Top 10 Challenges for Catalysis

1. $SO_2 \longrightarrow SO_3$

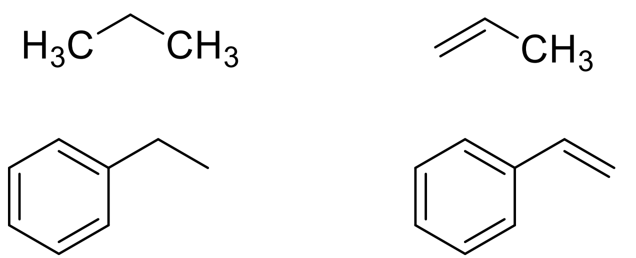
2. $CH_4 \longrightarrow CH_3OH$

3. $N_xO_y \longrightarrow N_2 + O_2$

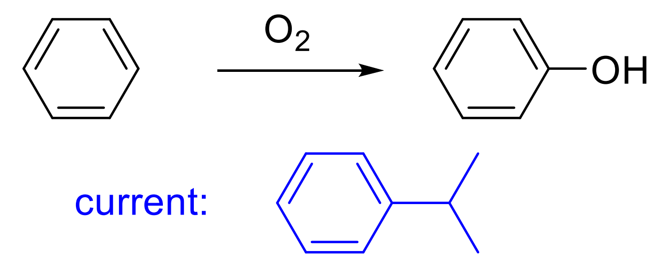
4. alkane $\longrightarrow$ alkene

$H_3C-CH_3 \qquad H_2C=CH_2$

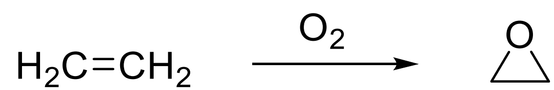
current: cracking

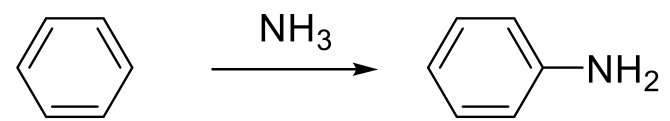


5. $CH_3OH \longrightarrow H_2C=CH_2$

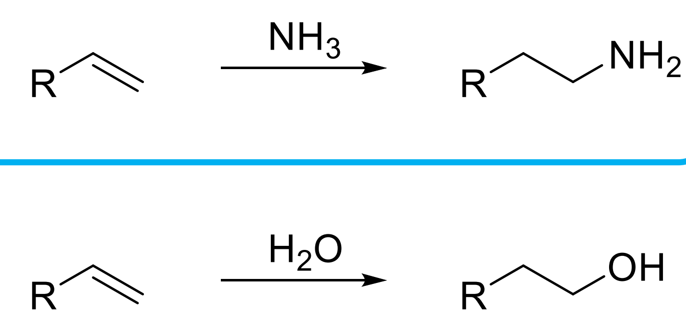
6. 

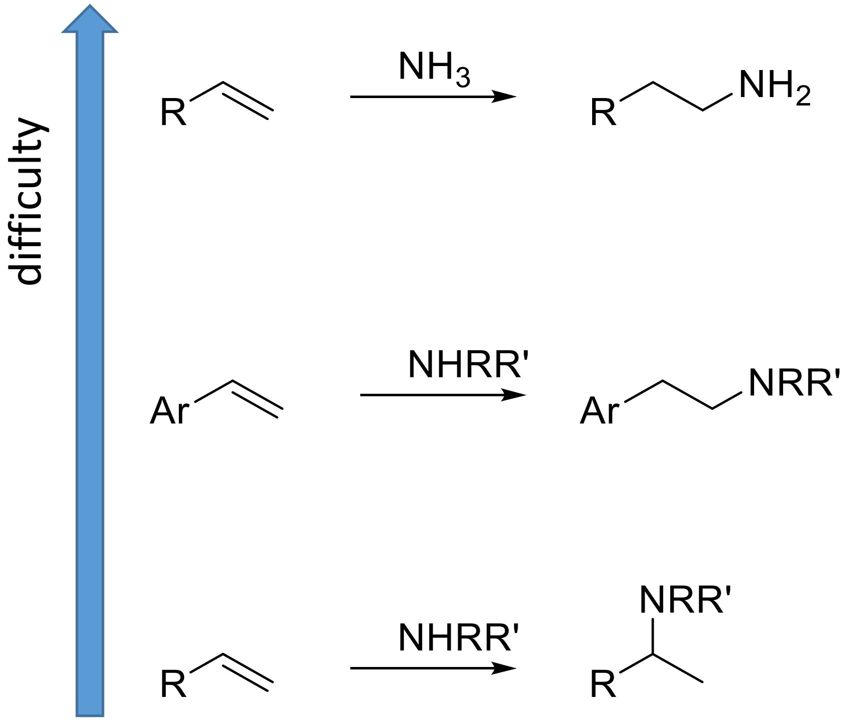
7. $H_2 + O_2 \longrightarrow H_2O_2$

8. 

9. 

current: nitration and Fe reduction

10. 



- ✓ Ammonia
- ✓ Anti-Markovnikov
- ✓ Hydroamination
- ✓ Olefin
- ✓ Not achieved

- ✓ Anti-Markovnikov
- ✓ Hydroamination
- ✓ Olefin (Aromatic Aliphatic)

- ✓ Hydroamination
- ✓ Olefin

Anti-Markovnikov Intermolecular Hydroamination of Olefins and Relative Mechanism Studies

Reporter: Fanyang Mo

Supervisor: Prof. Dr. Guangbin Dong

UT Ausitn

Content

Reactions

1. Anti-Markovnikov hydroamination of olefin
   a. Alkali-metal-catalyzed/mediated (Li, Na)
   b. Transition-metal-catalyzed (Rh, Ru, Cu…)
   c. Non-catalyzed

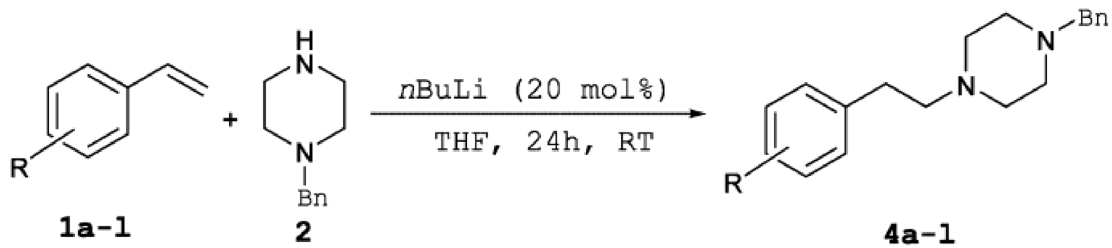
Mechanism and Insights

2. Migratory Insertion of Olefins into Metal–Nitrogen Bonds

3. Activation of N-H bond

1. Anti-Markovnikov hydroamination of olefin

a. Alkali-metal-catalyzed/mediated (Li, Na)



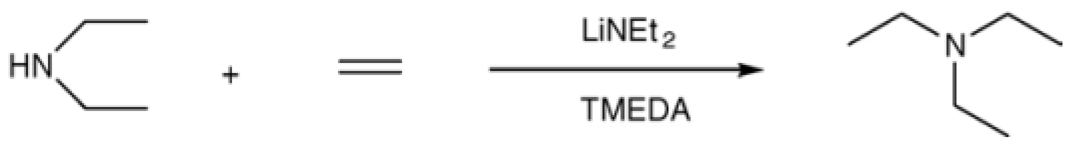
Entry	R	Olefin/ amine	Conv.[b] [%]	Product (Yield[c] [%])
1	H	2:1	82	**4a** (80)
2	4-Cl	2:1	99	**4b** (60)
3	4-Me	2:1	99	**4c** (96)
4	4-OMe	2:1	100	**4d** (99)
5	4-F	2:1	98	**4e** (87)
6	3-Cl	2:1	94	**4f** (85)
7	3-Me	2:1	80	**4g** (47)
8	3-Br	2:1	90	**4h** (41)
9	3-CF_3	2:1	78	**4i** (69)
10	2-Br	1:1	88	**4j** (59)
11	[d]	2:1	96	**4k** (94)
12	4-Ph	2:1	98	**4l** (98)

[a] Reaction conditions: **2** (2.2 mmol), olefin in THF (5 mL) in a pressure tube. [b] Determined by GC with hexadecane as internal standard (based on **2**). [c] Yield of isolated product. [d] 2-Vinylnaphthalene was used.

Kumar, K.; Michalik, D.; Garcia Castro, I.; Tillack, A.; Zapf, A.; Arlt, M.; Heinrich, T.; Böttcher, H.; Beller, M. *Chemistry – A European Journal* **2004**, *10*, 746.

1. Anti-Markovnikov hydroamination of olefin

a. Alkali-metal-catalyzed/mediated (Li, Na)



Entry	Solvent (ml)	Cat. (mol%)	Ligand (mol%)	Cat.:L ratio	Pressure (bar)	Temperature (°C)	Time (h)	Conversion (%)	Yield (%)	TON
6	Toluene	9	–	1:0	20	80	18	23	22	3
7	Toluene	5	10	1:2	20	80	18	100	96	19
11	Toluene	2.5	5	1:2	40	80	18	95	93	37
12	Toluene	2.5	5	1:2	40	r.t.	24	6	3	1
13	Toluene	2.5	5	1:2	40	40	12	10	8	3
14	Toluene	2.5	5	1:2	20	110	12	79	69	28

Reaction conditions: 0.029 mol diethylamine, 15 ml solvent, 0.5 ml *n*-octane as an internal GC standard.

Khedkar, V.; Tillack, A.; Benisch, C.; Melder, J.-P.; Beller, M. *J. Mol. Catal. A: Chem.* **2005**, *241*, 175.

1. Anti-Markovnikov hydroamination of olefin

a. Alkali-metal-catalyzed/mediated (Li, Na)

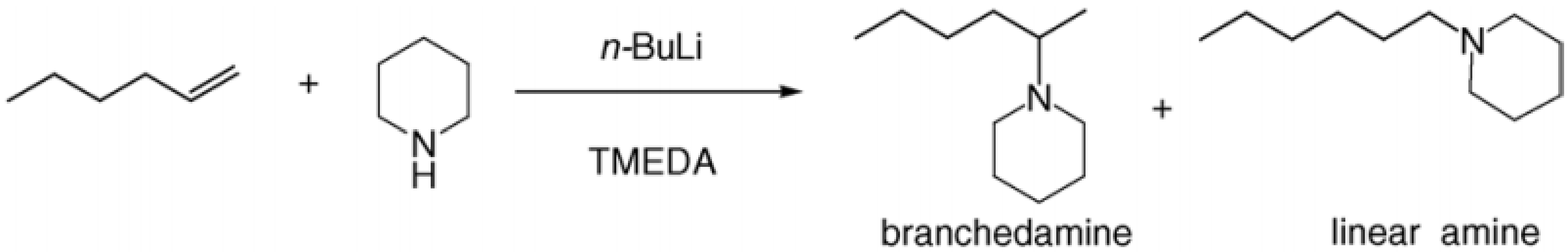


Table 3
Effect of solvent

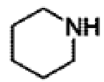
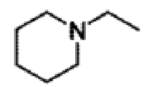
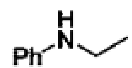
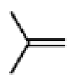
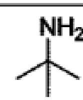
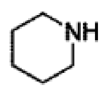
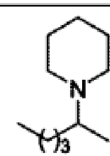
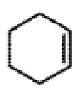
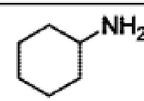
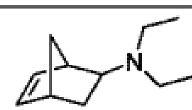
Entry	Solvent (ml)	*n*-BuLi (mol%)	TMEDA (mol%)	Temperature (°C)	Conversion (%)	Yield (%)	
						Branched amine	Linear amine
1	–	20	–	120	5	3	1
2	Toluene	20	20	120	8	4	1
3	THF	20	–	80	1	–	–
4	Diethyl ether	20	–	80	–	–	–
5	MTBE	20	–	80	–	–	–
6	Toluene	20	20	80	3	2	1
7	Toluene	20	20	120	8	4	1
8	Toluene	20	20	130	15	8	2
9	Toluene	20	20	160	5	4	1

Khedkar, V.; Tillack, A.; Benisch, C.; Melder, J.-P.; Beller, M. *J. Mol. Catal. A: Chem.* **2005**, *241*, 175.

1. Anti-Markovnikov hydroamination of olefin

a. Alkali-metal-catalyzed/mediated (Li, Na)

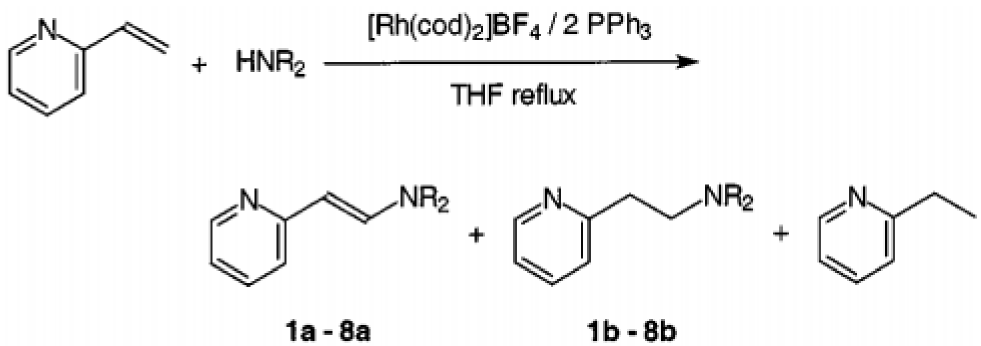
Table 73. Selected Examples for Alkali Metal-Catalyzed Amination of Aliphatic Olefins

Alkene	Amine	Product	Catalyst	Reaction conditions	Yield / %	Ref.
			Na, Py	100 °C 41-55 bar	80	455
	$PhNH_2$		$NaNH_2$	275 °C 41-55 bar	75	456
	NH_3		Na	250 °C 800-950 bar	32	456
			$NaNH_2$	225 °C	9	456
	NH_3		Na	250 °C 800-950 bar	17	456
			$LiNEt_2$/TMEDA	150 °C	18	457

Müller, T. E.; Hultzsch, K. C.; Yus, M.; Foubelo, F.; Tada, M. *Chem. Rev.* **2008**, *108*, 3795. P 3866

1. Anti-Markovnikov hydroamination of olefin (aromatic)

b. Transition-metal-catalyzed



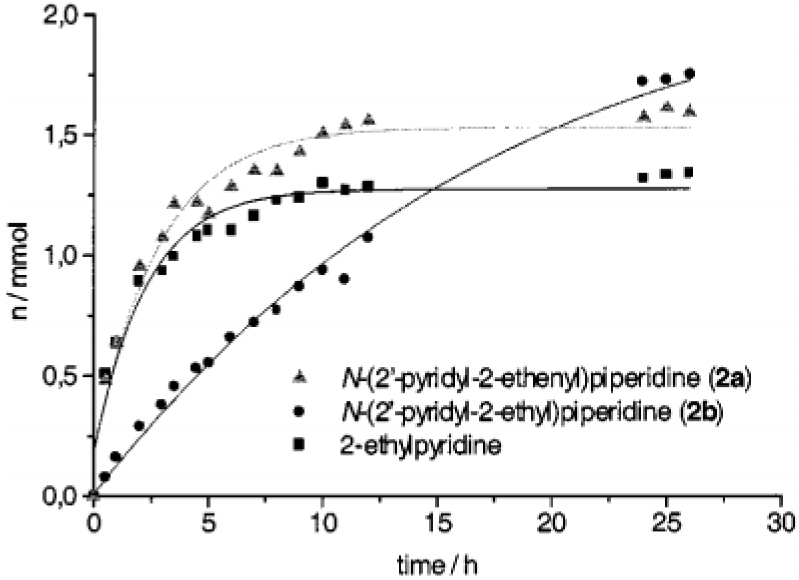


Figure 1. Time/concentration diagram for the reaction of 2-vinylpyridine and piperidine

Beller, M.; Trauthwein, H.; Eichberger, M.; Breindl, C.; Müller, T. E. *Eur. J. Inorg. Chem.* **1999**, *1999*, 1121.

1. Anti-Markovnikov hydroamination of olefin

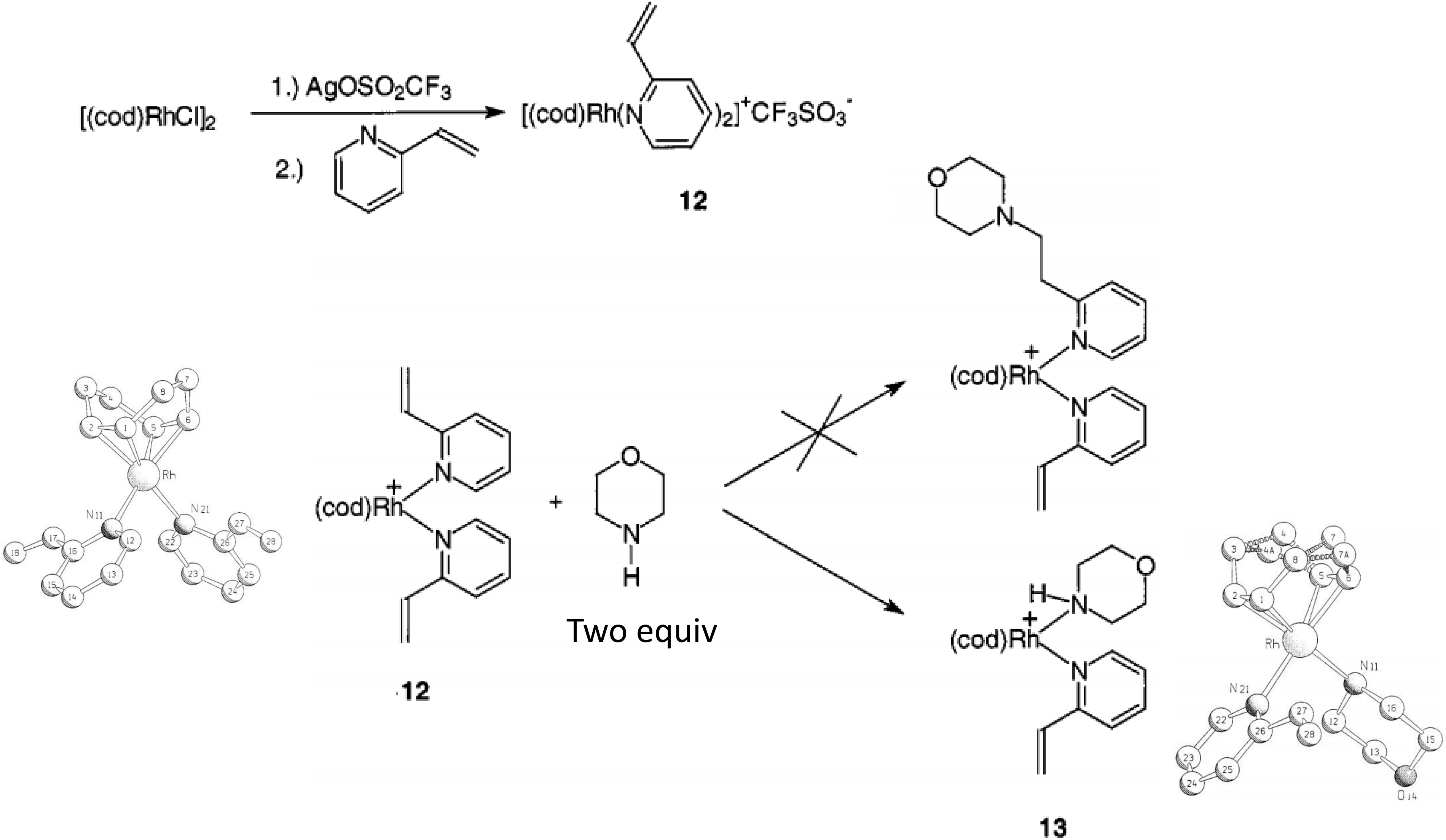
b. Transition-metal-catalyzed

Table 1. Rhodium-catalyzed reaction of 2-vinylpyridine and piperidine[a]

Entry	Olefin/Amine	Catalyst (mol-%)	Solvent, reaction time	Amine product (%)	Enamine (%)	Ethylpyridine (%)	Amine product/Enamine
1	4:1	$[Rh(cod)_2]BF_4/2\ PPh_3$ (2.5)	THF, reflux, 20 h	53	47	42	1.1
2	4:1	$[Rh(cod)_2]BF_4/2\ PPh_3$ (2.5)	Toluene, reflux, 20 h	61	30	24	2.0
3	4:1	$[Rh(cod)_2]BF_4/2\ PPh_3$ (2.5)	DMAC, 140 °C, 20 h	44	< 0.1	21	–
4	4:1	$[Rh(cod)_2]BF_4/2\ PPh_3$ (1.0)	THF, reflux, 20 h	47	8	7	5.9
5	4:1	$[Rh(cod)_2]BF_4$ (2.5)	THF, reflux, 20 h	97	2	2	48.5
6	2:1	$[Rh(cod)_2]BF_4/2\ PPh_3$ (2.5)	THF reflux, 20 h	16	82	46	0.2

[a] The yield was determined by GC with hexadecane as internal standard and is referred to amine.

Beller, M.; Trauthwein, H.; Eichberger, M.; Breindl, C.; Müller, T. E. *Eur. J. Inorg. Chem.* **1999**, *1999*, 1121.



Scheme 6. Reaction of [Rh(cod)(2-vinylpyridine)$_2$]CF_3SO_3 (**12**) with morpholine

Beller, M.; Trauthwein, H.; Eichberger, M.; Breindl, C.; Müller, T. E. *Eur. J. Inorg. Chem.* **1999**, *1999*, 1121.

1. Anti-Markovnikov hydroamination of olefin

b. Transition-metal-catalyzed

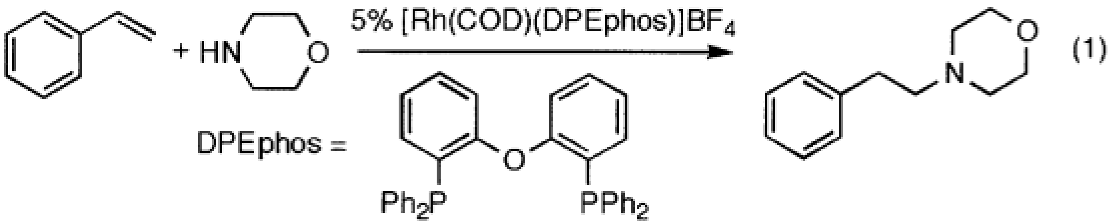
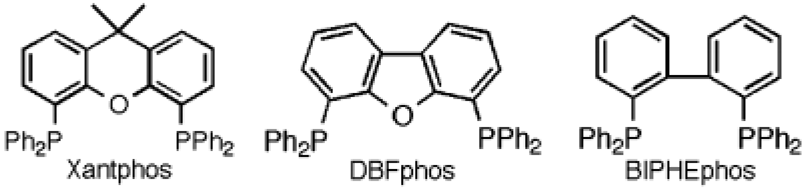


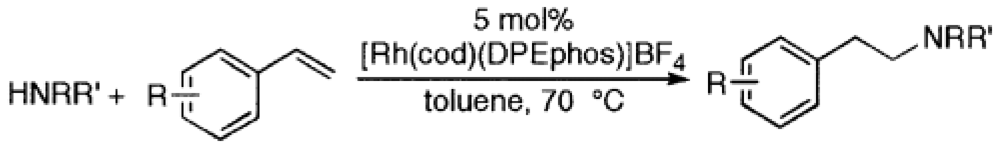
Table 1. Ligand Effects on the Reaction of Styrene with Morpholine in the Presence of Catalysts Containing DPEphos and Related Ligands[a]



entry	ligand	amine yield[b] (%)	enamine yield[b] (%)
1	DPEphos (eq 1)	62	20
2	PPh_3	17	78
3	DPPE[c]	0	1
4	DPPB[d]	0	0
5	DPPPent[e]	1	1
6	Xantphos (**1**)	trace	9
7	DBFphos (**2**)	3	40
8	BIPHEphos (**3**)	0	0

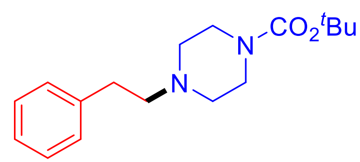
Utsunomiya, M.; Kuwano, R.; Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2003**, *125*, 5608.

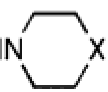
Table 2. Anti-Markovnikov Hydroamination of Vinylarenes with Secondary Amines[a]



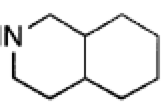
Amine : olefin = 1:4

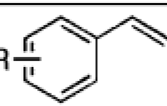
entry	amine	vinylarene	time (h)	yield[b] (%)	amine/enamine[c]
1	**1a**	**2a**	48	71	75:25
2	**1a**	**2b**	48	72	79:21
3	**1a**	**2c**	48	71	85:15
4	**1a**	**2d**	48	70	78:22
5[e]	**1a**	**2e**	72	48	60:40
6[e,f]	**1a**	**2f**	72	41	57:43
7[g]	**1b**	**2a**	72	57	63:37
8	**1b**	**2d**	48	66	77:23
9[g]	**1c**	**2a**	72	58	86:14
10	**1d**	**2a**	72	53	96:4
11[g,h]	**1e**	**2a**	72	51[k]	76:24
12	**1f**	**2c**	48	62[l]	72:28
13[i]	**1g**	**2b**	72	50[d]	54:46
14[i,j]	**1g**	**2d**	72	74	82:19
15[i]	**1g**	**2g**	48	79[d]	90:10



HNRR' = HN  X

1a : X = O
1b : X = CH_2
1c : X = N-Ph
1d : X = N-$CO_2{}^tBu$

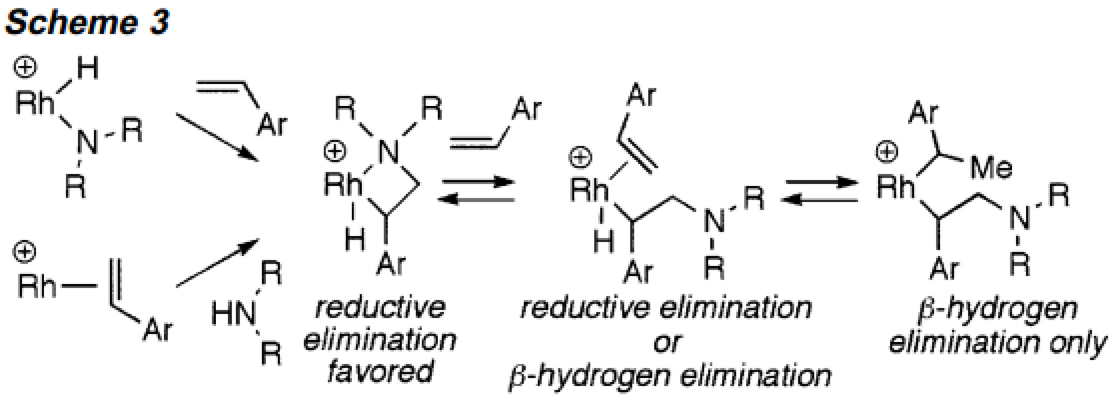
1e : 2,5-Me_2-morpholine
1f : HN 
1g : $HNMe_2$

vinylarene= R 

2a : R = H
2b : R = 4-Me
2c : R = 4-MeO
2d : R = 3,4-MeO
2e : R = 4-Cl
2f : R = 3-CF_3
2g : 2-vinylpyridine

Substrates limitation: Primary aliphatic amine and aromatic amine did not react.

Utsunomiya, M.; Kuwano, R.; Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2003**, *125*, 5608.

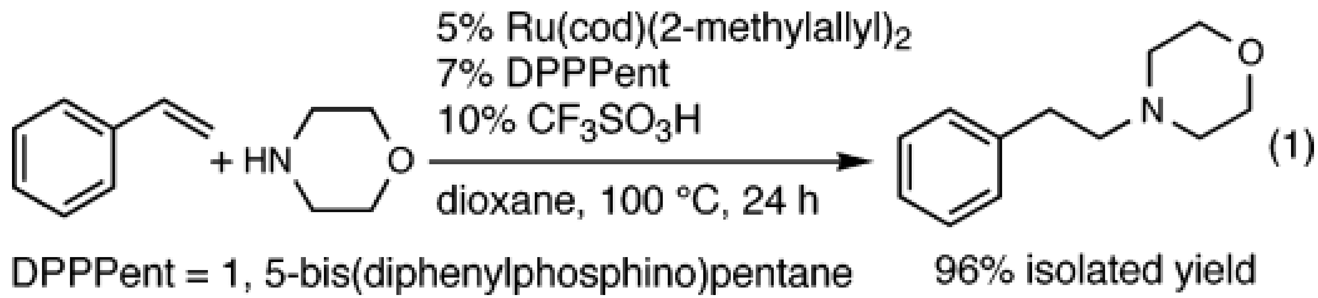


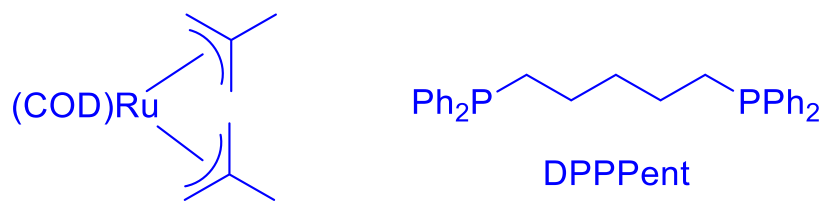
Concentration of olefin affected the amine:enamine ratio very much.

Utsunomiya, M.; Kuwano, R.; Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2003**, *125*, 5608.

1. Anti-Markovnikov hydroamination of olefin

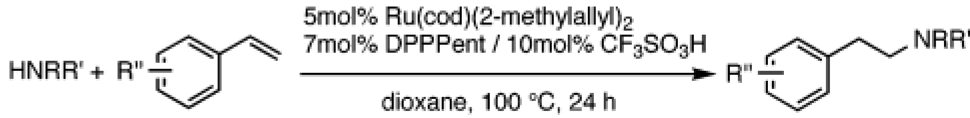
b. Transition-metal-catalyzed

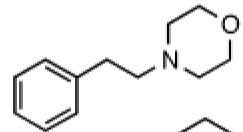
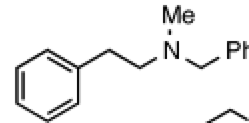
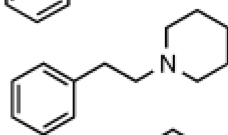
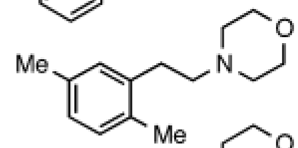
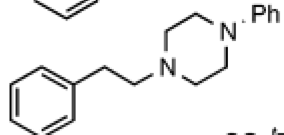
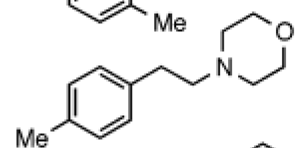
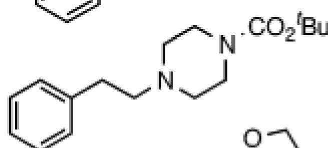
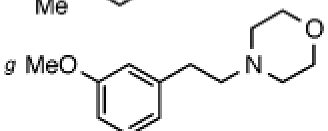
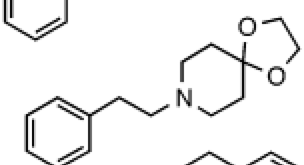
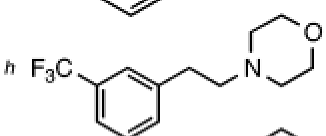
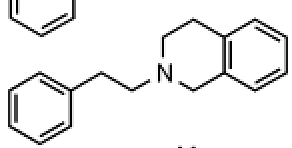
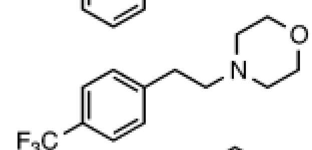
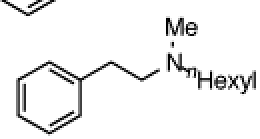
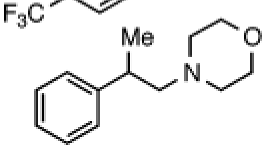




Utsunomiya, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2004**, *126*, 2702.

Table 2. Ruthenium-Catalyzed Hydroamination of Vinylarenes with Alkylamines[a]

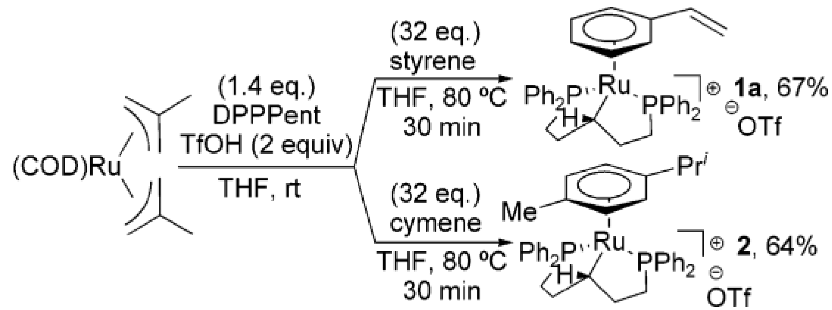


entry	product	yield[b]	entry	product	yield[b]
1		96%	8[c, d, e]		50%
2		91%	9		81%
3[c]		64%	10		72%
4		90%	11[e, f, g]		91%
5		82%	12[f, g, h]		71%
6[c]		65%	13[h]		51%
7[c, d, e]		63%	14[d, i, j]		40%

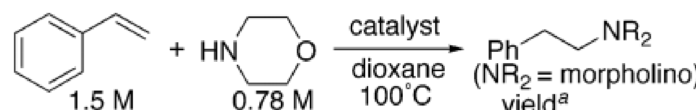
[a] Amine/vinylarene/Ru/DPPPent/TfOH = 1:2:0.05:0.07:0.10 (1 mmol of amine) in 0.50 mL of dioxane. [b] Isolated yield. [c] 4 mmol of vinylarene was used. [d] 80 °C. [e] 48 h. [f] 0.25 mL of dioxane. [g] 110 °C. [h] D*i*PPF was used as ligand. [i] 1.5 mmol of vinylarene was used. [j] 72 h.

Utsunomiya, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2004**, *126*, 2702.

Scheme 1



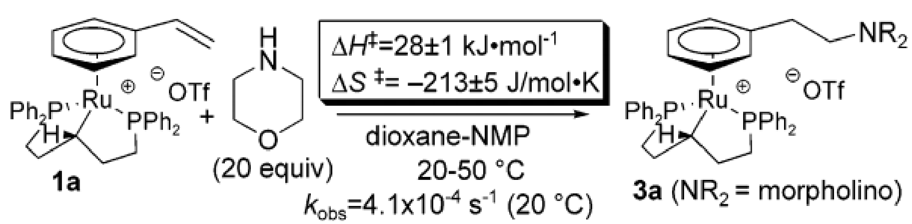
Scheme 2



cat.	yield[a] 15min	30min	1h	2h	5h
1a (5 mol%)	22%	40%	64%	80%	96%
2 (5 mol%)	10%	32%	56%	77%	94%
in situ[b]	9%	18%	40%	63%	87%

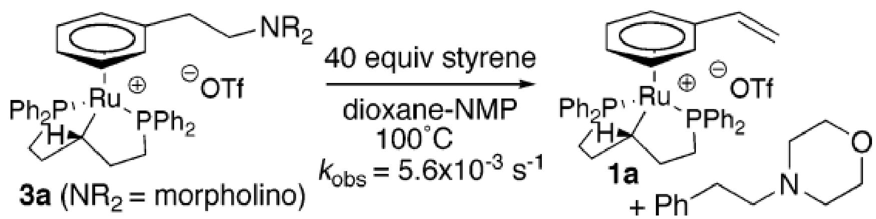
[a] Yield by GC. [b] Ru(COD)(2-methylallyl)$_2$ (5 mol %), DPPPent (7 mol %), TfOH (10 mol %).

Scheme 3

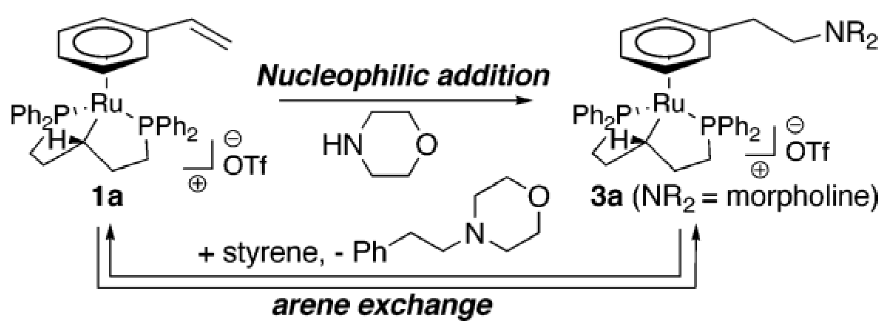


Takaya, J.; Hartwig, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 5756.

Scheme 4



Scheme 5



Takaya, J.; Hartwig, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 5756.

1. Anti-Markovnikov hydroamination of olefin

b. Transition-metal-catalyzed

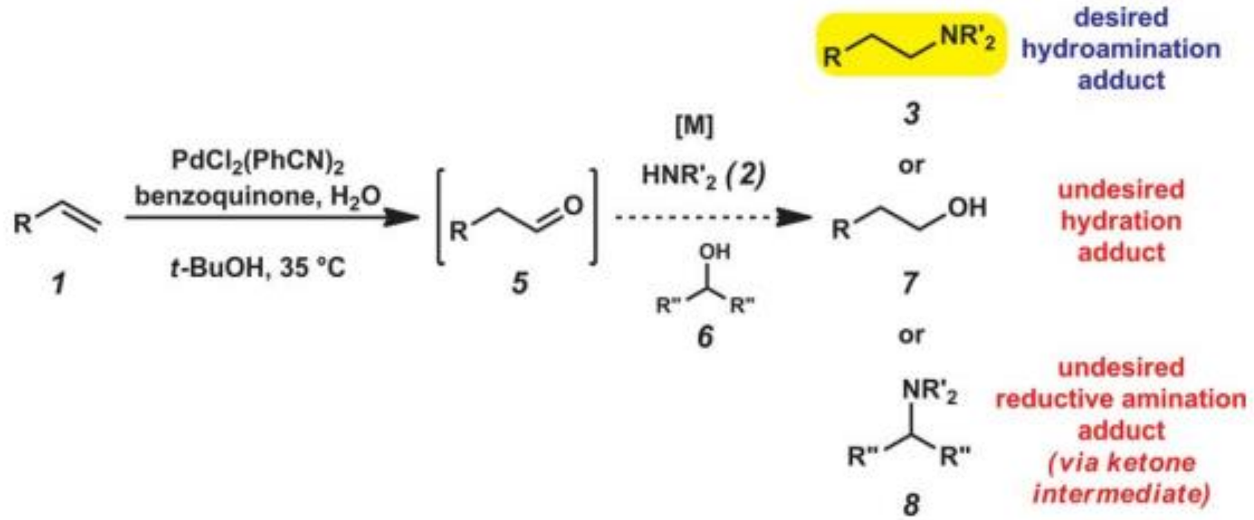
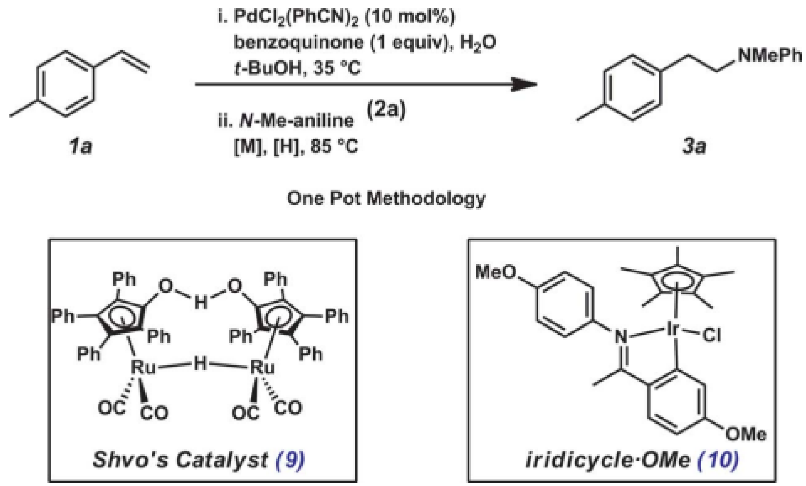


Fig. 2 Challenges of the formal anti-Markovnikov hydroamination methodology.

Bronner, S. M.; Grubbs, R. H. *Chem. Sci.* **2014**, *5*, 101.

Table 1 Optimization of hydroamination methodology

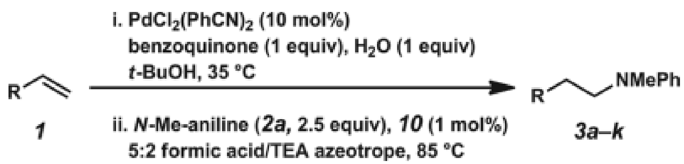


Entry	[M]	Mol% [M]	[H]	Additives (step)	Equiv. amine	Equiv. H_2O	Yield[a]
1	9	10%	Isopropyl alcohol	$CuCl_2$ (ii)	2.5	1	15%
2	9	10%	2,4-Dimethyl-3-pentanol	Mol. sieves (i); CuCl (ii)	2.5	0	25%
3	10	10%	5 : 2 HCO_2H/TEA	—	2.5	1	63%
4	10	10%	5 : 2 HCO_2H/TEA	—	2.5	2	59%
5	10	1%	5 : 2 HCO_2H/TEA	—	2.5	1	65%
6	10	10%	5 : 2 HCO_2H/TEA	—	1.3	1	66%
7	10	1%	5 : 2 HCO_2H/TEA	—	1.3	1	59%

[a] Yield determined from analysis of the ^{1}H NMR spectrum using 1,4-dioxane as an external standard.

Bronner, S. M.; Grubbs, R. H. *Chem. Sci.* **2014**, *5*, 101.

Table 2 Hydroamination of styrenes with *N*-methylaniline



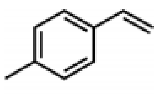
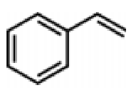
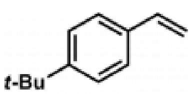
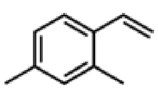
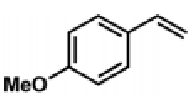
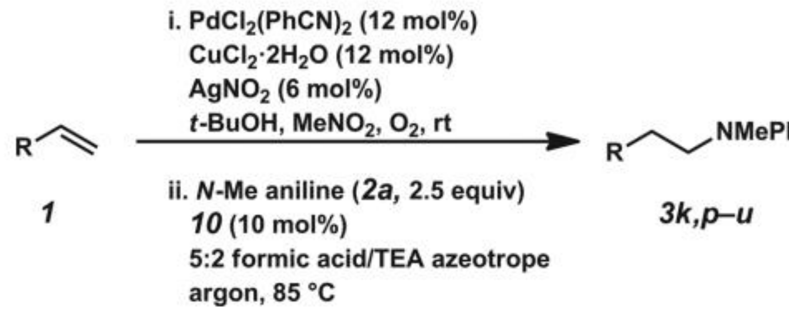
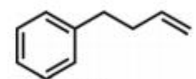
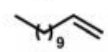
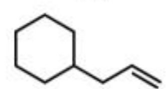
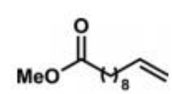
Entry	Substrate	Product	Yield[a]
1	 *1a*	**3a**	61% (66%[b])
2	 *1b*	**3b**	55%
3	 *1c*	**3c**	55%[c]
4	 *1d*	**3d**	62%
5	 *1e*	**3e**	65%

Table 4 Hydroamination of aliphatic olefins with *N*-methylaniline



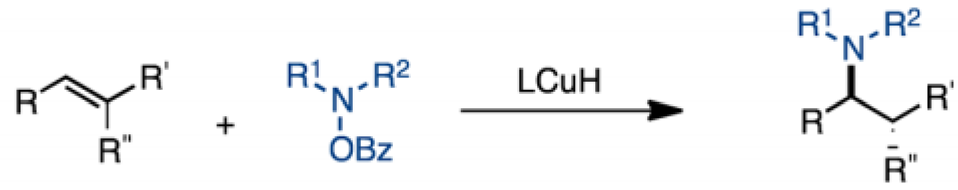
Entry	Substrate	Product	Yield[a]
1	 *1k*	**3k**	64%
2	 *1l*	**3p**	65%
3	 *1m*	**3q**	40%
4	 *1n*	**3r**	56%
5	 *1o*	**3s**	60%

Substrate limitation: aromatic amines

Bronner, S. M.; Grubbs, R. H. *Chem. Sci.* **2014**, *5*, 101.

1. Anti-Markovnikov hydroamination of olefin

b. Transition-metal-catalyzed



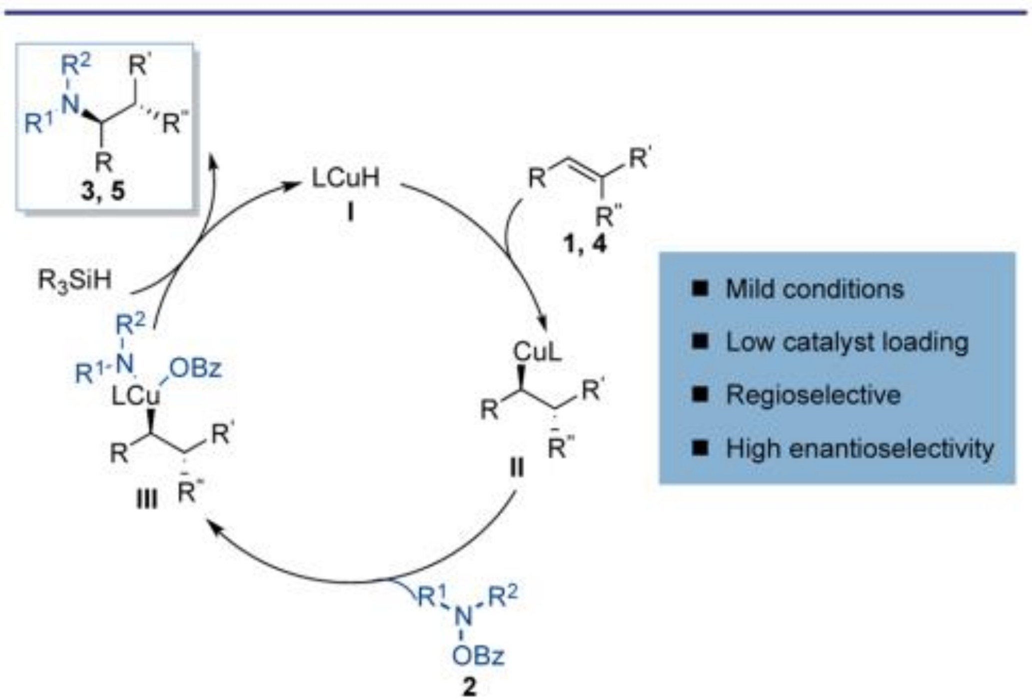
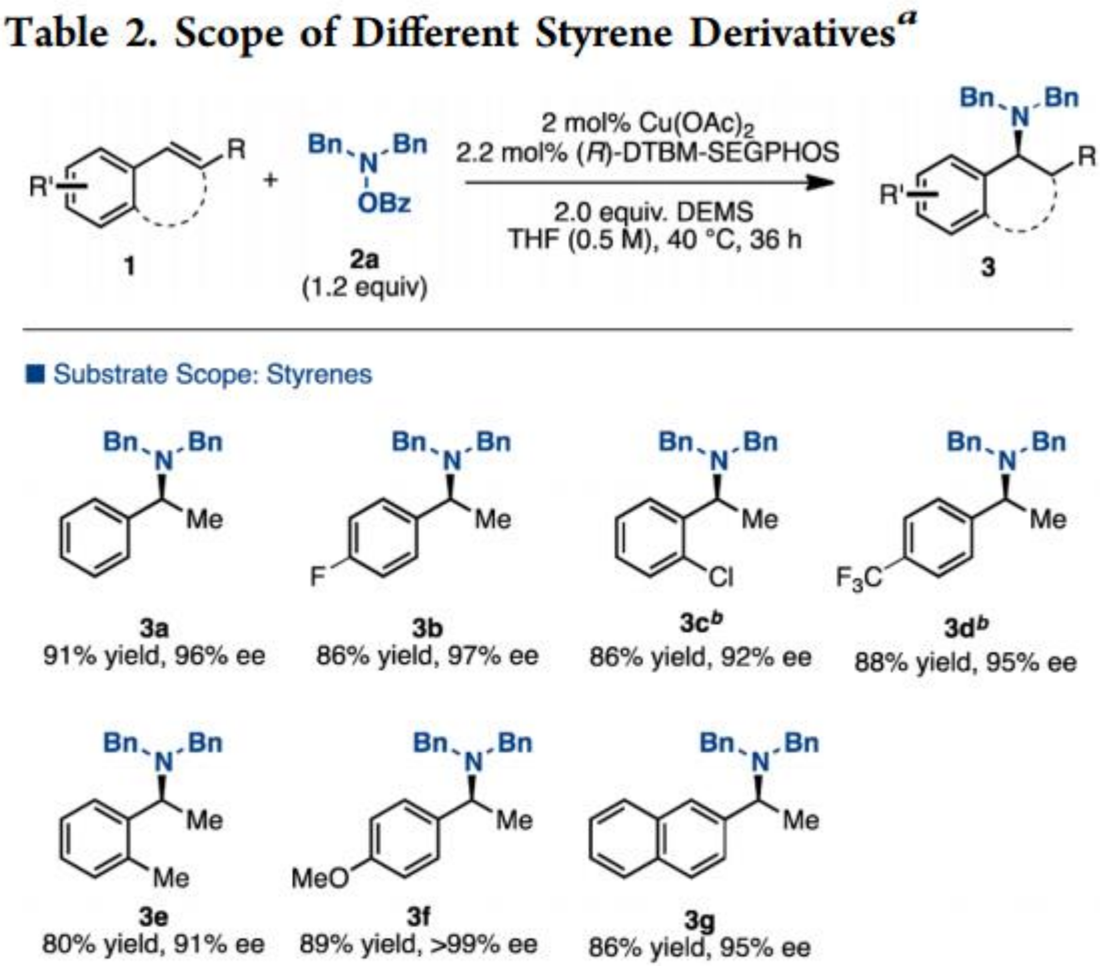


Figure 1. Proposed catalytic cycle for CuH-catalyzed hydroamination of alkenes.

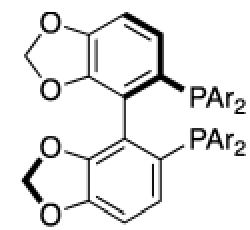
Zhu, S.; Niljianskul, N.; Buchwald, S. L. *J. Am. Chem. Soc.* **2013**, *135*, 15746.

1. Anti-Markovnikov hydroamination of olefin

b. Transition-metal-catalyzed



DEMS: di-EtMeSiH



Ar = Ph
(*R*)-SEGPHOS (**L4**)

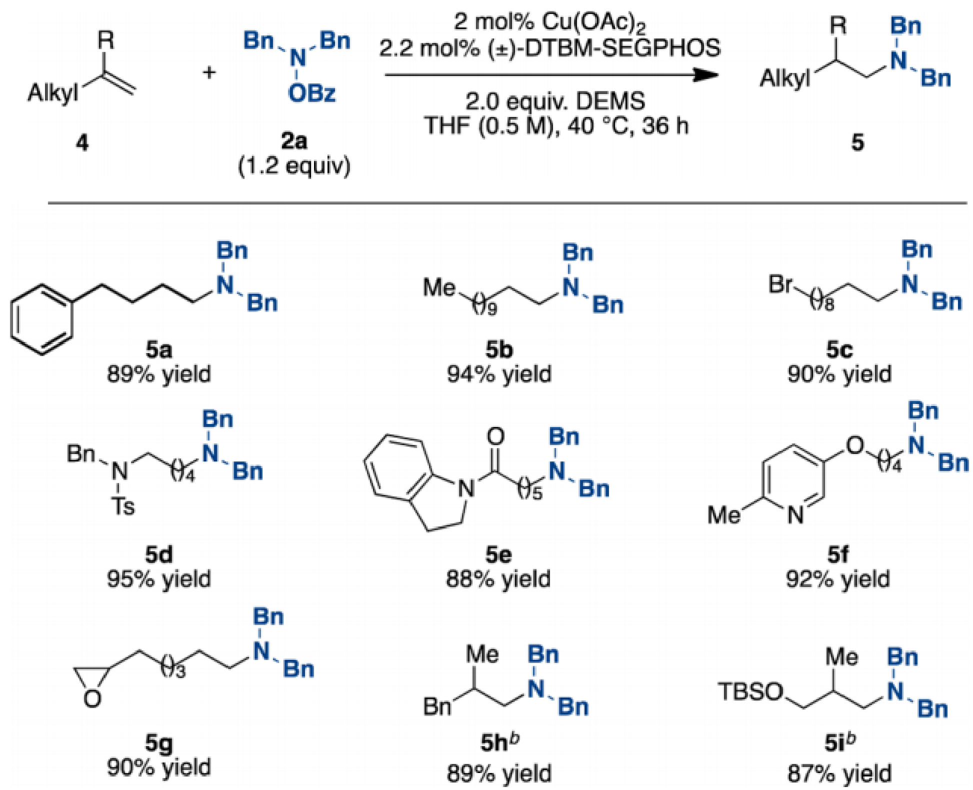
Ar = 3,5-*t*-Bu-4-MeOC$_6$H$_2$
(*R*)-DTBM-SEGPHOS (**L5**)

Zhu, S.; Niljianskul, N.; Buchwald, S. L. *J. Am. Chem. Soc.* **2013**, *135*, 15746.

1. Anti-Markovnikov hydroamination of olefin

b. Transition-metal-catalyzed

Table 4. Hydroamination of Terminal Aliphatic Alkenes[a]



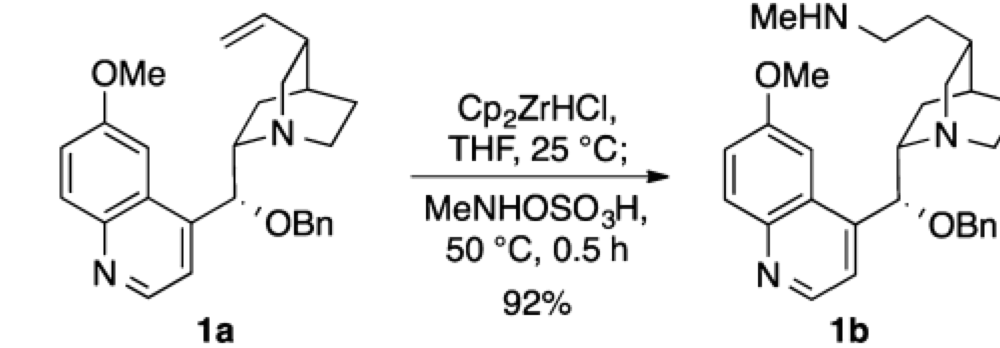
[a]Isolated yields (average of two runs). **2** (1 mmol), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (1.2 mmol), $Cu(OAc)_2$ (2 mol%), (±)-DTBM-SEGPHOS (2.2 mol%), DEMS (2 mmol), THF (0.5 M), 40 °C, up to 36 h. [b]THF (1 M).

Zhu, S.; Niljianskul, N.; Buchwald, S. L. *J. Am. Chem. Soc.* **2013**, *135*, 15746.

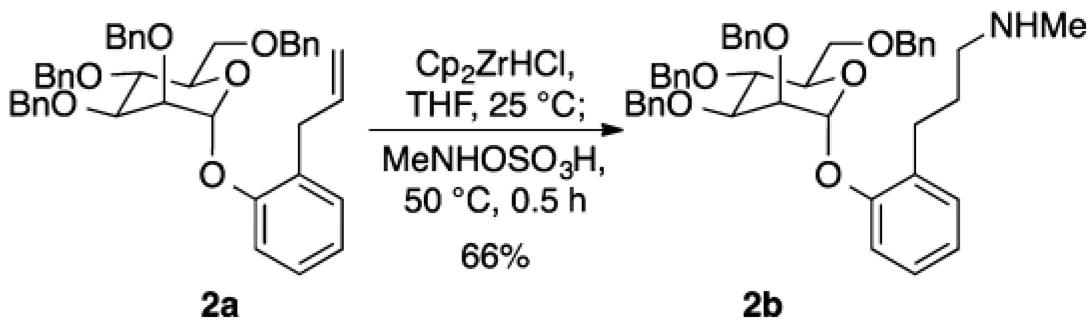
1. Anti-Markovnikov hydroamination of olefin

c. Non-catalyzed

Question 1:



b) Amination of D-mannose substrate



Strom, A. E.; Hartwig, J. F. *J. Org. Chem.* **2013**, *78*, 8909.

Content

Reactions

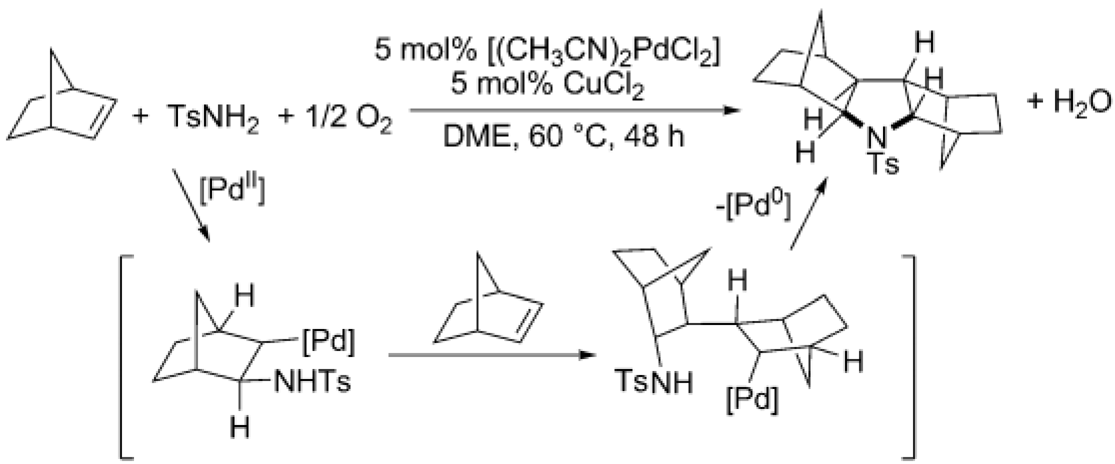
1. Anti-Markovnikov hydroamination of olefin
   a. Alkali-metal-catalyzed/mediated (Li, Na)
   b. Transition-metal-catalyzed (Rh, Ru, Cu…)
   c. Non-catalyzed

Mechanism and Insights

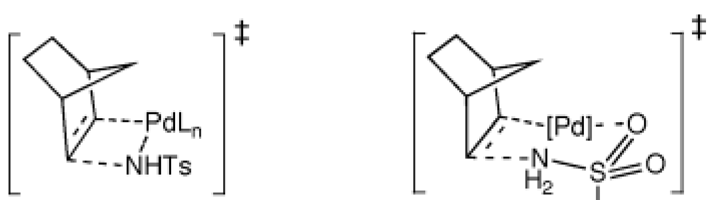
2. Migratory Insertion of Olefins into Metal–Nitrogen Bonds
3. Activation of N-H bond

2. Migratory Insertion of Olefins into Metal–Nitrogen Bonds

a. Pd-N bond



Scheme 18. Proposed reaction mechanism of the palladium-catalyzed oxidative amination of norbornene. DME = dimethoxyethane, Ts = 4-toluenesulfonyl.

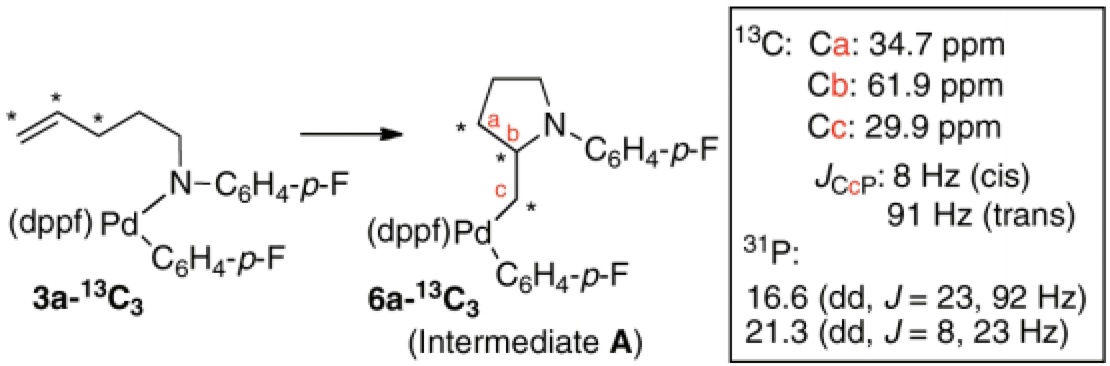


4 5

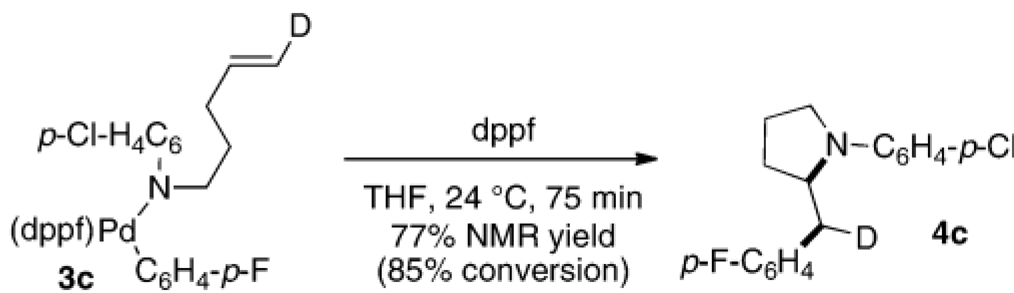
Brice, J. L.; Harang, J. E.; Timokhin, V. I.; Anastasi, N. R.; Stahl, S. S. *J. Am. Chem. Soc.* **2005**, *127*, 2868.

2. Migratory Insertion of Olefins into Metal–Nitrogen Bonds

a. Pd-N bond



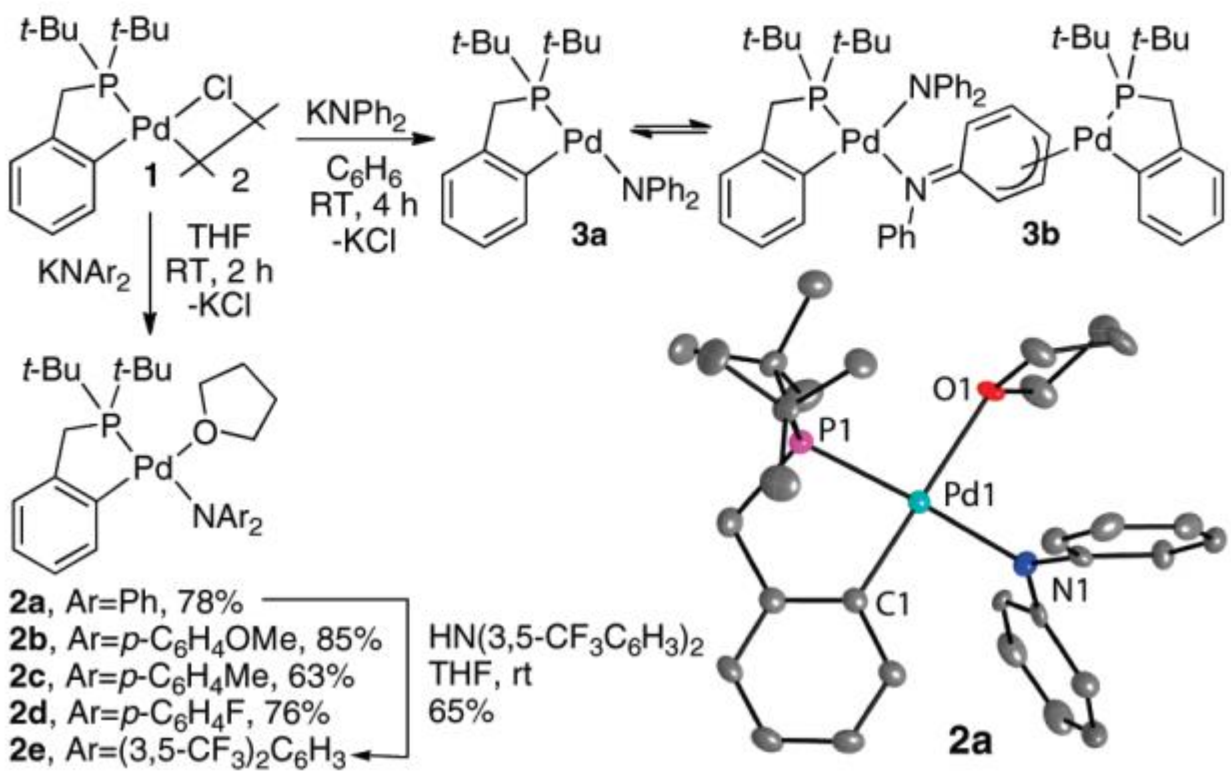
Question 3:



Neukom, J. D.; Perch, N. S.; Wolfe, J. P. *J. Am. Chem. Soc.* **2010**, *132*, 6276.

2. Migratory Insertion of Olefins into Metal–Nitrogen Bonds

a. Pd-N bond

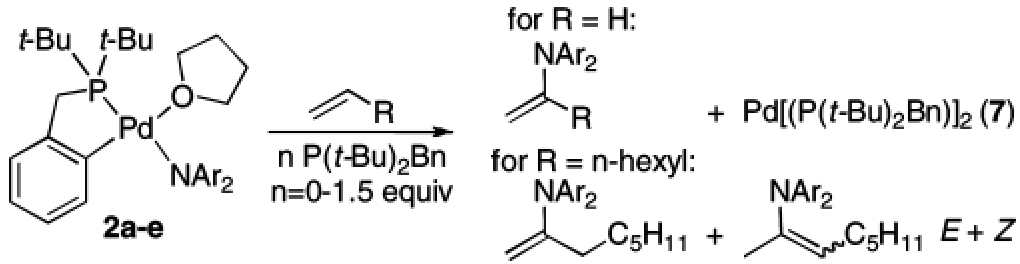


Hanley, P. S.; Marković, D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 6302.

2. Migratory Insertion of Olefins into Metal–Nitrogen Bonds

a. Pd-N bond

Table 1. Reactions of Ethylene and 1-Octene with Amides **2a–2e**[a]



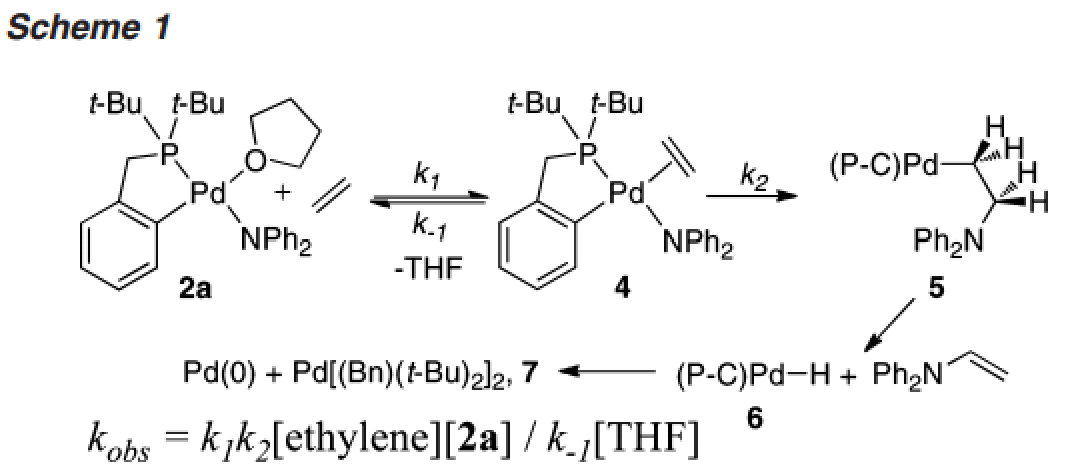
entry	complex	For R = H (yield)	for R = H $k_{obs} \times 10^3$ (s^{-1})	For R = C_6H_{13} (Yield)[b]
1	**2a**	89%	0.91	(neat) 74%
2	**2a**	–	–	(25 equiv) 69%
3	**2a**	–	–	(10 equiv) 48%
4	**2b**	94%	9.6	97%
5	**2c**	63%	4.3	64%
6	**2d**	60%	0.79	52%
7[c]	**2e**	98%	0.053	ND[d]

[a] Conditions for reactions with 1-octene: benzene, 80 °C for 30 min. Conditions for reactions with ethylene: toluene, −10 °C for 2 h, 20 equiv of ethylene. [b] Combined yield for all enamine isomers. [c] Reaction at 85 °C. [d] This reaction did not form detectable amounts of the enamine product.

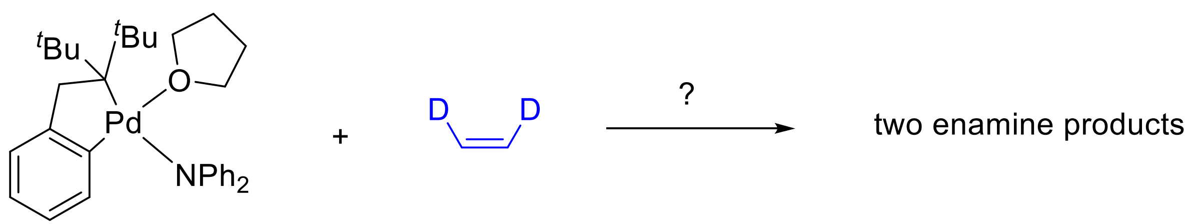
Hanley, P. S.; Marković, D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 6302.

2. Migratory Insertion of Olefins into Metal–Nitrogen Bonds

a. Pd-N bond



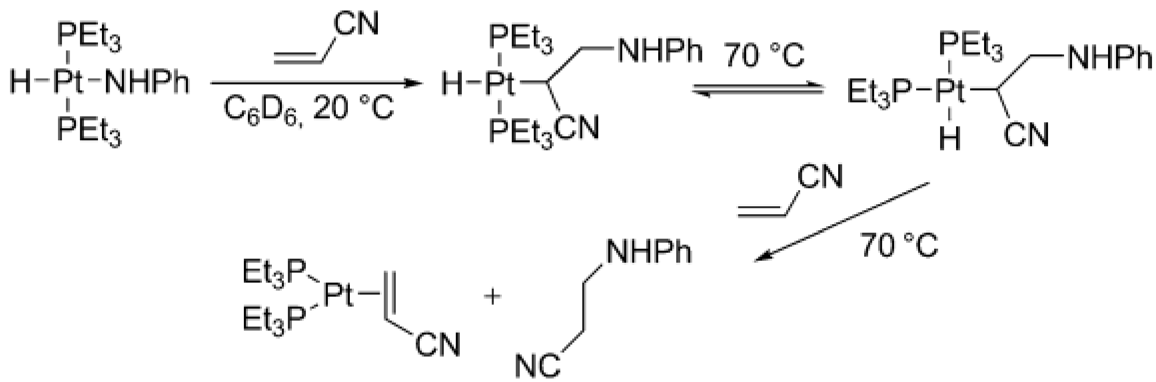
Question 2:



Hanley, P. S.; Marković, D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 6302.

2. Migratory Insertion of Olefins into Metal–Nitrogen Bonds

b. Pt-N bond

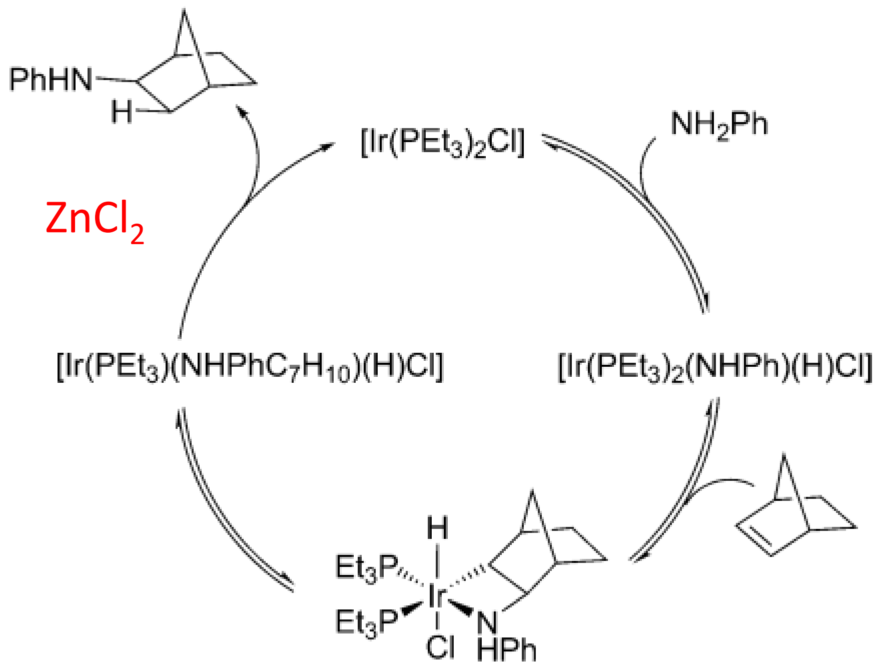


Scheme 21. Proposed reaction mechanism of platinum amides with acrylonitrile.

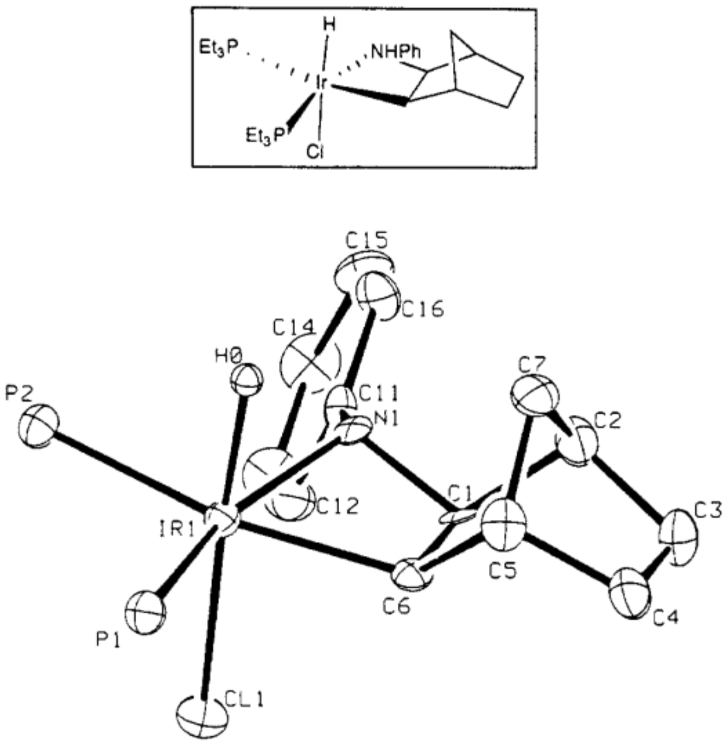
Cowan, R. L.; Trogler, W. C. *Organometallics* **1987**, *6*, 2451.

2. Migratory Insertion of Olefins into Metal–Nitrogen Bonds

c. Ir-N bond



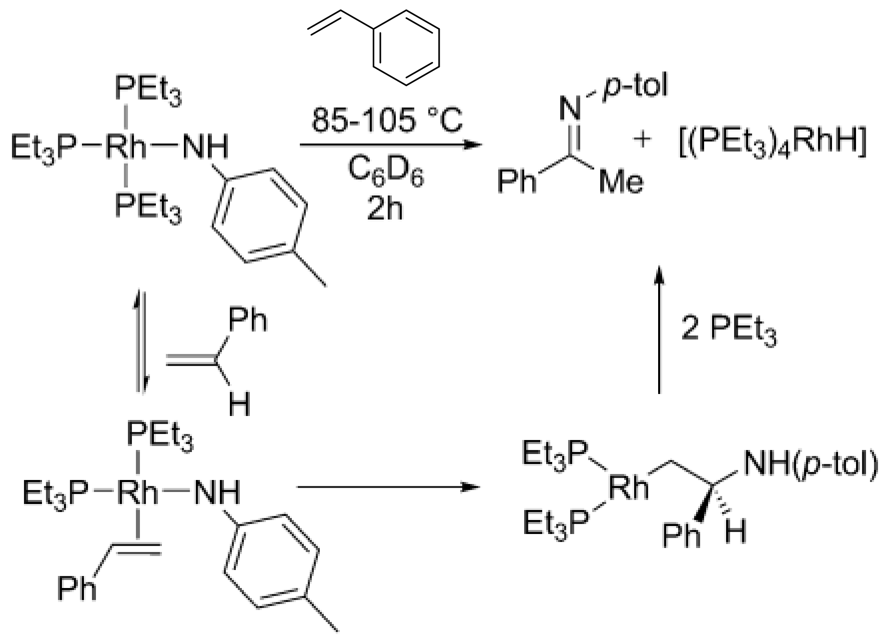
Scheme 22. Proposed reaction mechanism of iridium-catalyzed addition of aniline to norbornene.



Casalnuovo, A. L.; Calabrese, J. C.; Milstein, D. *J. Am. Chem. Soc.* **1988**, *110*, 6738.

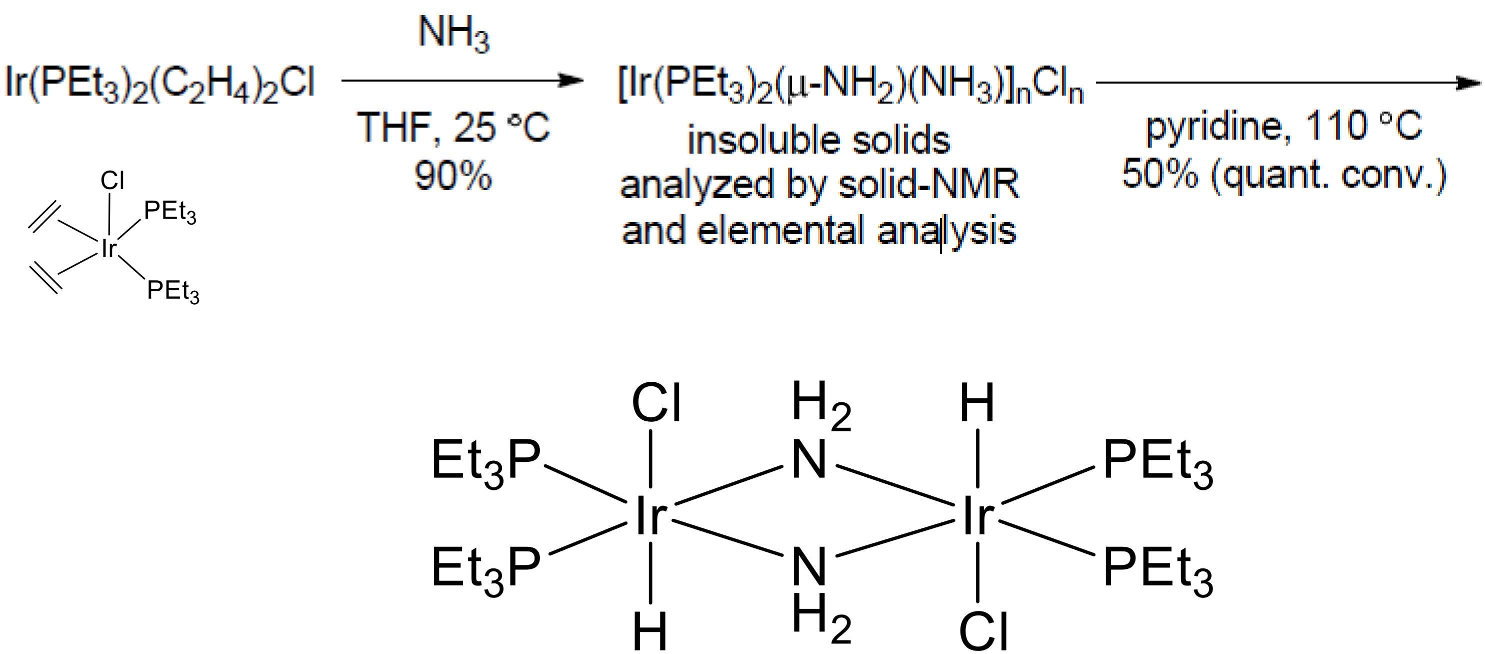
2. Migratory Insertion of Olefins into Metal–Nitrogen Bonds

d. Rh-N bond



Zhao, P.; Krug, C.; Hartwig, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 12066.

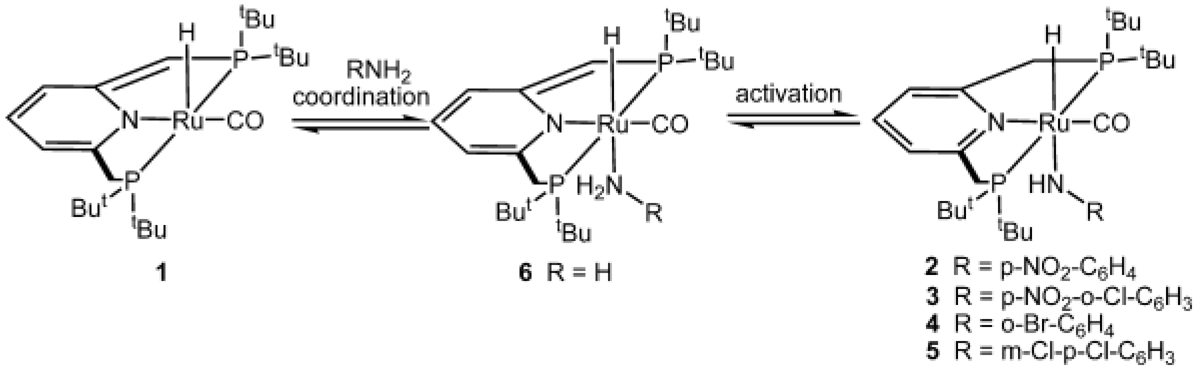
3. Activation of N-H bond



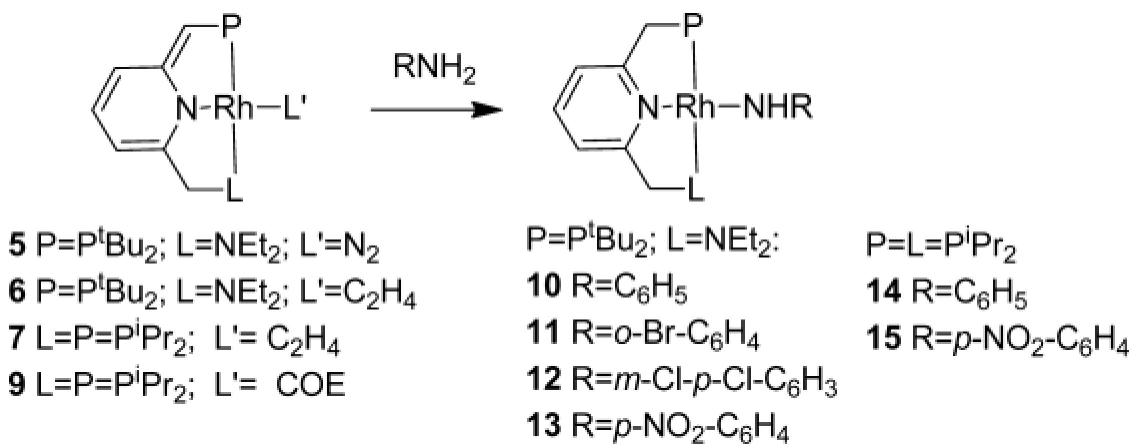
X-ray

Casalnuovo, A. L.; Calabrese, J. C.; Milstein, D. *Inorg. Chem.* **1987**, *26*, 971.

3. Activation of N-H bond

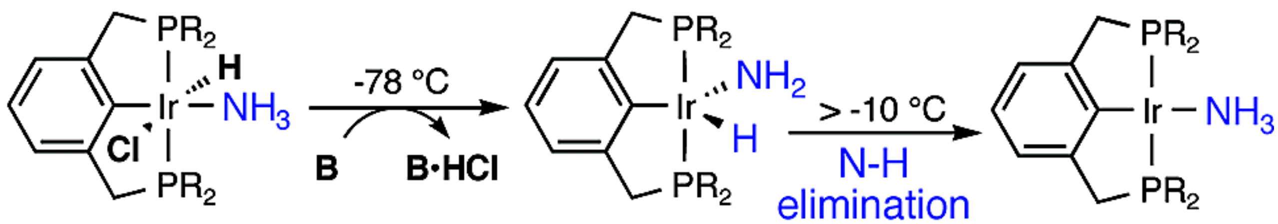


Khaskin, E.; Iron, M. A.; Shimon, L. J. W.; Zhang, J.; Milstein, D. *J. Am. Chem. Soc.* **2010**, *132*, 8542.



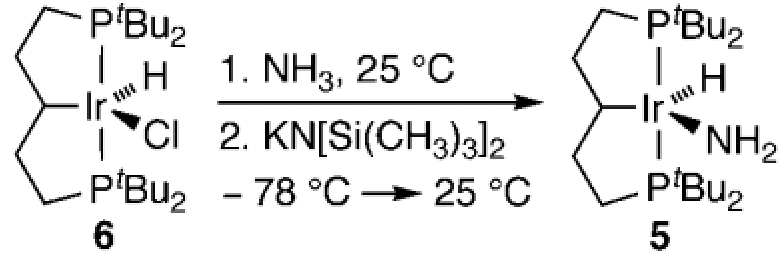
Feller, M.; Diskin-Posner, Y.; Shimon, L. J. W.; Ben-Ari, E.; Milstein, D. *Organometallics* **2012**, *31*, 4083.

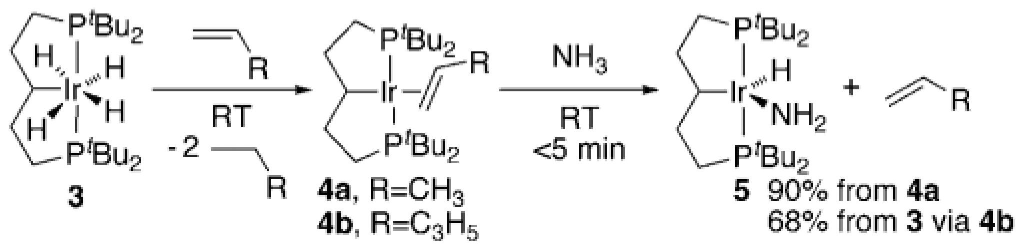
3. Activation of N-H bond

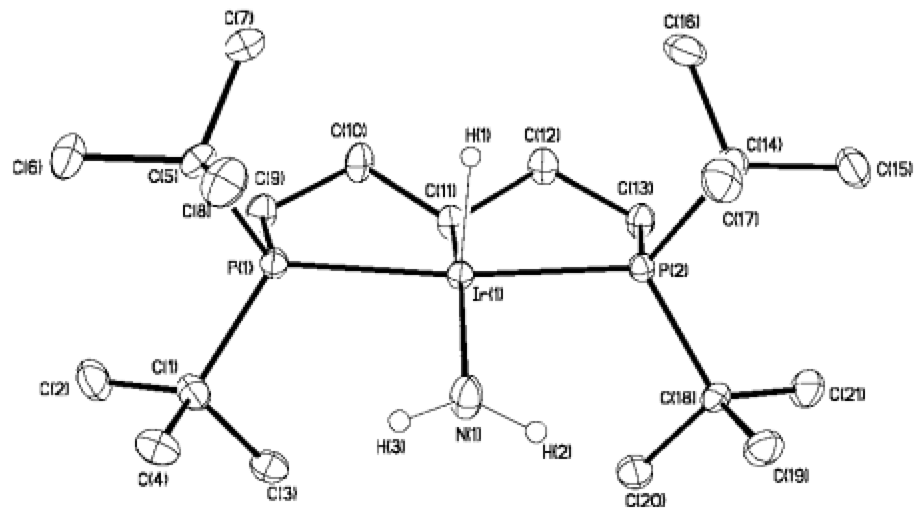


Kanzelberger, M.; Zhang, X.; Emge, T. J.; Goldman, A. S.; Zhao, J.; Incarvito, C.; Hartwig, J. F. *J. Am. Chem. Soc.* **2003**, *125*, 13644.

3. Activation of N-H bond



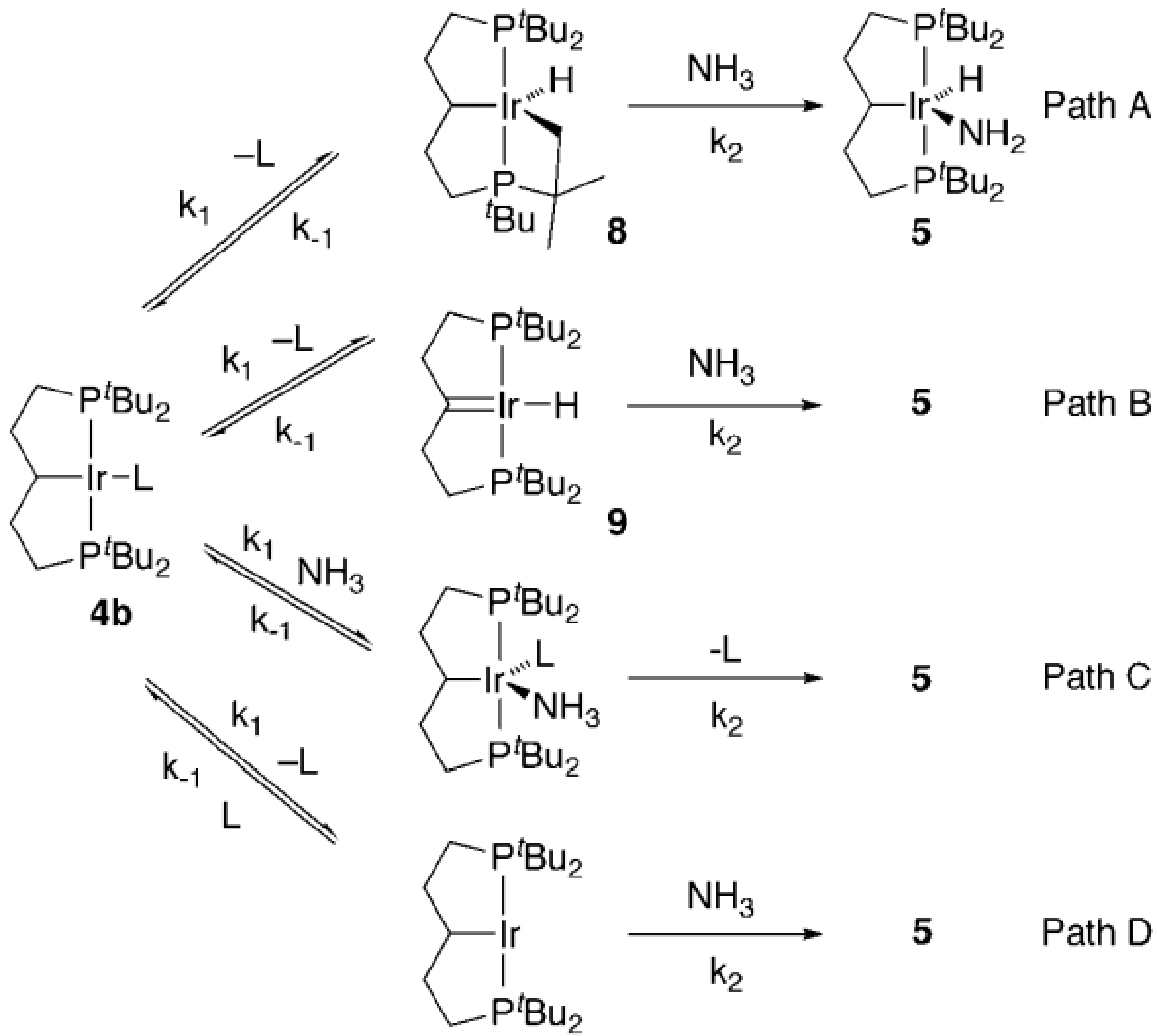




ORTEP diagram of **5**

Zhao, J.; Goldman, A. S.; Hartwig, J. F. *Science* **2005**, *307*, 1080.

3. Activation of N-H bond



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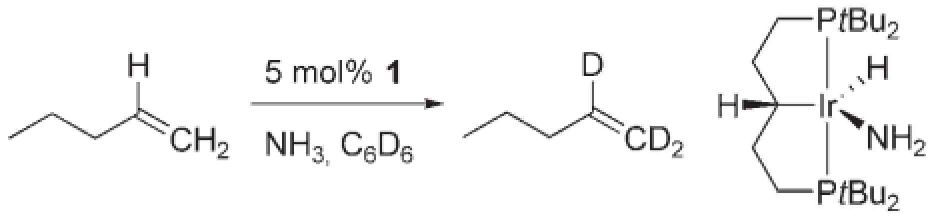
3. Activation of N-H bond



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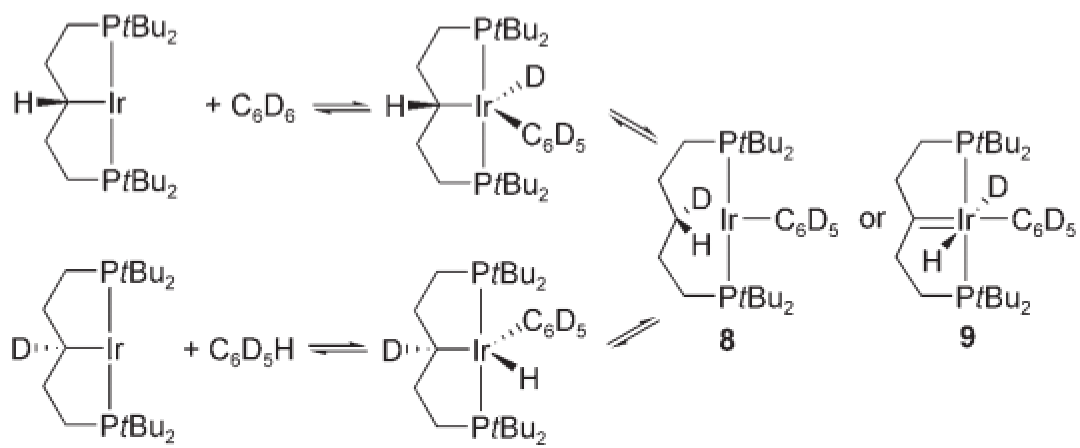
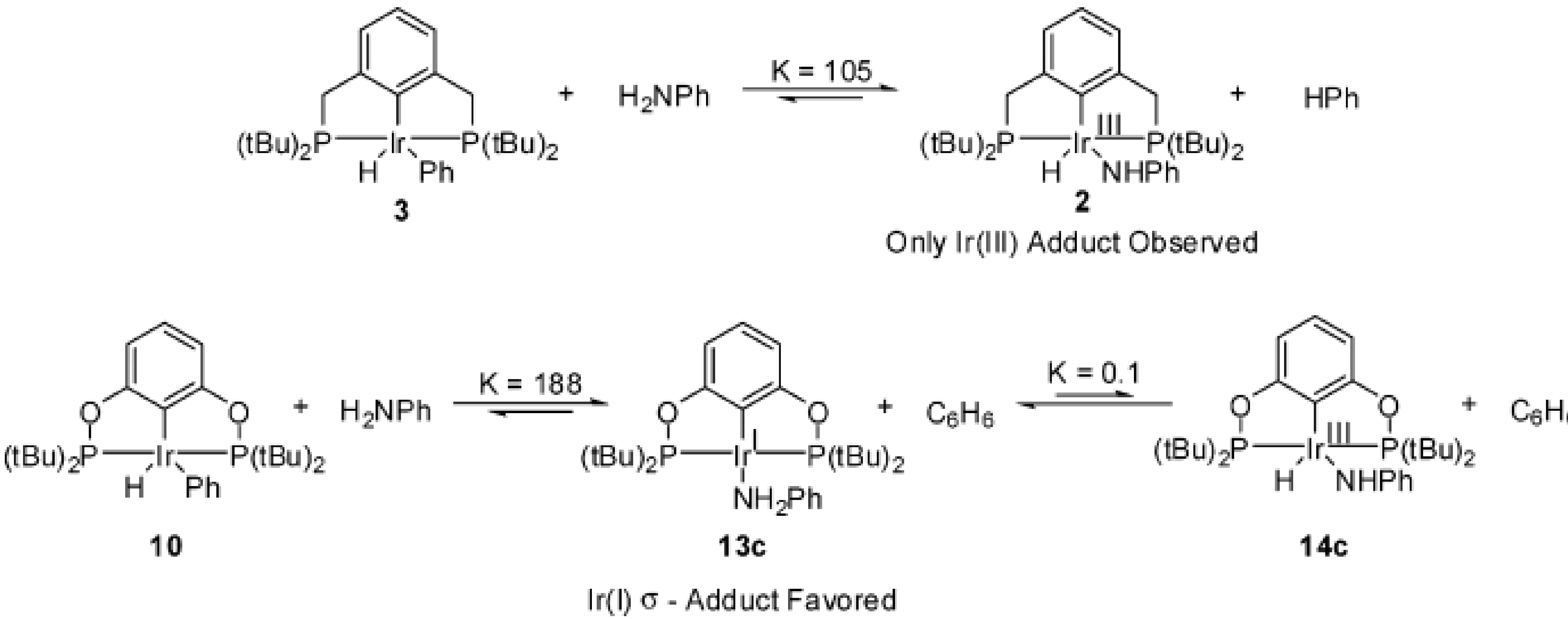


Scheme 1. Proposed pathways for the iridium-catalyzed H/D exchange in C_6D_6.

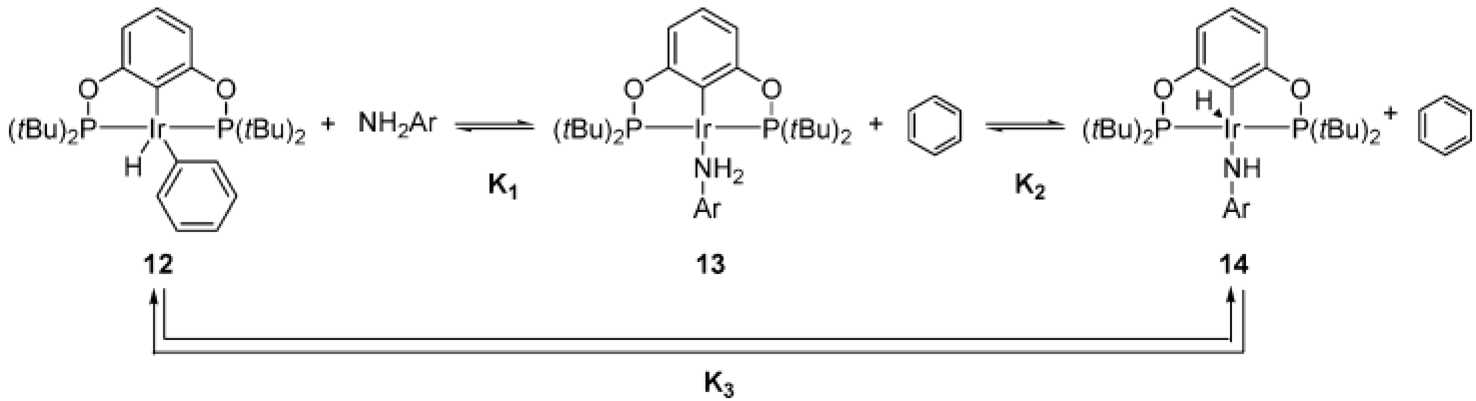
Zhou, J.; Hartwig, J. F. *Angew. Chem. Int. Ed.* **2008**, *47*, 5783.

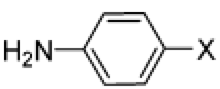
3. Activation of N-H bond



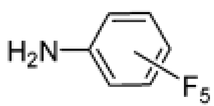
Sykes, A. C.; White, P.; Brookhart, M. *Organometallics* **2006**, *25*, 1664.

3. Activation of N-H bond

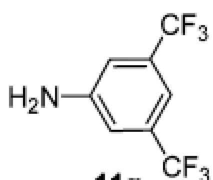




X = OMe (**11a**), Me (**11b**), H (**11c**), Cl (**11d**), CF_3 (**11e**)



11f



11g

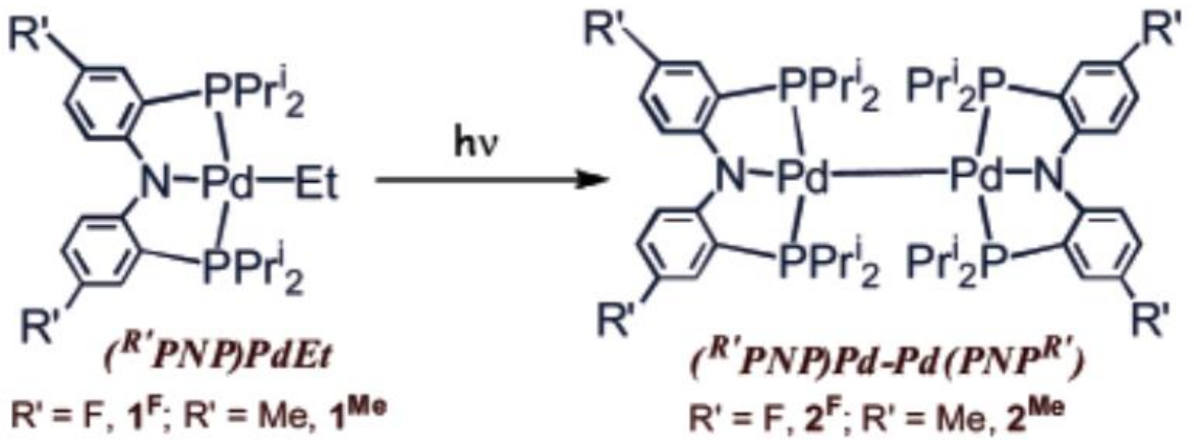
Table 1. Equilibrium Constants[a] for 12 + $NH_2Ar \rightleftharpoons$ 13 + Benzene $\rightleftharpoons$ 14 + Benzene at 25 °C

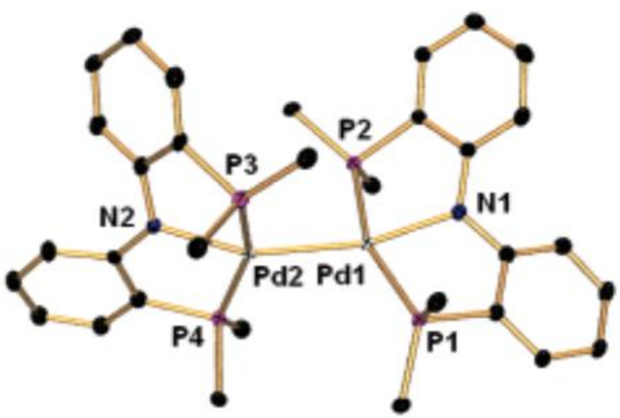
aniline (**11**)	K_1	K_2	K_3 (= K_1K_2)
a	1130	*b*	*b*
b	456	0.04	18
c	188	0.1	19
d	55	1	55
e	*c*	*c*	260
f	*c*	*c*	2190
g	*c*	*c*	2770

[a] Equilibrium values are based on an average of two to three runs. [b] Concentration of **14a** too low to detect. [c] Concentrations of **13e-g** too low to detect.

Sykes, A. C.; White, P.; Brookhart, M. *Organometallics* **2006**, *25*, 1664.

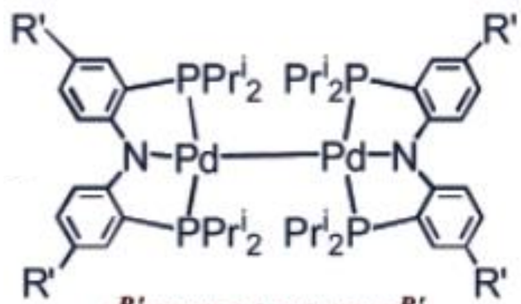
3. Activation of N-H bond





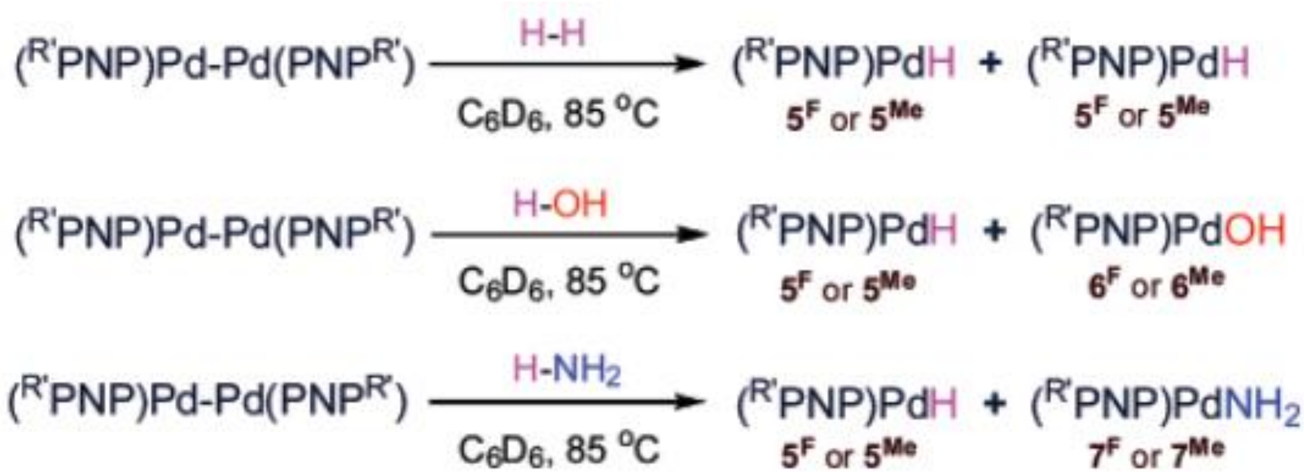
Fafard, C. M.; Adhikari, D.; Foxman, B. M.; Mindiola, D. J.; Ozerov, O. V. *J. Am. Chem. Soc.* **2007**, *129*, 10318.

3. Activation of N-H bond



($^{R'}$PNP)Pd-Pd(PNP$^{R'}$)

R' = F, **2^F**; R' = Me, **2^{Me}**



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4. Conclusion

a. NH_3 + Olefin

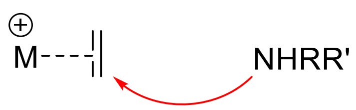
Catalytic utilization of ammonia in olefin hydroamination and in coupling with arenes were listed among the top ten challenges for catalysis over a decade ago, and these **remain unsolved** today.

b. NHRR' + Olefin

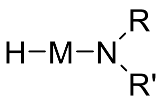
Markovnikov + aromatic olefin
Markovnikov + aliphatic olefin
Anit-Markovnikov + aromatic olefin
Anit-Markovnikov + aliphatic olefin

c. Any chance?

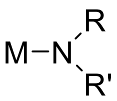
Activation of olefin



Activation of amine



oxidative addition



deprotonation

Markovnikov