

Tools for the Organic Chemist – Free stuff from the internet

ACDC – *Asymmetric Counteranion-Directed Catalysis* (*Catalysis with Chiral Phosphoric Acid Counteranions*)

- List, B. *et al. Angew. Chem. Int. Ed.* **2006**, 45, 4193.
List, B. *et al. J. Am. Chem. Soc.* **2006**, 128, 13368.
List, B. *et al. J. Am. Chem. Soc.* **2007**, 129, 11336.
Toste, D. *et al. Science* **2007**, 317, 496.
Rueping, M. *et al. Angew. Chem. Int. Ed.* **2007**, 46, 6903.

Aman Desai

21st Sep. 2007

A Group Meeting Literature Presentation

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Tools for the Organic Chemistry – *Free stuff from the internet*

General Websites

Tools

Research Group Websites

Lab Techniques

Blogs

Industrial/Pharmaceutical Links

The Fun Stuff

General Websites

1. Google Scholar (www.scholar.google.com)
 - Search across many disciplines and sources: peer-reviewed papers, theses, books, abstracts and articles, from academic publishers, professional societies, preprint repositories, universities and other scholarly organizations.
 - Features like Gmail.
2. Google Reader (www.reader.google.com)
 - Subscribe to various journals/news websites/blogs.
 - Get regular updates in your reader inbox from those websites – without going to those websites.
 - For example, ASAP articles from JACS.
 - Features like Gmail.
3. Organic Division (www.organicdivision.org)
 - A million links
 - Organic data tables – Chemical reaction/Chemical data/Spectroscopy/Organometallic topics/Nomenclature/Organic Compounds/Techniques *ands links therein!*
 - Organic weblinks – 9 categories and links therein.
 - *An amazing resource.*
4. Organic Syntheses (www.orgsynth.org)
 - Annual/collective volumes

Tools

1. Web of Science

(<http://portal.isiknowledge.com/portal.cgi?DestApp=WOS&Func=Frame&Init=Ye>)

- For citation alerts.
- *Room service* – Every time a reference cites your selected articles, they send you an email.

2. e-EROS – Encyclopedia of Reagents for Organic Synthesis

(<http://www3.interscience.wiley.com/cgi-bin/mrwhome/104554785/HOME?CRETR>)

- Database of 70,000 reactions & 4,000 most frequently consulted reagents.
- Search by: chemical structure – substructure – reagent – reaction type – experimental conditions – etc.
- *Very useful and practical.*

3. NMR Databases

- Spectral database for organic compounds, SDBS
(http://riodb01.ibase.aist.go.jp/sdbs/cgi-bin/cre_index.cgi?lang=eng)
- <http://www.chem.wisc.edu/areas/organic/index-chem.htm>
- www.sigmaaldrich.com

4. Boiling point calculation at different temperatures/pressures

- <http://www.ch.cam.ac.uk/magnus/boil.html>
- [http://www.sigmaaldrich.com/Area_of_Interest/Research_Essentials/Solvents/Key Resources/nomograph.html](http://www.sigmaaldrich.com/Area_of_Interest/Research_Essentials/Solvents/Key_Resources/nomograph.html)

Tools

5. Named Reactions

- <http://themerckindex.chemfinder.com/TheMerckIndex/NameReactions/TOC.asp>
- <http://www.monomerchem.com/display4.html>
- <http://orgchem.chem.uconn.edu/namereact/named.html>
- http://www.geocities.com/chempen_software/reactions.htm

Research Group Websites

1. Allison Frontier – Not Voodoo (Demystifying Synthetic Organic Lab. Techniques)
(<http://chem.chem.rochester.edu/~nvd/>)
 - Tour of collective wisdom – browse by experience level.
 - Magic formulas eg. work up formulas etc.
 - Interesting, funny statistics.
 - Troubleshooting, tips and advices – practical and lab level.
2. David Evans, Harvard University
3. Douglas Taber (www.organic-chemistry.org)

Lab Techniques

1. Allison Frontier – Not Voodoo (Demystifying Synthetic Organic Lab. Techniques) (<http://chem.chem.rochester.edu/~nvd/>)
2. Al's Notebook (www.alsnotebook.com)
 - A collection of commonly used experimental procedures and other interesting stuff for synthetic chemists

Blogs

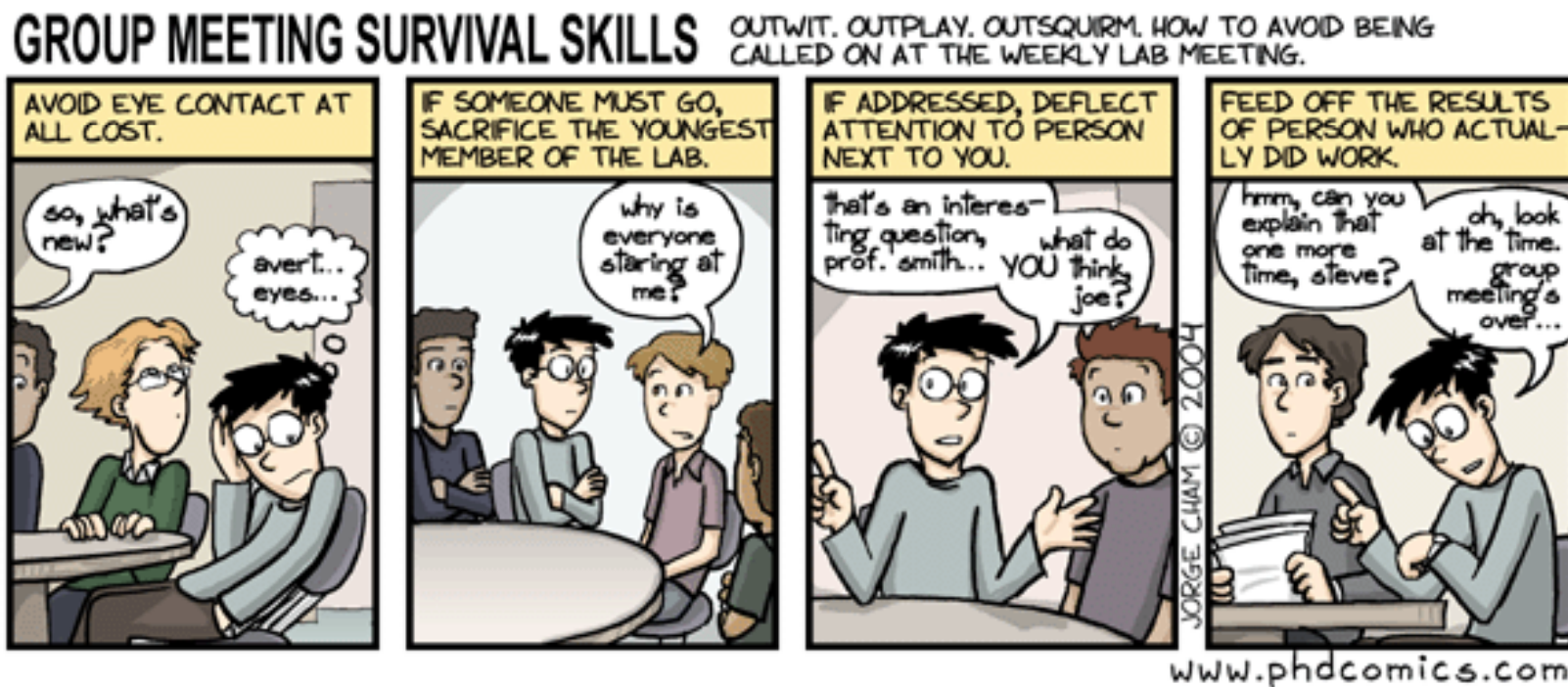
1. Corante “In The Pipeline” – Derek Lowe (www.pipeline.corante.com)
 - Pharmaceutical industry blog.
2. www.totallysynthetic.com
 - The latest and best total syntheses – dissected nicely.
 - Retrosynthesis and key forward steps.
3. www.blog.chembark.com

Industrial/Pharmaceutical Links

1. Product/chemical search – product information/vendors/suppliers
 - www.emolecules.com – Over 7 million chemicals
 - www.chemnet.com – Chinese website with good information about Indian/Chinese vendors
 - www.globalspec.com – Engineering Search Engine – Product/Suppliers
2. Patents
 - www.uspto.gov – US patents
 - www.espacenet.com – Worldwide/European patents
 - www.freepatent.com
 - www.pat2pdf.org
 - www.patentstorm.us
 - www.google.com/patents
3. MSDS (Material Safety Data Sheets)
 - www.msds.com

The Fun Stuff

1. Molecules with silly/unusual names
 - <http://www.chm.bris.ac.uk/sillymolecules/silymols.htm>
2. www.phdcomics.com
 - *you are not a phd student if you haven't spent hours on this website!*



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ACDC – ***Asymmetric Counteranion-Directed Catalysis***
(*Catalysis with Chiral Phosphoric Acid Counteranions*)

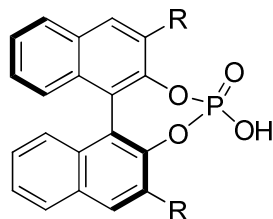
- List, B. *et al. Angew. Chem. Int. Ed.* **2006**, 45, 4193.
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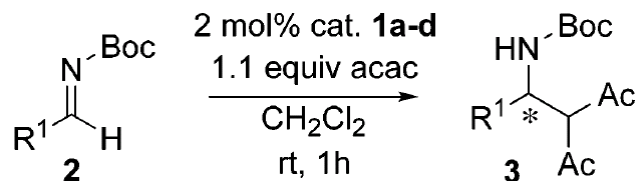
A Group Meeting Literature Presentation

Chiral Phosphoric Acids – Powerful Organocatalysts



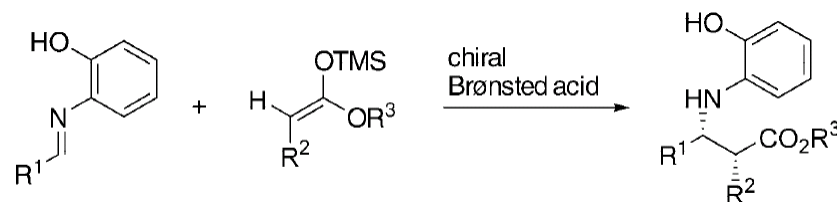
Terada, *JACS* **2004**, 5356

Mannich Reaction: R = 4-(β -naph.)-C₆H₄



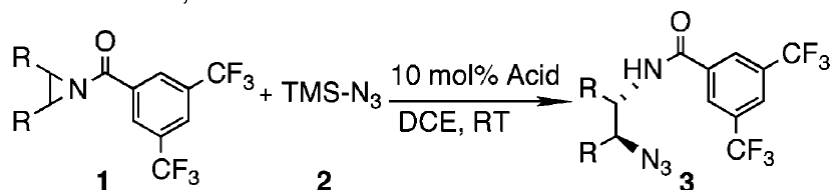
Akiyama, *ACIEE* **2004**, 1566

Mannich Reaction: R = 4-NO₂C₆H₄

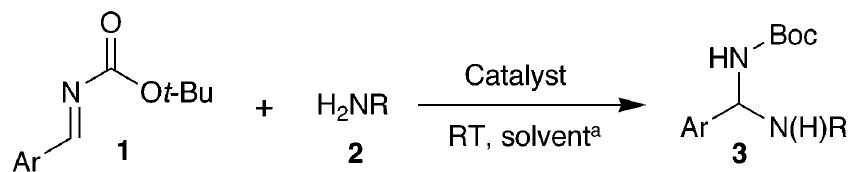


Explosive growth in the field in the last 4 years

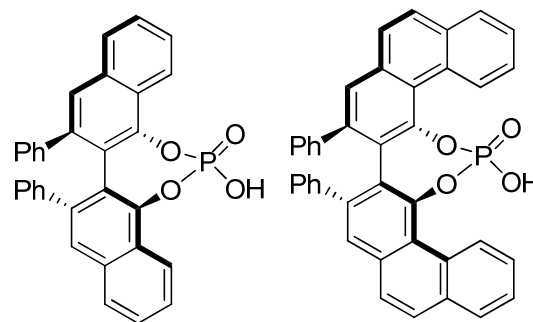
JACS **2007**, ASAP.



JACS **2005**, 127, 15696



Jon C. Antilla, Wulff Group Alumni



Chiral Counteranions – Emerging Field in Catalysis

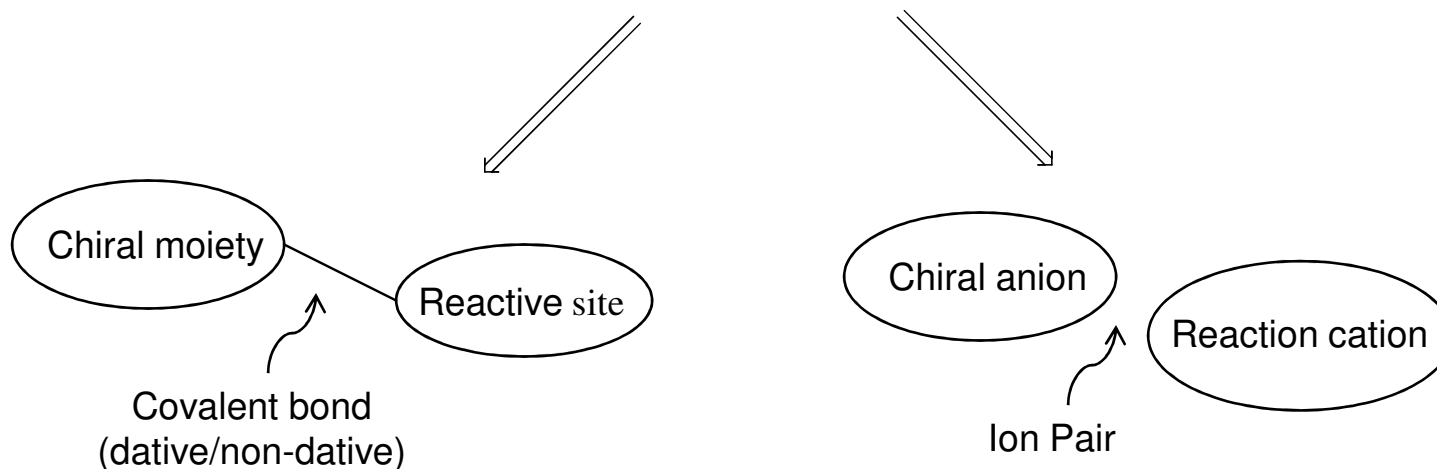
Chiral compounds – requirement for agrochemical/pharmaceutical purposes



Nature's "chiral pool" or

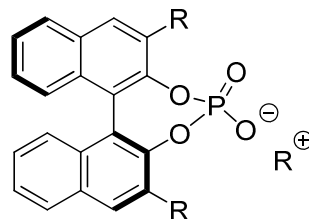
Resolution of a racemate or

Asymmetric synthesis by chiral catalysts



Same or small library of chiral anionic counteranions –
make a wide range of cationic catalysts enantioselective

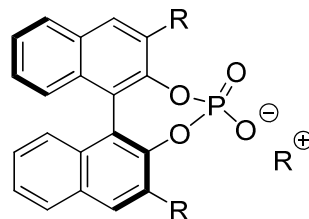
Chiral Phosphoric Acid Counteranions – Emerging Field in Catalysis



Benjamin List – *ACDC*



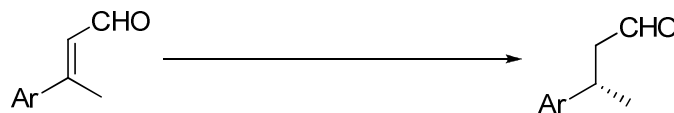
Chiral Phosphoric Acid Counteranions – Emerging Field in Catalysis



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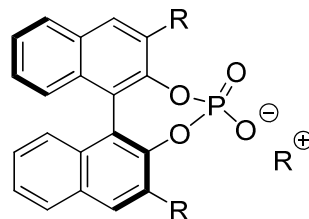
*A*symmetric *C*ounteranion-*D*irected *C*atalysis

“....catalytic reactions that proceed via cationic intermediates can be conducted asymmetrically via the use of a chiral enantiomerically enriched anion incorporated into the catalyst.”

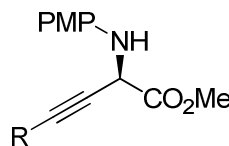
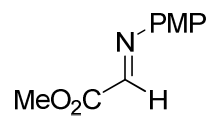
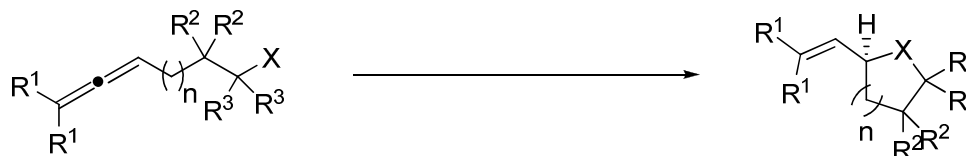


List, *ACIEE*, **2006**, 4193

Chiral Phosphoric Acid Counteranions – Emerging Field in Catalysis

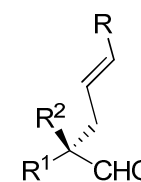
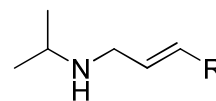
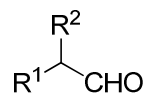


Toste, *Science* **2007**, 496

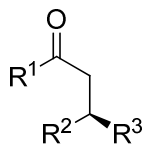
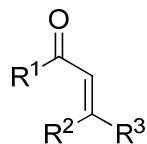


Rueping, *ACIEE* **2007**, 46, 6903.

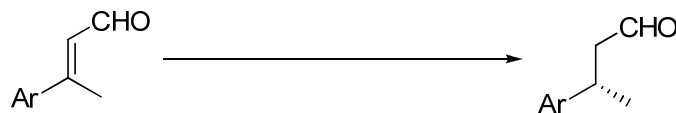
List, *JACS*, **2007**, 11336



List, *JACS*, **2006**, 13368

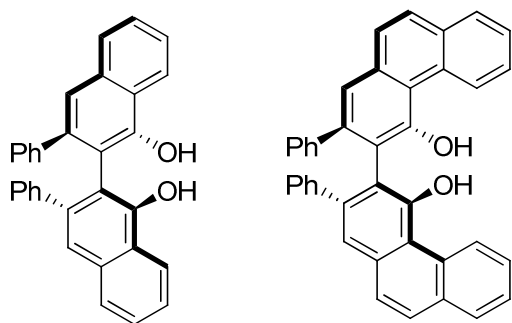


List, *ACIEE*, **2006**, 4193

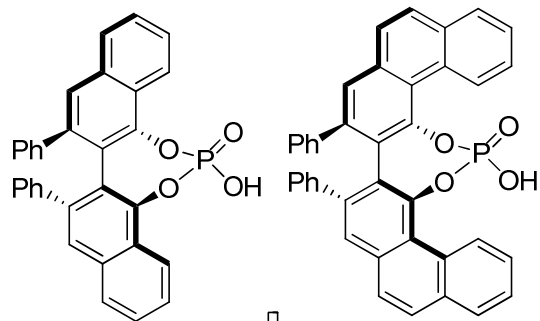


But Why Do I Care?

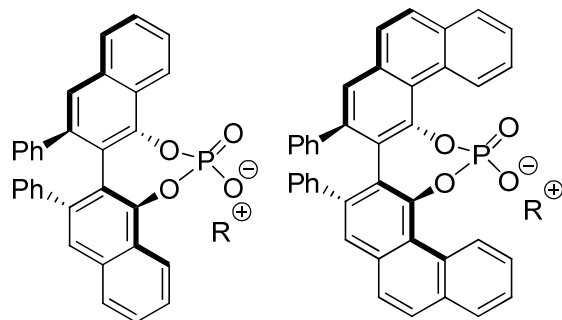
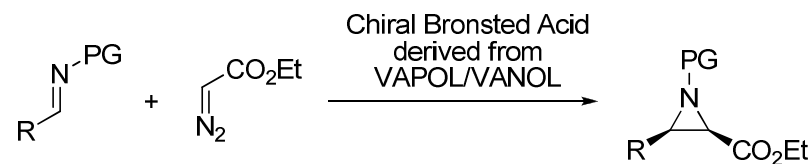
The Ultimate Dream VAPOL & VANOL – “Privileged” Ligands



Successfully applied in various catalytic asymmetric protocols



Promising Bronsted acid catalysts

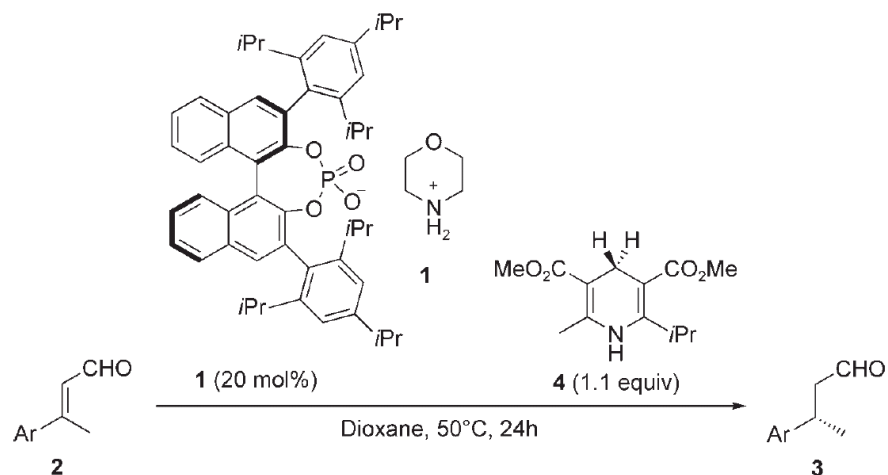


Dual Catalysts????

Now wouldn't that be cool???

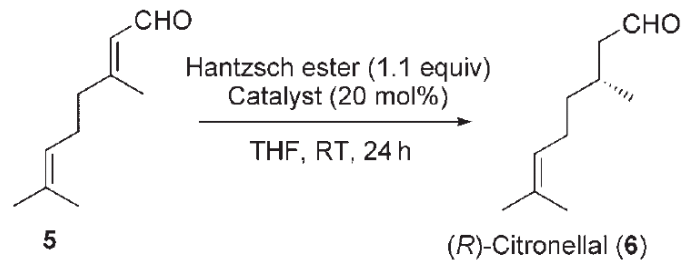
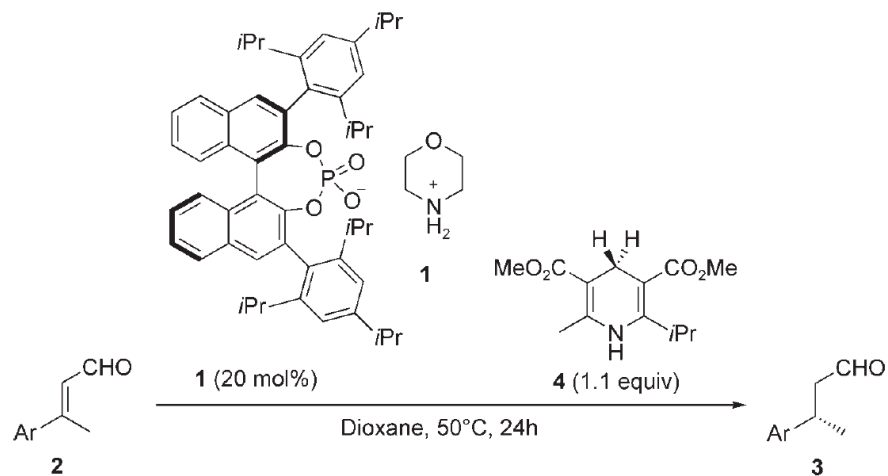
Ideas anyone? ☺

List's *ACDC* – Transfer H₂ of Enals

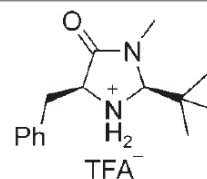


Substrate	Product	Yield [%]	e.r. ^[a]
		87	98:2
		84	99:1
		90	99:1
		67	98:2
		63	99:1
		72	>99:<1
		<5	n.d.

List's *ACDC* – Transfer H₂ of Enals



List, *ACIEE* 2005, 110

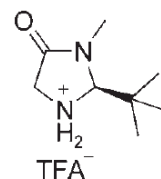


(*S*)-**6**

58^[a]

70:30^[c]

Macmillan *JACS* 2005, 32



(*S*)-**6**

82^[a]

70:30^[d]

This work

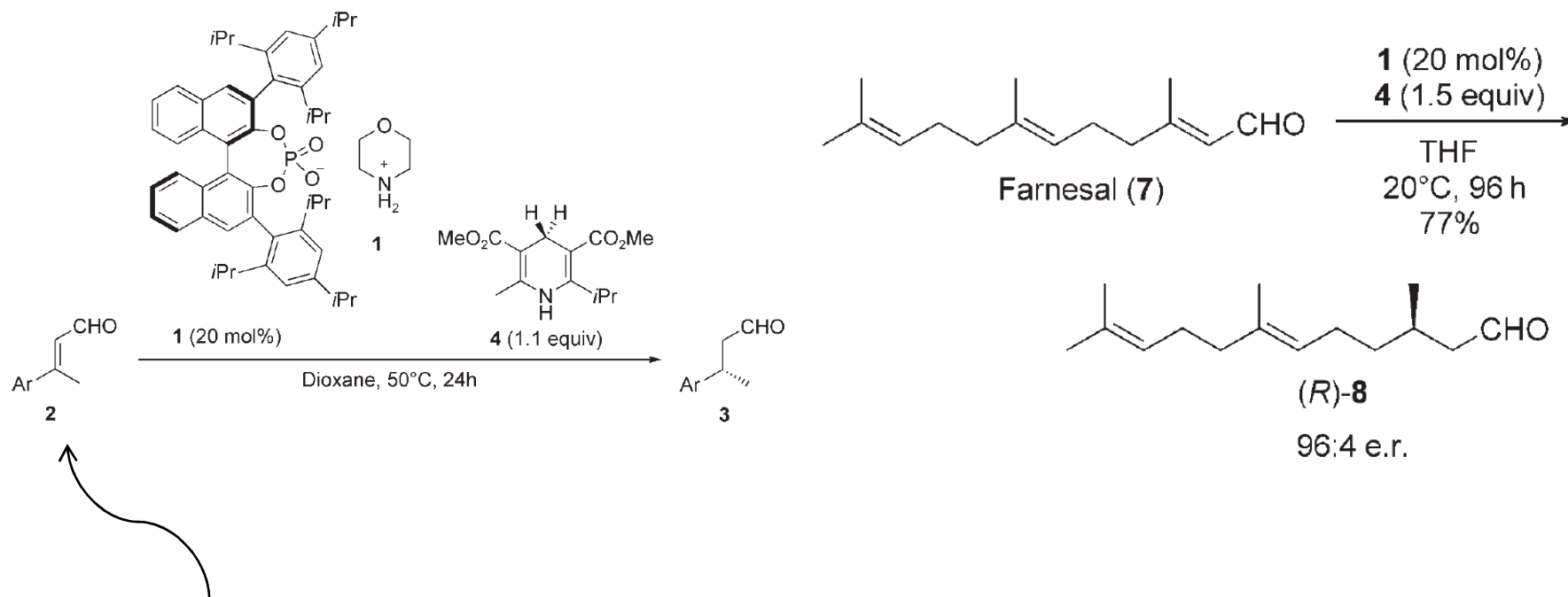
1

(*R*)-**6**

71

95:5

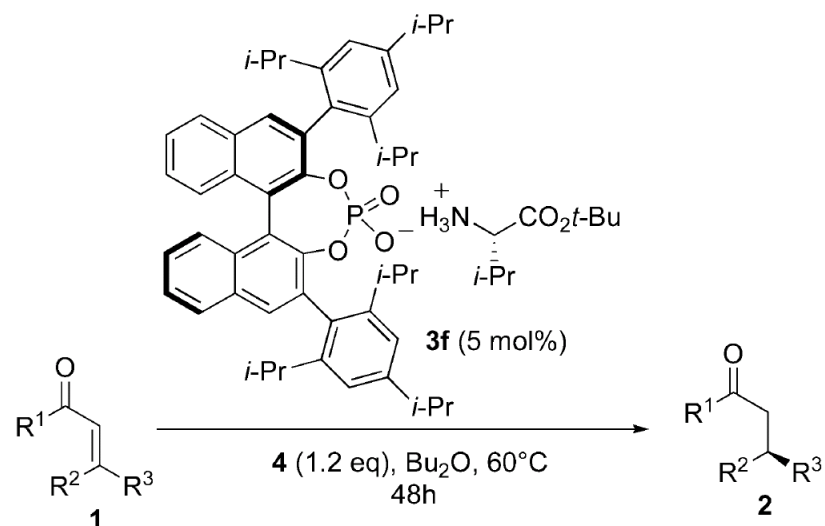
List's *ACDC* – Transfer H₂ of Enals



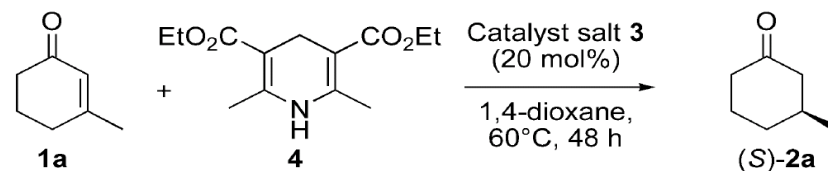
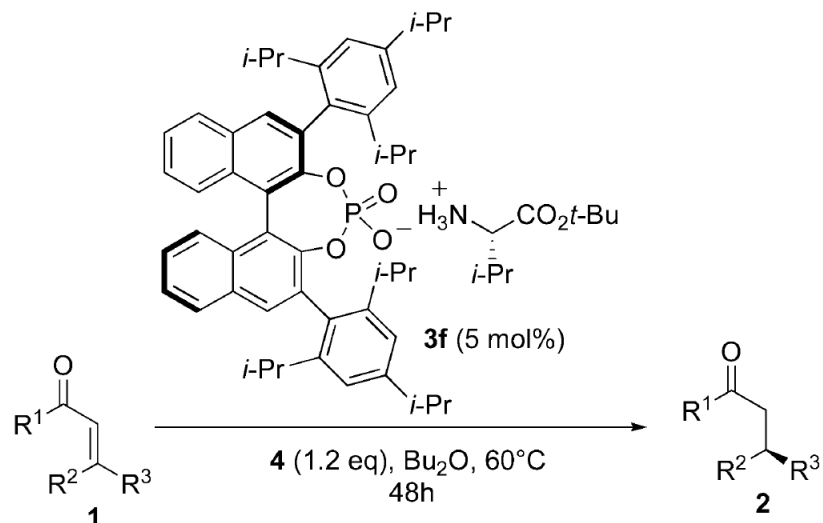
Both E & Z isomers and mixtures provide same enantiomer – Stereoconvergent process

Protocol not good for α,β -unsaturated ketones

List's *ACDC* – Transfer H₂ of Enones

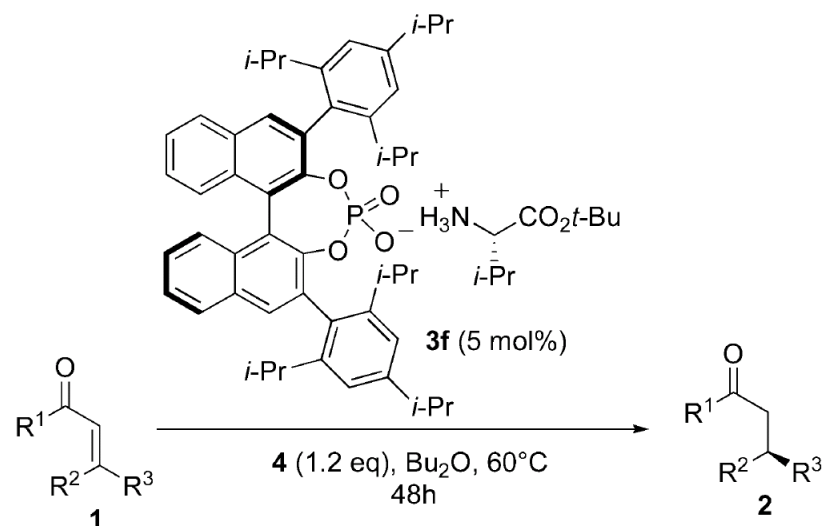


List's *ACDC* – Transfer H₂ of Enones



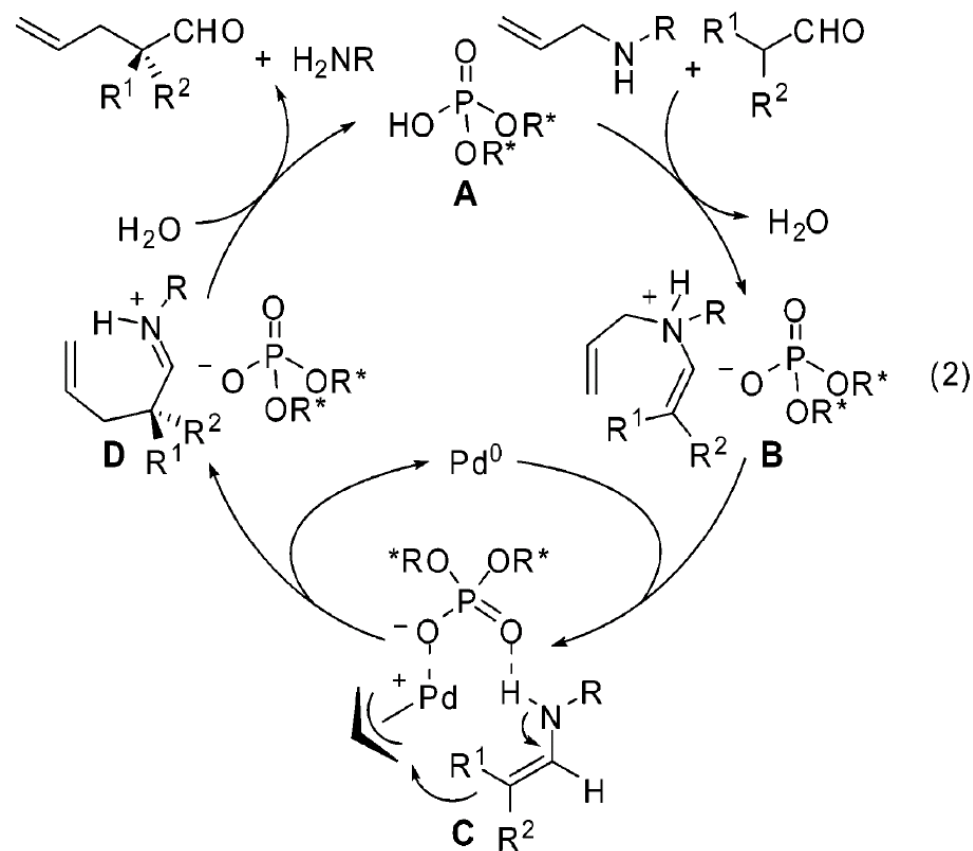
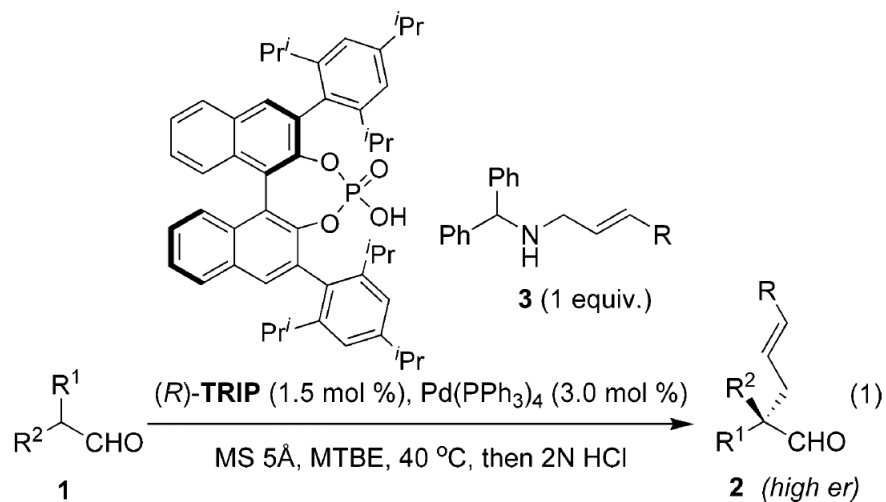
entry	catalyst-cation	-anion	cat.	conv. [%] ^b	er ^b
1		CF ₃ COO ⁻	3a	23	75:25
2		CF ₃ COO ⁻	3b	66	77:23
3		CF ₃ COO ⁻	3c	72	76:24
4		CF ₃ COO ⁻	3d	42	64:36
5 ^c			3e	25	87:13
6		R = 2,4,6-(<i>i</i> -Pr) ₃ C ₆ H ₂	3f	14	95:5
7 ^c		R = 2,4,6-(<i>i</i> -Pr) ₃ C ₆ H ₂	3f	81	97:3
8		R = 2,4,6-(<i>i</i> -Pr) ₃ C ₆ H ₂	3g	66	74:26
9 ^c	H ⁺	R = 2,4,6-(<i>i</i> -Pr) ₃ C ₆ H ₂	3h	5	40:60
10 ^c		R = 2,4,6-(<i>i</i> -Pr) ₃ C ₆ H ₂ (S)-Enantiomer	3i	45	58:42

List's *ACDC* – Transfer H₂ of Enones

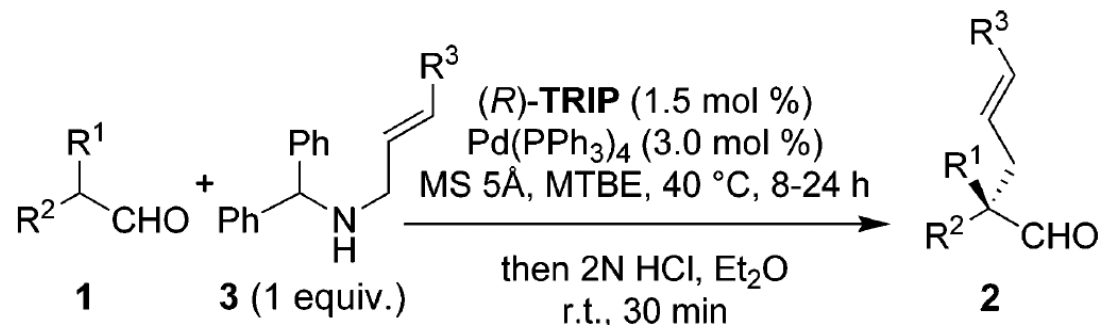


enone	product	yield [%] ^a	er ^{a,b}
R= Me	2a	99	97:3
R= Et	2b	98	98:2
R= <i>i</i> -Bu	2c	89	98:2
R= <i>i</i> -Pr	2d	94	99:1
R= CH ₂ CH ₂ Ph	2e	99 ^c	98:2 ^d
R= Ph	2f	99	92:8
R= Me	2g	78 ^e	99:1
R= Et	2h	71 ^e	98:2
R= CH ₂ CH ₂ Ph	2i	68 ^{d,e}	98:2 ^d
		>99	98:2
R= CO ₂ Et	2k	>99	92:8
R= Ph	2l	81	85:15

List's *ACDC* – α -Allylation of Aldehydes



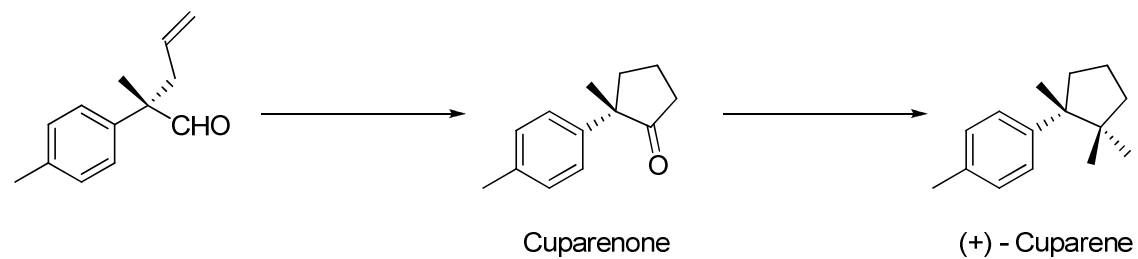
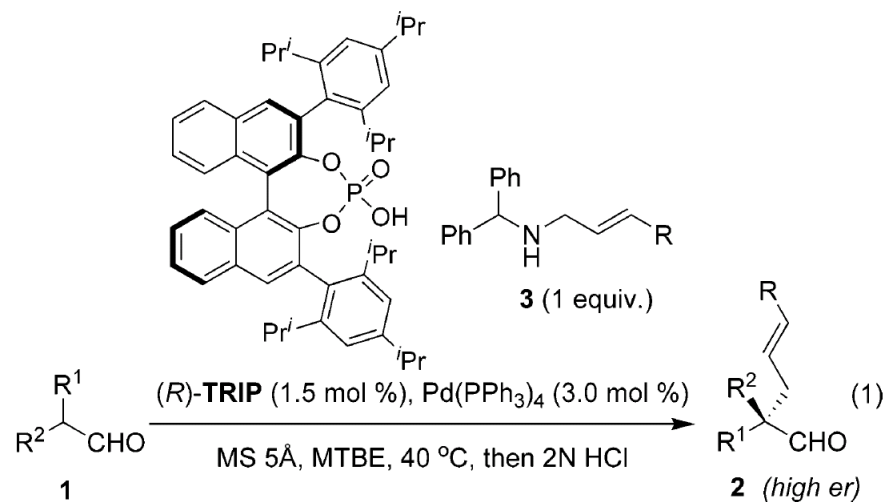
List's *ACDC* – α -Allylation of Aldehydes



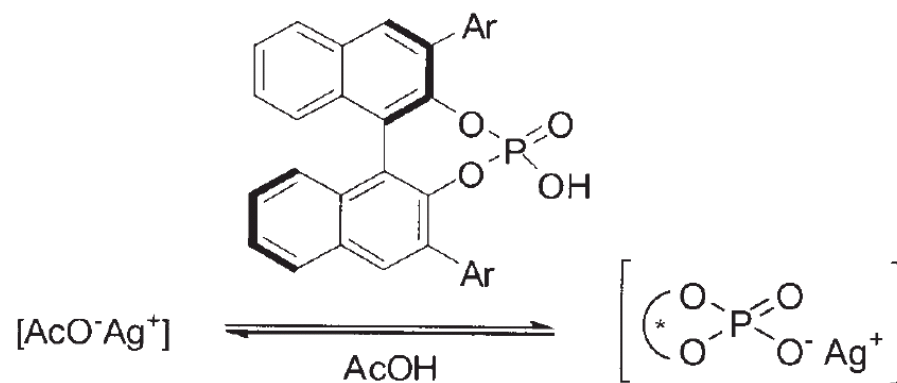
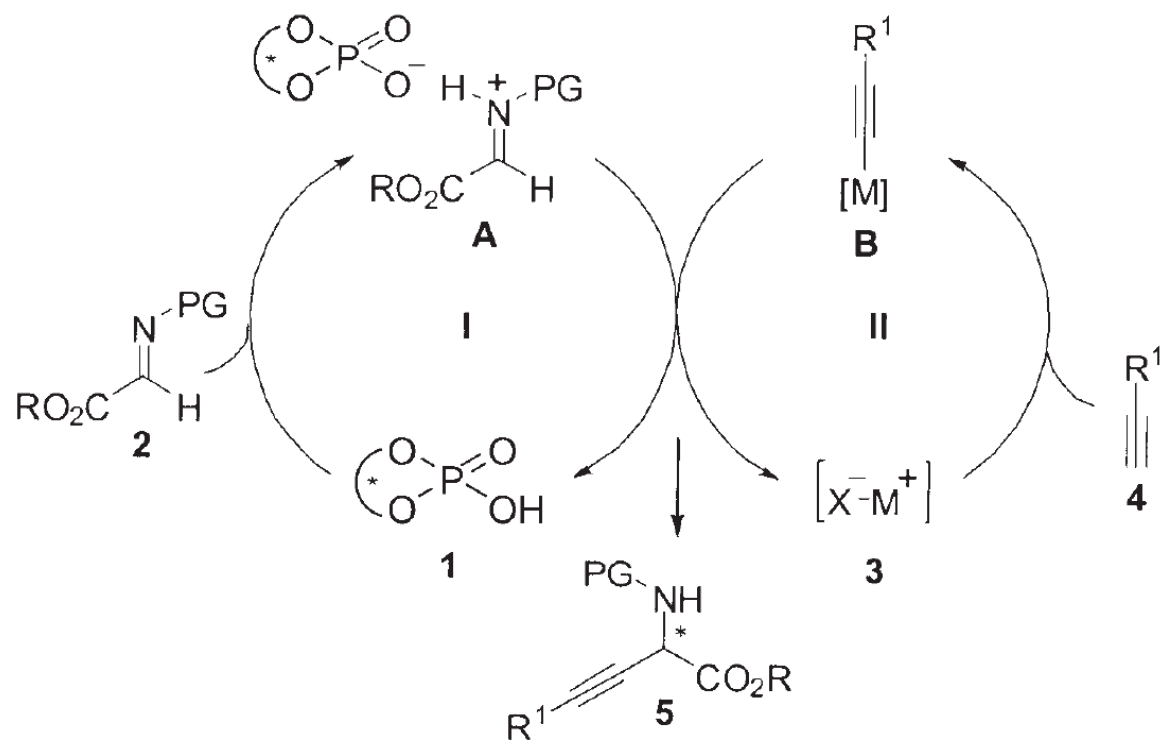
entry	R^1	R^2	R^3		yield (%)	er ^a
1	Me	Ph	H	2a	85	98.5:1.5
2	Me	4-Me-C ₆ H ₄	H	2b	89	97:3
3	Me	3-Me-C ₆ H ₄	H	2c	84	98:2
4	Me	3-F-C ₆ H ₄	H	2d	85	98:2
5 ^b	Me	2-F-C ₆ H ₄	H	2e	74	97:3
6	Me	4- <i>i</i> -Bu-C ₆ H ₄	H	2f	76	97.5:2.5
7	Me	2-naph	H	2g	71	97:3
8	Me	2-thiophenyl	H	2h	80	93:7
9			H	2i	45	95:5
10 ^c	Me	<i>c</i> -hex	H	2j	65	85:15
11 ^{d,e}	Me	Ph	Me	2k	40	96:4
12 ^{d,e}	Me	Ph	Ph	2l	82	91:9

^a From GC or HPLC. ^b Reaction run at 50 °C. ^c Reaction run at 110 °C in toluene. ^d Reaction run at 60 °C. ^e Reaction run for 72 h.

List's *ACDC* – α -Allylation of Aldehydes

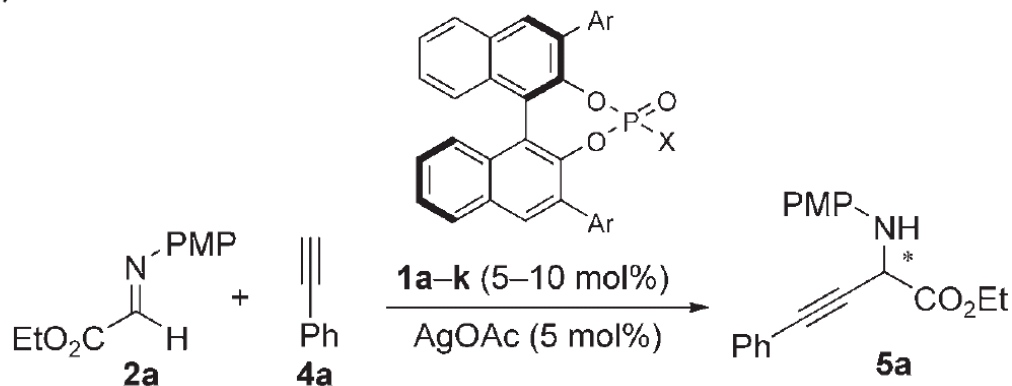


Rueping's *ACOC* – Alkynylation of α -Imino Esters



Rueping's *ACDC* – Alkynylation of α -Imino Esters

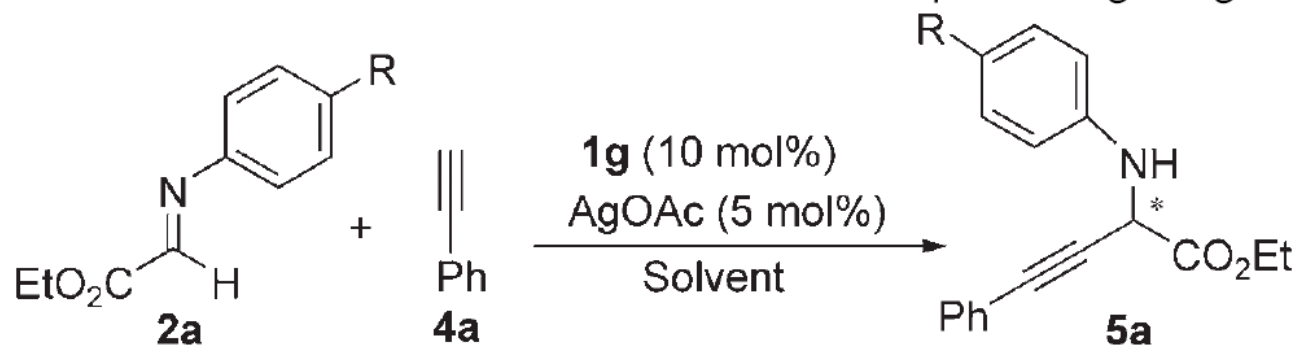
Table 1: Chiral Brønsted acids in the enantioselective silver-catalyzed alkyne addition.



Entry ^[a]	1	Ar	X	1 [mol %]	e.r. ^[b]
1	1a	phenyl ^[c]	OH	10	57:14
2	1b	4-biphenyl	OH	5	55:45
3	1c	1-naphthyl ^[c]	OH	10	55:45
4	1d	2-naphthyl	OH	10	54:46
5	1e	3,5-(CF ₃) ₂ -C ₆ H ₃	OH	5	62:38
6	1f	3,5- <i>t</i> Bu ₂ -PMP	OH	5	49:51
7	1g	9-phenanthryl	OH	5	86:14
8	1g	9-phenanthryl	OH	10	91:9
9	1h	[H] ₈ Ph ₃ Si	OH	5	69:31
10	1i	9-anthracenyl	OH	10	91:9
11	1j	9-phenanthryl ^[d]	NHTf	10	41:59
12	1k	9-anthracenyl ^[d]	NHTf	10	31:69

Rueping's *ACOC* – Alkynylation of α -Imino Esters

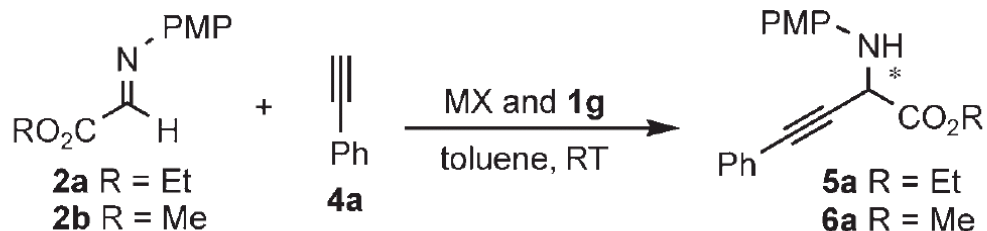
Table 2: Evaluation of solvents and protecting groups.



Entry ^[a]	Solvent	R	e.r. ^[b]
1	benzene	OMe	86:14
2	toluene	OMe	91:9
3	p-xylene	OMe	84:16
4	CH ₂ Cl ₂	OMe	76:24
5	CHCl ₃	OMe	53:47
6	(<i>n</i> Bu) ₂ O	OMe	73:27
7	toluene	OEt	82:18
8	toluene	Opentyl	88:12
9	toluene	OCF ₃	58:42
10	toluene	OPh	76:24

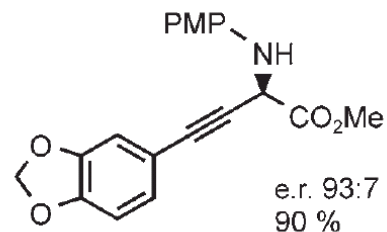
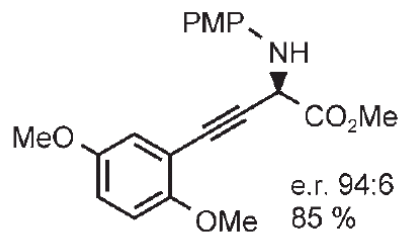
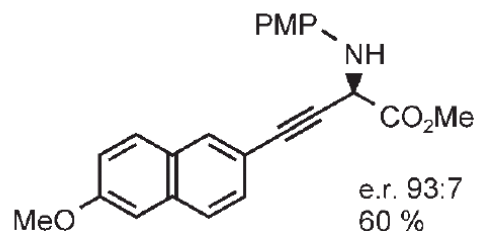
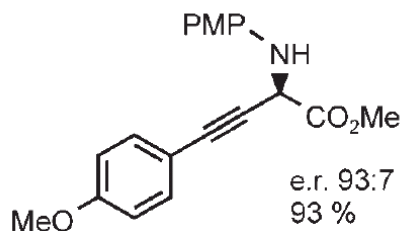
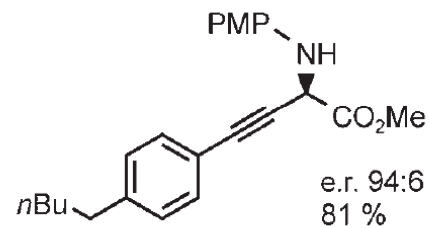
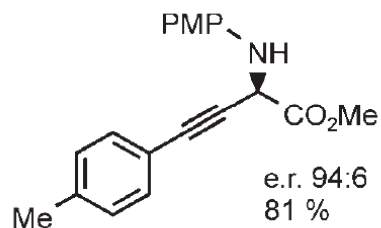
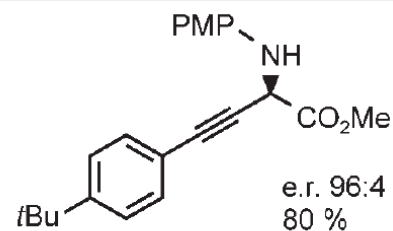
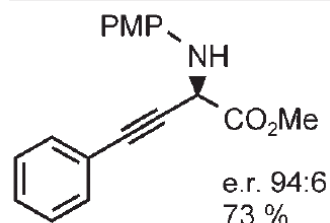
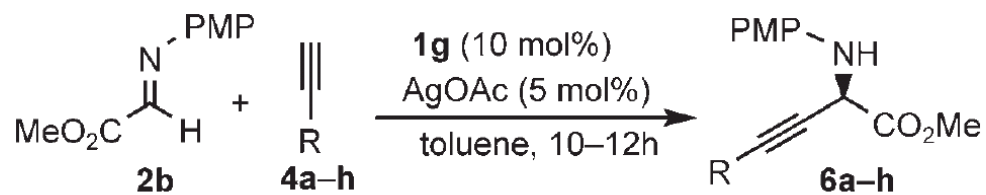
Rueping's *ACDC* – Alkynylation of α -Imino Esters

Table 3: Variation of the metal salts, catalyst loading, and *N*-PMP-imino ester.

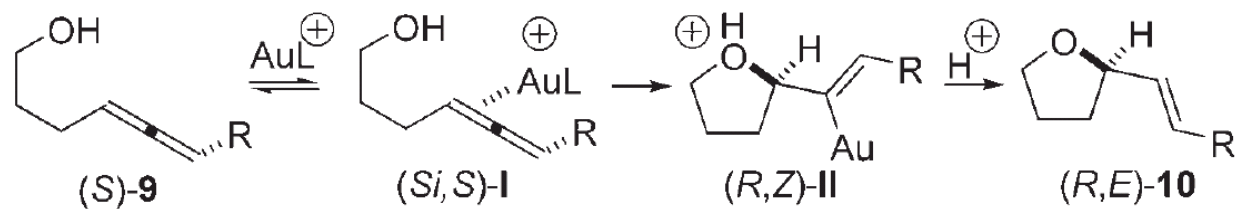
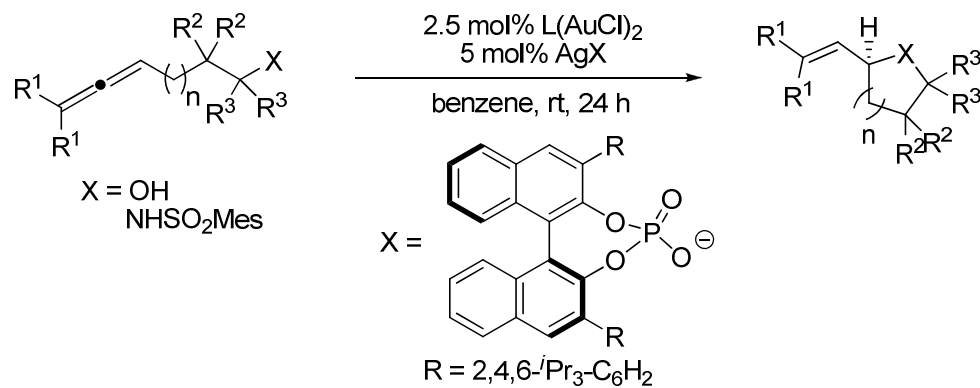


Entry ^[a]	MX	MX [mol %]	1 g [mol %]	R	e.r. ^[b]
1	–	–	10	Et	n.d. ^[c]
2	AcOAc	10	–	Et	n.d.
3	AgOAc	5	2	Et	76:24
4	AgOAc	5	5	Et	86:14
5	AgOAc	5	10	Et	91:9
6	AgOAc	5	10	Me	94:6
7	AgOAc	5	20	Et	87:13
8	AgOBz	5	5	Et	65:35
9	Ag ₂ O	2.5	5	Et	55:45
10	Ag ₂ CO ₃	2.5	5	Et	73:27
11	AgCO ₂ CF ₃	5	10	Et	85:15
12	AgSO ₃ CF ₃	5	10	Et	72:28
13	AgNO ₃	5	10	Et	81:19
14	AgBF ₄	5	10	Et	79:21
15	CuOAc	5	10	Et	92:8
16	Cu(OAc) ₂	5	10	Et	93:7

Rueping's *ACOC* – Alkynylation of α -Imino Esters

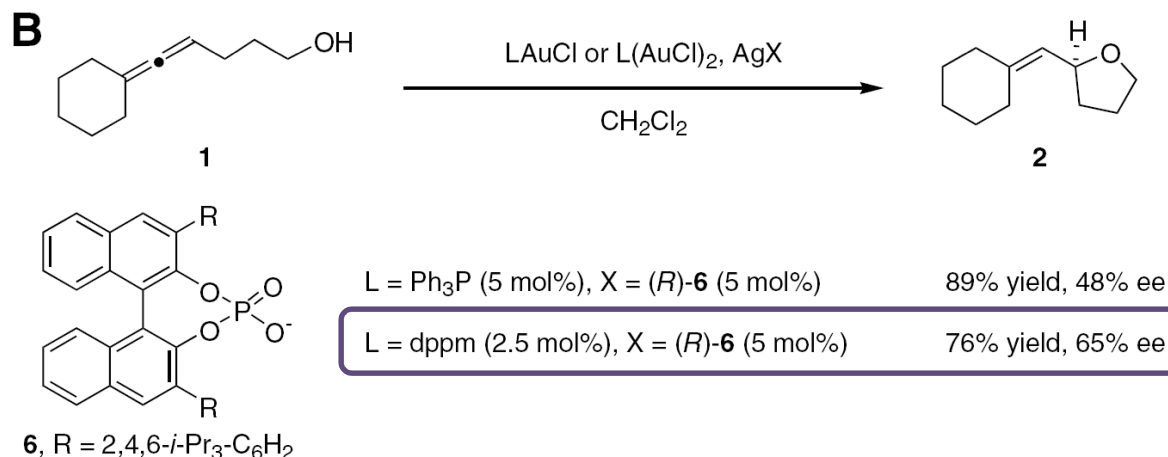
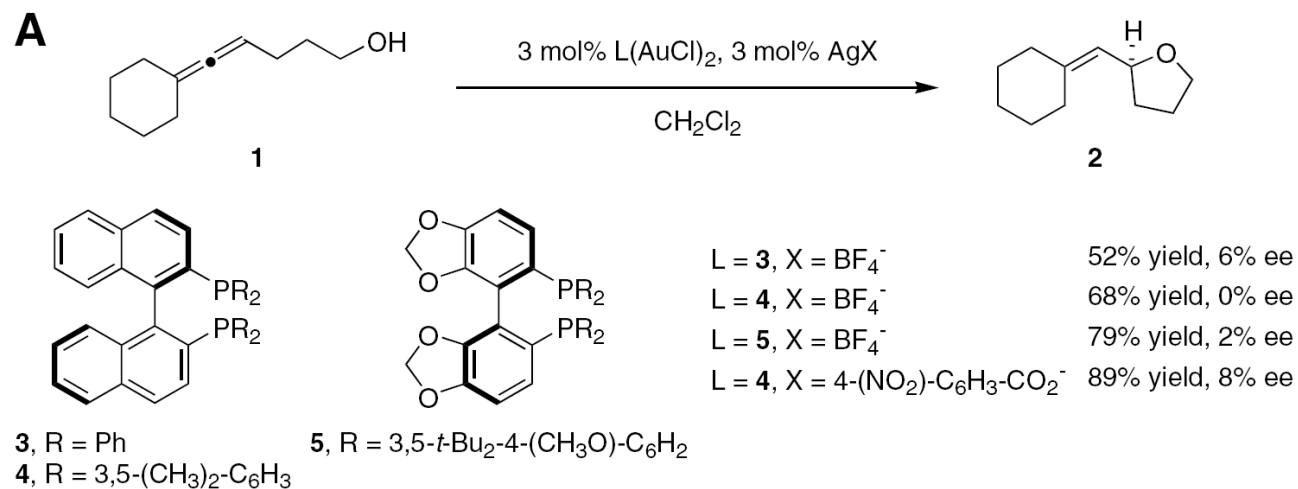


Toste's *ACDC* – Hydro-Alkoxylation/Amination of Allenes

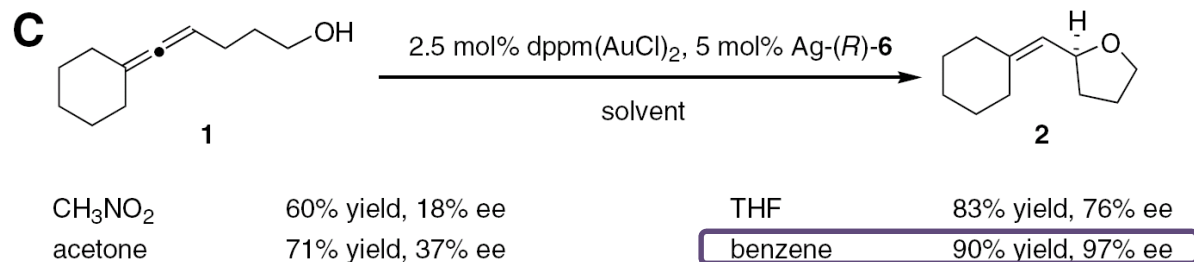
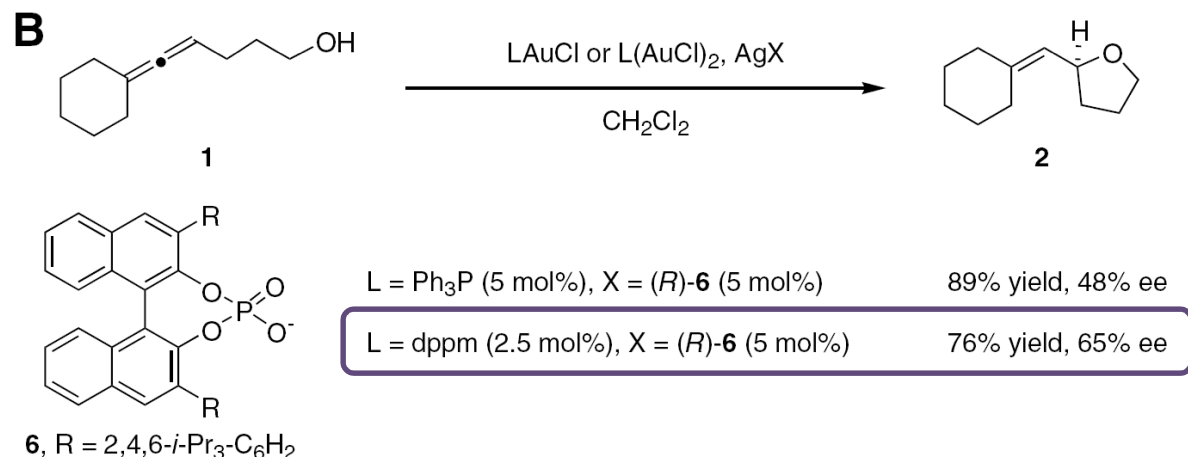
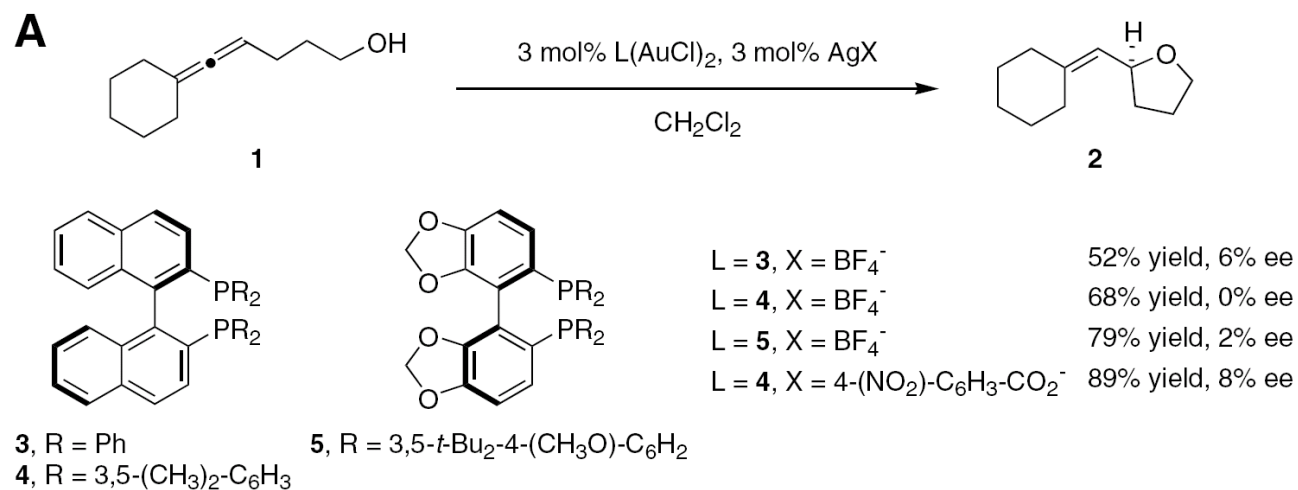


Zhang, Z.; Weidenhofer, R. *ACIEE* **2007**, 46, 283.

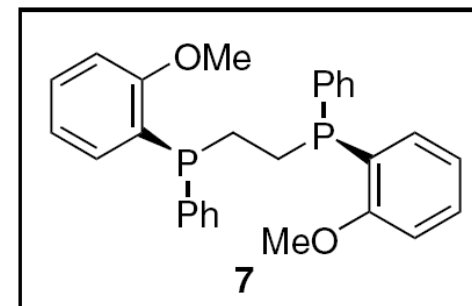
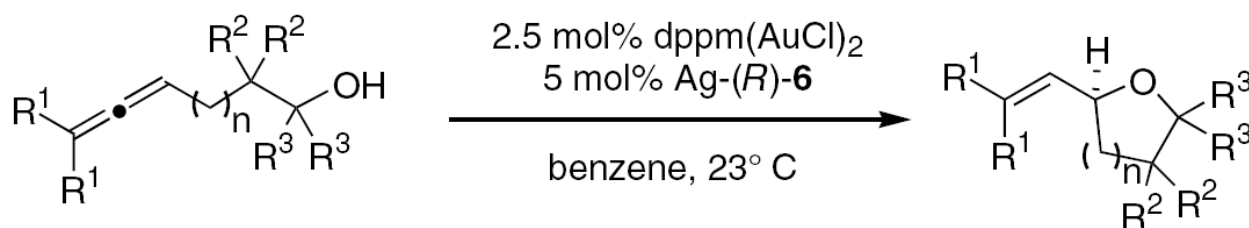
Toste's *ACDC* – Hydro-Alkoxylation/Amination of Allenes



Toste's *ACDC* – Hydro-Alkoxylation/Amination of Allenes



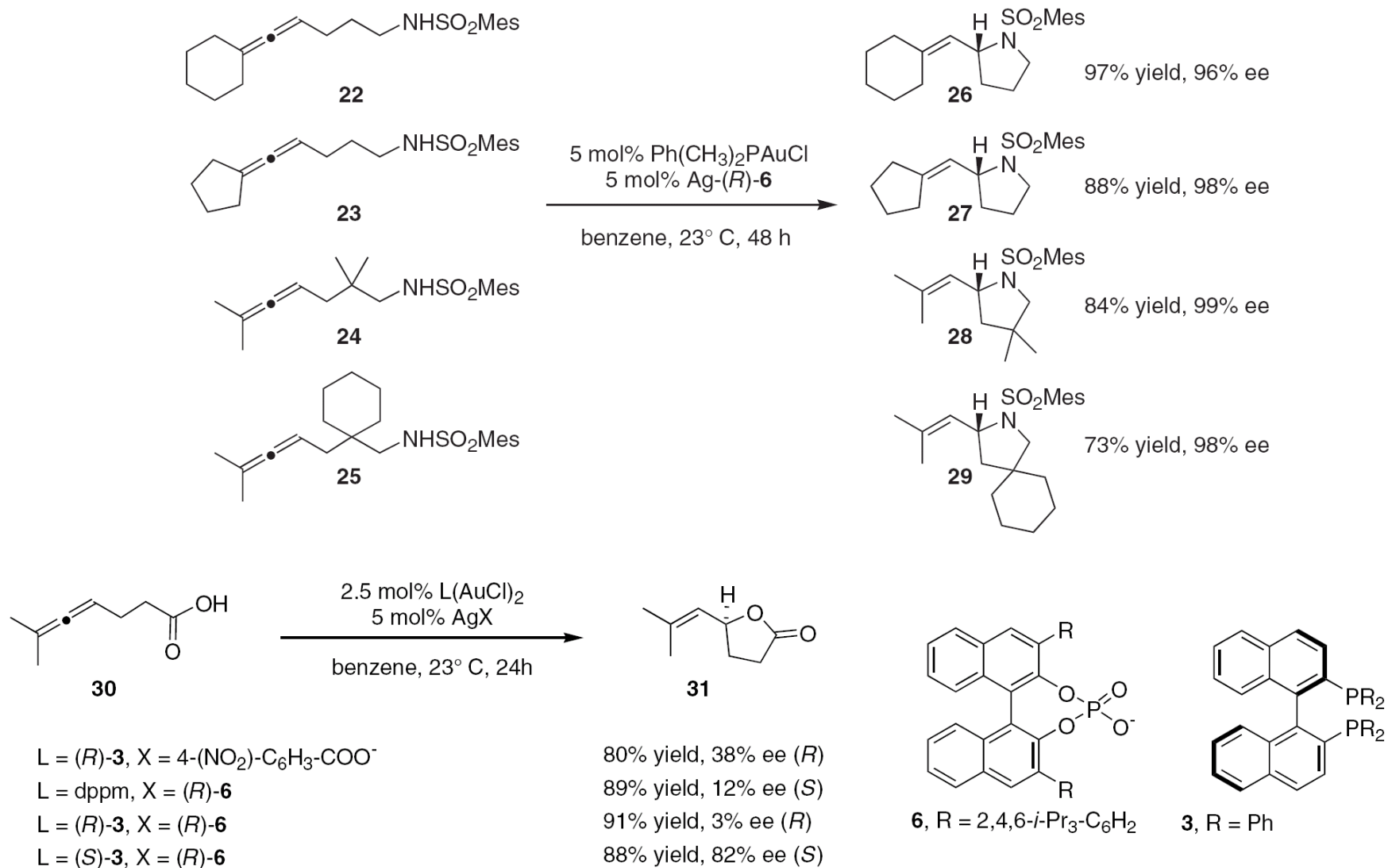
Toste's *ACDC* – Hydro-Alkoxylation/Amination of Allenes



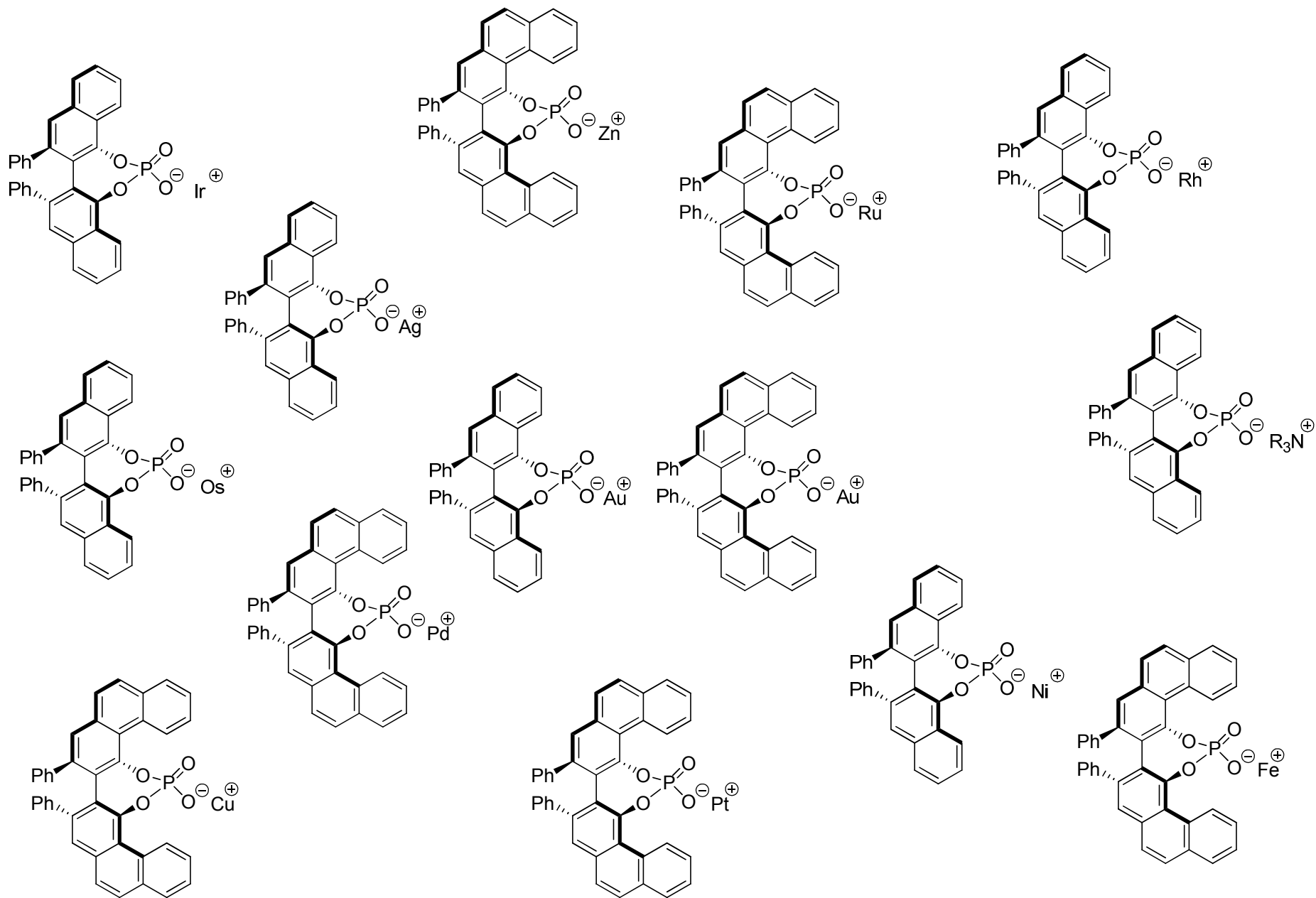
Entry	Substrate	n	R^1	R^2	R^3	Time (h)	Product	% Yield	% ee
1	1	1	$-(CH_2)_4-$	H	H	1	2	90	97
2	8	1	CH_3	H	H	1	15	91	95
3	9	1	CH_2CH_3	H	H	5	16	89	96
4	10	1	$-(CH_2)_4-$	H	CH_3	2	17	79	99
5	11	1	$-(CH_2)_4-$	H	Ph	30	18	86	92
6	12	1	$-(CH_2)_4-$	CH_3	H	13	19	90	90
7	13	2	CH_3	H	H	15	20	81	90
8	14	2	H	H	H	24	21	96	92 (80)

Match / Mismatched studies

Toste's *ACDC* – Hydro-Alkoxylation/Amination of Allenes



The Ultimate Dream – VAPOL & VANOL: “Privileged” Ligands



The Original – and the Best *AC/DC*



The Original – and the Best *AC/DC*

Australian rock band – formed in 1973 by two brother guitarists – Malcolm & Angus Young.

Phil Rudd – drums, Mark Evans – bass, Bon Scott – lead vocals.

Present: Malcolm & Angus, Phil, Mark & Brian Johnson.

Pioneers of heavy metal, alongwith Led Zeppelin, Deep Purple & Black Sabbath.

150 million albums worldwide.

Back in Black – 42 million worldwide & 21 million in USA (5th highest selling album in USA).

Ranked 4th on VH1 list of the Rock's Greatest 100.

Ranked 7th on MTV's Greatest Heavy Metal Bands of All Time.

Damn good!

The Original – and the Best AC/DC

