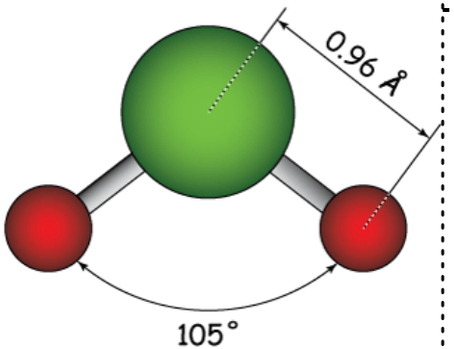
Jie Wang

Organic Reactions in the Presence of Water

Baran Group Meeting
06/25/16

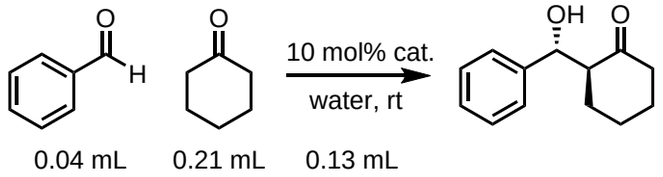
Water

Maximum density: 1.0 g/mL at 3.98 ^{o}C
Surface tension: 71.97 at 25 ^{o}C
Heat capacity: 4.187 kJ/kgK
Heat of melting: 334 kJ/kg
Heat of vaporization: 2257 kJ/kg
BDE: 493.4 kJ/mol (423.0 for ethane)
Dielectric constant: 80.1 at 20 ^{o}C
Cohesive energy density: 2.2973 GPa
Critical temperature: 380-386 ^{o}C
Critical pressure: 22.1 MPa



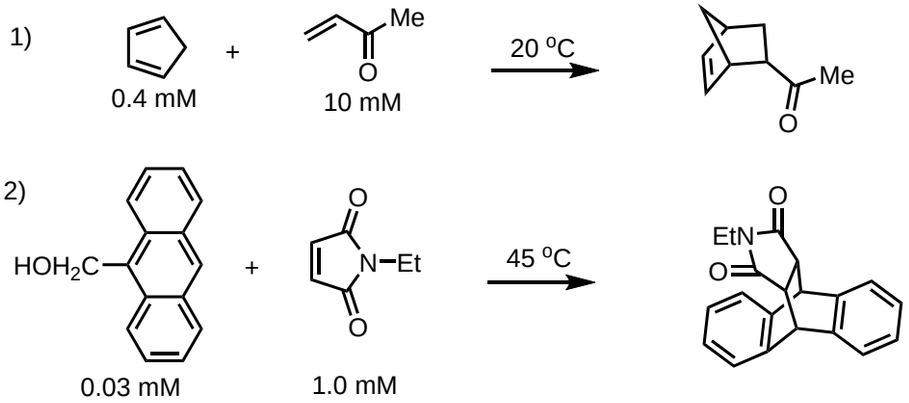
Terminology:

in water
on water
aqueous
micelle
emulsion
microemulsion
concentrated organic phase
in the presence of water



Y. Hayashi, *Angew. Chem. Int. Ed.* **2006**, *45*, 958
K. Janda, *Angew. Chem. Int. Ed.* **2006**, *45*, 8100
Y. Hayashi, *Angew. Chem. Int. Ed.* **2006**, *45*, 8103

"Big Bang"



Advantages:

Not inflammable, No smell, Nontoxic, environment friendly
Good separation with organics
Ubiquitous, inexpensive
Unique fluid properties
Anhydrous solvents are not needed
Protection of OH, CO_2H may not be necessary
Control of pH

Disadvantages:

Large heat of evaporation
Chelation to metal prevents catalysis
Limit the use of water sensitive organics?

Part I: Reactivities and Selectivities in the Presence of Water

- Different reactivity and selectivity w/ water
- Conterintuitively water toleration

Part II: Designed Catalysis in Water

- Water-tolerant ligand design
- Green chemistry

Topics not covered:

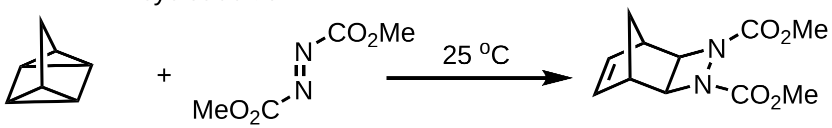
Organocatalysis
Phase-transfer catalysis
Solid supported catalysis in water
Supermolecular chemistry in water
Reactions in near- or super-critical water
Peptide synthesis
Porphyrin catalysis

solvent	k_2 (1) x10^5 $M^{-1}S^{-1}$	k_2 (2) x10^5 $M^{-1}S^{-1}$
isooctane	6	796
MeOH	76	344
H_2O	4400	22600
LiCl (aq, 4.86 M)	10800	56500
$C(NH_2)_3^+Cl^-$ (4.86 M)	4300	18830
β-cyclodextrin	10900	13800
α-cyclodextrin	2610	

solvent	conc.	endo/exo (1)
neat	-	3.85
EtOH	0.15 M	8.5
H_2O	0.15 M	21.4
H_2O	0.30 M	18.6
H_2O	0.45 M	17.2
H_2O	0.48 M	15.0
H_2O,(SDS)	0.15 M	19.5
H_2O	7 mM	22.5
LiCl	10 mM	28.0
$C(NH_2)_3^+Cl^-$	10 mM	22.0

R. Breslow, *J. Am. Chem. Soc.* **1980**, *102*, 7816
R. Breslow, *Tetrahedron Lett.* **1983**, *24*, 1901
R. Breslow, *Tetrahedron Lett.* **1984**, *25*, 1239

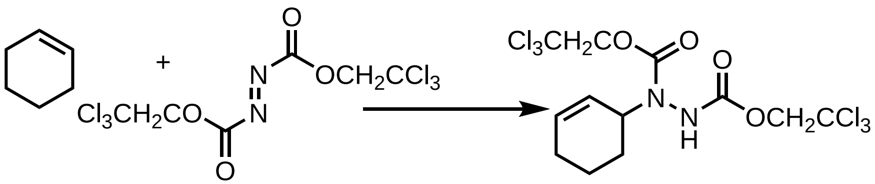
$2\sigma+2\sigma+2\pi$ cycloaddition



Solvent	Conc. [M]	Time to Completion
CH_3CN	2	84 h
DMSO	2	36 h
MeOH	2	18 h
neat	4.53	48 h
'on H_2O'	**4.53**	**10 min**
$MeOH/H_2O$ (3:1, homogeneous)	2	4 h
$MeOH/H_2O$ (1:1, heterogeneous)	-	10 min
$MeOH/H_2O$ (1:3, heterogeneous)	-	10 min

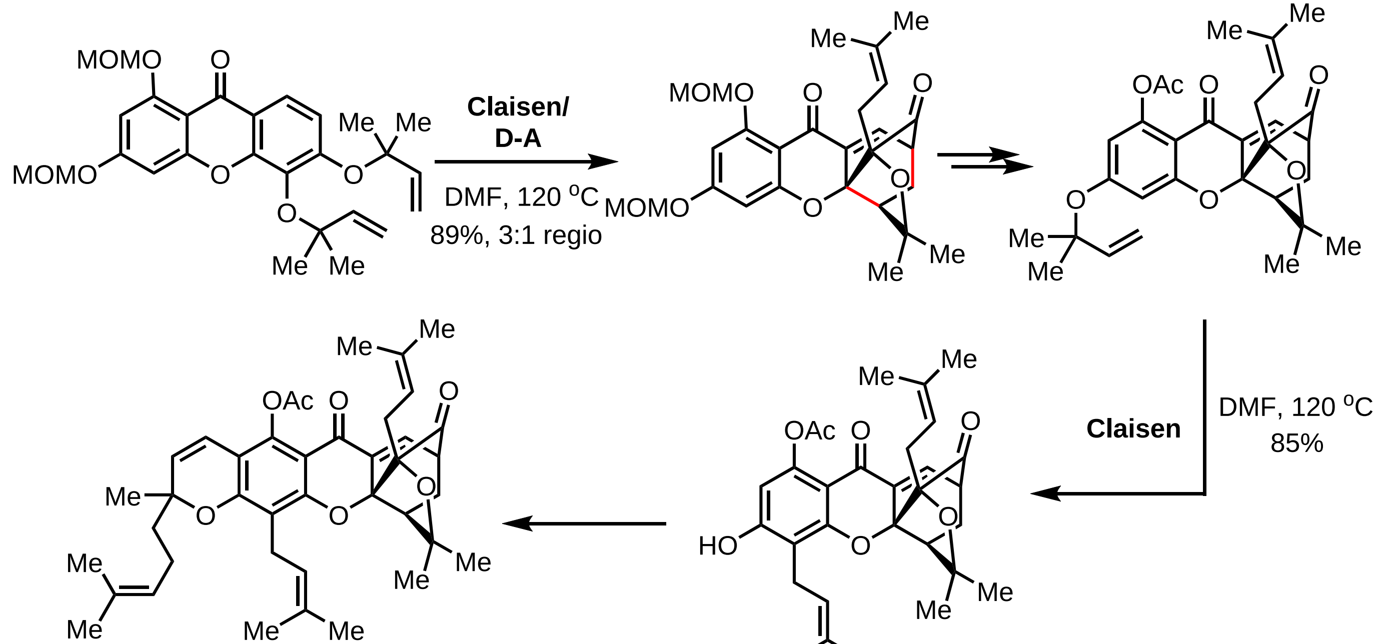
K. B. Sharpless, *Angew. Chem. Int. Ed.* **2005**, *44*, 3275

Ene reaction



Solvent	Temp (°C)	Time	Yield
benzene	80	24 h	70%
neat	50	36 h	62%
'on H_2O'	50	8 h	91%

K. B. Sharpless, *Angew. Chem. Int. Ed.* **2005**, *44*, 3275



For Claisen/D-A

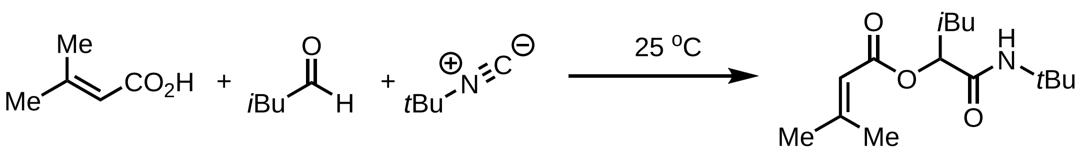
Solvent	Temp (°C)	Time (h)	Conv.
MeOH	65	4	0
TFE	65	4	0
EtOH	65	4	0
$MeOH/H_2O$ (1:1)	65	4	100
TFE/H_2O (1:1)	65	4	100
$EtOH/H_2O$ (1:1)	65	4	100

For Claisen

Solvent	Temp (°C)	Time (h)	Conv.
MeOH	50	4.5	50
TFE	25	4	0
EtOH	25	4	0
$MeOH/H_2O$ (1:1)	50	2.5	100
TFE/H_2O (1:1)	25	75	100
$EtOH/H_2O$ (1:1)	25	72	100

K. C. Nicolaou, *Angew. Chem. Int. Ed.* **2005**, *44*, 756

Passerini Reaction

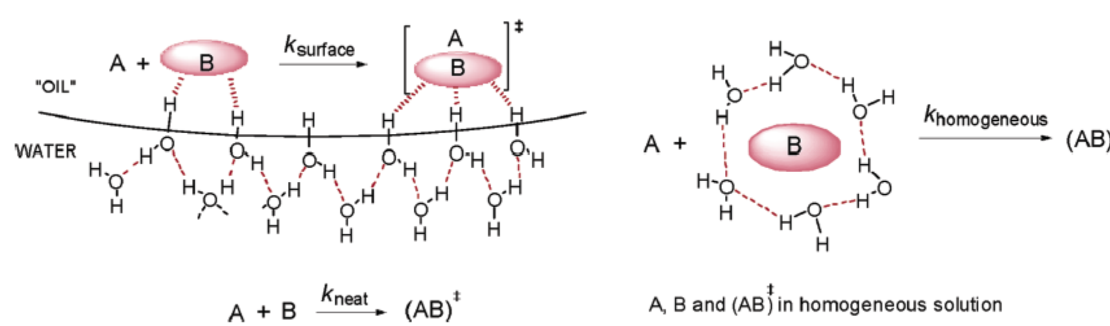


Solvent	Rate
DCM	1
H_2O	18
0.5 M aq. glucose	129
1 M aq LiCl	286

M. C. Pirrung, *J. Am. Chem. Soc.* **2004**, *126*, 444
M. C. Pirrung, *Tetrahedron,* **2005**, *61*, 11456
M. C. Pirrung, *Chem. Eur. J.* **2006**, *12*, 1312

$k_{surface}/k_{neat} = 1.5 \times 10^5$

$k_{surface}/k_{homogeneous} = 600$



Hydrophobic effect
Hydrogen bonding

R. A. Marcus, *J. Am. Chem. Soc.* **2007**, *129*, 5492
A. Kumar, *J. Phys. Chem. A* **2013**, *117*, 2446

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Organic Reactions in the Presence of Water

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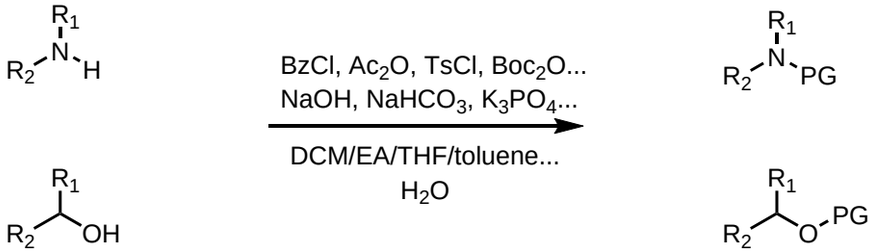
Schotten-Baumann Acylation

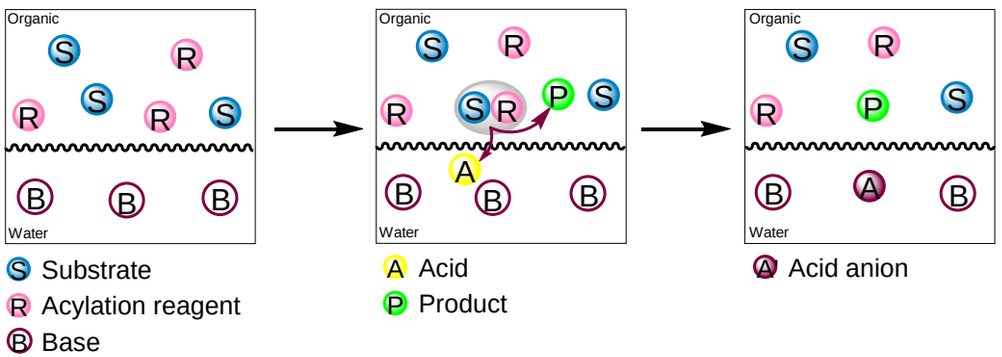


Relative rate:

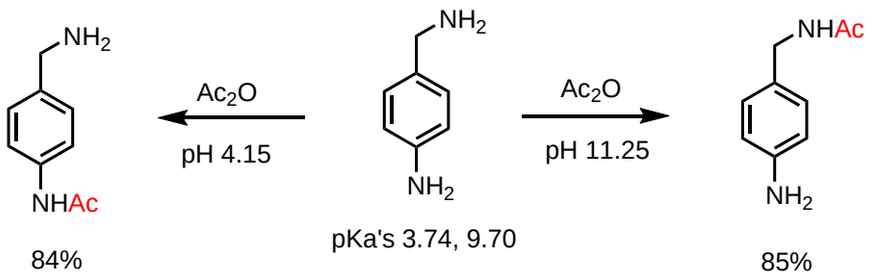
	MeOH	H_2O	*m*-Nitroaniline
AcCl	8	1	400
BzCl	39	1	50000

- Slower hydrolysis for higher acyl chlorides
- Slower hydrolysis for aromatic acyl chlorides
- Heterogenous important for hydrolysis more labileacyl chlorides

C. Schotten, *Chem. Ber.* **1884**, *21*, 2544
E. Baumann, *Chem. Ber.* **1886**, *19*, 3218
N. O. V. Sonntag, *Chem. Rev.* **1953**, *52*, 237
C. Yuan, *J. Am. Chem. Soc.* **1955**, *77*, 332
C. N. Hinshelwood, *J. Chem. Soc.* **1934**, 1079
T. W. Bentley, *J. Org. Chem*. **1996**, *61*, 7927

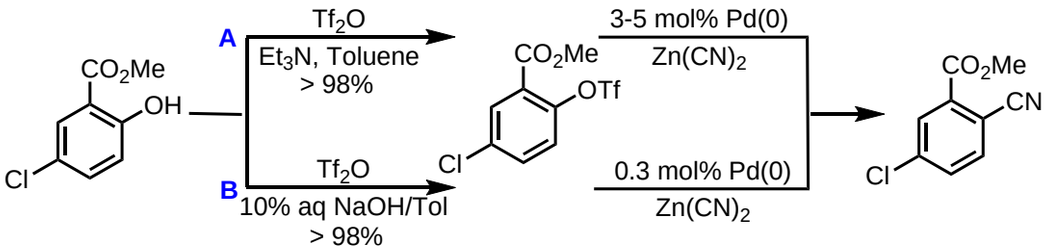


pH tuned selectivity



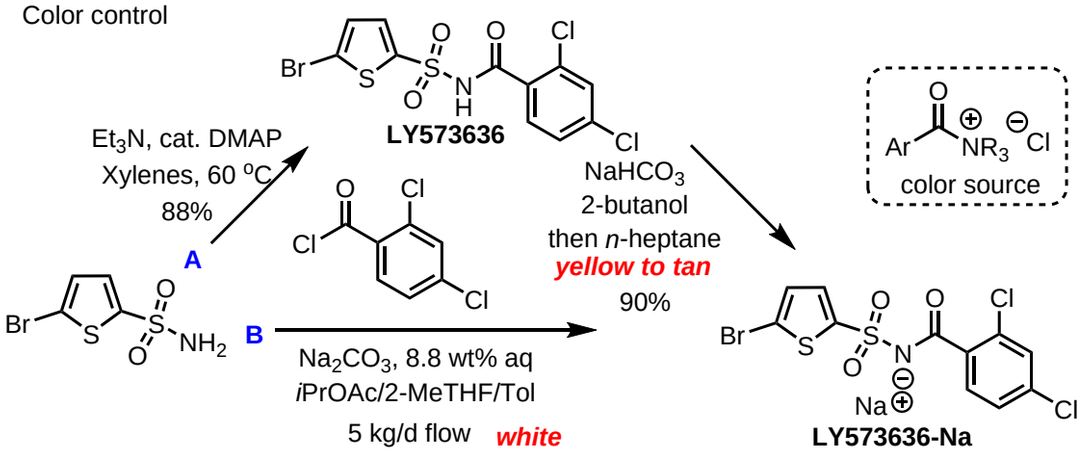
J. F. King, *J. Am. Chem. Soc.* **1992**, *114*, 3028

Impurity control

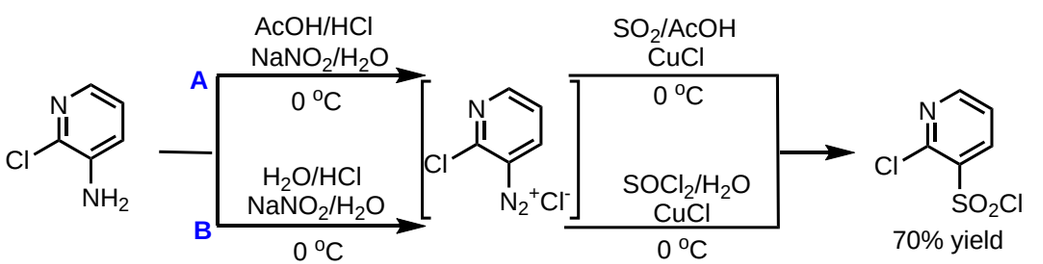


D. E. Frantz, *Org. Lett*. **2002**, *4*, 4717

Color control



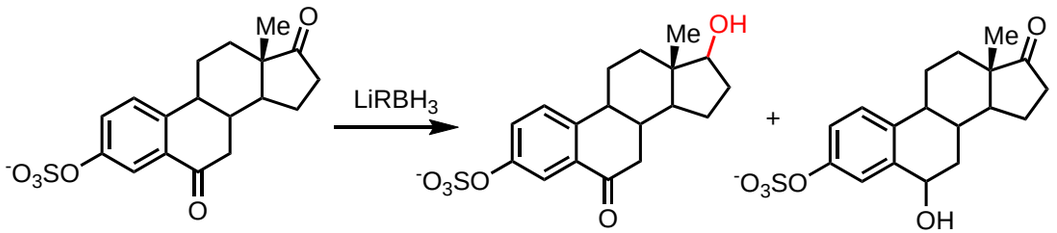
T. D. White, *Org. Process Res. Dev.* **2012**, *16*, 939
M. H. Yates, *Org. Process Res. Dev.* **2009**, *13*, 255



Hydrolysis

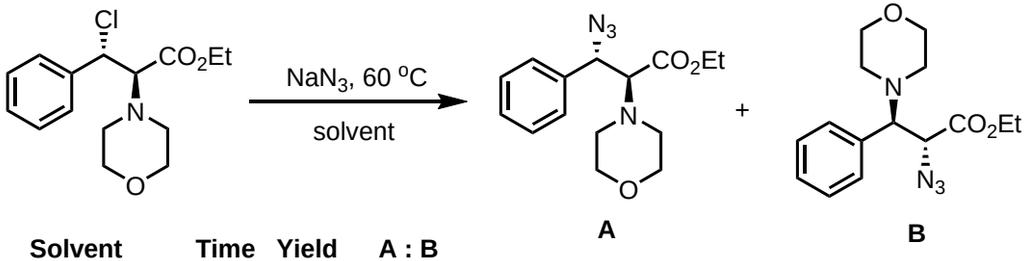
AcCl	250
BzCl	1
$PhSO_2Cl$	0.001

C. Wang, *Org. Process Res. Dev.* **2007**, *11*, 52
P. J. Hogan, *Org. Process Res. Dev.* **2009**, *13*, 875



	4M LiCl	CD_3OD
R = H	86/14	90/10
R = C_6F_5	15/85	54/46

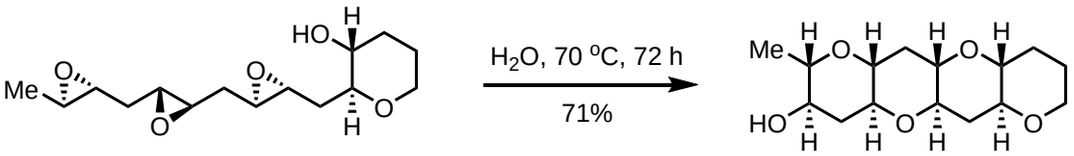
R. Breslow, *Org. Lett.* **2004**, *6*, 4331

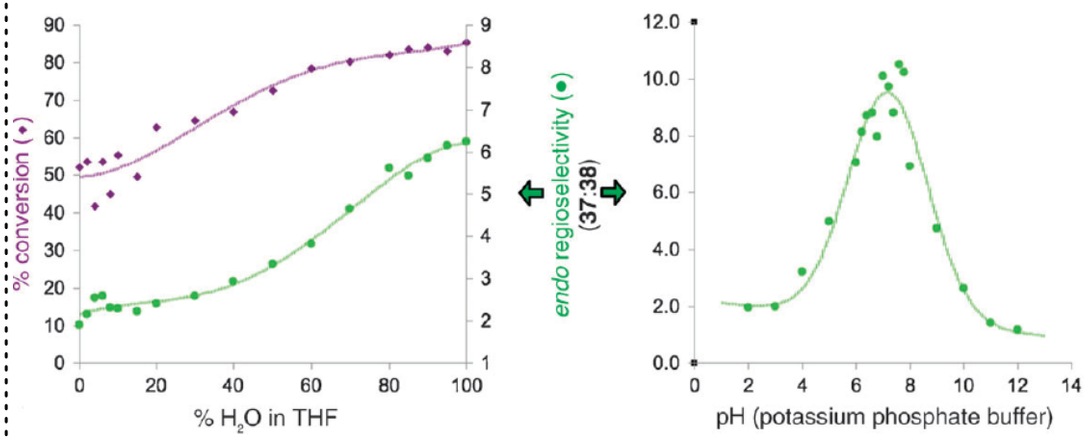


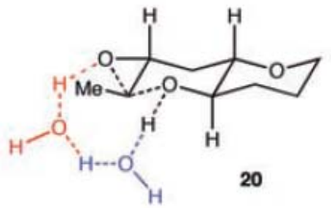
Solvent	Time	Yield	A : B
CH_3CN	12 h	85%	60 : 40
EtOH/H_2O (4:1)	12 h	97%	88 : 12
EtOH/H_2O (1:4)	6 h	92%	93 : 7
H_2O	6 h	99%	95 : 5

K. B. Sharpless, *Org. Lett.* **1999**, *1*, 1435
K. B. Sharpless, *Org. Lett.* **2000**, *2*, 3555
K. B. Sharpless, *Helv. Chim. Acta.* **2000**, *83*, 1734

Polyether synthesis

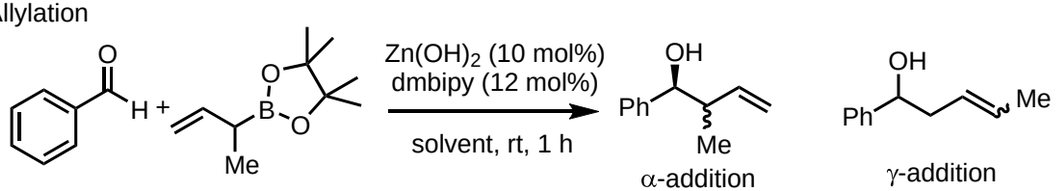






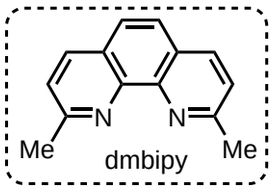
T. F. Jamison, *Science*, **2007**, *317*, 1189
T. F. Jamison, *Chem. Soc. Rev*, **2009**, *38*, 3175
T. F. Jamison, *J. Am. Chem. Soc.* **2011**, *133*, 1902

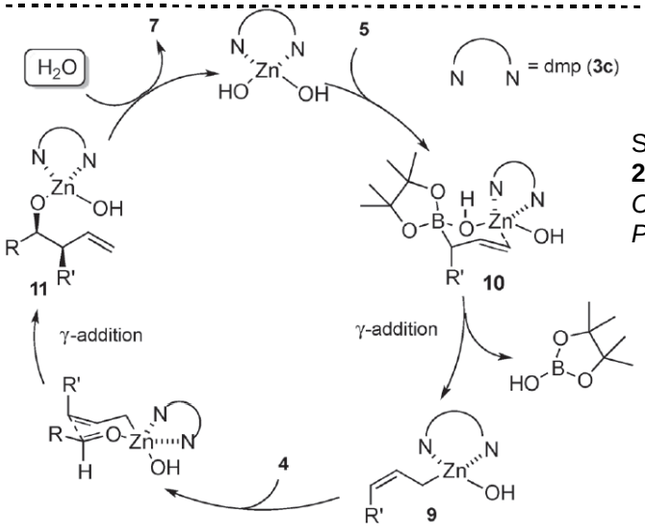
Allylation



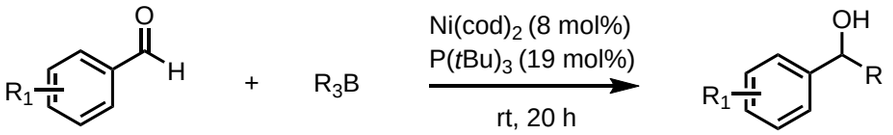
Solvent	Zn/Ligand	Yield	α/γ	Syn/Anti (α)
CH_3CN/H_2O (4:1)	N/N	77	5/95	-
CH_3CN/H_2O (4:1)	Y/N	81	85/15	69/31
CH_3CN/H_2O (4:1)	Y/Y	82	>98/2	93/7
CH_3CN	Y/Y	61	<2/98	-

14 exaples
81-92% yield
>98/2 α/γ



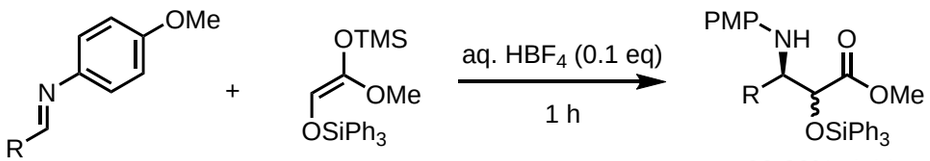


S. Kobayashi, *J. Am. Chem. Soc.* **2008**, *130*, 2914
Chem. Commun. **2010**, *46*, 1260
Pure Appl. Chem. **2013**, *85*, 1089



Solvent	Additive	Yield
toluene (0.05 M)	-	<2%
toluene (0.05 M)	Cs_2CO_3 (3 eq)	88%
toluene (0.05 M)	H_2O (3 eq)	<2%
H_2O (0.1 M)	-	33%
H_2O (0.05 M)	-	63%
H_2O (0.025 M)	-	90%

K. Oshima, *Chem. Commun.* **2008**, 3234



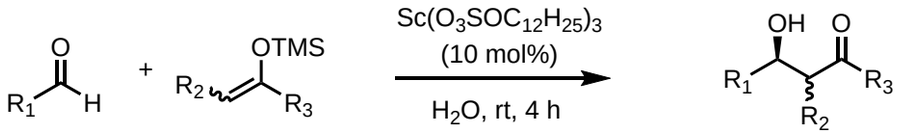
*i*PrOH, -20 °C, 39:61
H_2O, SDS (0.4 eq), rt, 86:14

66-99% yield
up to 95:5 sny/anti

T. Akiyama, *Tetrahedron Lett.* **2001**, 42, 4025

Lewis acid-surfactant-combined catalyst (LASC)

Also see Hai Dao, *Shū Kobayashi*, GM 2013

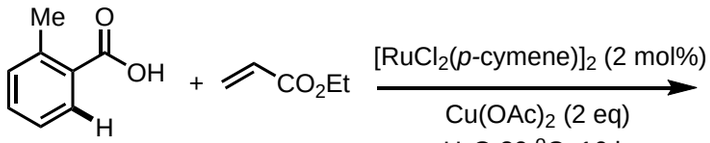


reaction proceed slow in organic sol.

80-98% yield
up to 4:1 sny/anti

S. Kobayashi, *J. Am. Chem. Soc.* **2000**, *122,* 7202

C-H activation

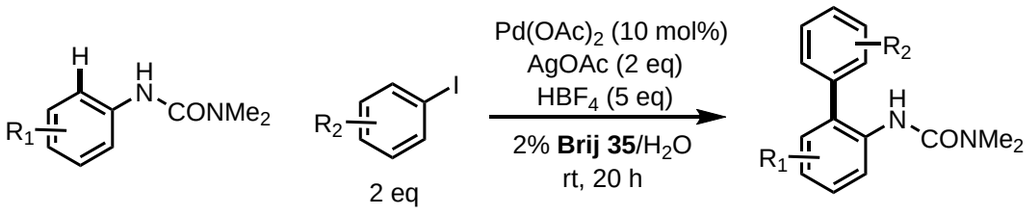


xylene, 0%
MeOH, 28%
t-AmOH, 34%
H_2O, 95%

16 examples
66%-95%

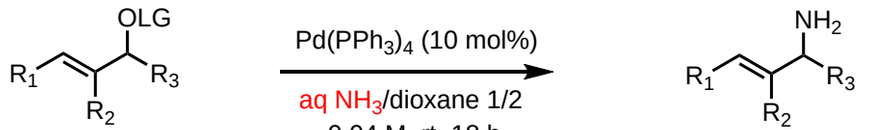
L. Ackermann, *Org. Lett.* **2011**, *13*, 4153

C-H activation



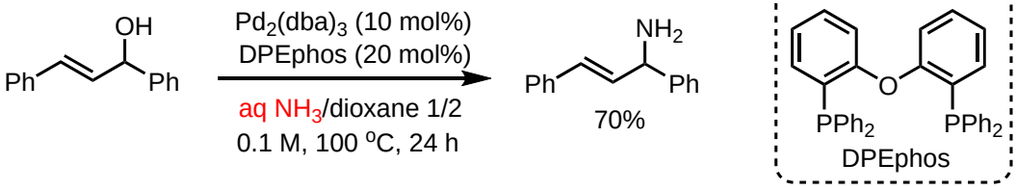
Birj 35 = $C_{12}H_{25}(OCH_2CH_2)_nOH$, n~23

B. H. Lipshutz, *Angew. Chem. Int. Ed.* **2010**, *49*, 781



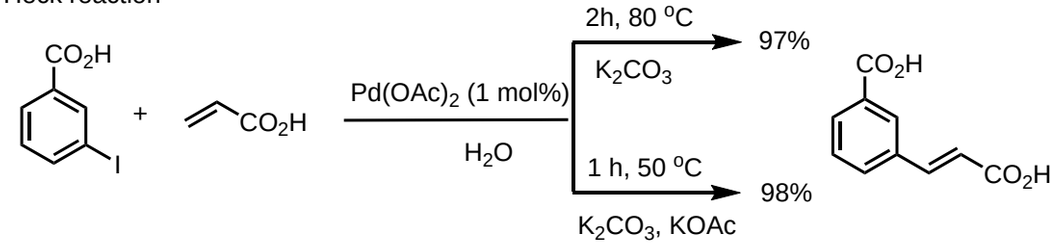
R_1, R_3 = Ph, R_2 = H, 87% ee w/ BINAP

S. Kobayashi, *J. Am. Chem. Soc.* **2009**, *131*, 4200



S. Kobayashi, *Pure Appl. Chem.* **2013**, *85*, 1089

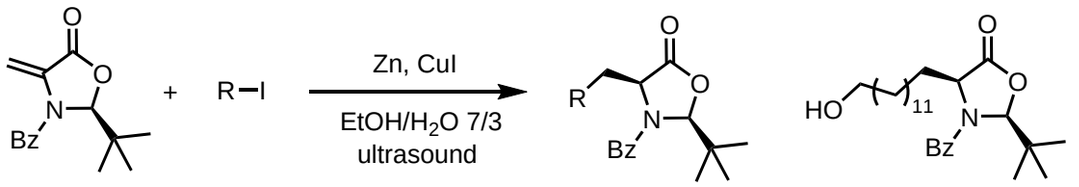
Heck reaction



bromide works when tetraalkylammonium salts added

I. P. Beletskaya, *J. Organomet. Chem*. **1989**, *371*, 397
I. P. Beletskaya, *J. Organomet. Chem*. **1995**, *486*, 259

Conjugate addition

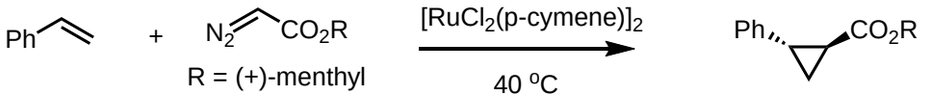


45-95% yield
> 92/8 cis/transi

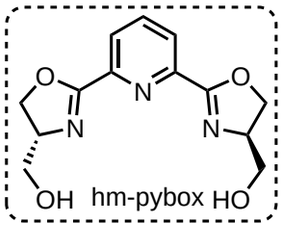
57%
92/8 cis/transi

J. P. Sestelo, *Chem. Eur. J*. **2003**, *9,* 4179
For micelle assisted conjugate addition, see:
B. H. Lipshutz, *J. Am. Chem. Soc.* **2012**, *134*, 19985

Carbene reaction

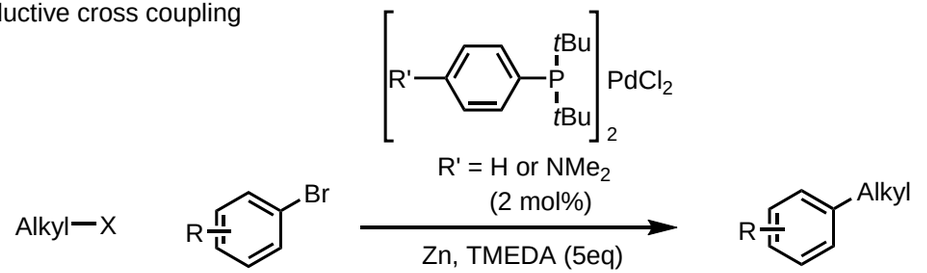


Solvent	Ee
THF	8
Tol	8
THF/H_2O 5/1	78
Tol/H_2O 4/1	94
2nd cycle	97



H. Nishiyama, *Chem. Commun*. **2001**, 59

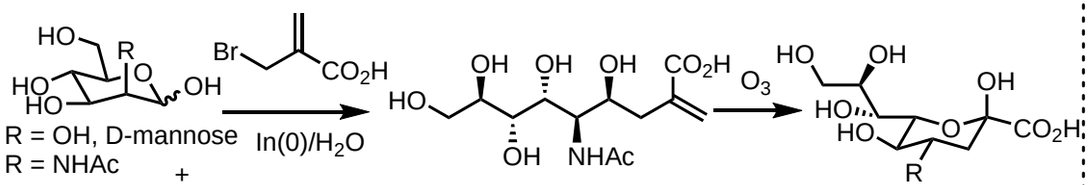
Reductive cross coupling



16 examples
65-96% yield

B. H, Lipshutz, *J. Am. Chem. Soc.* **2009**, *131*, 15592

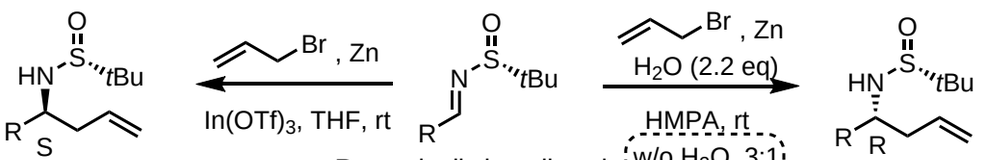
Barbier reaction



R = OH, 77%, *dr* 5:1
R = NHAc, 77%, *dr* 3:1

R = OH, (+)-KDN, 95%
R = NHAc, (+)-N-acetyl neuraminic acid, 74%

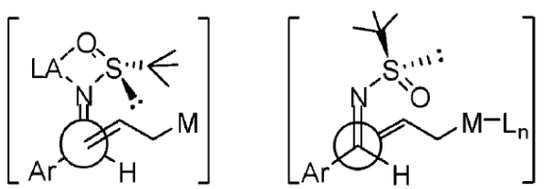
T.-H. Chan, *J. Org. Chem.* **1995**, *60*, 4228



16 examples
81-99% yield
76-98% de

R = aryl, alkyl or alkenyl

16 examples
73-99% yield
90-99% de



G.-Q. Lin, *Org. Lett*. **2006**, *8*, 4979

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Organic Reactions in the Presence of Water

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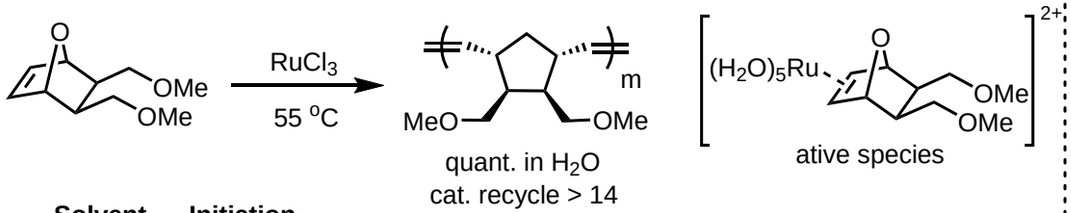
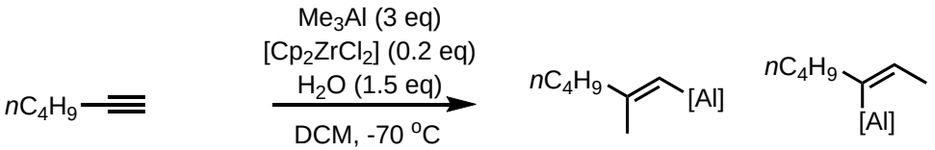
Ring-opening metathesis polymerization



Solvent	Initiation
organic	22-24 h
H_2O	30-35 min
3rd cycle	10-12 s

R. H. Grubbs,, *J. Am. Chem. Soc.* **1988**, *110*, 7543

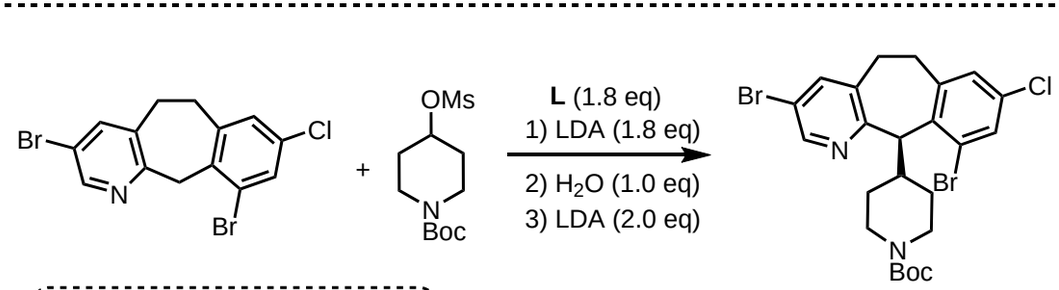
Carboalumination

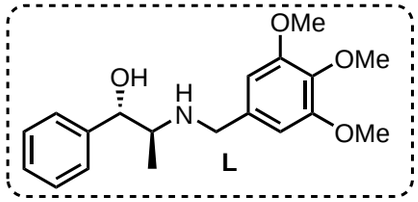


100% yield, 97 : 3

w/o water, rt, 3 h
w/ water, -70 °C, 10 min

P. Wipf, *Angew. Chem. Int. Ed.*. **1993,** *32*, 1068

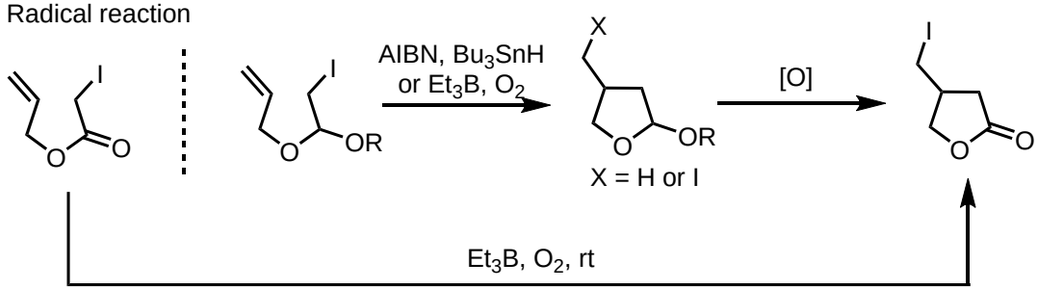




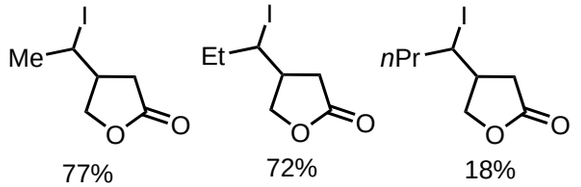
Water	Yield	Ee
0.0 eq	50%	55%
0.7 eq	92%	85%
1.0 eq	95%	95%

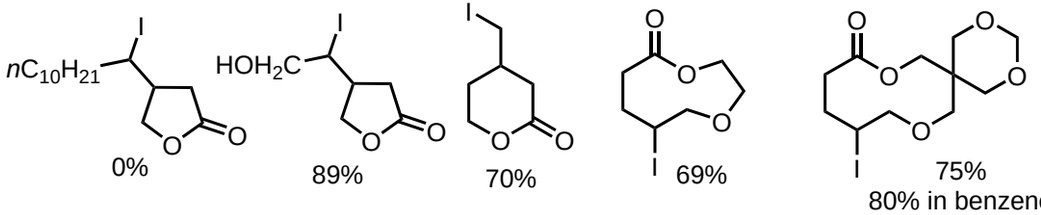
G. G. Wu, *J. Org. Chem*. **2003**, *68*, 4984

Radical reaction



hexane 0.03 M, 0%
benzene 0.03 M, 0%
H_2O, 0.03 M, 67%
H_2O, 0.01 M, 78%

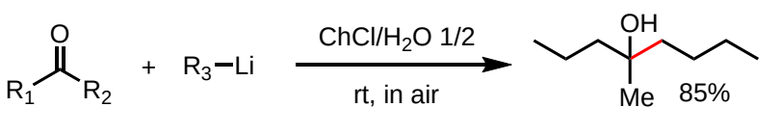




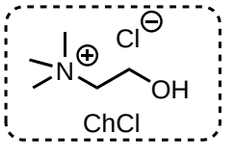
H. Fujimoto, *J. Am. Chem. Soc.* **2000**, *122*, 11041

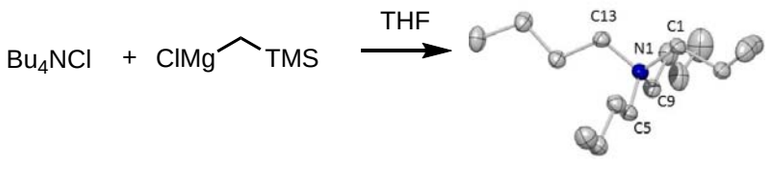
For SmI_2-H_2O mediated radical reaction, see C. A. Lewis, *Samarium (II) Iodide*, GM **2010**

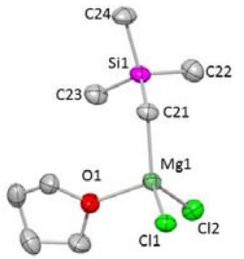
Deep Eutectic Solvent



7 examples
68-90% yield







E. Hevia, *Angew. Chem. Int. Ed.* **2014**, *53*, 5969

For reviews about DES, see: a) Q. Zhang, *Chem. Soc. Rev*. **2012**, *41*, 7108; b) Y. Gu, *Chem. Soc. Rev.* **2013**, *42*, 9550; c) M. C. Kroon, *Angew. Chem. Int. Ed.* **2013**, *52*, 3074; d) E. L. Smith, *Chem. Rev*. **2014**, *114*, 11060

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Organic Reactions in the Presence of Water

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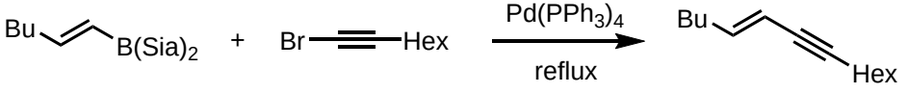
Designed Catalysis in water

Aqueous Pd-catalyzed cross-coupling dates back to the early development of Suzuki coupling, which uses aqueous base to activate the organoboron nucleophile.



NaOMe, THF-MeOH, 97%
NaOH, THF-H_2O, 86%

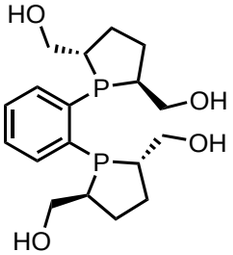
N, Miyaura, *J. Am. Chem. Soc.* **1985**, *107*, 972

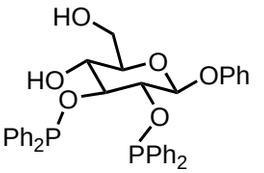
Mass transport/green chemistry:

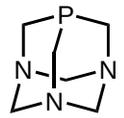
1) Water-miscible organic co-solvent
2) Surfactant or micellar chemistry
3) Phase-transfer catalysis
4) Catalyst immobilization
5) Water-soluble cat/ligand design

For micellar chemistry: G. Oehme, *Angew. Chem. Int. Ed*. **2005**, *44*, 7174; A. Daniela, *Chem. Rev.* **2016**, *116*, 2023
For PTC: K. Maruoka, *Angew. Chem. Int. Ed.* **2007**, *46*, 4222; B. I. Andrews, *Acc. Chem. Res.* **2004**, *37*, 518; Maruoka, K. *Asymmetric Phase-Transfer Catalysis,* Wiley-VCH, Weinheim, Germany, **2008**
For catalyst immobilization: T. Turec, *Heterogeneous Catalysis and Solid Catalysts ,* Wiley-VCH, Weinheim, Germany, **2009**; K. D. Janda, *Tetrahedron*, **2001**, *57*, 4637

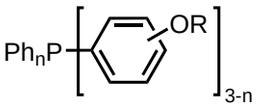
Non-ionic substituents: polyol, polyamine, carbonhydrate, polyether







PTA

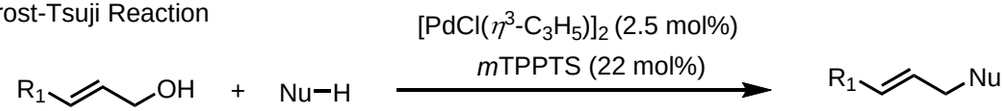


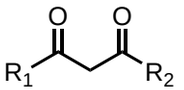
R = $(CH_2CH_2\text{-}O)_mH$
n= 0-2, m = 8-25

Most studied reactions:

Hydrogenation
Hydroformylation
Hydrodimerization
Oxidation
Hydrocyanation
Carbonylation
Alkene metathesis
Cross-coupling

Trost-Tsuji Reaction

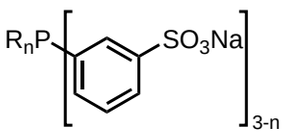


NuH =  or amine

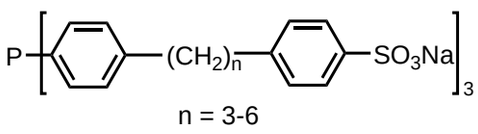
K. Oshima, *Org. Lett*. **2004**, *6*, 4085

Ligand design: attach water-solubilizing groups to hydrophobic ligands:

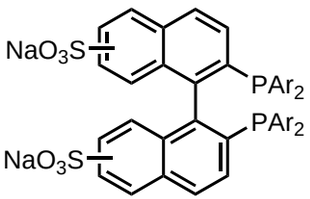
Ionic substituents: $-SO_3^-$, $-CO_2^-$, $-PO_3^{2-}$, $-NMe_3^+$



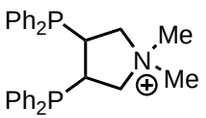
n = 2, *m*TPPMS
n = 1, *m*TPPDS
n = 0, *m*TPPTS

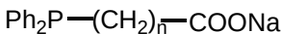


n = 3-6



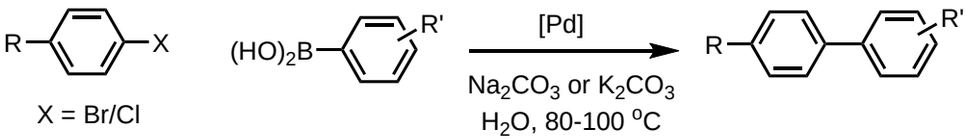
Ar = 3/4-C_6H_4-SO_3Na



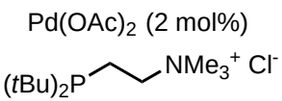


n = 1-5, 7

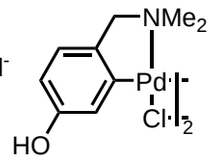
Suzuki



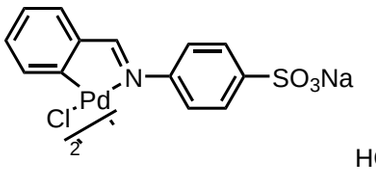
X = Br/Cl



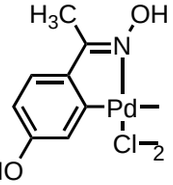
***t*Bu-Amphos**
(2 mol%)
TON: 730,000
3 cycles



4 cycles



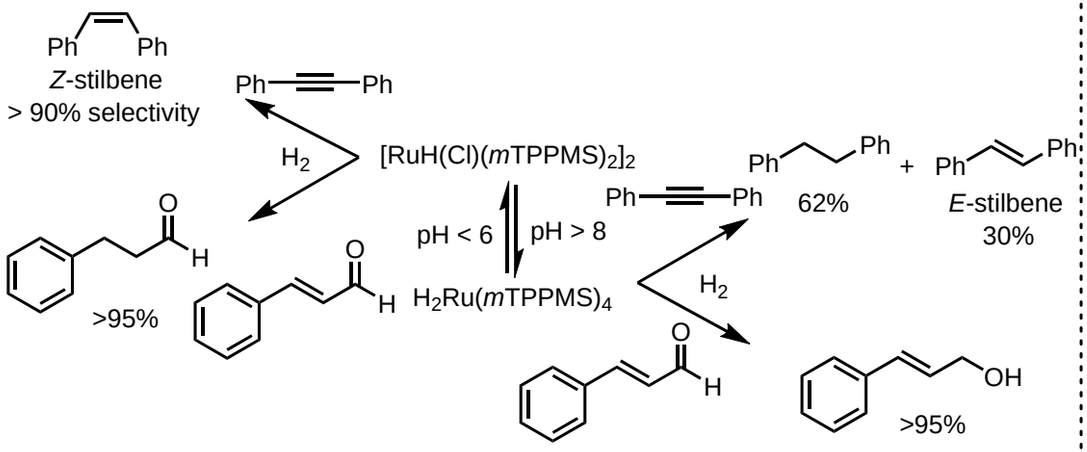
11 cycles



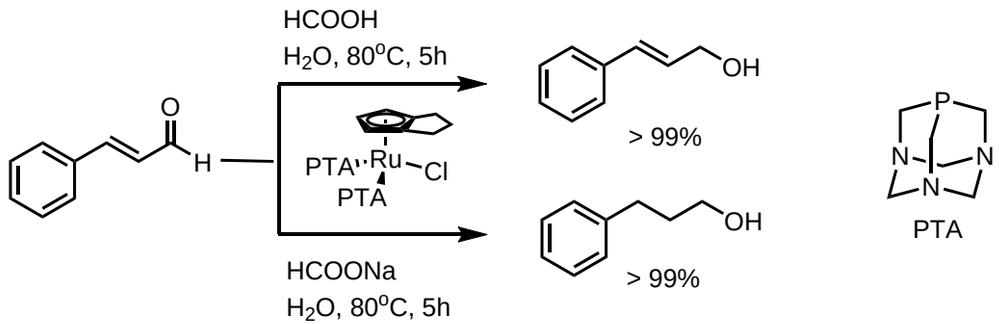
0.01 mol%

L. Botella, *Angew. Chem. Int. Ed.*, **2002**, *41*, 179
L. Botella, *J. Organomet. Chem.*, **2002**, *663*, 46
R. Huang, *Organometallics*, **2006**, *25*, 4105

pH-dependence

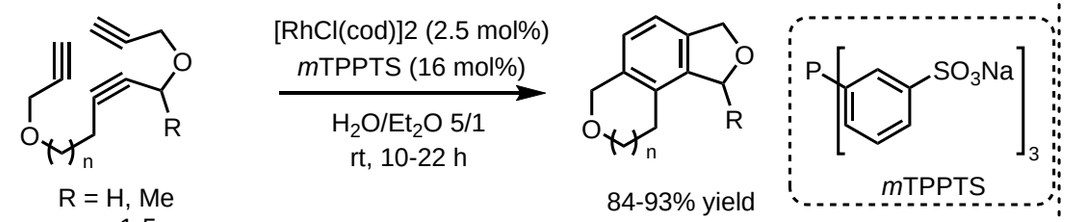


Y. Dror, *J. Mol. Catal.* **1977**, *2*, 219
F. Joo, *Angew. Chem. Int. Ed*. **1998**, *37*, 969



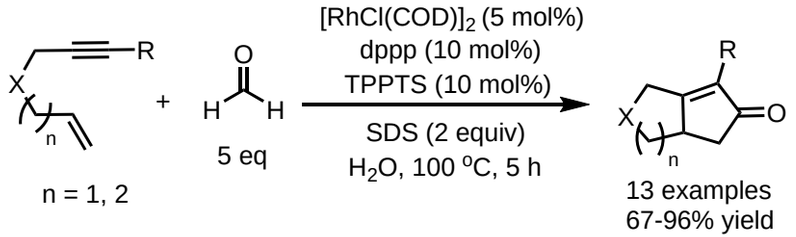
C. A. Mebi, *Organometallics*. **2007**, *26*, 429

[2+2+2]



Koichiro Oshima, *J. Am. Chem. Soc*. **2003**, *125*, 7784

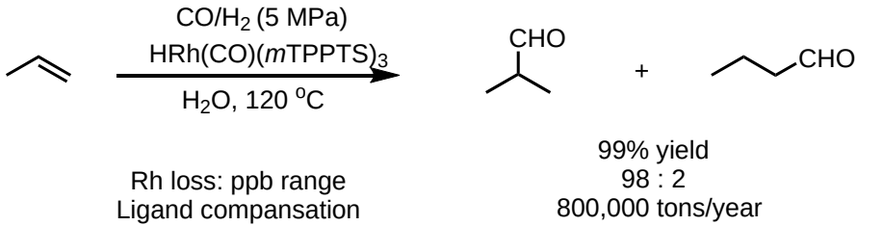
Pauson-Khand type



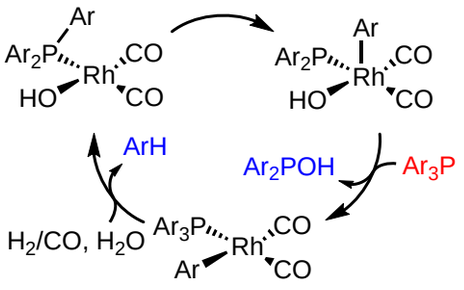
K. Kakiuchi, *Angew. Chem. Int. Ed*. **2003**, *42*, 2409

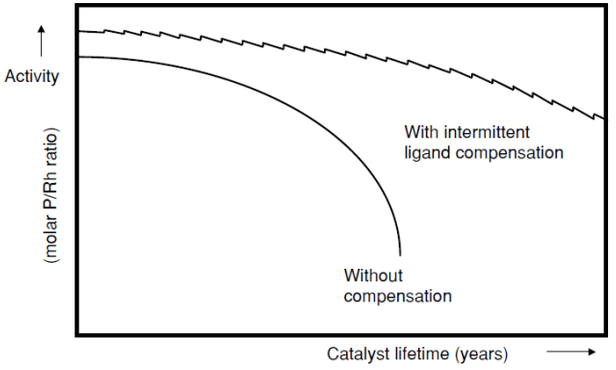
Industrial processes

1) Wacker process covered by J Cornella, *Metal Pairs*, GM **2016**
2) Ruhrchemie/Rhone Poulenc process-Hydroformylation



B. Cornils, *Org. Process Res. Dev*. **1998**, *2*, 121





E. G. Kuntz, *Chemtech*, **1987**, *17*, 570.
E. G. Kuntz, *French Patent*, 2,314,910, **1975**
E. G. Kuntz, *French Patent*, 2,349,562, **1976**
M. Lindstrom, *Organic Reactions in Water*, **2006**, chapter 12