

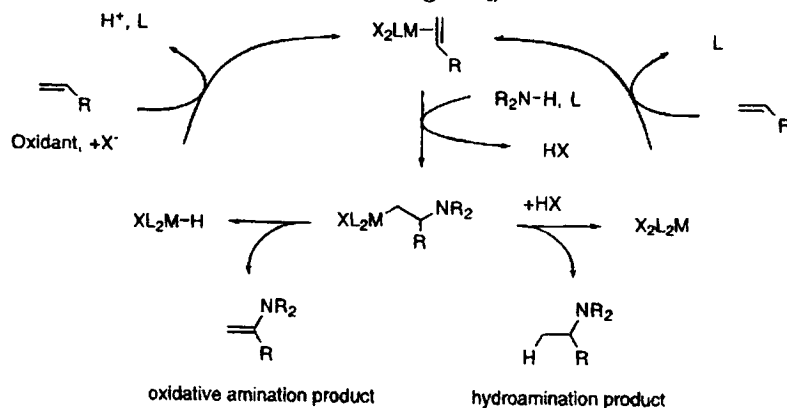


But alkenes are more inexpensive and can directly give amines, so this seminar will discuss the recent development about hydroamination of alkenes.

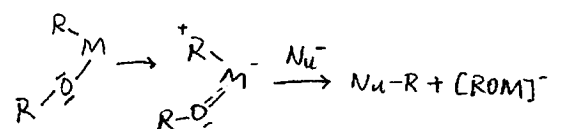
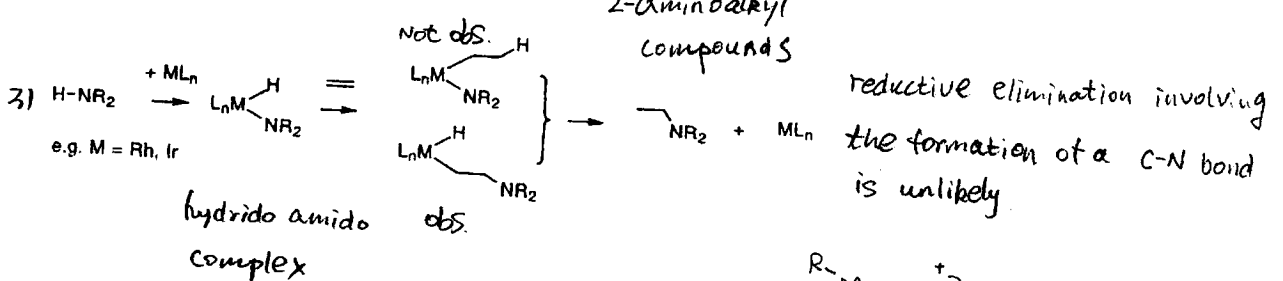
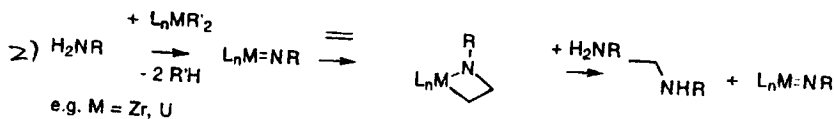
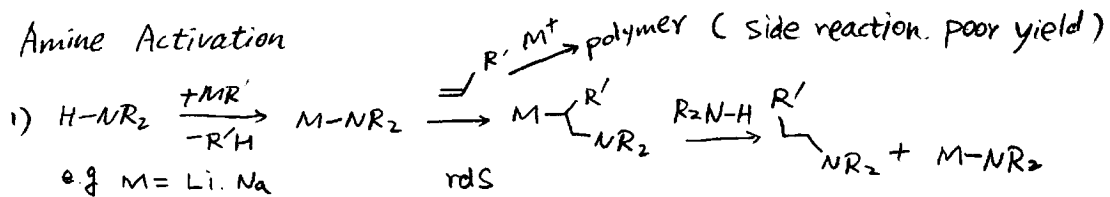
In general, hydroamination reactions are hindered by two major problems:

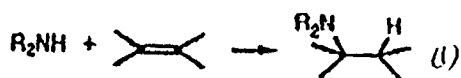
- 1) a high activation barrier for the direct addition of amines across C=C double bonds exists which arises from electrostatic repulsion between the electron lone pair at the nitrogen atom and the electron-rich C=C bond;
- 2) the general negative reaction entropy  $\Delta S^\circ$  of the reaction is responsible for the fact that the equilibrium of hydroamination reactions is shifted towards the starting materials at the higher temperatures that are necessary to overcome the activation barrier. This combination of facts makes it indispensable to develop catalytic hydroamination processes, which involve either activation of the C=C multiple bond or activation of the amine.

Scheme 6. Regeneration of the Active Catalyst from 2-Aminoalkyl Complexes via a Protonolytic or an Oxidative Pathway (M = Pd, Pt; X = e.g. Cl<sup>-</sup>, Br<sup>-</sup>; L = e.g. PR<sub>3</sub>)

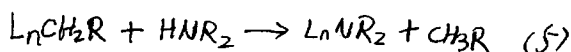
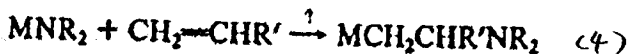
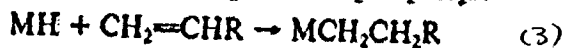
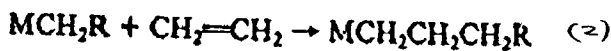


Amine Activation

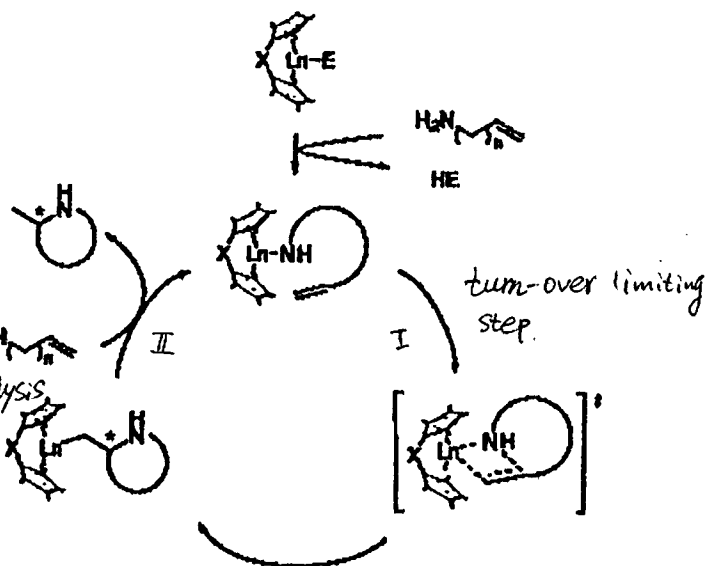




Organolanthanide complexes of the type  $Cp'_2LnR$  ( $Cp' = \eta^5-Me_5C_5$ ;  $R = H, CH(TMS)_2$ ;  $Ln = La, Nd, Sm, Y, Lu$ ) have been shown to be highly reactive with respect to olefin insertion processes (e.g.,  $N_i \approx 1500 s^{-1}$  for ethylene polymerization by  $Cp'_2La$  centers at 25 °C, 1 atm ethylene).<sup>15,16</sup> That this metal-ligand array supports olefin insertion into Ln-C and Ln-H bonds (eqs 2 and 3) with such extraordinary kinetic facility suggests that this may be an ideal environment in which to effect heretofore unrealized olefin insertion processes such as those involving metal-N bonds (eq 4).<sup>17,18</sup> Additionally, thermo-

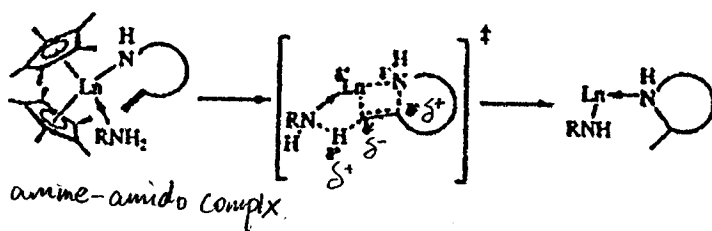


a



$k_H/k_D = 4.1 (25^\circ)$  suggests the cleavage of D-N bond or/and D-C formation.

Scheme III. Possible Sources of the NH/ND Kinetic Isotope Effect



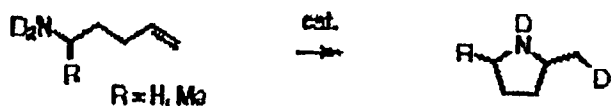
proton transfer occurs from coordinated amine to the partially polarized  $\alpha$ -carbon in the 4-member insertion TS. Such a transfer would stabilize the negative charge buildup.

hydrocarbon solvent.  
 Table II. Catalytic Results for the Organolanthanide-Catalyzed Hydroamination/Cyclization of Amino Olefins<sup>a</sup>

entry	substrate	product	$N_i, h^{-1} (^\circ C)$
1			140 (60) <sup>b</sup>
2			5 (60) <sup>b</sup>
3			45 (25) <sup>b</sup>
4			36 (25) <sup>b</sup>
5			95 (25) <sup>b</sup>
6			11 (25) <sup>c</sup>
7			12 (80) <sup>d</sup>
8			0.3 (60) <sup>c</sup>

<sup>a</sup>All rates measured in toluene- $d_6$ . <sup>b</sup>Rate measured using  $Cp'_2LaCH(TMS)_2$  as the precatalyst. <sup>c</sup>Rate measured using  $Me_2SiCp'_2NdCH(TMS)_2$  as the precatalyst.

Scheme 13. Deuterium Disposition Pattern

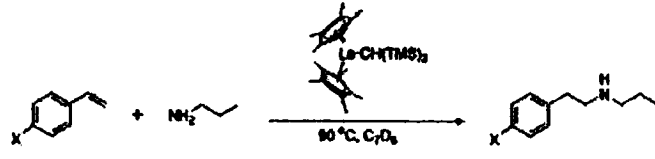


About I: cyclization depressed when THF used as solvent due to competition for the empty coordination site within the  $Cp'_2LnX$ .

**Organolanthanide-Catalyzed Regioselective Intermolecular Hydroamination of Alkenes, Alkynes, Vinylarenes, Di- and Trivinylarenes, and Methylenecyclopropanes. Scope and Mechanistic Comparison to Intramolecular Cyclohydroaminations**

Jae-Sang Ryu, George Yanwu Li,<sup>†</sup> and Tobin J. Marks\* *J. Am. Chem. Soc.* 2003, 125, 12584.

**Table 5.** Organolanthanide-Catalyzed Intermolecular Hydroamination of Vinylarenes<sup>a</sup>

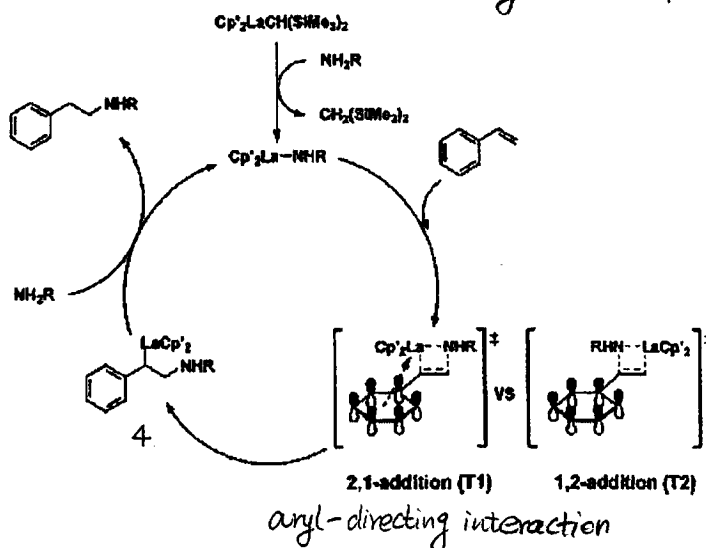


Entry	Olefin	Product	$N_t$ (h <sup>-1</sup> ) <sup>a</sup>	Conversion <sup>b</sup> (Reaction Yield %) <sup>c</sup>
1.	<i>e</i> -neutral	8	2.0 (90 °C)	93 (90)
2.	H <sub>3</sub> C	10	1.5 (90 °C)	> 95 (93) <sup>d</sup>
3.		11	1.6 (90 °C)	> 95 (92) <sup>d</sup>
4.	F	12	0.94 (120 °C)	94 (88)
5.	<i>e</i> poor	13	3.4 (90 °C)	93 (83) <sup>d</sup>
6.	<i>e</i> rich	14	0.2 (90 °C)	89 (82) <sup>d</sup>
7.		15	0.05 (90 °C)	55 (30)
8.		16	3.6 (90 °C)	89 (85)
9.		17	strongly coordinating substrate — instant precipitation No reaction	

<sup>a</sup> Turnover frequencies ( $N_t$ ) measured in C<sub>7</sub>D<sub>8</sub>. NMR reaction conditions: [cat]:[amine]:[vinylarene] = 1:10:100 employed for pseudo-zero-order kinetic plot; [cat] = 0.03 mM. <sup>b</sup> Isolated yield in preparative-scale reaction: the reactions were conducted in C<sub>6</sub>D<sub>6</sub>. Preparative reaction conditions: [cat]:[amine]:[vinylarene] = 1:20:40 employed; [cat] = 0.05 mM. <sup>c</sup> Isolated yield of the corresponding HCl salt in preparative-scale reaction. <sup>d</sup> [anti-Markovnikov]:[Markovnikov] = 96:4 regiochemistry was observed.

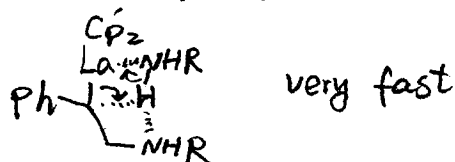
[olefin]:[amine] = 100:1 is to minimize amine inhibition and to shorten time. The relative reactivities of vinylarene can be compared by  $N_t$ .

Entry 5. *p*-CF<sub>3</sub> decreased styrenic olefin electron density lowered the barrier to insertion into Ln-N and also resulted in lessened arene coordinative tendency →  $N_t$  ↑



Weak Lewis basic arene  $\pi$  electrons stabilize the electron-deficient Lewis acidic Lanthanide center and deliver lanthanide to the benzylic position.

The reason why 2-aminophenylethyl does not undergo  $\beta$ -elimination



# Rational Design in Homogeneous Catalysis. Ir(1)-Catalyzed Addition of Aniline to Norbornylene via N-H Activation

Albert L. Casalnuovo,\* Joseph C. Calabrese, and David Milstein<sup>1</sup>

J. Am. Chem. Soc. 1988, 110, 6738-6744

Scheme 1

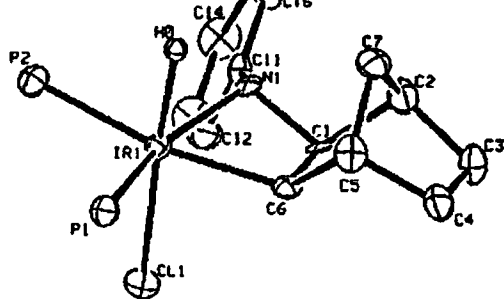
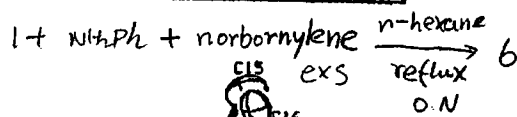
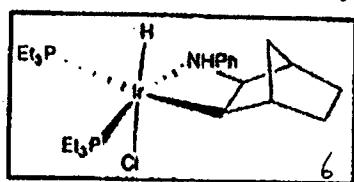
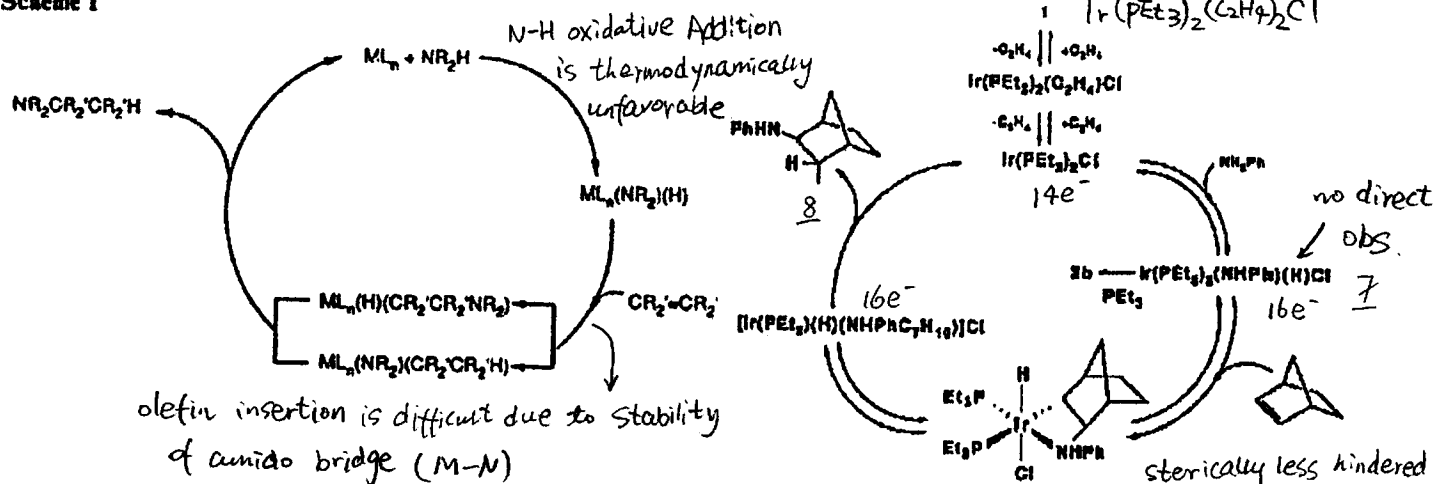
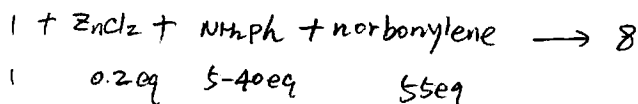


Figure 1. ORTEP and stick drawings of the solid-state structure of 6. H atoms and ethyl groups have been omitted from the ORTEP drawing for clarity.

with Lewis acid, effective barrier for reductive elimination (R.E) is greatly reduced by accelerate the dissociation of Cl

based on the decomposition results. 8 was obtained by:



formation of 8 is irreversible because  $8 + 1 \xrightarrow{\text{aniline or norbornylene}}$

No 8 resulted without cat 1

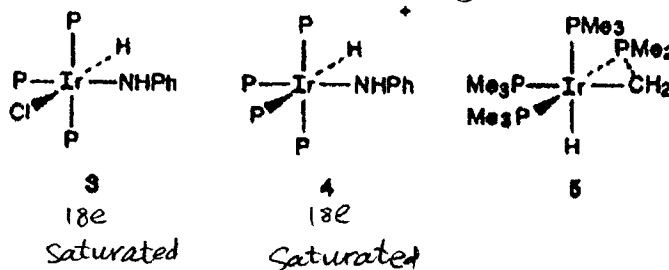


Table III. Effect of Added Reagents on Decomposition of 6

reagent <sup>a</sup>	norbornylene (%)	7 (%)	major inorganic product
none	53	43	hydride
PEt <sub>3</sub>	92	3	3b anilido 7 resulted
C <sub>2</sub> H <sub>4</sub> <sup>b</sup>	88	11	1 reversible
1,5-cyclooctadiene	44	56	Ir(PEt <sub>3</sub> ) <sub>x</sub> (COD)Cl <sup>c</sup>
LiCl <sup>d</sup>	82	12	
ZnCl <sub>2</sub> <sup>d</sup>	0	100	
TiPF <sub>6</sub> <sup>d</sup>	0	100	
CH <sub>2</sub> Cl <sub>2</sub> <sup>e</sup>	95	5	

<sup>a</sup>THF solution of 6 and 2 equiv of reagent heated at 80 °C for 1 h. <sup>b</sup>60 psi. <sup>c</sup>Saturated THF solution. <sup>d</sup>Reaction carried out at room temperature in THF. <sup>e</sup>Decomposition of 6 in CH<sub>2</sub>Cl<sub>2</sub> at 45 °C. <sup>f</sup>Same species observed from the addition of 1,5-cyclooctadiene to 1.

the formation of 8 is intramolecular process.

mixture of <sup>15</sup>N labeled 6 and deuterium-labeled 6 (Ir-D) were decompose to give, ca. 95% of 8 corresponded to a singly labeled species (either <sup>15</sup>N or D)

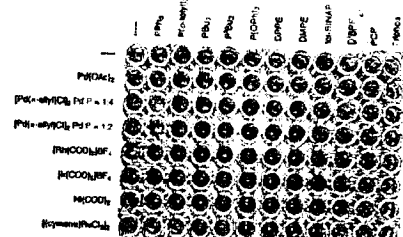


Figure 1. Use of a simple spot test to screen catalyst for the hydroamination of cyclohexadiene with aniline. A red color indicates remaining aniline reactant.

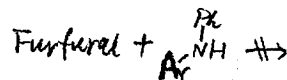
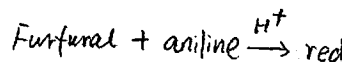
3. Activation of the Olefin

a. markovnikov addition

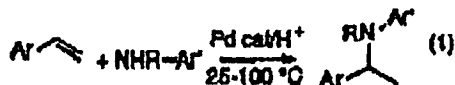
Palladium-Catalyzed Intermolecular Hydroamination of Vinylarenes Using Arylamines

Motoi Kawatsura and John F. Hartwig\*

J. Am. Chem. Soc. 2000, 122, 9546-9547



Colorimetric Assay



The catalytic, intermolecular hydroamination of olefins is a highly desired, but difficult process. Efficient, intramolecular, lanthanide-catalyzed hydroaminations of alkenes have been developed by Marks, but intermolecular reactions are generally slow, but reaction of piperidine or aniline with styrene gives enamine by oxidative amination<sup>14</sup> or product mixtures.

An efficient, palladium-catalyzed hydroamination of vinylarenes using aromatic amines to give *sec*-phenethylamine products in the presence of acid cocatalyst (eq 1). Was reported.

$Pd(PPh_3)_4/AcOH$  effectively catalyzed add. of amine to diene

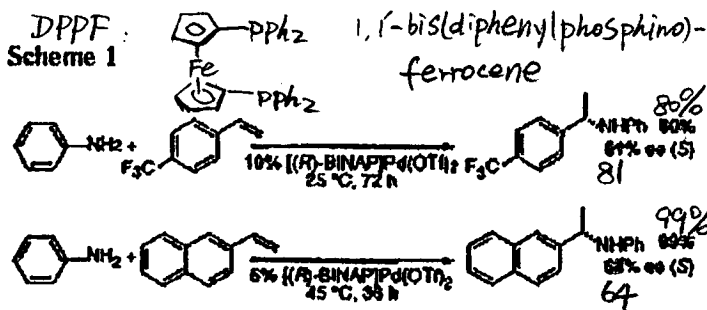
Table 2. Palladium-Catalyzed Hydroamination of Styrene<sup>a</sup>

Table 1. Effect of Catalyst Components and Acid on the Hydroamination of Styrene with Aniline<sup>a</sup>

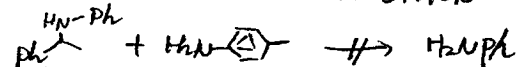
entry	catalyst	yield, % <sup>b</sup>
1	2% $[Pd(PPh_3)_4]$	0
2	2% $Pd(OC(O)CF_3)_2/8\% PPh_3$ in situ	28
3	2% $[Pd(PPh_3)_4]/20\%$ TFA weaker acid NG	67
A 4	2% $[Pd(PPh_3)_4]/20\%$ TfOH	83
5	2% $Pd(OC(O)CF_3)_2/8\% PPh_3/20\%$ TFA	68
6	2% $[Pd(OC(O)CF_3)_2]/3\%$ DPPF	78
B 7	2% $[Pd(OC(O)CF_3)_2]/3\%$ DPPF/20% TfOH	> 99
8	2% $[(DPPF)Pd(OTf)_2]$ Counterion effect	96

	Amine	Olefin	Cond.	time	Yield <sup>b</sup>
1			A	12 h	83%
2			B	7 h	>99%
3			A	12 h	93%
4			B	7 h	78%
6			A	12 h	64%
6			B	7 h	88%
7			B	7 h	68%
8			B	7 h	99%
9			B	7 h	85%
10			B	7 h	98%
11			C	72 h	98%
12			B	12 h	55%
13			A	12 h	65%
14			B <sup>c</sup>	12 h	54%

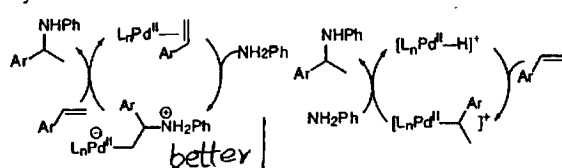
<sup>a</sup> Reactions were run for 6 h in toluene solvent at 100 °C. Reactions with lower yields did not show complete conversion. <sup>b</sup> Yields are for isolated material and are an average of two runs.



hydroamination is irreversible



Scheme 2. Two Potential General Mechanisms for the Hydroamination



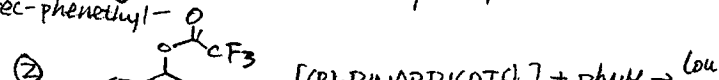
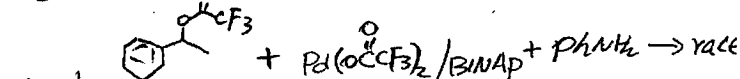
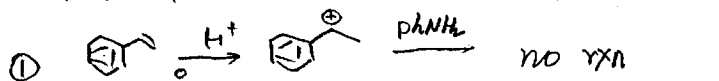
the aminoalkyl complex must undergo

protonolysis faster than  $\beta$ -hydrogen elimination  
 $\alpha$ -C of styrene is  $\delta^+$  after coordination to Pd and easier to attacked by aniline.

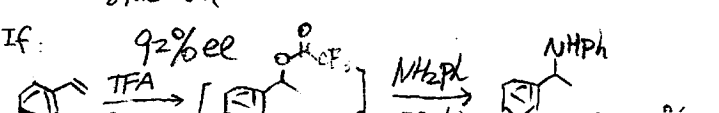
b/c

<sup>a</sup> Reaction conditions: A, 2%  $Pd(PPh_3)_4/20\%$  triflic acid, 100 °C; B, 2%  $Pd(TFA)_2/3\%$  DPPF, 20% TfOH, 100 °C; C, 5%  $(DPPF)Pd(OTf)_2$ , generated from  $(DPPF)Pd(OTf)_2$  and  $AgOTf$ , 25 °C. <sup>b</sup> Yields are for pure, isolated material and are an average of two runs. <sup>c</sup> 5 mol % catalyst used.

Role of Acid: no involve of add. of acid to arene

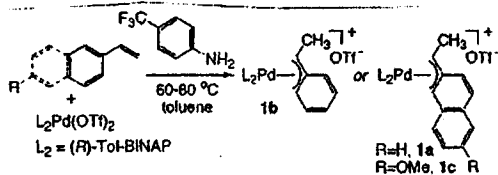


benzylic trifluoroacetate



**A New Pathway for Hydroamination. Mechanism of Palladium-Catalyzed Addition of Anilines to Vinylarenes**  
Ulrike Nettekoven and John F. Hartwig\*  
*J. Am. Chem. Soc.* 2002, 124, 1166

In last paper, a new Pd-cat hydroamination of vinylarene with arylamine is reported. This paper will explain the mechanism.



[(R)-Tol-BINAP][1-(2-naphthyl)-ethyl]Pd(OTf)

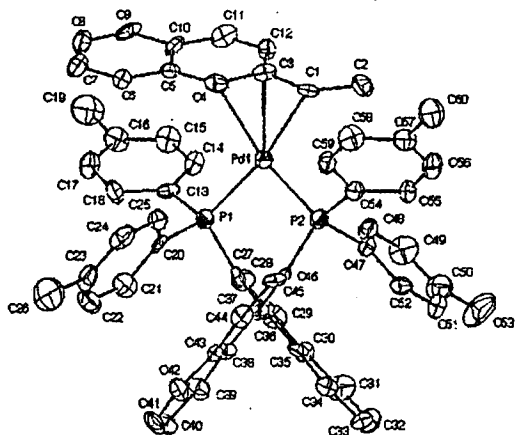


Figure 1. ORTEP plot of 1a at 50% probability level (hydrogen atoms, triflate anion, and solvent molecules are omitted for clarity). Selected bond lengths: Pd-C1 = 2.157(9) Å; Pd-C4 = 2.323(10) Å; Pd-P1 = 2.329(3) Å; Pd-P2 = 2.285(2) Å.

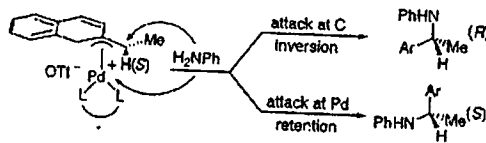
1a give corresponding N-(1-aryl)ethylamine at ca. 80% yield.

but alternative catalyst produced by deinsertion of olefin can also be reasonable.

To obtain strong evidence for the intermediacy of 1a-c, we allowed the methoxy-substituted complex 1c to react with aniline

and free 2-vinylnaphthalene. If 1a-c deinserted vinylarene to form the active catalyst, then the catalyst generated in this manner would react with the free vinylarene present in the highest concentration,

which is the unsubstituted 2-vinylnaphthalene in this case. Control experiments catalyzed by [(R)-Tol-BINAP]Pd(OTf)<sub>2</sub> and employing 2-vinylnaphthalene and 6-methoxy-2-vinylnaphthalene as well as a 1:1 mixture as substrates showed that the two olefins were comparable in reactivity. Reactions of 1c in the presence of 2 equiv of free 2-vinylnaphthalene were conducted with 100 equiv of aniline to ensure that reaction with aniline occurred faster than generation of other isomers or diastereomers of 1a. <sup>1</sup>H NMR spectra obtained at the early stages of the reaction showed that N-1-(6-methoxy-2-naphthyl)ethylaniline formed prior to the unsubstituted naphthylamine. These data strongly support the intermediacy of the isolated complexes in the catalytic process.



major isolated da → (R) prod. (da=diastereome)  
Catalytic Reaction → (S) ~60%

minor da reacts faster to give major enantiomer

Rate constant is measured as

$$k_{\text{major da}} = 2.3(2) \times 10^{-5} \text{ M}^{-1} \text{ s}^{-1}$$

$$k_{\text{overall cat.}} = 7.7(2) \times 10^{-5} \text{ M}^{-1} \text{ s}^{-1}$$

The major isolated da is 80%

3 isomers make up the rest 17-20% (8:5:4)

Although which isomer mainly give (S)-prod is unknown

This can explain why the ee is not so good.

Rf. the famous example to show minor, but more active species can determine ee of product

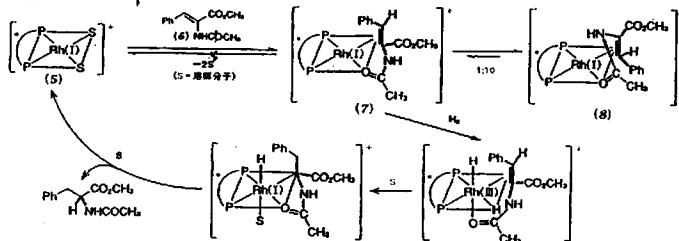


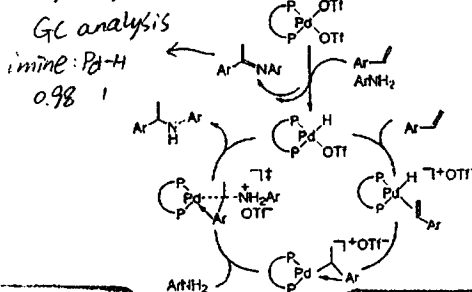
図8 Pd-ジホスフィン錯体による不斉水素化の反応機構

現代化学 2002年1月

19

unstable complex 7 undergoes hydrogenation 600 times faster than 8

Scheme 1. Catalytic Cycle for the Hydroamination of Vinylarenes Catalyzed by Palladium-diphosphine Complexes



7/14

# Intermolecular, Markovnikov Hydroamination of Vinylarenes with Alkylamines

Masaru Utsunomiya and John F. Hartwig\*

J. Am. Chem. Soc. 2003, 125, 14286-14287

Late transition-metal catalysts are likely to be more convenient to handle and tolerant of functional groups than lanthanide or early metal catalysts. However, late metal-catalyzed pathways for hydroaminations with alkylamines initiated by activation of amine or activation of olefin have been challenging to develop. Activation of alkylamines by oxidative addition remains unknown, and although addition of amines to coordinated olefins is common, the aminoalkyl group resulting from this addition is difficult to cleave from the metal under catalytic conditions. Acid could cleave this group in a catalytic cycle,<sup>12</sup> but the high basicity of alkylamine reagents level the strength of strong acids.

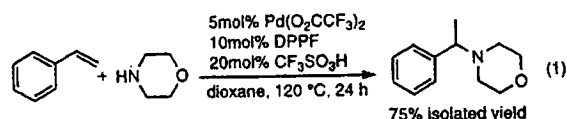


Table 1. Effects of Catalyst, Acid, and Solvent on the Hydroamination of Styrene with Morpholine at 120 °C<sup>a</sup>

entry	catalyst	solvent	yield <sup>b</sup>
1	5% Pd(O <sub>2</sub> CF <sub>3</sub> ) <sub>2</sub> /10% DPPF/20% TfOH	dioxane	79
2	5% Pd(O <sub>2</sub> CF <sub>3</sub> ) <sub>2</sub> /10% DPPF/20% TfOH	toluene	25
3	5% Pd(O <sub>2</sub> CF <sub>3</sub> ) <sub>2</sub> /5% DPPF/20% TfOH	dioxane	2
4	5% Pd(DPPF)(OTf) <sub>2</sub>	dioxane	1
5	5% Pd(DPPF)(OTf) <sub>2</sub> /5% DPPF/10% TfOH	dioxane	74
6	5% Pd(PPh <sub>3</sub> ) <sub>4</sub> /20% TfOH	dioxane	6
7	20% TfOH	dioxane	1
8	5% Pd(O <sub>2</sub> CF <sub>3</sub> ) <sub>2</sub> /20% TfOH	dioxane	1
9	5% Pd(O <sub>2</sub> CF <sub>3</sub> ) <sub>2</sub> /10% DPPF	dioxane	2
10	5% Pd(O <sub>2</sub> CF <sub>3</sub> ) <sub>2</sub> /10% DPPF/20% TFA	dioxane	19
11	5% Pd(O <sub>2</sub> CF <sub>3</sub> ) <sub>2</sub> /10% DPPF/20% NFA <sup>c</sup>	toluene	72
12	5% Pd(O <sub>2</sub> CF <sub>3</sub> ) <sub>2</sub> /10% DPPF/20% NFA <sup>c</sup>	dioxane	67

<sup>a</sup> Reaction conditions: 0.4 mmol morpholine, 0.8 mmol styrene, 0.2 mL dioxane, 24 h. <sup>b</sup> GC yields, in percent. <sup>c</sup> NFA = nonafluorobutane sulfonic acid.

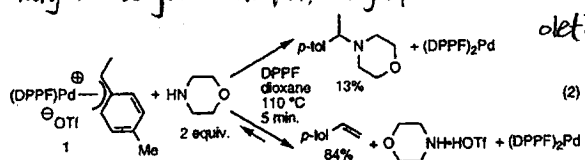
Entry 2 - Two phase

Entry 4 - active when arylamine used

Entry 7-8-9: Pd ligand Acid indispensable

Entry-10: weaker acid NG

Entry-11: longer chain FA, single phase in Tol.



olefin elimination occurs faster than C-N formation

Compared with reaction using arylamine.

Con Pd(0) is higher because  $\sigma$ -C<sub>6</sub>H<sub>4</sub>HOTf is easier to form.

To understand the differences in reactions of alkyl and arylamines, we evaluated if the C-N bond in the alkylamine products was formed by addition of alkylamine to an  $\eta^3$ -phenethylpalladium complex as it was during palladium-catalyzed additions of arylamines to vinylarenes.<sup>13</sup> Thus, DPPF-ligated  $\eta^3$ -4-methylphenylethylpalladium complex 1 in eq 2 was allowed to react with 2 equiv of morpholine in the presence of added DPPF to trap a Pd(0) product. Reaction at 110 °C for 5 min formed (DPPF)<sub>2</sub>Pd in 93% yield, N-1-(4-methylphenylethyl)morpholine in 13% yield, and morpholinium triflate together with free 4-methylstyrene in 84% yield.

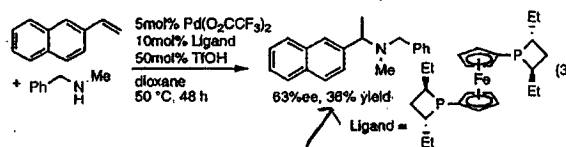
To determine if the 13% of hydroamination product was generated directly from the reaction of amine with 1 or from a catalytic reaction of the amine with the released vinylarene, the reaction of 1 with morpholine was conducted in the presence of 2 equiv of added styrene. The initial N-arylethylamine product contained the tolyl group of 1. This result demonstrates that morpholine reacted directly with 1 to form the arylethylamine product.

Table 2. Pd-Catalyzed Hydroamination of Alkylamines with Vinylarenes

entry	product	yield <sup>b</sup>	entry	product	yield <sup>b</sup>
1		75%	8 <sup>a</sup>		63%
2 <sup>c</sup>		51%	9 <sup>a</sup>		71%
3		76%	10		58%
4 <sup>d</sup>		79%	11 <sup>a</sup>		52%
5 <sup>e,f</sup>		51%	12 <sup>h</sup>		63%
6 <sup>e,f</sup>		48%	13 <sup>e,f,g</sup>		43%
7		72%	14 <sup>g,i</sup>		53%

best.

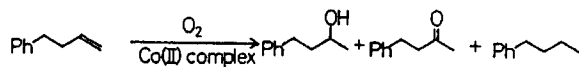
<sup>a</sup> Amine/vinylarene/Pd(TFA)<sub>2</sub>/DPPF/TfOH = 1:2:0.05:0.10:0.20 (1 mmol of amine) in 0.50 mL of dioxane. <sup>b</sup> Isolated yield. <sup>c</sup> 48 h. <sup>d</sup> 100 °C. <sup>e</sup> 4.0 mmol of vinylarene was used. <sup>f</sup> 0.20 mL of dioxane. <sup>g</sup> 110 °C. <sup>h</sup> 80 °C. <sup>i</sup> 10% of dibenzylmethylamine was obtained as side product. <sup>j</sup> 18 h.



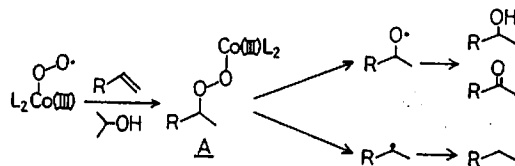
The low yield cause by alkyl exchange, which can give dibenzyl methylamine



The use of simple Cobalt complexes and Silanes for the oxyfunctionalization of olefins has been pioneered by Isayama and Mukaiyama.



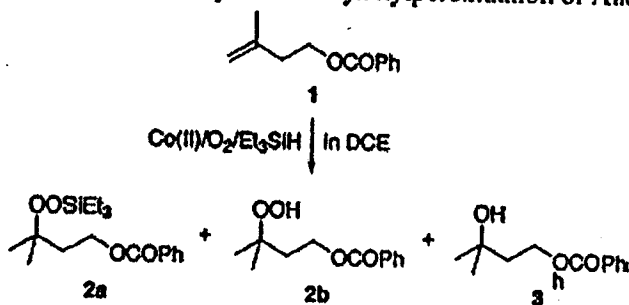
Scheme 1.



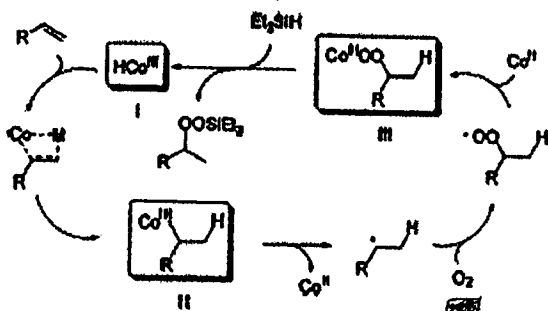
Co(acac)<sub>2</sub> IPA(sol) 46 8 17.

**Co(III)-Alkyl Complex- and Co(III)-Alkylperoxy Complex-Catalyzed Triethylsilylperoxidation of Alkenes with Molecular Oxygen and Triethylsilane**  
 Takahiro Tokuyasu, Shigeki Kunikawa, Araki Masuyama, and Masatomo Nojima\*  
 Org. Lett., 2002, 4, 3595

Table 1. Co(III)-Catalyzed Triethylsilylperoxidation of Alkene 1

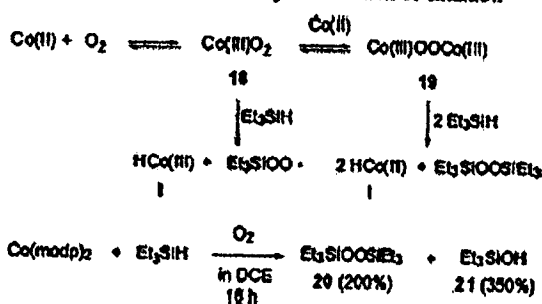


Scheme 3. Proposed Mechanism



how about displace O<sub>2</sub> with a  $\alpha$ -dicarboxylates?

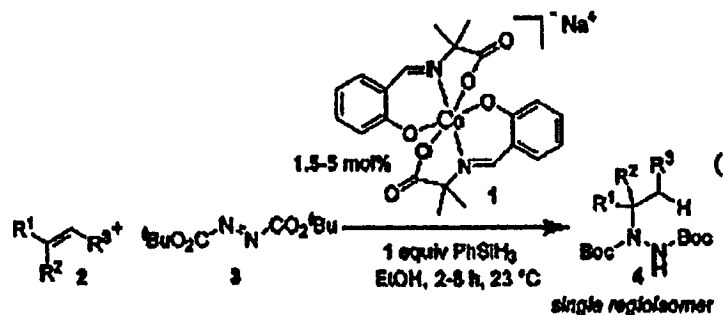
Scheme 7. Most Likely Mechanism of Initiation



Alkyl hydrazine can serve as useful precursors to amine and other synthetic building blocks. The synthesis of *N*-alkyl hydrazide by direct  $C=C$  functionalization of unactivated olefins is unprecedented.

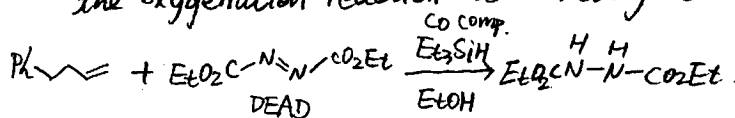
### Convenient Synthesis of Alkylhydrazides by the Cobalt-Catalyzed Hydrohydrazination Reaction of Olefins and Azodicarboxylates

Jerome Waser and Erick M. Carreira\* *J. Am. Chem. Soc.* 2004, 126, 5676.



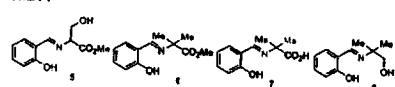
#### Screen of Catalyst:

- 1) complexes and conditions proven successful in the oxygenation reaction were investigated

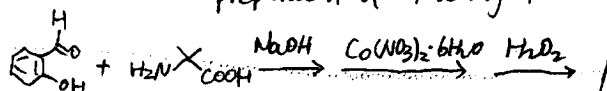


- 2) Various cobalt known to mediate epoxidation or peroxidation reaction of alkenes or alkanes.

Chart 1



preparation of 1 using 7



Scheme 1

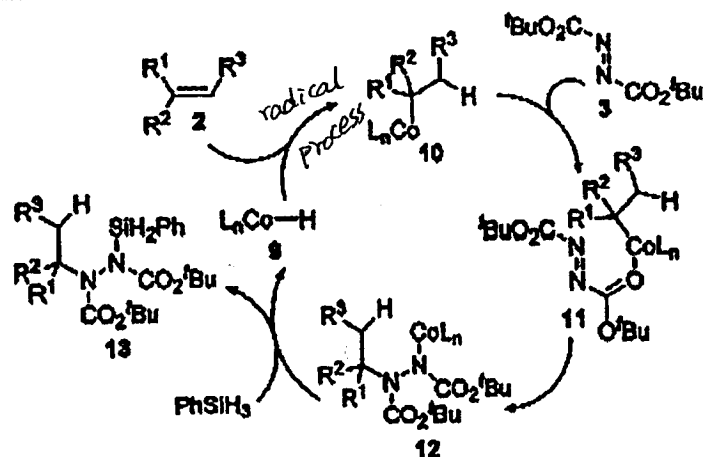


Table 1. Hydrohydrazination Reaction of Olefins (Eq 1)

Entry	Alkene	Product	Yield <sup>a)</sup>
1	Ph-CH=CH <sub>2</sub>	BocNHNBoc-CH(Ph)-CH <sub>3</sub>	86% <sup>b)</sup>
2	Ph-C(CH <sub>3</sub> )=CH <sub>2</sub>	BocNHNBoc-CH(Ph)-C(CH <sub>3</sub> ) <sub>2</sub> -H	88% <sup>b)</sup>
3	Ph-CH=CH-CH <sub>3</sub>	BocNHNBoc-CH(Ph)-CH <sub>2</sub> -CH <sub>3</sub>	88%
4	Ph-CH=CH-CH <sub>2</sub> -OH	BocNHNBoc-CH(Ph)-CH <sub>2</sub> -CH <sub>2</sub> -OH	91%
5	Indene	BocNHNBoc-Indene-2-yl	94%
6	Ph-Cyclohexene	BocNHNBoc-Cyclohexane-1-yl-Ph	80% <sup>c)</sup>
7	CH <sub>2</sub> =CH-CH <sub>2</sub> -OH	BocNHNBoc-CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -OH	78%
8	CH <sub>2</sub> =CH-CH <sub>2</sub> -OBn	BocNHNBoc-CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -OBn	76%
9	CH <sub>2</sub> =CH-CH(OH)-CH <sub>3</sub>	BocNHNBoc-CH <sub>2</sub> -CH(OH)-CH <sub>2</sub> -CH <sub>3</sub>	73% (d.r. 1:1)
10	CH <sub>2</sub> =CH-CH <sub>2</sub> -C(=O)-R	BocNHNBoc-CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -C(=O)-R	76%
11	CH <sub>2</sub> =CH-CH <sub>2</sub> -Br	BocNHNBoc-CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -Br	90%
12	CH <sub>2</sub> =CH-CH <sub>2</sub> -Ph	BocNHNBoc-CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -Ph	85%
13	CH <sub>2</sub> =CH-CH(OMe)-CH <sub>2</sub> -OMe	BocNHNBoc-CH <sub>2</sub> -CH(OMe)-CH <sub>2</sub> -OMe	70%
14	CH <sub>2</sub> =CH-CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>3</sub>	BocNHNBoc-CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>3</sub>	88% <sup>c)</sup>
15	Bicyclic alkene	BocNHNBoc-Bicyclic-1-yl	84% dr 2:1-3:1
16	Bicyclic alkene	BocNHNBoc-Bicyclic-1-yl	69% dr >5:1
17	Cyclohexene	BocNHNBoc-Cyclohexane-1-yl	90%
18	CH <sub>2</sub> =CH-COOEt	BocNHNBoc-CH <sub>2</sub> -CH <sub>2</sub> -COOEt	66% <sup>c)</sup>
19	CH <sub>2</sub> =CH-CH <sub>2</sub> -OH	BocNHNBoc-CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -OH	70%
20	Bicyclic alkene	BocNHNBoc-Bicyclic-1-yl	66%
21	Cyclooctene	BocNHNBoc-Cyclooctane-1-yl	62% <sup>c)</sup>
22	Cyclopentene	BocNHNBoc-Cyclopentane-1-yl	74% <sup>c)</sup>

<sup>a)</sup> Standard conditions: 0.5 mmol of alkene, 0.5 mmol of  $\text{PhSiH}_3$ , 0.75 mmol of 3, 5 mol % of catalyst 1, 2.5 mL of ethanol at 23 °C under  $\text{N}_2$ .  
<sup>b)</sup> 0.5 mmol of alkene was added as a solution in 1 mL of  $\text{CH}_2\text{Cl}_2$  using 1.5 mol % of catalyst 1. <sup>c)</sup> 0.5 mmol of alkene, 0.75 mmol of  $\text{PhSiH}_3$ , and 1.0 mmol of 3 were used.

Philip Magnus et al. T. L 2000 41, 9725-9730.

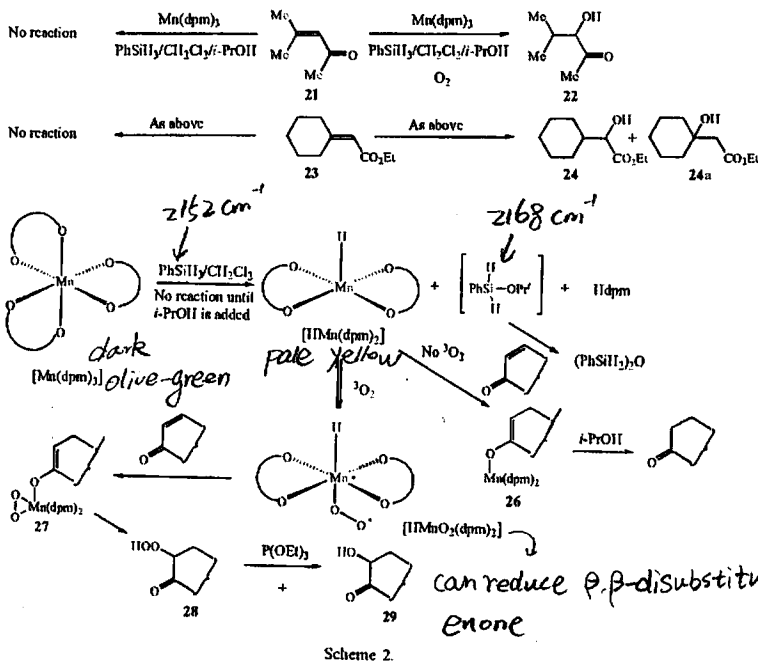


Table 1: Hydrohydrazination reactions of simple alkenes with  $[\text{Mn(dpm)}]_2$  (1).

Entry	Alkene	Product <sup>[a]</sup>	Regioselectivity <sup>[a]</sup>	Yield [%] <sup>[a]</sup>
1			> 20:1	94
2			5.5:1	94
3			9:1	87
4			> 20:1	86
5			> 20:1	88
6			1.8:1	90 $\leftarrow 25\% \text{ (Co)}$

[a] Major product shown. [b] With the Co catalyst, the regioselectivity was generally higher than 20:1, except for entry 6 (3:1). [c] Standard conditions: alkene (0.5 mmol),  $\text{PhSiH}_2$  (0.5 mmol), 3 (0.75 mmol), catalyst 1 (2 mol%), 2-propanol (2.5 mL),  $\text{N}_2$ ,  $0^\circ\text{C}$ .

Compared with Co System

- 1) wider scope
- 2) higher yield
- 3) faster (5 min v.s 6-23 h)

Table 2: Hydrohydrazination reactions of more-challenging alkenes.

Entry	Alkene	Product	Yield [%] <sup>[a]</sup>	$\text{Mn}^{\text{III}}$
8			16	78
9			18	79
10			10	74
11			13 <sup>[c]</sup>	51 <sup>[c]</sup>

[a] Standard conditions: alkene (0.5 mmol),  $\text{PhSiH}_2$  (0.5 mmol), 3 (0.75 mmol), Co catalyst<sup>[a]</sup> (5 mol%), ethanol (2.5 mL),  $\text{N}_2$ ,  $23^\circ\text{C}$ .  
 [b] Standard conditions: alkene (0.5 mmol),  $\text{PhSiH}_2$  (0.5 mmol), 3 (0.75 mmol), catalyst 1 (2 mol%), 2-propanol (2.5 mL),  $\text{N}_2$ ,  $0^\circ\text{C}$ .  
 [c] Only one regioisomer was observed.

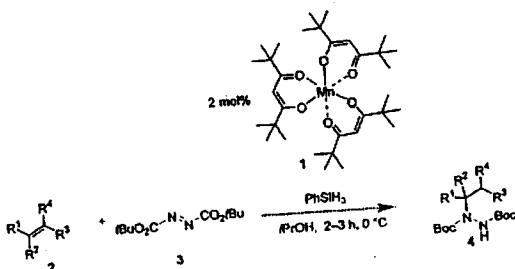
Given the observation of unique reactivity for the Mn complex, we proceeded to investigate whether this catalyst would permit the use of other silanes. We were pleased to note that in the hydrohydrazination reaction of 4-phenylbutene with  $[\text{Mn(dpm)}]_2$  (2 mol%) the hydrazide adduct is obtained when using PMHS (poly(methylhydrosiloxane)), a considerably less-expensive and more-stable silane, in 88% yield in 12 h at  $23^\circ\text{C}$ , whereas the Co system showed less than 20% conversion after 24 h when using this silane.

The reaction to convert an  $\alpha,\beta$ -unsaturated ester into an  $\alpha$ -hydroxy ester in a single step also be pioneered by Isayama and Mukaiyama.

The Mn(II) used by Isayama was corrected to be Mn(III) by X-ray analysis.

Erick M Correia Angew Chem Int Ed  
 2004, 43, 4099-4102

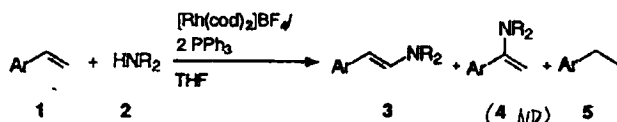
A broad-based study of numerous metal salts and complexes led us to examine  $[\text{Mn(dpm)}]_2$  (1).<sup>[29]</sup> This complex has been studied in the hydration of  $\alpha,\beta$ -unsaturated ketones and esters to give  $\alpha$ -hydroxyketones and -esters, respectively,<sup>[27,28,30]</sup> as well as for epoxidation of alkenes,<sup>[31]</sup> reduction of ketones,<sup>[32]</sup> and conjugate reduction of  $\alpha,\beta$ -unsaturated ketones.<sup>[33]</sup> Based on our speculations regarding the similarities between the metal-catalyzed functionalization of alkenes using oxygen and phenylsilane<sup>[27,28,34]</sup> and the hydrohydrazination reaction, we hypothesized that this complex could also catalyze the reaction of alkenes and azodicarboxylates.



## b. Anti-Markovnikov product formation

### Anti-Markovnikov Functionalization of Olefins: Rhodium-Catalyzed Oxidative Aminations of Styrenes\*\*

Matthias Beller, Martin Eichberger, and Harald Trauthwein  
*Angew. Chem. Int. Ed. Engl.* 1997, 36, 2225

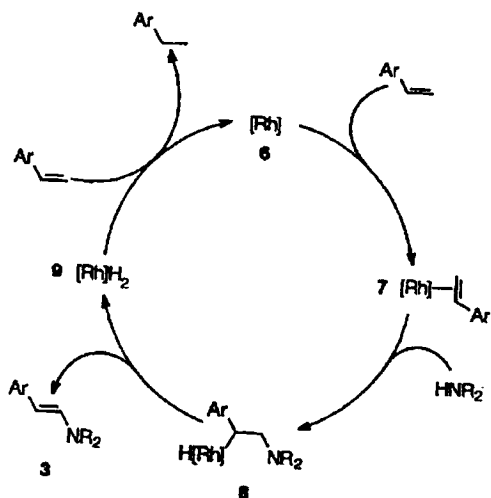


Scheme 2. Rhodium-catalyzed regioselective oxidative amination of styrenes. Ar = aryl; R = alkyl, aryl; cod = (Z,Z)-1,5-cyclooctadiene.

Table 1. Oxidative aminations of styrene [a].

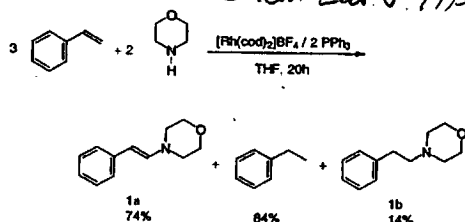
Amine	Yield [%]	
	enamine	ethyl benzene
diethylamine	40	54
di-n-butylamine	48	44
piperidine	55	57
hexahydroazepine	45	80
N-methylaniline	9	9

[a] Ratio of styrene:amine 4:1, 2.5 mol% [Rh(cod)<sub>2</sub>]BF<sub>4</sub>/2 PPh, relative to amine, 20 h reflux in THF.

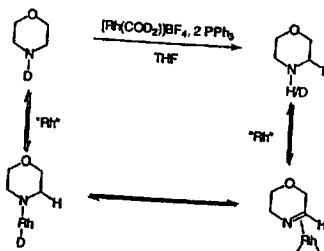


Postulated mechanism of the oxidative amination. Ar = aryl; R = alkyl.

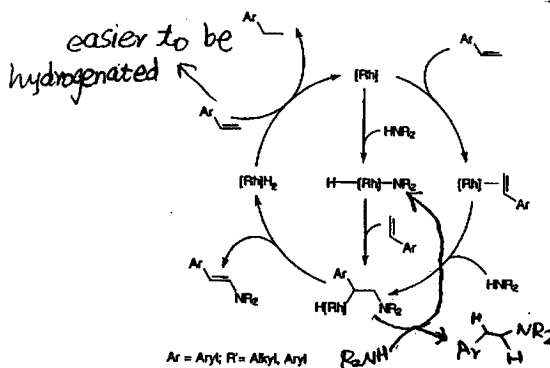
First Anti-Markovnikov Hydroamination.  
*Chem. Eur. J.* 1995, 5, 1306



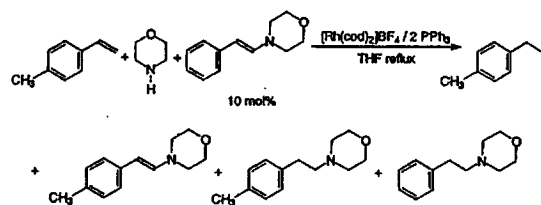
Scheme 3. anti-Markovnikov oxidative amination and anti-Markovnikov hydroamination of styrene with morpholine.



Scheme 8. Reaction of N-deuterated morpholine with [Rh(cod)<sub>2</sub>]BF<sub>4</sub>/2 PPh<sub>3</sub>.



Scheme 9. Possible mechanisms for the oxidative amination of styrene.



para-substituent	enamine [%]	alkylamine [%]	enamine / alkylamine
Methyl	76	15	5.3
H	9.8	0.2	54.4

Scheme 5. Reaction of 4-methylstyrene and morpholine in the presence of 10 mol% N-(2-phenylethenyl)-morpholine.

No hydrogenation to enamine.

Both enamine have similar reactivity.

Interestingly, morpholine generated a comparatively high yield of the hydroamination product compared with other amines that we studied. One possibility is that the hemilabile oxygen atom of morpholine coordinates to the rhodium center and stabilizes the alkylrhodium complex, thus decreasing the possibility of  $\beta$ -hydride elimination (Scheme 11).



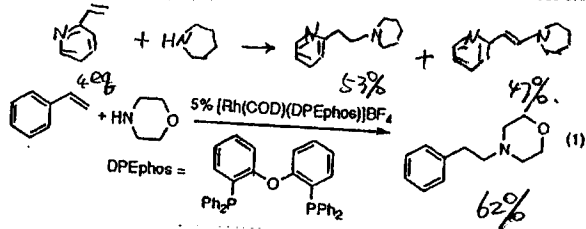
Scheme 11. Hypothetical coordination of the rhodium-alkyl species with morpholine to suppress  $\beta$ -hydride elimination.

The proposed protolysis step is supported by the fact that an increase in the concentration of the amine or of protons also increases the amount of the hydroamination product. In addition, the formation of the alkylamine is dependent on the styrene concentration. An excess of styrene also promotes the formation of the hydroamination product. This is in agreement with an independent hydroamination cycle, because at higher concentrations of styrene a hydrogenation of enamine by a rhodium-dihydride species is unlikely.

Rhodium-Catalyzed Anti-Markovnikov Hydroamination of Vinylarenes

Masaru Utsunomiya, Ryoichi Kuwano, Motoi Kawatsura, and John F. Hartwig\*

Department of Chemistry, Yale University, P.O. Box 208107, New Haven, Connecticut 06520-8107



enamine from oxidative amination — minor along with same equivalent ethylbenzene.

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

entry	ligand	amine yield (%)	enamine yield (%)
1	DPEphos (eq 1)	62	20
2	PTB <sub>3</sub>	17	78
3	DPPE <sup>b</sup>	0	1
4	DPPF <sup>c</sup>	0	0
5	DPPFent <sup>d</sup>	1	0
6	Xantphos (1)	trace	1
7	DBPphos (2)	3	40
8	BiHPEphos (3)	0	0

\* Reaction were run for 48 h at 70 °C. Morpholine:styrene:[Rh(cod)]BF<sub>4</sub>:ligand = 1:4:0.05:0.15 (0.2 mmol of morpholine, PPh<sub>3</sub> = 0.1) in 0.2 mL of toluene. <sup>b</sup> GC yield. <sup>c</sup> 1,2-Bis(diphenylphosphino)ethane. <sup>d</sup> 1,4-Bis(diphenylphosphino)butane. <sup>e</sup> 1,5-Bis(diphenylphosphino)pentane.

faster with higher styrene con but the selectivity (hydroamination:oxi:amine) is lower

e rich olefin, less reactive, gave better yield and selectivity  
e poor olefin, to get better h.A v.s O.A. can react with lower olefin con (2:1 olefin:amine) because e poor olefin is more reactive to  $\beta$ -H eliminated (entry 4, 6).

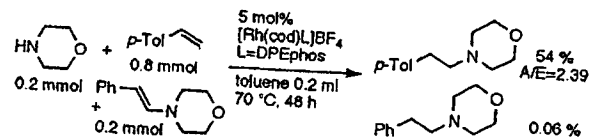
Table 2. Anti-Markovnikov Hydroamination of Vinylarenes with Secondary Amines\*

entry	amine	vinylarene	time (h)	yield (%)	amine:enamine <sup>b</sup>
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 <sup>c</sup>	1a	2e	72	48	60:40
6 <sup>d</sup>	1a	2f	72	41	57:43
7 <sup>e</sup>	1b	2a	72	57	63:37
8	1b	2d	48	66	77:23
9	1c	2a	72	58	86:14
10	1d	2a	72	51 <sup>f</sup>	76:24
11 <sup>g</sup>	1e	2a	72	51 <sup>f</sup>	72:28
12	1f	2c	48	62 <sup>f</sup>	54:46
13 <sup>h</sup>	1g	2b	72	50 <sup>f</sup>	82:18
14 <sup>i</sup>	1g	2d	72	74	82:18
15 <sup>j</sup>	1g	2g	48	79 <sup>f</sup>	90:10

HNRR' = 1a: 2,5-Me<sub>2</sub>-morpholine; 1b: N-Me-morpholine; 1c: N-Et-morpholine; 1d: N-Pr-morpholine; 1e: N-Bu-morpholine; 1f: N-Pipecolone; 1g: N-Pipecolone; 1h: N-Pipecolone; 1i: N-Pipecolone; 1j: N-Pipecolone. Vinylarenes: 2a: R = H; 2b: R = 4-Me; 2c: R = 4-MeO; 2d: R = 3-CF<sub>3</sub>; 2e: R = 4-MeO; 2f: R = 3-CF<sub>3</sub>; 2g: 2-vinylpyridine; 2h: R = 3,4-MeO.

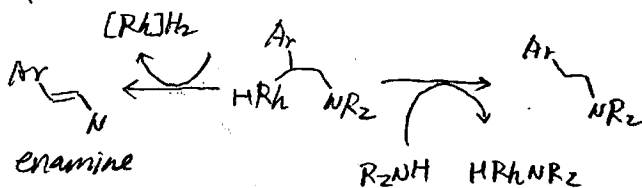
\* Amine: vinylarene: Rh catalyst = 1:4:0.05 (1 mmol of amine) in 1 mL of toluene. <sup>b</sup> Isolated yield by silica gel column chromatography. <sup>c</sup> Selectivity was calculated from the GC area. <sup>d</sup> GC yield = 10 mol % Rh catalyst was used. <sup>e</sup> 2.0 equiv of vinylarene was used. <sup>f</sup> 75 °C. <sup>g</sup> 0.5 mL of toluene was used. <sup>h</sup> Dimethylamine 2.0 M in THF solution (0.5 mL) and 0.5 mL toluene was used. <sup>i</sup> No toluene was added. <sup>j</sup> Diastereomer ratio of starting amine was 74:26, ratio of products was 82:18. The ratio was determined by GC area. <sup>k</sup> Diastereomer ratio of starting amine was 7:93, ratio of products was 17:83. The ratio was determined by GC area.

Scheme 1



Beller, Eur J Inorg Chem 1999, 1121 in parallel, because amine and enamine are formed

- 1) the ratio is constant over the course
- 2) in Scheme 1, only trace phenylamine formed



Scheme 2

entry	3 (mmol)	4 (mmol)	5:6 <sup>a</sup>	7:8 <sup>a</sup>
1	0.4	0.4	50:50	47:53
2	0.8	0.0	72:28	—
3	0.0	0.8	—	38:62

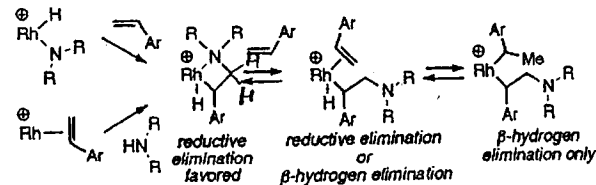
<sup>a</sup> Ratios were determined from GC peak areas and are uncorrected.

Entry 1, 2

amine reduced, enamine raised, means 5 is easier to be  $\beta$ -H eliminated with existence of another vinylarene.

The lower amine:enamine ratios at higher concentrations of vinylarene suggest that two vinylarenes are present in the transition state that controls selectivity. If the vinylarene is both a reactive and an ancillary ligand, then one vinylarene should affect the product ratio formed from another. To test this prediction, the reaction of morpholine with a mixture of styrene and *m*-trifluoromethylstyrene was conducted. Compared to ratios from reactions of the two vinylarenes alone, the ratio of amine to enamine formed from styrene was lower and the ratio of amine to enamine formed from *m*-trifluoromethylstyrene was higher (Scheme 2).<sup>38</sup> This result supports the presence of two vinylarenes in the complex that controls selectivity. A second amine does not participate in a similar way. The ratios of amine:enamine from reaction of morpholine and piperidine together were indistinguishable from the ratios produced from reactions of the two amines conducted separately.

Scheme 3



bigger coord. constant

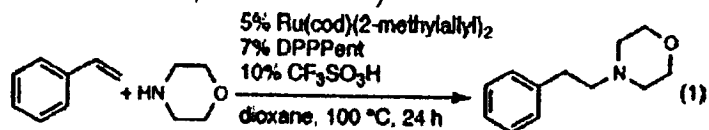
rationalizes the effect of the second styrene. A metallacyclic  $\beta$ -amino,  $\alpha$ -arylalkyl complex could form by either attack on coordinated olefin or insertion into a species formed by N-H activation. This metallacyclic would favor formation of amine because the  $\beta$ -hydrogen would be inaccessible to the metal, but the alkyl and hydride could be mutually cis. Coordination of a second vinylarene<sup>31</sup> could then open the metallacyclic to allow  $\beta$ -hydrogen elimination, or insertion of the vinylarene could generate a dialkyl complex that must undergo  $\beta$ -hydrogen elimination. Coordination of the electron-poor vinylarene is likely to be favored.<sup>41</sup> Reaction solutions containing electron-poor vinylarene would, therefore, create more enamine from  $\beta$ -hydrogen elimination than those with only electron-rich vinylarene. We cannot explain at this time the low selectivity from reactions of piperidine, but

# Ruthenium-Catalyzed Anti-Markovnikov Hydroamination of Vinylarenes

Masaru Utsunomiya and John F. Hartwig\*

J. Am. Chem. Soc. 2004, 126, 2702

In last report, oxidative amination to form enamine compete with hydroamination.



DPPPPent = 1, 5-bis(diphenylphosphino)pentane 96% isolated yield  
 polymerization compete with hydroamination  
 but no enamine formed from oxidative amination

We disclose here selected ruthenium complexes that catalyze with exquisite chemo- and regioselectivity the anti-Markovnikov hydroamination of vinylarenes. Reactions of cyclic or acyclic, functionalized or unfunctionalized secondary amines with vinylarenes form terminal amines. In addition to demonstrating high selectivity for formation of terminal amines, these results demonstrate the tolerance of these late-metal catalysts toward Lewis basic and acid-labile functionality.

Markov →

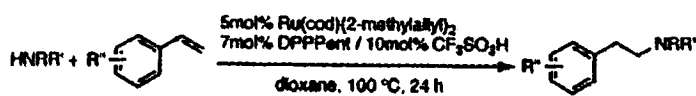
Table 1. Effects of Catalyst Components on the Hydroamination of Styrene and Morpholine in Dioxane at 100 °C<sup>a</sup>

c1ccc(cc1)/C=C + HN1CCOCC1 >> c1ccc(cc1)CN1CCOCC1 + c1ccc(cc1)CN1CCOCC1
  
 Ru(cod)(methylallyl)<sub>2</sub> Ligand / Acid
   
 dioxane, 100 °C, 24 h

entry	Ru (%)	ligand	acid	1 <sup>b</sup> (%)	2 <sup>b</sup> (%)
1	5	7% DPPPPent	10% TfOH	96	<1
2	5	—	10% TfOH	0	<1
3	5	7% DPPPPent	—	0	0
4	5	7% DPPPPent	10% TFA	8	0
5	2	3% DPPPPent	5% TfOH	90	<1
6	5	14% PPh <sub>3</sub>	10% TfOH	36	9
7	5	14% PEtPh <sub>2</sub>	10% TfOH	61	3
8	5	7% DPPB <sup>c</sup>	10% TfOH	54	12
9	5	7% DPPHex <sup>d</sup>	10% TfOH	33	2
10	5	7% DPPF <sup>e</sup>	10% TfOH	55	44
11	5	7% DPEphos <sup>f</sup>	10% TfOH	19	2

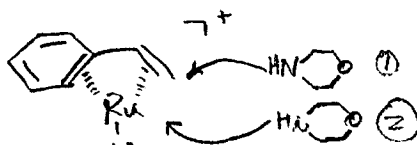
<sup>a</sup> Reaction conditions: morpholine 0.4 mmol, styrene 0.8 mmol, dioxane 0.2 mL, 100 °C, 24 h. <sup>b</sup> GC yields. <sup>c</sup> 1,4-Bis(diphenylphosphino)butane. <sup>d</sup> 1,6-Bis(diphenylphosphino)hexane. <sup>e</sup> 1,1'-Bis(diphenylphosphino)ferrocene. <sup>f</sup> Bis(2-diphenylphosphino)phenyl) ether.

Table 2. Ruthenium-Catalyzed Hydroamination of Vinylarenes with Alkylamines<sup>a</sup>

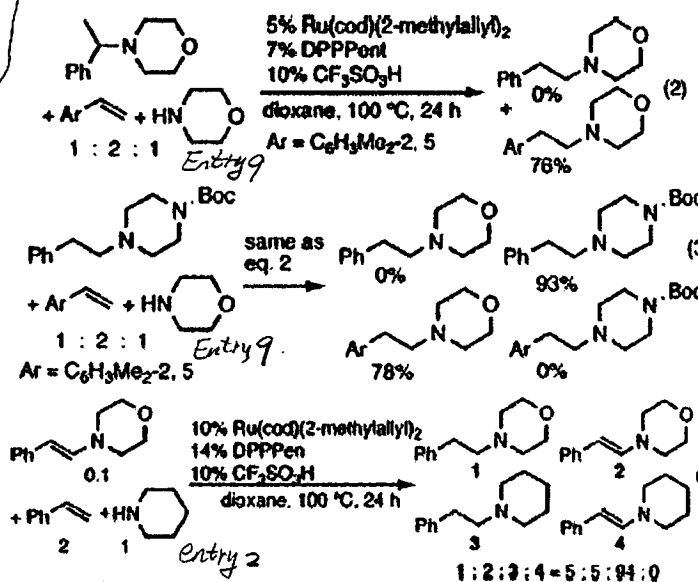


entry	product	yield <sup>b</sup>	entry	product	yield <sup>b</sup>
1	<chem>c1ccc(cc1)CN1CCOCC1</chem>	96%	8 <sup>c,d,e</sup>	<chem>c1ccc(cc1)CN(C)Cc2ccccc2</chem>	50%
2	<chem>c1ccc(cc1)CN1CCOCC1</chem>	91%	9	<chem>Cc1ccc(C)cc1CN1CCOCC1</chem>	81%
3 <sup>c</sup>	<chem>c1ccc(cc1)CN1CCOCC1</chem>	64%	10	<chem>Cc1ccc(C)cc1CN1CCOCC1</chem>	72%
4	<chem>c1ccc(cc1)CN1CCOCC1</chem>	90%	11 <sup>e,f,g</sup>	<chem>COc1ccc(C)cc1CN1CCOCC1</chem>	91%
5	<chem>c1ccc(cc1)CN1CCOCC1</chem>	82%	12 <sup>f,g,h</sup>	<chem>Fc1ccc(C)cc1CN1CCOCC1</chem>	71%
6 <sup>c</sup>	<chem>c1ccc(cc1)CN1CCOCC1</chem>	65%	13 <sup>h</sup>	<chem>Fc1ccc(C)cc1CN1CCOCC1</chem>	51%
7 <sup>c,d,e</sup>	<chem>Cc1ccc(C)cc1CN1CCOCC1</chem>	63%	14 <sup>d,i,j</sup>	<chem>Cc1ccc(C)cc1CN1CCOCC1</chem>	40%

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



no benzyl exchange between amine.  
 this is to say, no Br<sub>2</sub>NMe obtained



- irreversible.
- NO isomerization of Markovnikov product to terminal amine
- No amine exchange between terminal amine, no ArEt. NO<sub>2</sub>
- direct (?)
  - compound 1 resulted
  - additional exp 2 4 hydrogenation.