Career Review of Dean Toste I

2015/9/9

Zhi Ren

Introduction

- F. Dean Toste, now in UC Berkeley

- Career:

Full Professor since 2009-now
Associate Professor 2006-2009
Assistant Professor 2002-2006
Faculty Scientist Lawrence National Lab Since 2007

- Education:

B.Sc&M.Sc in University of Toronto with Prof. Ian Still (1989-95)
Ph.D. in Stanford University with Prof. Barry M. Trost (1995-2000)
Postdoc in CalTech with Prof. Robert H. Grubbs (2000-2002)

- Place of Birth:

Portugal, then moved to Canada

Introduction

- Publications:

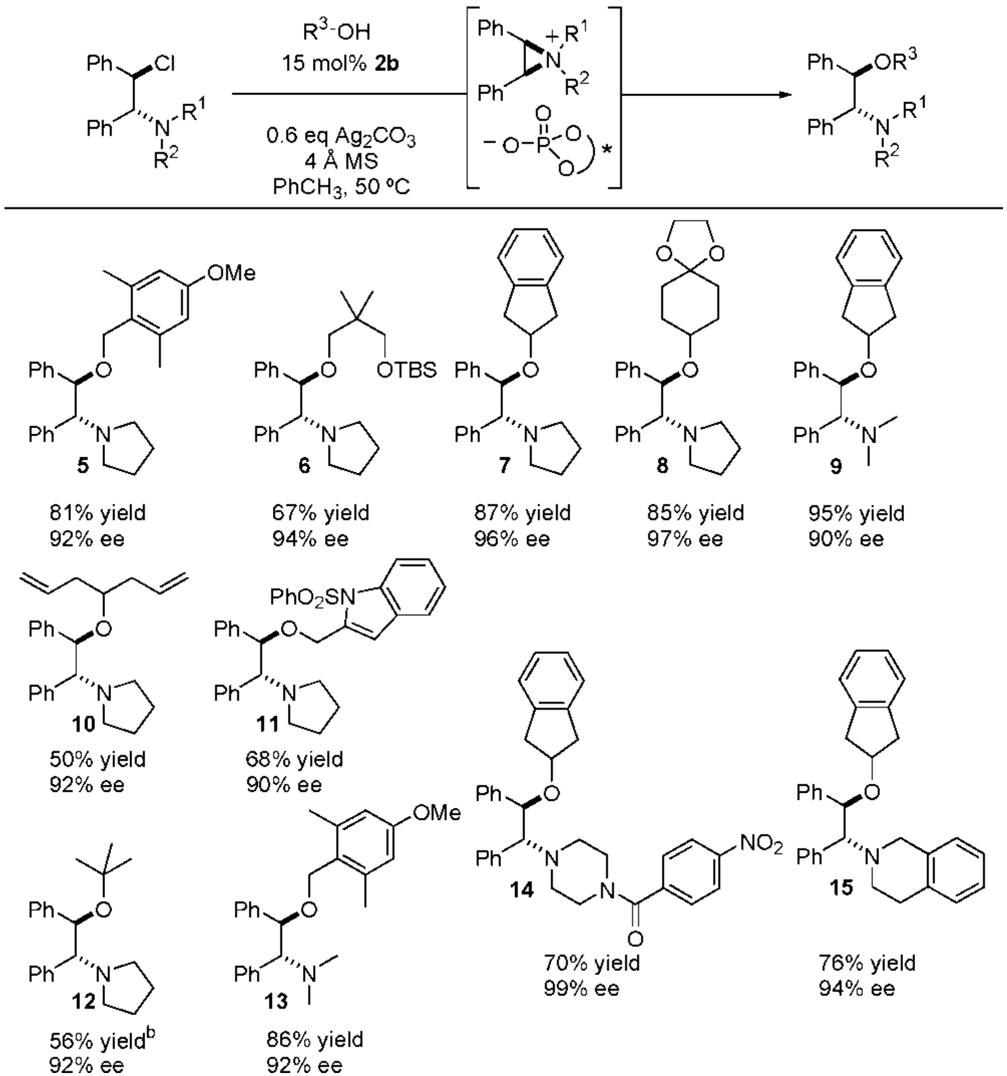
- Ph.D.12 papers
- Postdoc 1 paper

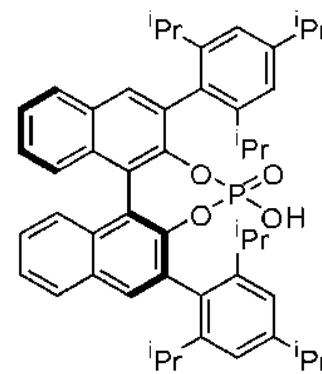
- Independent career: 163 papers so far
- Gold related: 79 papers
- Chiral anion phase transfer related: 19 papers
- Over 73 papers are assymmetric transformations
- TM involved: Au, Ag, Pd, Re, Ru, Ga, V, Co, Cu

Chiral Anion Phase Transfer Catalysis

Asymmetric Ring Opening

- Ring Opening of Aziridinium



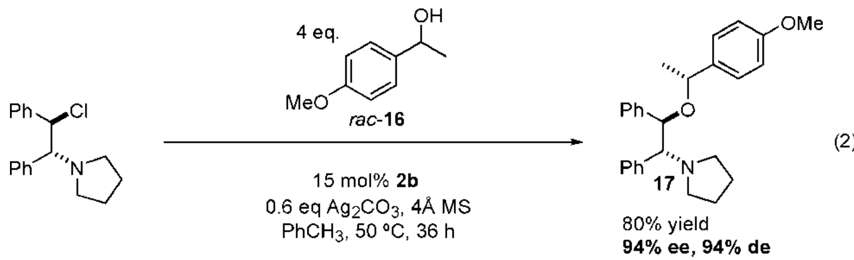


2b

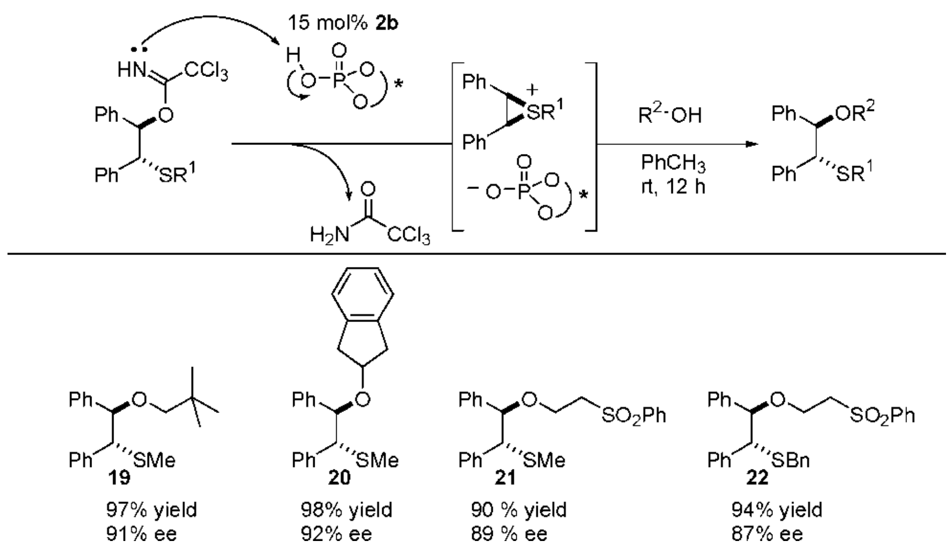
Hamilton, G. L.; Kanai, T.; Toste, F. D. *J. Am. Chem. Soc.* **2008**, *130*, 14984.

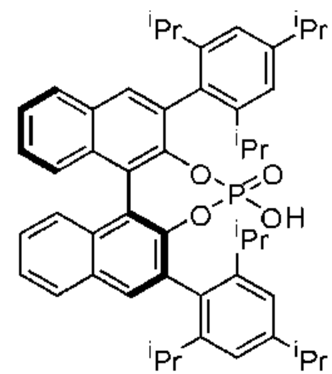
Asymmetric Ring Opening

- React with Racemic Nucleophile



- Ring Opening of Episulfonium Ions





2b

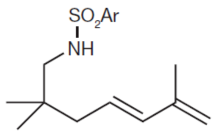
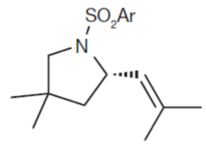
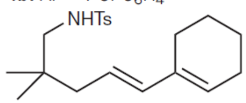
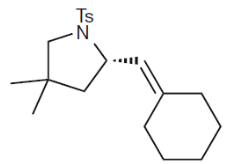
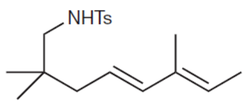
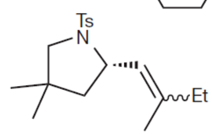
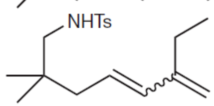
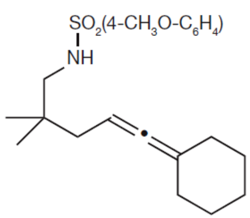
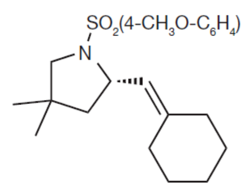
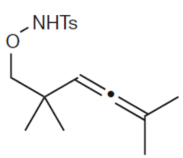
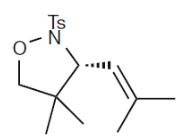
Hamilton, G. L.; Kanai, T.; Toste, F. D. *J. Am. Chem. Soc.* **2008**, *130*, 14984.

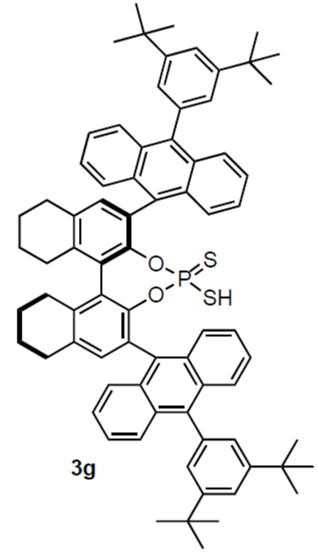
Asymmetric Additions to Dienes

- Intramolecular Hydroamination

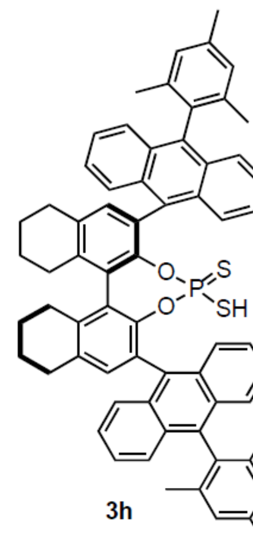
Reactions were run in fluorobenzene for 48 h using 10% catalyst, with 4 A MS

Table 2 | Performance of various 1,2- and 1,3-dienes in the enantioselective hydroamination reaction

Entry	Diene (4a–4n)	No.	Temperature (°C)	Product (5a–5n)	No.	Yield (%E:%Z)	e.e. (%)
1	 **4a:** Ar = 3,5-$(CH_3)_2C_6H_3$	**4a**	23		**5a**	99	92
2	**4b:** Ar = 4-Cl-C_6H_4	**4b**	23		**5b**	99	95
3		**4c**	30		**5c**	70	94
4		**4d**	30		**5d**	90 (4.7:1)	95 (*E*) 90 (*Z*)
5	 6:1 E/Z	**4e**	23		**5d**	75 (1:2)	91 (*E*) 99 (*Z*)
12		**4l**	40		**5l**	67	97
13		**4m**	23		**5m**	70	90



3g



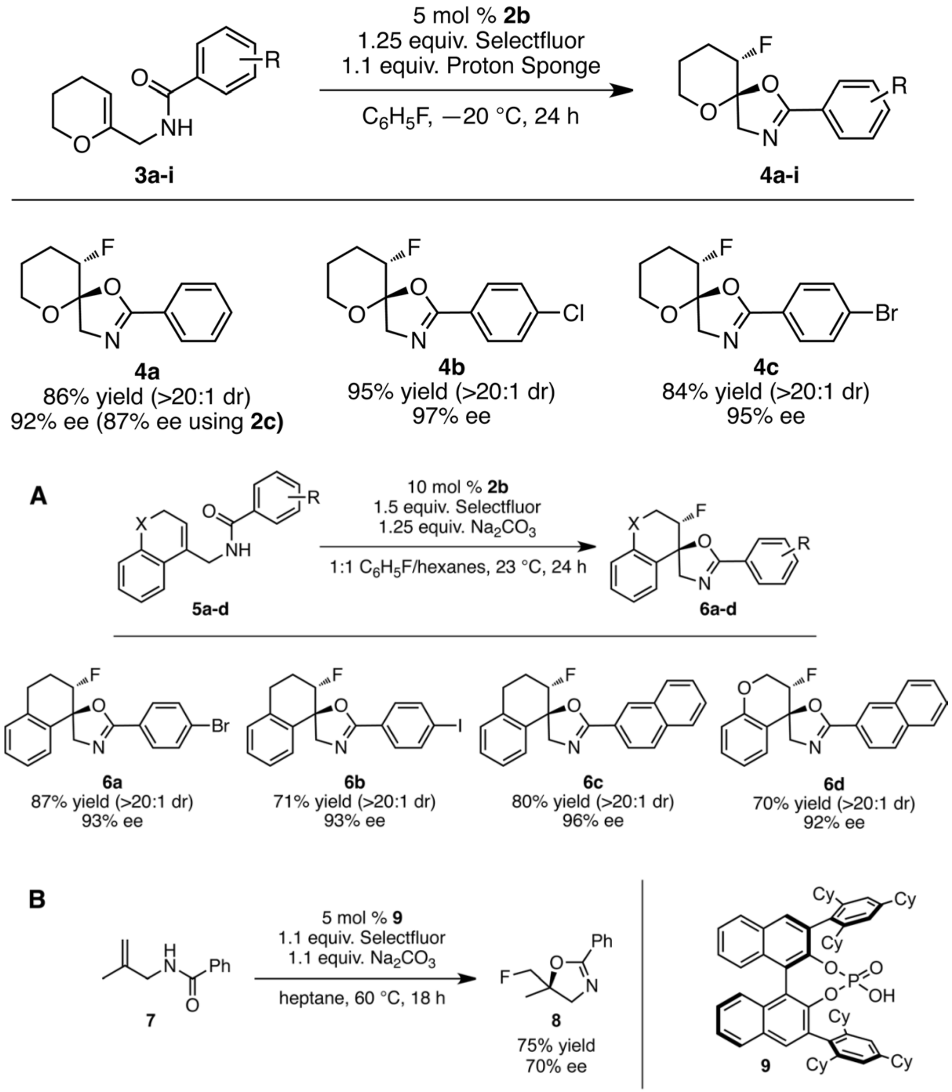
3h

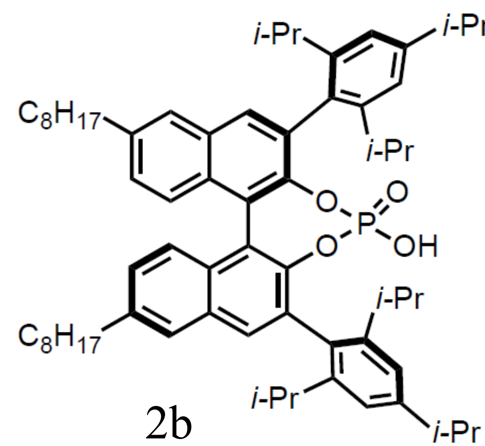
most cases

Shapiro, N. D.; Rauniyar, V.; Hamilton, G. L.; Wu, J.; Toste, F. D. *Nature* **2011**, *470*, 245.

Asymmetric Electrophilic Fluorination

- Asymmetric Fluorocyclization



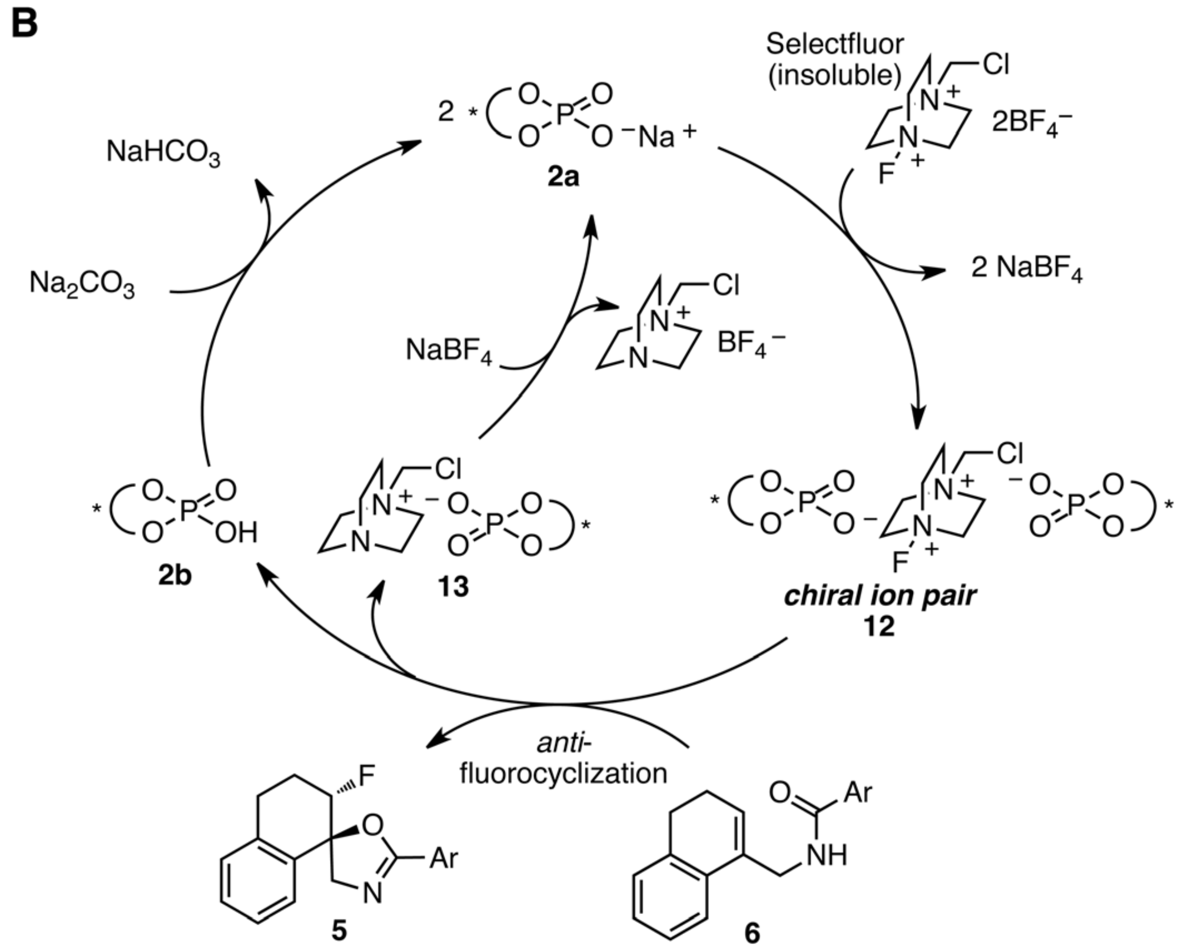


2b

Rauniyar, V.; Lackner, A. D.; Hamilton, G. L.; Toste, F. D. *Science* **2011**, *334*, 1681.

Asymmetric Electrophilic Fluorination

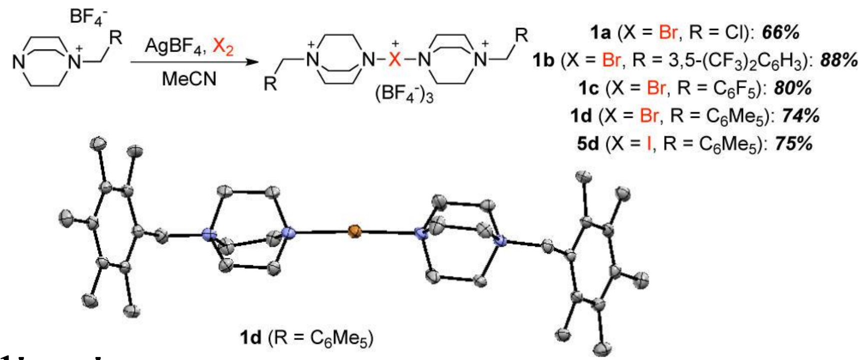
- Proposed Mechanism for Asymmetric Fluorocyclization



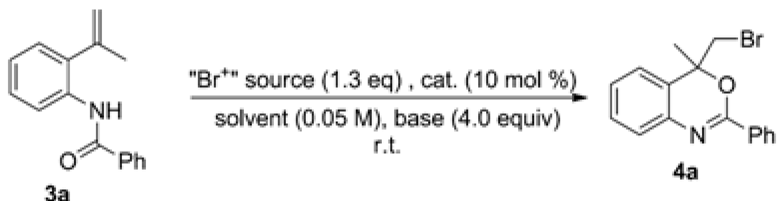
Rauniyar, V.; Lackner, A. D.; Hamilton, G. L.; Toste, F. D. *Science* **2011**, *334*, 1681.

Asymmetric Electrophilic Halogenation

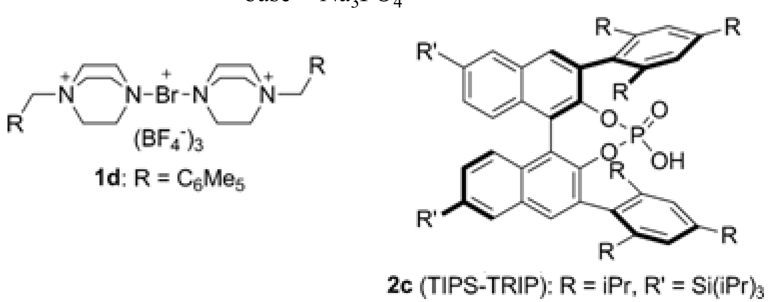
- Prepare the Halogenation Reagents

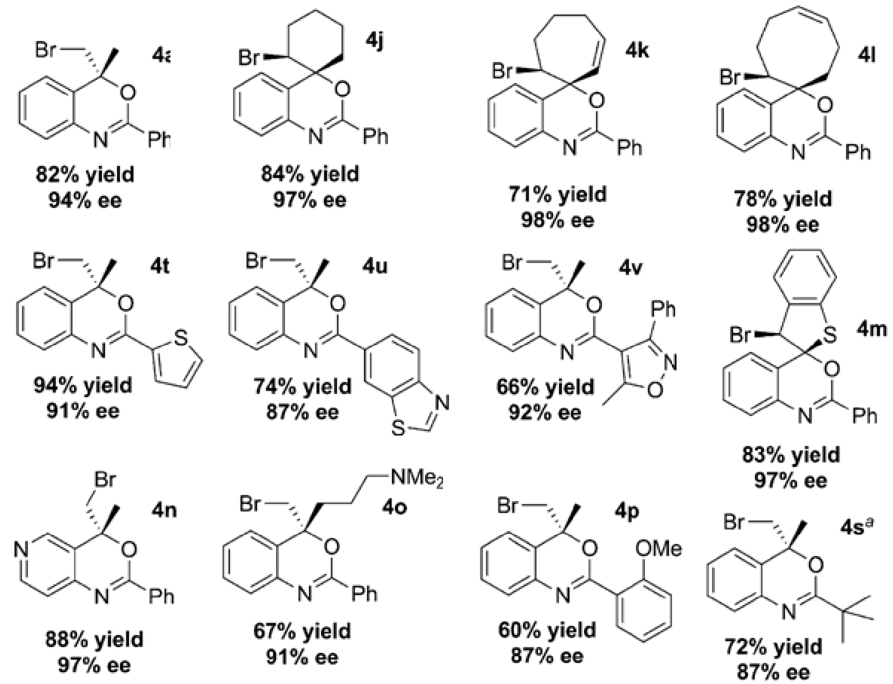


- Scope of Enantioselective Bromocyclization



solvent = p-Xyl/hex (1:1)
base = Na_3PO_4

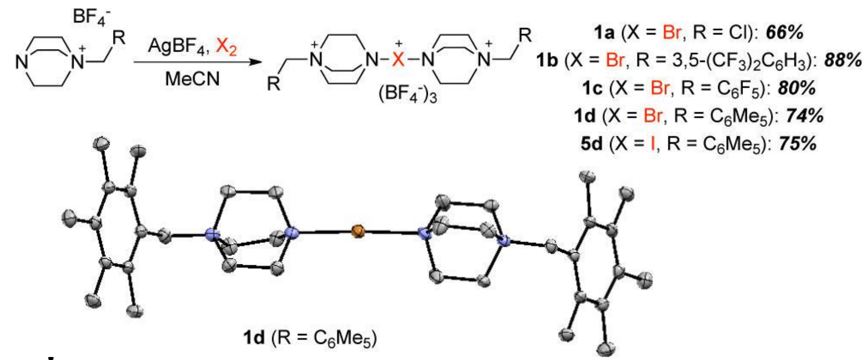




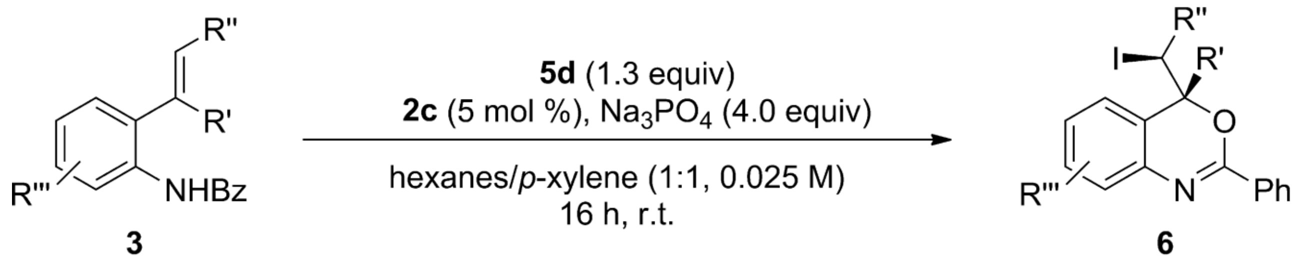
Wang, Y. M.; Wu, J.; Hoong, C.; Rauniyar, V.; Toste, F. D. *J. Am. Chem. Soc.* **2012**, *134*, 12928.

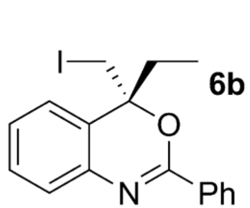
Asymmetric Electrophilic Halogenation

- Prepare the Halogenation Reagents

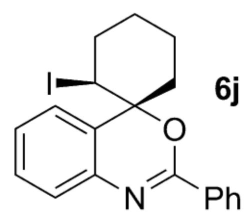


- Scope of Enantioselective Iodocyclization

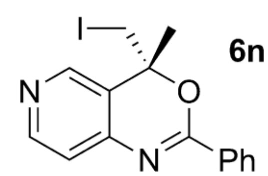




74% yield
94% ee



82% yield
99% ee

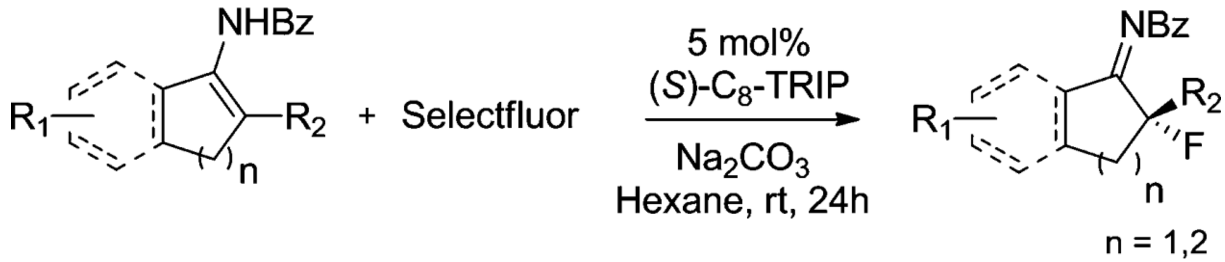


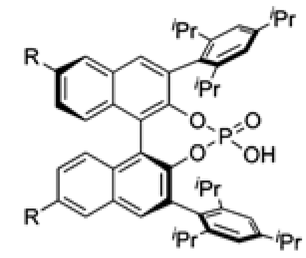
79% yield
92% ee

Wang, Y. M.; Wu, J.; Hoong, C.; Rauniyar, V.; Toste, F. D. *J. Am. Chem. Soc.* **2012**, *134*, 12928.

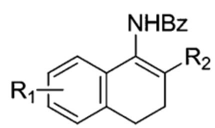
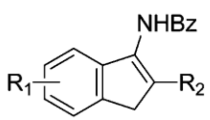
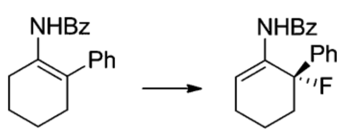
Asymmetric Fluorination of Enamides

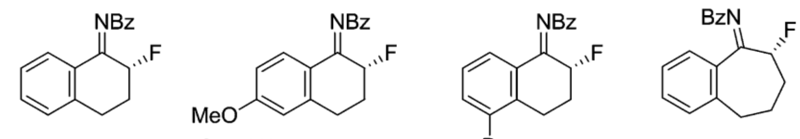
- Scope of the Reaction



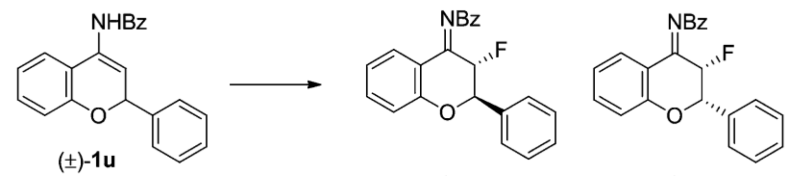


R = C_8H_{17}, **C_8-TRIP**

Entry	Substrate **1**	R_1	R_2	Product	% yield **2**[a]	%ee **2**[b,c]
1		H	Me	**2d**	88	96
2[d]		H	Allyl	**2e**	80	96
3		H	Bn	**2f**	92	99
4[e]		6-OMe	Me	**2g**	94	92
5		H	Me	**2h**	66	96
6[d,f]		H	Ph	**2i**	79	90
7		H	Bn	**2j**	84	98
8		5-OMe	Bn	**2k**	68	96
9[g]		5-F	Bn	**2l**	75	94
10[d]		5-Cl	Bn	**2m**	85	93
11		H	(3-OMe)Bn	**2n**	83	98
12[h]				**2o**	58	87



2q, 76% yield, 93 % ee; **2r**, 78% yield, 92 % ee; **2s**[c], 79% yield, 88 % ee; **2t**[c], 78% yield, 82 % ee



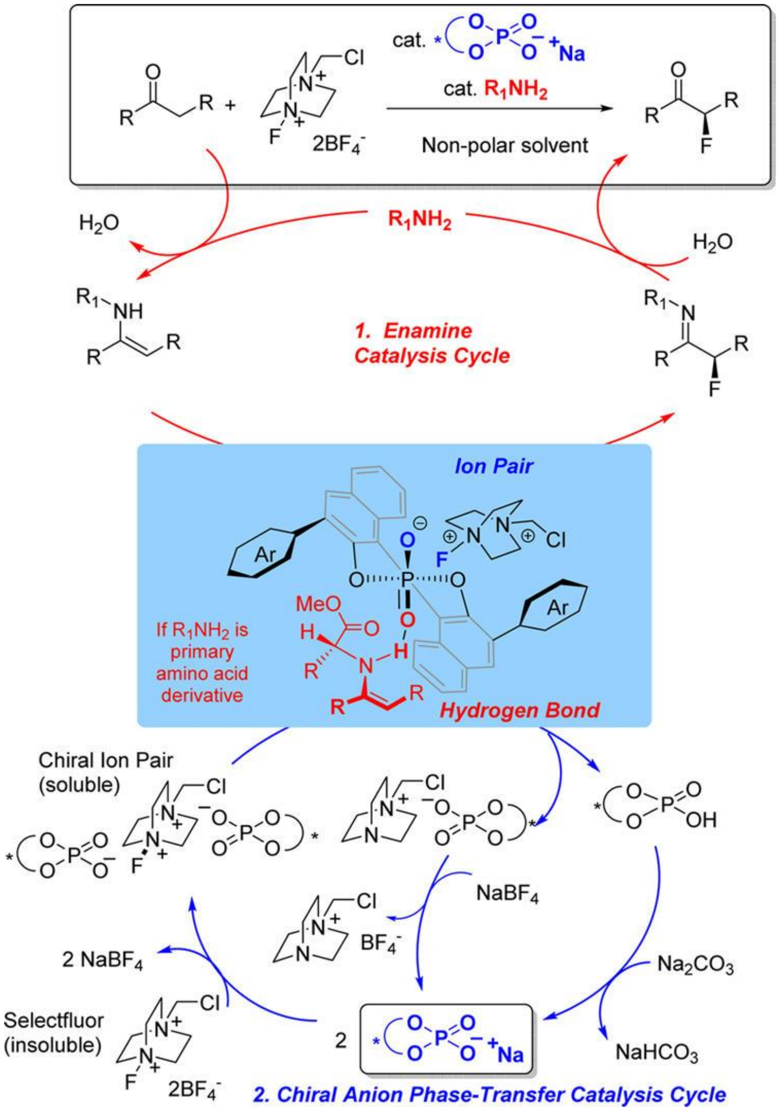
(±)-**1u**; ***anti*-2u**[c], 41% yield, 93% ee; **syn-2u**[c], 20% yield, 99% ee

[a]Isolated yields after chromatography on silica gel. [b]ee's were determined by HPLC. [c]Reaction was run in the presence of 5 equiv of 3-hexanol.

Phipps, R. J.; Hiramatsu, K.; Toste, F. D. *J. Am. Chem. Soc.* **2012**, *134*, 8376.

Asymmetric α-Fluorination of Cyclohexanones

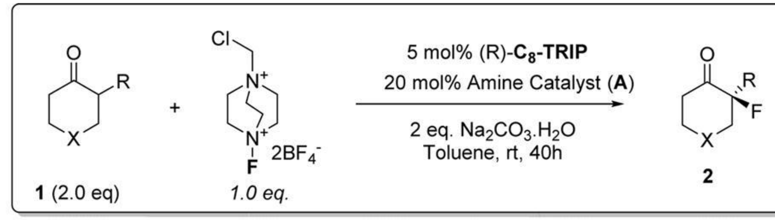
- Proposed Mechanism

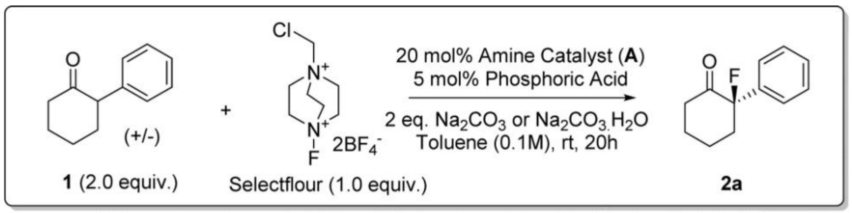


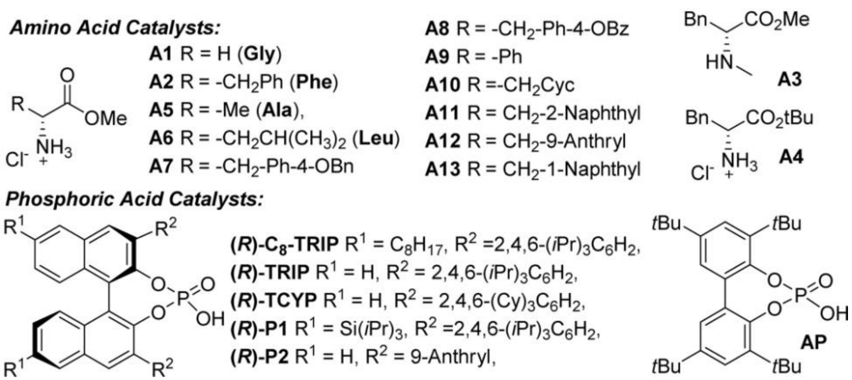
Yang, X. Y.; Phipps, R. J.; Toste, F. D. *J. Am. Chem. Soc.* **2014**, *136*, 5225.

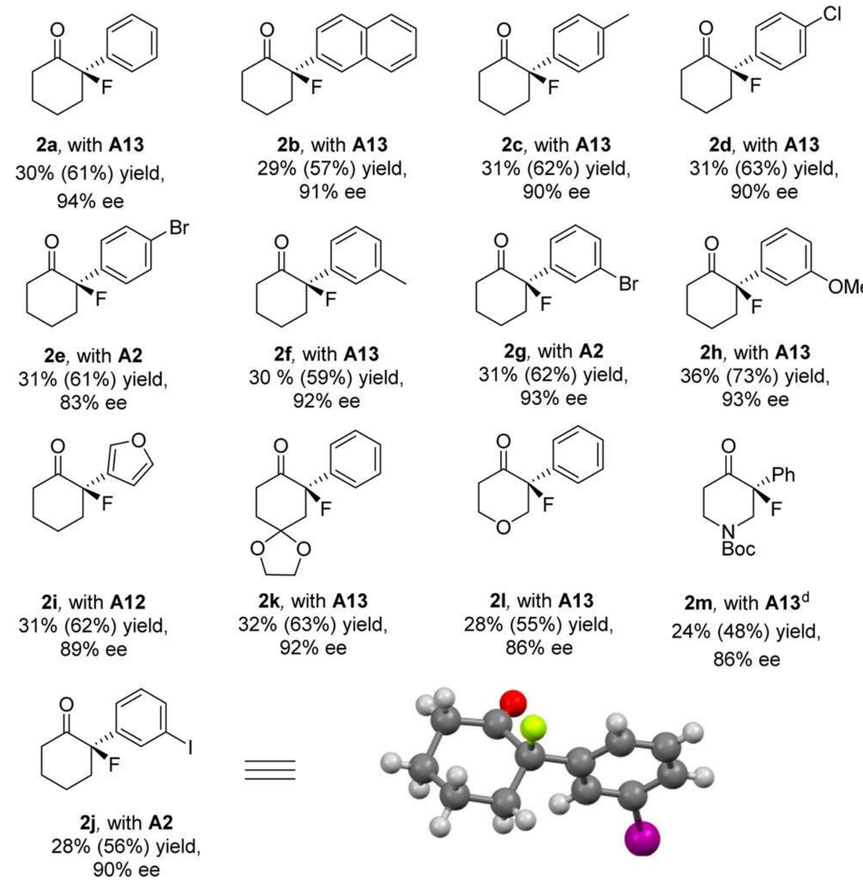
Asymmetric α-Fluorination of Cyclohexanones

- Reaction Scopes







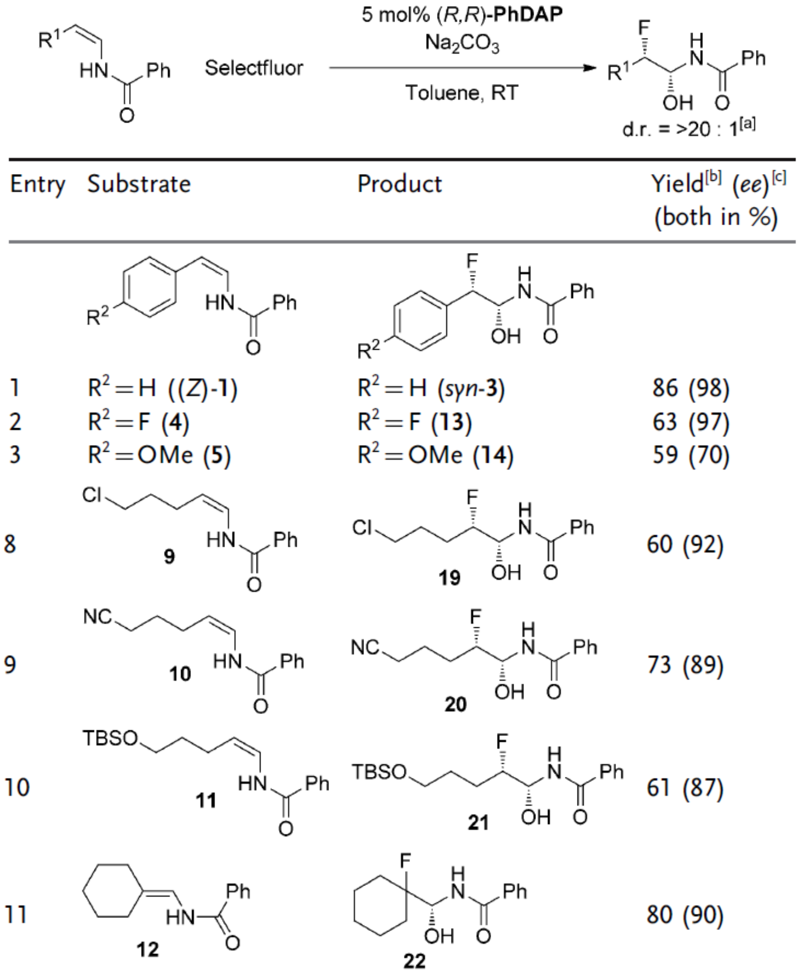


Yang, X. Y.; Phipps, R. J.; Toste, F. D. *J. Am. Chem. Soc.* **2014**, *136*, 5225.

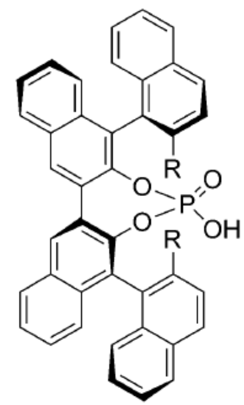
Asymmetric Oxyfluorination of Enamides

- Scope of the Reaction

Table 2: Substrate scope of fluorohydration of enamides.



Entry	Substrate	Product	Yield[b] (ee)[c] (both in %)
1	R^2 = H ((Z)-1)	R^2 = H (syn-3)	86 (98)
2	R^2 = F (4)	R^2 = F (13)	63 (97)
3	R^2 = OMe (5)	R^2 = OMe (14)	59 (70)
8	9	19	60 (92)
9	10	20	73 (89)
10	11	21	61 (87)
11	12	22	80 (90)



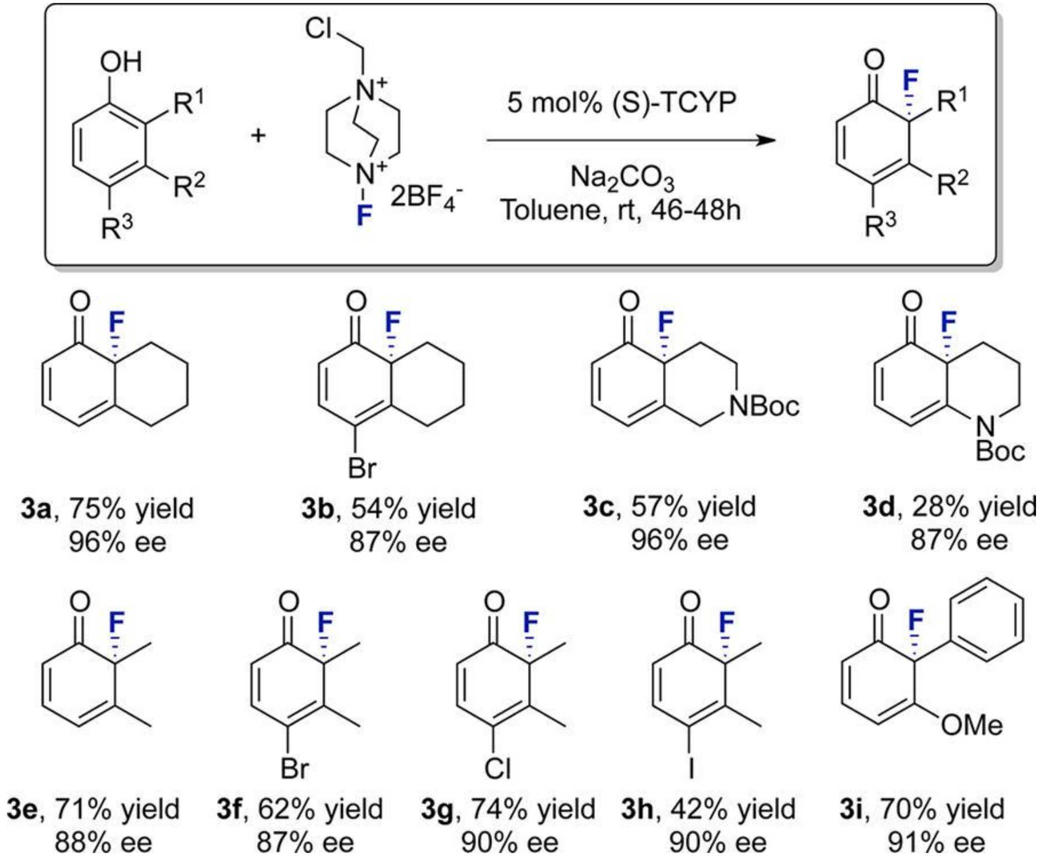
R = OCy, (R,R)-**2i**
R = Ph, (R,R)-**PhDAP** (**2j**)

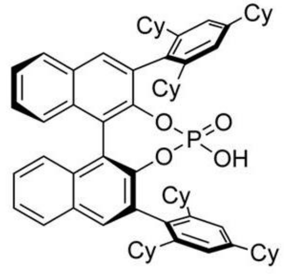
Water comes from Selectfluor!

Honjo, T.; Phipps, R. J.; Rauniyar, V.; Toste, F. D. *Angew. Chem. Int. Ed.* **2012**, *51*, 9684.

Asymmetric Fluorinative Dearomatization

- Scope of the *ortho*-Fluorinative Dearomatization Reaction





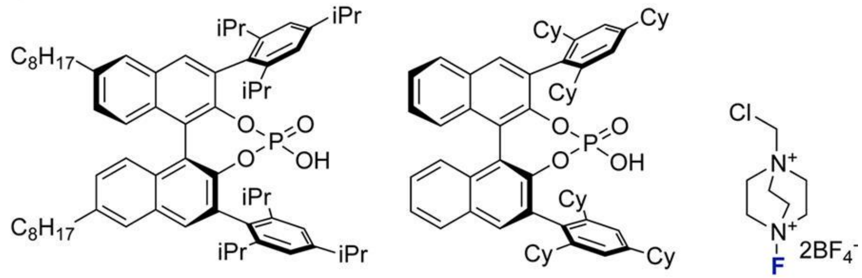
(S)-TCYP

Phipps, R. J.; Toste, F. D. *J. Am. Chem. Soc.* **2013**, *135*, 1268.

Asymmetric Fluorinative Dearomatization

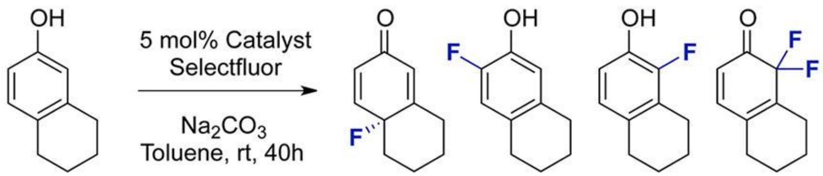
- Scope of the *para*-Fluorinative Dearomatization Reaction

(a) Catalysts/reagents employed



(S)-C$_8$-TRIP **(S)-TCYP** **Selectfluor**

(b) Initial findings - *Para*-fluorination



1a **2a** **2b** **2c** **2d**

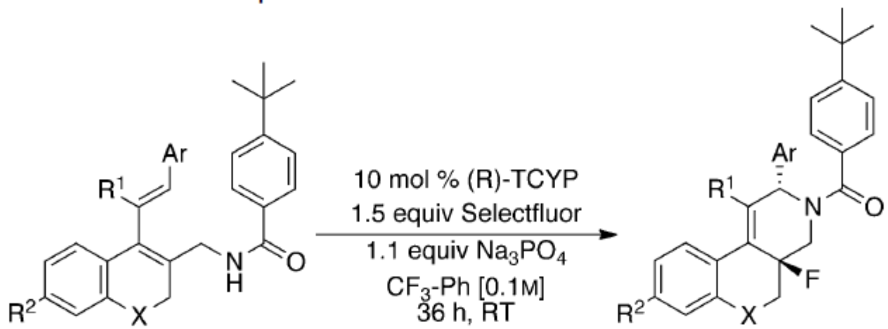
Catalyst	**Ratio 2a:2b:2c:2d**	**Net *para:ortho***	**Yield 2a (% conv)**	***ee* 2a**
(*S*)-C$_8$TRIP	1 : 0.28 : 0.51 : 0.15	1.1 : 1	41% (>95)	27%
(*S*)-TCYP	1 : 0.19 : 0.51 : 0.32	1.0 : 1	41% (>95)	63%
none	1 : 0.11 : 0.23 : 0.00	2.9 : 1	17%[c] (23)	--

Phipps, R. J.; Toste, F. D. *J. Am. Chem. Soc.* **2013**, *135*, 1268.

Asymmetric Fluoroamination of Conjugated Dienes

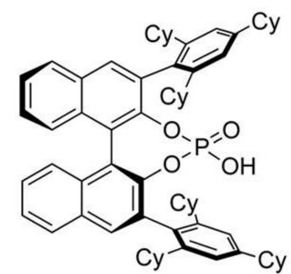
- 1,4-Difunctionalization of Conjugated Dienes

Table 2: Substrate scope with Selectfluor.



Entry	Product	Ar	R[1]	R[2]	R[2]	Yield [%][a]	ee [%][b]	d.r.[c]
1	**2a**	2-MeC_6H_4	H	H	-CH_2-	91	96	>20:1
2	**2b**	3-MeC_6H_4	H	H	-CH_2-	92	92	5.9:1
3	**2c**	C_6H_5	H	H	-CH_2-	90	92	6.9:1
4	**2d**	C_6H_5	H	OMe	-CH_2-	90	93	6.9:1
5	**2e**	C_6H_5	H	H	O	85	91	5.5:1
6	**2f**	4-$CF_3C_6H_4$	H	H	-CH_2-	94	95	10:1
7	**2g**	4-MeOC_6H_4	H	H	-CH_2-	89	93	7.5:1
8[d]	**2h**	C_6H_5	*n*Bu	H	-CH_2-	85	94	>20:1

[a] Yield given after purification as a combination of both diastereomers. [b] % *ee* determined by chiral-phase HPLC. [c] d.r. calculated by integration of ^{1}H NMR spectra. [d] Reaction run in benzene.



(S)-TCYP

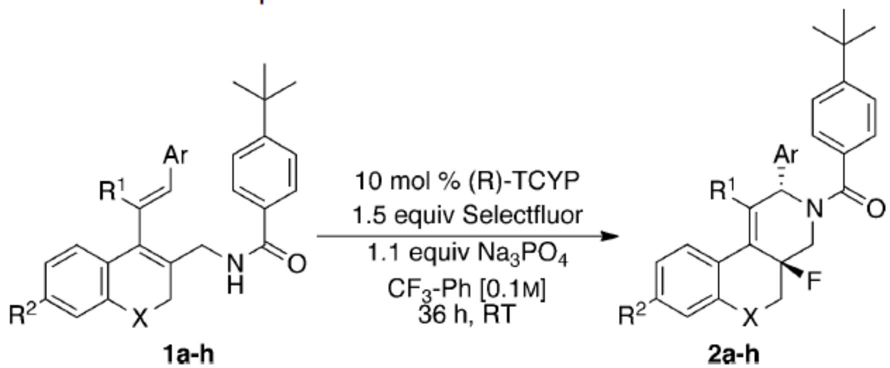
R-catalyst for this reaction

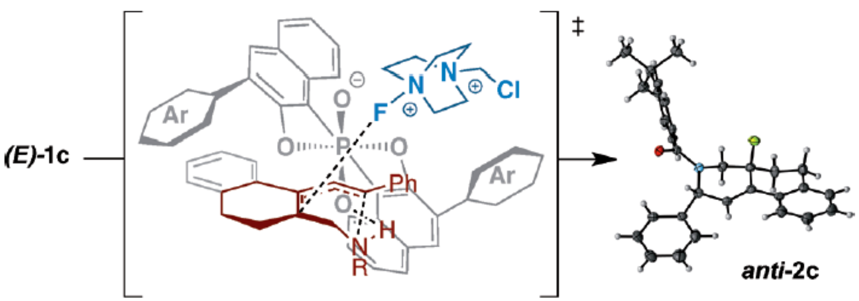
Shunatona, H. P.; Fruh, N.; Wang, Y. M.; Rauniyar, V.; Toste, F. D. *Angew. Chem. Int. Ed.* **2013**, *52*, 7724.

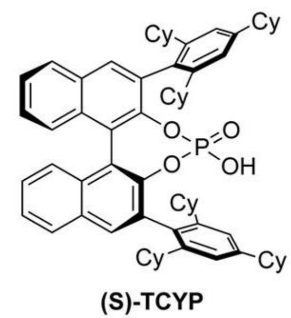
Asymmetric Fluoroamination of Conjugated Dienes

- 1,4-Difunctionalization of Conjugated Dienes

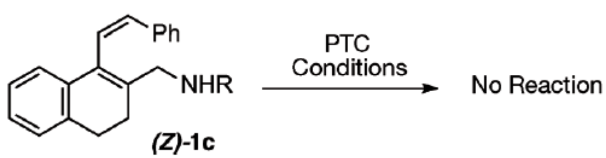
Table 2: Substrate scope with Selectfluor.







R-catalyst for this reaction

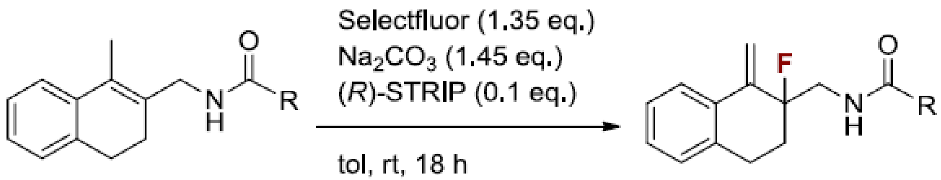


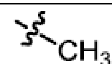
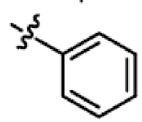
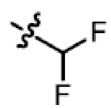
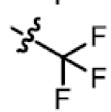
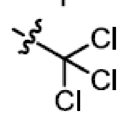
Z-diastereomer give no reactivity, as the $A^{1,3}$ strain in TS will increase.

Shunatona, H. P.; Fruh, N.; Wang, Y. M.; Rauniyar, V.; Toste, F. D. *Angew. Chem. Int. Ed.* **2013**, *52*, 7724.

Directed Asymmetric Fluorination of Alkenes

- Steric Factors for Amide DGs on % ee

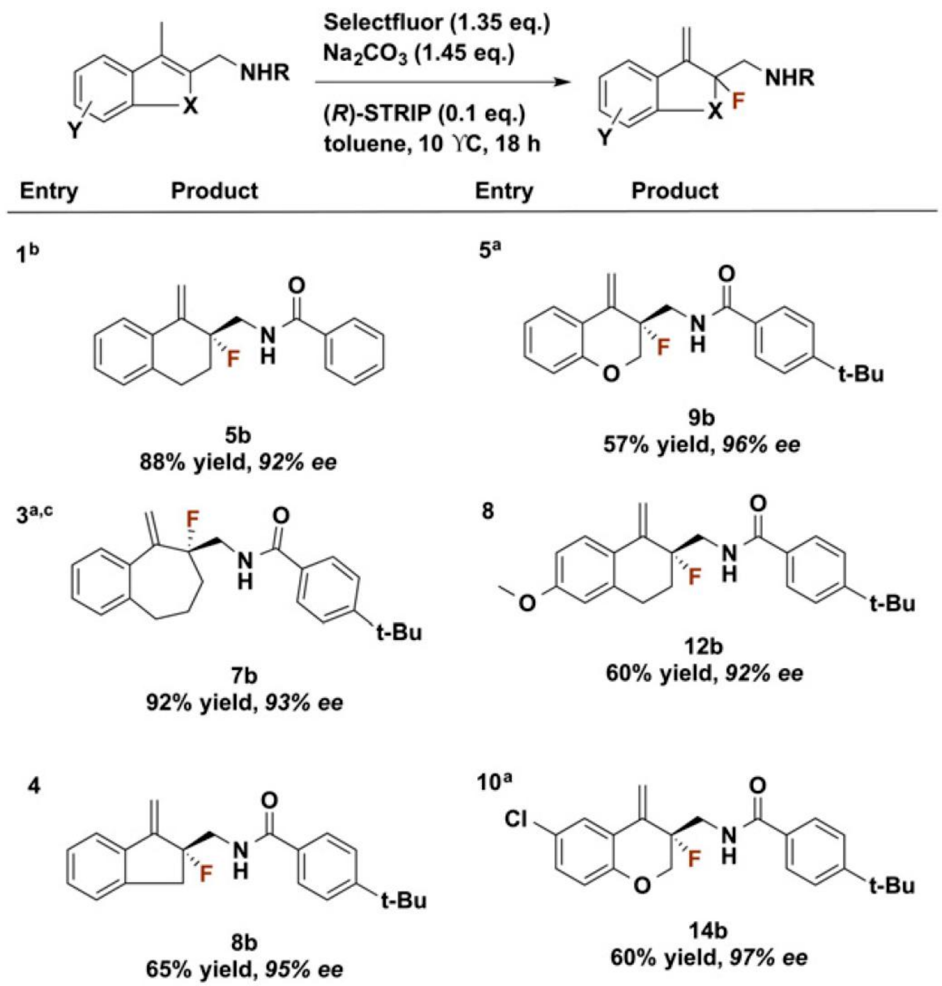


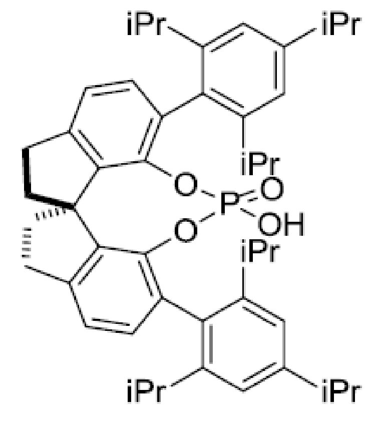
Entry	R =	% ee
1		30
2		51
3		75
4		92
5		30
6		82
7		93

Wu, J.; Wang, Y. M.; Drljevic, A.; Rauniyar, V.; Phipps, R. J.; Toste, F. D. *Proc. Natl. Acad. Sci.* **2013**, *110*, 13729.

Directed Asymmetric Fluorination of Alkenes

- Reaction Scope





(*R*)-**3** (STRIP)

Wu, J.; Wang, Y. M.; Drljevic, A.; Rauniyar, V.; Phipps, R. J.; Toste, F. D. *Proc. Natl. Acad. Sci.* **2013**, *110*, 13729.

Directed Asymmetric Fluorination of Alkenes

- Phenol as DG

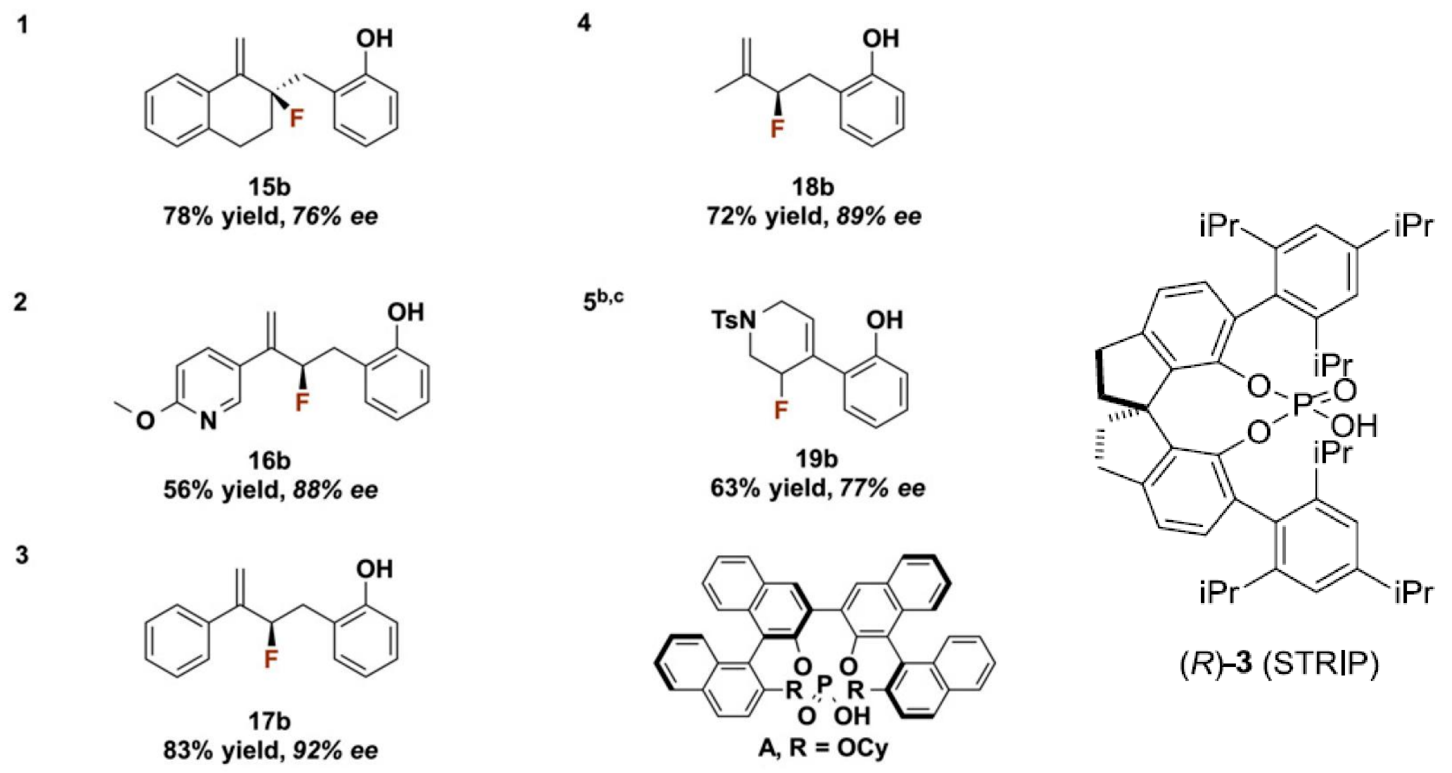


Fig. 5. 2-Hydroxyphenyl DG effective for various alkenes. *a*, Selectfluor (1.35 eq), Na_2CO_3 (1.45 eq), (*R*)-STRIP (0.1 eq), tol, rt, 18 h; *b*, reaction run for 36 h; *c*, catalyst A (39) used instead of (*R*)-STRIP.

Wu, J.; Wang, Y. M.; Drljevic, A.; Rauniyar, V.; Phipps, R. J.; Toste, F. D. *Proc. Natl. Acad. Sci.* **2013**, *110*, 13729.

Directed Asymmetric Fluorination of Alkenes

- Possible Mechanisms

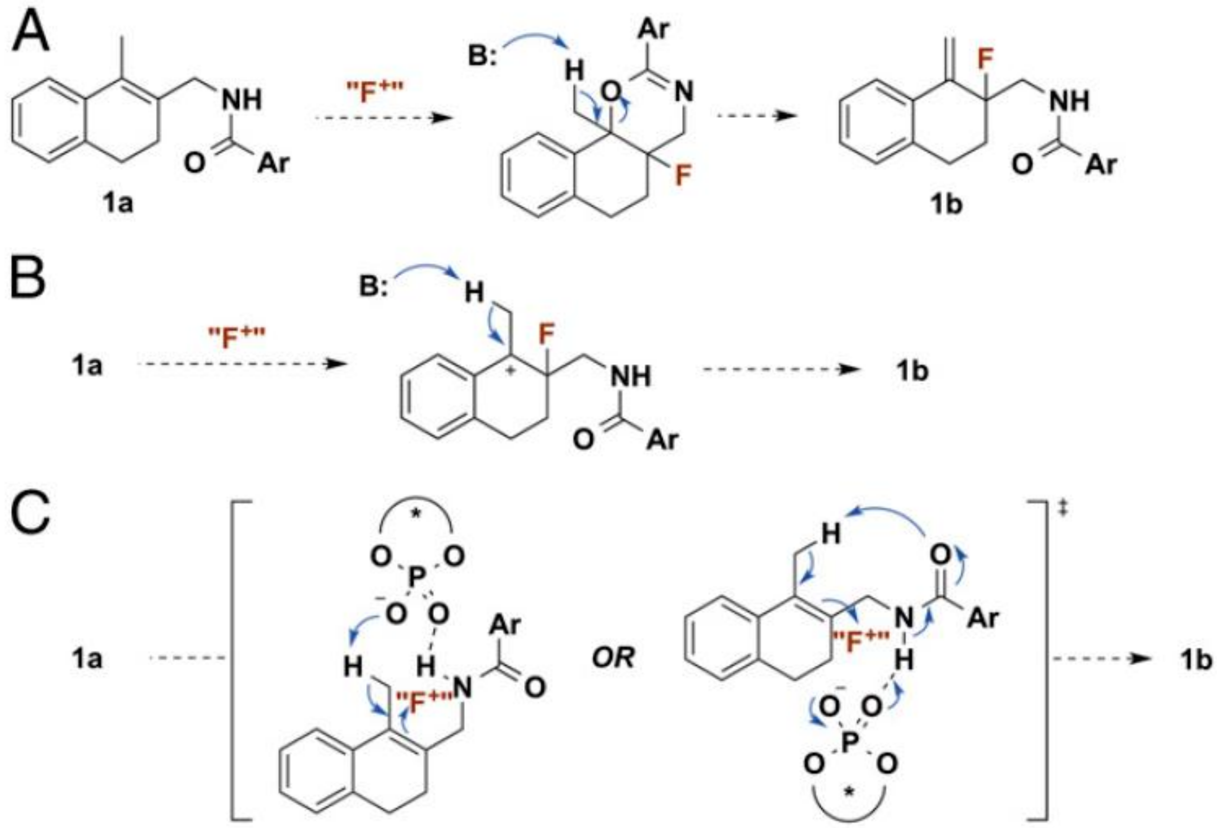
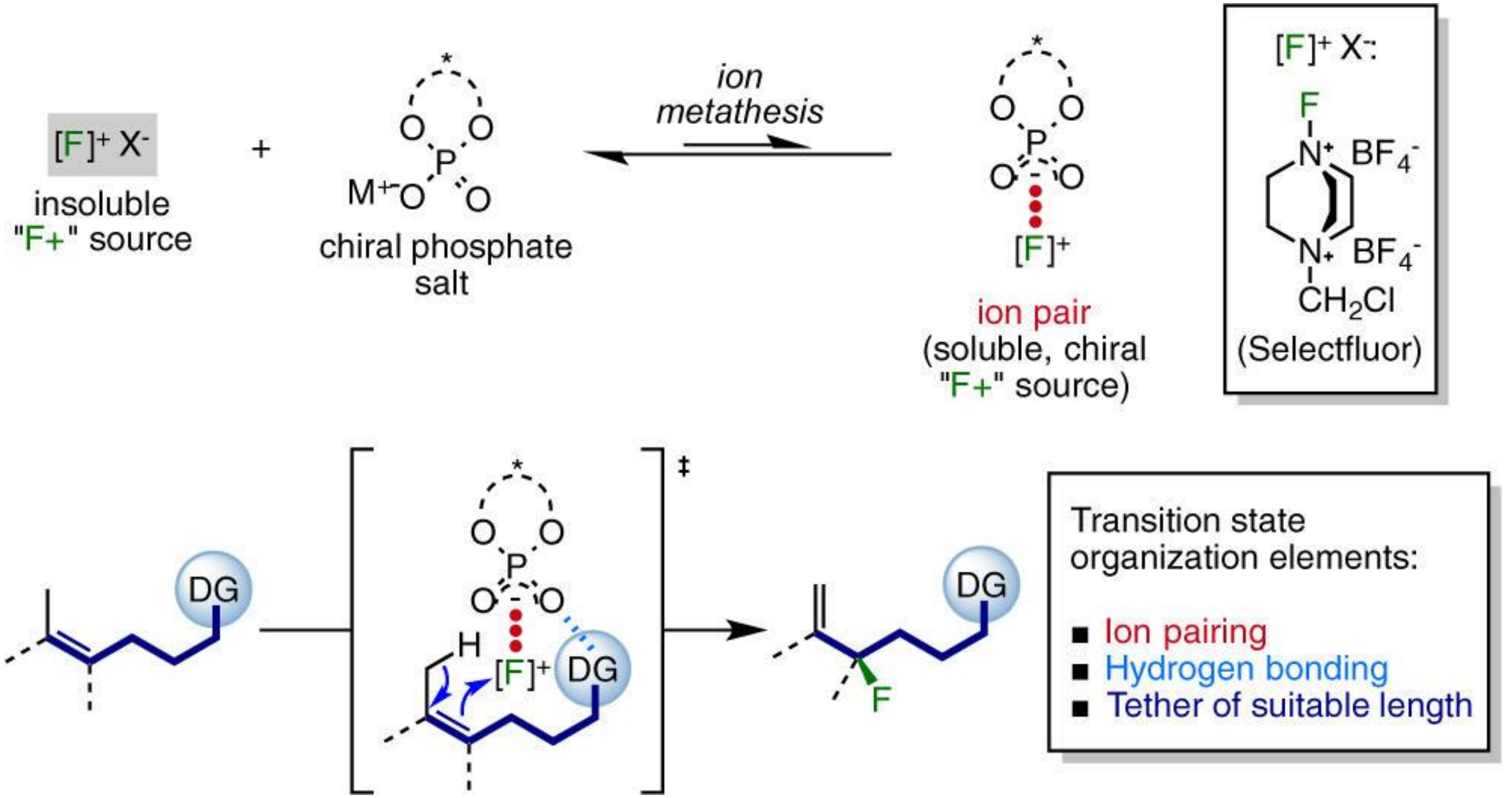


Fig. 3. (*A–C*) Possible mechanisms for the formation of allylic fluoride **1b** from substrate **1a**.

Wu, J.; Wang, Y. M.; Drljevic, A.; Rauniyar, V.; Phipps, R. J.; Toste, F. D. *Proc. Natl. Acad. Sci.* **2013**, *110*, 13729.

In Situ Directed Fluorination of Allylic Achohols

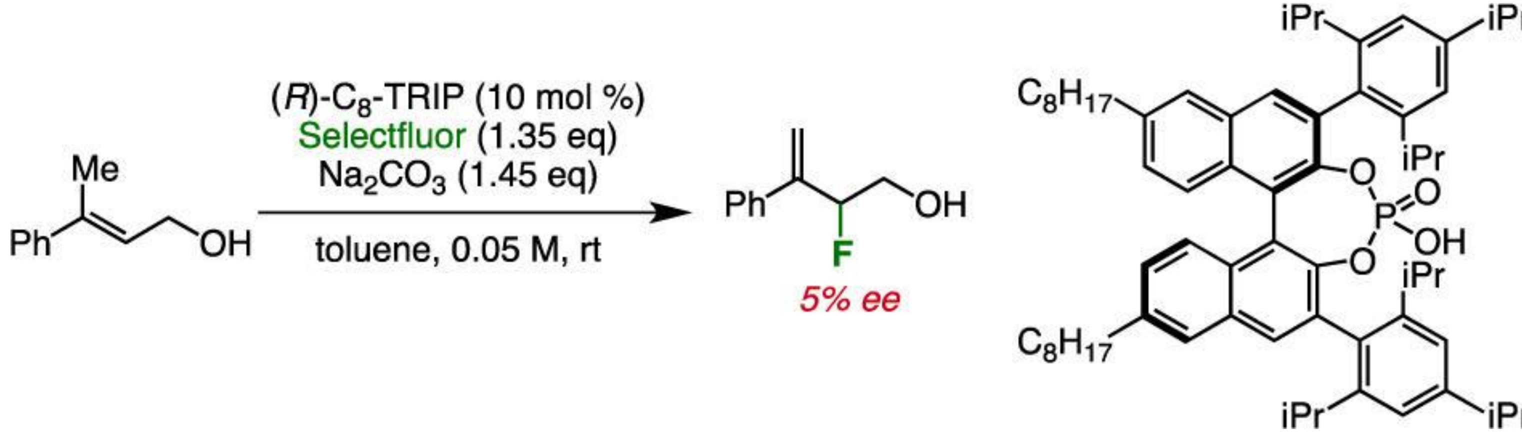
- Reaction Design



Zi, W. W.; Wang, Y. M.; Toste, F. D. *J. Am. Chem. Soc.* **2014**, *136*, 12864.

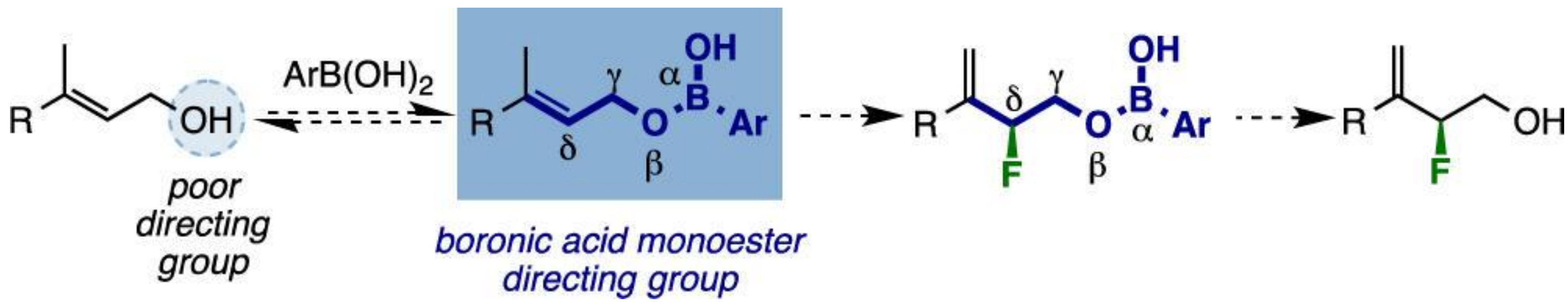
In Situ Directed Fluorination of Allylic Achohols

- Preliminary Results



(1)

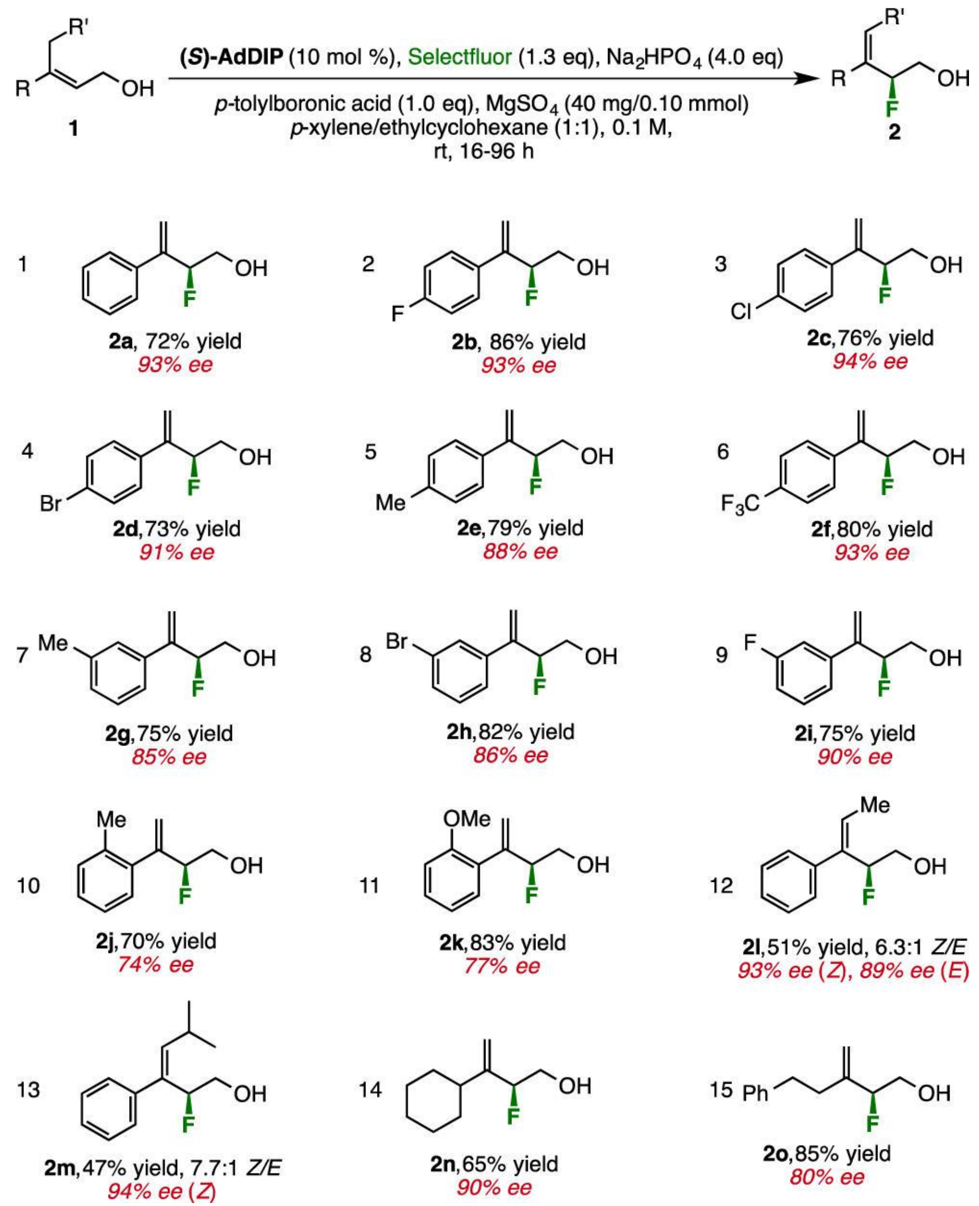
- Boronic Acid Monoester-Directed Transformation



Zi, W. W.; Wang, Y. M.; Toste, F. D. *J. Am. Chem. Soc.* **2014**, *136*, 12864.

In Situ Directed Fluorination of Allylic Achohols

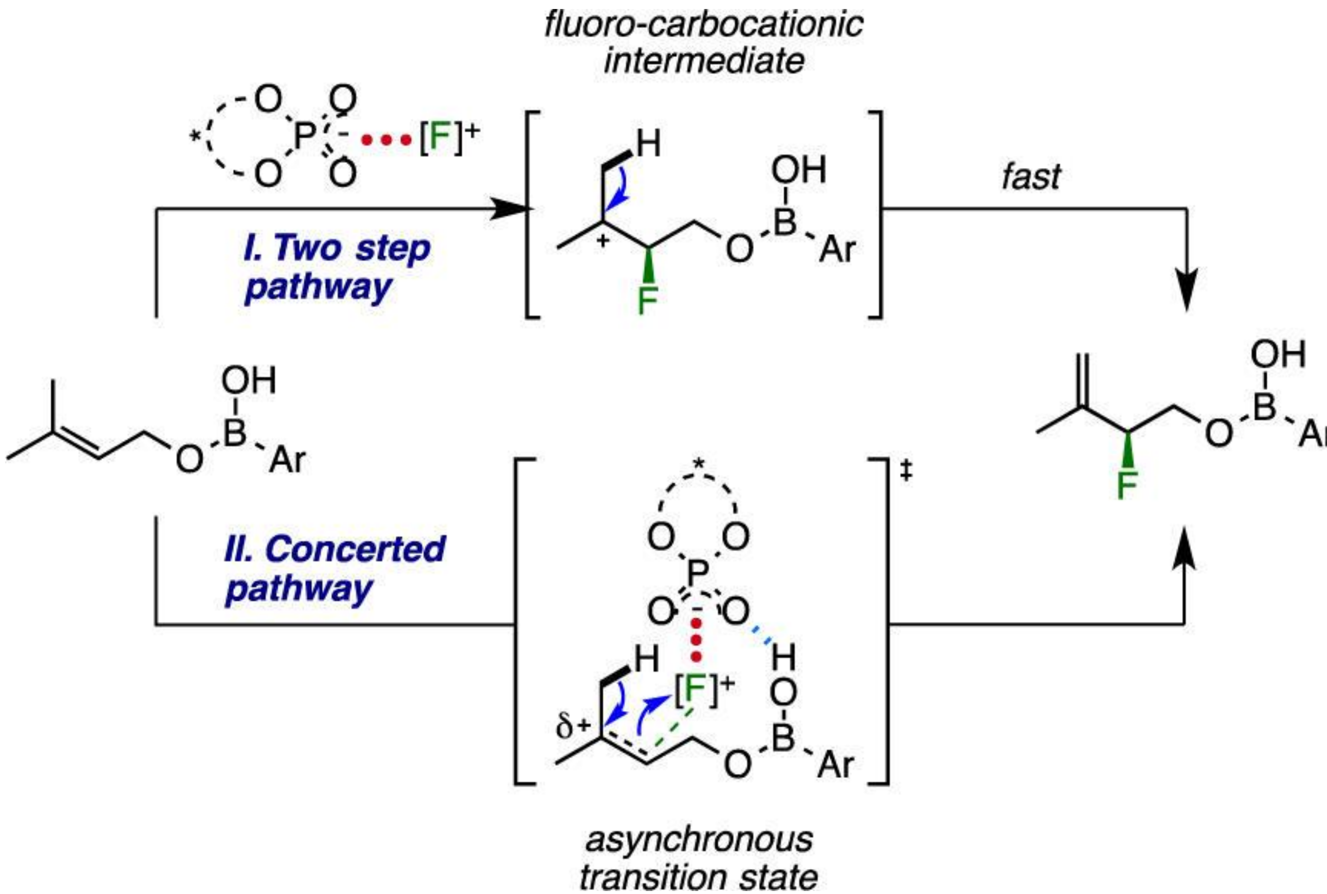
- Reaction Scope



Zi, W. W.; Wang, Y. M.; Toste, F. D. *J. Am. Chem. Soc.* **2014**, *136*, 12864.

In Situ Directed Fluorination of Allylic Achohols

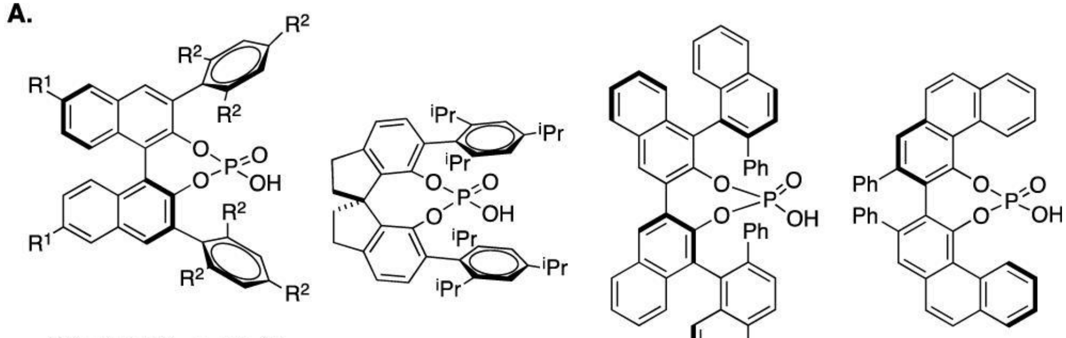
- Two Possible Mechanisms



Zi, W. W.; Wang, Y. M.; Toste, F. D. *J. Am. Chem. Soc.* **2014**, *136*, 12864.

Asymmetric Cross-Dehydrogenative Coupling

- Existing Phosphoric Acids



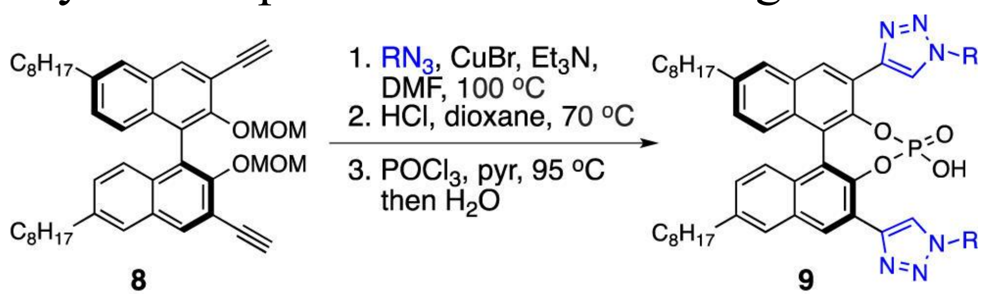
(S)-TRIP: R^1= H, R^2= ^iPr
(S)-C8-TRIP: R^1= C_8H_{17}, R^2= ^iPr
(S)-TCYP: R^1= H, R^2= C_6H_{11}

(R)-STRIP

(R,R)-Ph-DAP

(S)-VAPOL PA

- Catalyst Library of Phosphoric Acids Containing Triazole

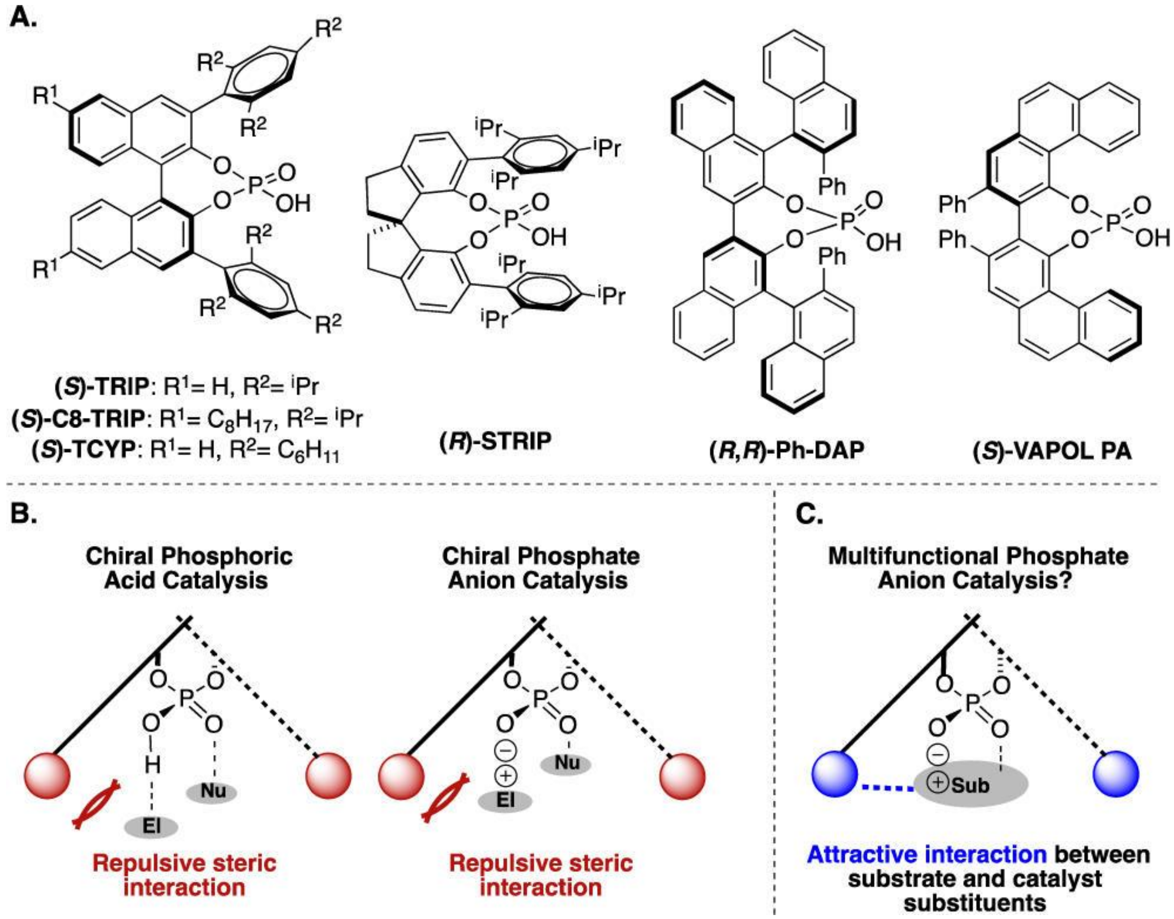


9a	R = Bn[a]	**9g**	R = 2,4,6-$(Me)_3C_6H_3$
9b	R = $CH(Ph)_2$	**9h**	R = 2,4,6-$(^iPr)_3C_6H_3$
9c	R = $CH(1\text{-}Naph)_2$	**9i**	R = 2,4,6-$(c\text{-}C_6H_{11})_3C_6H_3$
9d	R = 1-naphthyl	**9j**	R = 4-$(^tBu)C_6H_5$
9e	R = 9-anthracyl	**9k**	R = 3,5-$(^tBu)_2C_6H_4$
9f	R = 1-pyrenyl	**9l**	R = 1-adamantyl

Neel, A. J.; Hehn, J. P.; Tripet, P. F.; Toste, F. D. *J. Am. Chem. Soc.* **2013**, *135*, 14044.

Asymmetric Cross-Dehydrogenative Coupling

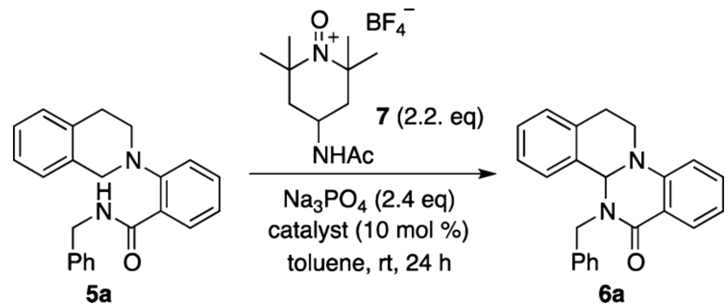
- Design Principles

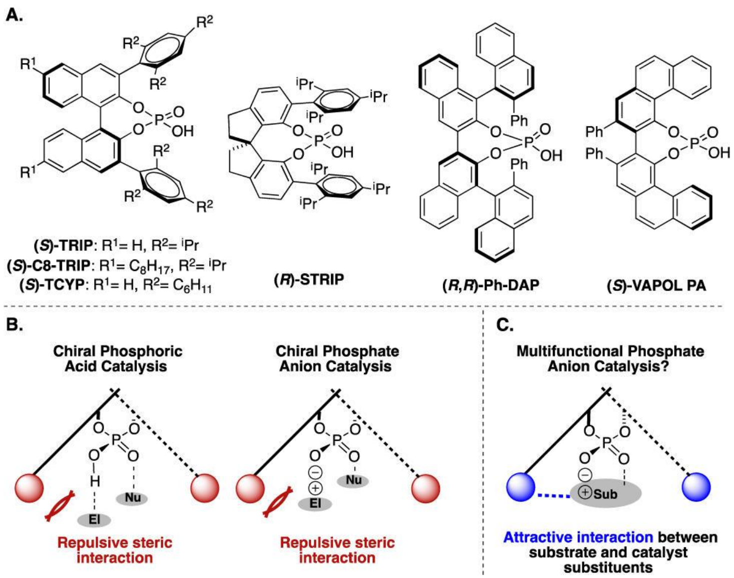


Neel, A. J.; Hehn, J. P.; Tripet, P. F.; Toste, F. D. *J. Am. Chem. Soc.* **2013**, *135*, 14044.

Asymmetric Cross-Dehydrogenative Coupling

- Selected Optimization Data





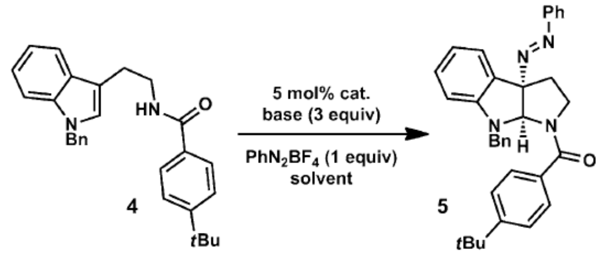
entry	catalyst	conversion (%)[b]	ee (%)[c]
1	(*S*)-C8-TRIP	86	8
2	(*S*)-TCYP	95	16
3	(*R*)-STRIP	64	30
4	(*R,R*)-Ph-DAP	69	−10[d]
5	(*S*)-VAPOL PA	97	31
6	(*S*)-**9b**	99	−69
7	(*S*)-**9g**	92	−78
8	(*S*)-**9h**	92	−80
9	(*S*)-**9i**	91	−77
10	(*S*)-**9l**	75	−81
11[e]	(*S*)-**9l**	91(83)[f]	−84
12	none	82	nd

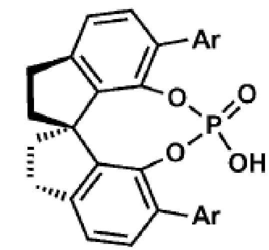
[a]See Supporting Information for complete optimization data. [b]Determined by HPLC using 1,4-dinitrobenzene internal standard. [c]Determined by chiral HPLC. [d]Negative sign indicates that opposite enantiomer predominates. [e]*p*-Xylene was used as solvent with 5 mol % catalyst. [f]Value in parentheses reflects isolated yield.

Neel, A. J.; Hehn, J. P.; Tripet, P. F.; Toste, F. D. *J. Am. Chem. Soc.* **2013**, *135*, 14044.

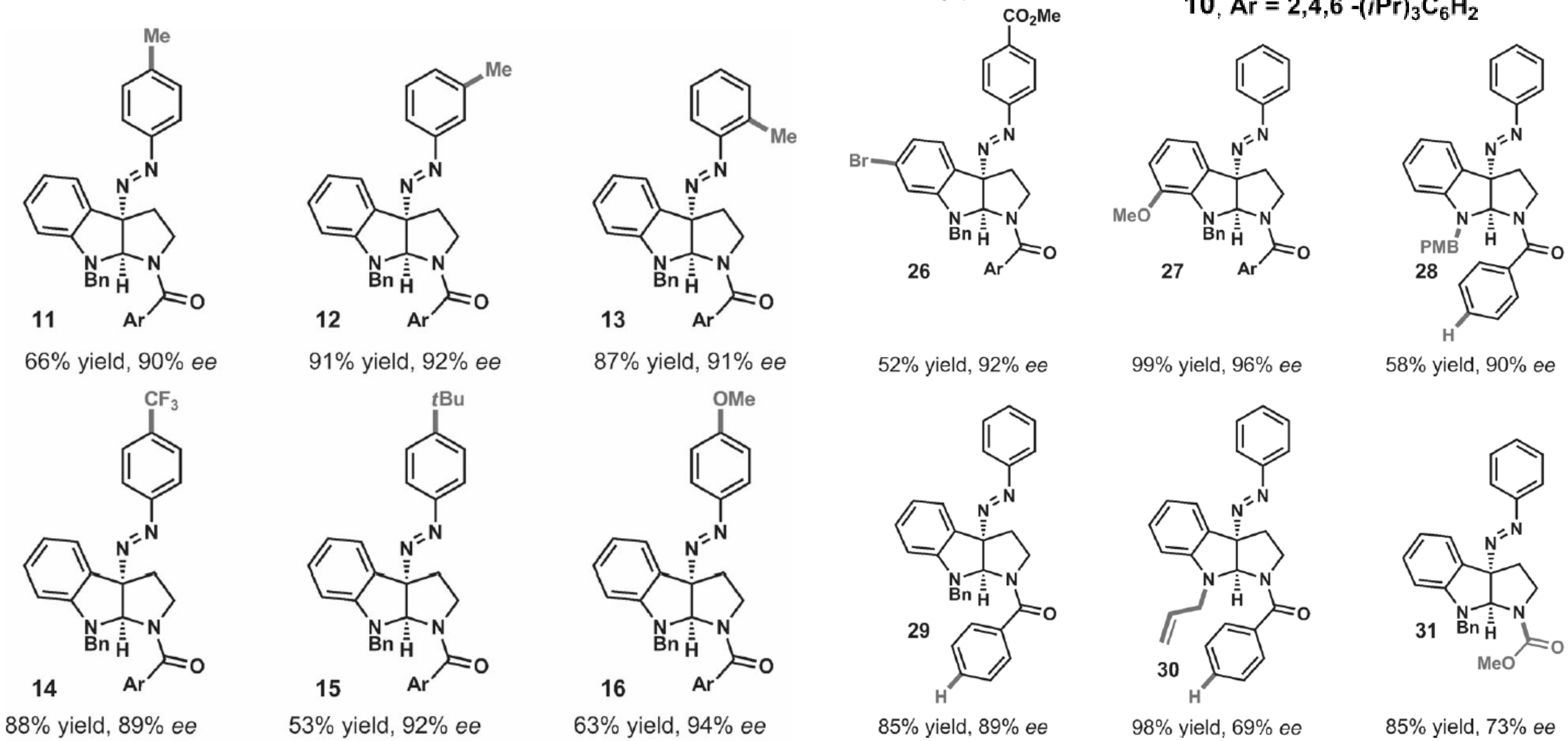
Asymmetric synthesis of C3-Diazenated Pyrolodindolines

- Reaction Scope





10, Ar = 2,4,6 -(iPr)$_3C_6H_2$

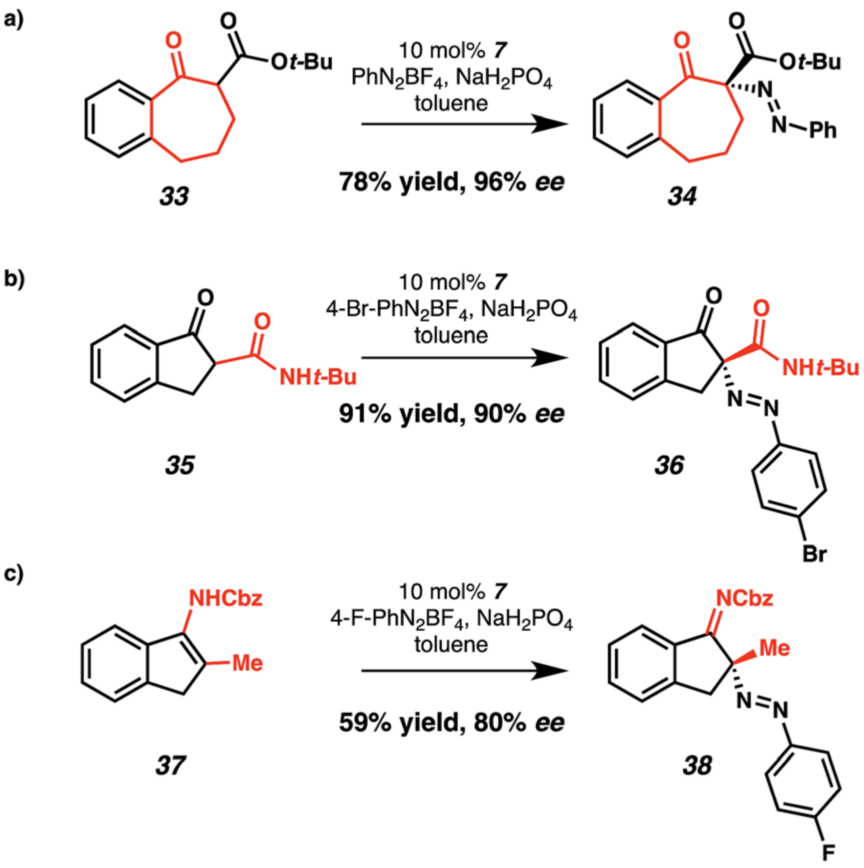


Scheme 2. Aryldiazonium scope. Conditions: **4** (1 equiv), (R)-STRIP (**10**; 5 mol%), Na_3PO_4 (3 equiv), ArN_2BF_4 (1 equiv), MTBE, RT, 2–8 h. Yields are of isolated products. The *ee* values were determined by HPLC on a chiral stationary phase. The relative and absolute configuration was assigned by analogy to **5**. Ar = 4-(tBu)C_6H_4.

Nelson, H. M.; Reisberg, S. H.; Shunatona, H. P.; Patel, J. S.; Toste, F. D. *Angew. Chem. Int. Ed.* **2014**, *53*, 5600.

Asymmetric α-Amination of 1,3-Dicarbonyl Compound

- Few Examples

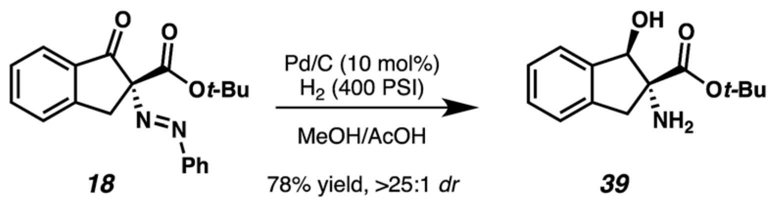


Nelson, H. M.; Patel, J. S.; Shunatona, H. P.; Toste, F. D. *Chem. Sci.* **2015**, *6*, 170.

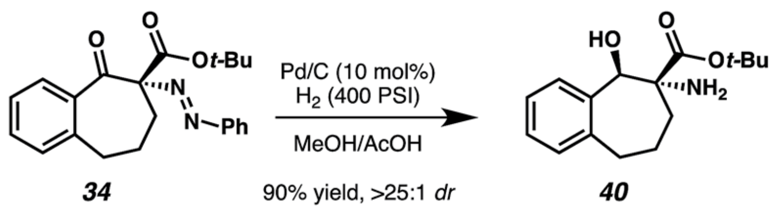
Asymmetric α-Amination of 1,3-Dicarbonyl Compound

- More Interesting Reactions

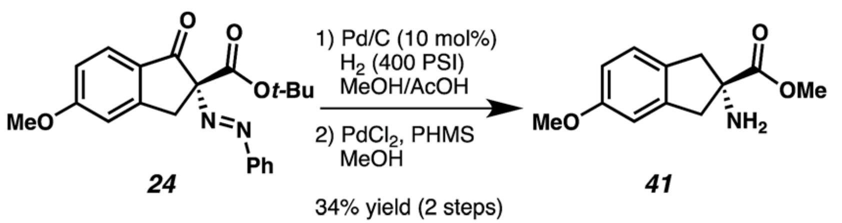
a)

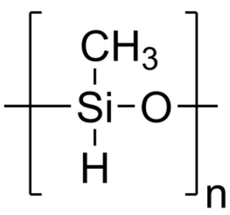


b)



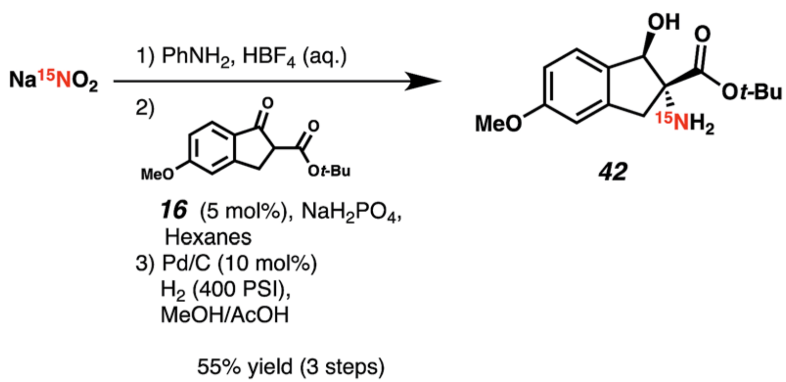
c)





PHMS

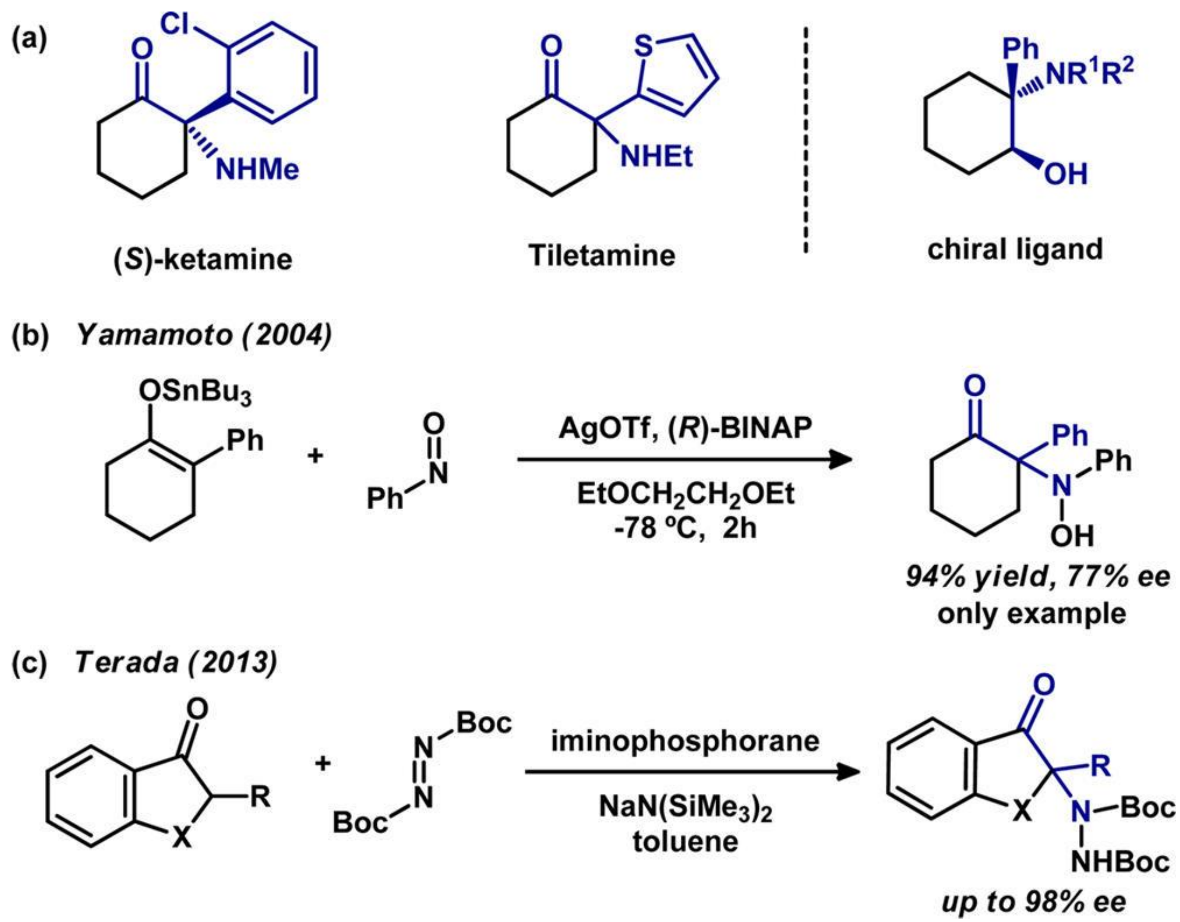
d)



Nelson, H. M.; Patel, J. S.; Shunatona, H. P.; Toste, F. D. *Chem. Sci.* **2015**, *6*, 170.

Asymmetric α-Amination of Cyclic Ketones

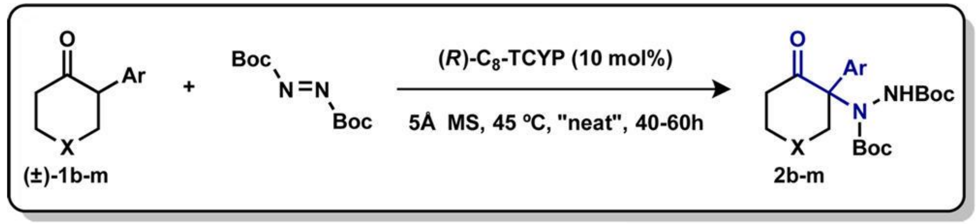
- Introduction

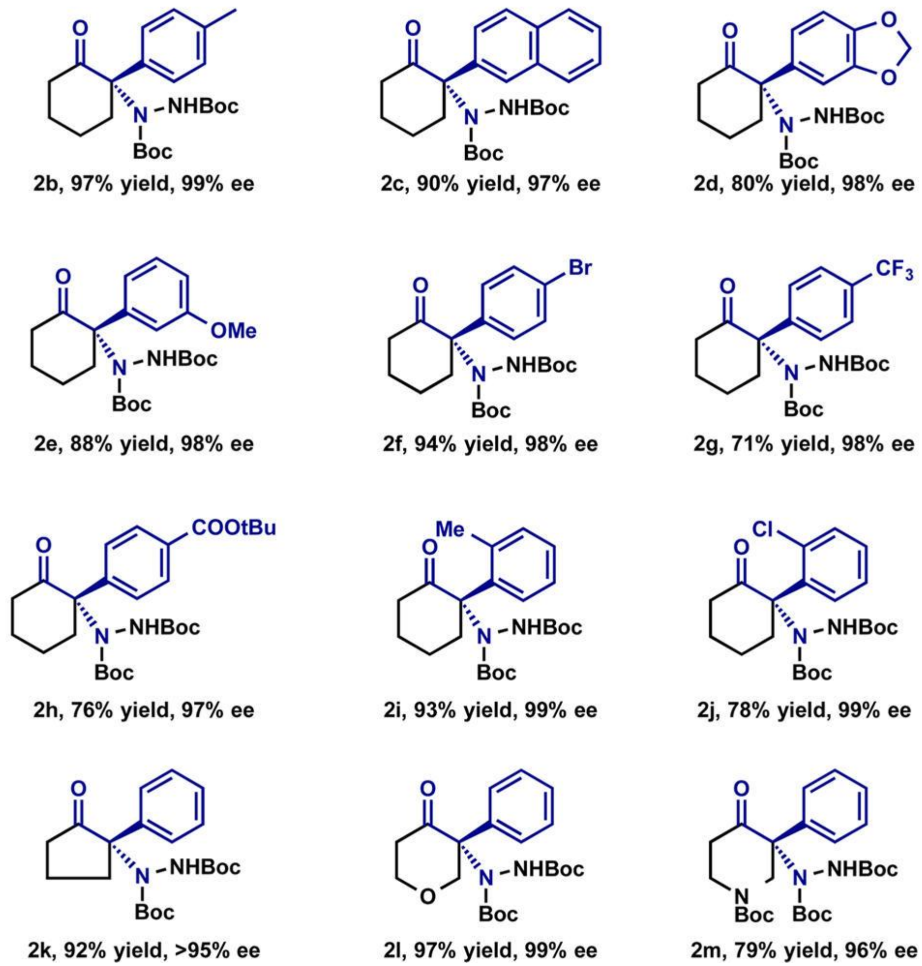


Yang, X. Y.; Toste, F. D. *J. Am. Chem. Soc.* **2015**, *137*, 3205.

Asymmetric α-Amination of Cyclic Ketones

- Substrate Scope

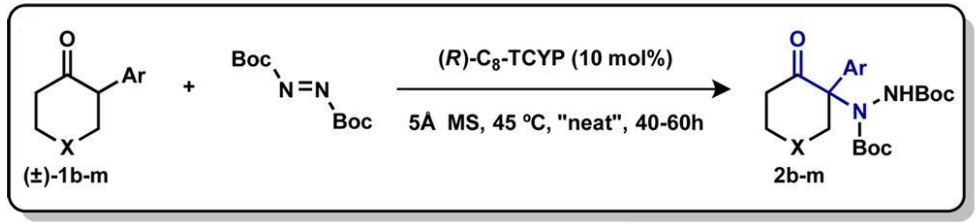


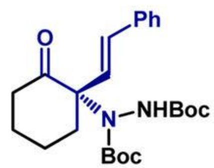


Yang, X. Y.; Toste, F. D. *J. Am. Chem. Soc.* **2015**, *137*, 3205.

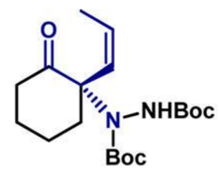
Asymmetric α-Amination of Cyclic Ketones

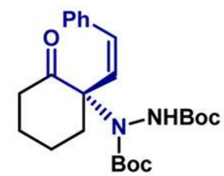
- Substrate Scope

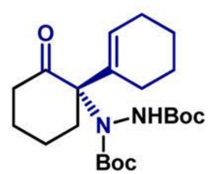


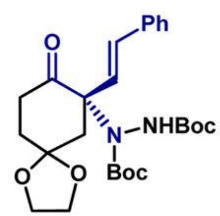

2n, 99% yield, 99% ee

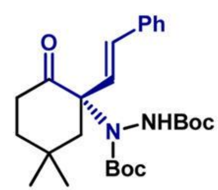

2o, 89% yield, 98% ee

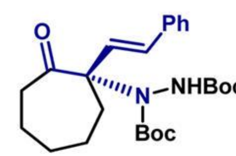

2p, 98% yield, 99% ee

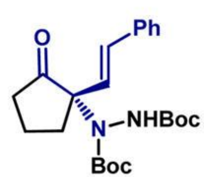

2q, 99% yield, 99% ee

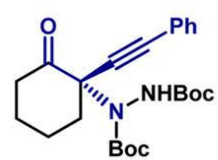

2r, 96% yield, 95% ee

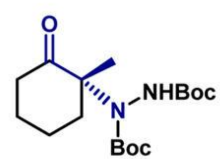

2s, 82% yield, 97% ee

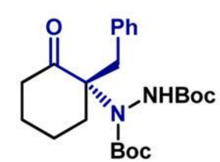

2t, 82% yield, 98% ee


2u, 60% yield, 72% ee


2v, 99% yield, 99% ee


2w, 33% yield, 93% ee

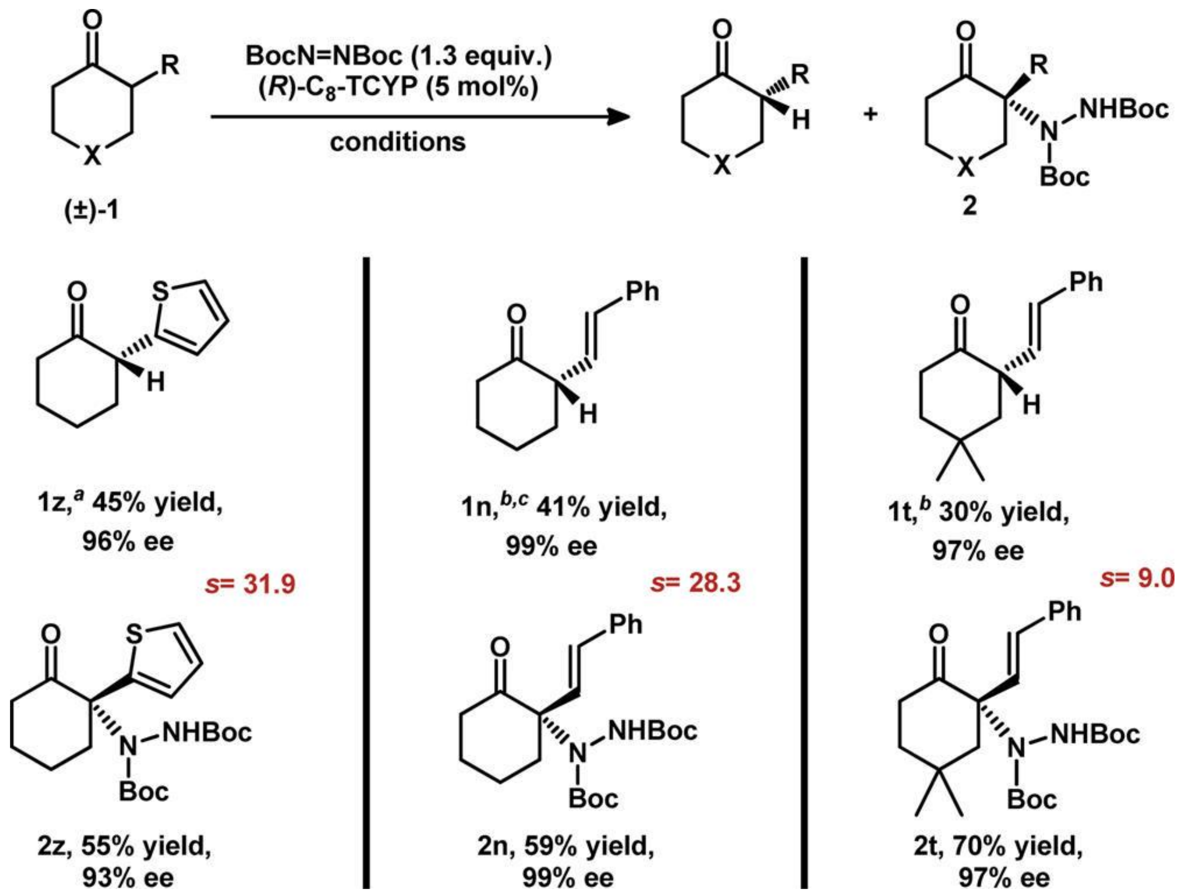

2x[b], 94% yield, 86% ee


2y[c], 89% yield, 99% ee

Yang, X. Y.; Toste, F. D. *J. Am. Chem. Soc.* **2015**, *137*, 3205.

Asymmetric α-Amination of Cyclic Ketones

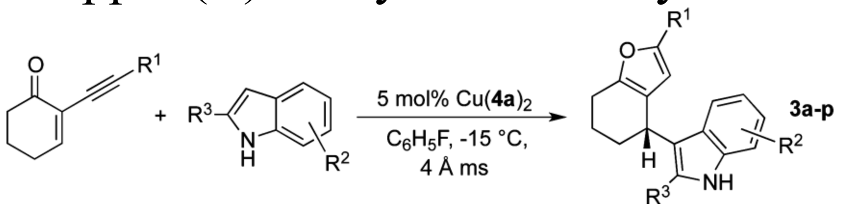
- Substrate Scope of Kinetic Resolution and Asymmetric Amination of α-Branched Cyclic Ketones



Yang, X. Y.; Toste, F. D. *J. Am. Chem. Soc.* **2015**, *137*, 3205.

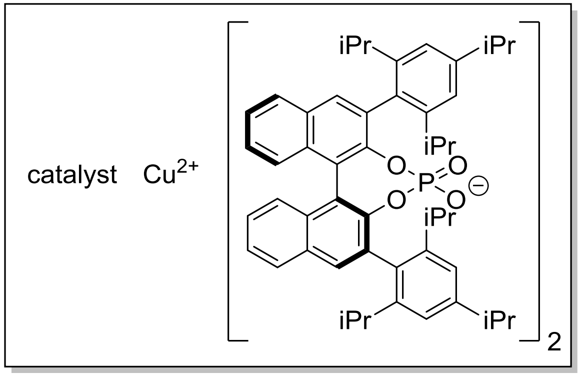
Combine Chiral Anion with Copper (II)

- Copper (II) catalyzed Furan Synthesis



Entry	R^1	R^2	R^3	Product	% yield[b]	%ee[c]
1	Ph	H	H	**3a**	92	91
2	4-MeO-C_6H_4	H	H	**3b**	82	92
3	4-Me-C_6H_4	H	H	**3c**	85	90
4	4-F-C_6H_4	H	H	**3d**	76	88
5	4-*t*-Bu-C_6H_4	H	H	**3e**	85	90
6	3-Me-C_6H_4	H	H	**3f**	75	90
7	Cyclopentyl	H	H	**3g**	80	87
8	Bn	H	H	**3h**	84	73
9	Cyclohexyl	H	H	**3i**	85	94
10	Ph	5-Br	H	**3j**	90	93
11	Ph	6-Br	H	**3k**	94	90
12	Ph	5-MeO	H	**3l**	74	81
13	Ph	6-Me	H	**3m**	76	85
14	Ph	5-Cl	H	**3n**	81	90
15	Ph	5-F	H	**3o**	73	90
16[d]	Ph	H	Me	**3p**	16	85

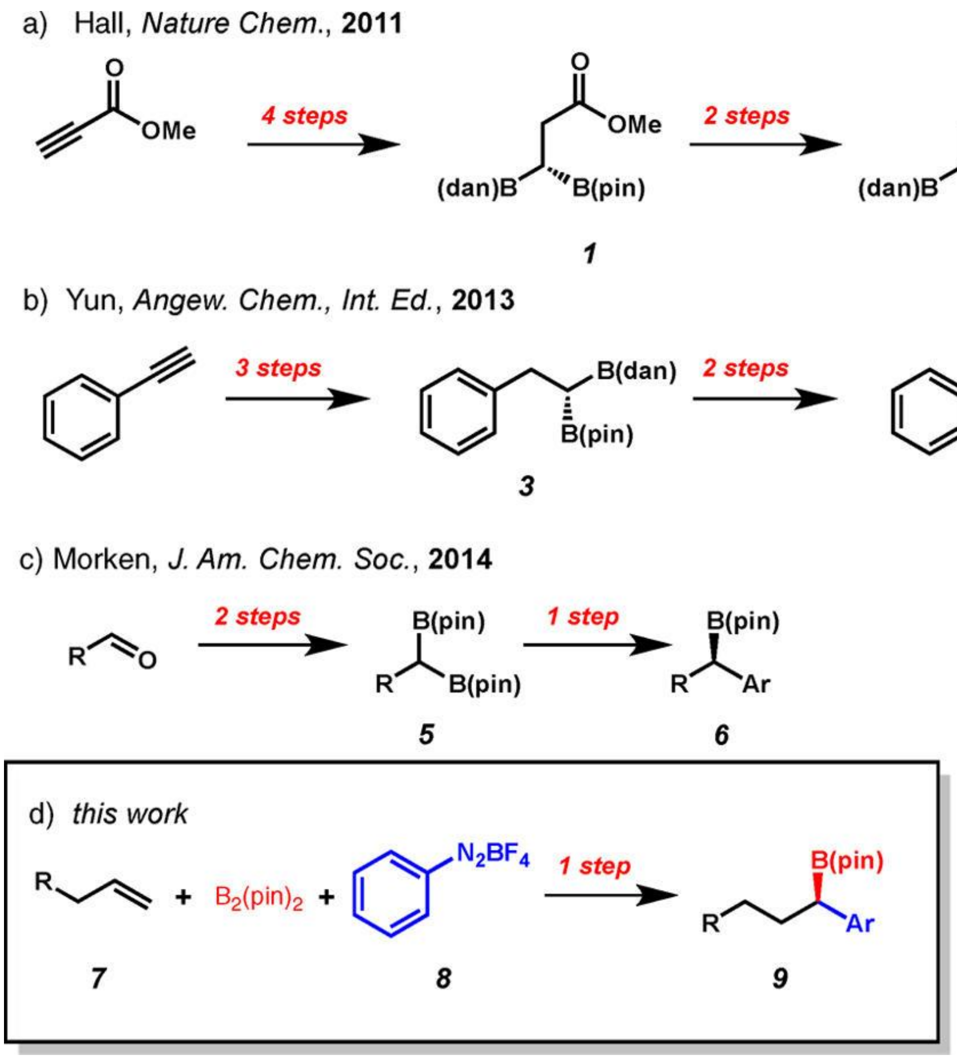
[a] Conditions: 5 mol % Cu(**4a**)$_2$ added to a solution of 1.0 equiv of **1** (0.2 M) and 1.05 equiv of **2**, 50 h. [b] Isolated after chromatography. [c] Determined by HPLC analysis. [d] Conducted at 5 °C.



Rauniyar, V.; Wang, Z. J.; Burks, H. E.; Toste, F. D. *J. Am. Chem. Soc.* **2011**, *133*, 8486.

Combine Chiral Anion with Pd

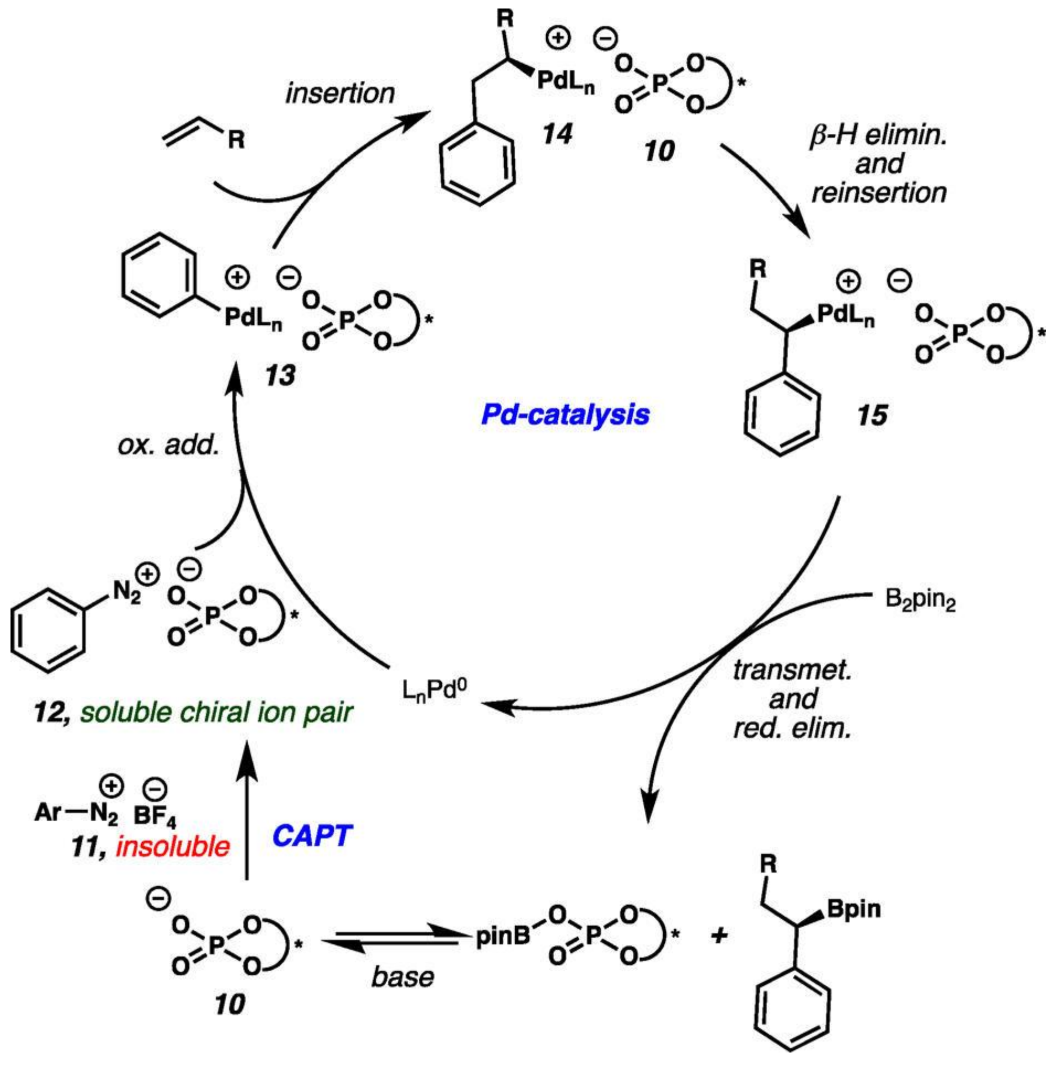
- Enantioselective 1,1-Arylborylation of Alkenes



Nelson, H. M.; Williams, B. D.; Miro, J.; Toste, F. D. *J. Am. Chem. Soc.* **2015**, *137*, 3213.

Combine Chiral Anion with Pd

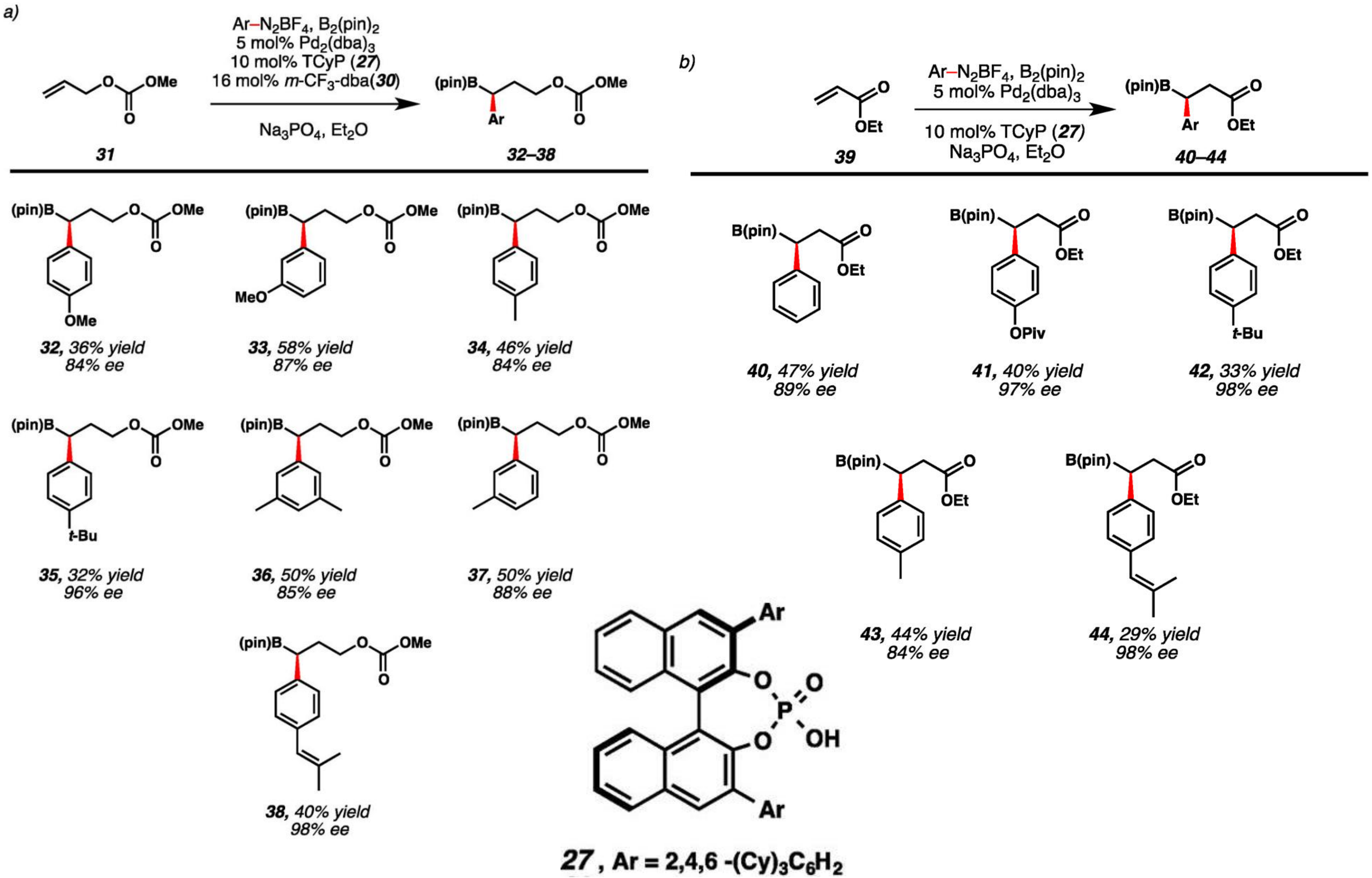
- Proposed Mechanism



Nelson, H. M.; Williams, B. D.; Miro, J.; Toste, F. D. *J. Am. Chem. Soc.* **2015**, *137*, 3213.

Combine Chiral Anion with Pd

- Enantioselective Scope



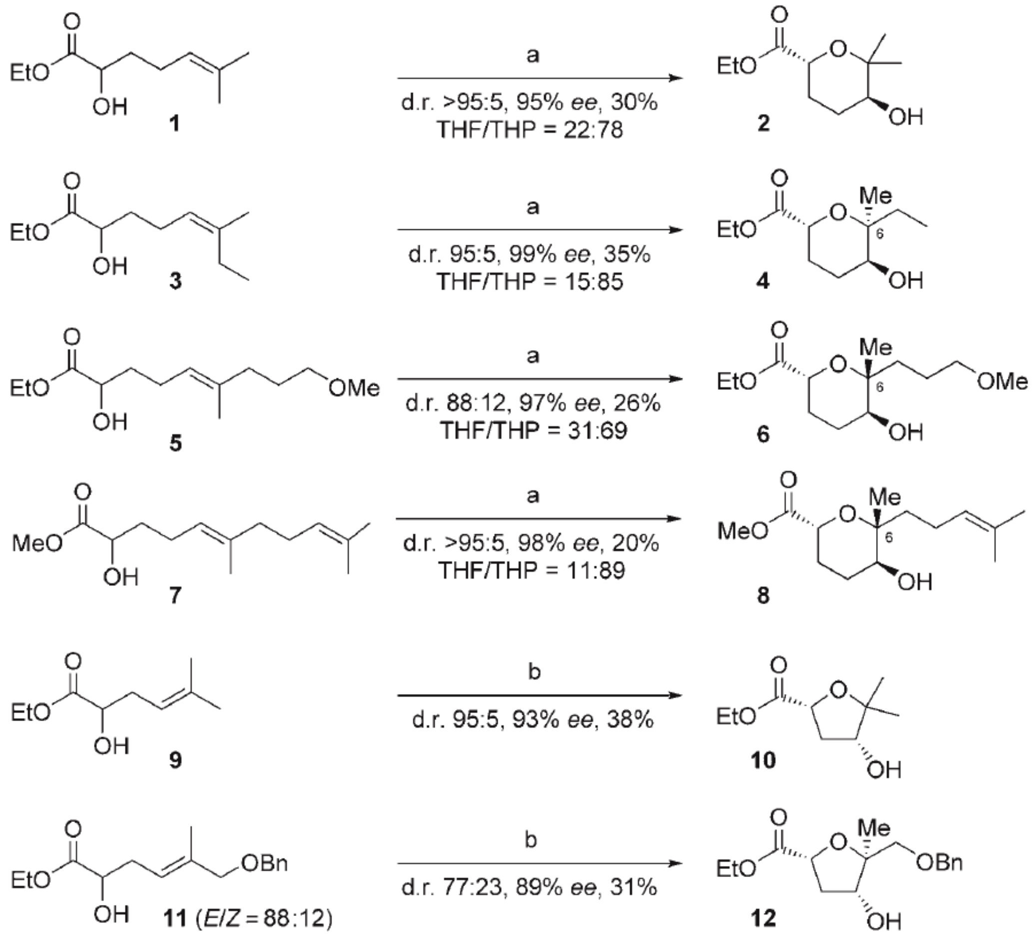
Nelson, H. M.; Williams, B. D.; Miro, J.; Toste, F. D. *J. Am. Chem. Soc.* **2015**, *137*, 3213.

Redox Chemistry

- Vanadium-Catalyzed Oxidation
- Vanadium-Catalyzed Reduction
- Rhenium-Catalyzed Reduction

Vanadium-Catalyzed Oxidation

- Enantioselective synthesis of Cyclic Ethers

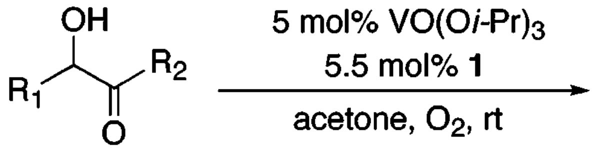


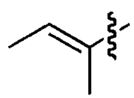
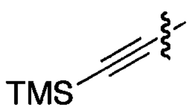
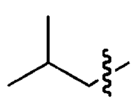
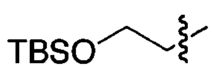
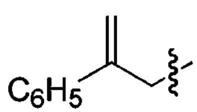
Scheme 1. Vanadium-catalyzed resolution/oxidative cyclization. Reagents and conditions: a) [VO(O*i*Pr)$_3$] (10 mol%), **L1** (11 mol%), O_2, acetone, 30 °C, 30–48 h (≈50% conversion); then TBHP (0.55 equiv), $CHCl_3$, RT, 24–72 h; b) [VO(O*i*Pr)$_3$] (10 mol%), **L1** (11 mol%), O_2, acetone, 30 °C, 30–48 h; TBHP (0.55 equiv), $CHCl_3$, RT, 3 h; then CSA (5 mol%), RT, 16 h.

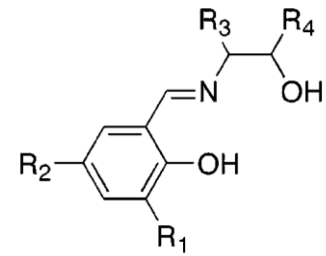
Blanc, A.; Toste, F. D. *Angew. Chem. Int. Ed.* **2006**, *45*, 2096.

Vanadium-Catalyzed Oxidation

- Asymmetric Oxidation of α-Hydroxy Esters



entry	R_1	R_2	time (h)	conversion	isolated yield[b]	ee[c]	*s*
1	Ph–	OEt	10	51%	49% (95%)	99% (*R*)	> 50
2	*p*-$MeOC_6H_4$–	OMe	5.5	62%	38% (69%)	95% (*R*)	13
3	*p*-$CF_3C_6H_4$–	OMe	4.0	57%	35% (88%)	98% (*R*)	29
4		OBn	16	57%	45% (90%)	92% (*R*)	18
5		OEt	16	47%	53% (85%)	50% (*R*)	6
6		O*i*-Pr	90	55%	37% (86%)	98% (*R*)	30
7		OMe	144	51%	48% (95%)	90% (*R*)	42
8		OEt	72	48%	48% (88%)	90% (*R*)	34
9[d]	Ph–	NH^tBu	12	52%	48% (97%)	72% (*R*)	12

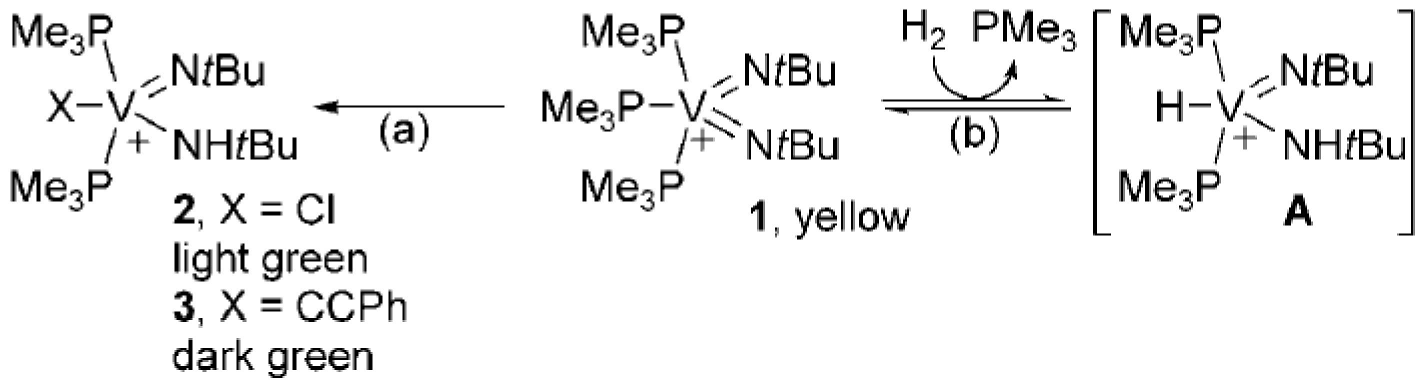


(**1**) R_1= *t*-Bu; R_2= *t*Bu
R_3= (*S*)-*t*-Bu; R_4= H

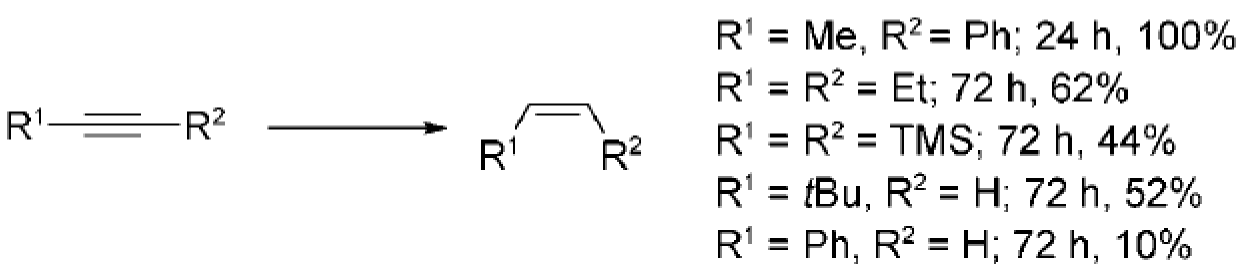
Radosevich, A. T.; Musich, C.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 1090.

Vanadium-Catalyzed Reduction

- Z-Selective Hydrogenation of Alkynes



Scheme 1. Conditions: a) 1.05 equiv 2.0 M HCl in Et_2O, RT, over night, 46%; b) 1.05 equiv phenylacetylene in Et_2O, RT, 71%; c) 1 atm H_2, $PhCF_3$. In complexes **1**, **2**, **3**, and **A** the counteranion, $[Al(PFTB)_4]^-$, is not depicted for clarity.

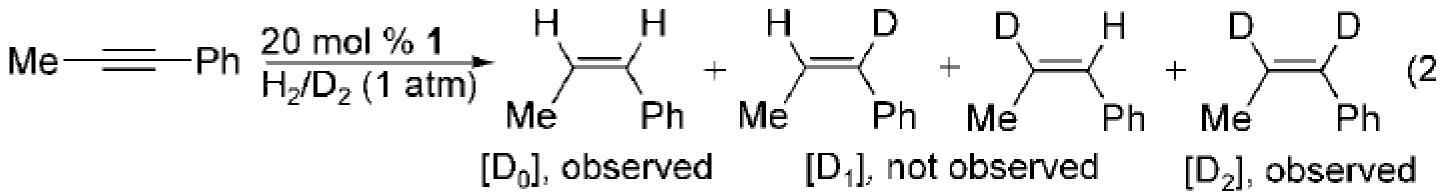


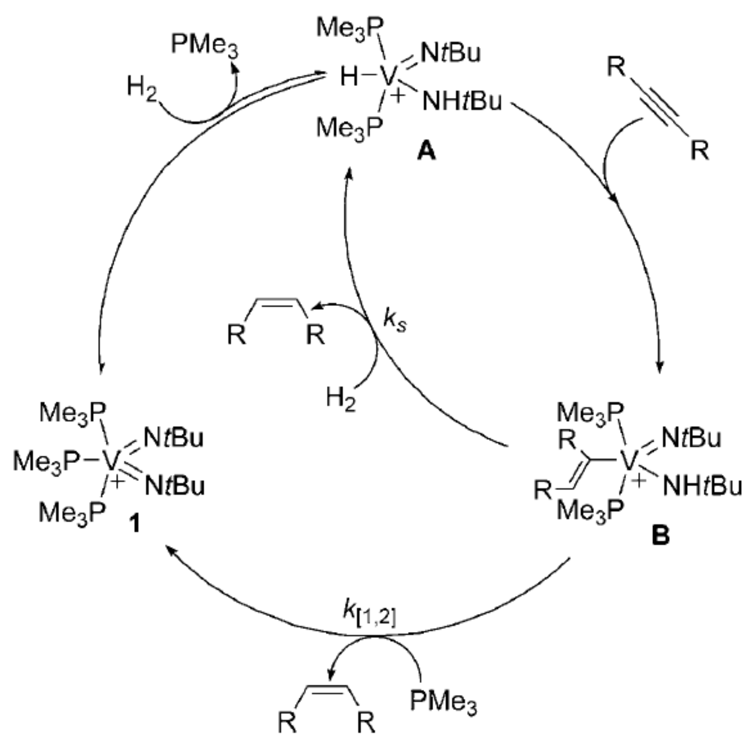
(1)

La Pierre, H. S.; Arnold, J.; Toste, F. D. *Angew. Chem. Int. Ed.* **2011**, *50*, 3900.

Vanadium-Catalyzed Reduction

- Mechanism



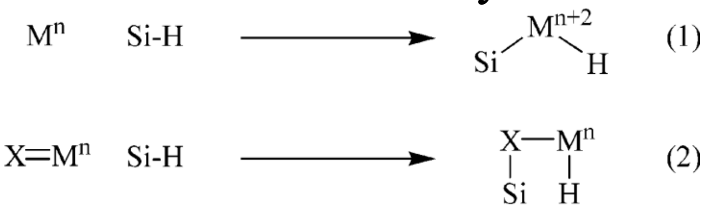


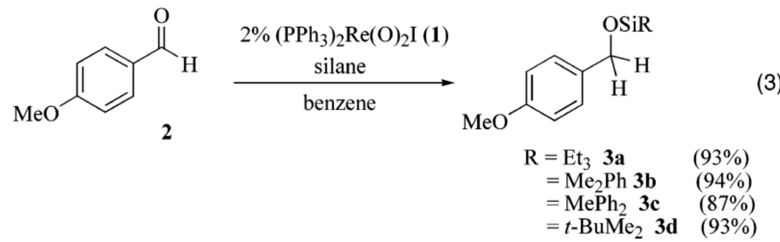
$k_{[1,2]} \gg k_s$

La Pierre, H. S.; Arnold, J.; Toste, F. D. *Angew. Chem. Int. Ed.* **2011**, *50*, 3900.

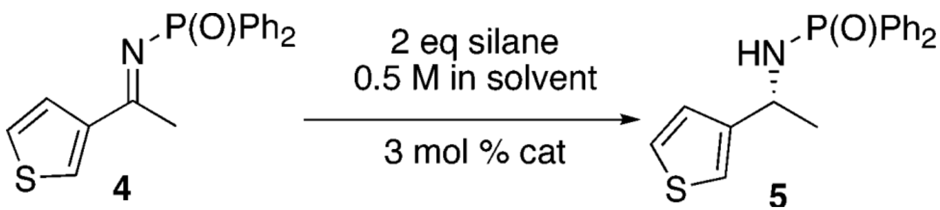
Rhenium-Catalyzed Reduction

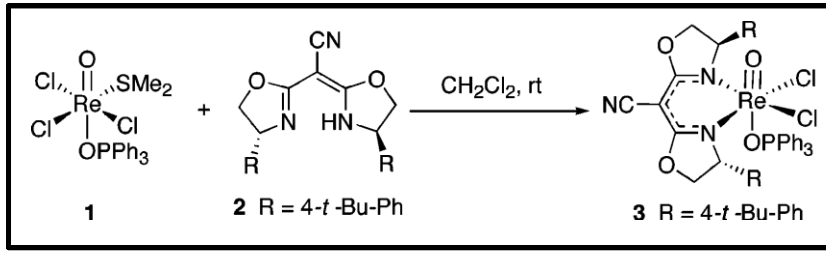
- 1. Reduction of Aldehydes





- 2. Enantioselective Reduction of Imines





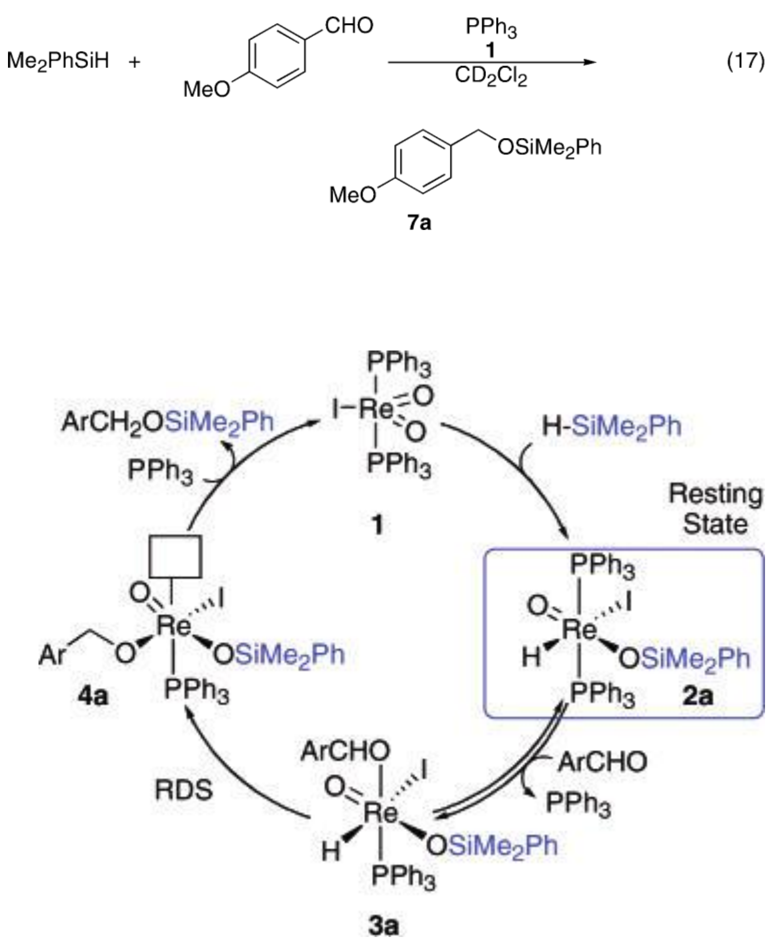
entry	silane	solvent	temp	% yield	% ee
1	DMPS−H	CH_2Cl_2	rt	75	99
2	DMPS−H	THF	rt	96	99
3	DMPS−H	EtOAc	rt	58	99
4	DMPS−H	toluene	rt	51	99
5	DPMS−H	CH_2Cl_2	rt	77	98
6	DMPS−H	CH_2Cl_2	40 °C	81	98

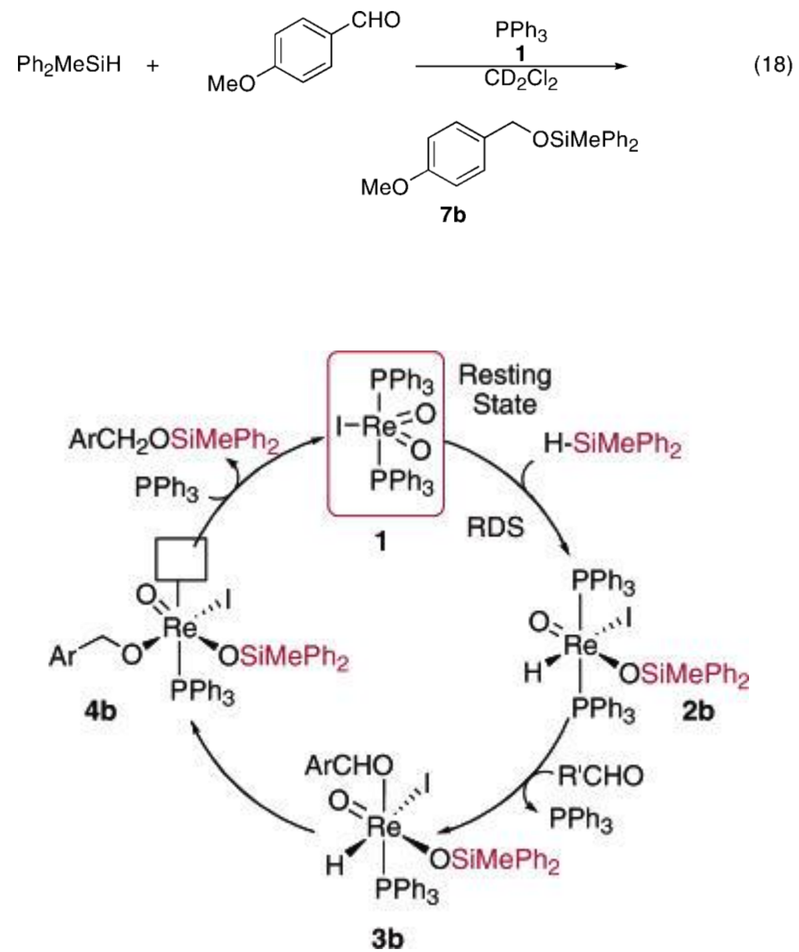
1. Kennedy-Smith, J. J.; Nolin, K. A.; Gunterman, H. P.; Toste, F. D. *J. Am. Chem. Soc.* **2003**, *125*, 4056.

2. Nolin, K. A.; Ahn, R. W.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 12462.

Rhenium-Catalyzed Reduction

- Mechanisms





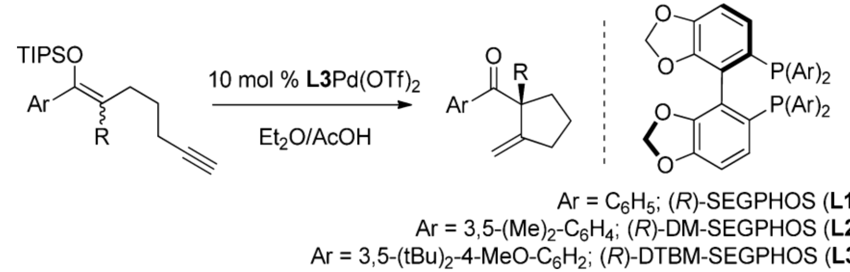
Nolin, K. A.; Krumper, J. R.; Pluth, M. D.; Bergman, R. G.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 14684.

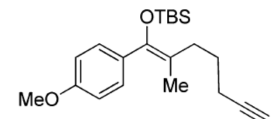
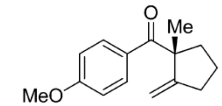
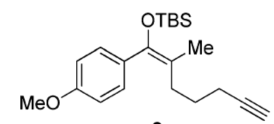
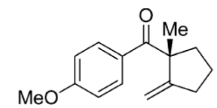
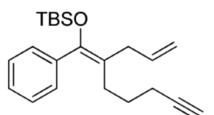
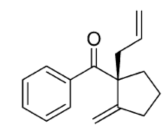
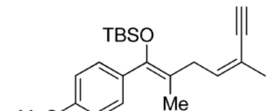
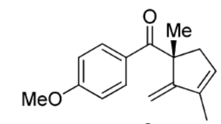
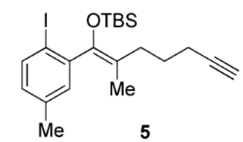
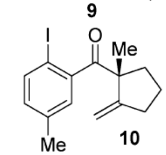
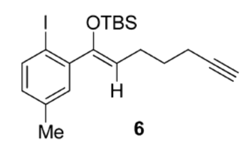
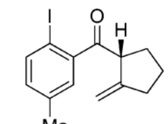
Palladium Chemistry

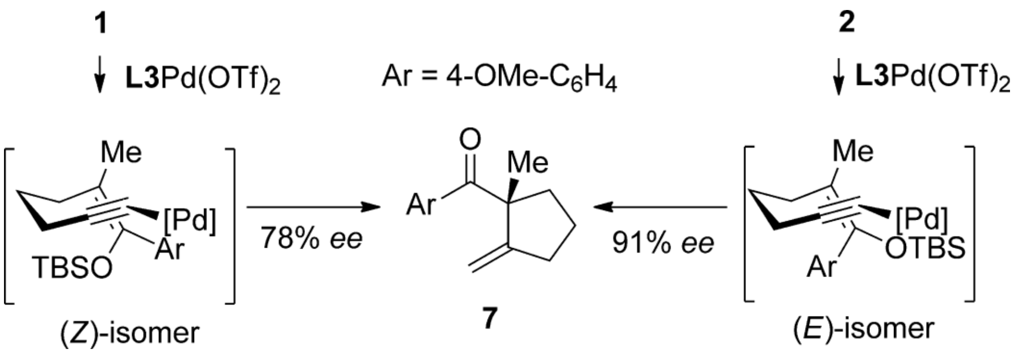
- Enyne Cyclization Reactions
- Conia Ene Reactions
- Coupling Reaction
- Palladium Nanoparticle Catalyst

1,6-Enyne Cyclization Reactions

- Pd-Cyclization of Silyloxy-1,6-enynes



Entry	Substrate	Product	Yield (%)[b]	ee (%)[c]
1	 **1**	 **7**	80	78
2	 **2**	 **7**	93	91
3	 **3**	 **8**	92	88
4	 **4**	 **9**	70	73
5	 **5**	 **10**	96	95
6[d]	 **6**	 **11**	86	85



Acknowledgment. We gratefully acknowledge the University of California, Berkeley, NIHGMS (R01 GM073932-01), Merck Research Laboratories, Bristol-Myers Squibb, Amgen Inc., DuPont, GlaxoSmithKline, and Eli Lilly & Co. for financial support. We thank Takasago for their generous donation of the SEGPHOS ligands.

Brazeau, J. F.; Zhang, S. Y.; Colomer, I.; Corkey, B. K.; Toste, F. D. *J. Am. Chem. Soc.* **2012**, *134*, 2742.

Thanks for Your Time!

- Portugal Equals

Dean Toste

Egg Tarts

To Me