The Conferience Experience

Modern Synthetic Methods & Chiral USA
(11 – 13 July, Philadelphia)

234th ACS National Meeting & Exposition
(19 – 23 August, Boston)

Aman Desai

A Group Meeting Presentation

7th Sep. 2007

What, Why & How many?

Modern Synthetic Methods & Chiral USA – *Reaction to reality* (11 – 13 July, Boston)

What? A three day conference and exhibition.

What? Entire focus on asymmetric methodology/synthesis, at the academic as well as the industrial level.

Why? Provide a forum where industry and academia can meet to discuss new synthetic methodology & chiral chemistry.

Why did I attend? In 3 days, I could get to know the latest in chiral chemistry at the academic as well as the industrial level.

Got an awesome discount!

How many? 13 academic talks

11 industrial talks

~ 10 exhibiting companies

1 poster (mine!)

Who?

From academia:

Steven Nolan (ICIQ, Spain)

Barry Trost (Stanford)

Xumu Zhang (SUNY, Rutgers)

Michael Krische (U. Texas)

Mathew Gaunt (U. Cambridge, UK)

Erick Carreira (ETH-Zurich)

Dean Toste (U. Cal. Berkeley)

John Montgomery (U. Michigan)

Vadim Soloshonok (U. Oklohoma)

Clark Landis (U. Wisconsin)

Patrick Walsh (U. Penn.)

Marisa Kozlowski (U. Penn.)

Kevin Burgess (TAMU)

From industry:

Scott May (Eli Lilly)

Johan Wennerberg (DuPont)

Kevin Campos (Merck)

Ian Lennon (Dowpharma)

Fred Hancock (Johnson Matthey Catalysis)

Michel Guillaume (Johnson & Johnson)

Michael Schwarm (Degussa)

Xudong Wei (Boehringer)

Surendra Singh (Sepracor)

Brian Freer (Chiral Technologies)

Benoit Pugin (Solvias)

Who?

From industry:

Scott May (Eli Lilly)	*Asymmetric hydrogenation*
Johan Wennerberg (DuPont)	*Lewis acid catalyzed Michael reactions*
Kevin Campos (Merck)	*Asymmetric hydrogenation*
Ian Lennon (Dowpharma)	*Asymmetric hydrogenation*
Fred Hancock (Johnson Matthey Catalysis)	*Asymmetric hydrogenation*
Michel Guillaume (Johnson & Johnson)	*Chiral pool*
Michael Schwarm (Degussa)	*Biocatalysis*
Xudong Wei (Boehringer)	*Olefin metathesis*
Surendra Singh (Sepracor)	*Asymmetric hydrogenation*
Brian Freer (Chiral Technologies)	*Chiral chromatography*
Benoit Pugin (Solvias)	*Asymmetric hydrogenation*

Asymmetric hydrogenation by and large the only asymmetric synthesis methodology really explored in industry till now!

Industrial chiral chemistry is in its infancy.

Asymmetric synthesis is and will remain a hot field for a long time.

A lot of unexplored territory.

A world of potential.

So…

Yeah Aziridinations!

Go VAPOL/VANOL!

Rock on Carbene Complexes!

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SCIENTIFIC UPDATE

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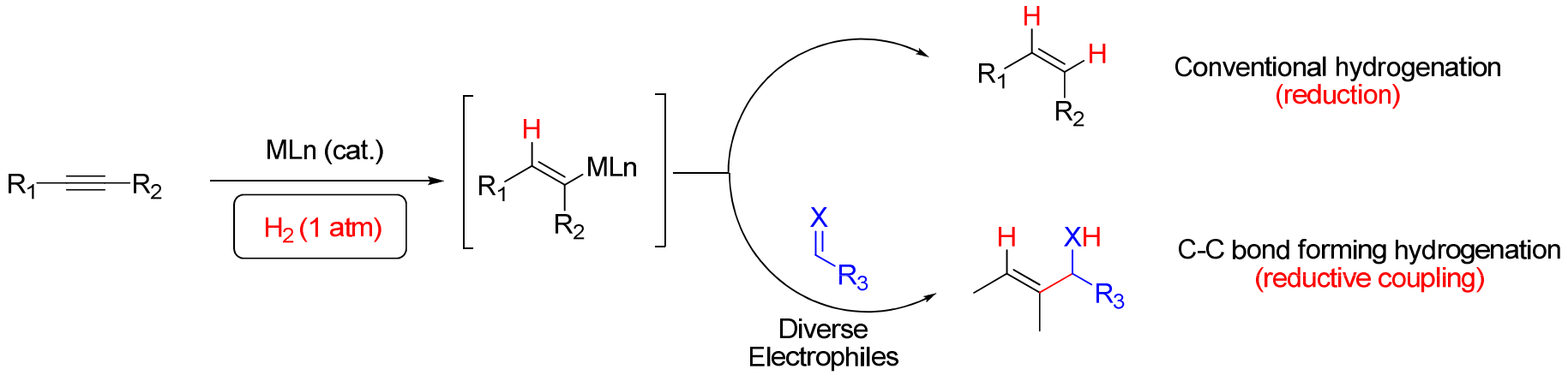
Michael Krische – Formation of C-C bonds via Catalytic Hydrogenation

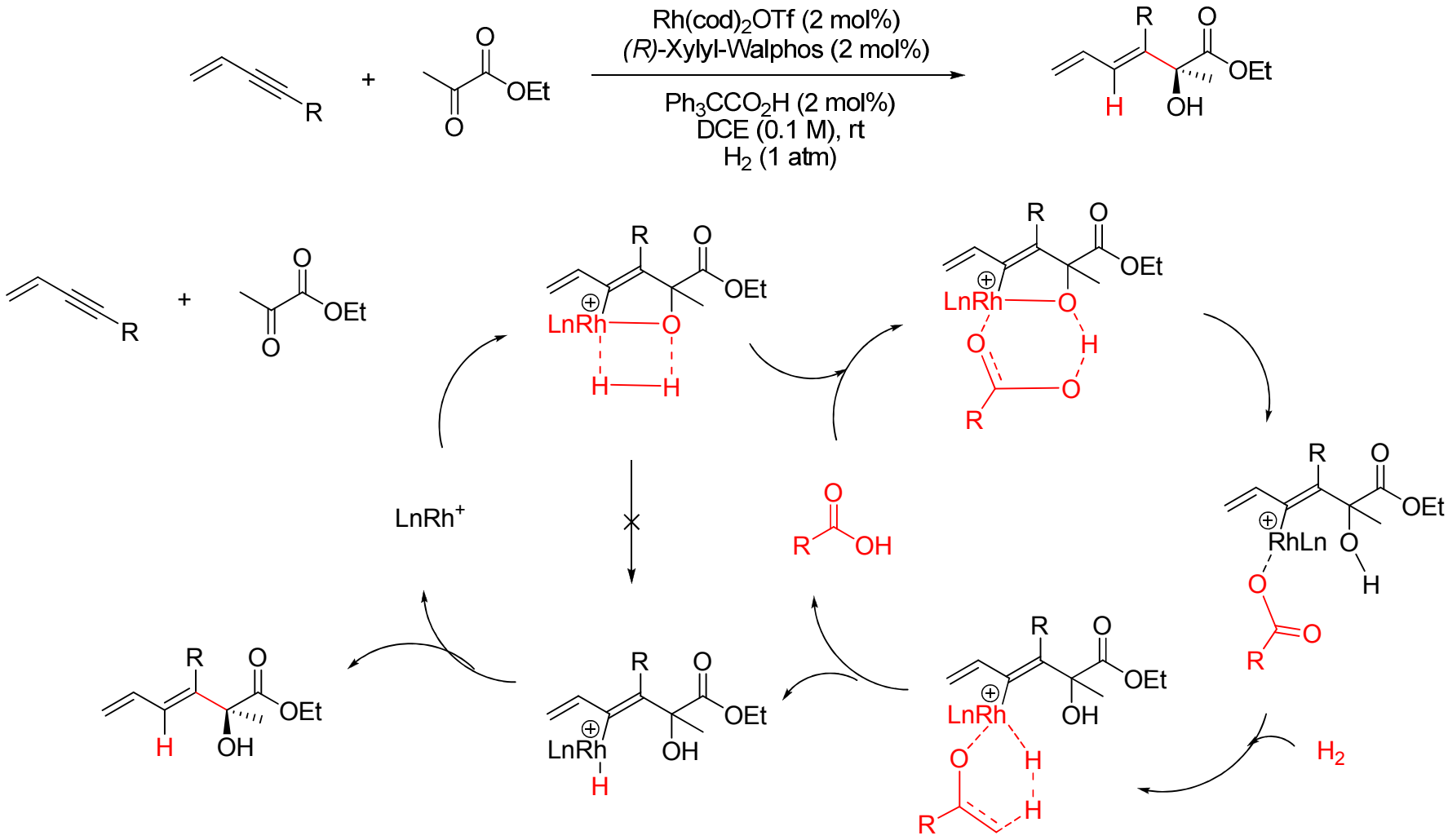
Awarded the Dowpharma prize for "Creativity in Chiral Chemistry"



Can Hydrogenation Intermediates be intercepted and rerouted to products of C-C coupling?

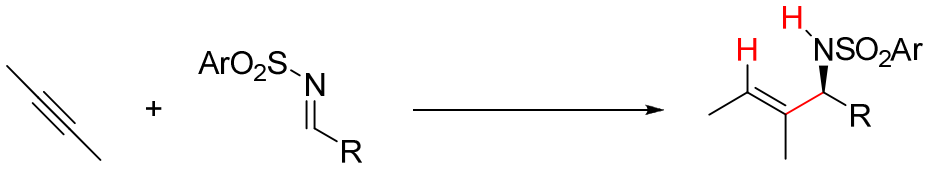
Michael Krische – Formation of C-C bonds via Catalytic Hydrogenation

H_2 Mediated Synthesis of α-Hydroxy Esters: *JACS* **2006**, 718.

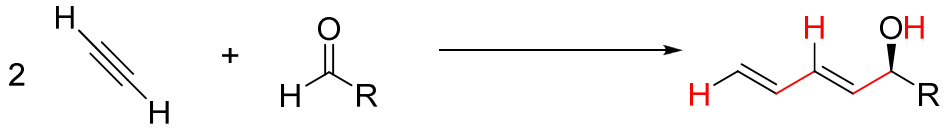


Michael Krische – Formation of C-C bonds via Catalytic Hydrogenation

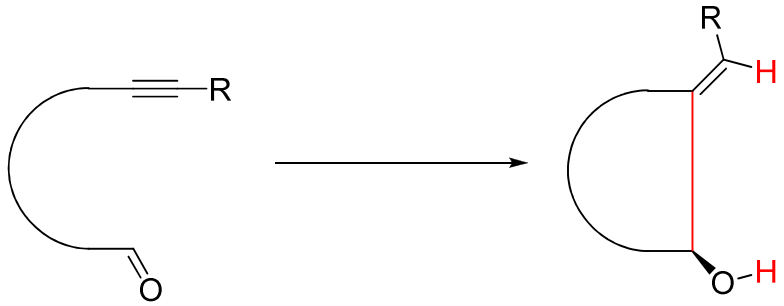
Alkyne-Imine H_2-Coupling: *JACS* **2007**, ASAP



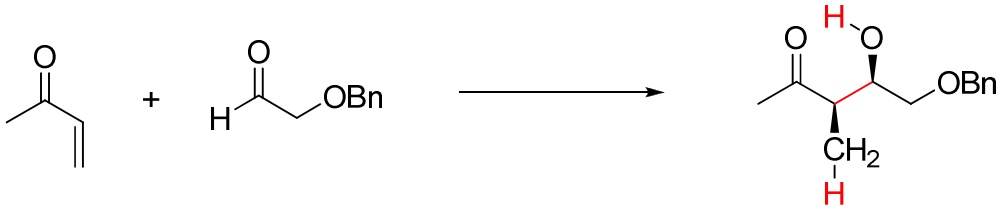
Acetylene Couplings: *JACS* **2006**, 16040



Unactivated Alkynes – Intramolecular Coupling: *JACS* **2006**, 10674



Enantioselective Reductive Aldol Coupling



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Brian Freer – Chiral Chromatography

Discussions with process chemists show a consistent message – chromatography is considered to be:

- Last resort
- Temporary Solution
- Inelegant
- Difficult to use

Conference Presentations often include:

"Benefit is no chromatography"

"Removed expensive chromatography step"

But, several months to develop a 3 stage asymmetric route using metal catalysis (higher variable and fixed costs) – to give 50% yield.

Chiral chromatography would have give an overall enantiomer yield of 45%

To date 6 drugs are produced at multi-tonne scale.

DAICEL (Japan): SMB multi-tonne production of a chiral drug.

UCB (Belgium): Chiral SMB multi-tonne production of 2 drugs.

Honeywell/SAFC (Ireland): Chiral SMB system > 10 MTA

Productivity vs. Scale

50 mm column (diameter) for 12 kg enantiomer/week

Upto

800 mm column for 2020 kg enantiomer/week.

Success rate = 75%

Guaranteed yield = 90% (per enantiomer)

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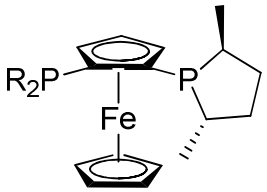
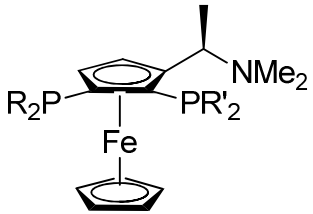
Benoit Pugin – New Ligands for Asymmetric Catalytic Hydrogenation

New Ferrocenyl Diphosphine Ligands in the Solvias Pipeline

5-ring-chelates

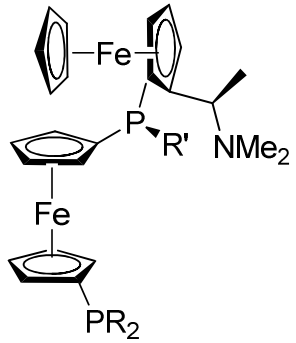


Kephos



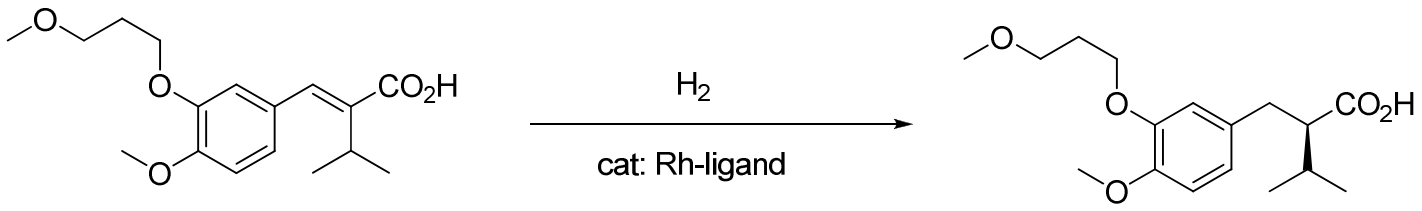
Fengphos

P-chiral phosphines



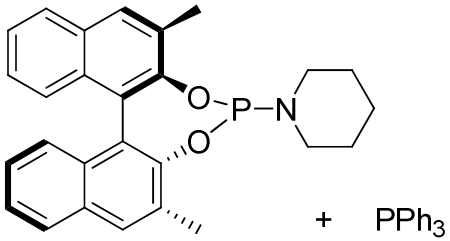
Chenphos

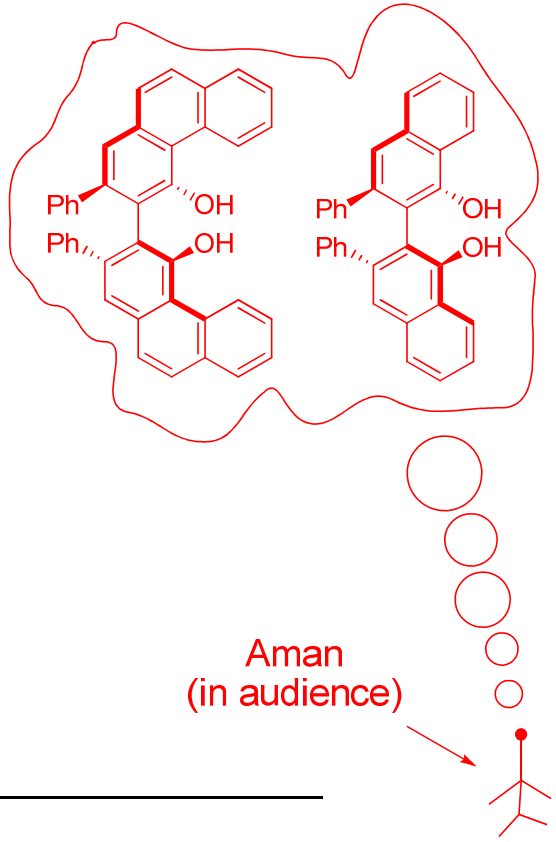
Benoit Pugin – New Ligands for Asymmetric Catalytic Hydrgenation



Monophos (DSM)

- TON > 5000
- ee 90%
- currently used in production!





De Vries et al., *Chem. Eur. J.* **2006**, *12*, 4722.

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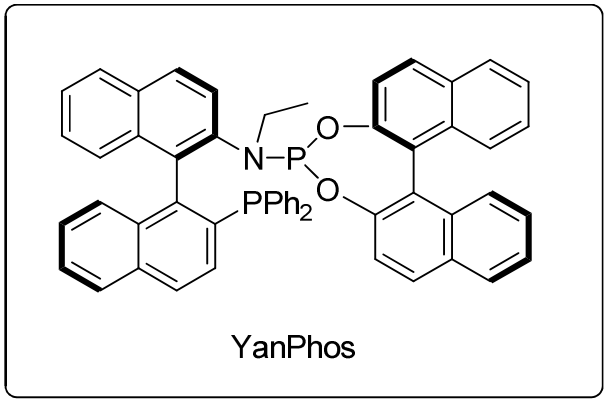
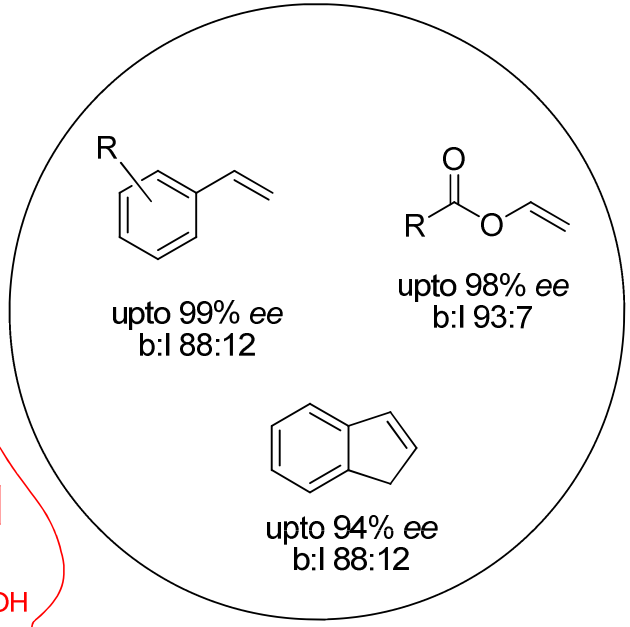
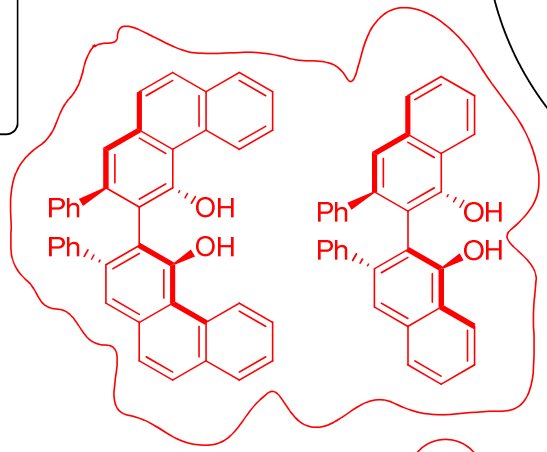
Xumu Zhang - Innovative Phosphines for Regioselective and Enantioselective Hydroformylation



Hydroformylation





Aman
(in audience)

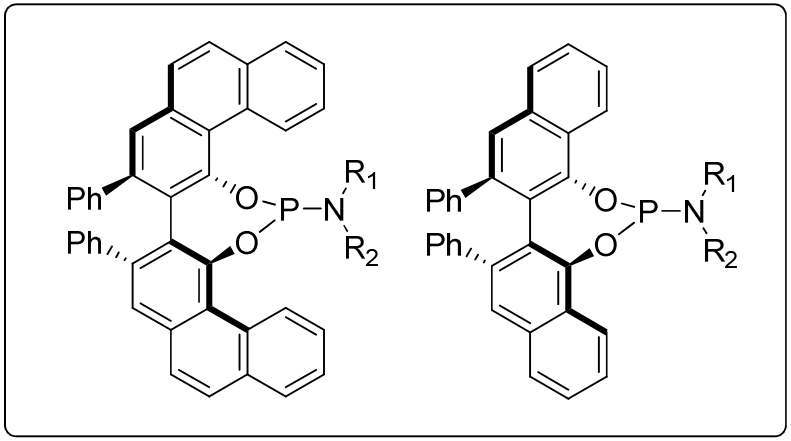
Yan, Y.; Zhang, X. *J. Am. Chem. Soc.* **2006**, *128*, 7198.

A New Future Project Maybe?…

New Phosphoramidite Ligands
Based on VAPOL and VANOL

asymmetric hydroformylation

asymmetric hydrogenation

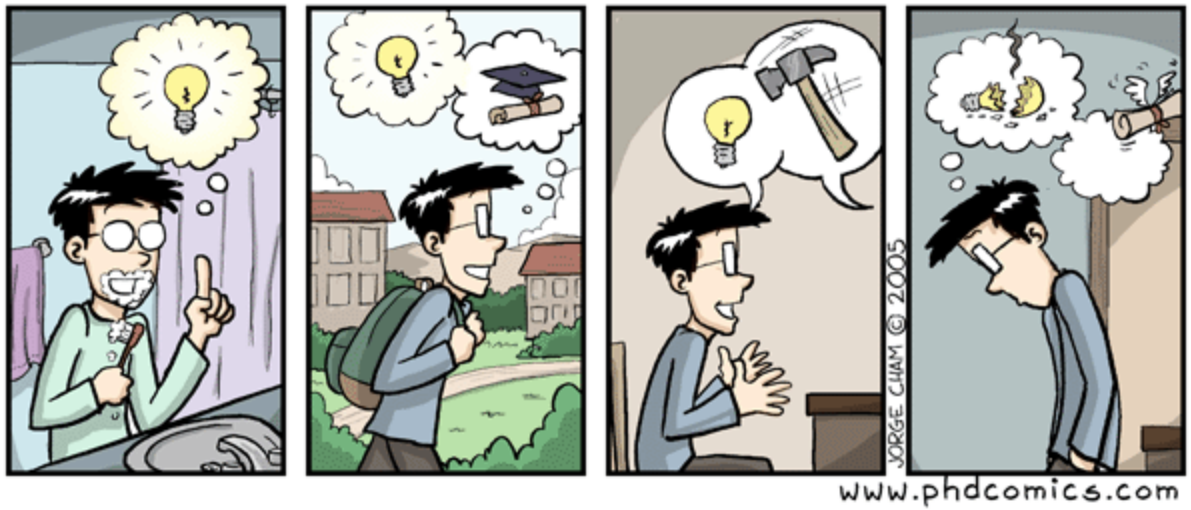


asymmetric allylic substitution

asymmetric hydroboration

Easy synthesis

Fast screening



What, Why & How many?

234th ACS National Meeting (19 - 23 August, Boston)

What? A five day conference and exhibition.

What? The biggest chemistry meeting in America, and probably in the world.

Why did I attend? To learn about the latest research in my field, and others.

To get new ideas.

To revel in the atmosphere that is created by the presence of thousands of graduate students/professors/chemists under a single roof!

How many? 15344 total registrants.

3518 students.

324 exhibitors.

9560 papers presented.

844 half-day oral sessions.

97 poster sessions.

Who?

George Whitesides (Harvard)

Scott Denmark (UIUC)

Masakatsu Shibasaki (U. Tokyo)

Elias J. Corey (Harvard)

Hisashi Yamamoto (U. Chicago)

David Macmillan (Princeton U.)

Scott Schaus (Boston U.)

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Student Speakers

Student Posters

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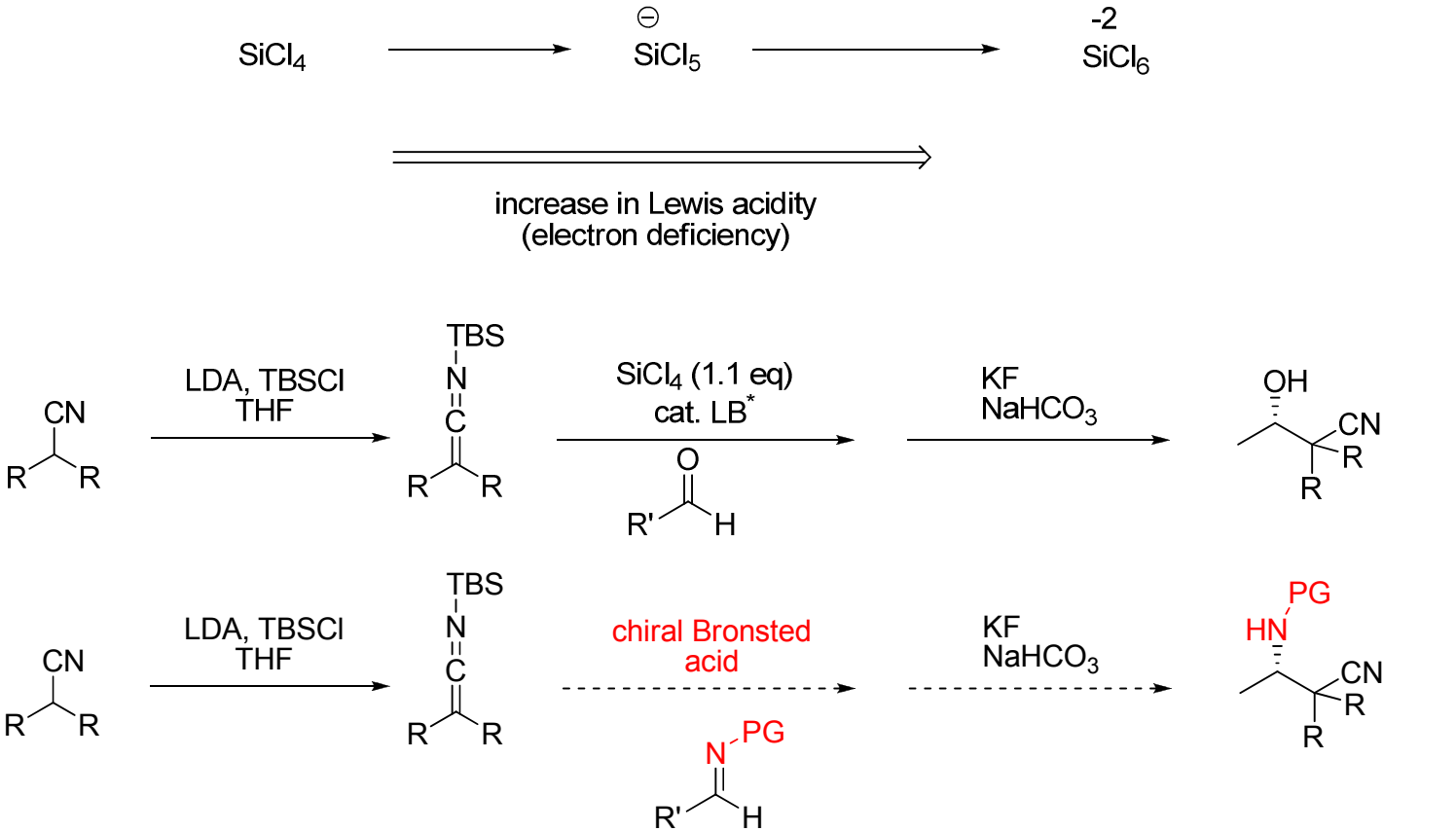
Exposition

Scott Denmark - Lewis Base Activation of Lewis Acids



Scott Denmark, Unpublished results.

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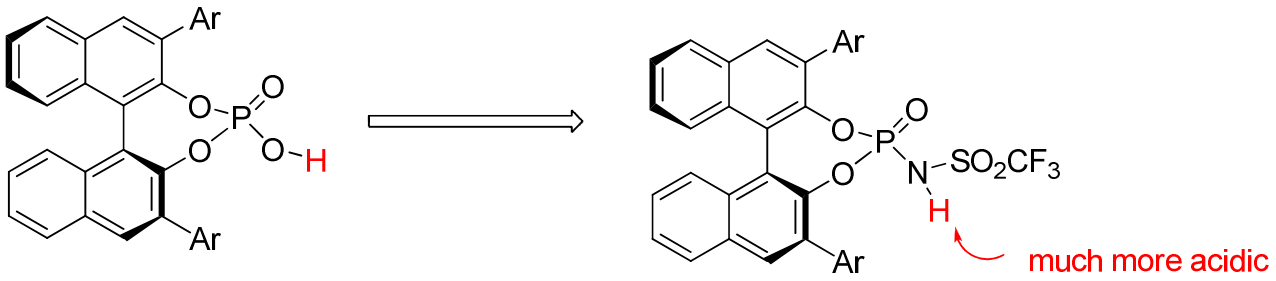
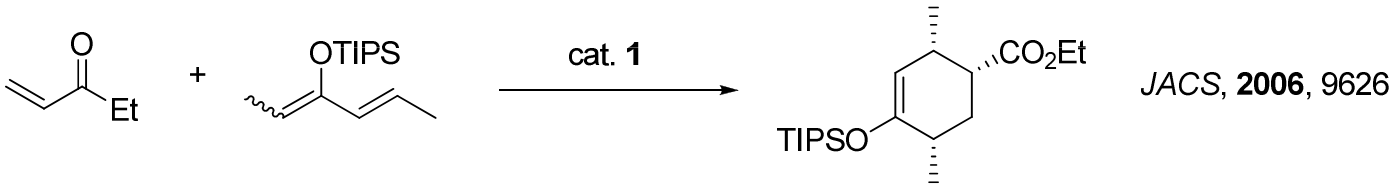
Hisashi Yamamoto - Design of Super Bronsted Acids

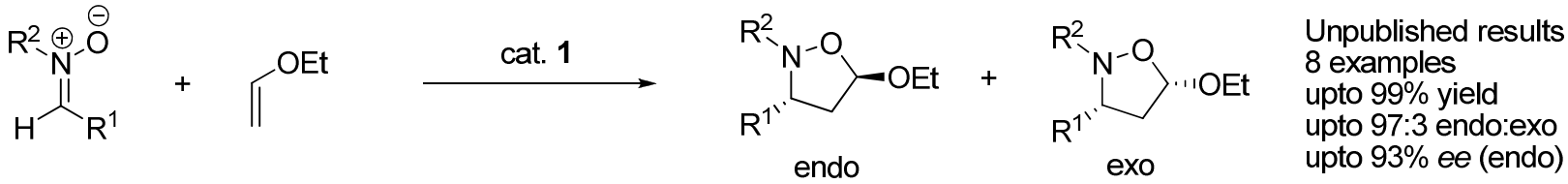


1

Ar = 2,4,6-(*i*-Pr)$_3$C$_6$H$_2$

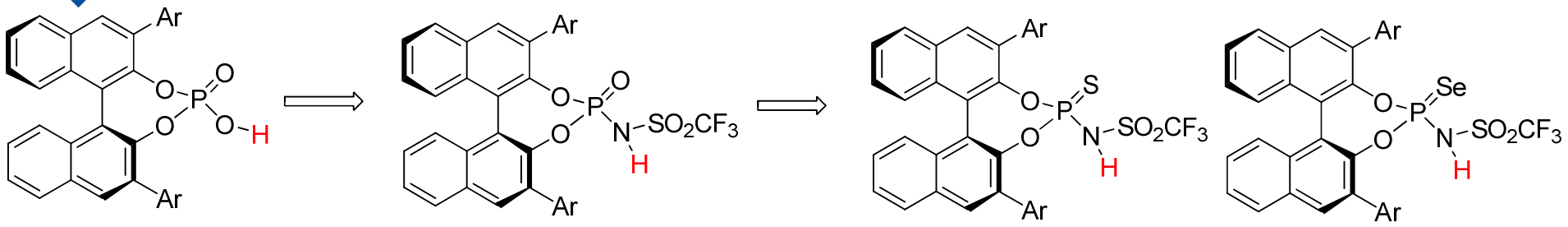


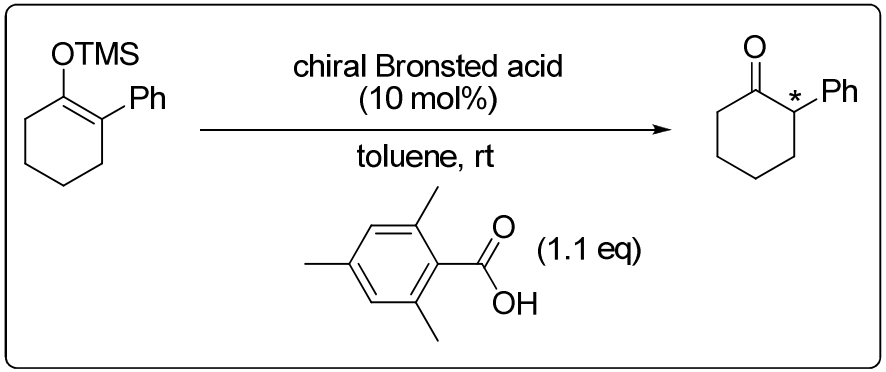
JACS, **2006**, 9626

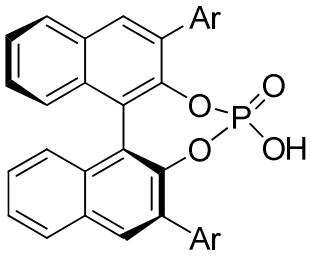


Unpublished results
8 examples
upto 99% yield
upto 97:3 endo:exo
upto 93% *ee* (endo)

Hisashi Yamamoto - Even More Acidic Systems?



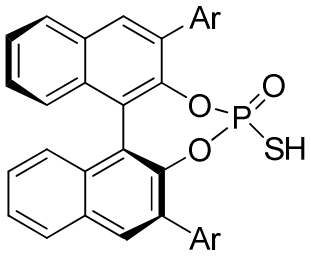




72 h

0% conversion

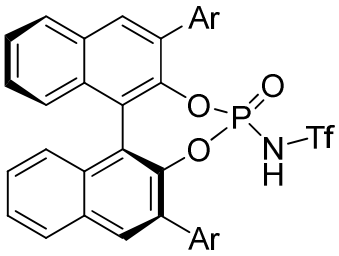
no *ee*



72 h

trace

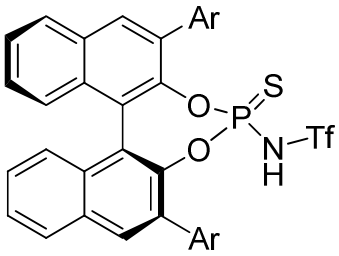
no *ee*



4.5 h

100% conversion

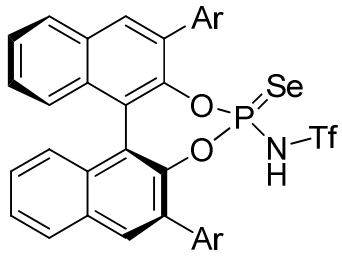
54% *ee*



3.5 h

100% conversion

78% *ee*



3.5 h

100% conversion

72% *ee*

Who?

George Whitesides (Harvard)

Scott Denmark (UIUC)

Masakatsu Shibasaki (U. Tokyo)

Elias J. Corey (Harvard)

Hisashi Yamamoto (U. Chicago)

David Macmillan (Princeton U.)

Scott Schaus (Boston U.)

Samuel Danishefsky (Columbia)

Kevin Campos (Merck)

Yoshinori Yamamoto (Tohoku U., Japan)

Amir Hoveyda (Boston College)

Vladimir Birman (Washington U.)

Phil Baran (Scripps)

Amos Smith (U. Penn.)

Dale Boger (Scripps)

Gregory Fu (MIT)

John Hartwig (UIUC)

Michael Krische (U. Texas)

Student Speakers

Student Posters

Exposition

The Schaus Group - Asymmetric Boration with Chiral Diols

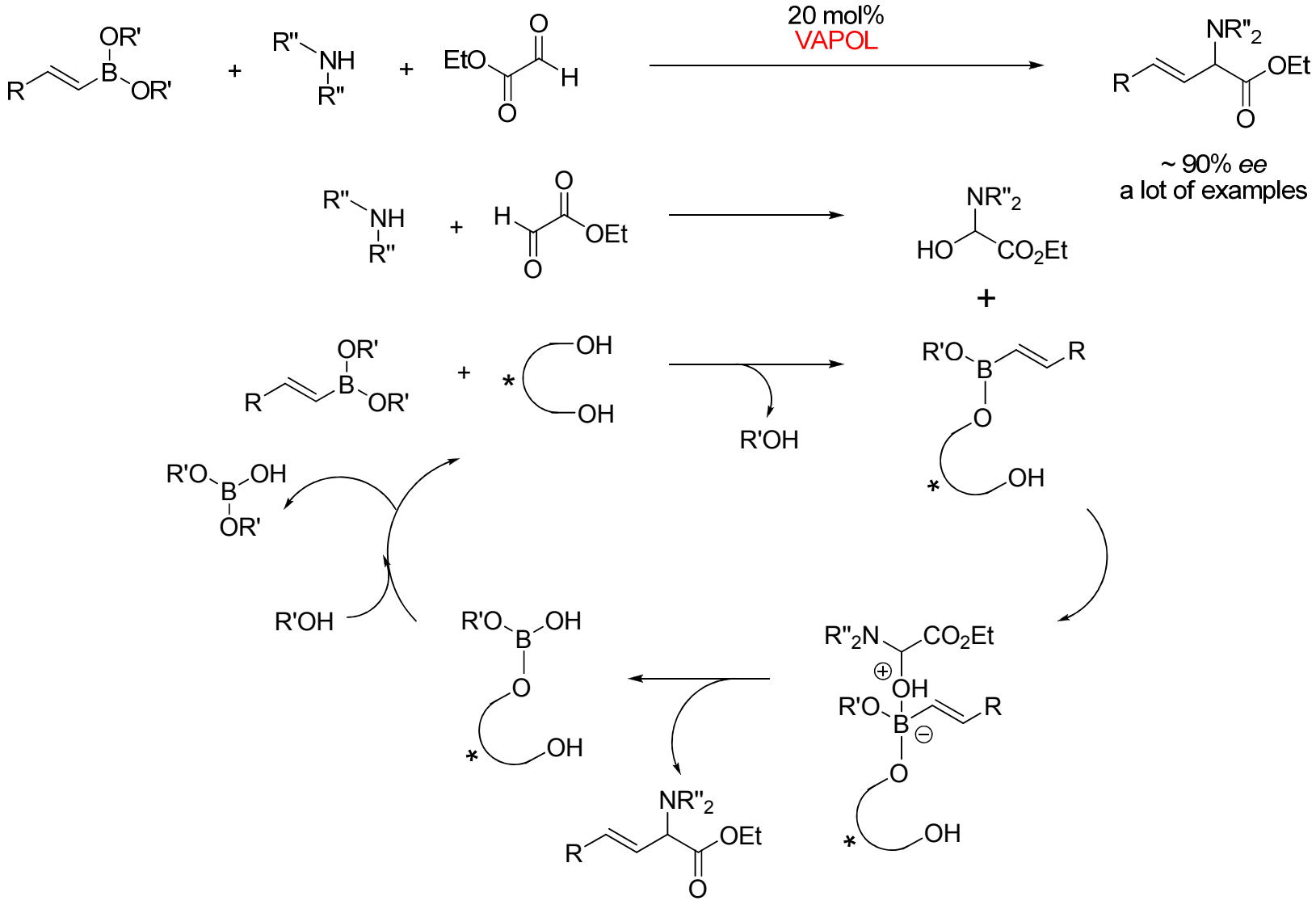
First General Catalytic Asymmetric Petathesis Reaction

~ 90% *ee*
a lot of examples

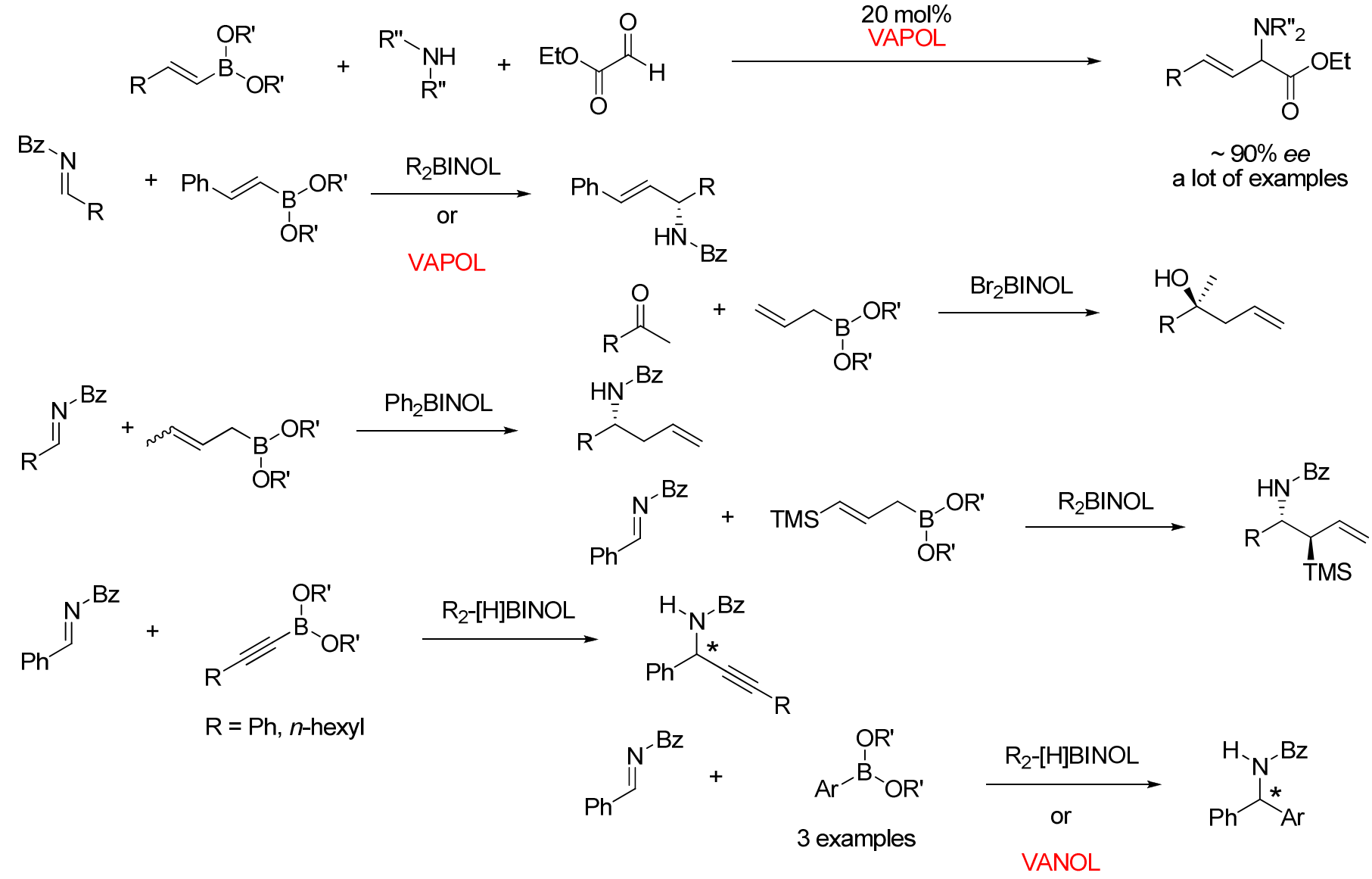
R	R'	some variation of the amine
Ph	^{i}Pr	match/mismatch studies
p-OMeC$_6$H$_4$	*n*-Bu	
p-BrC$_6$H$_4$	Et	
m-CF$_3$C$_6$H$_4$		
m-FC$_6$H$_4$		
2-thiophenyl		
cyclohexyl		
n-butyl		
primary alkyl		
1,1-disubstituted		

The Schaus Group - Asymmetric Boration with Chiral Diols

First General Catalytic Asymmetric Petathesis Reaction



The Schaus Group - Asymmetric Boration with Chiral Diols



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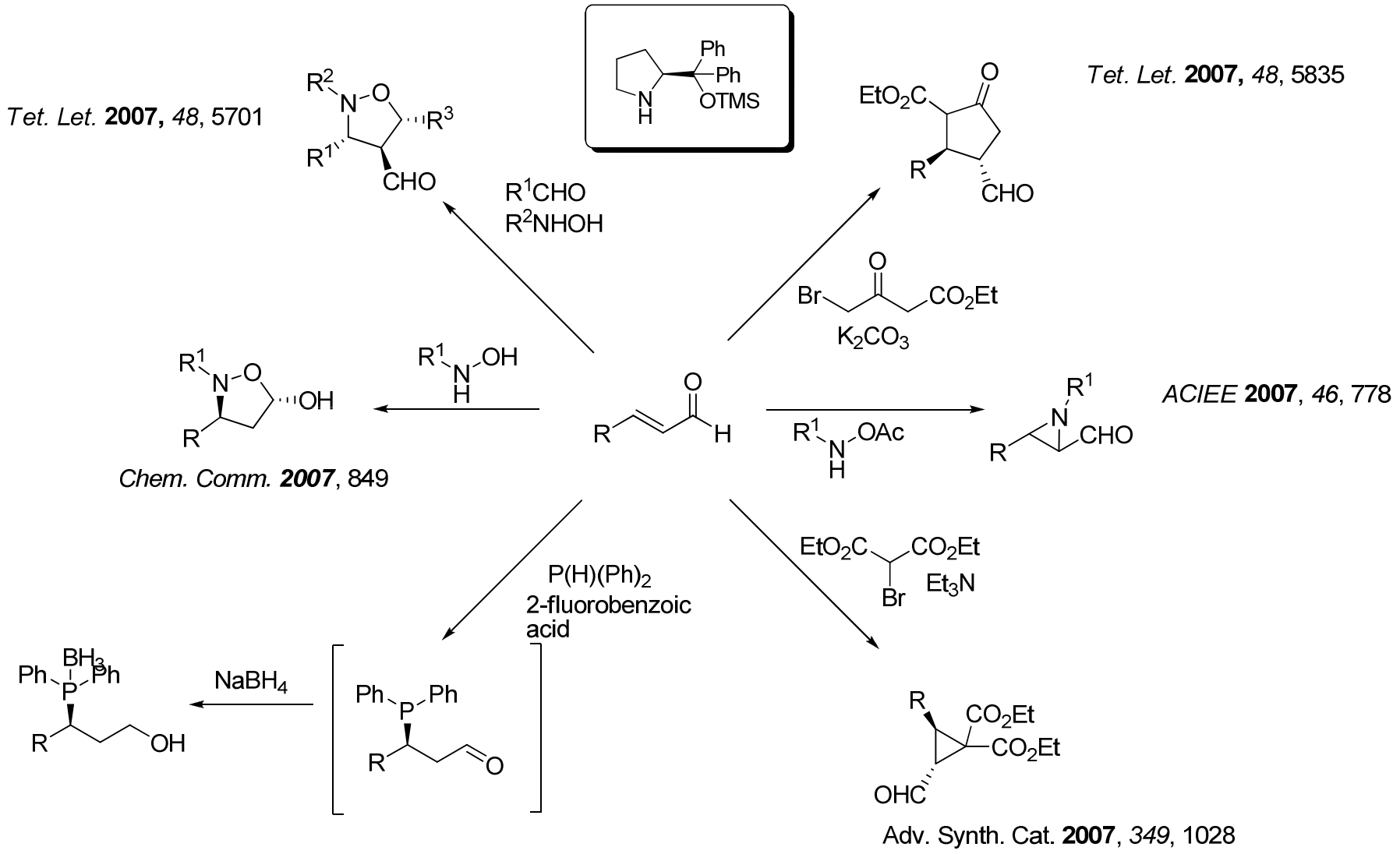
Exposition

The Cordova Group - Proline Catalysis (6 posters!)



Tet. Let. **2007,** *48*, 5701

Tet. Let. **2007,** *48*, 5835

Chem. Comm. ***2007***, 849

ACIEE **2007**, *46*, 778

Adv. Synth. Cat. **2007**, *349*, 1028

The Take-Home Message

It is good to go to conferences because…

Expand your knowledge of chemistry in your field.

Get lots of new ideas/dreams *(getting them to work is your problem).*

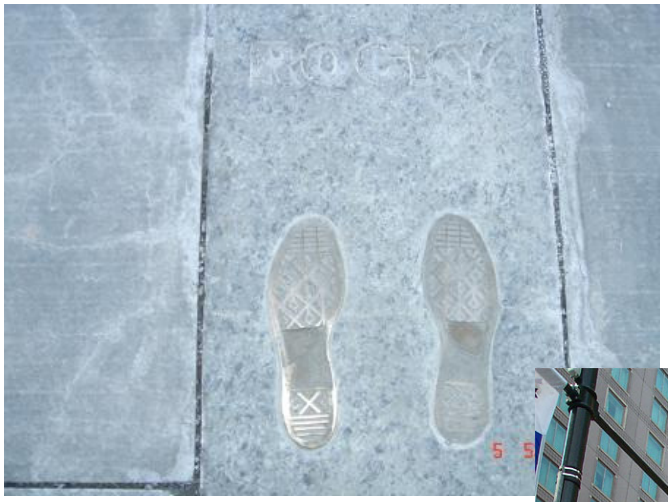
Networking.

Meet new people.

See new places.

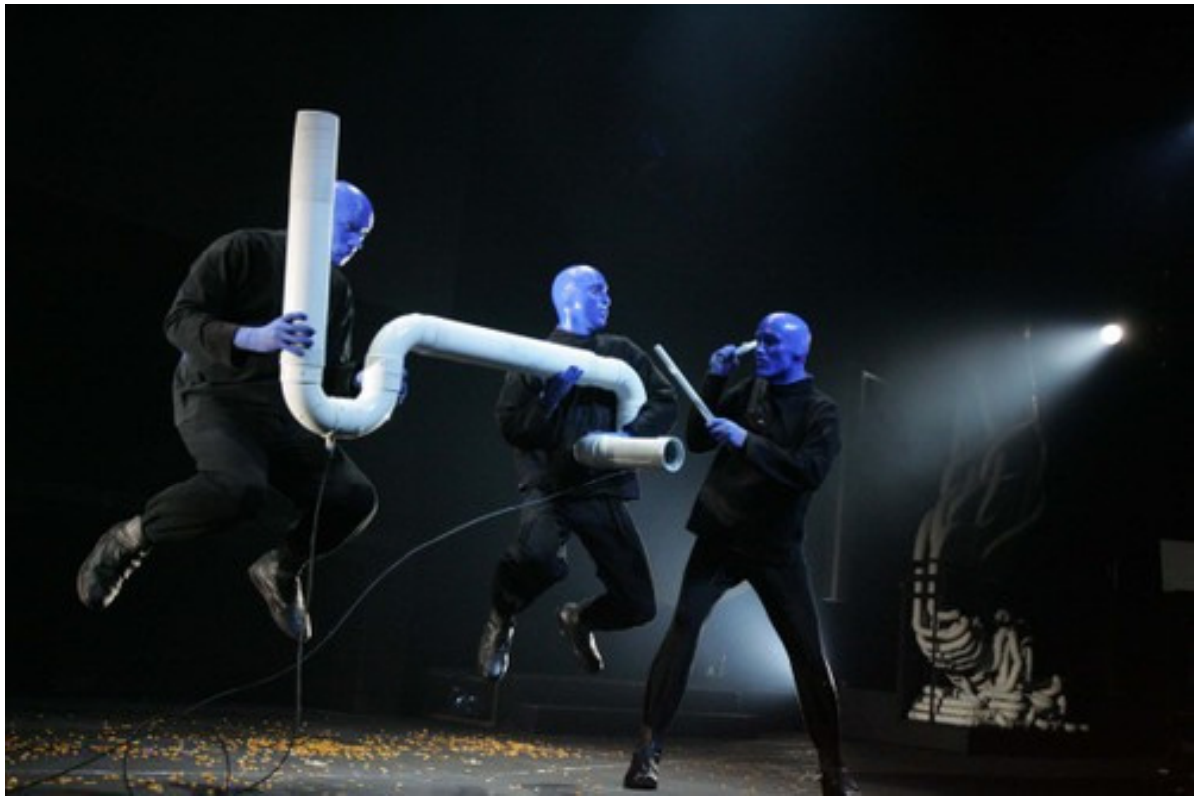
A lot of fun!

All Work And No Play Makes Jack A Dull Boy



Philadelphia

All Work And No Play Makes Jack A Dull Boy



Boston = ACS + Blue Man Show + Restaurants + Bars

- Parents + Friends