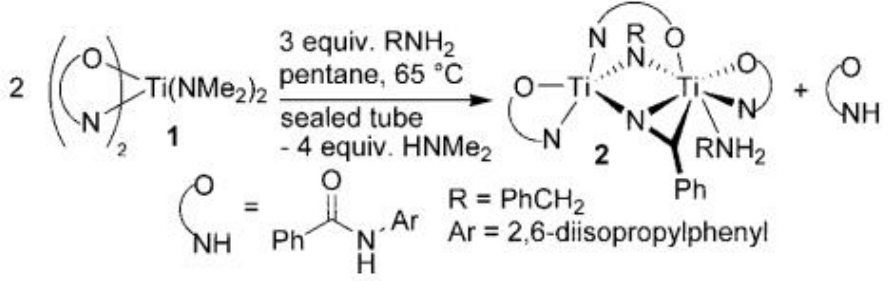
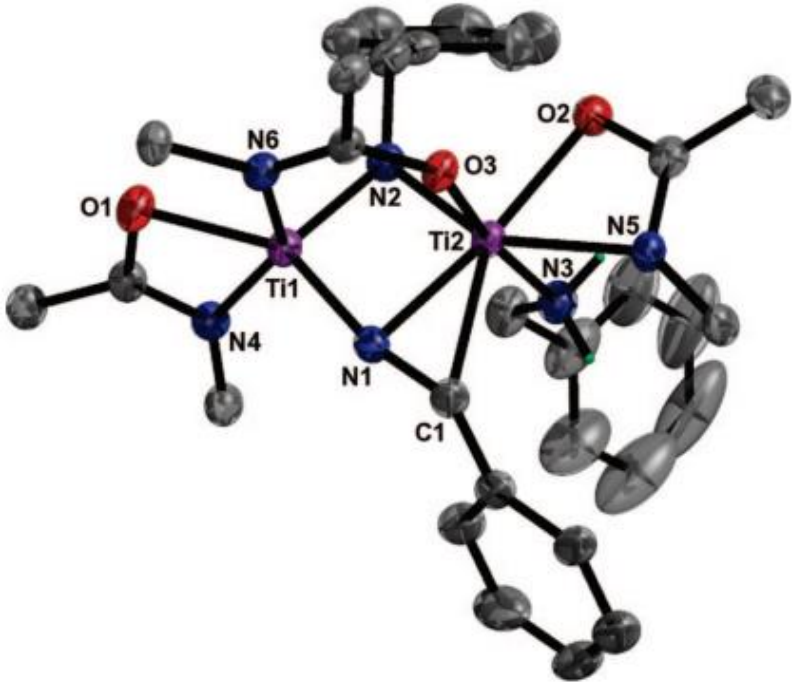


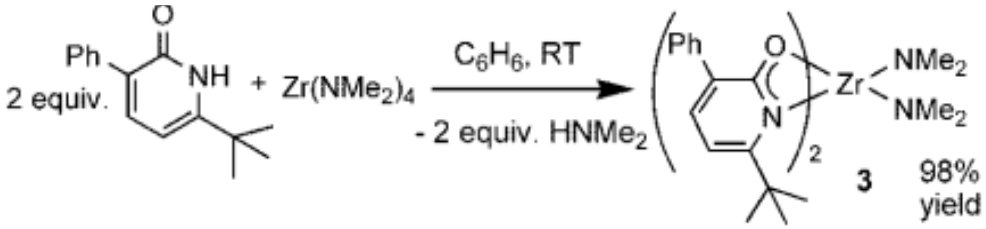




Laurel L. Schafer *J. Am. Chem. Soc.*, **2009**, *131*, 2116

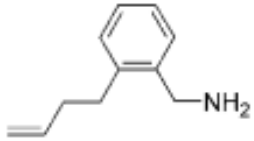
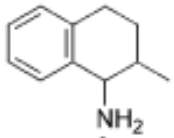
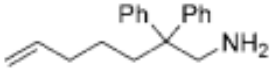
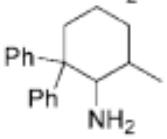
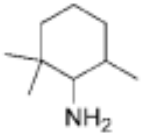
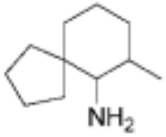
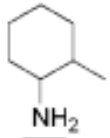
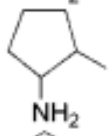
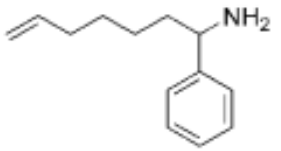
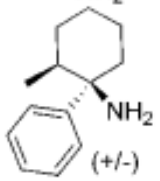




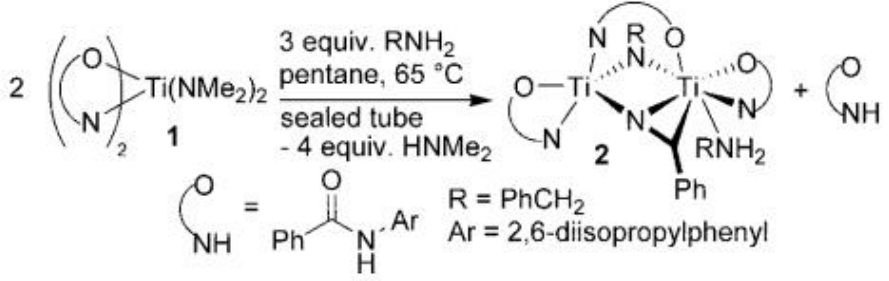


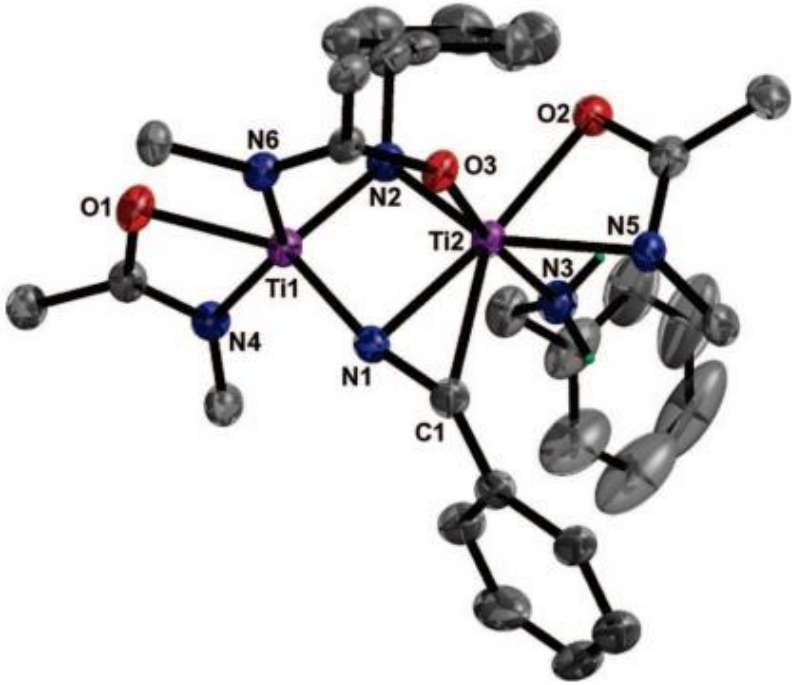
Zr: larger metal center

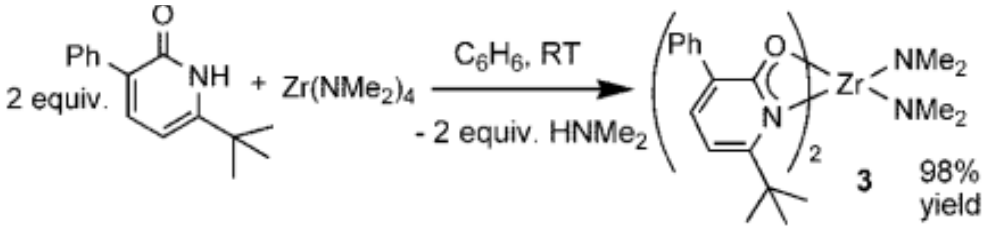
2-pyridonate ligand: less sterically demanding

Entry	Aminoalkene	Product	Time (h)	Yield (%) *trans:cis*
1			24[a]	90[d] (3:1)[c]
2			96[a]	63[d] (2:1)[c]
3			24[a]	50[d] (3:1)[c]
4			22[a]	91[d] (2:1)[c]
5			72[b]	43[d] (74)[e] (2:1)[c]
6			20[b]	54[d] (98)[e] (1:2)[c]
7			120[b]	51[f] (1: 19)[c]

[a] 20 mol% catalyst at 145 °C. [b] 40 mol% catalyst at 155 °C. [c] Ratio from ^{1}H NMR spectroscopy. [d] Isolated yield of derivatized products. [e] Consumption of starting material, determined by NMR. [f] NMR yield with 1,3,5-trimethoxybenzene as internal standard.







Zr: larger metal center

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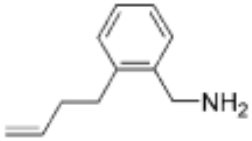
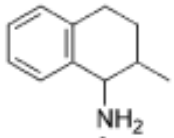
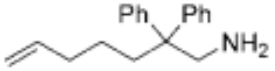
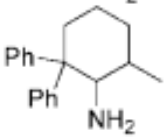
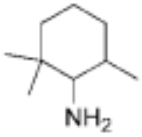
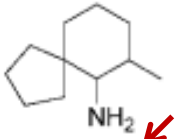
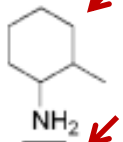
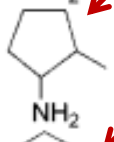
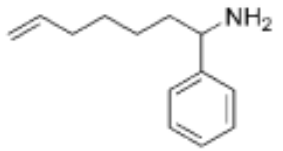
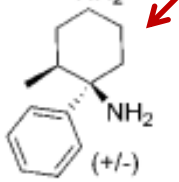
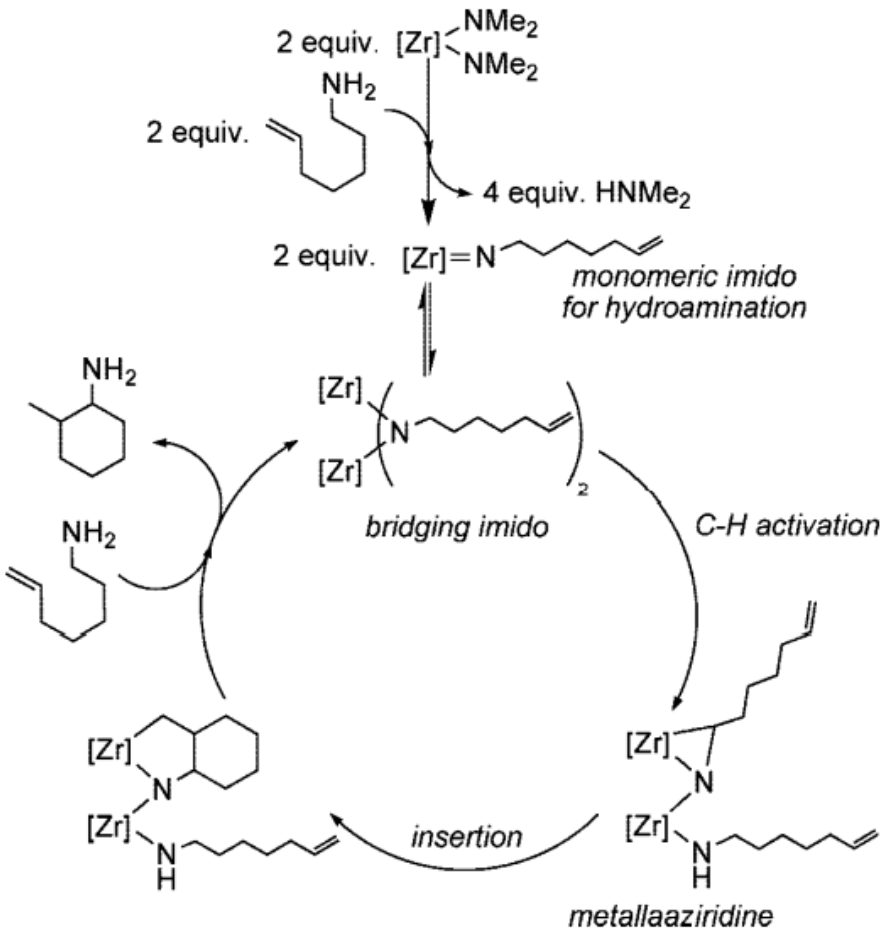
Entry	Aminoalkene	Product	Time (h)	Yield (%) *trans:cis*
1			24[a]	90[d] (3:1)[c]
2			96[a]	63[d] (2:1)[c]
3			24[a]	50[d] (3:1)[c]
4			22[a]	91[d] (2:1)[c]
5			72[b]	43[d] (74)[e] (2:1)[c]
6			20[b]	54[d] (98)[e] (1:2)[c]
7			120[b]	51[f] (1: 19)[c]

[a] 20 mol% catalyst at 145 °C. [b] 40 mol% catalyst at 155 °C. [c] Ratio from ^{1}H NMR spectroscopy. [d] Isolated yield of derivatized products. [e] Consumption of starting material, determined by NMR. [f] NMR yield with 1,3,5-trimethoxybenzene as internal standard.


2 equiv. [Zr]NMe2 NMe2
NH2
2 equiv.
4 equiv. HNMe2
2 equiv. [Zr]=N
monomeric imido for hydroamination
NH2
[Zr]
N
[Zr]
2
bridging imido
C-H activation
NH2
[Zr]
N
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N
H
insertion
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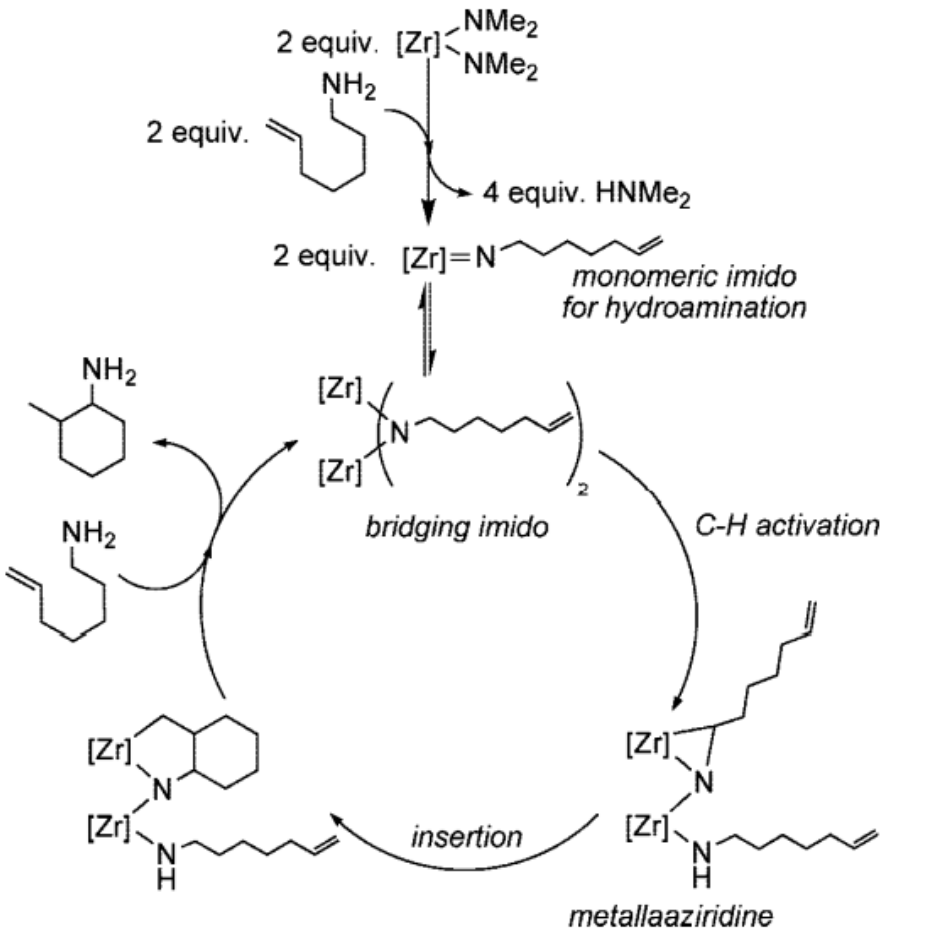
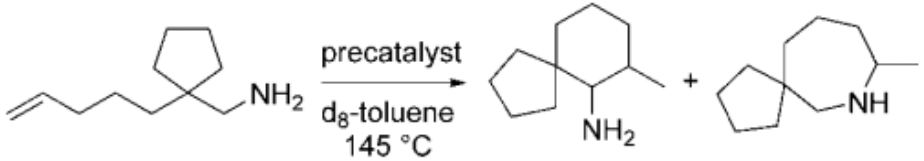
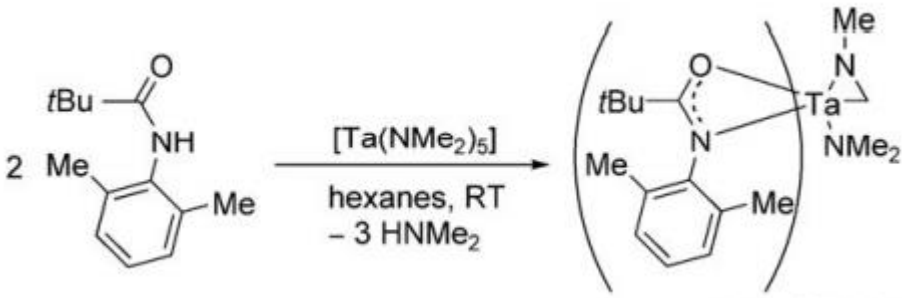
N
[Zr]
N
H
metallaaziridine

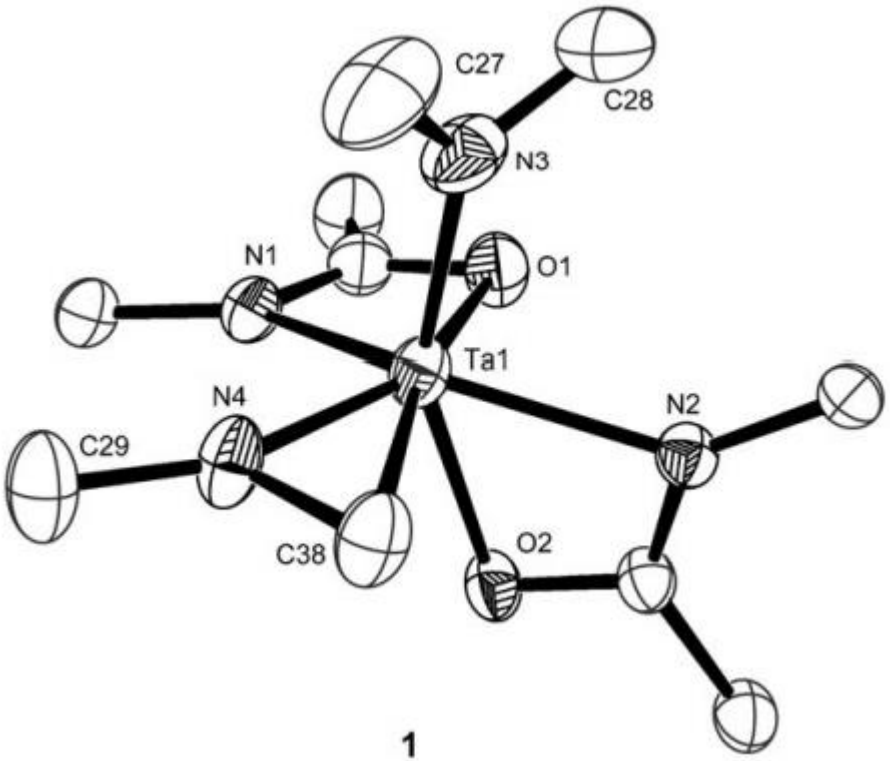




entry	precatalyst[a]	time (h)	conv (%) (CH/HA)
1	**3**, 40 mol%	6	96 (23:1)
2	**3**, 20 mol%	22	92 (5:1)
3	**3**, 10 mol%	48	86 (3:1)
4	**3**, 5 mol%	148	84 (2:1)



1, 84% yield



1

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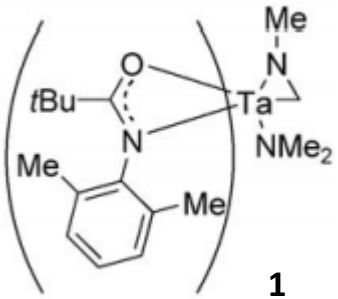
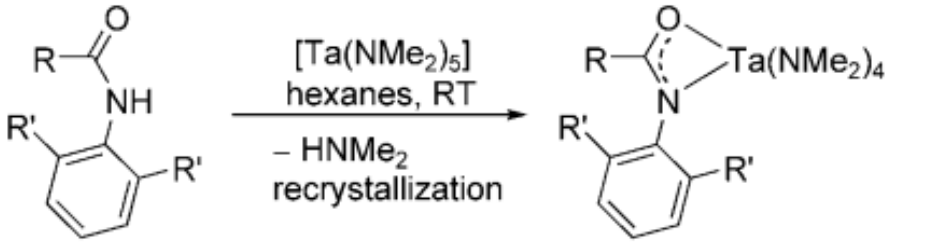
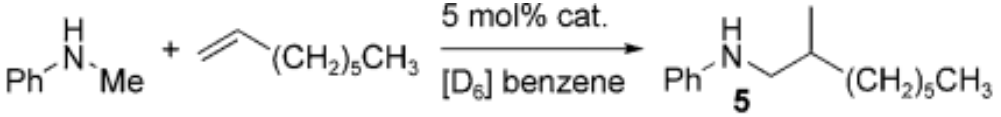


1



R=*t*Bu, R'=Me: **2**, 65% yield
R=*t*Bu, R'=*i*Pr: **3**, 69% yield
R=Ph, R'=*i*Pr: **4**, 50% yield

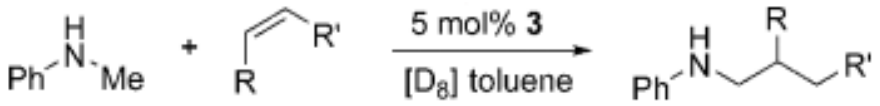


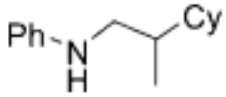
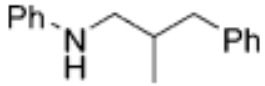
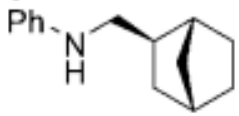
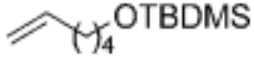
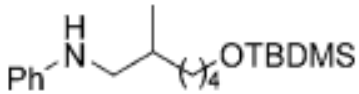
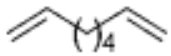
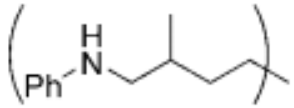
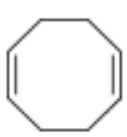
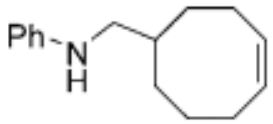
5

Entry	Catalyst	Conditions	Conversion [%][a]
1	**1**[b]	130 °C, 1 week[c,d,e]	71
2	**2**	130 °C, 24 h[c,e,f]	84
3	**2**	110 °C, 68 h[c,f]	69
4	**3**	110 °C, 63 h[c,f]	96 (92)
5	**4**	110 °C, 77 h[c,f]	85
6	$[Ta(NMe_2)_5]$	110 °C[c,f]	n.r.
7	$[Ta(NMe_2)_5]$	130 °C, 67 h[c,f]	89 (80)

[a] Yield of isolated product given in brackets; conversion was estimated by ^{1}H NMR spectroscopy. [b] 10 mol %; [c] [*N*-methylaniline] = 1 M. [d] *N*-methylaniline/1-octene 1:1.05. [e] [D_8]toluene as solvent. [f] *N*-methylaniline/1-octene 1:1.5. n.r. = no reaction.

Laurel L. Schafer *Angew. Chem. Int. Ed.* **2009**, *48*, 8361



Entry	Alkene	Conditions	Product	Yield [%][a]
1		145 °C, 15 h[b,c]	 **6**	90
2		130 °C, 19 h[b,c]	 **7**	85
3		110 °C, 96 h[b,c]	 **8**	93[d]
4		130 °C, 11 h[b,c]	 **9**	85
5		130 °C, 19 h[e]	 **10**	75[f]
6		165 °C, 96 h[b,g]	 **11**	83

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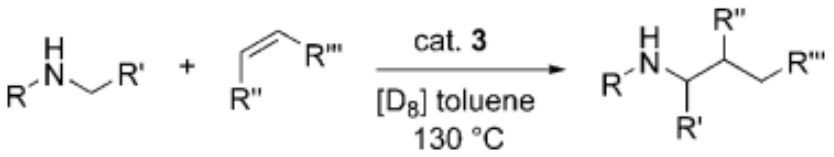
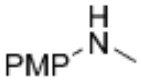
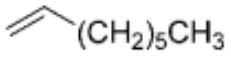
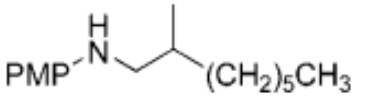
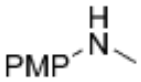
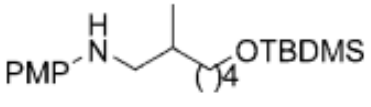
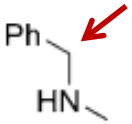
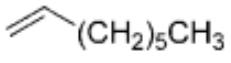
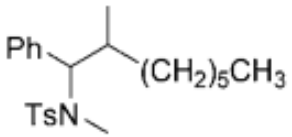
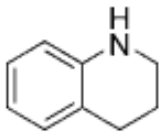
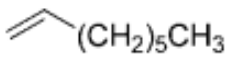
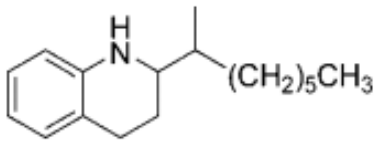
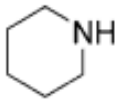
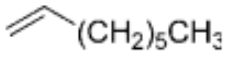
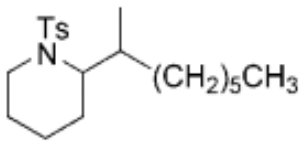


Entry	Amine	Alkene	*t* [h]	Product	Yield [%][a]
1			20[b,c]	 **12**	87
2			20[b,c]	 **13**	90
3			50[b,c]	 **14**	75[d,e,f]
4			37[b,g]	 **15**	92[e]
5			134[g,h]	 **16**	74[d,e,f]

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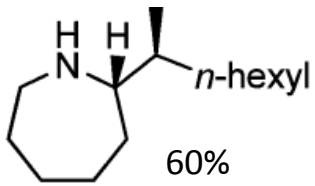
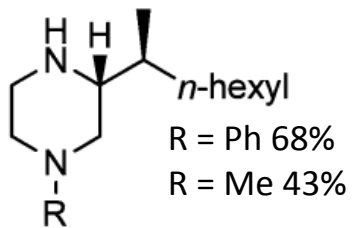
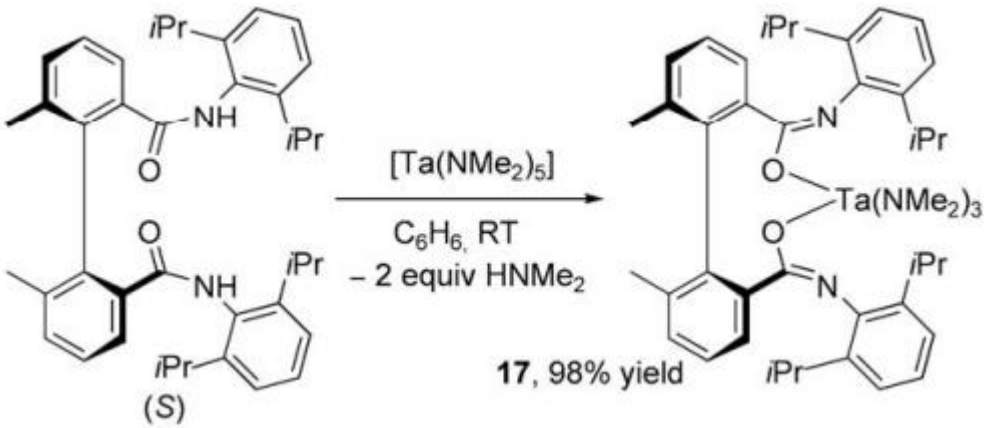


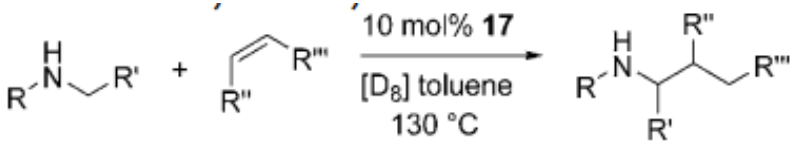
60%

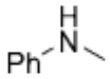
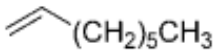
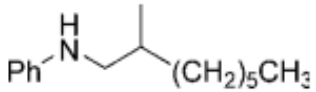
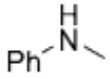
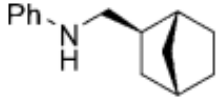
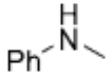
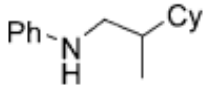


R = Ph 68%
R = Me 43%

See: Org. Lett., **2013**, *15*, 2182





Entry	Amine	Alkene[a]	*t* [h]	Product	Yield [%][b]	*ee* [%][c]
1			68	 **5**	86	44
2			46	 **8**	80	61[d]
3			48	 **6**	92	43

For further improvement, See:
Guofu Zi, *Chem. Commun*., **2010**, *46*, 6296
Guofu Zi, *Dalton. Trans*., **2011**, *40*, 1547

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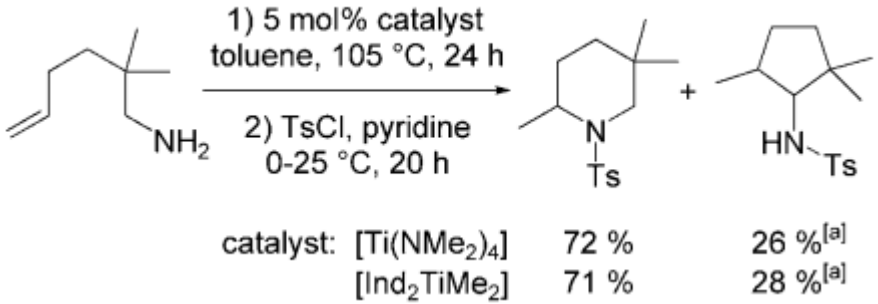
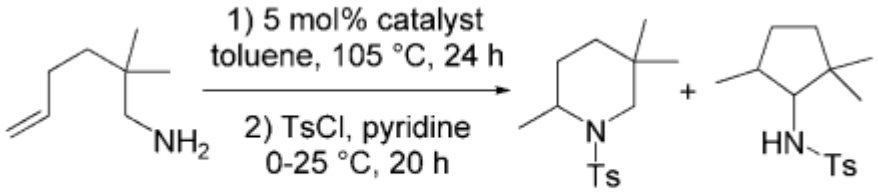


Sven Doye *Angew. Chem. Int. Ed*. **2009**, *48*, 1153

Only 105 °C: is this catalyst able to solve the styrene problem?

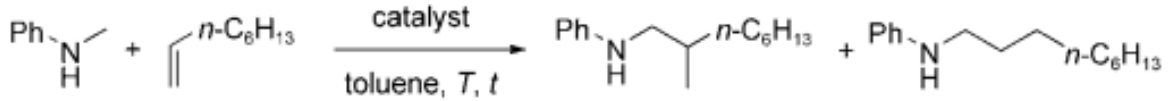
Sven Doye *Angew. Chem. Int. Ed.* **2010**, *49*, 2626



catalyst:		
$[Ti(NMe_2)_4]$	72 %	26 %[a]
$[Ind_2TiMe_2]$	71 %	28 %[a]

Sven Doye *Angew. Chem. Int. Ed*. **2009**, *48*, 1153

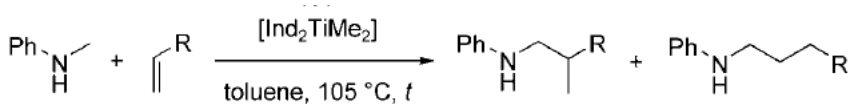
Only 105 °C: is this catalyst able to solve the styrene problem?



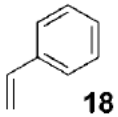
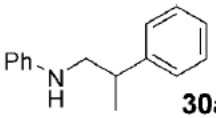
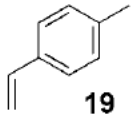
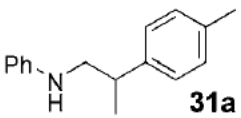
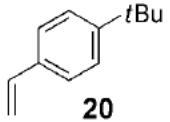
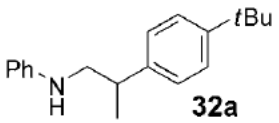
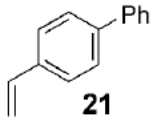
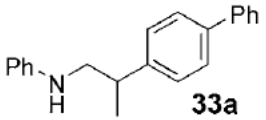
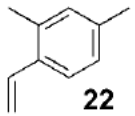
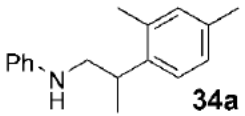
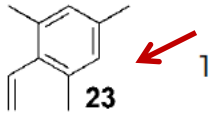
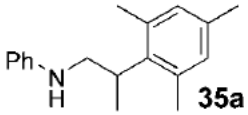
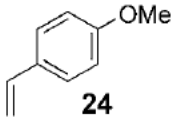
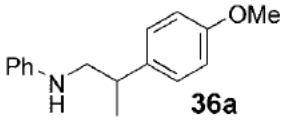
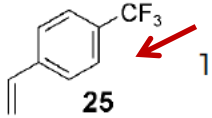
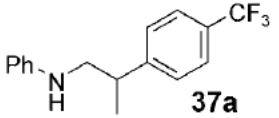
1 **2** **3a** **3b**

Entry	Catalyst	mol%	*T* [°C]	*t* [h]	Yield **3a** + **3b** [%][a]	Selectivity **3a**/**3b**[b]
1	$[Ti(NMe_2)_4]$	10	160	96	32	93:7
2		10	105	96	< 5	n.d.
3	$[Ind_2TiMe_2]$	10	160	96	84	> 99:1
4		10	105	96	97	> 99:1
5		10	105	24	96	> 99:1
6		5	105	24	96	> 99:1
7		5	90	24	81	> 99:1
8		5	80	24	86	> 99:1
9		5	70	24	< 5	n.d.
10		2	105	24	90	> 99:1
11		1	105	24	6	n.d.

Sven Doye *Angew. Chem. Int. Ed.* **2010**, *49*, 2626



1 **18-29** **30-41a** **30-41b**

Entry	Alkene	mol %	*t* [h]	Branched product	Yield **a** + **b** [%][a]	Selectivity **a**/**b**[b]
1	 **18**	5	24	 **30a**	13	85:15
2		5	96		71	85:15
3		10	96		91	85:15
4	 **19**	10	96	 **31a**	99	90:10
5	 **20**	10	96	 **32a**	97	87:13
6	 **21**	10	96	 **33a**	97	82:18
7	 **22**	10	96	 **34a**	94	75:25
8	 **23**	10	96	 **35a**	<5	n.d.
9	 **24**	10	96	 **36a**	95	92:8
10	 **25**	10	96	 **37a**	<5	n.d.

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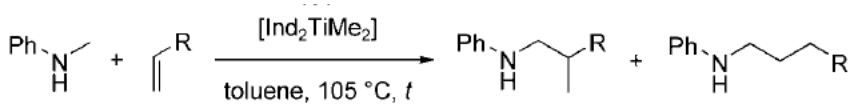
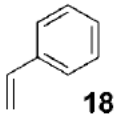
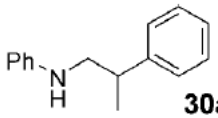
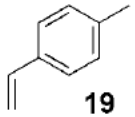
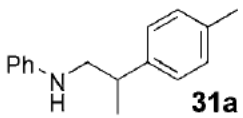
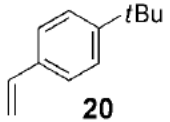
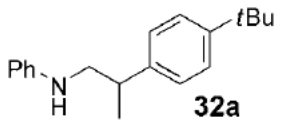
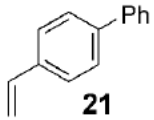
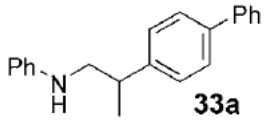
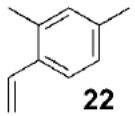
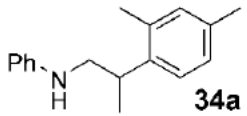
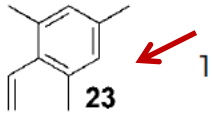
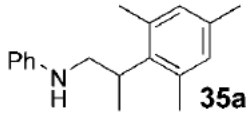
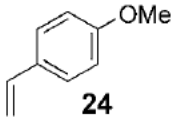
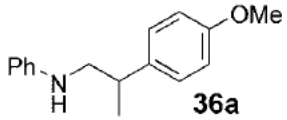
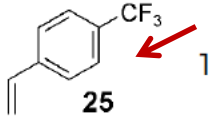
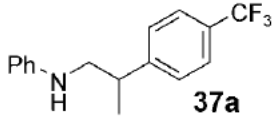
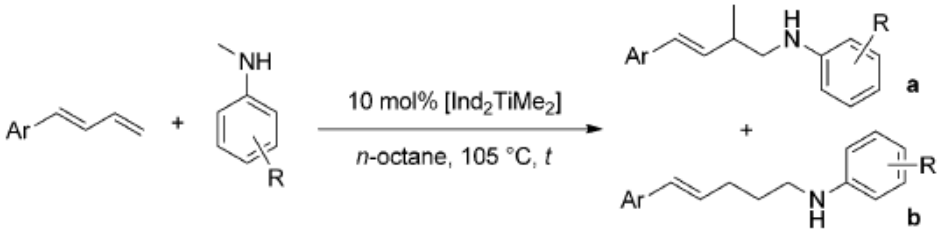


1 **18-29** **30-41a** **30-41b**

Entry	Alkene	mol%	t [h]	Branched product	Yield a + b [%][a]	Selectivity a/b[b]
1	 **18**	5	24	 **30a**	13	85:15
2		5	96		71	85:15
3		10	96		91	85:15
4	 **19**	10	96	 **31a**	99	90:10
5	 **20**	10	96	 **32a**	97	87:13
6	 **21**	10	96	 **33a**	97	82:18
7	 **22**	10	96	 **34a**	94	75:25
8	 **23**	10	96	 **35a**	<5	n.d.
9	 **24**	10	96	 **36a**	95	92:8
10	 **25**	10	96	 **37a**	<5	n.d.



Sven Doye *Chem. Eur. J.* **2013**, *19*, 3833

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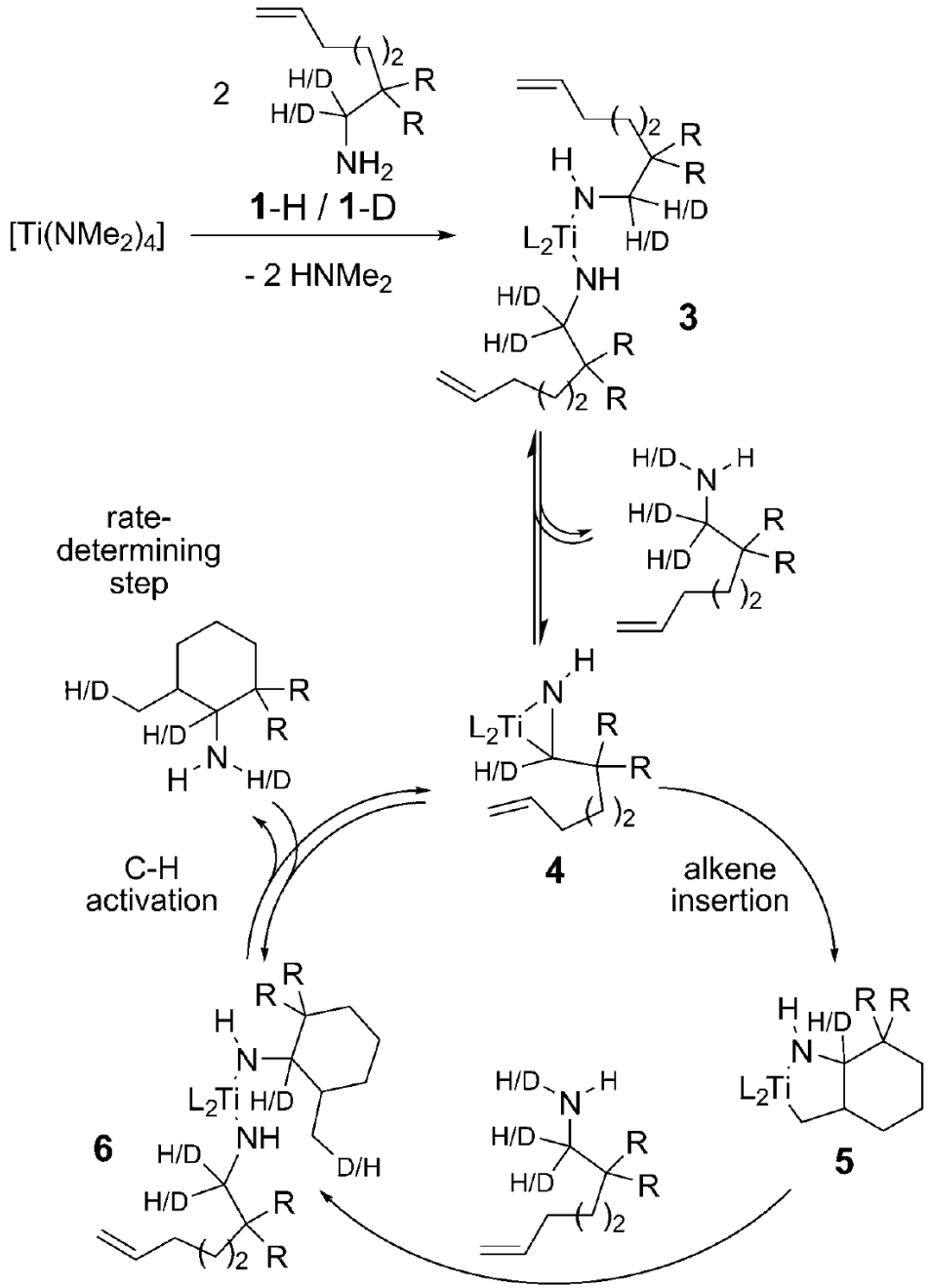

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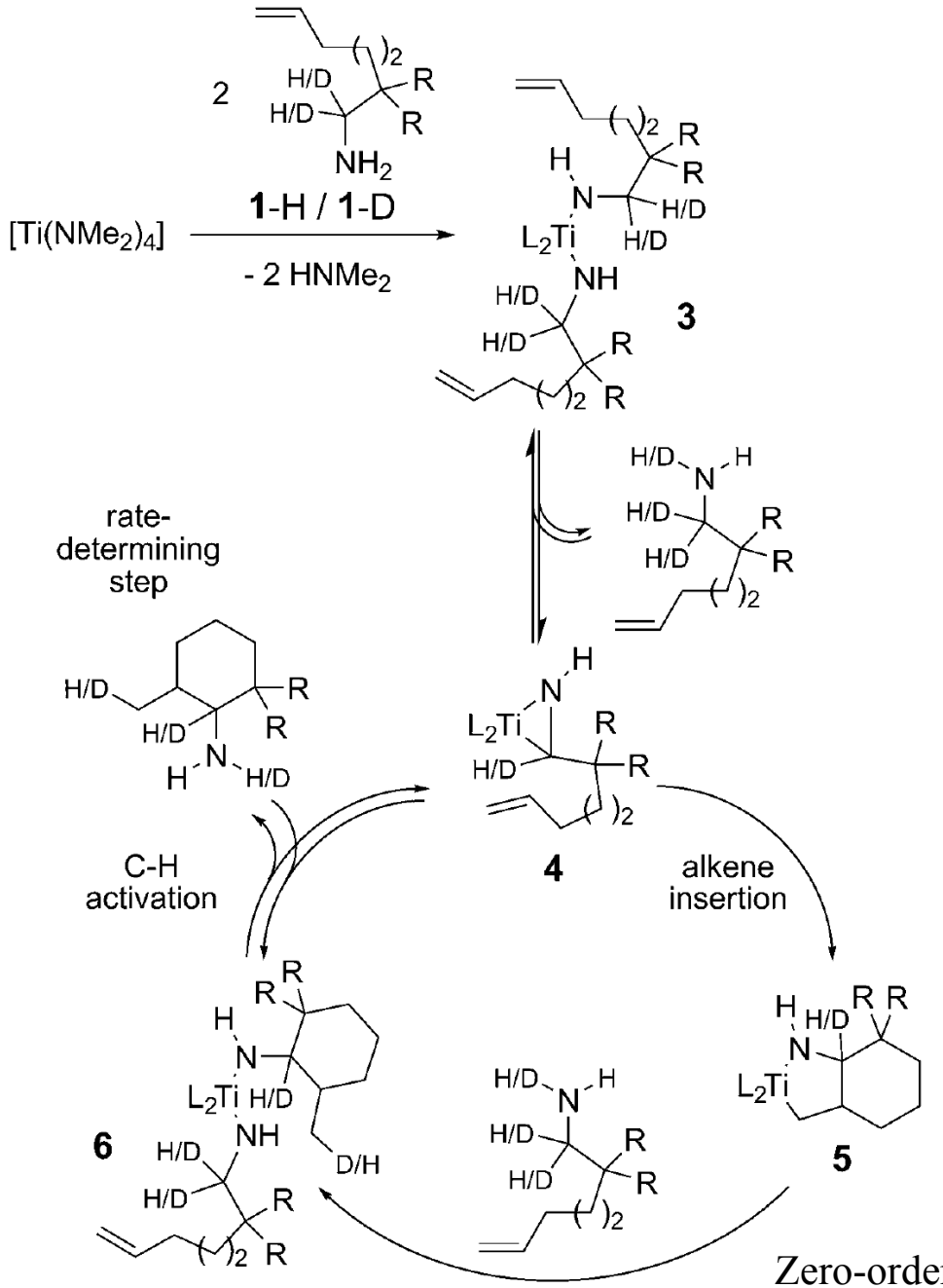
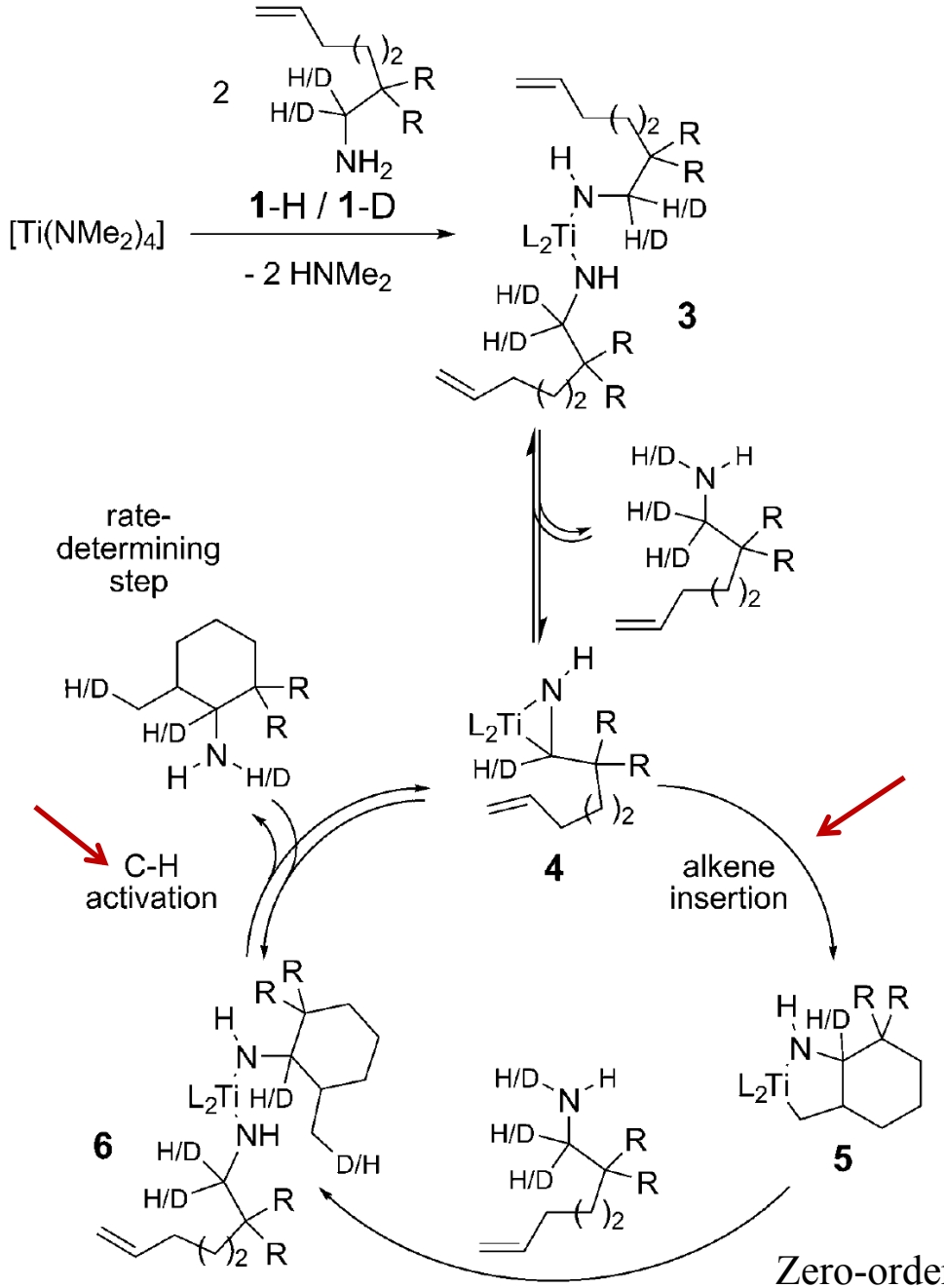


Zero-order rate dependence on aminoalkene

L = NMe_2
$NH\text{-}CH_2\text{-}CR_2\text{-}(CH_2)_3\text{-}CH{=}CH_2$

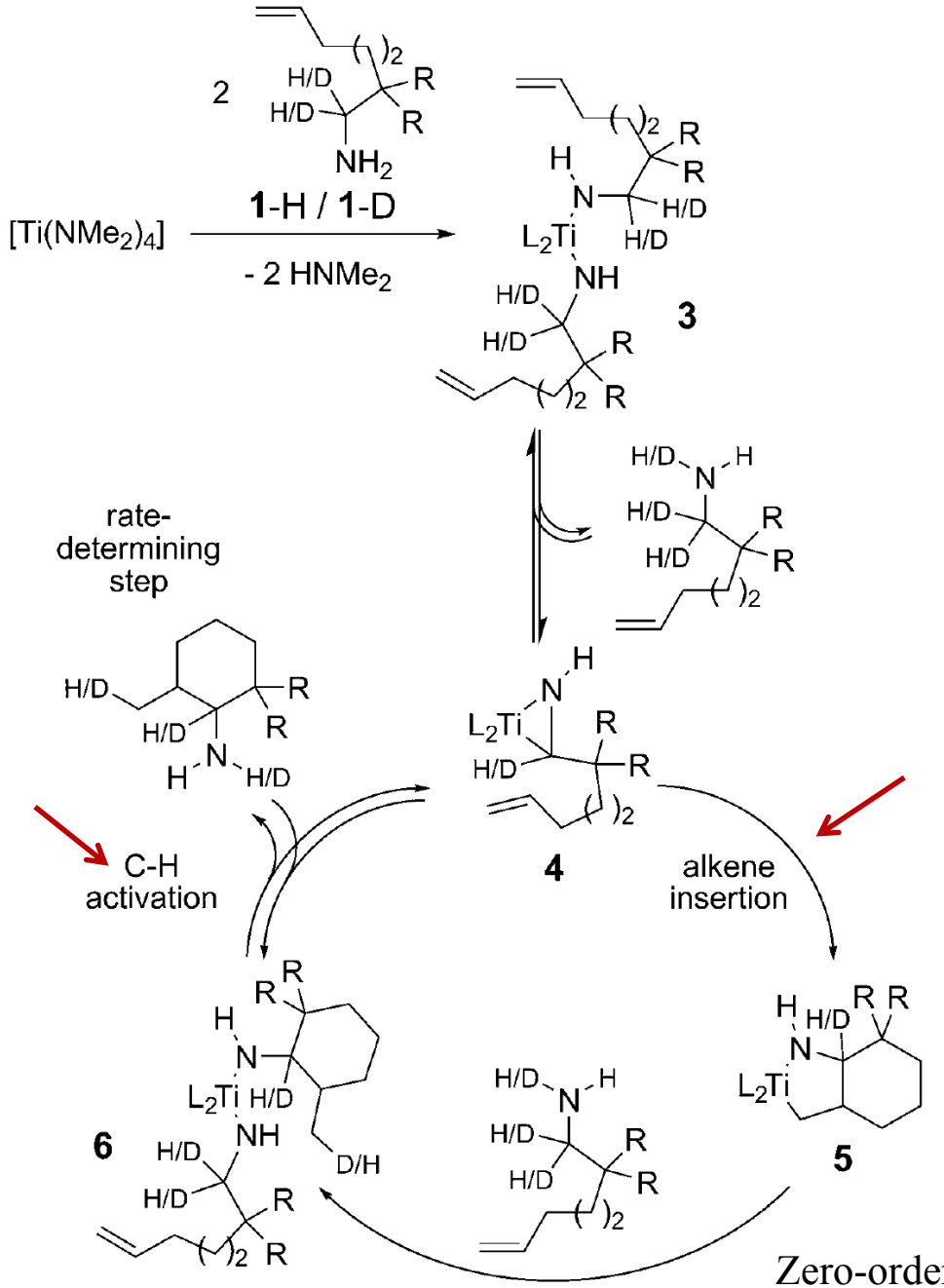
Sven Doye, *Angew. Chem. Int. Ed*. **2011**, *50*, 6401

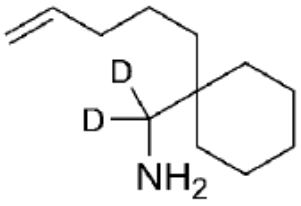


Zero-order rate dependence on aminoalkene

L = NMe_2
NH-CH_2-CR_2-$(CH_2)_3$-$CH=CH_2$

Sven Doye, *Angew. Chem. Int. Ed*. **2011**, *50*, 6401



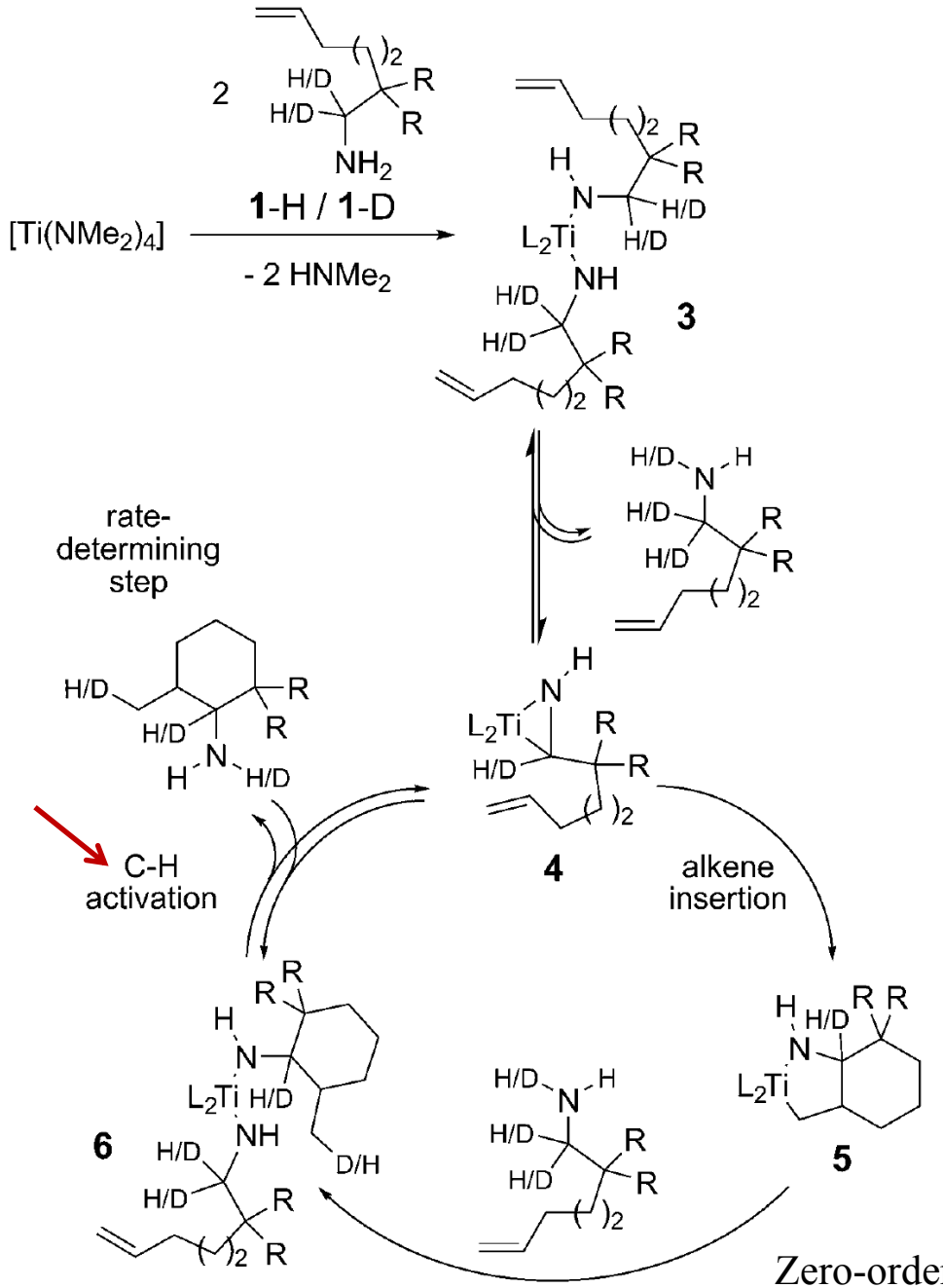


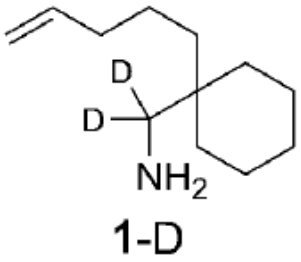
1-D

k_{obs}(1-H)/k_{obs} (1-D) = 7.3 at 130°C
with 5 mol% and 10 mol% [$Ti(NMe_2)_4$]

Zero-order rate dependence on aminoalkene

Sven Doye, *Angew. Chem. Int. Ed*. **2011**, *50*, 6401





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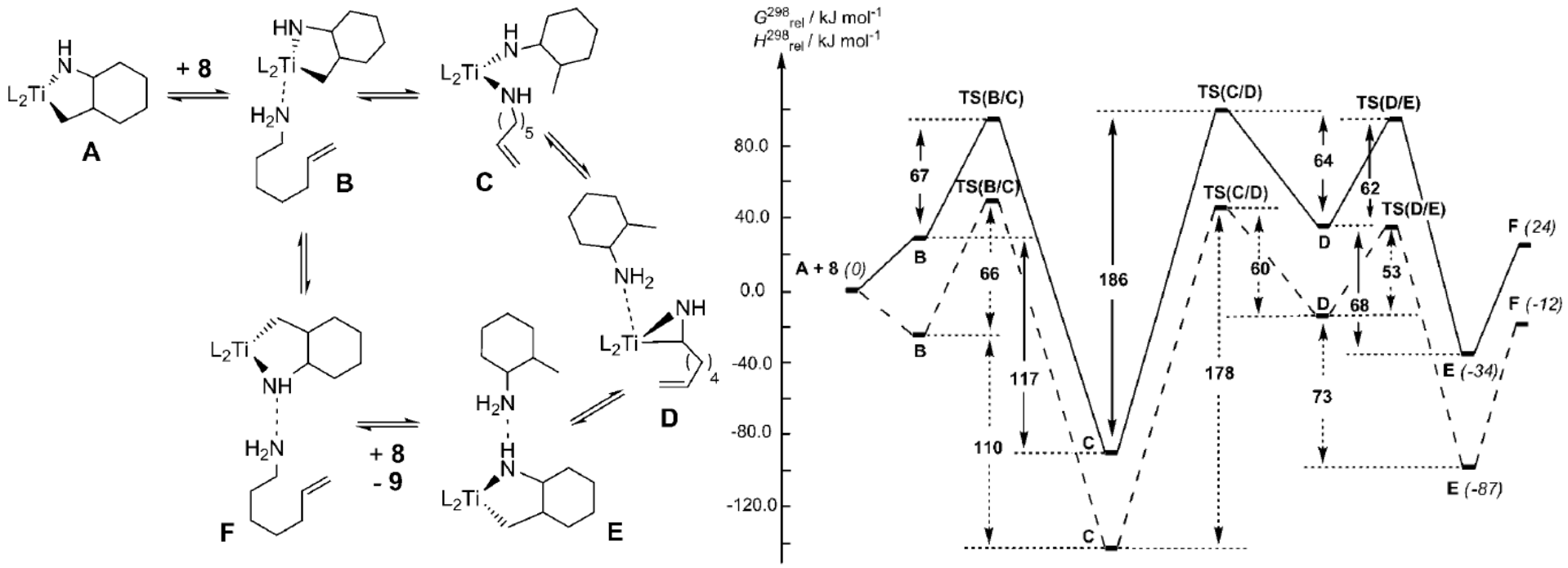
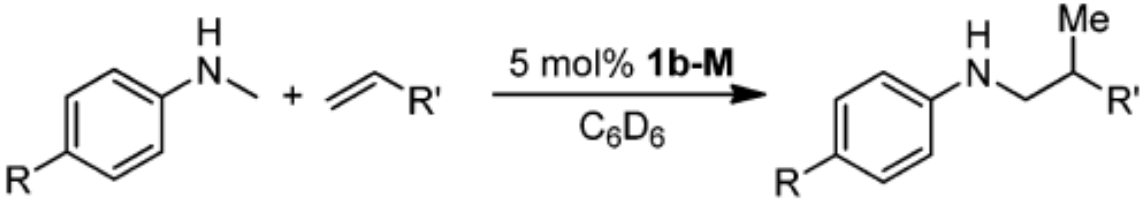
Zero-order rate dependence on aminoalkene

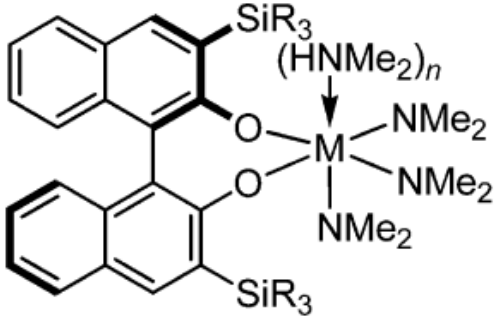
Sven Doye, *Angew. Chem. Int. Ed*. **2011**, *50*, 6401



Sven Doye, *Angew. Chem. Int. Ed*. **2011**, *50*, 6401



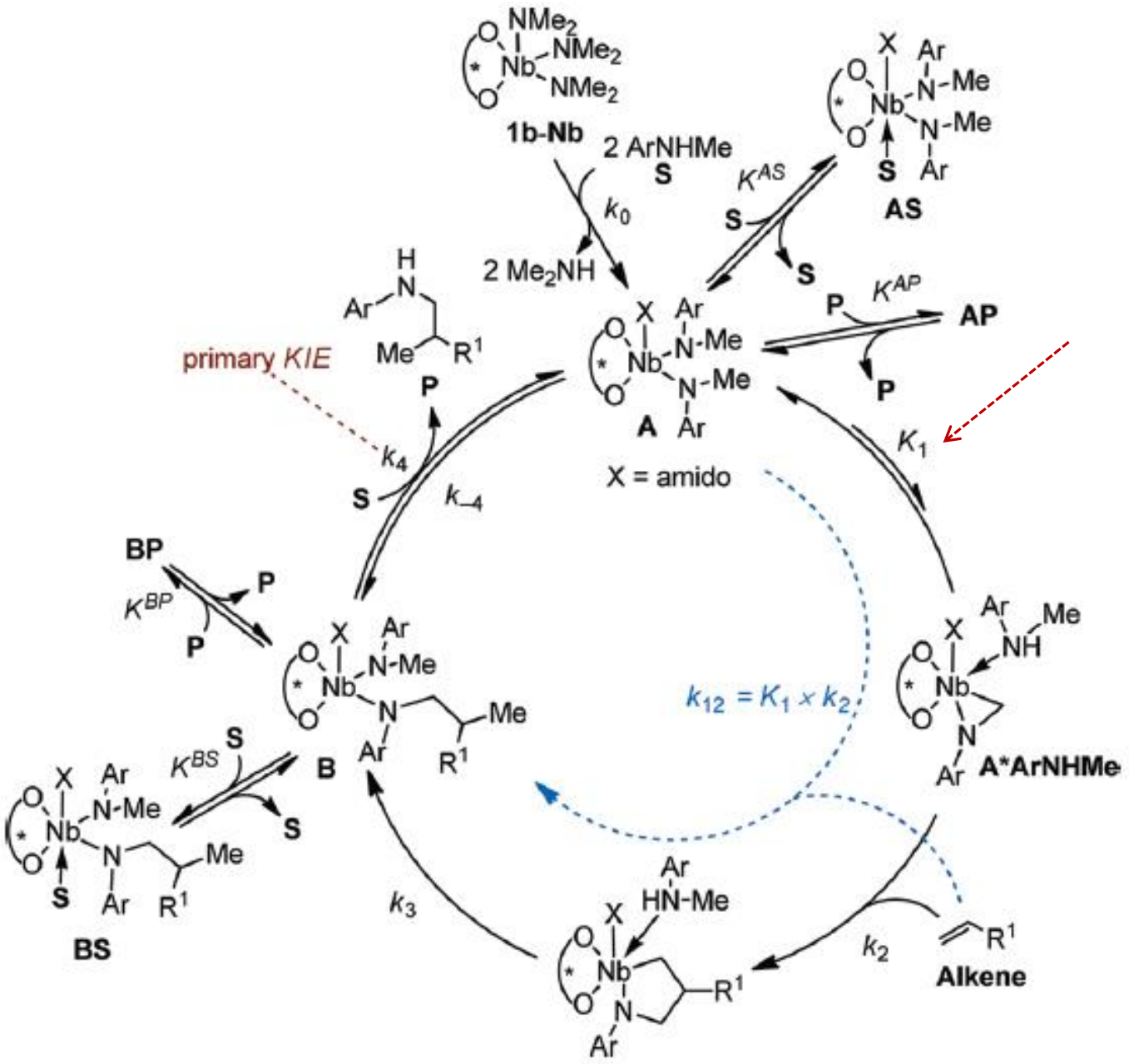
59-98% ee
61-95% yield



M = Ta, Nb

	SiR_3	*n*
1a-M	$Si\textit{i}Pr_2Me$	1 (Ta) / 0 (Nb)
1b-M	$SiPh_2Me$	1
1c-M	$SiMe_2\textit{t}Bu$	0
1d-M	$SiMe_3$	1

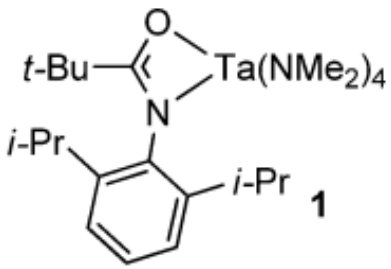
Kai C. Hultzsch J. Am. Chem. Soc., **2012**, *134*, 3300



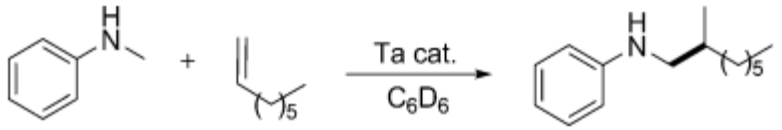
- Non-dissociative
- Fast
- reversible

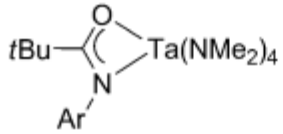
r.d.s:
Either by amide exchange
Or by alkene insertion

Catalyst activity can be enhanced by a more electron deficient ligand



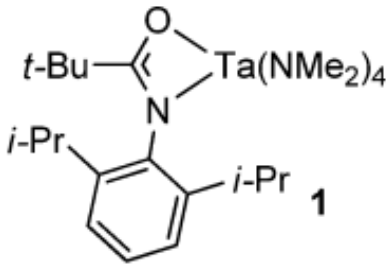
$TaMe_3Cl_2$



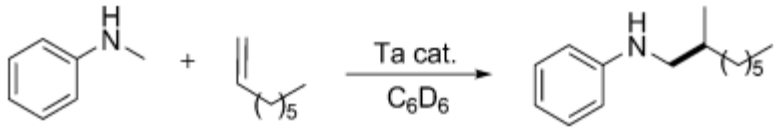
Entry	Catalyst	Conditions	Conv. [%]
1	$Ti(NMe_2)_4$	10 mol %, 160 °C, 96 h	32[a,4c]
2	$TiBn_4$	10 mol %, 160 °C, 96 h	77[a,4c]
3	Ind_2TiMe_2	2 mol %, 105 °C, 24 h	90[a,4d]
4	$Ta(NMe_2)_5$	5 mol %, 110 °C	n.r.
5	$[Cl_3Ta(NMePh)_2]_2$	2 mol %, 90 °C, 24 h	72[a,5b]
6		5 mol %, 110 °C, 63 h	96[a,5c]
7	$TaMe_3Cl_2$	10 mol %, 110 °C, 30 h	91

[a] Reported yields; n.r. = no reaction.

Laurel L. Schafer *Chem. Eur. J.* **2013**, *19*, 8751



$TaMe_3Cl_2$



Entry	Catalyst	Conditions	Conv. [%]
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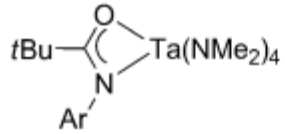
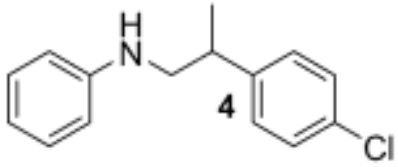
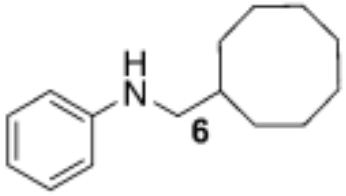
2	$TiBn_4$	10 mol %, 160 °C, 96 h	77[a,4c]
3	Ind_2TiMe_2	2 mol %, 105 °C, 24 h	90[a,4d]
4	$Ta(NMe_2)_5$	5 mol %, 110 °C	n.r.
5	$[Cl_3Ta(NMePh)_2]_2$	2 mol %, 90 °C, 24 h	72[a,5b]
6		5 mol %, 110 °C, 63 h	96[a,5c]
7	$TaMe_3Cl_2$	10 mol %, 110 °C, 30 h	91

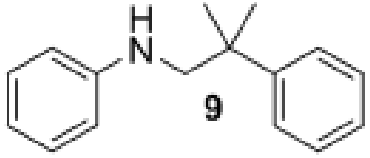
[a] Reported yields; n.r. = no reaction.



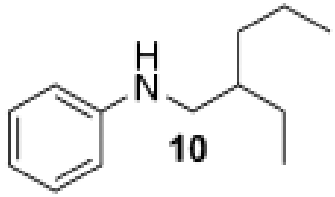
84%



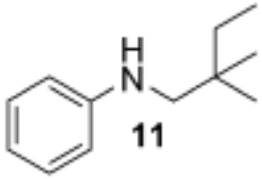
73%



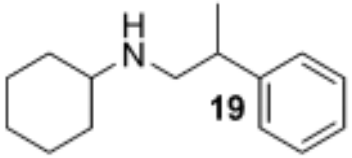
61%
130 °C



36%
145 °C



16%
145 °C



85%

- Styrene
- disubstituted terminal alkenes
- internal unstrained alkenes
- dialkylamines.

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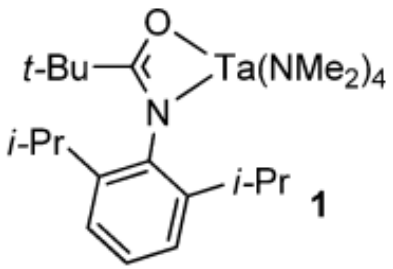
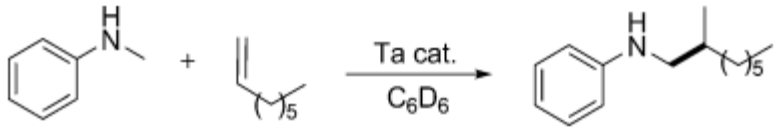
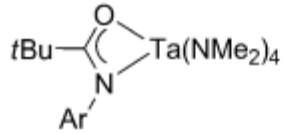
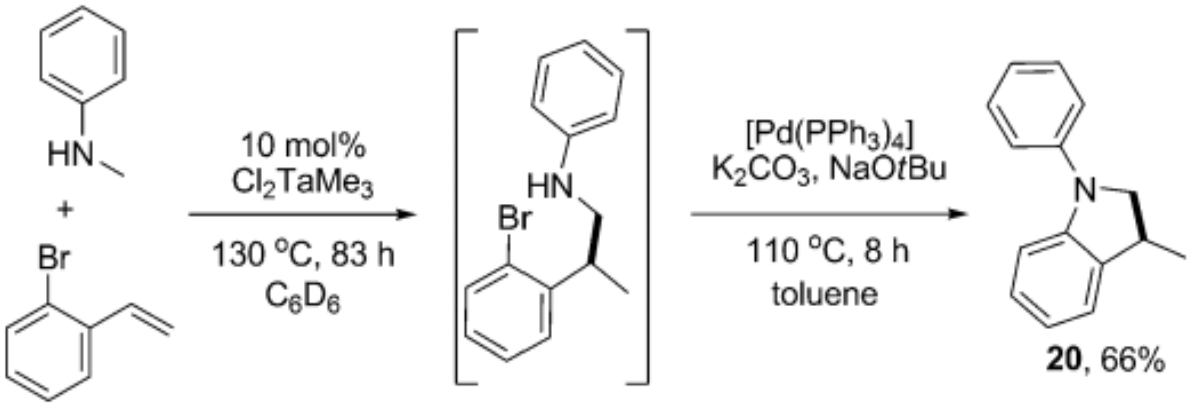


$TaMe_3Cl_2$



Entry	Catalyst	Conditions	Conv. [%]
1	$Ti(NMe_2)_4$	10 mol %, 160 °C, 96 h	32[a,4c]
2	$TiBn_4$	10 mol %, 160 °C, 96 h	77[a,4c]
3	Ind_2TiMe_2	2 mol %, 105 °C, 24 h	90[a,4d]
4	$Ta(NMe_2)_5$	5 mol %, 110 °C	n.r.
5	$[Cl_3Ta(NMePh)_2]_2$	2 mol %, 90 °C, 24 h	72[a,5b]
6		5 mol %, 110 °C, 63 h	96[a,5c]
7	$TaMe_3Cl_2$	10 mol %, 110 °C, 30 h	91

[a] Reported yields; n.r. = no reaction.



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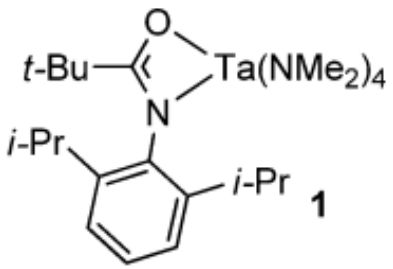
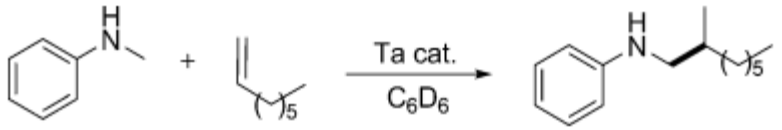
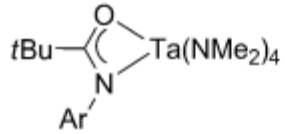


$TaMe_3Cl_2$



Entry	Catalyst	Conditions	Conv. [%]
1	$Ti(NMe_2)_4$	10 mol %, 160 °C, 96 h	32[a,4c]
2	$TiBn_4$	10 mol %, 160 °C, 96 h	77[a,4c]
3	Ind_2TiMe_2	2 mol %, 105 °C, 24 h	90[a,4d]
4	$Ta(NMe_2)_5$	5 mol %, 110 °C	n.r.
5	$[Cl_3Ta(NMePh)_2]_2$	2 mol %, 90 °C, 24 h	72[a,5b]
6		5 mol %, 110 °C, 63 h	96[a,5c]
7	$TaMe_3Cl_2$	10 mol %, 110 °C, 30 h	91

[a] Reported yields; n.r. = no reaction.

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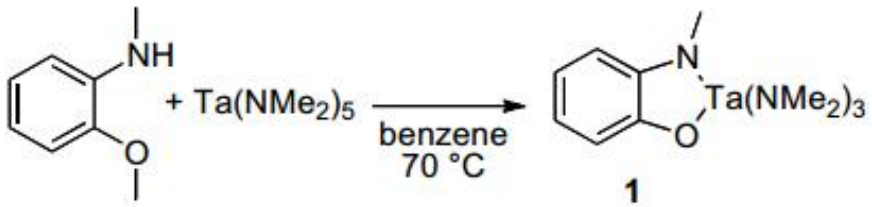
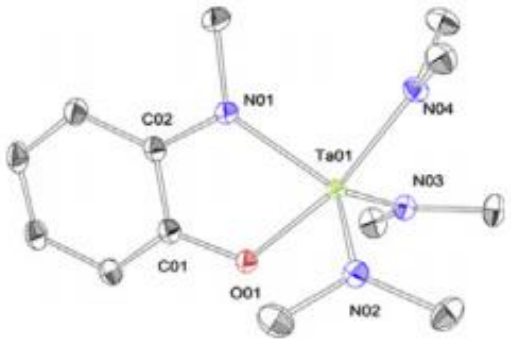
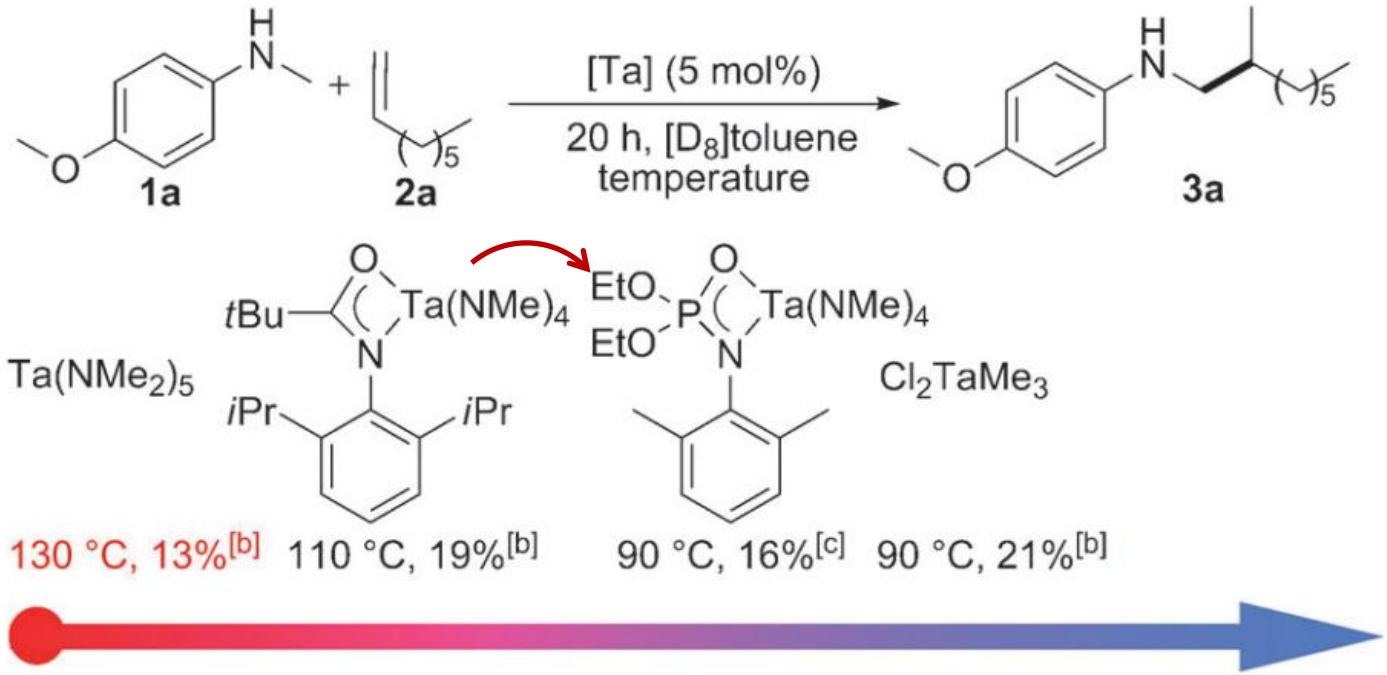




Laurel L. Schafer *Tetrahedron* **2013,** *69*, 5737



minimum temperature required to achieve at least three turnovers within 20 h

- sufficient steric bulk is critical
- Electron withdrawing ligand is critical

Phosphoramidates

- increased electronwithdrawing properties
- tunable steric bulk at both phosphorus and nitrogen

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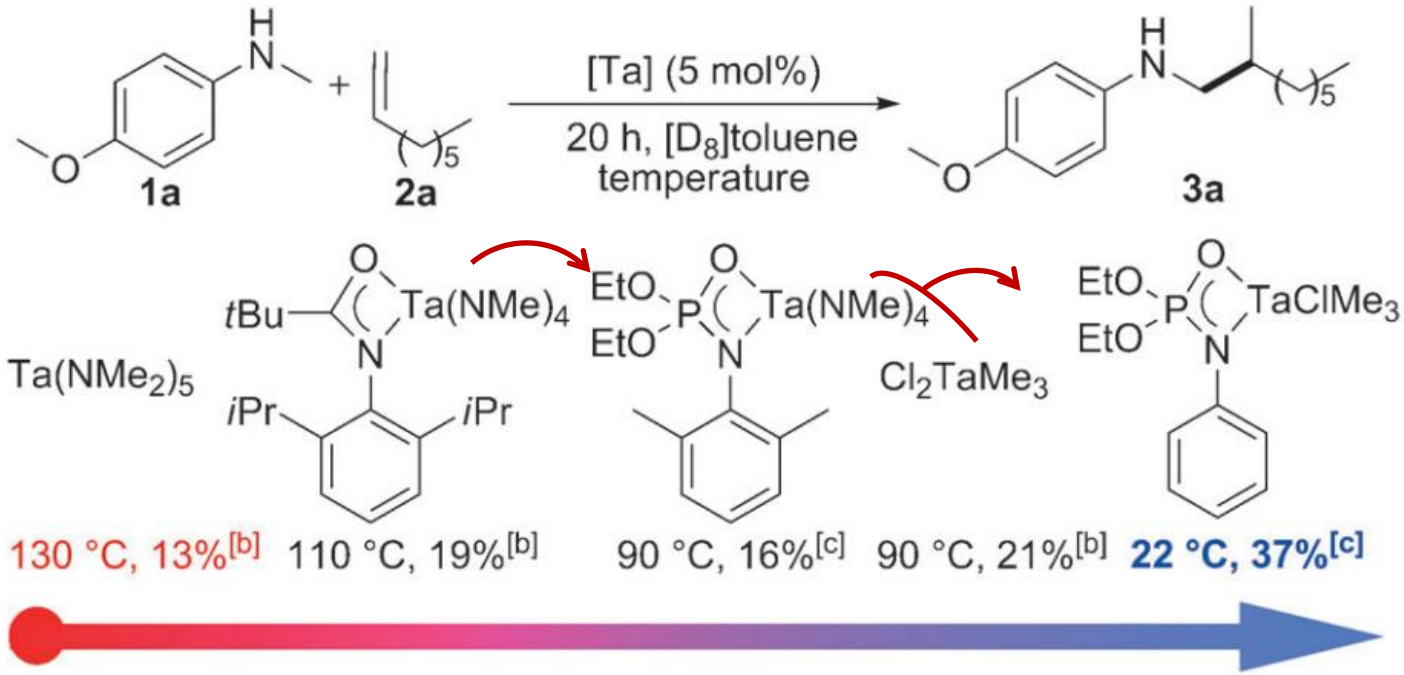

minimum temperature required to achieve at least three turnovers within 20 h

- sufficient steric bulk is critical
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Phosphoramidates

- increased electronwithdrawing properties
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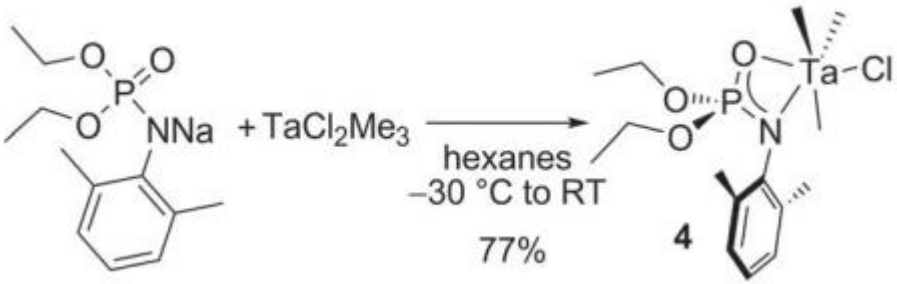

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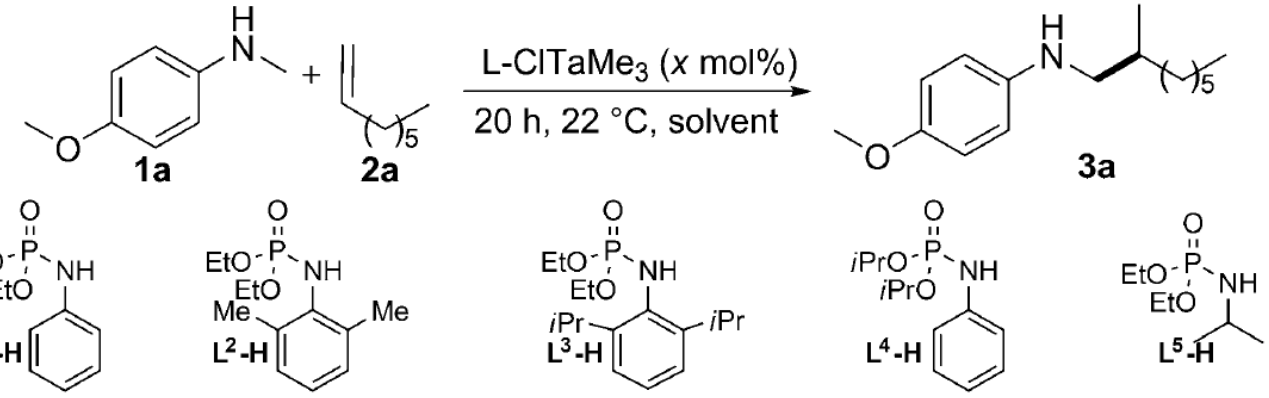

Entry	L	*x* mol%	Solvent	Conv. [%]
1[b]	**L**^{1}	5	[D$_8$]toluene	37
2[b]	**L**^{2}	5	[D$_8$]toluene	52
3[b]	**L**^{3}	5	[D$_8$]toluene	28
4[b]	**L**^{4}	5	[D$_8$]toluene	24
5[b]	**L**^{5}	5	[D$_8$]toluene	0
6[b]	**L**^{2}	10	[D$_8$]toluene	76
7[b]	**L**^{2}	10	hexanes	62
8[c]	**L**^{2}	10	[D$_8$]THF	26
9[c]	**L**^{2}	10	[D$_8$]toluene	86

[a] Reaction conditions: **1a** (0.5 mmol), **2a** (0.75 mmol), solvent (0.6 mL), [Ta] (*x* mol%), 20 h. Conversion determined by ^{1}H NMR spectroscopy. [b] In situ generated complex. [c] Isolated complex.

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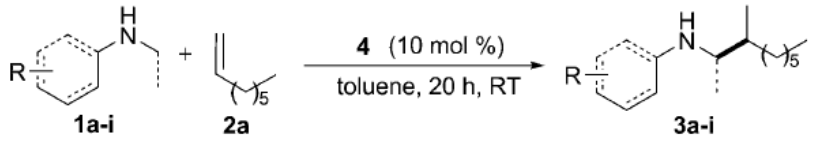
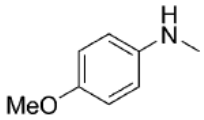
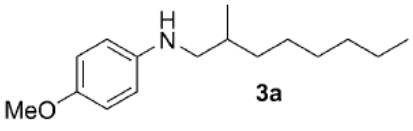
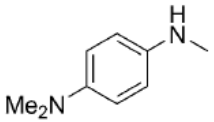
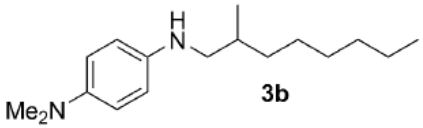
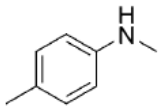
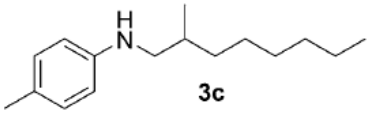
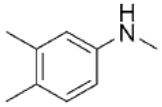
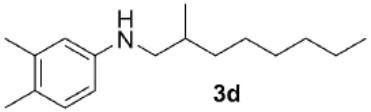
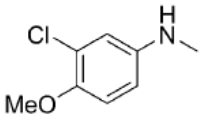
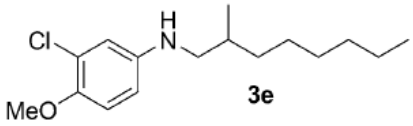
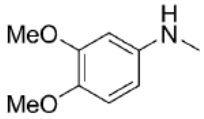
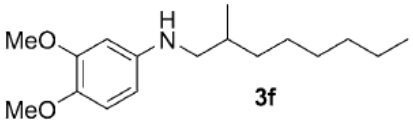
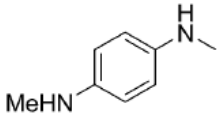
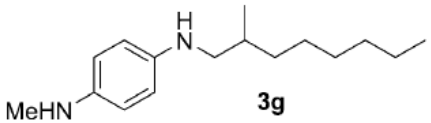
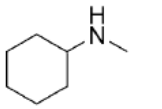
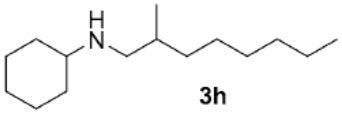
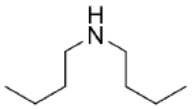
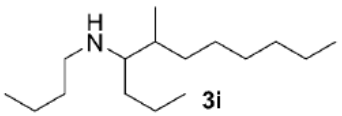
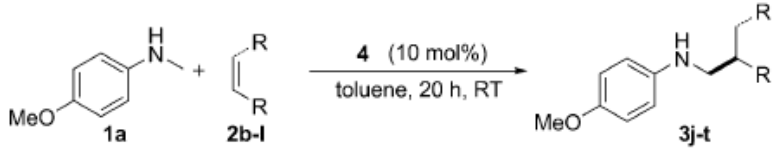
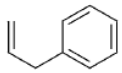
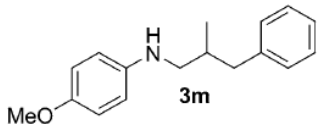
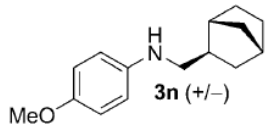
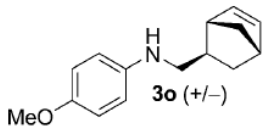
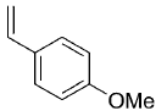
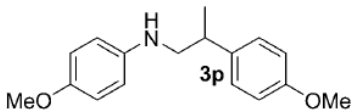
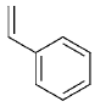
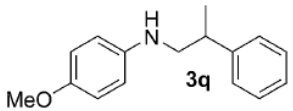
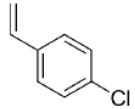
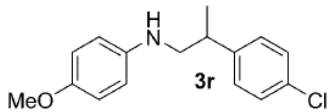
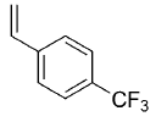
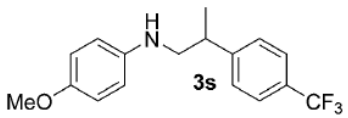
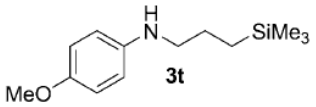
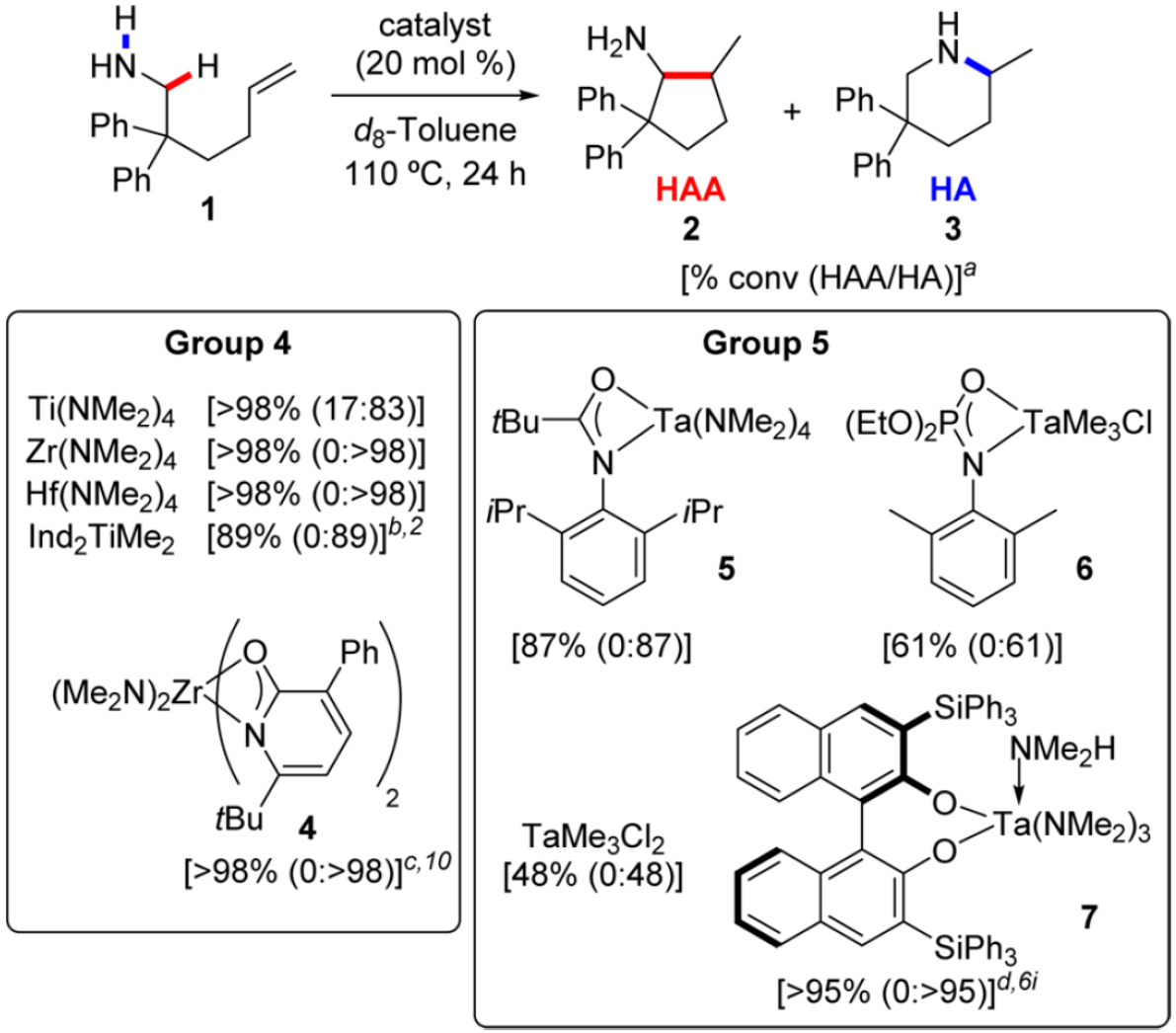


Entry	Amine	Product	Yield [%]
1		 **3a**	84
2		 **3b**	87
3		 **3c**	46
4		 **3d**	62 (44 h)
5		 **3e**	41
6		 **3f**	80 (64 h)
7		 **3g**	52
8		 **3h**	84 (50 °C) 62 (168 h)
9		 **3i**	15



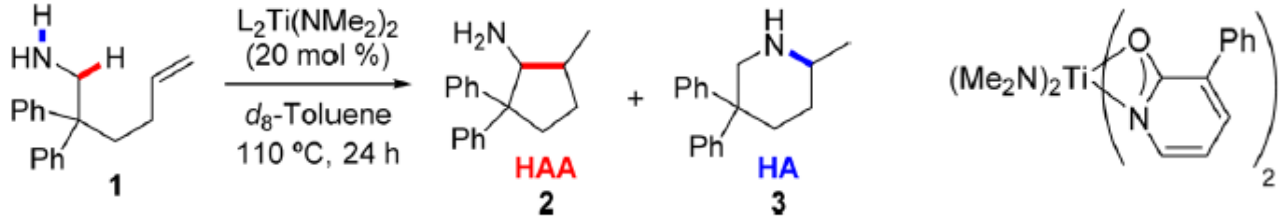
Entry	Amine	Product	Yield [%]
4		 **3m**	70
5		 **3n** (+/–)	86
6		 **3o** (+/–)	56
7		 **3p**	88 [*68:1*][b] (50 °C) 87 (168 h)
8		 **3q**	87 [*14:1*][b] (50 °C) 93 [*26:1*][b] (168 h)
9		 **3r**	58 [*10:1*][b] (50 °C) 93 [*10:1*][b] (168 h)
10		 **3s**	91 [*1.6:1*][b] (50 °C) 78 [*1.8:1*][b] (168 h)
11		 **3t**	66 [*1:7*][c]

Laurel L. Schafer *Angew. Chem. Int. Ed*. **2013**, *52*, 9144



[a] Determined by ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. [b] 5 mol %, 105 °C. [c] 10 mol %, 5 h. [d] 5 mol %, 120 °C, 36 h, C_6D_6.

Laurel L. Schafer Org. Lett., **2013**, *15*, 6002



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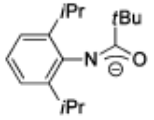
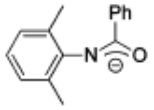
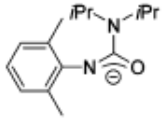
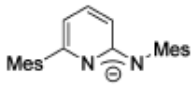
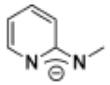
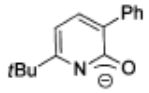
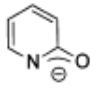
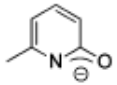
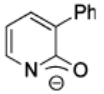
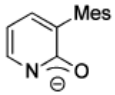
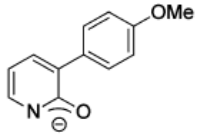
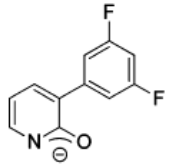
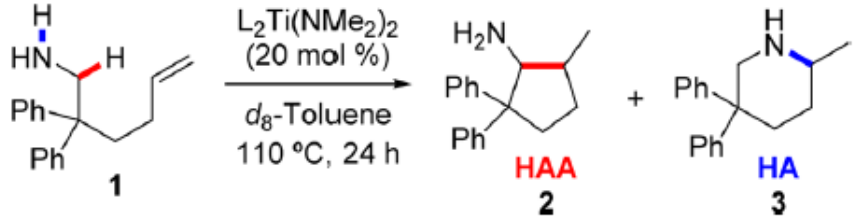
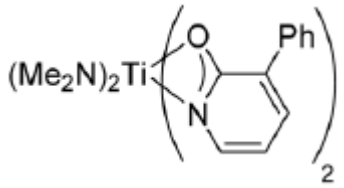
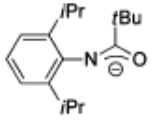
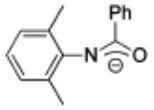
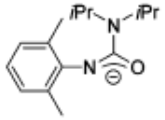
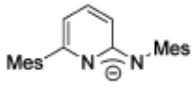
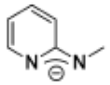
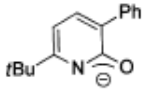
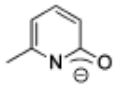
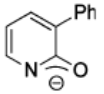
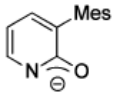
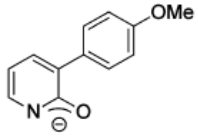
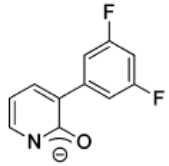
1		91	0:91
2		58	0:58
3		8	0:8
4[c]		>98	0:>98
5[d]		(97)[e] 87	(20:77)[e] 52:35
6		3	n.d.
7		9	8:1
8		4	n.d.
9		45	37:8

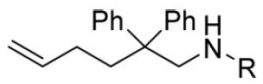
entry	L	conv (%)[b]	HAA/HA[b]
10		76	71:5
11		16	8:8
12		75	70:5
13		86	54:32





entry	L	conv (%)[b]	HAA/HA[b]
1		91	0:91
2		58	0:58
3		8	0:8
4[c]		>98	0:>98
5[d]		(97)[e] 87	(20:77)[e] 52:35
6		3	n.d.
7		9	8:1
8		4	n.d.
9		45	37:8

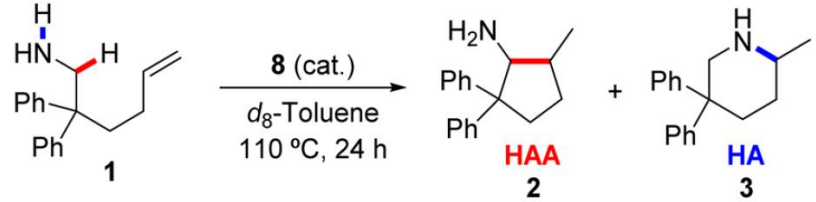
entry	L	conv (%)[b]	HAA/HA[b]
10		76	71:5
11		16	8:8
12		75	70:5
13		86	54:32



R = Me, Ph

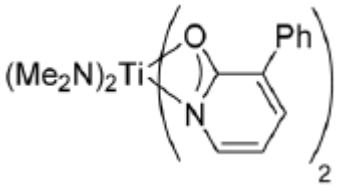
8 (20 mol %)
d_8-Toluene
145 ºC, 48 h

NO REACTION



[catalyst] = 0.025 M, 10 mol %
0.050 M, 20 mol %
0.100 M, 40 mol %

% conv (HAA/HA) = 64 (12:1)
76 (14:1)
82 (20:1)



e-withdrawing and steric less hindered ligand!

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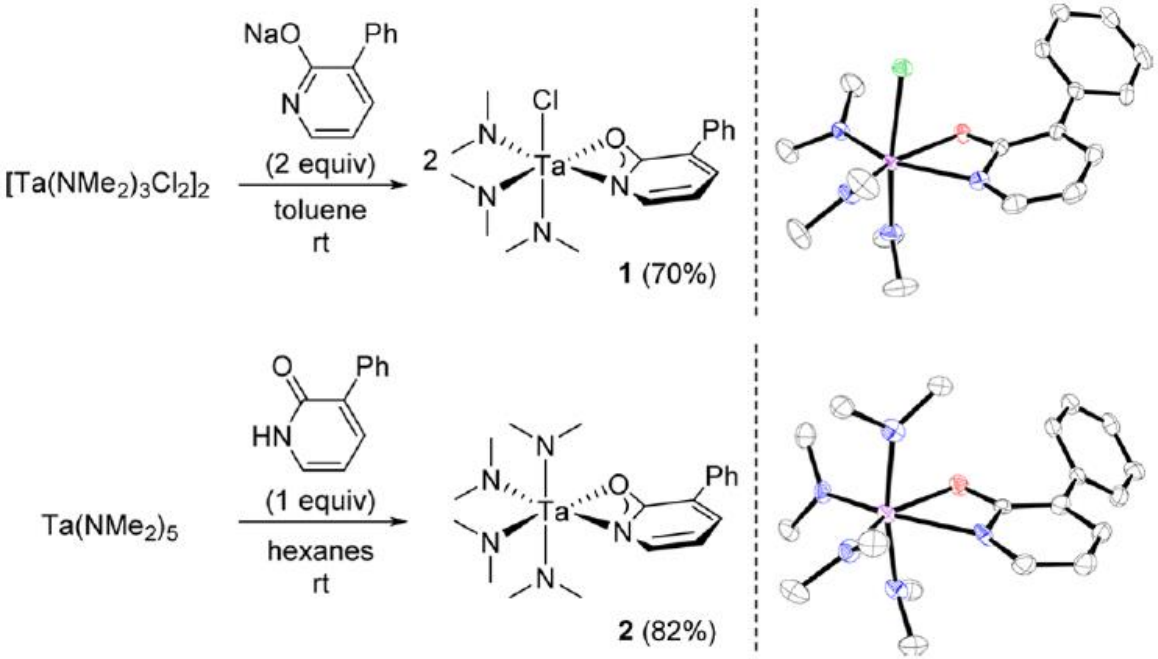

- Ta−Cl bond [2.4959(8) Å] is significantly longer than Ta−NMe2(axial) bond [1.970(3) Å]
- the bonding the of Ta−N amido bond lengths are shorter in 1 than in 2

Improved metal accessibility
increased electrophilic nature of the metal center

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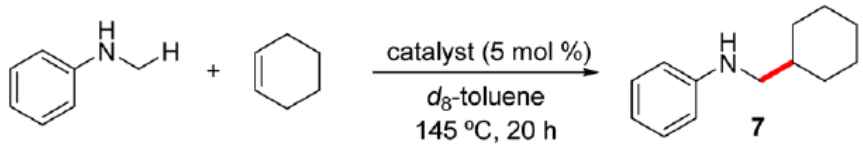
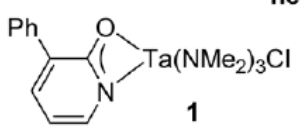


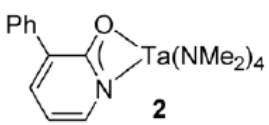
$TaMe_3Cl_2$	$Ta(NMe_2)_5$	$[Ta(NEt_2)_2Cl_3]_2$	$[Ta(NMe_2)_3Cl_2]_2$
3%	n.r.	n.r.	6%

new



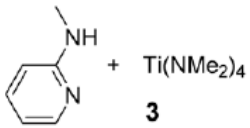
1

>95% (88%)[b]



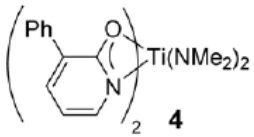
2

10%



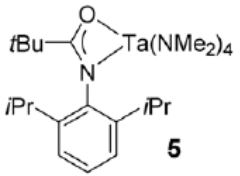
3

(1:1) n.r.
(2:1) n.r.



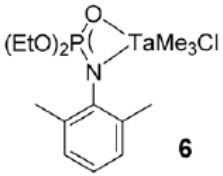
4

n.r.



5

n.r.



6

4%

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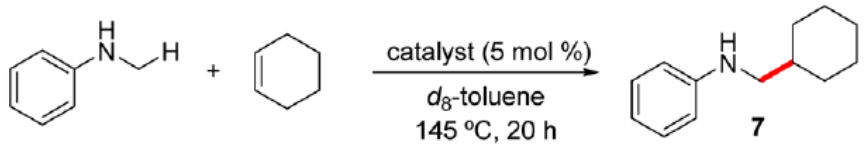
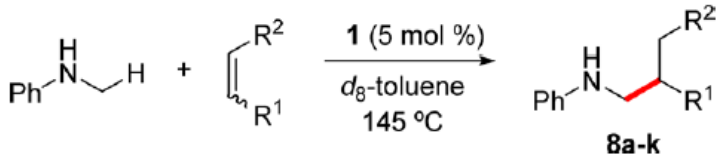
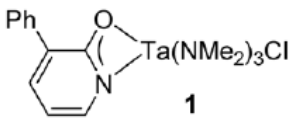


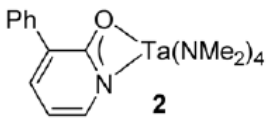


$TaMe_3Cl_2$	$Ta(NMe_2)_5$	$[Ta(NEt_2)_2Cl_3]_2$	$[Ta(NMe_2)_3Cl_2]_2$
3%	n.r.	n.r.	6%

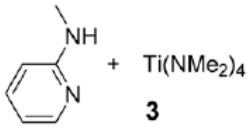
new



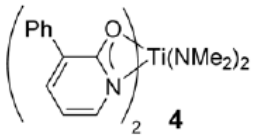
>95% (88%)[b]



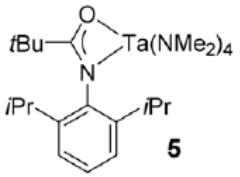
10%



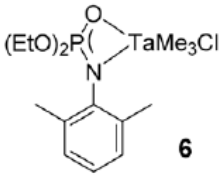
(1:1) n.r.
(2:1) n.r.



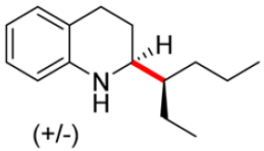
n.r.



n.r.

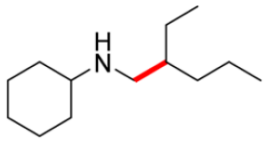


4%

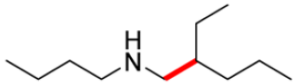


(+/-)

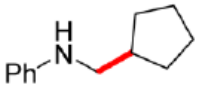
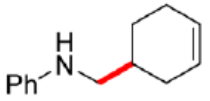
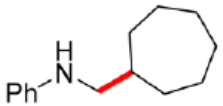
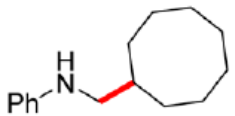
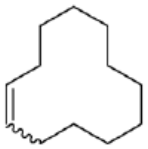
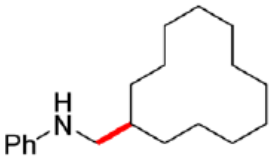
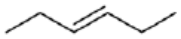
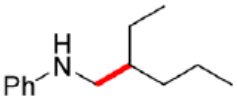
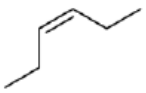
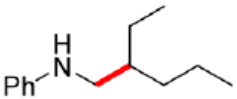
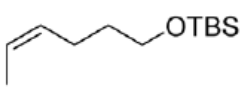
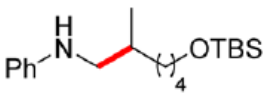
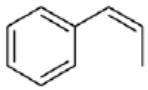
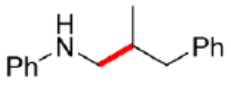
9i
82%[c]



9j
88%[d]



9k
64%[b,e]

entry	alkene	product		cond.	yield (%)
1			**8a**	44 h	73
2[b]			**8b**	20 h	72
3			**8c**	130 °C 20 h	95
4			**8d**	20 h	93
5			**8e**	44 h	88
6			**8f**	44 h	79
7			**8f**	44 h	69
8			**8g**	44 h	70[c] (2.3:1)[d]
9			**8h**	24 h	92[c] (4.4:1)[d]

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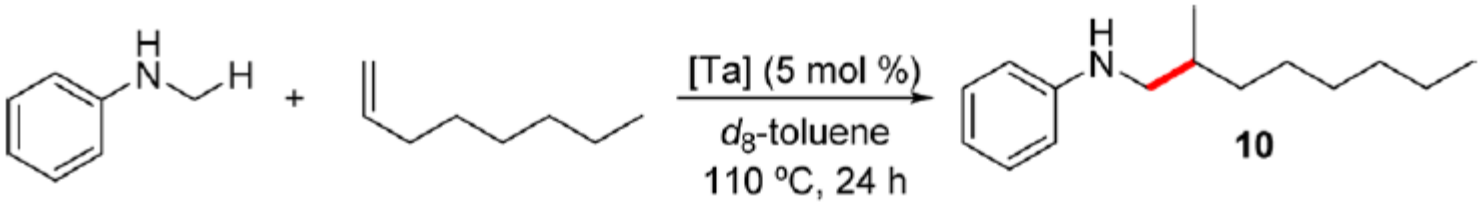

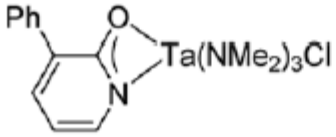

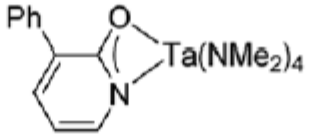

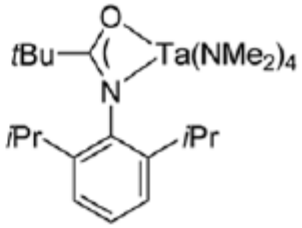

catalyst:	**1**	**2**	**5**
conv.[a]:	40%	>95% (93%)[b]	(92%)[b,6e] (63 h)

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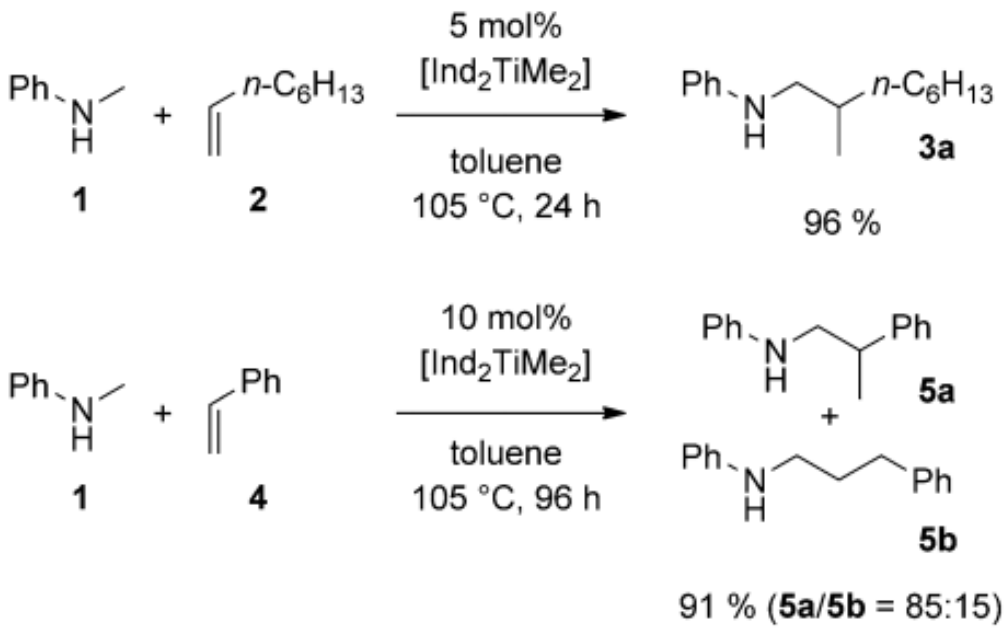
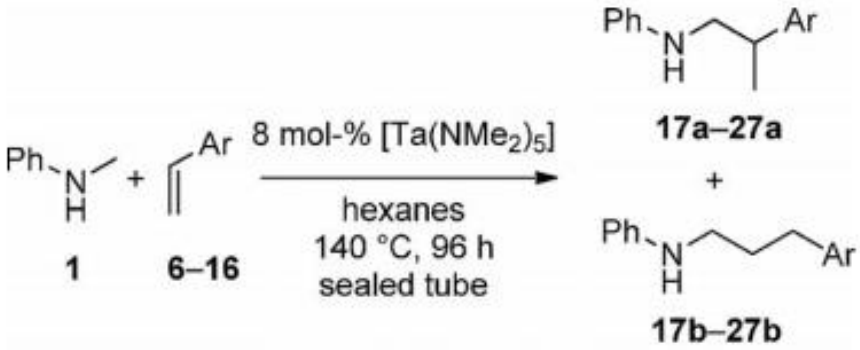
Another unsolved problem: Styrene selectivity w/ [Ti]



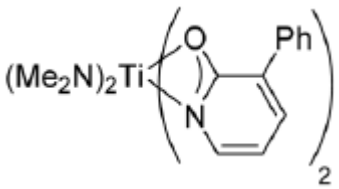
Branched selectivity: has already been achieved by [Ta]



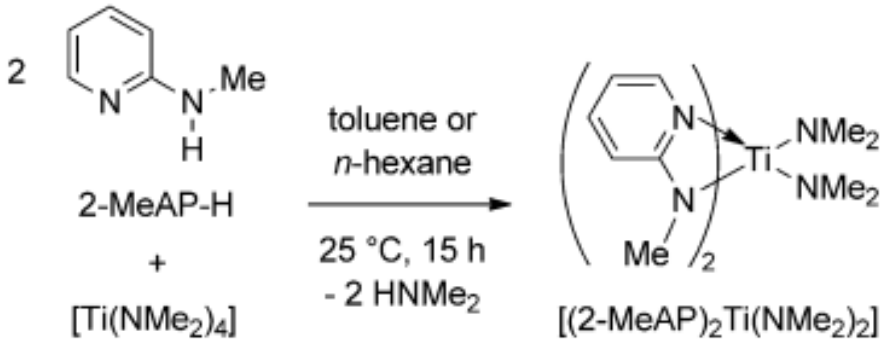
a:b>99:1

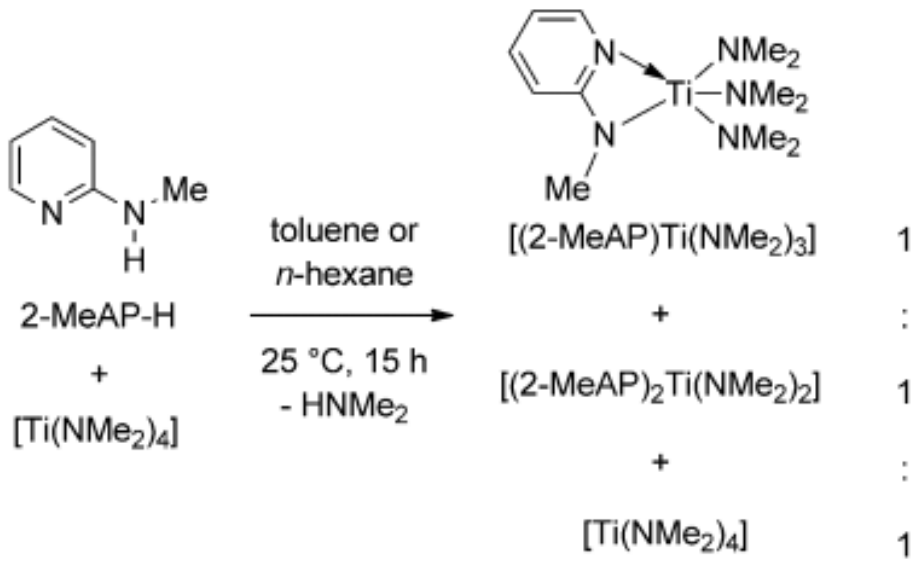
Eur. J. Org. Chem. **2014**, 2790

Linear selectivity?



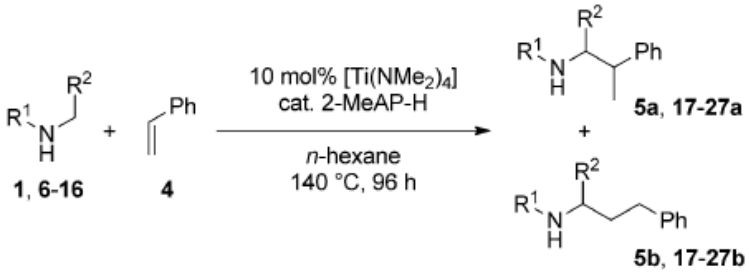
Schafer's catalyst for intramaleculor HAA reaction

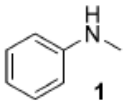
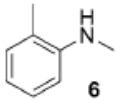
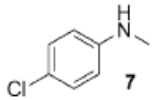
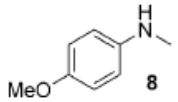
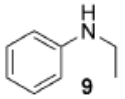
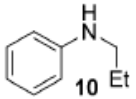
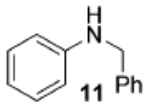
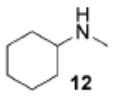
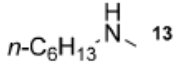


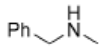
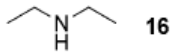


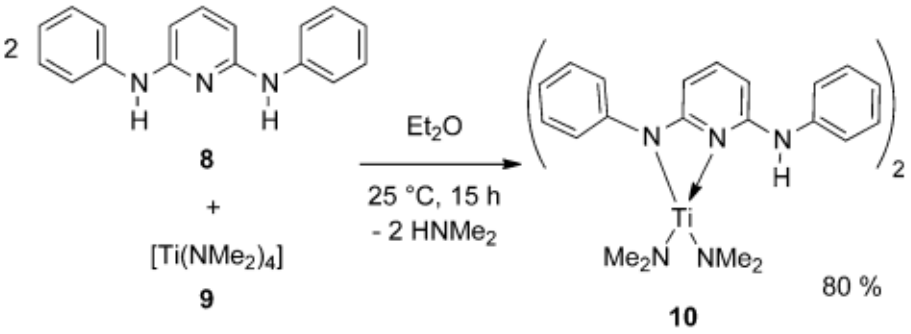
By NMR

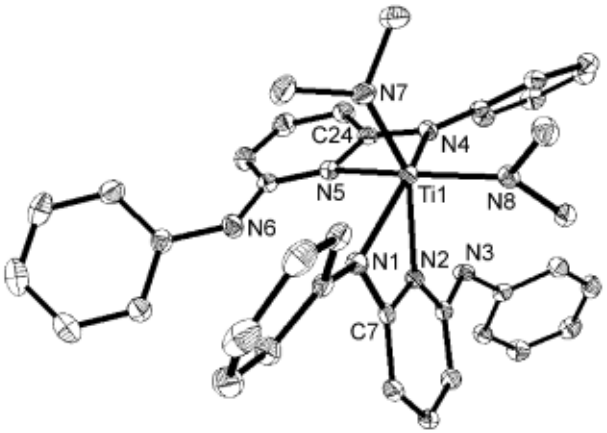
Sven Doye *Angew. Chem. Int. Ed*. **2013**, *52*, 1806

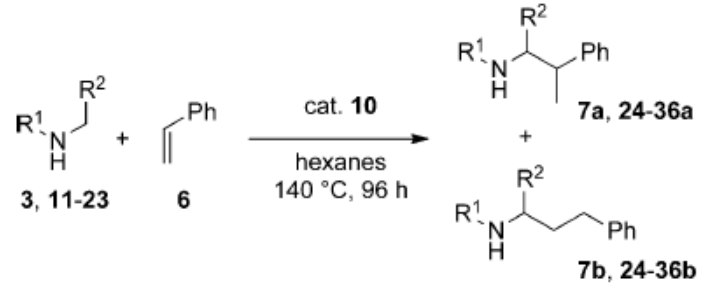


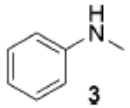
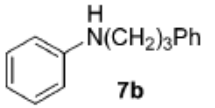
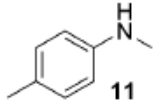
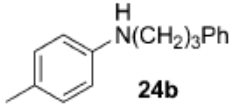
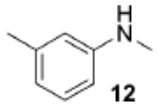
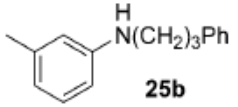
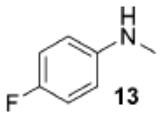
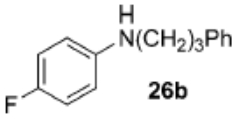
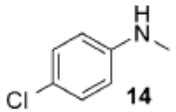
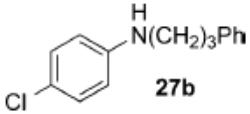
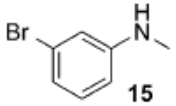
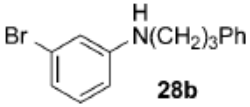
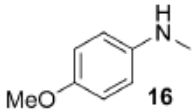
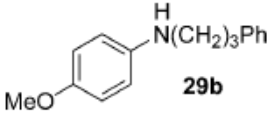
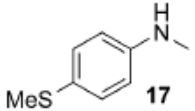
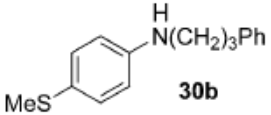
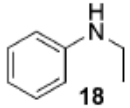
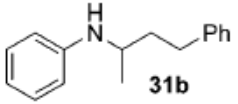
Entry	Amine	2-MeAP-H [mol%]	Yield a + b [%][a]	Selectivity a/b[b]
1	 1	10	79 (5a/b)	32:68
2		20	76 (5a/b)	34:66
3	 6	10	31 (17a/b)[c]	32:68
4		20	4 (17a/b)	33:67
5	 7	10	31 (18a/b)	43:57
6		20	2 (18a/b)	30:70
7	 8	10	50 (19a/b)	35:65
8		20	15 (19a/b)	25:75
9	 9	10	61 (20a/b)	21:79
10		20	32 (20a/b)[d]	21:79
11	 10	10	48 (21a/b)	9:91
12		20	4 (21a/b)	1:99
13	 11	10	85 (22a/b)	8:92
14		20	30 (22a/b)	7:93
15	 12	10	71 (23a/b)[e,f]	42:58
16		20	60 (23a/b)[e,f,g]	27:73
17	 13	10	22 (24a/b)[e,f]	20:80
18		20	5 (24a/b)[e,f]	12:88

Entry	Amine	2-MeAP-H [mol%]	Yield a + b [%][a]	Selectivity a/b[b]
19	 14	10	69 (25a/b)[e,h]	7:93
20		20	40 (25a/b)[e,h]	35:65
21	15	10	5 (26a/b)[e]	12:88
22		20	17 (26a/b)[e]	12:88
23	 16	10	26 (27a/b)[e]	15:85
24		20	8 (27a/b)[e]	12:88







Entry	Amine	10 [mol %]	Product	Yield [%][a]	Selectivity a/b[b]
1	 **3**	5	 **7b**	81 (7 b)	6:94
2	 **11**	5	 **24b**	73 (24 b)	5:95
3	 **12**	5	 **25b**	74 (25 b)	5:95
4	 **13**	5	 **26b**	72 (26 b)	6:94
5	 **14**	5	 **27b**	31 (27 b)	6:94
6	 **15**	5	 **28b**	23 (28 b)	5:95
7	 **16**	5	 **29b**	74 (29 b)	5:95
8	 **17**	10	 **30b**	46 (30 b)	6:94
9	 **18**	10	 **31b**	33 (31 b)	1:99

Summary

- sp^3 C-H alkylation has been achieved via many different machanism
- Metal: d^0 & d^8
- Logical development of ligand and catalyst is critical
- Inspiration of our own work

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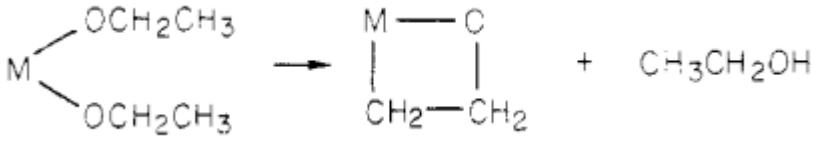
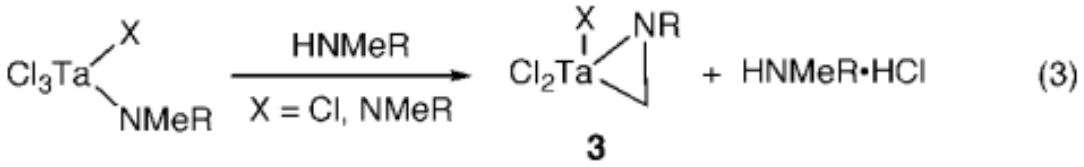
Table II. H-D Exchange in CH_3CH_2OD Catalyzed by Transition-Metal Ethoxides[a]

catalyst	temp, °C	% H-D exchange[c]	distributn of ^2H label,[b] %		
			CH_2D	CD_2H	CD_3
$Ti(OEt)_4$	180	0[e]			
$Zr(OEt)_4$	200	14	5	25	70
$Nb_2(OEt)_{10}$	200	18	27	41	32
$Ta_2(OEt)_{10}$	180	9			
$Ta_2(OEt)_{10}$	200	23	28	39	33
$Ta_2(OEt)_{10}$	220	47			
$Ta_2(OEt)_{10}$ + C_6H_5N[d]	200	55	38	39	23
$Ta_2(OEt)_{10}$ + Et_3N[d]	200	50			
$W(OEt)_6$	200	0[e,f]			

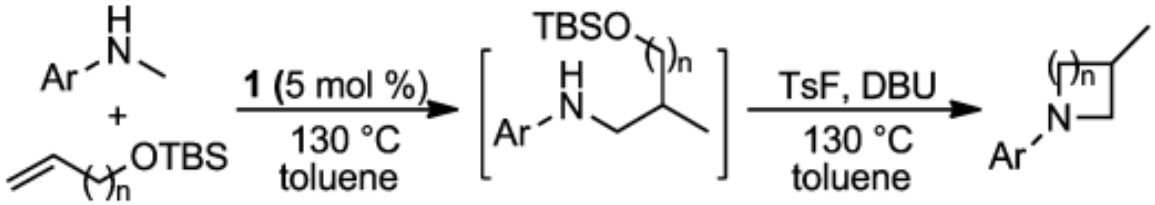


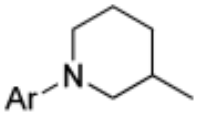
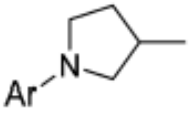
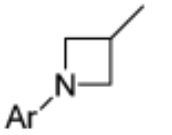
"The predominance of multiply deuterated products, especially from the Zr catalyst, suggests that further metalation of the intermediate metallacycle is fast compared with the reverse reaction."

In contrast to reactions catalyzed by bis(anilide) **4**, little product was obtained when the mono(anilide) **5** was used instead (Table 2, entry 3). This result suggests that the key η^2-imine intermediate **3** does not form as readily by elimination of HCl·amine (eq 3) as by elimination of amine.



(3)



entry	Ar	n	product	yield (%)[a]
1	Ph	3		67
2	PMP			67[b]
3	*p*-Cl Ph			57[b]
4	PMP	2		72
5	Ph			69
6	PMP	1		48