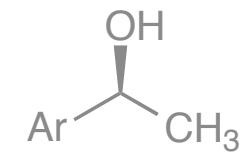
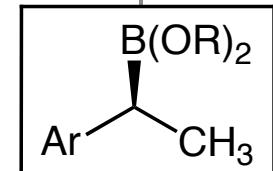
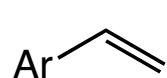
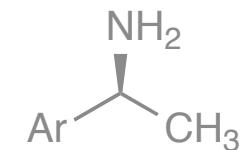
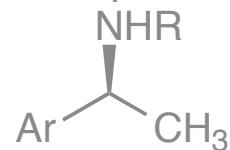
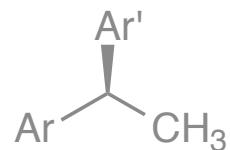


Catalytic Olefin Hydroboration

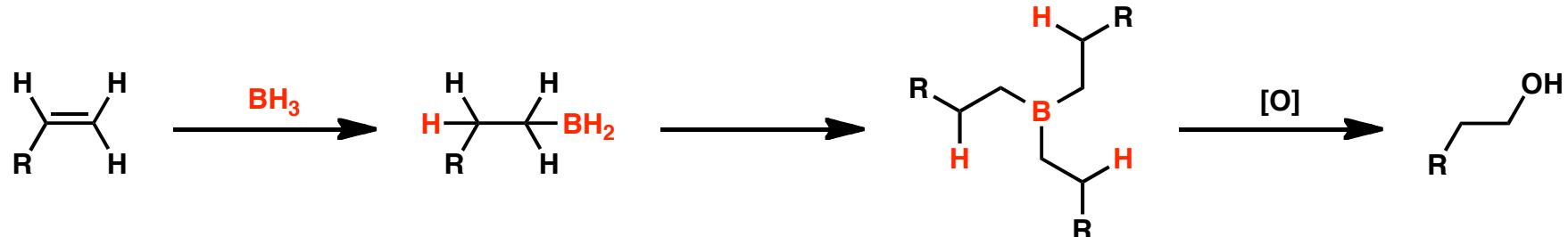
Mechanistic Features, Practical Considerations and Synthetic Applications



Alexander Goldberg
Stoltz Group Literature Presentation
March 1, 2010
8 PM, 147 Noyes

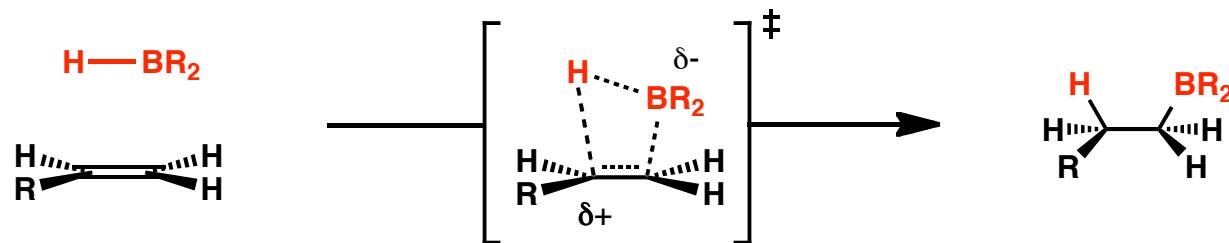


Introduction to Hydroboration



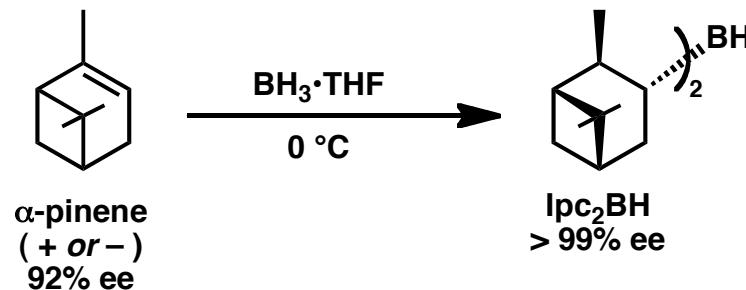
- Convenient method for ***anti-Markovnikoff*** hydration of olefins

Mechanism:

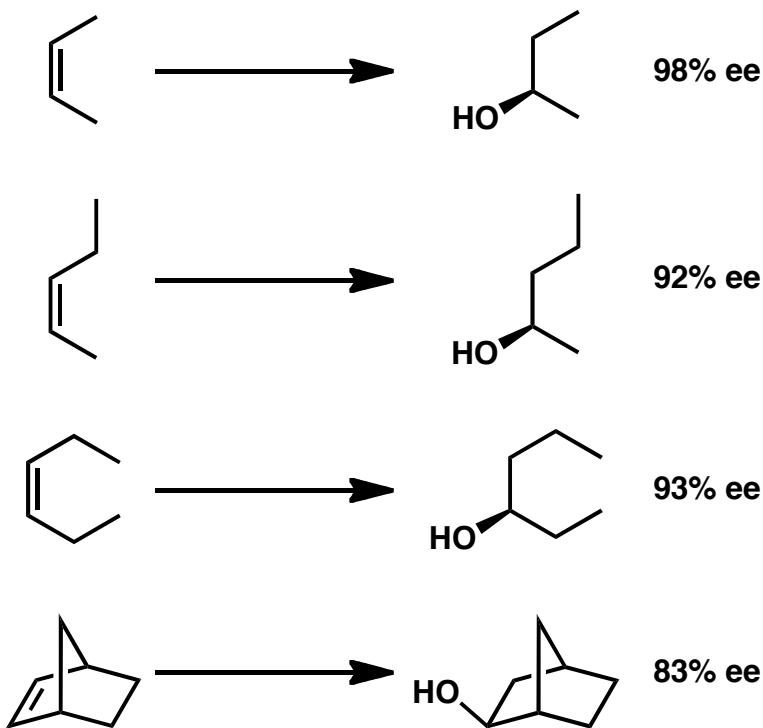


- Asynchronous transition state: partial charge buildup
- Substituent most capable of stabilizing partial positive charge receives proton

Stoichiometric Enantioselective Hydroboration



Diiisopinocampheylborane (Ipc_2BH)

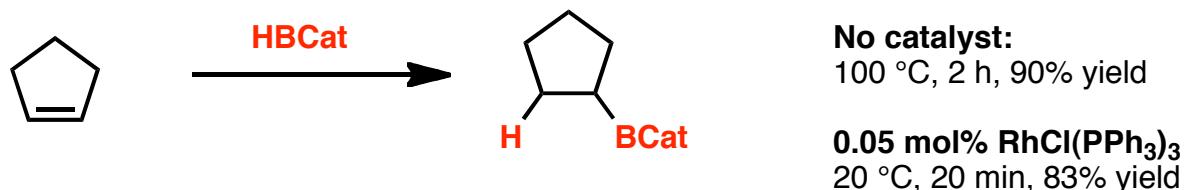
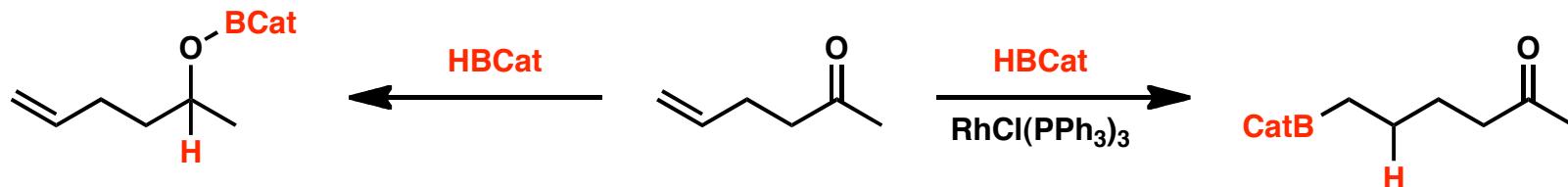


- Allowing Ipc_2BH to stand @ $0\text{ }^\circ\text{C}$ in presence of slight excess of $\alpha\text{-pinene}$ gives enantiopure reagent

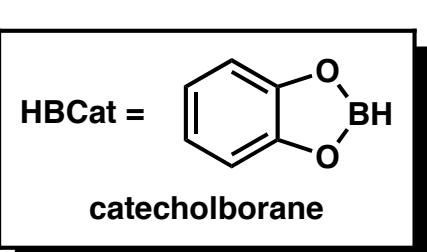
- "The first truly successful, nonenzymatic, asymmetric synthesis"

First Publication: Brown, H. C. *J. Am. Chem. Soc.* **1961**, *83*, 486–487.
Review: Brown, H. C. *Acc. Chem. Res.* **1988**, *21*, 287–293.

Late Transition Metal Catalysis

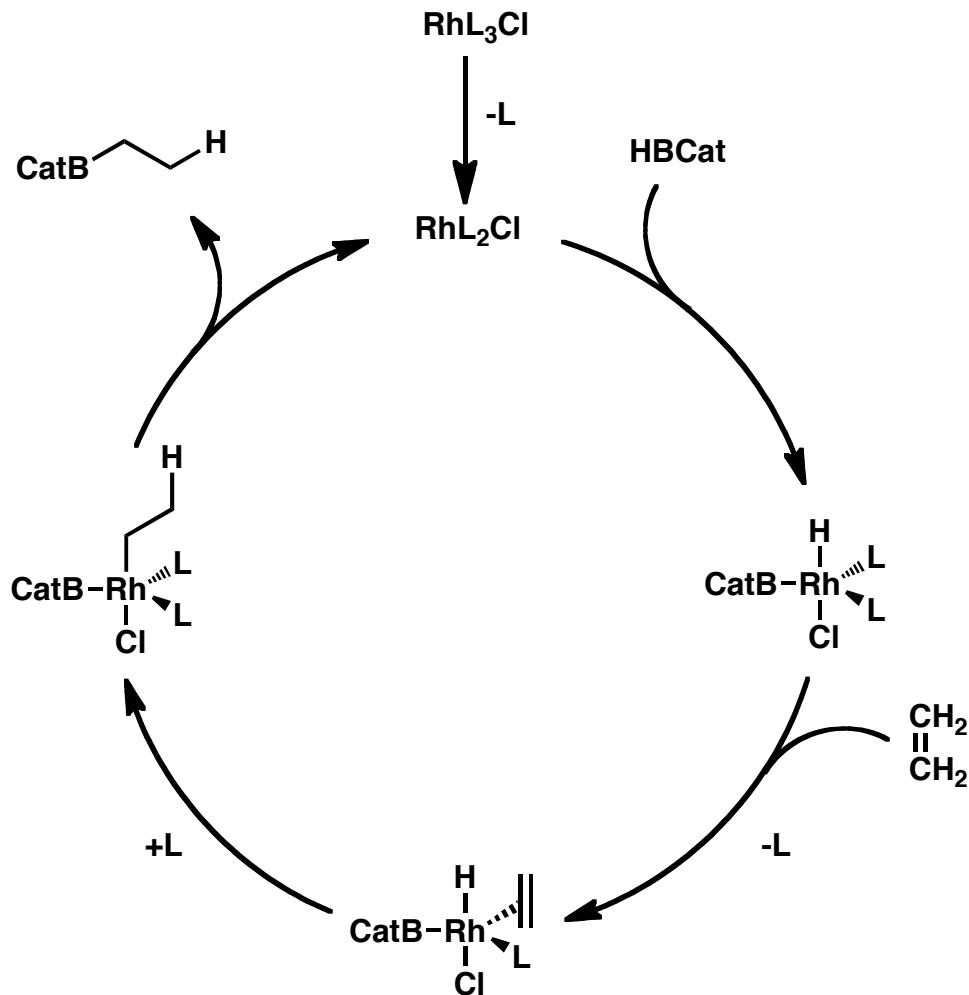


- ~4:1 selectivity for olefin in presence of ketone with Wilkinson's catalyst
- Temperature & Reaction time greatly reduced for catalyzed variant
- No noticeable rate difference for BH₃
- Catecholborane is much less lewis acidic than borane: slower uncatalyzed hydroboration



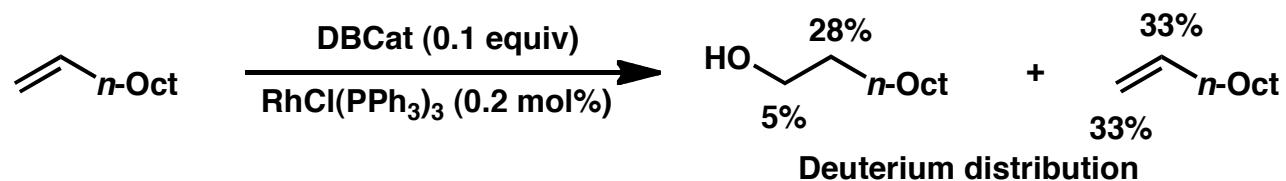
Catecholborane: Brown, H. C. *J. Am. Chem. Soc.* **1971**, *93*, 1816–1818
Catalyzed: Nöth, H. *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 878–879.

Initial Proposed Mechanism

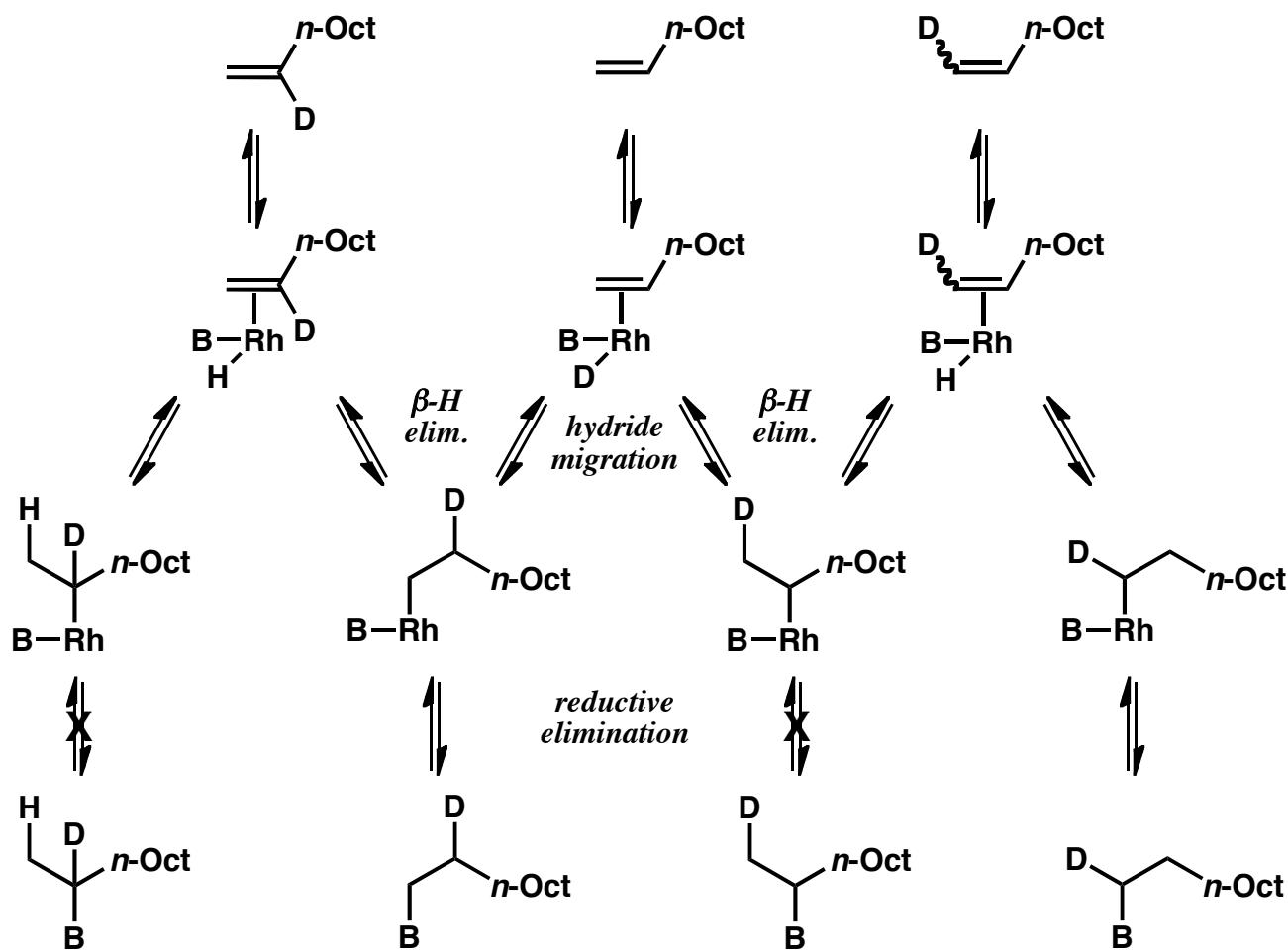
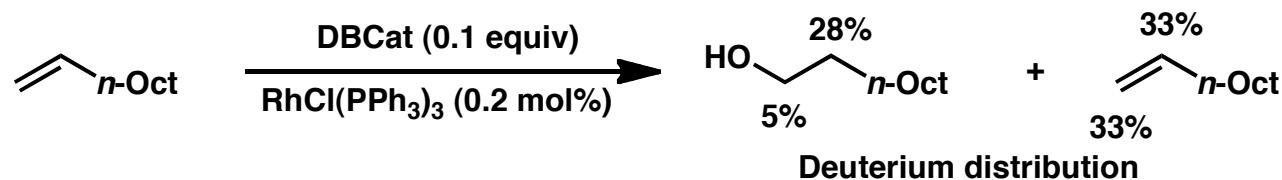


- Supported by catalytic viability of catecholborane adduct
- Loose ends: reversibility of each step?
- Boryl v. Hydride insertion?

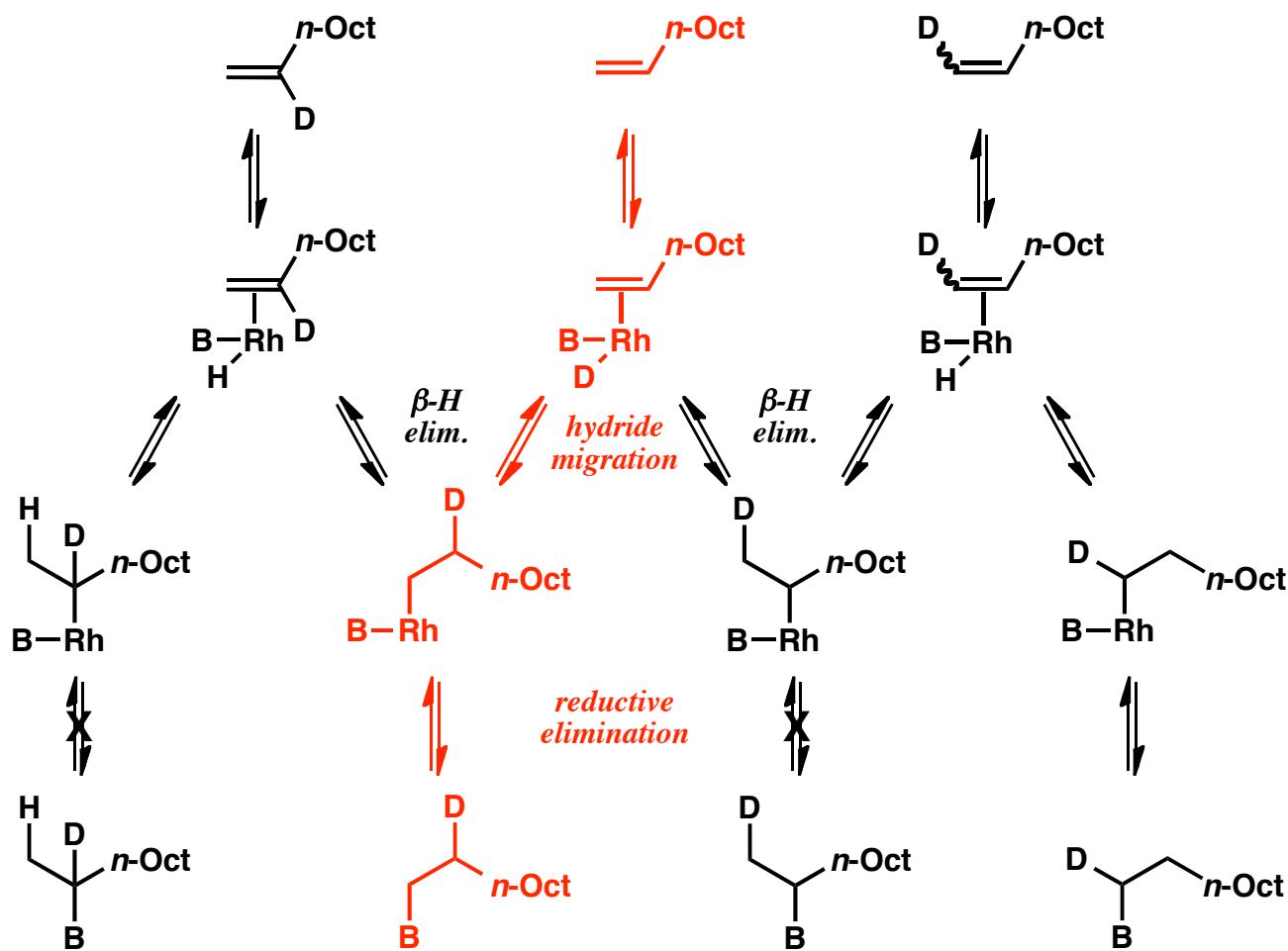
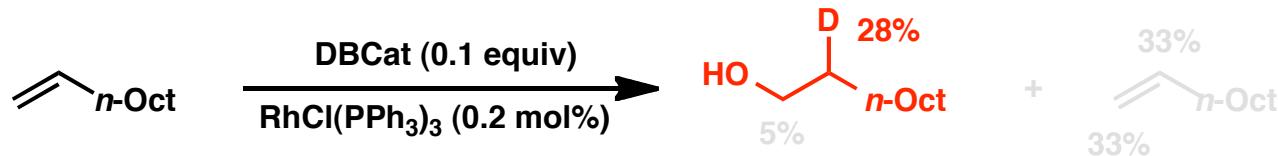
Deuterium Labelling Studies



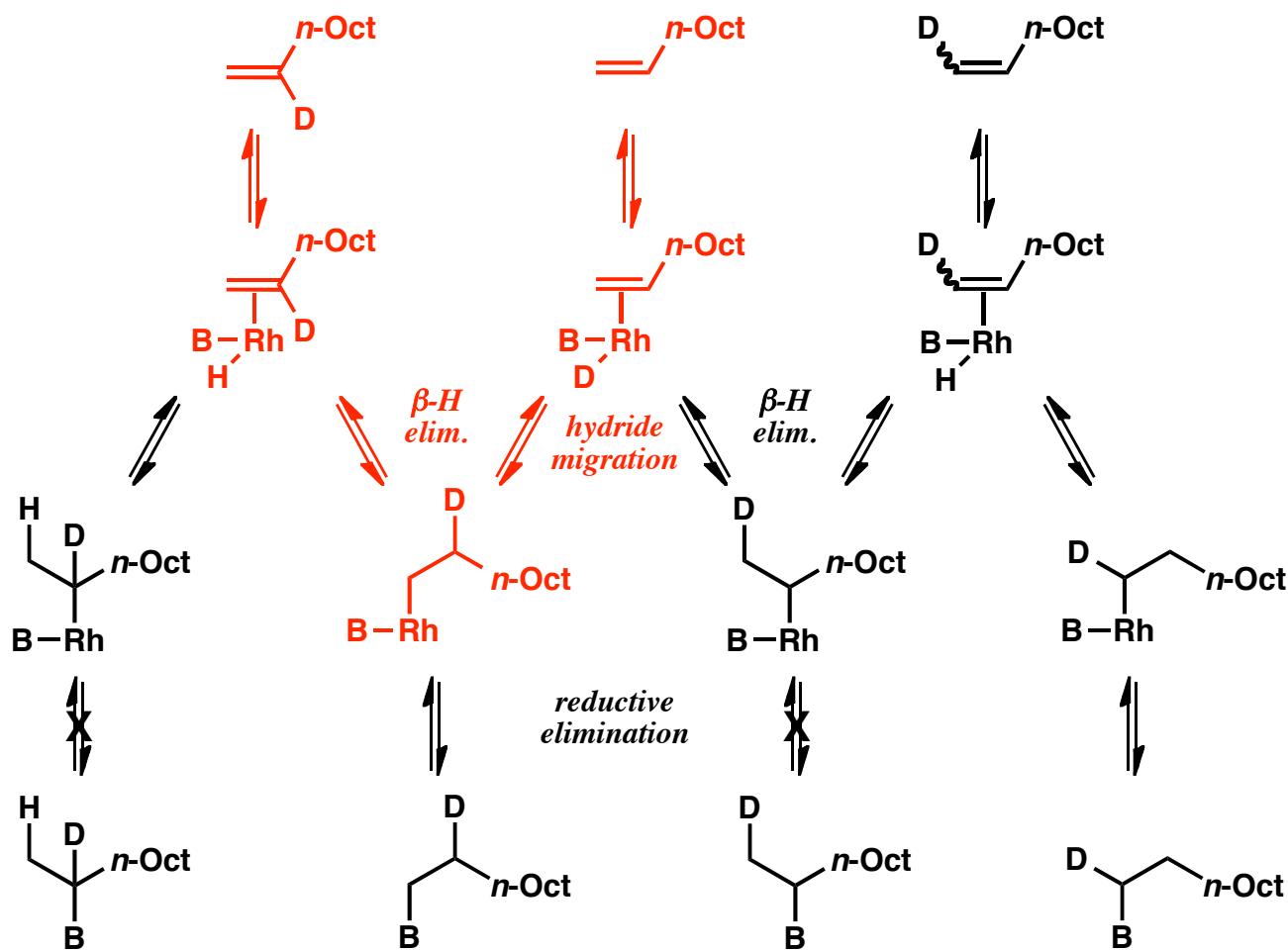
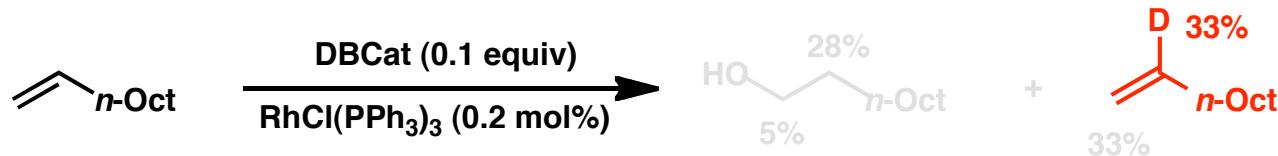
Deuterium Labelling Studies



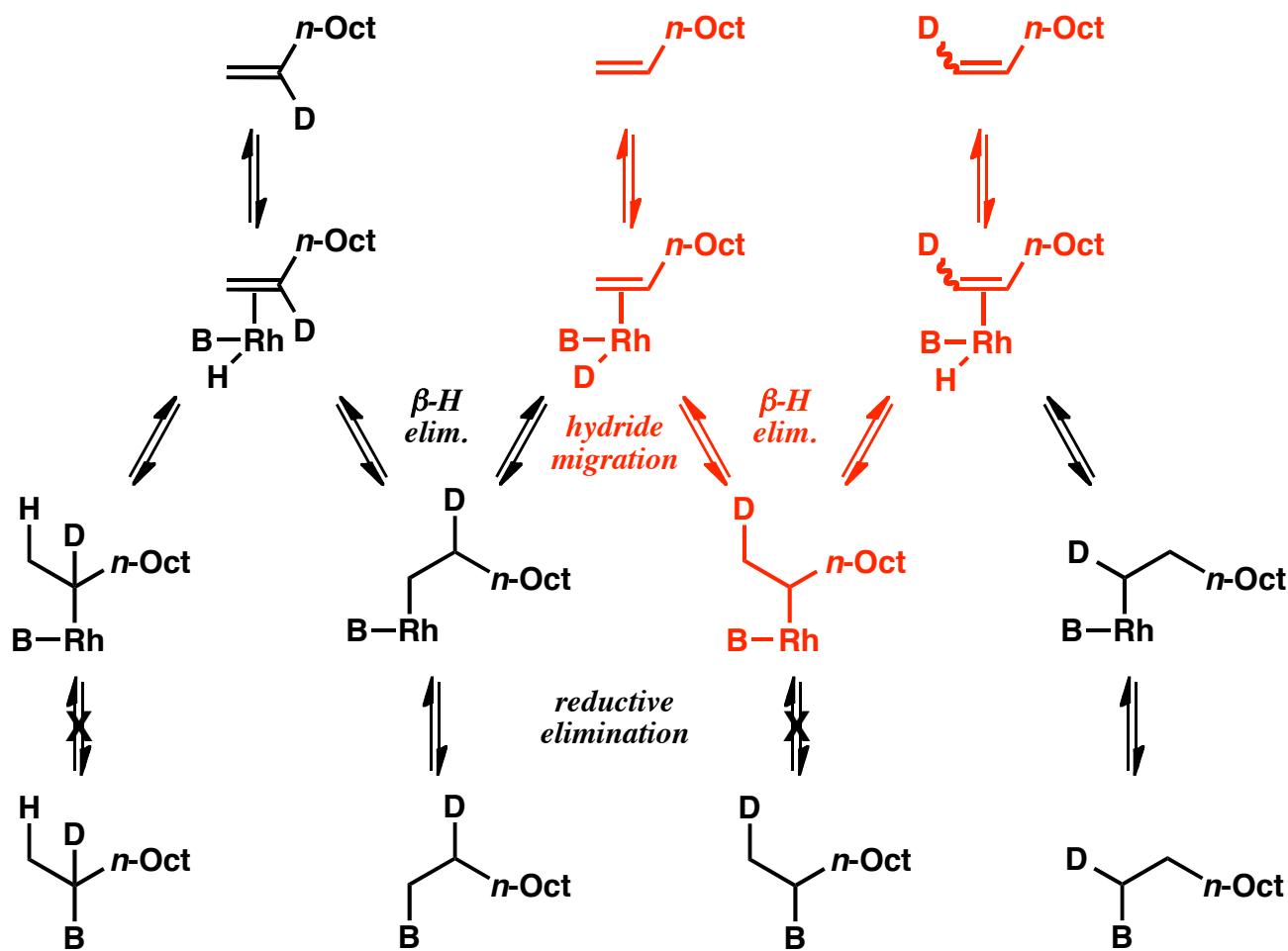
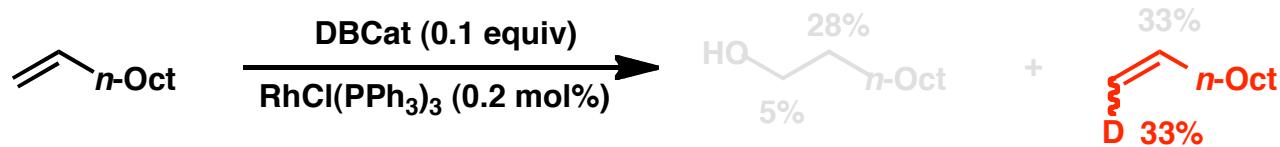
Deuterium Labelling Studies



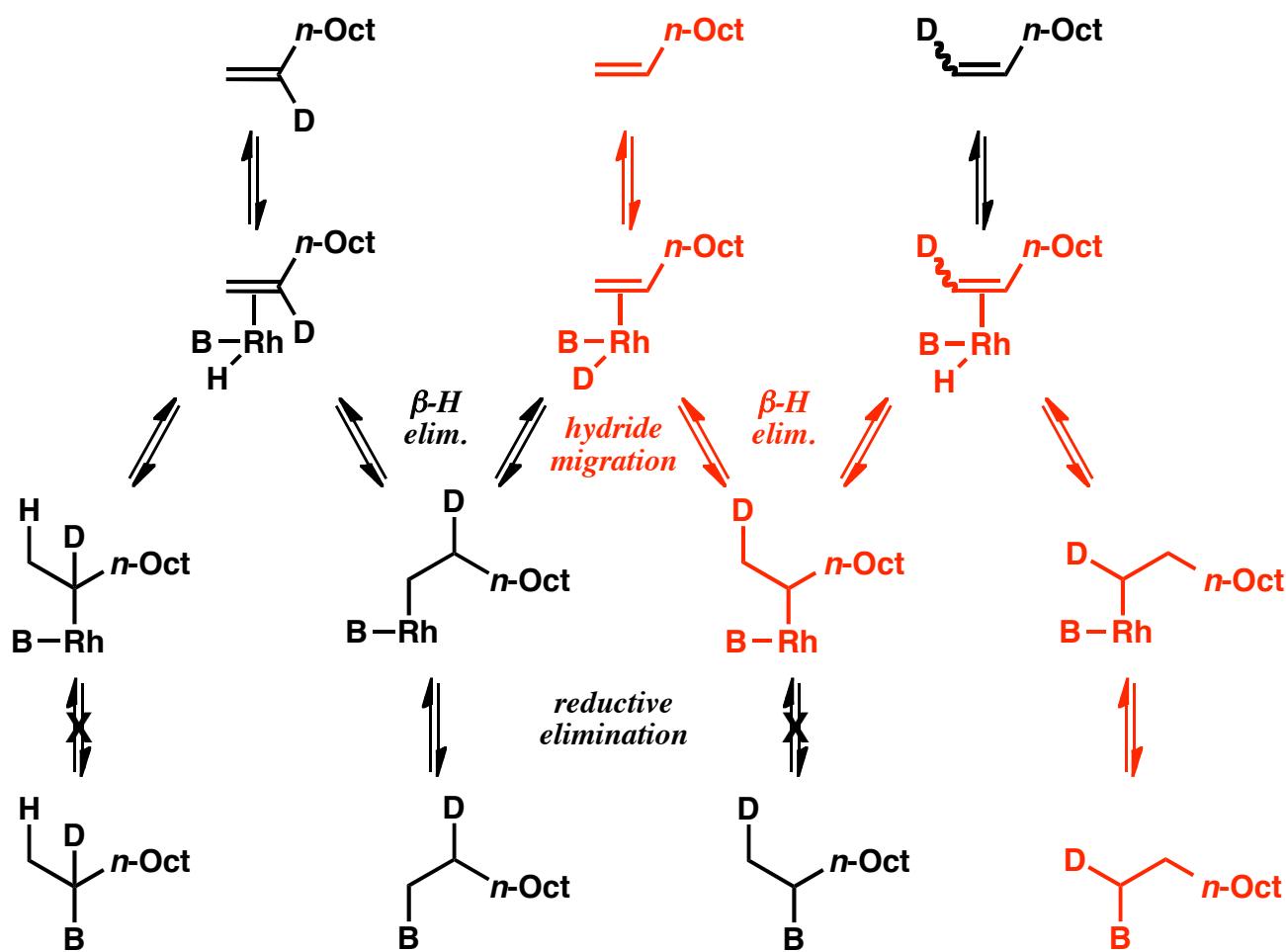
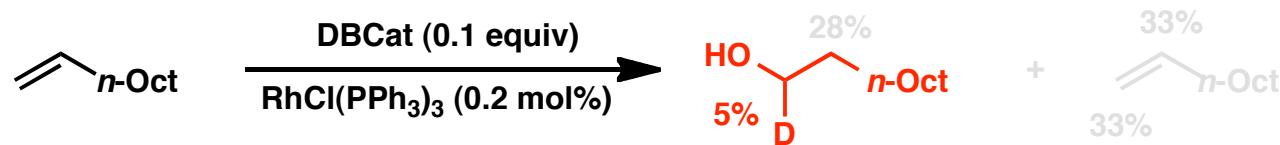
Deuterium Labelling Studies



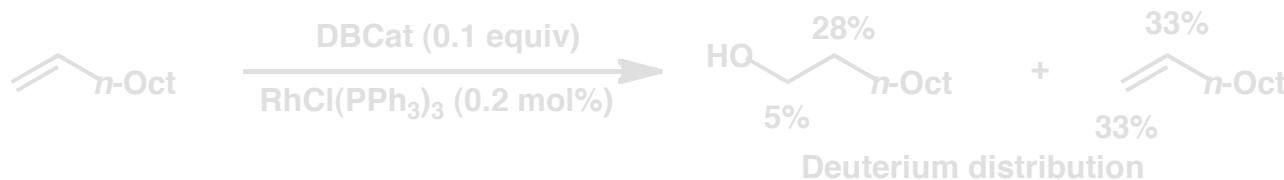
Deuterium Labelling Studies



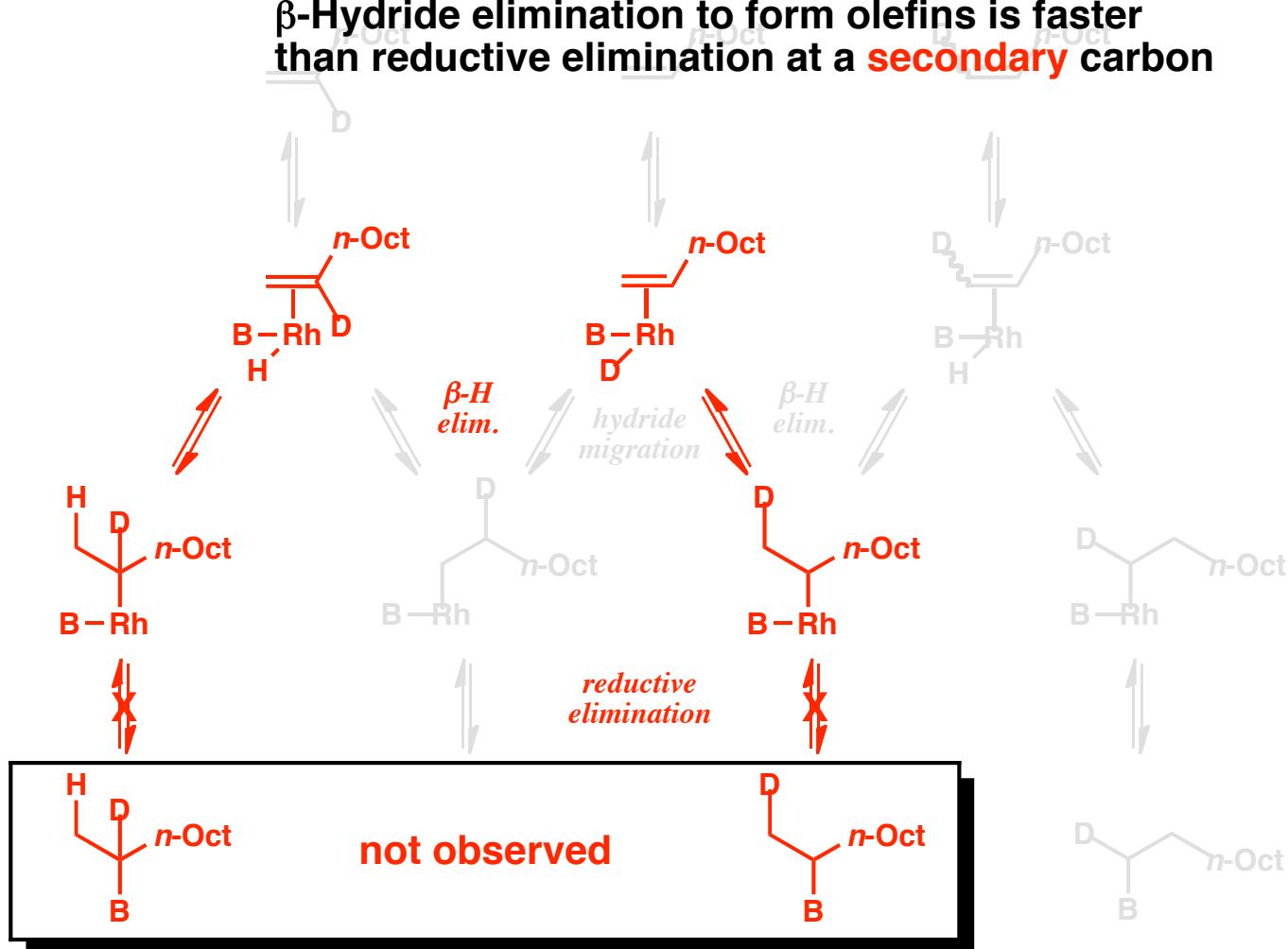
Deuterium Labelling Studies



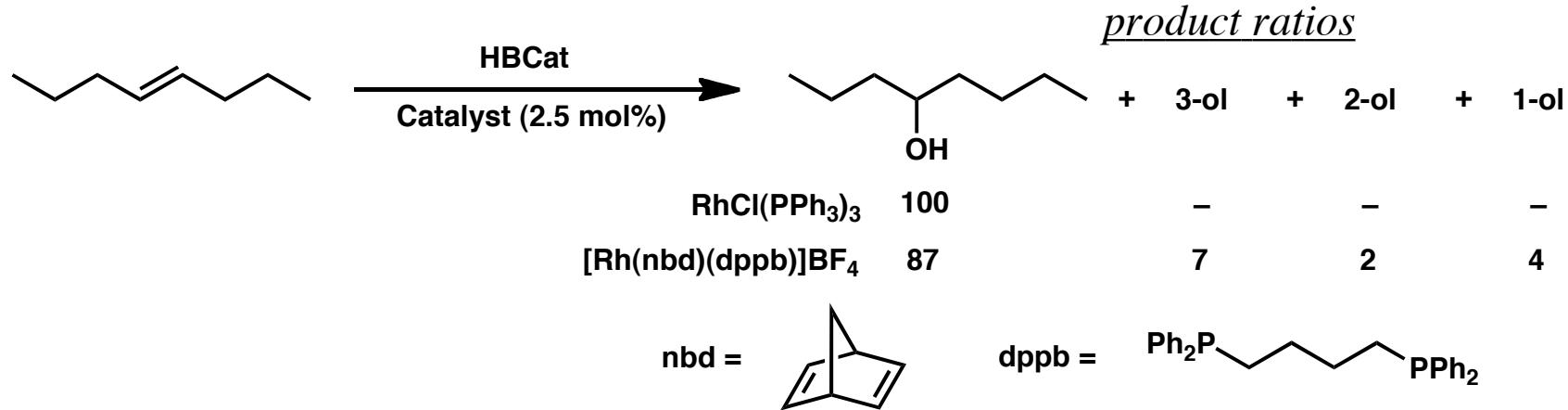
Deuterium Labelling Studies



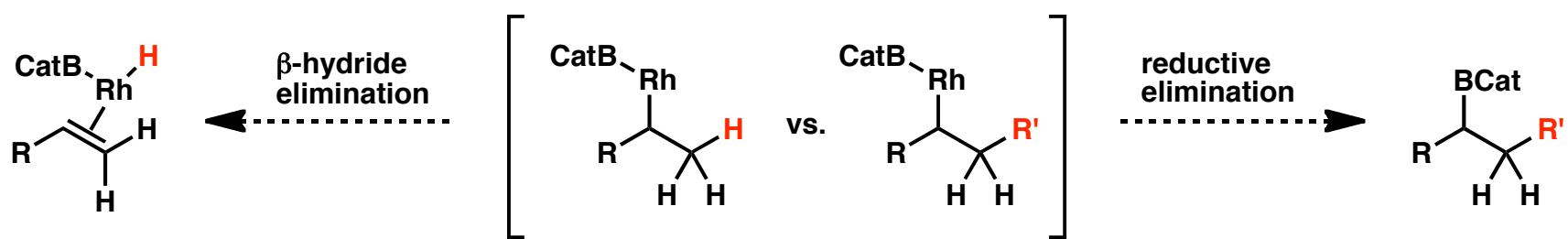
β -Hydride elimination to form olefins is faster than reductive elimination at a **secondary carbon**



Internal v. Terminal Olefin Isomers



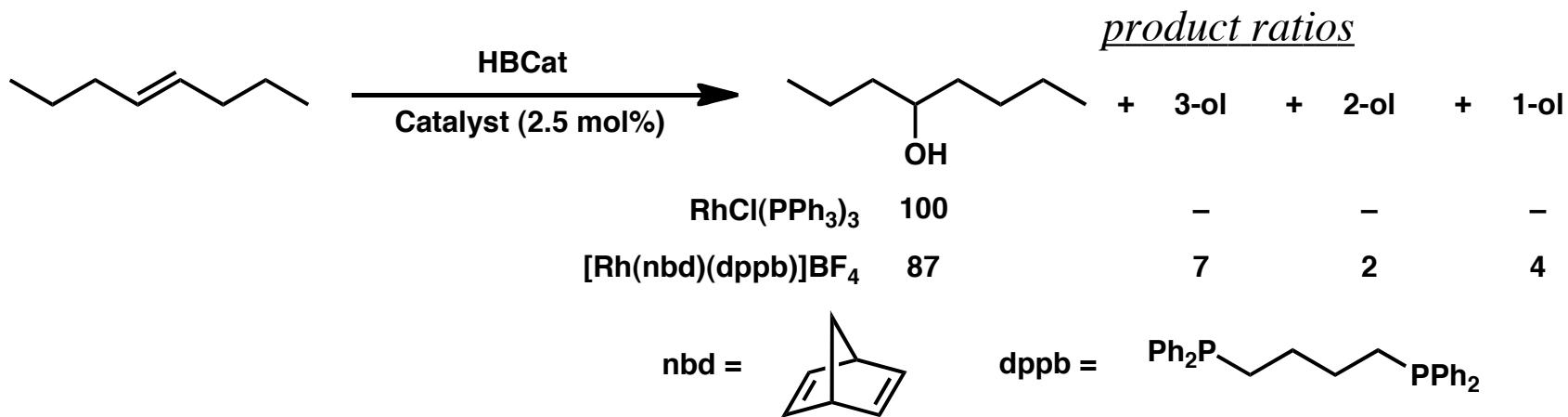
- Generation of an **internal olefin** complex: less facile than reductive elimination?



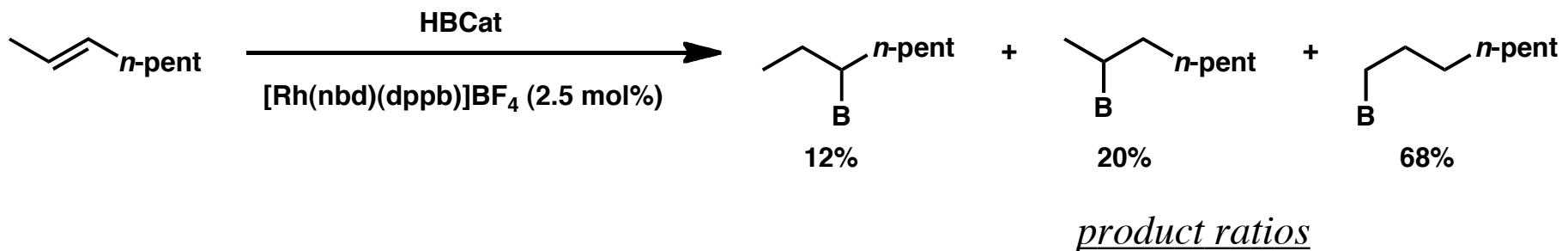
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Evans, D. A. *J. Am. Chem. Soc.* **1992**, *114*, 6679–6685.

Internal v. Terminal Olefin Isomers



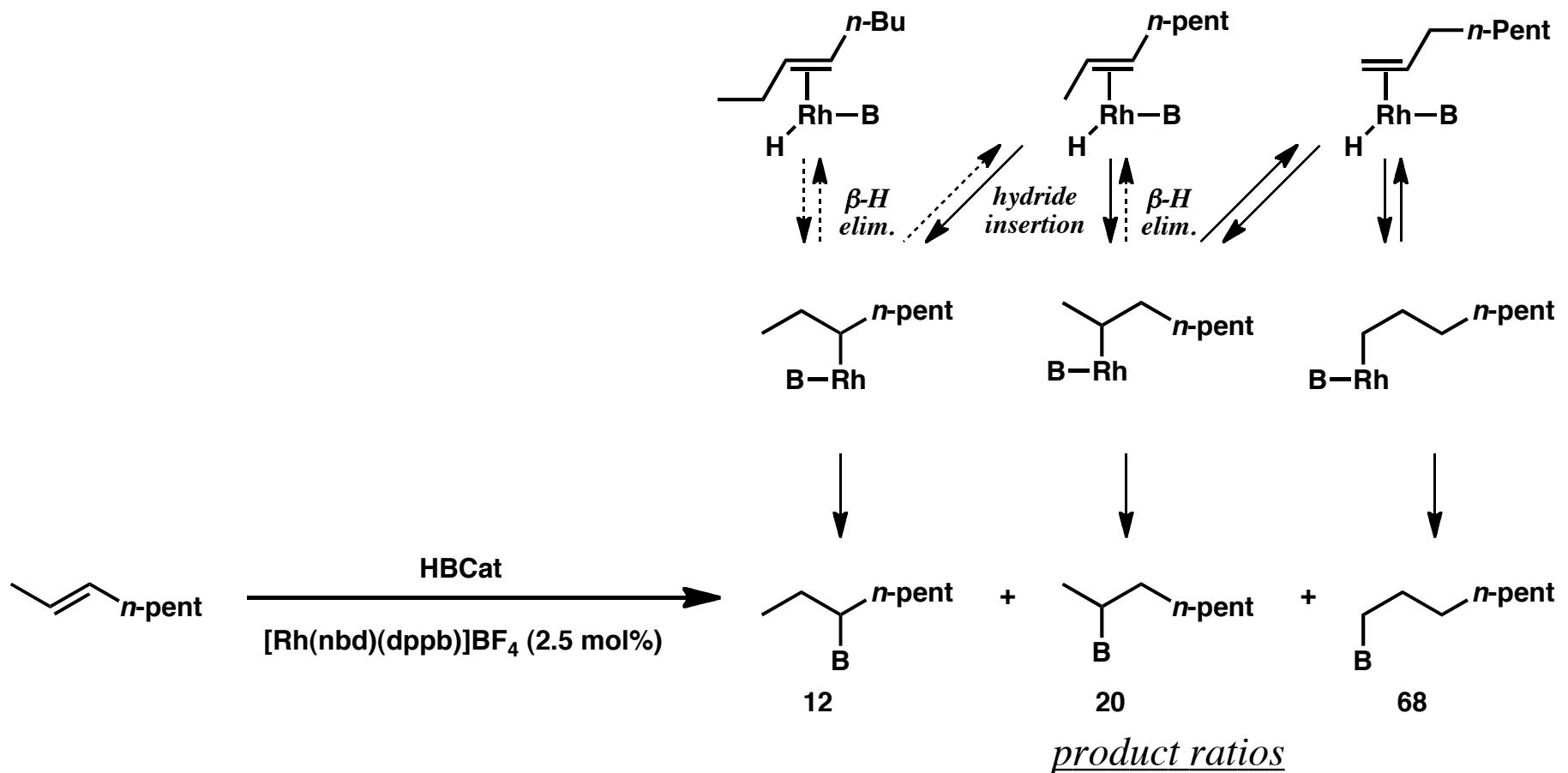
- Generation of an internal olefin complex: less facile than reductive elimination?
 - Examine a system which has access to both **internal** and **terminal** olefin complexes



β -Hydride elimination to form terminal olefins is faster than reductive elimination at a secondary carbon

Evans, D. A. *J. Am. Chem. Soc.* **1992**, *114*, 6679–6685.

Internal v. Terminal Olefin Isomers

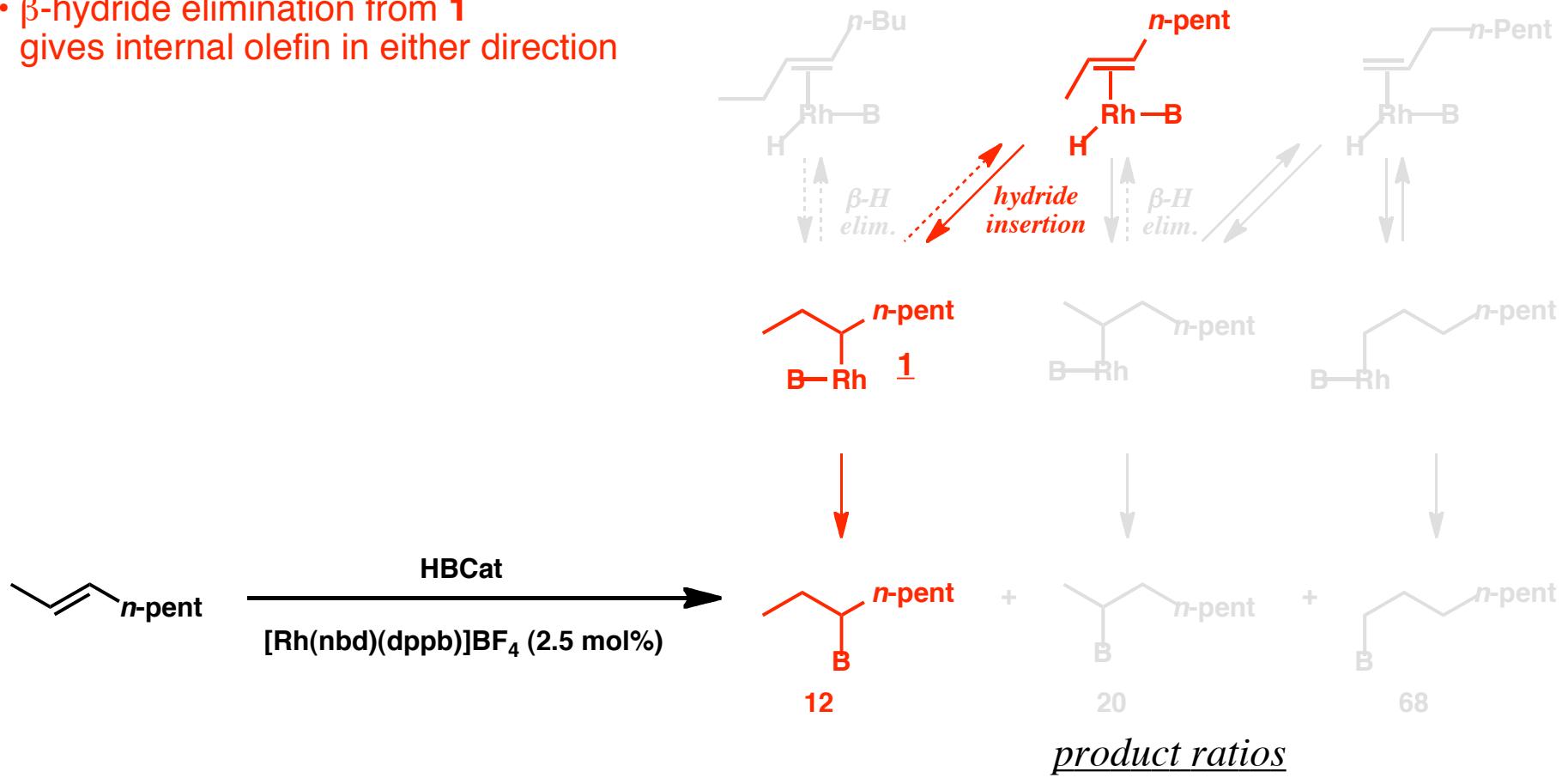


β -Hydride elimination to form **terminal** olefins is faster than reductive elimination at a secondary carbon

Evans, D. A. *J. Am. Chem. Soc.* **1992**, 114, 6679–6685.

Internal v. Terminal Olefin Isomers

- β -hydride elimination from **1** gives internal olefin in either direction

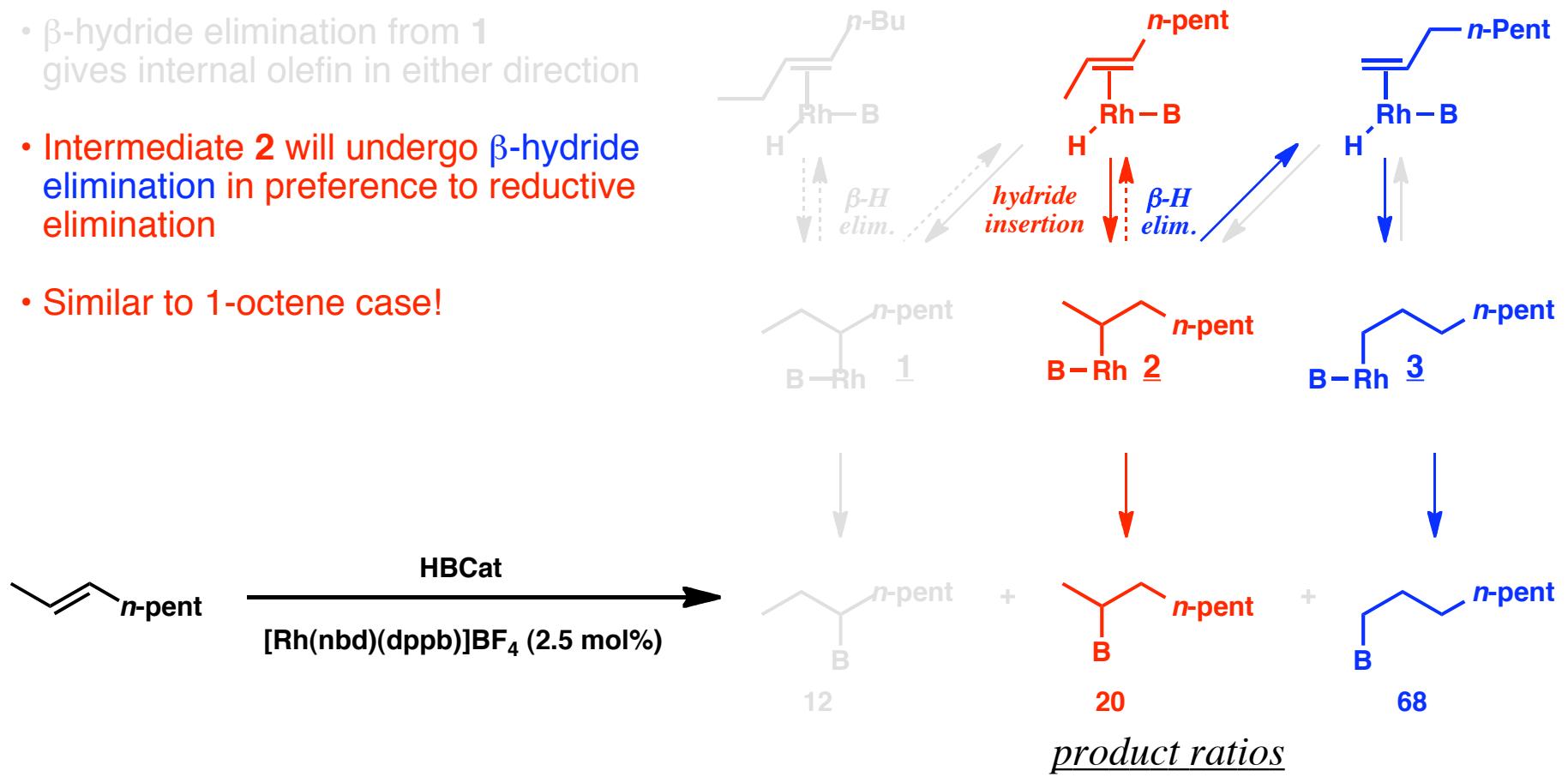


β -Hydride elimination to form **terminal** olefins is faster than reductive elimination at a secondary carbon

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Internal v. Terminal Olefin Isomers

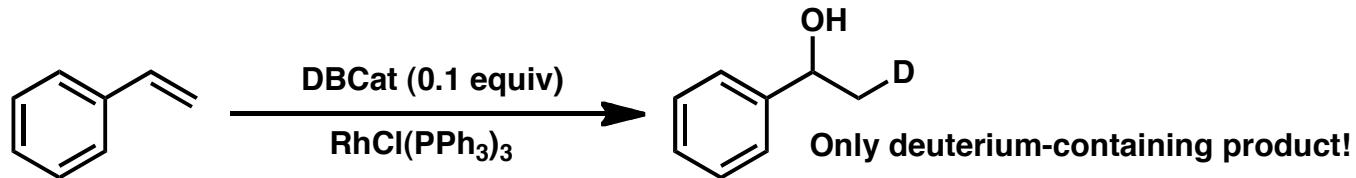
- β -hydride elimination from **1** gives internal olefin in either direction
- Intermediate **2** will undergo β -hydride elimination in preference to reductive elimination
- Similar to 1-octene case!



β -Hydride elimination to form **terminal** olefins is faster than reductive elimination at a secondary carbon

Evans, D. A. *J. Am. Chem. Soc.* **1992**, *114*, 6679–6685.

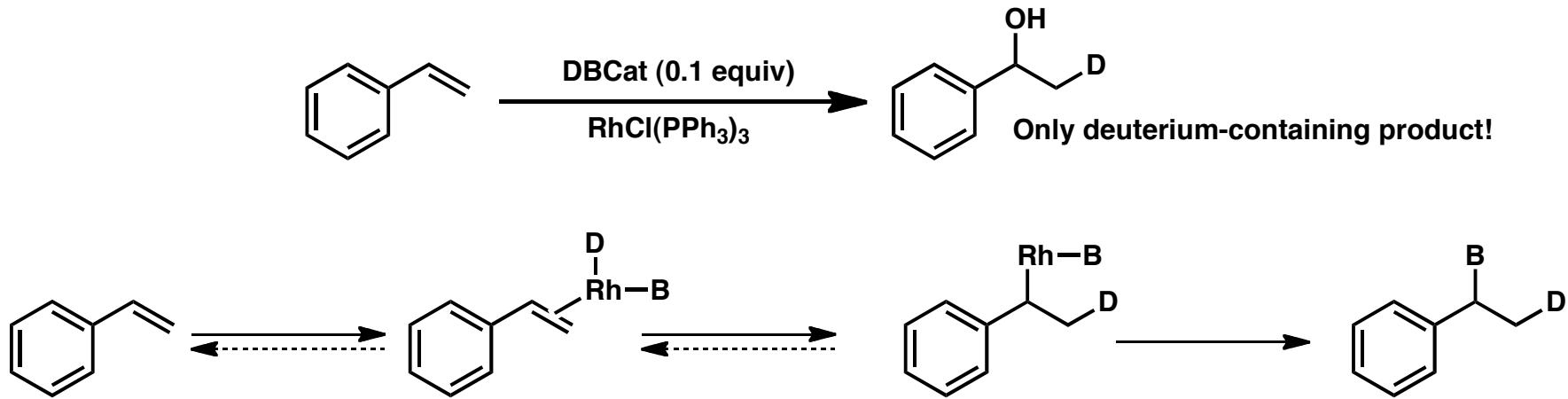
Aryl substituents – Regioselectivity Inverted!



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Evans, D. A. J. Am. Chem. Soc. 1992, 114, 6679–6685.

Aryl substituents – Regioselectivity Inverted!

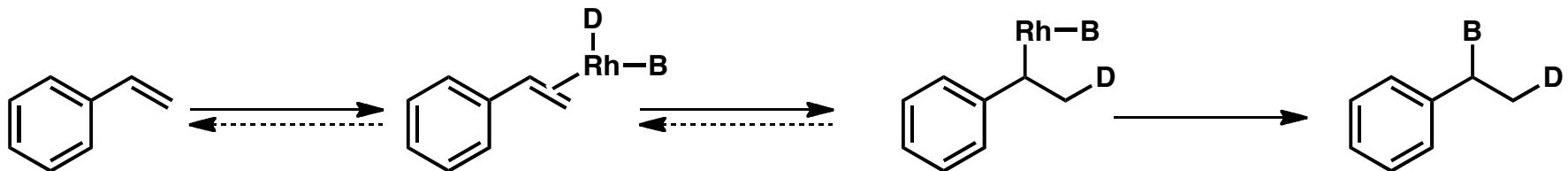
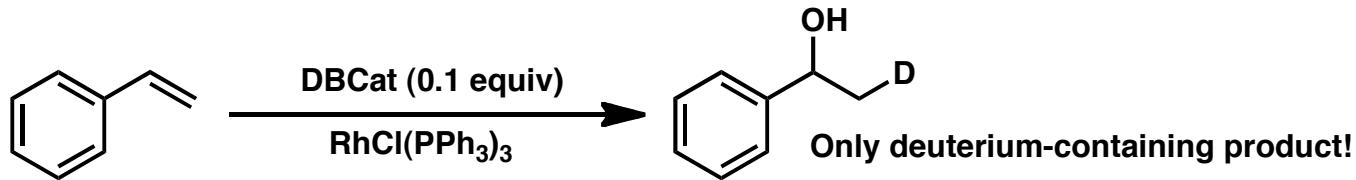


- Either the insertion or complexation must be irreversible
- hydride (deuteride) migration only occurs in one direction

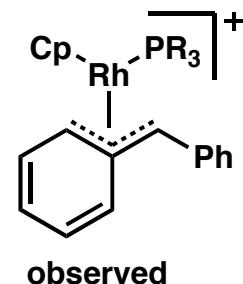
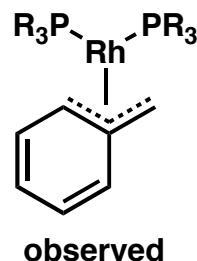
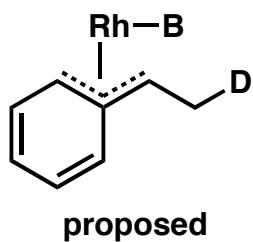
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Evans, D. A. J. Am. Chem. Soc. 1992, 114, 6679–6685.

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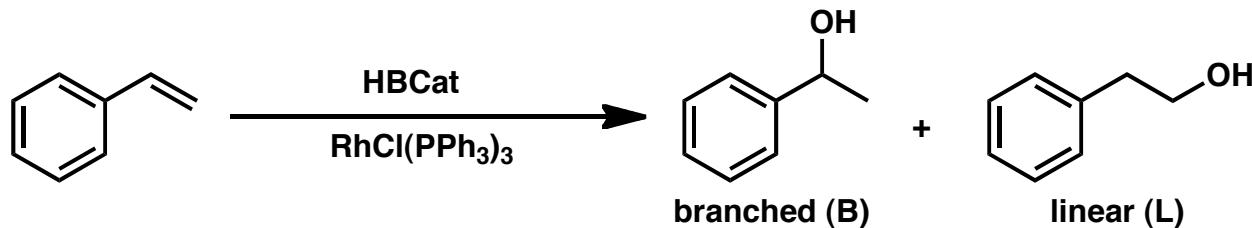


π -benzylic interaction: proposed stabilizing effect

β -Hydride elimination to form terminal olefins is faster than reductive elimination at an **aliphatic** secondary carbon

Evidence for π -benzyl interaction, see (inc. refs) in:
 Hayashi, T. *J. Am. Chem. Soc.* **1989**, *111*, 3426–3428.
 Crudden, C. M. *Angew. Chem. Int. Ed.* **2007**, *46*, 7799–7802
 Evans, D. A. *J. Am. Chem. Soc.* **1992**, *114*, 6679–6685.

Technical Challenges - Catalyst Oxidation

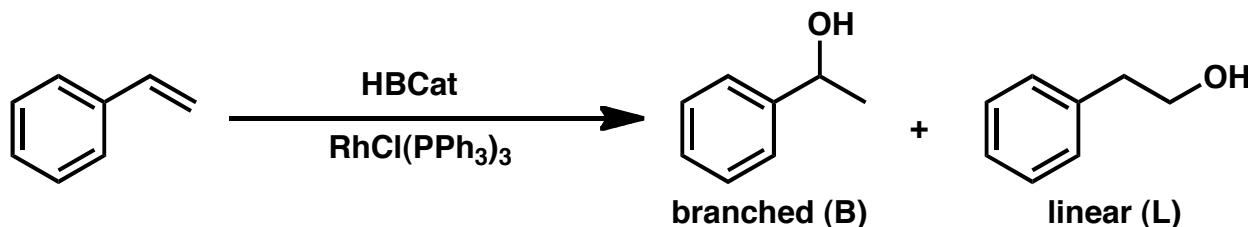


Reference	mol ratio			
	styrene	HBCat ^a	catalyst	B:L
Evans	10	1	0.02	>99:1
(a)	1	2	0.02	86:4
(b)	10	1	0.02	20:80
(c)	1	1.1	0.01	10:90

^aDBCat used in Evans, ref (a)

- (a) Dai, L. *J. Org. Chem.* **1991**, *56*, 1670–1672.
(b) Burgess, K. *J. Org. Chem.* **1991**, *56*, 2949–2951
(c) Hayashi, T. *Tetrahedron: Asymmetry* **1991**, *2*, 601–612
Evans, D. A. *J. Am. Chem. Soc.* **1992**, *114*, 6679–6685.

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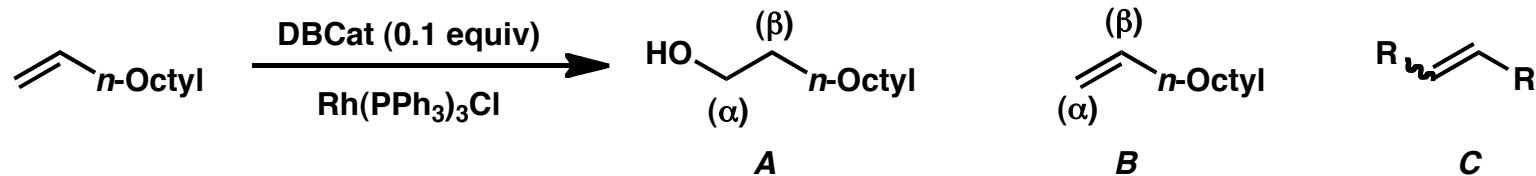
^aDBCat used in Evans, ref (a)

	catalyst	yield (%)	B:L
	Rh(PPh ₃) ₃ Cl	80	>99:1
	Rh(PPh ₃) ₃ Cl, O ₂ treated	85	60:40
	[Rh(COD)Cl] ₂	45	20:80
	[Rh(COD)Cl] ₂ , 2 PPh ₃	67	60:40
	[Rh(COD)Cl] ₂ , 4 PPh ₃	90	98:2
	Rh(PPh ₃) ₃ Cl, O ₂ treated then 2 PPh ₃	85	99:1

- Freshly Prepared Wilkinson's catalyst vs. old or even *Commercially Available* Wilkinson's catalyst react differently!
- May restore regioselectivity by addition of triphenylphosphine

- (a) Dai, L. *J. Org. Chem.* **1991**, *56*, 1670–1672.
 (b) Burgess, K. *J. Org. Chem.* **1991**, *56*, 2949–2951
 (c) Hayashi, T. *Tetrahedron: Asymmetry* **1991**, *2*, 601–612
 Evans, D. A. *J. Am. Chem. Soc.* **1992**, *114*, 6679–6685.

Technical Challenges - Impure Reagents

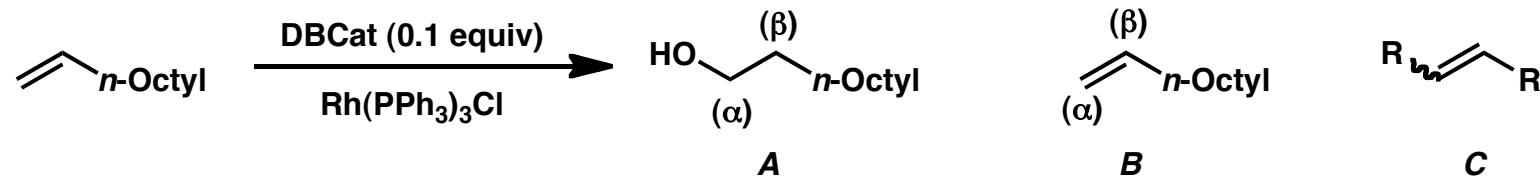


catalyst	% D distribution		
	A ($\alpha:\beta$)	B ($\alpha:\beta$)	B:C
Rh($PPh_3)_3Cl$ (Evans)	67 (11:89)	33 (46:54)	$\geq 95:5$
Rh($PPh_3)_3Cl$ (Burgess)	*	*	$\leq 5:95$

* D label found in all possible C-D positions.

Burgess, K. *J. Org. Chem.* **1991**, *56*, 2949–2951.
Evans, D. A. *J. Am. Chem. Soc.* **1992**, *114*, 6679–6685.

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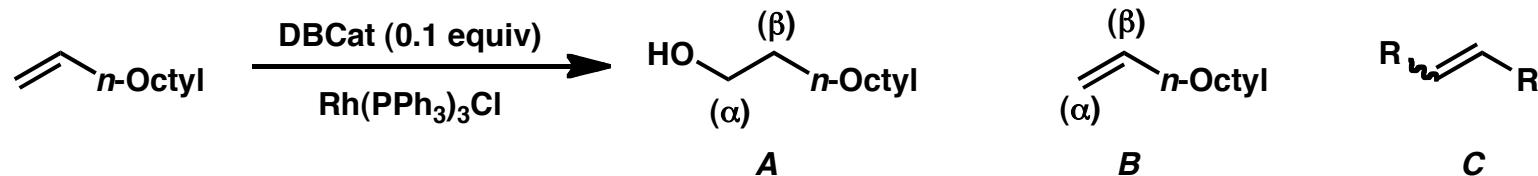


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Rh($PPh_3)_3Cl$ O_2 treated	74	26	15:85
Rh($PPh_3)_3Cl$ undistilled olefin	(16:84)	—	5: ≥ 95
Rh($PPh_3)_3Cl$ 3% $t\text{-}BuO}_2\text{H}$	79 (11:89)	21 (50:50)	70:30
Rh($PPh_3)_3Cl$ O_2 treated, 2 PPh_3	62 (11:89)	38 (44:56)	$\geq 95:5$

* D label found in all possible C-D positions.

Burgess, K. *J. Org. Chem.* **1991**, *56*, 2949–2951.
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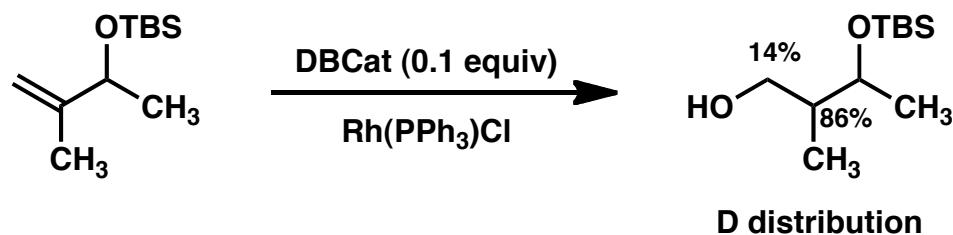
* D label found in all possible C-D positions.

- Vast discrepancies between Burgess and Evans data
- Fresh Wilkinson's cat. necessary, as well as purified starting materials

**PURIFY YOUR
STARTING MATERIALS!**

**BE MINDFUL OF YOUR
CATALYST SOURCE!**

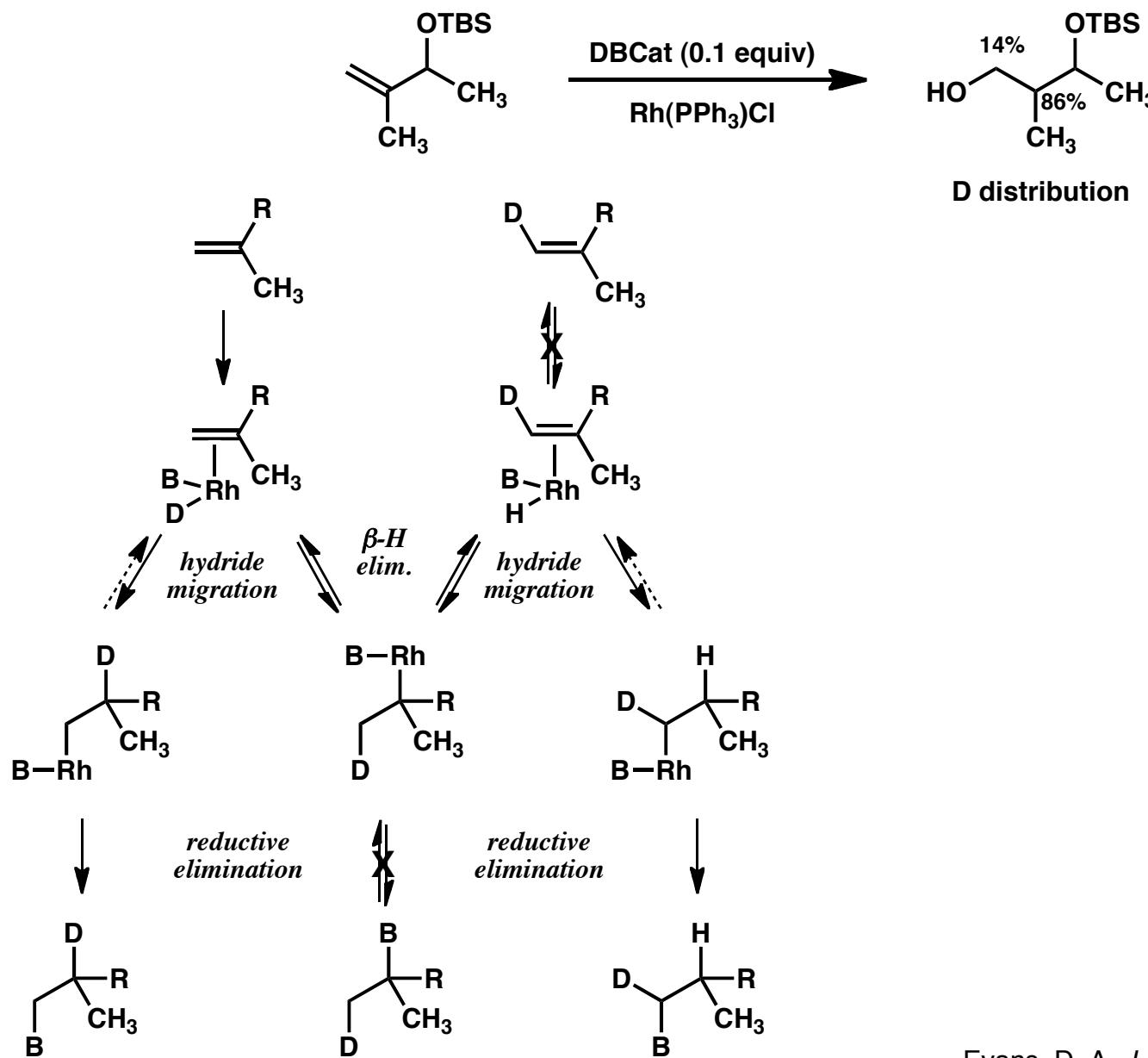
1,1-Disubstitution: Raising even more questions!



D distribution

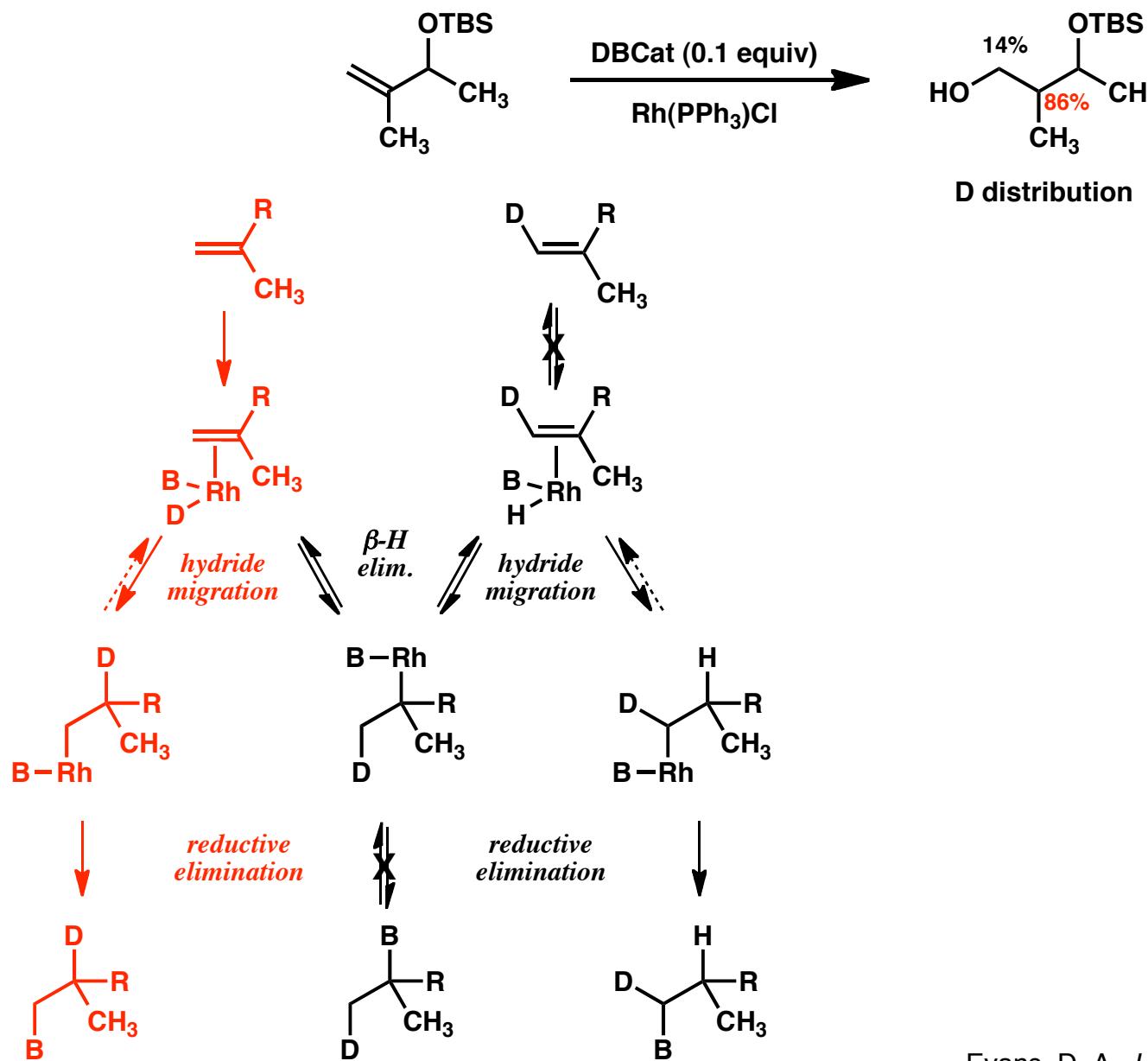
Evans, D. A. *J. Org. Chem.* **1990**, *55*, 2280–2282.
Evans, D. A. *J. Am. Chem. Soc.* **1992**, *114*, 6679–6685.

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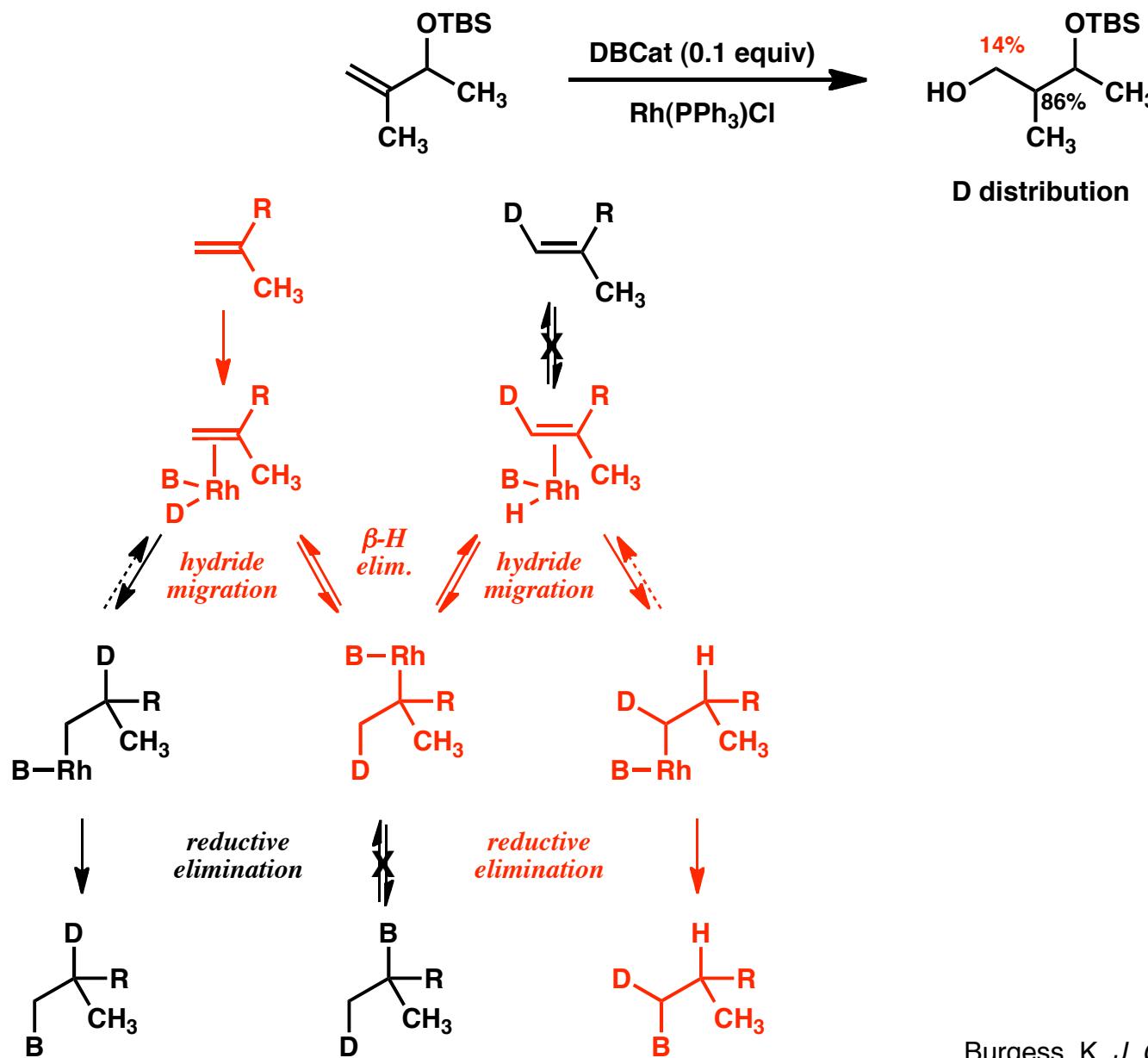
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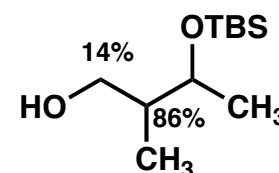
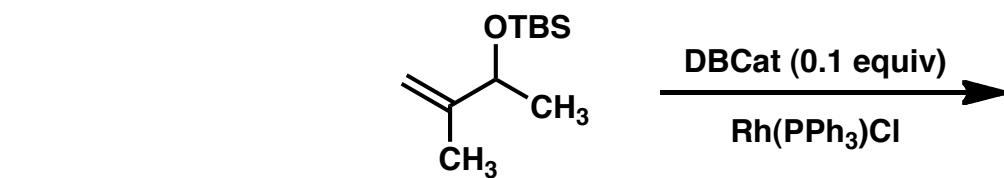
Evans, D. A. *J. Org. Chem.* 1990, 55, 2280–2282.
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1,1-Disubstitution: Raising even more questions!



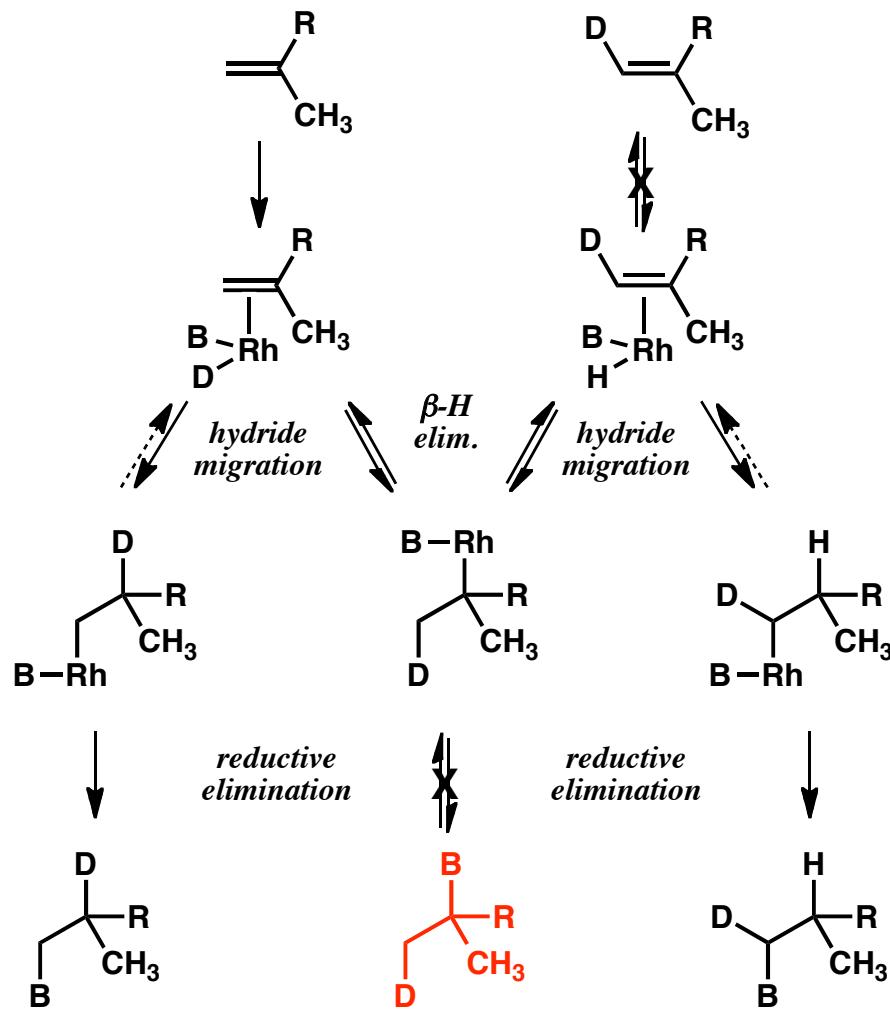
Burgess, K. *J. Org. Chem.* **1991**, *56*, 2949–2951.
 Evans, D. A. *J. Am. Chem. Soc.* **1992**, *114*, 6679–6685.

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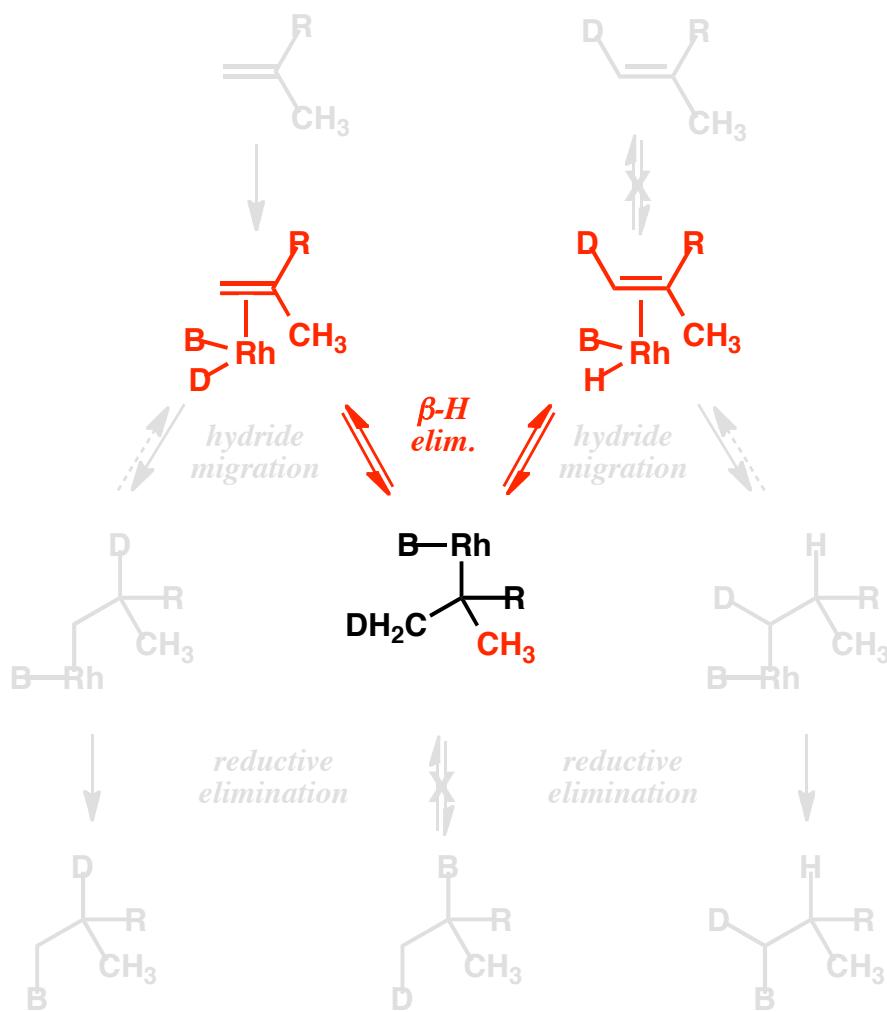
D distribution

- Not surprising that tertiary product not observed



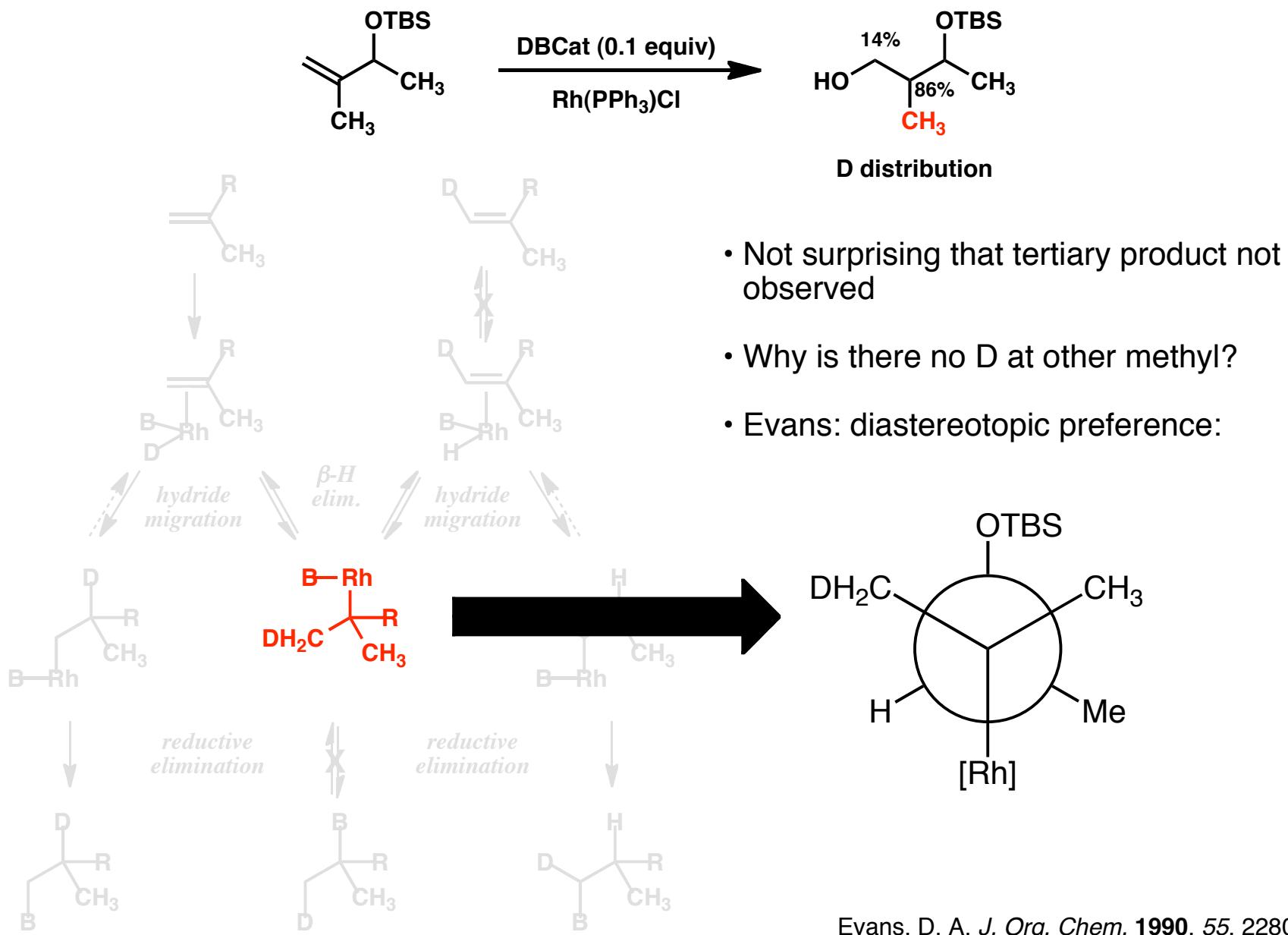
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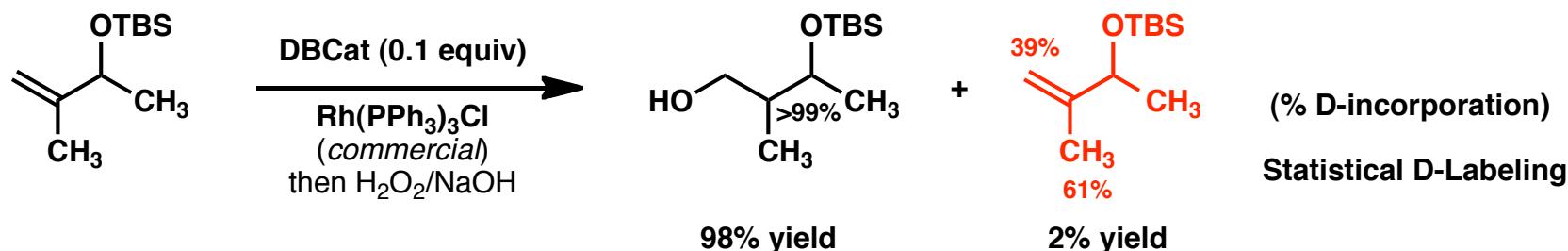
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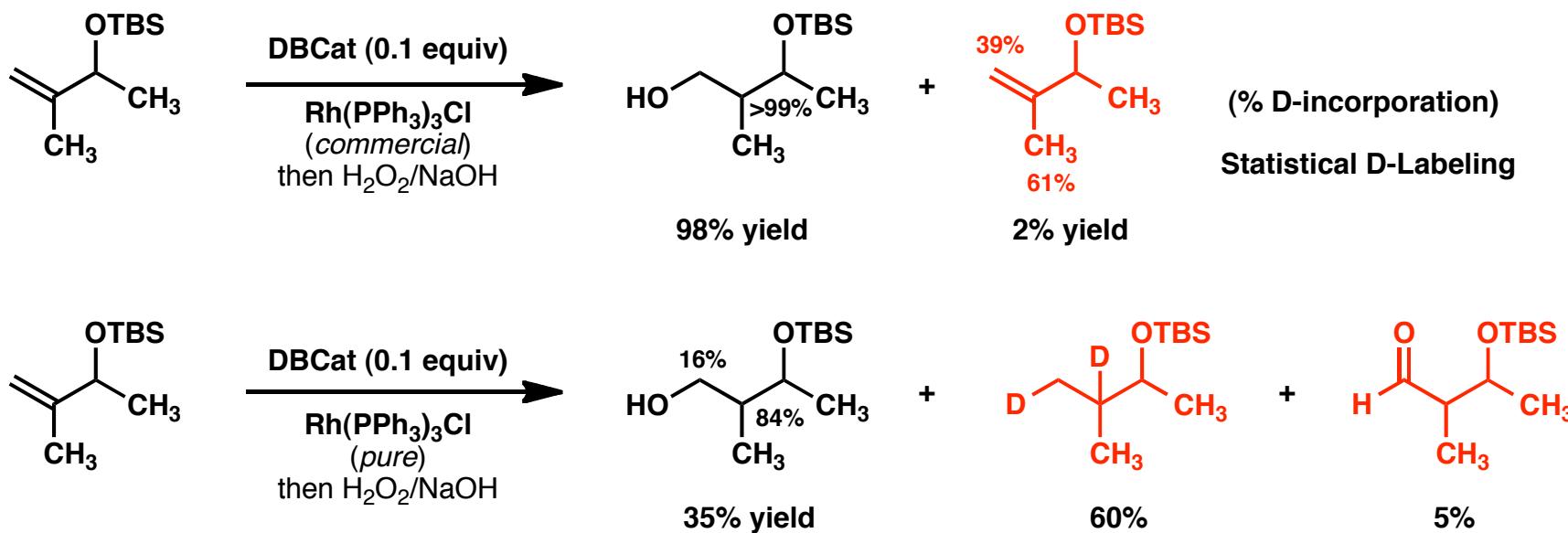


Evans, D. A. *J. Org. Chem.* **1990**, *55*, 2280–2282.
 Evans, D. A. *J. Am. Chem. Soc.* **1992**, *114*, 6679–6685.

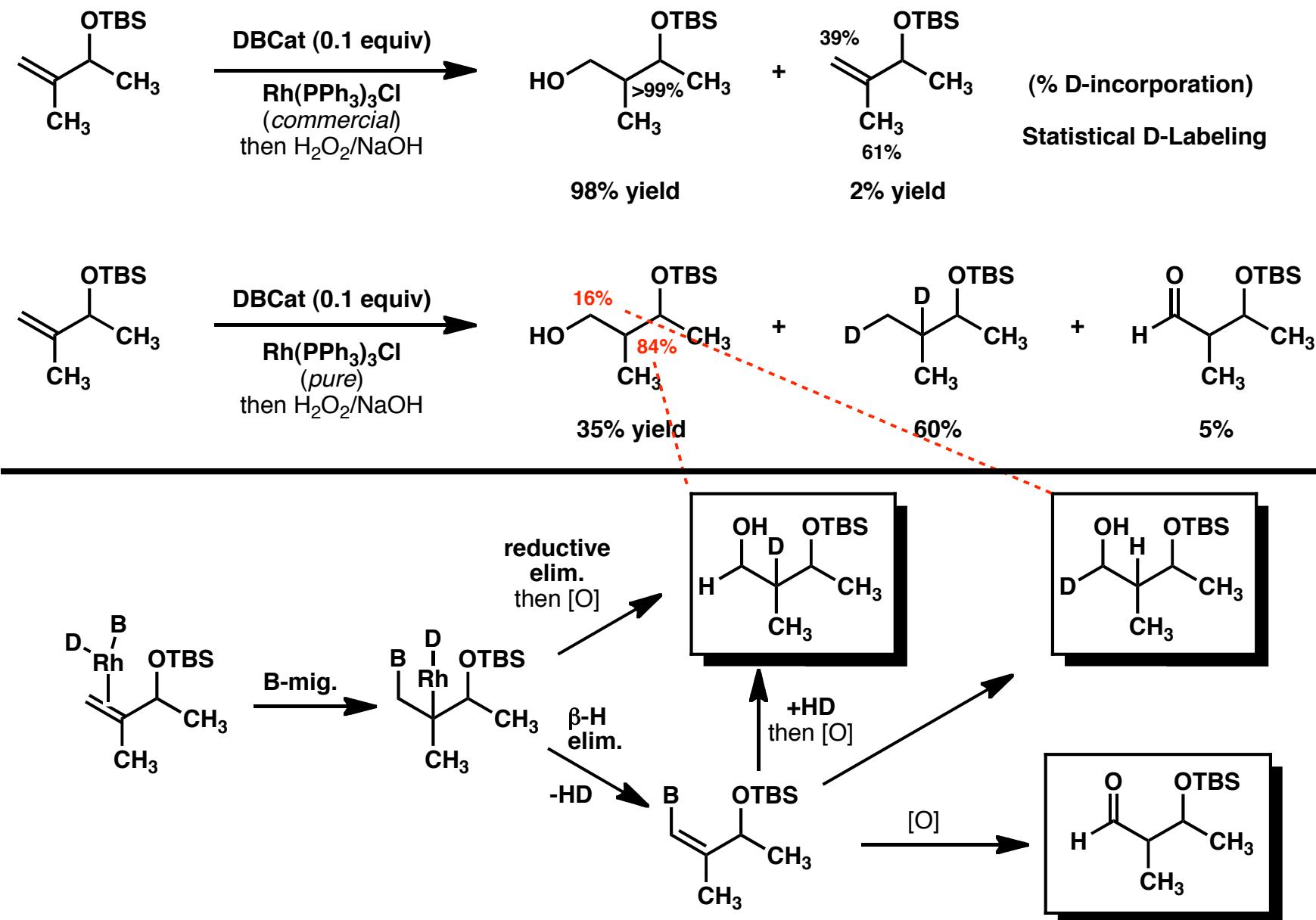
1,1-Disubstitution: Burgess with the answers.



1,1-Disubstitution: Burgess with the answers.

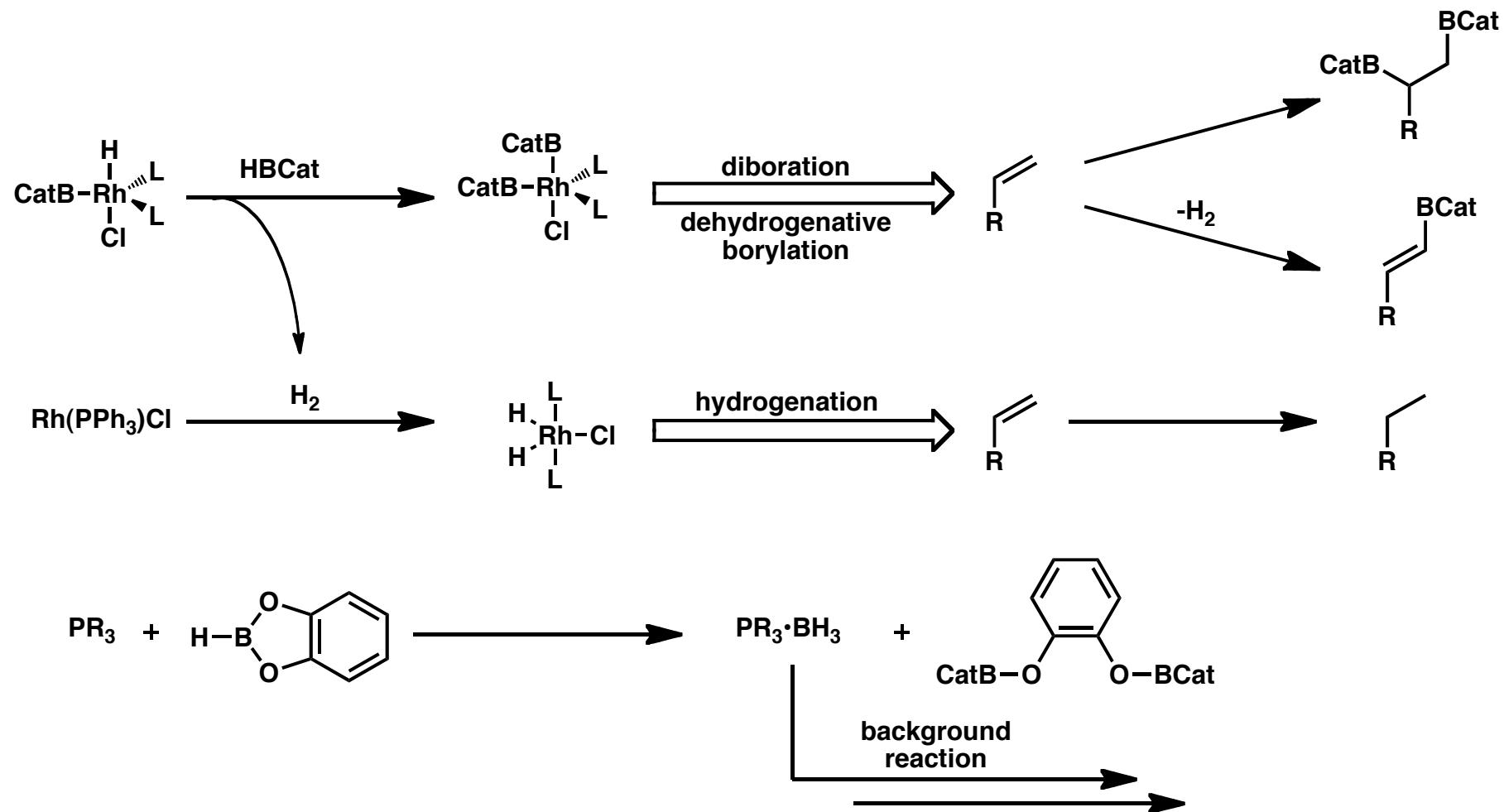


1,1-Disubstitution: Burgess with the answers.



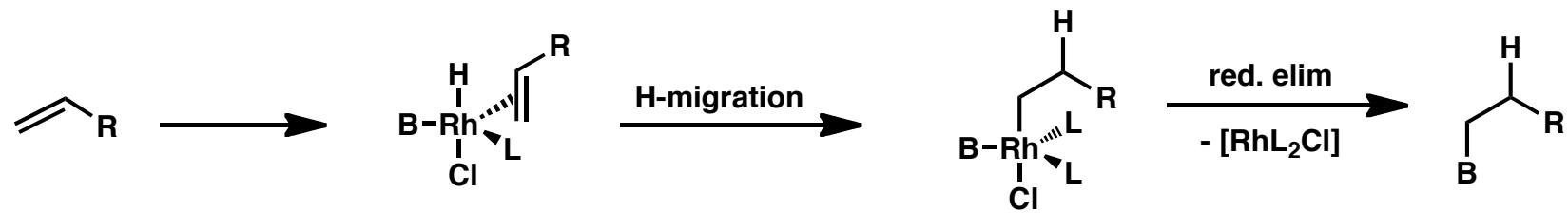
Side Reactions of Catecholborane

Difficulties arise with unreactive substrates – Excess catecholborane in solution

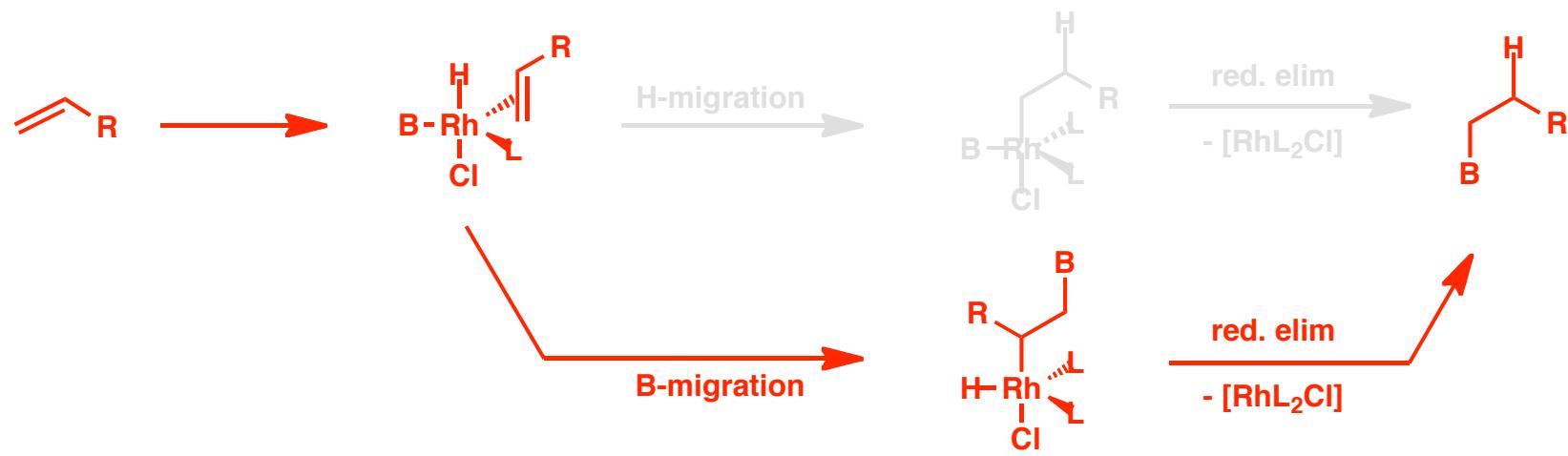


More details in: Westcott, S. A. *Inorg. Chem.* 1993, 32, 2175–2182.
Review: Crudden, C. M. *Eur. J. Org. Chem.* 2003, 24, 4695–4712.

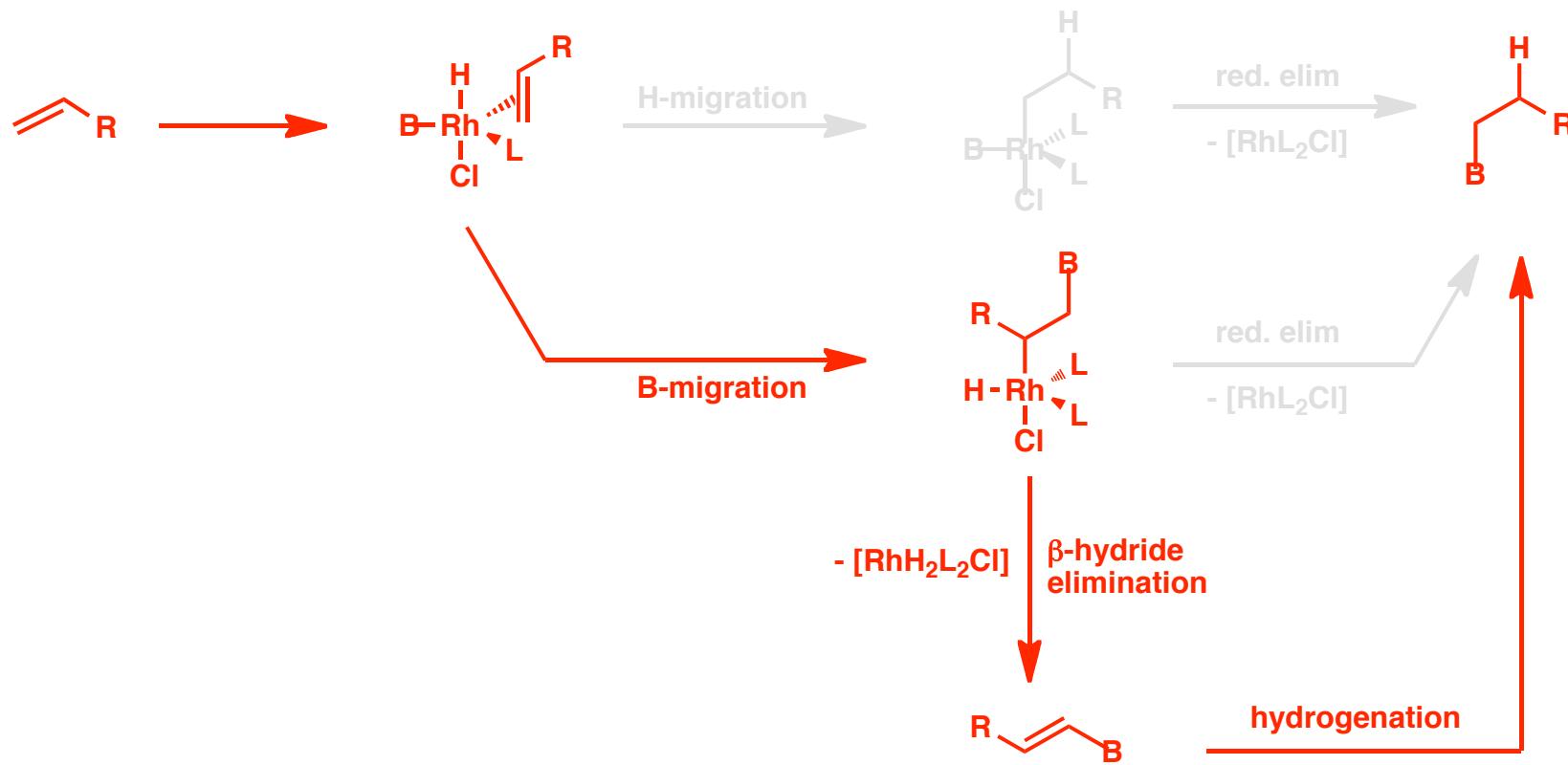
Mechanistic Implications



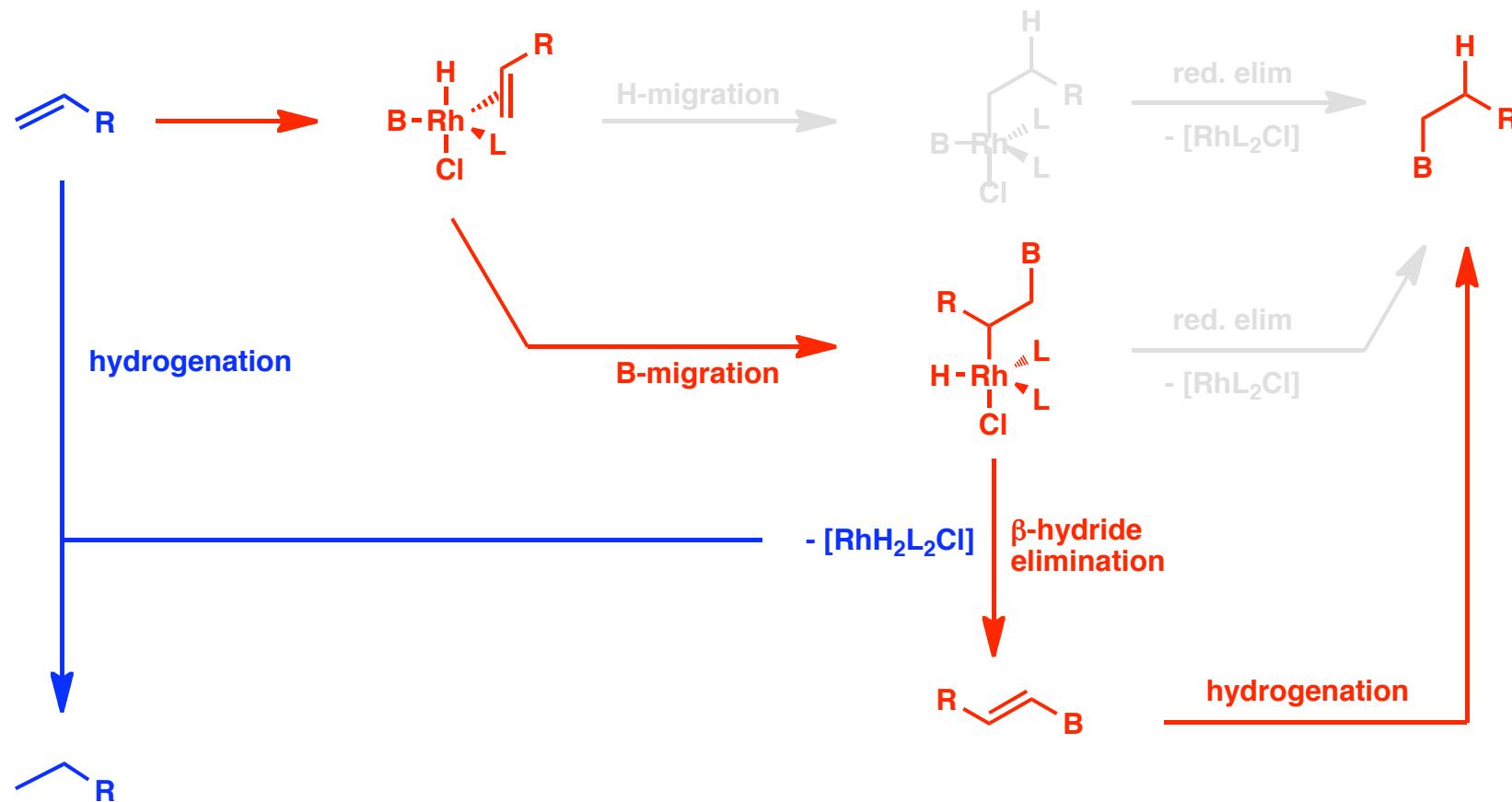
Mechanistic Implications



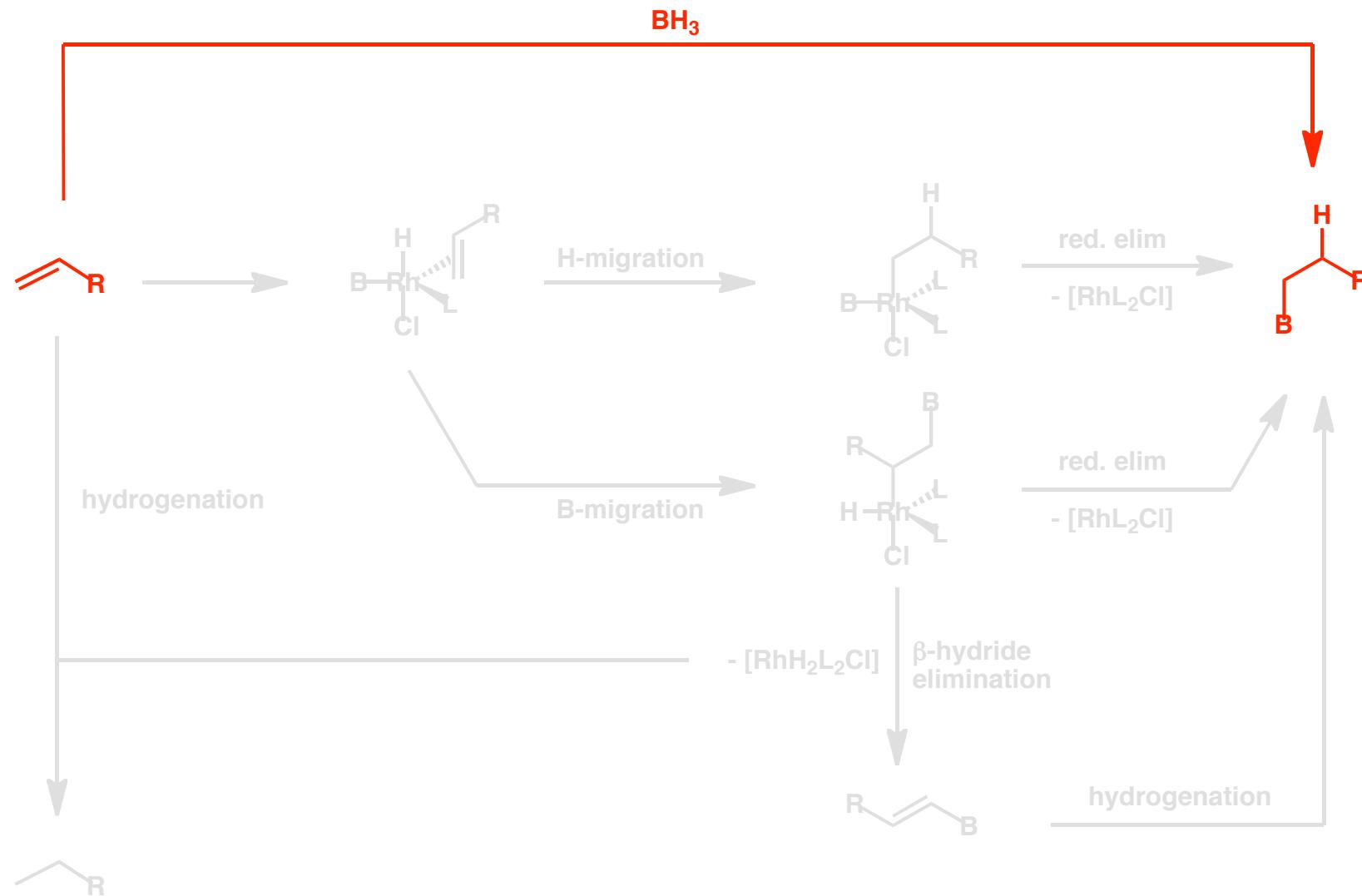
Mechanistic Implications



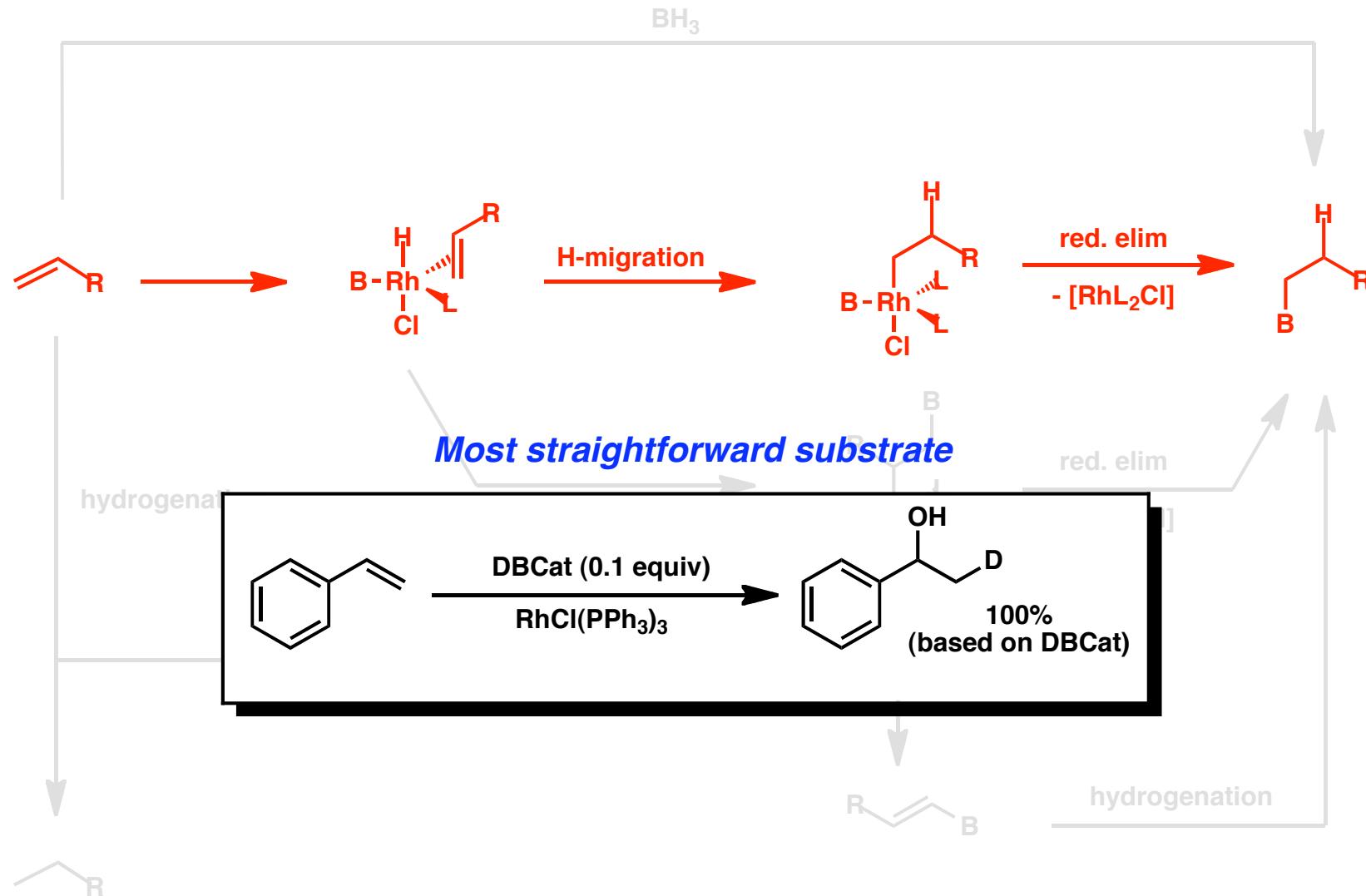
Mechanistic Implications



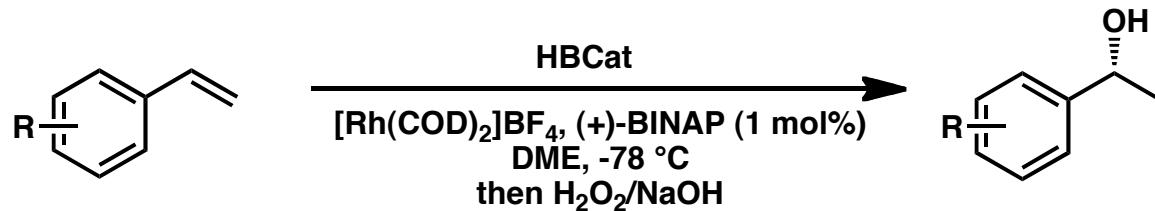
Mechanistic Implications



Mechanistic Implications



Asymmetric Hydroborations of Styrenes



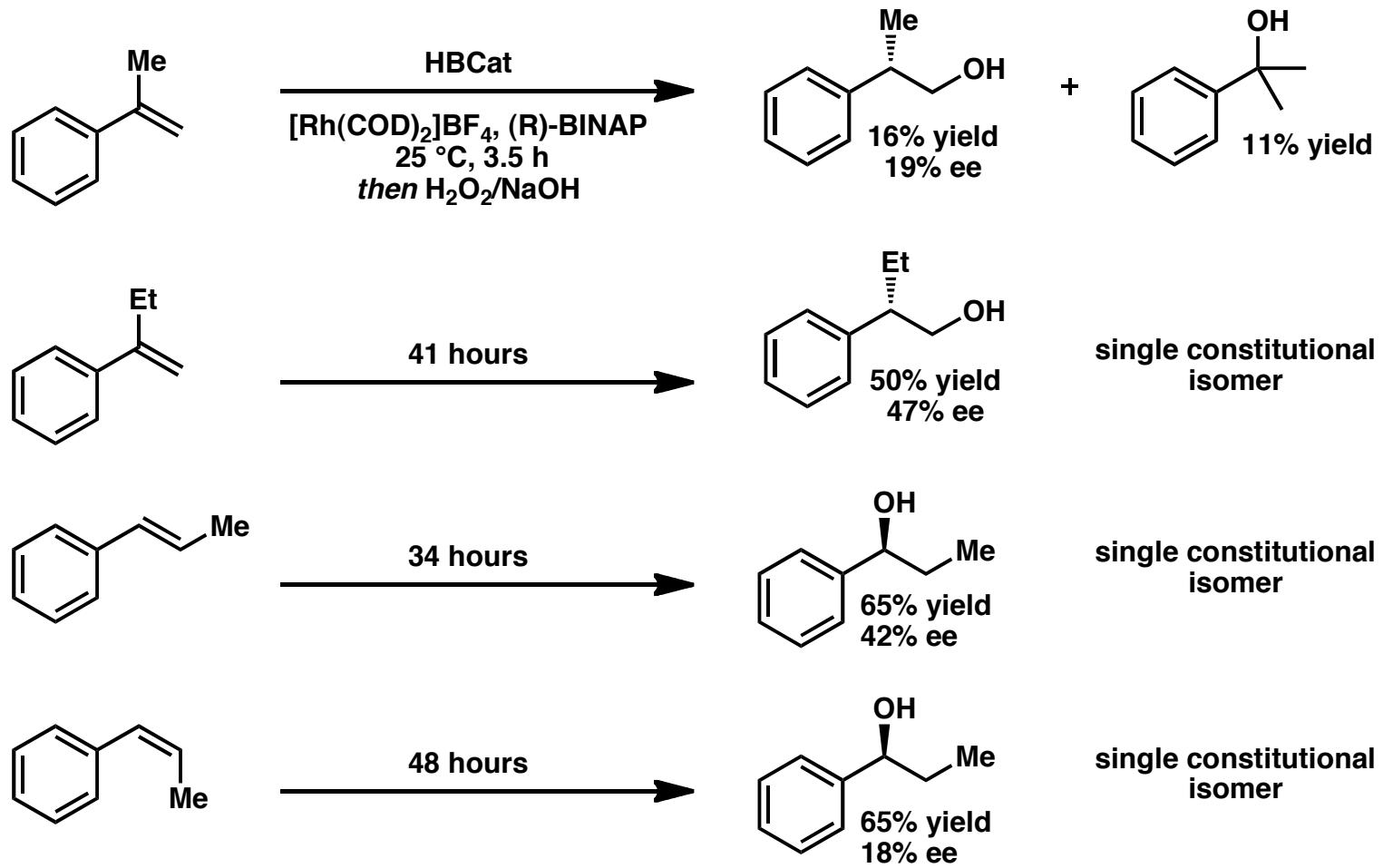
Ar =	solvent	temp (°C)	time (h)	yield (%)	% ee
H	THF	25	0.5	92	57
H	THF	-30	0.5	90	76
<i>o</i> -MeO	THF	-30	0.5	84	82
<i>p</i> -MeO	THF	-30	0.5	74	85
H	DME	-78	2	91	96
<i>m</i> -Cl	DME	-78	2	99	85
<i>p</i> -MeO	DME/THF	-78	6	54	89
<i>p</i> -Me	DME	-78	6	77	94
<i>p</i> -Cl	DME	-78	6	98	91

high regioselectivity observed for electron donating *and* withdrawing groups

COD = 1,5-cyclooctadiene

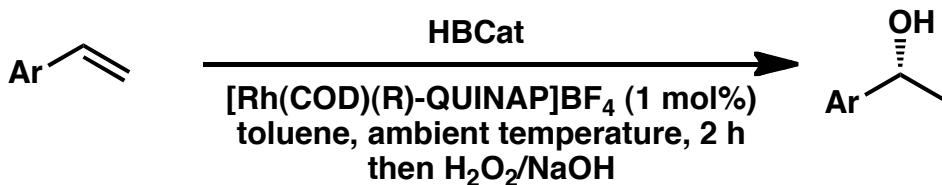
Hayashi, T. J. Am. Chem. Soc. 1989, 111, 3426–3428.

Limitations of Hayashi's System



Steric bulk requires higher temperatures: lower ee's result.

Asymmetric Hydroborations of Styrenes



substrate	yield (%)	branched/linear	% ee	substrate	yield (%)	regioselectivity	% ee
	75	97/3	89		81	97/3	86
	82	93/7	92		82	93/7	92
	21 ^a	63/37	77		82	96/4	94
	80 ^b	99/1	93		80 ^b	99/1	95
	82	96/4	82		78	99/1	96

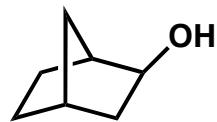
^a 5% excess ligand added ^b triflate catalyst, THF solvent

Brown, J. M. *Chem. Eur. J.* **1999**, *5*, 1320–1330.

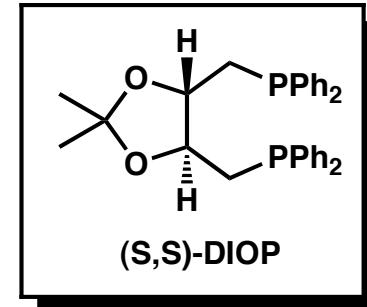
Other Substrates: Norbornene



HBCat
 $[\text{RhCl}(\text{C}_2\text{H}_4)]_2$, (S,S)-DIOP
 PhMe, -5 °C, 3 days
 then $\text{H}_2\text{O}_2/\text{NaOH}$



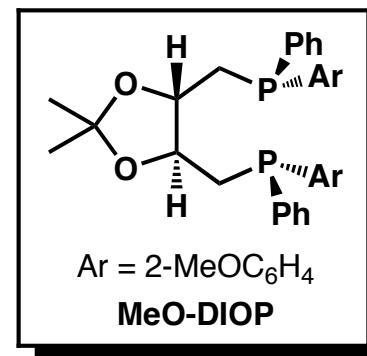
81% yield
 59% ee



HBCat
 $[\text{RhCl}(\text{COD})]_2$, MeO-DIOP
 THF, -25 °C
 then $\text{H}_2\text{O}_2/\text{NaOH}$

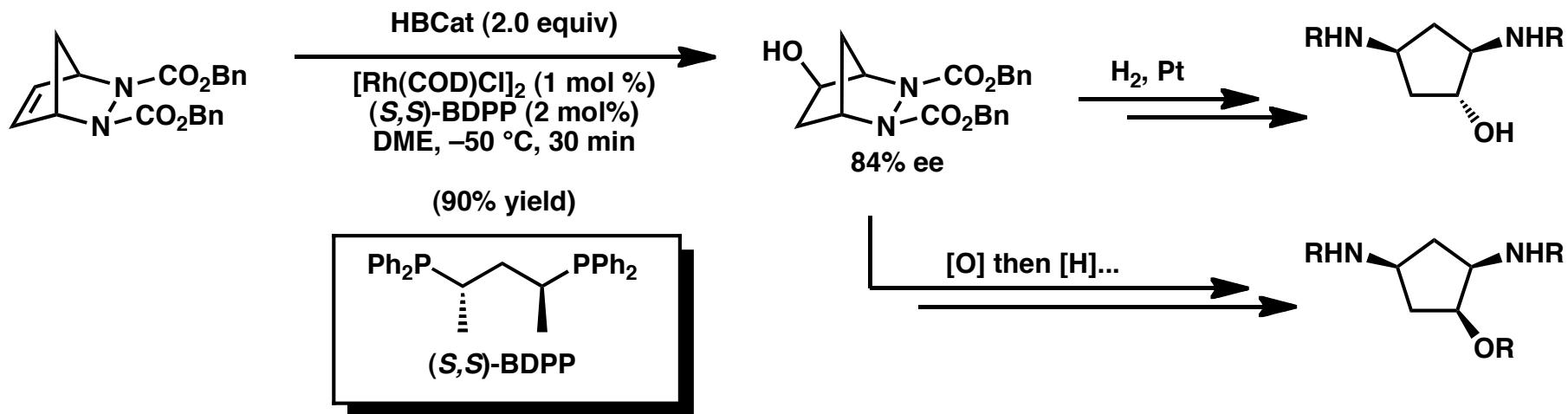


no yield reported
 84% ee



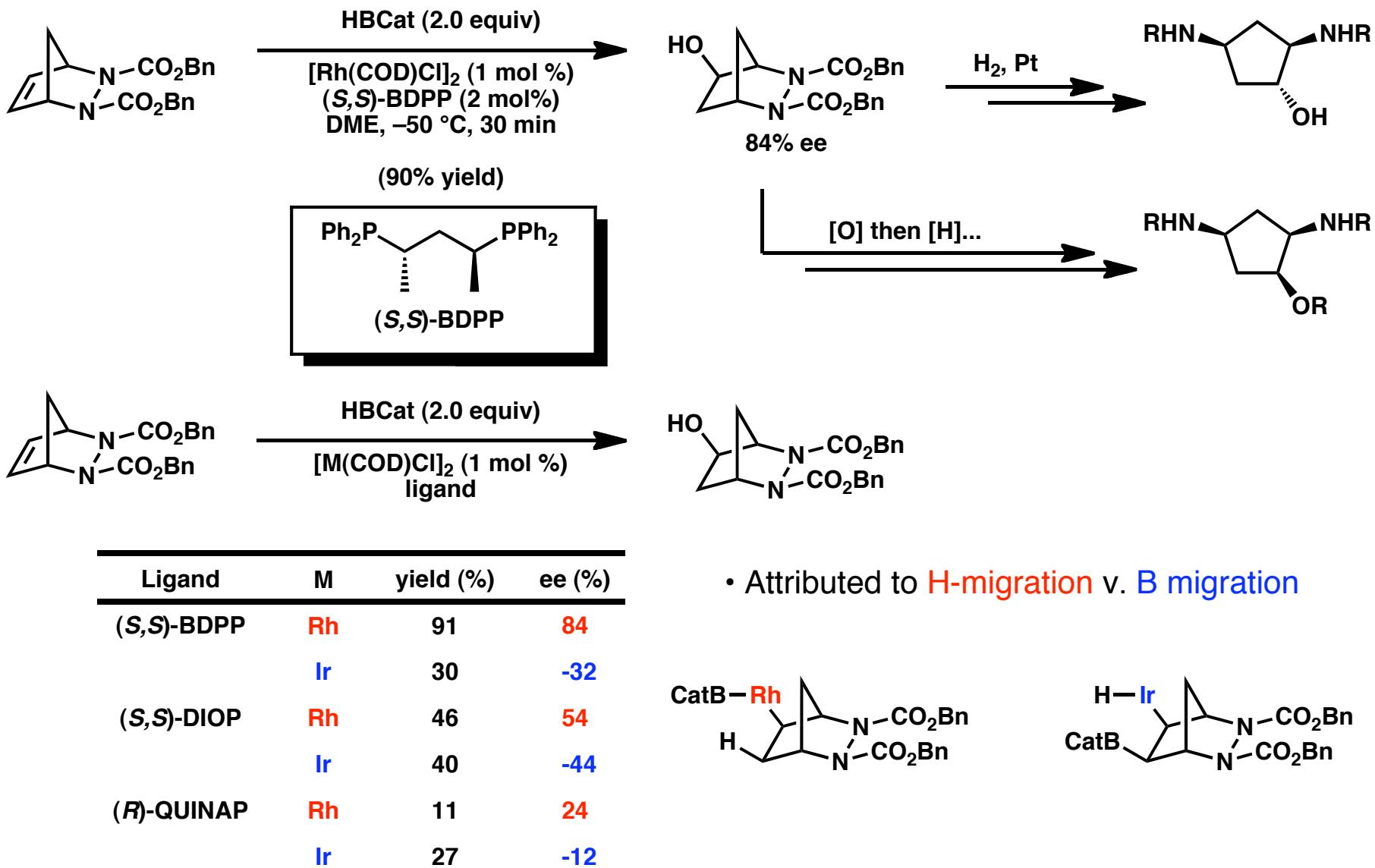
- β -hydride elimination pathways are limited
- Symmetric substrate: regioselectivity not a concern

Enantioselectivity - Bicyclic Hydrazines



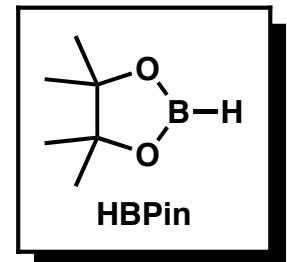
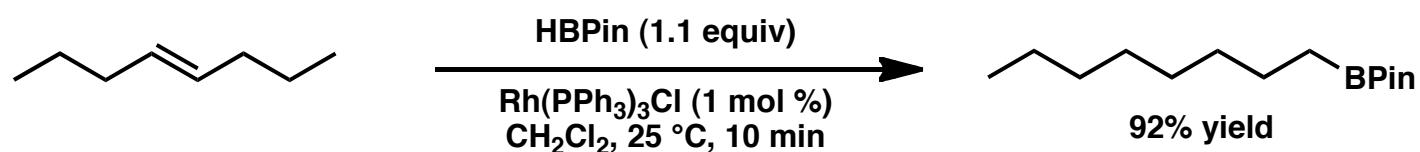
Bonin, M.; Micouin, L.; *J. Org. Chem.* **2002**, *67*, 3522–3524.
Bonin, M.; Micouin, L. *J. Am. Chem. Soc.* **2002**, *124*, 12098–12099.

Enantioselectivity - Bicyclic Hydrazines



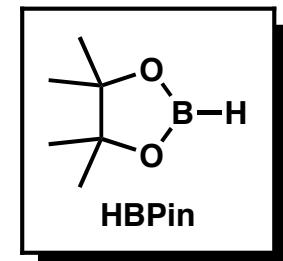
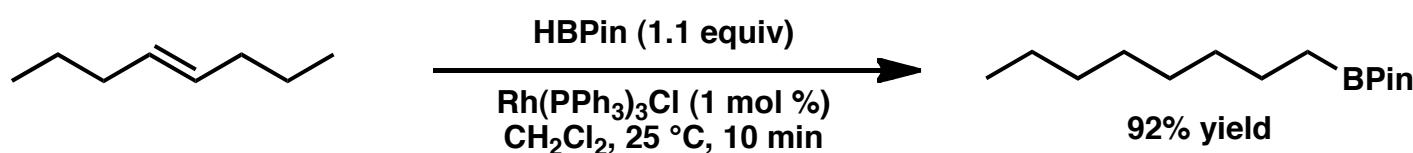
Bonin, M.; Micouin, L.; *J. Org. Chem.* **2002**, *67*, 3522–3524.
 Bonin, M.; Micouin, L. *J. Am. Chem. Soc.* **2002**, *124*, 12098–12099.

Alternatives to HBCat: Pinacolborane

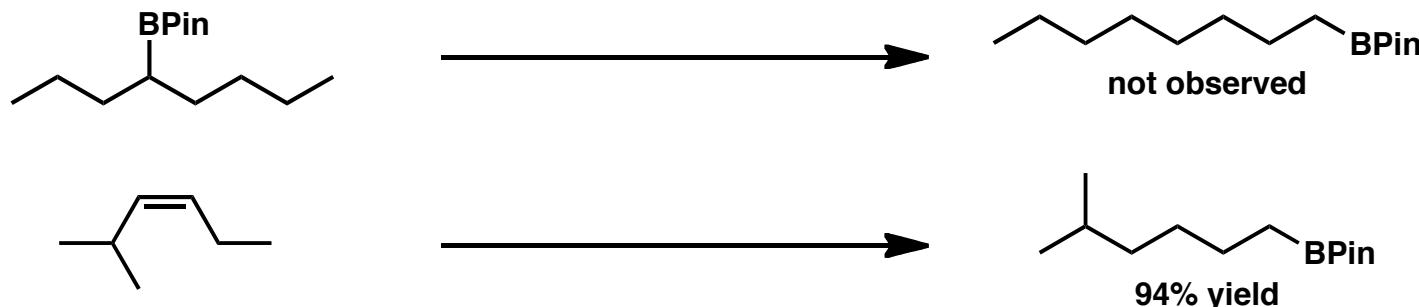


- Reversible reductive elimination *or* fast β-hydride elimination?

Alternatives to HBCat: Pinacolborane

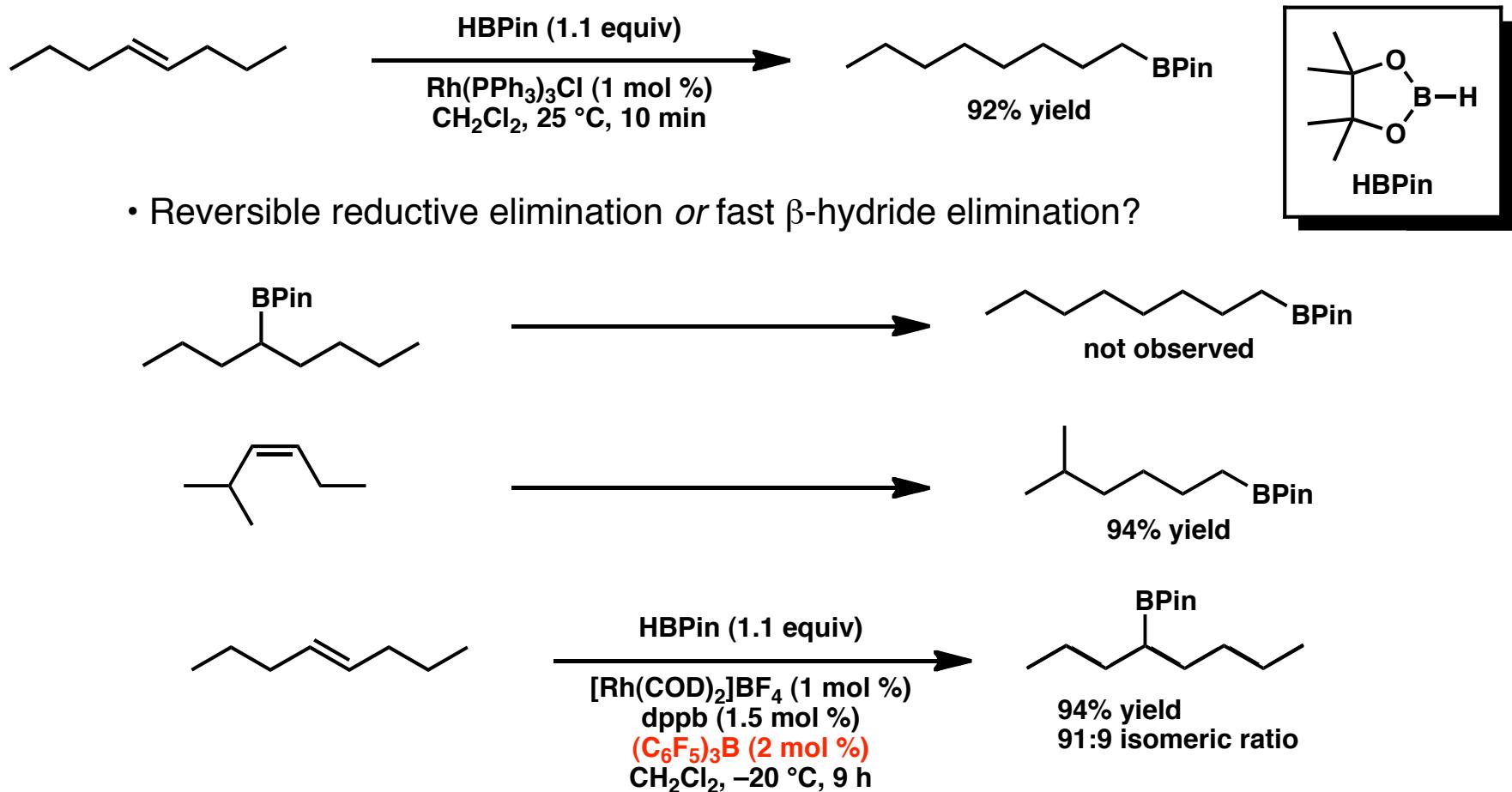


- Reversible reductive elimination *or* fast β-hydride elimination?



- HBPin: Reductive elimination at *secondary* carbons is slower than β-hydride elimination
- Attributed to greater steric demand and lower lewis acidity of **HBPin** vs. **HBCat**

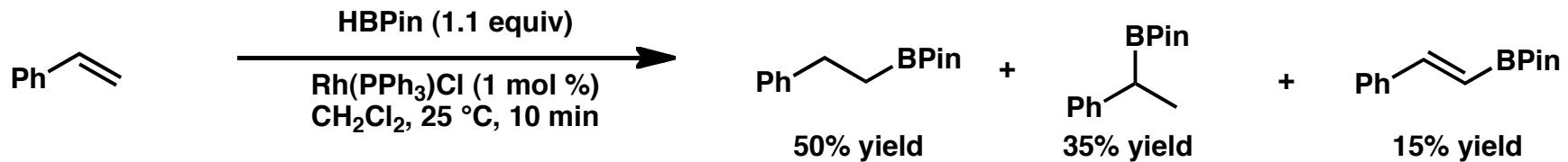
Alternatives to HBCat: Pinacolborane



- HBPin: Reductive elimination at *secondary* carbons is slower than β -hydride elimination
- Attributed to **greater steric demand** and **lower lewis acidity** of **HBPin** vs. **HBCat**
- Selectivity reversed with **addition of lewis acid**

Srebnik, M. *J. Am. Chem. Soc.* **1996**, *118*, 909–910.
 Lata, C. J.; Crudden, C. M. *J. Am. Chem. Soc.* **2010**, *132*, 131–137.

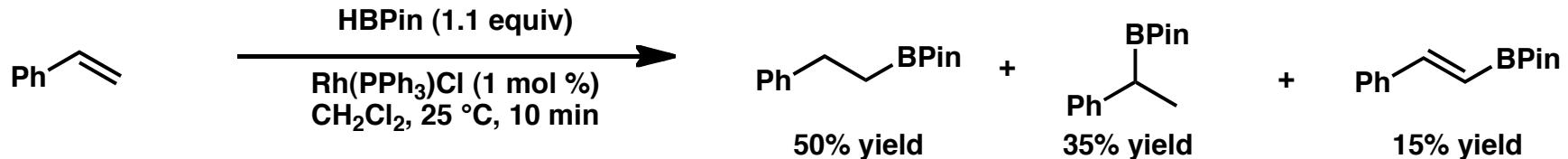
Pinacolborane - Aryl Substrates



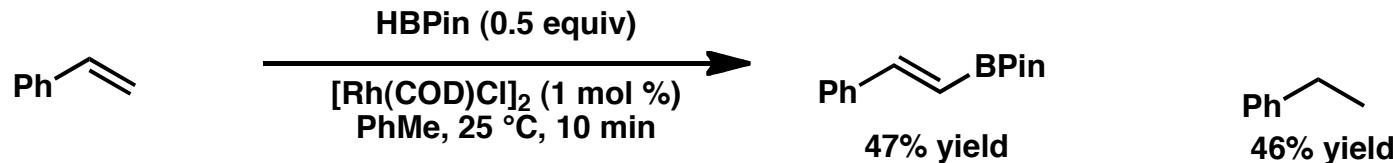
- However, later studies suggested that this work was performed with oxidized catalyst!

Srebnik, M. *J. Am. Chem. Soc.* **1996**, *118*, 909–910.
Masuda, Y. *Tetrahedron Lett.* **1999**, *40*, 2585–2588.
Crudden, C. M.; Hleba, Y. B.; Chen, A. C. *J. Am. Chem. Soc.* **2004**, *126*, 9200–9201.

Pinacolborane - Aryl Substrates

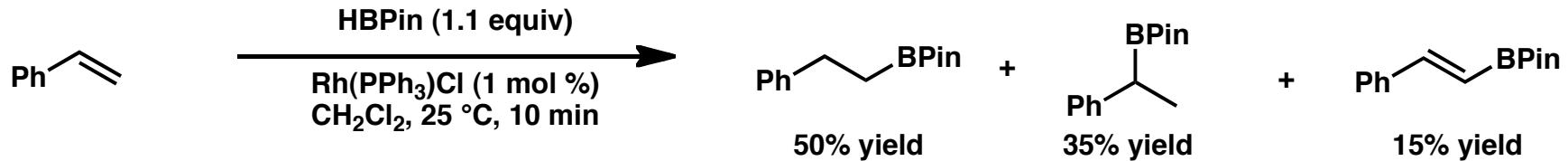


- However, later studies suggested that this work was performed with oxidized catalyst!

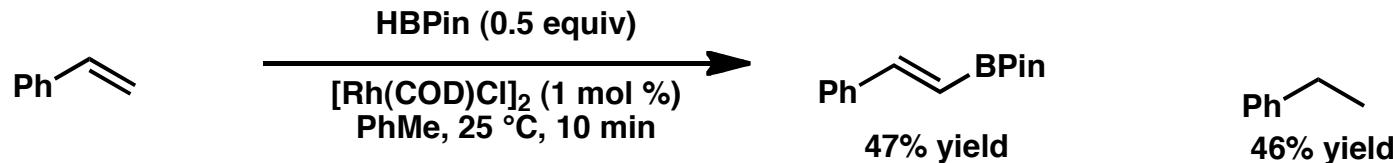


- Recall: phosphene-deficient catalysts (with HBCat) result in unusual product mixtures.

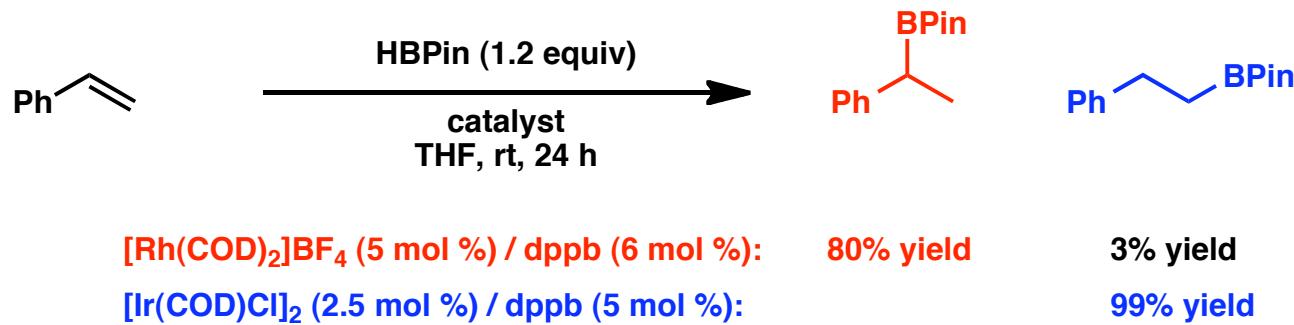
Pinacolborane - Aryl Substrates



- However, later studies suggested that this work was performed with oxidized catalyst!

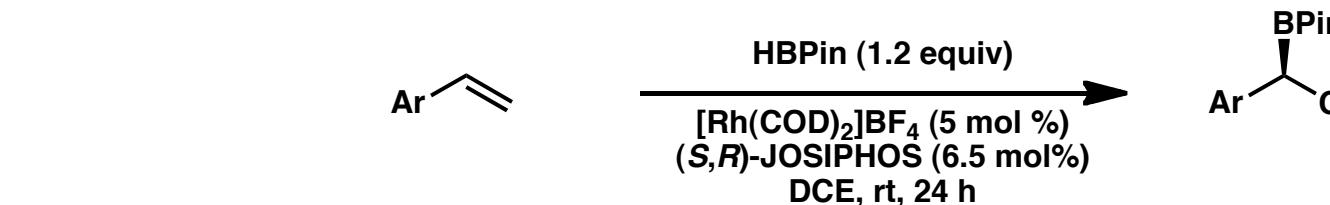


- Recall: phosphene-deficient catalysts (with HBCat) result in unusual product mixtures.

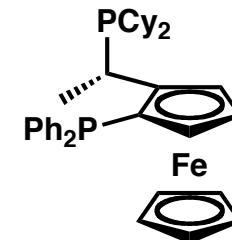


Srebnik, M. *J. Am. Chem. Soc.* **1996**, *118*, 909–910.
 Masuda, Y. *Tetrahedron Lett.* **1999**, *40*, 2585–2588.
 Crudden, C. M.; Hleba, Y. B.; Chen, A. C. *J. Am. Chem. Soc.* **2004**, *126*, 9200–9201.

Enantioselectivity with Pinacolborane: Vinyl Arenes



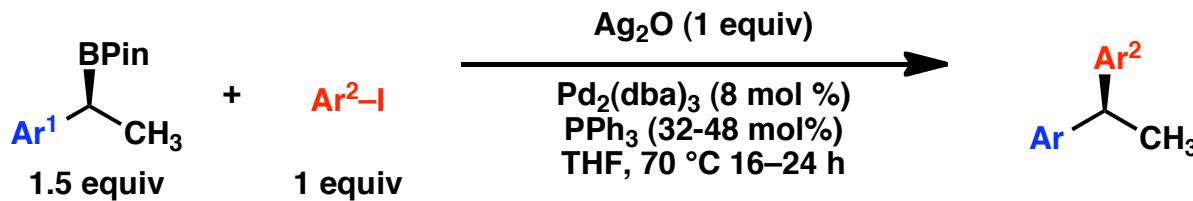
substrate	branched:linear	yield (%)	ee (%)
	83:17	87	84
	82:18	39	88
	72:28	90	80
	83:17	87	84
	83:17	69	76
	95:5	67	86
	95:5	83	88
	91:9	51	84



(S,R)-JOSIPHOS

- Gives complementary enantioselectivity to HBCat with same ligand

Suzuki Couplings of Chiral Secondary Boronic Esters



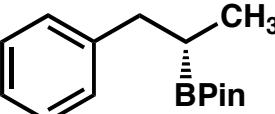
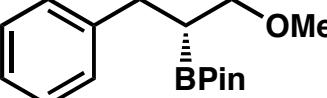
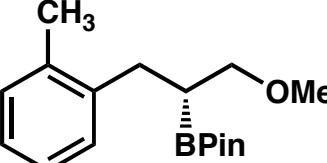
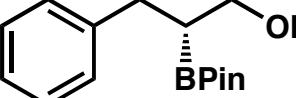
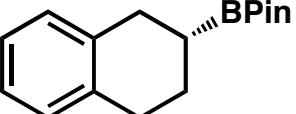
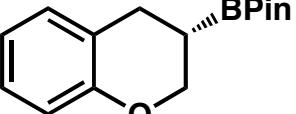
Ar ¹	Ar ² -I	yield (%)	stereoretention
Ph	p-CH ₃ COPhI	65% (63)	92%
Ph	p-CIPhI	81% (63)	91%
Ph	p-CH ₃ PhI	86% (60)	92%
Ph	3,5-diMePhI	86% (64)	93%
Ph	p-MeOPhI	48%	93%
Ph	o-CH ₃ PhI	48%	93%
p-CIPh	PhI	84% (64)	84%
p-CH ₃ Ph	PhI	54% (38)	94%

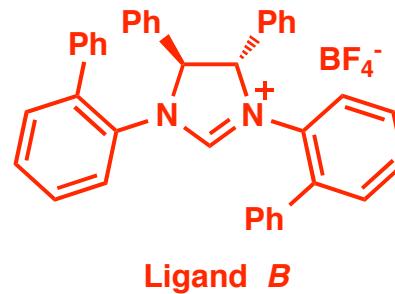
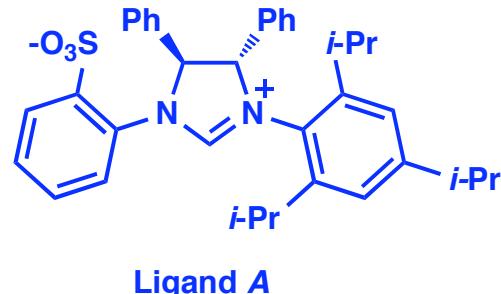
yields determined by ¹H NMR, internal standard
isolated yields in parentheses

- Silver base: speeds transmetallation
- Primary boronate esters unreactive under these conditions

Complementary Regioselectivity with Cu-NHC Catalysts

$\text{Ar}-\text{CH}=\text{CH}-\text{R} \xrightarrow[\substack{\text{CuCl, Ligand (7.5 mol \%)} \\ \text{30 mol\% KOT-Bu} \\ \text{THF, } -50^\circ\text{C, 48 h}}]{\substack{\text{B}_2(\text{Pin})_2 (1.1 \text{ equiv}), \text{MeOH (2 equiv)}}} \text{Ar}-\text{CH}(\text{BPin})-\text{CH}_2-\text{R}$
>98:2
regioselectivity
in all cases

Product	Ligand	yield (%)	ee (%)
	A	80	98
	A	75	96
	A	51	89
	A	74	96
	B	63	72
	B	98	89



Complementary Regioselectivity with Cu-NHC Catalysts

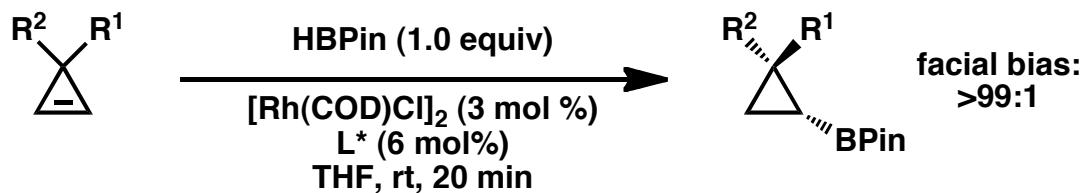
<chem>Ar-CH=CR</chem>	<chem>B2(Pin)2</chem> (1.1 equiv), MeOH (2 equiv)	<chem>Ar-CH(CBPin)-CR</chem>	>98:2 regioselectivity in all cases
	CuCl, Ligand (7.5 mol %) 30 mol% KOT-Bu THF, -50 °C, 48 h		
Product	Ligand	yield (%)	ee (%)
<chem>c1ccccc1CC(CBPin)C2</chem>	A	80	98
<chem>c1ccccc1CC(CBPin)CO</chem>	A	75	96
<chem>c1ccccc1CC(CBPin)COCC2</chem>	A	51	89
<chem>c1ccccc1CC(CBPin)COCC(O)C2</chem>	A	74	96
<chem>c1ccccc1C2CC(BPin)C3</chem>	B	63	72
<chem>c1ccccc1C2CC(BPin)C3OC</chem>	B	98	89

Ligand A

Ligand B

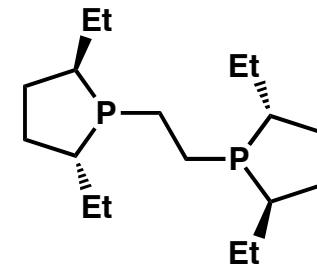
$\left[\begin{array}{c} \text{[Cu]} \\ \text{Ar}-\text{CH}(\text{CBPin})-\text{CR} \end{array} \right] \xrightarrow{\text{MeOH}} \begin{array}{c} \text{H} \\ | \\ \text{Ar}-\text{CH}(\text{CBPin})-\text{R} \end{array}$

Enantioselectivity for Other Substrates - Cyclopropenes

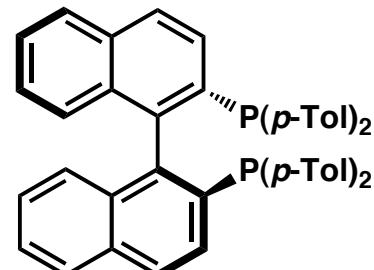


substrate	ligand	product	yield (%)	ee (%)
	(R)-BINAP		94	94
	(R)-BINAP		99	97
	(R)-BINAP		99	92
	(S)-Tol-BINAP		99	>98
	(R,R)-Et-BPE		98	87

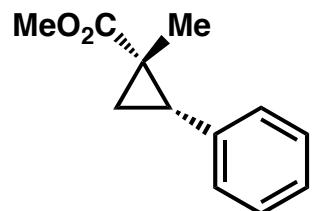
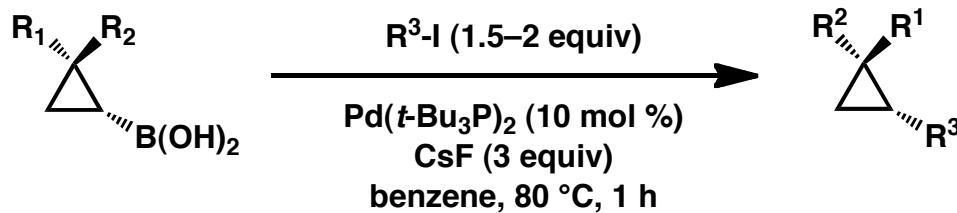
(R,R)-Et-BPE:



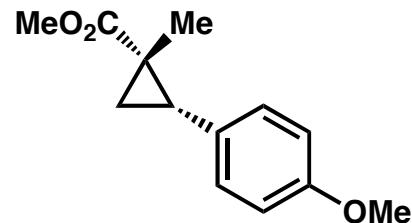
(S)-Tol-BINAP:



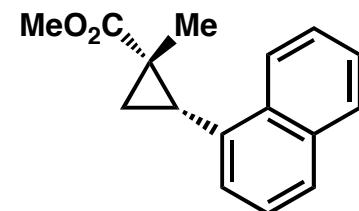
Suzuki Coupling of Cyclopropylboronic Acids



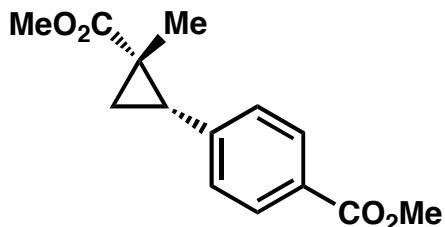
76% yield



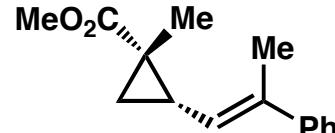
77% yield



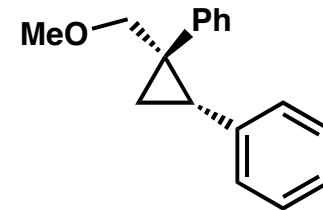
85% yield



64% yield



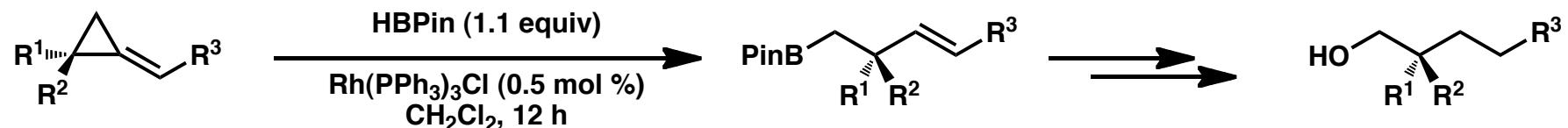
65% yield
(0.5 h)



85% yield
($NaOH$, 7 h)

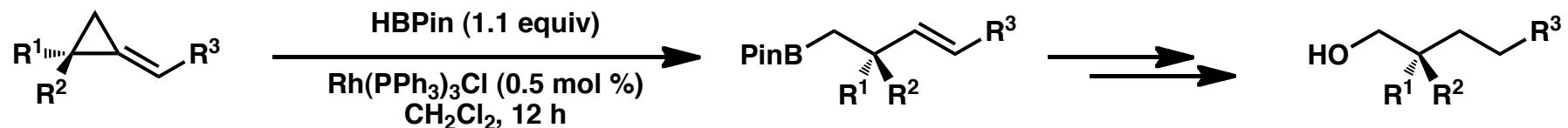
- Cross coupling was not successful with boronate esters
- Only two cyclopropylboronic acids discussed

Alkylidenecyclopropane Ring Openings

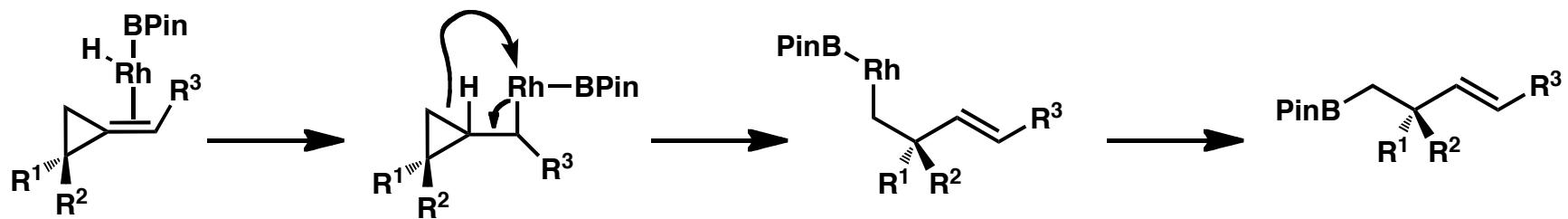


R1	R2	R3	yield (%)
Bu	Hex	H	90
Me	Ph	H	89
Me	Et	(CH ₂) ₂ Ph	83
Bu	Et	Me	81
Me	Ph	(CH ₂) ₂ Ph	83
Me	Et	Ph	80
Me	Bu	Ph	84
Me	Bu	Ph	84
Me	Hex	Ph	90

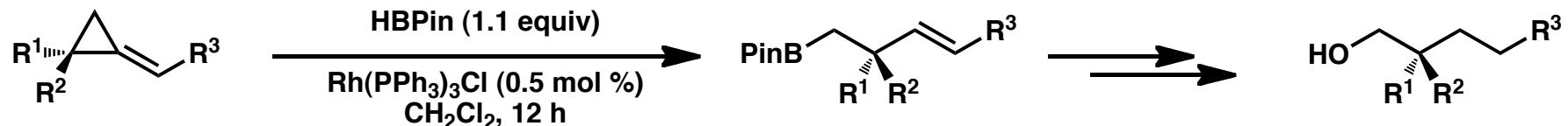
Alkylidenecyclopropane Ring Openings



R1	R2	R3	yield (%)
Bu	Hex	H	90
Me	Ph	H	89
Me	Et	(CH ₂) ₂ Ph	83
Bu	Et	Me	81
Me	Ph	(CH ₂) ₂ Ph	83
Me	Et	Ph	80
Me	Bu	Ph	84
Me	Bu	Ph	84
Me	Hex	Ph	90

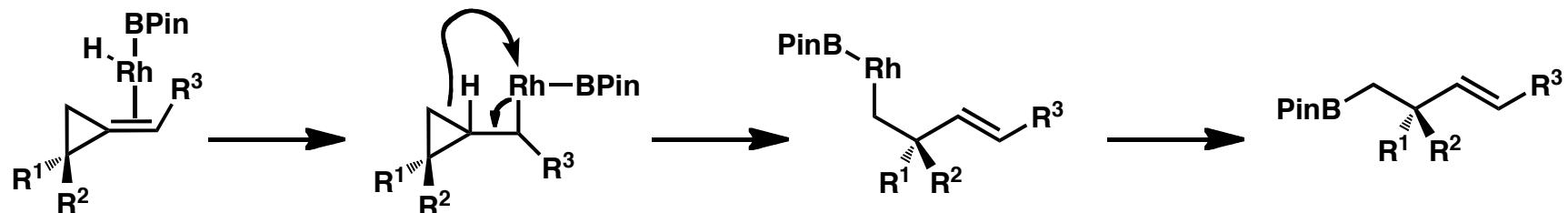


Alkylidenecyclopropane Ring Openings

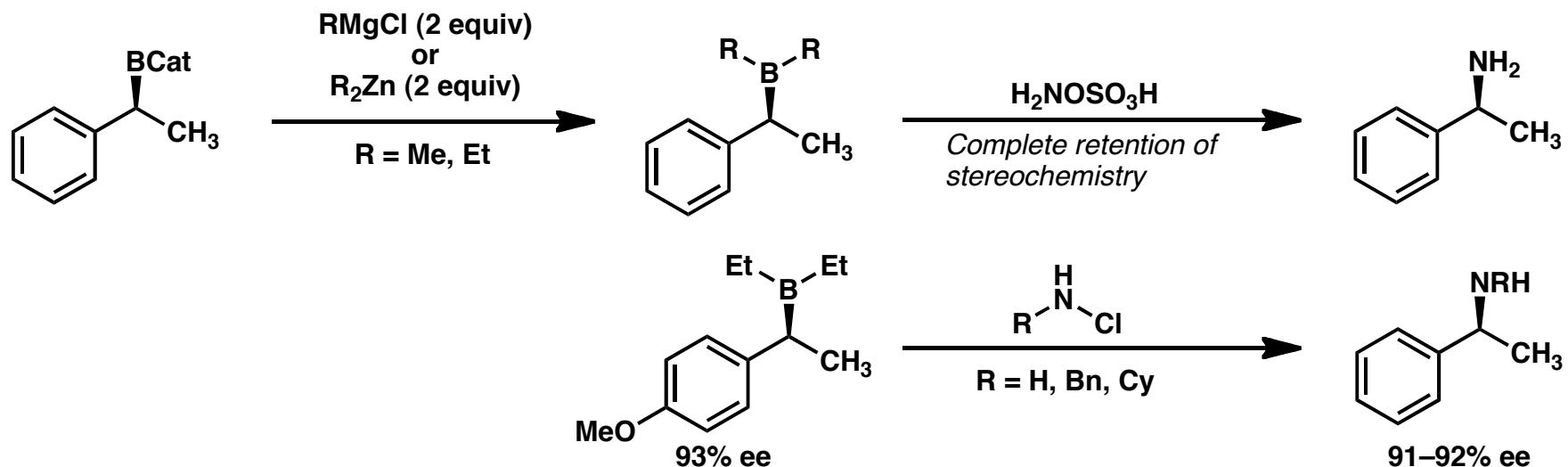


R1	R2	R3	yield (%)
Bu	Hex	H	90
Me	Ph	H	89
Me	Et	(CH ₂) ₂ Ph	83
Bu	Et	Me	81
Me	Ph	(CH ₂) ₂ Ph	83
Me	Et	Ph	80
Me	Bu	Ph	84
Me	Bu	Ph	84
Me	Hex	Ph	90

- No direct olefin addition observed
- High selectivity for desired bond cleavage
- Good stereoretention, but olefin isomerizes.
- 98% SM; 96% ee product
2:1 E:Z after ring opening
- Route to enantioenriched acyclic 4° stereocenters



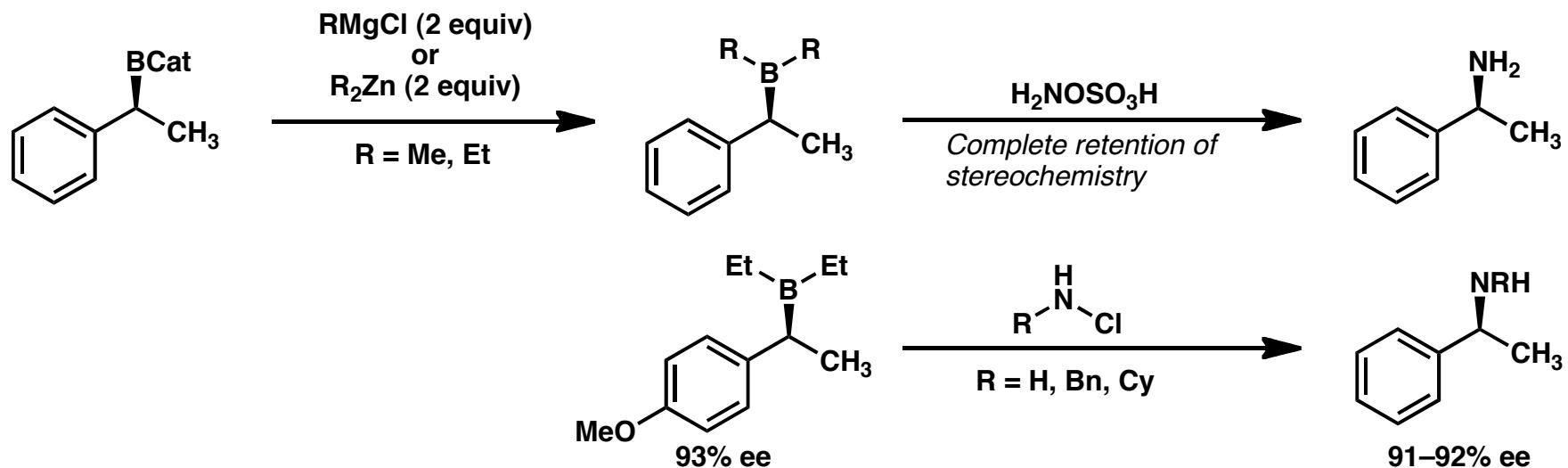
Carbon-Boron Bond Functionalization - Amination



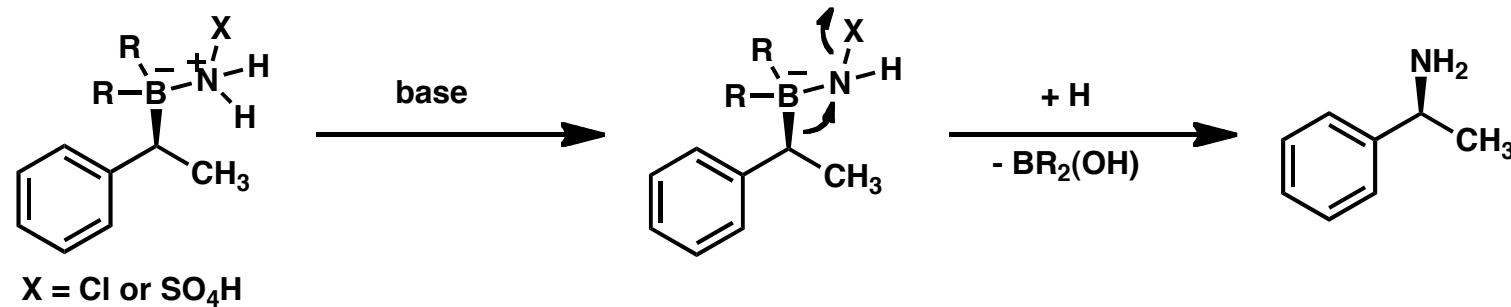
Features:

- Boronate esters are not electrophilic enough for reaction
- Can be performed in one-pot
- Chloramines formed in situ from R-NH₂ and NaOCl

Carbon-Boron Bond Functionalization - Amination



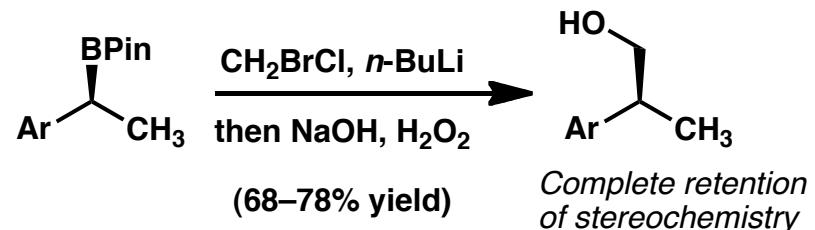
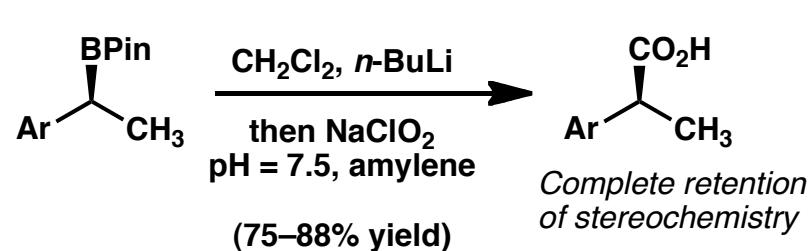
Mechanism:



Features:

- Boronate esters are not electrophilic enough for reaction
- Can be performed in one-pot
- Chloramines formed in situ from $\text{R}-\text{NH}_2$ and NaOCl
- Analogous to H_2O_2 / NaOH workup
- Formation of tertiary amines: low yielding and racemic: radical mechanism likely.

Carbon-Carbon Bonds - 1 Carbon Homologation

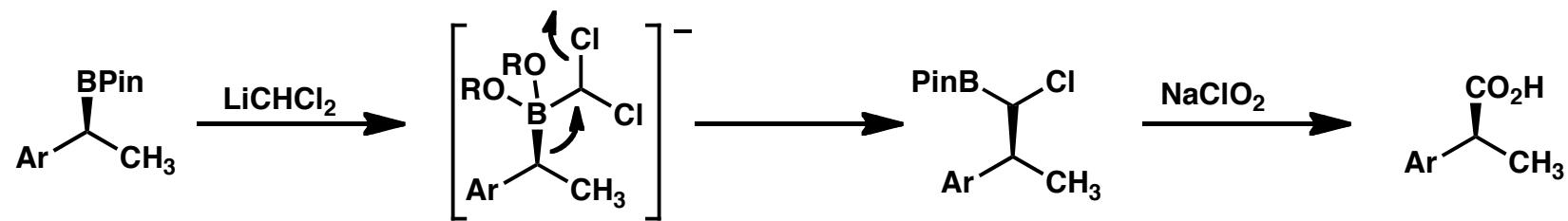


Matteson, D. S. *Tetrahedron* **1998**, *54*, 10555–10606.
Chen, A.; Ren, L.; Crudden, C. M. *J. Org. Chem.* **1999**, *64*, 9704–9710.

Carbon-Carbon Bonds - 1 Carbon Homologation



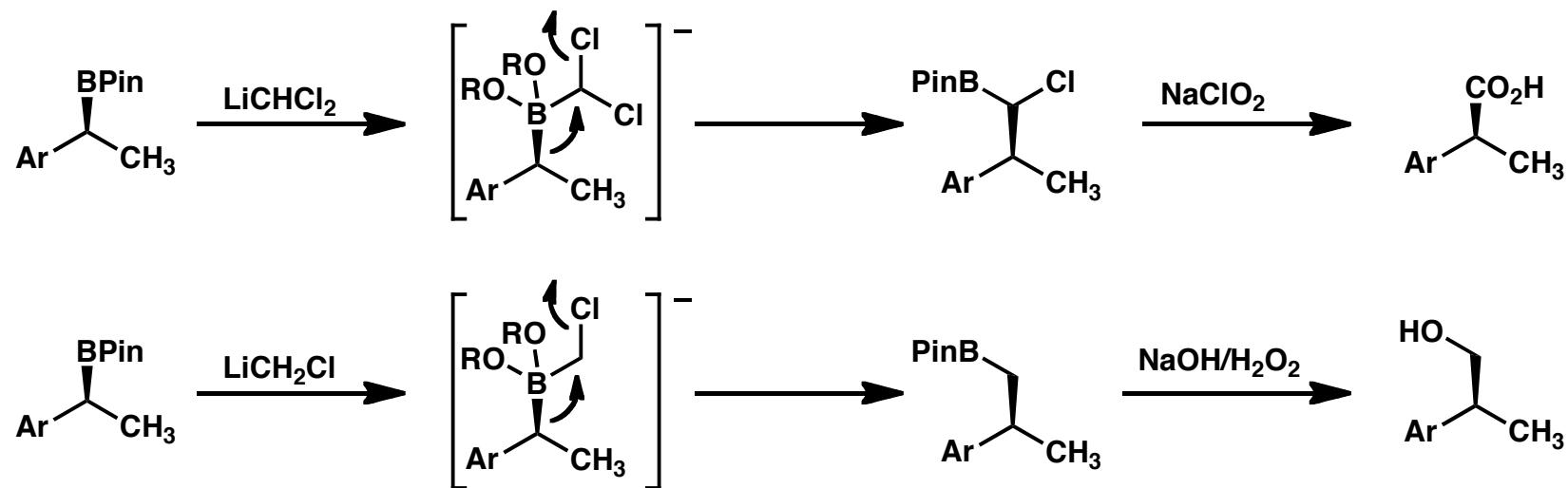
Mechanism:



Carbon-Carbon Bonds - 1 Carbon Homologation



Mechanism:

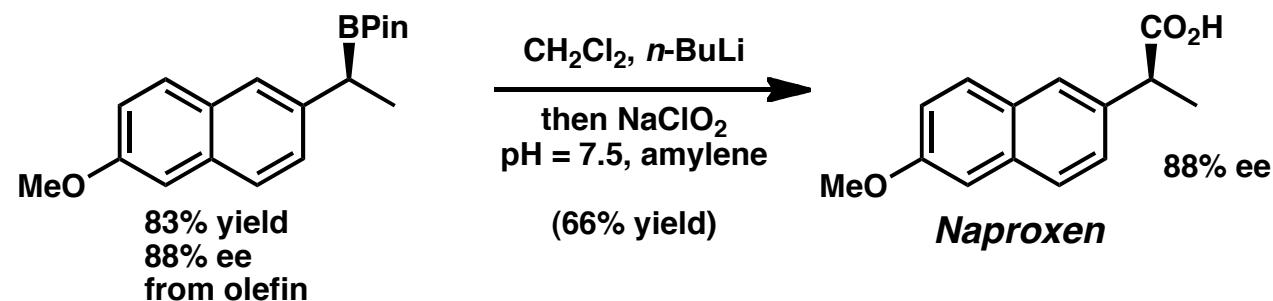
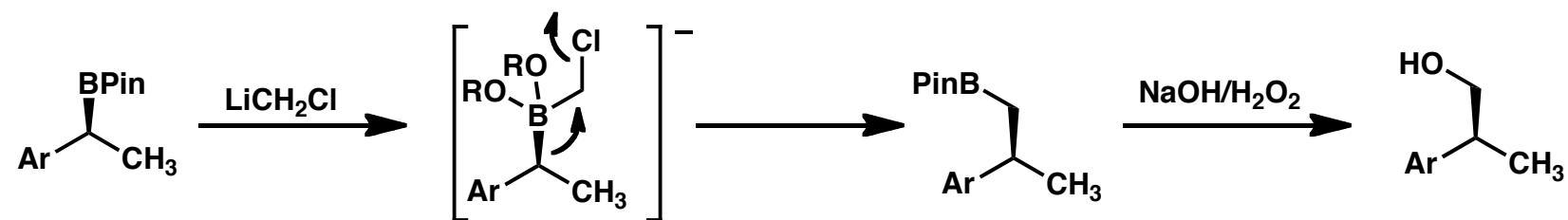
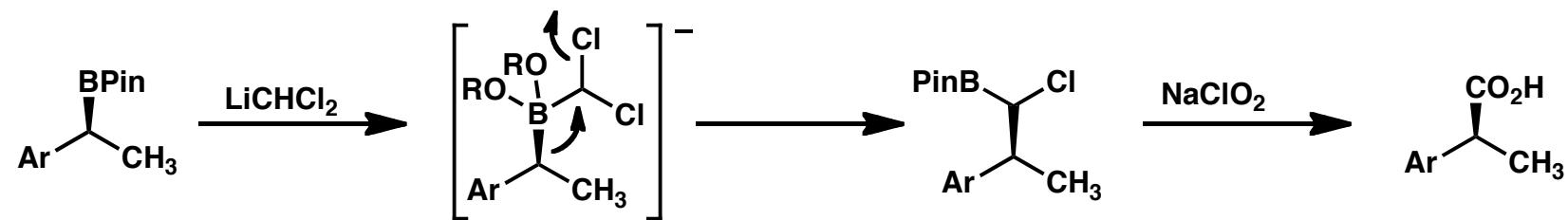


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Carbon-Carbon Bonds - 1 Carbon Homologation



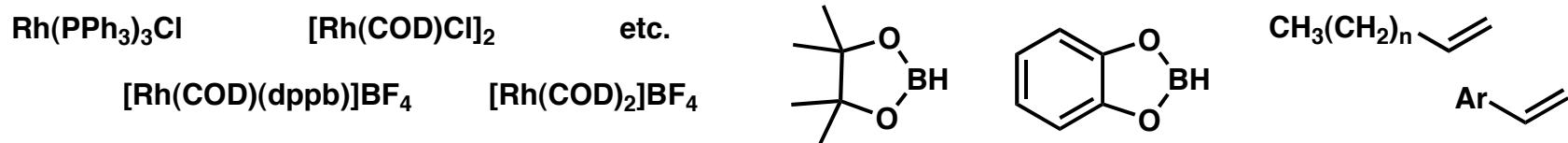
Mechanism:



Matteson, D. S. *Tetrahedron* **1998**, *54*, 10555–10606.
Chen, A.; Ren, L.; Crudden, C. M. *J. Org. Chem.* **1999**, *64*, 9704–9710.

Summary

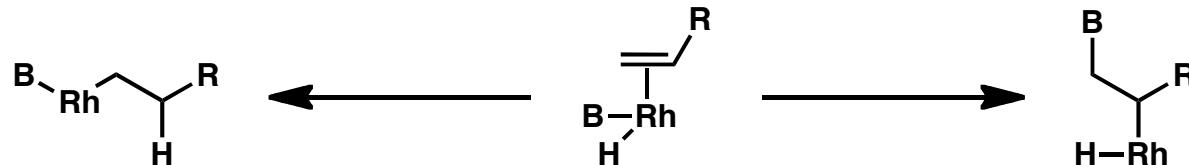
- Mechanism strongly dependent on catalyst and ligands, boronate, substrate



- Integrity of Wilkinson's Catalyst plays important role in regioselectivity:
Phosphine-deficient catalysts behave like 'aged' Wilkinson's catalyst.



- Reversibility of steps, bond-formation play role in regioselectivity and enantioselectivity



- Substrate scope for enantioselective reaction remains rather limited

Reviews:

Beletskaya, I.; Pelter, A. *Tetrahedron* **1997**, *53*, 4957–5026.
Crudden, C. M.; Edwards, D. *Eur. J. Org. Chem.* **2003**, 4695–4712.
Guiry, P. J. *Adv. Synth. Catal.* **2005**, *347*, 609–631.