聲明

本檔案之內容僅供下載人自學或推廣化學教育之非營利目的使用。並請於使用時註明出處。[如本頁取材自〇〇〇教授演講內容]。

試劑與觸媒

蔡蘊明
台大化學系

Outline

- 趨勢
- Biocatalysis
- Organocatalysis
- Catalytic hydrogenation
- Green oxidation reagents
- CO_2 and CO fixation
- Greener biaryl couplings

US Presidential Green Chemistry Challenge Awards

Summary of hot key words in the past five years

• Catalysts	15
• Biomass and related	10
• Polymers	9
• Commodity chemicals	5
• Organic solvent & VOCs reduction	5
• Fuels	4
• Drugs and pesticides	4
• Paints	2
• Water	2
• Analysis	2

Targets with high impact

- Fuels
- Polymers
- Paints
- Papers
- Drugs
- Pesticides
- Commodity chemicals

} With high demands worldwide

Biocatalysis

Advantages:

- Highly efficient
- Aqueous phase
- Enantioselective
- Regioselective
- Chemoselective
- Mild conditions
  - low pH
  - low temperature
  - low pressure
- Fewer byproducts
- Simplified processing

Thayer, A. M. *C&EN* **2012**, *90*, 13

Enabling technologies

- Enzyme evolution methods
- Microbial genomic sequencing
- Bioinformatics
- Protein engineering
- DNA synthesis
- Robotic screening

Established biocatalysts

- Lipases
- Esterases
- Amidase
- Hydrolases
- Ketoreductases
- Transaminases

Clouthierzab, C. M.; Pelletier, J. N. *Chem. Soc. Rev.,* 2012, **41**, 1585

Identifying a suitable biocatalyst

Three levels

- Where a similar reaction has been reported
  - www.enzymedirectory.com
  - www.bio-catalyst.com/enzyme-sources
  - www.coebio3.org
  - borgc185.kfunigraz.ac.at
  - World Federation for Culture Collections
- Require biocatalyst library screening
- Screening fails and biocatalyst engineering is required

Clouthierzab, C. M.; Pelletier, J. N. *Chem. Soc. Rev.,* 2012, **41**, 1585

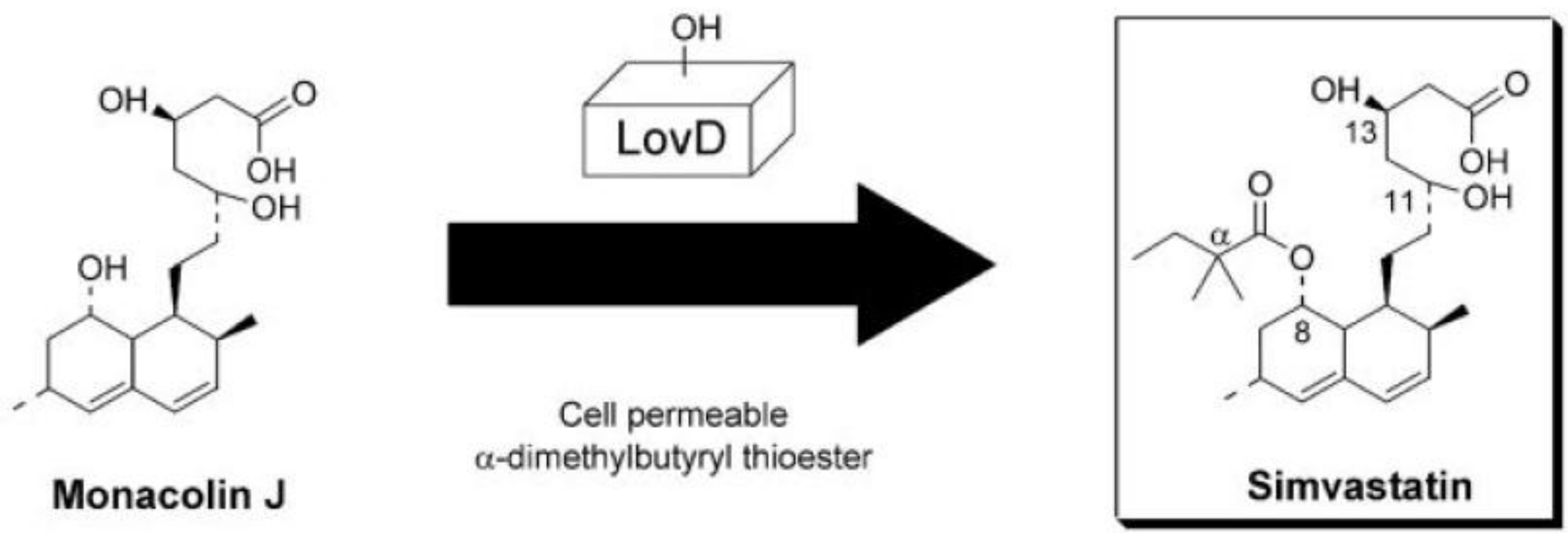
US Presidential Green Chemistry Challenge Awards

2012 Greener Synthetic Pathways Award

Codexis, Inc.; Prof. Y. Tang (UCLA)

An efficient biocatalytic process to manufacture simvastatin

one-step, whole-cell biocatalytic process



>99% conversion
>90% recovery
>98% purity

Appl. Environ. Microbio. **2007**, *73*, 2054

Codexis carried out nine iterations of in vitro evolution,
creating 216 libraries
and screening 61,779 variants
to develop a LovD variant
with improved activity,
in-process stability,
and tolerance to product inhibition

2010 Academic Award

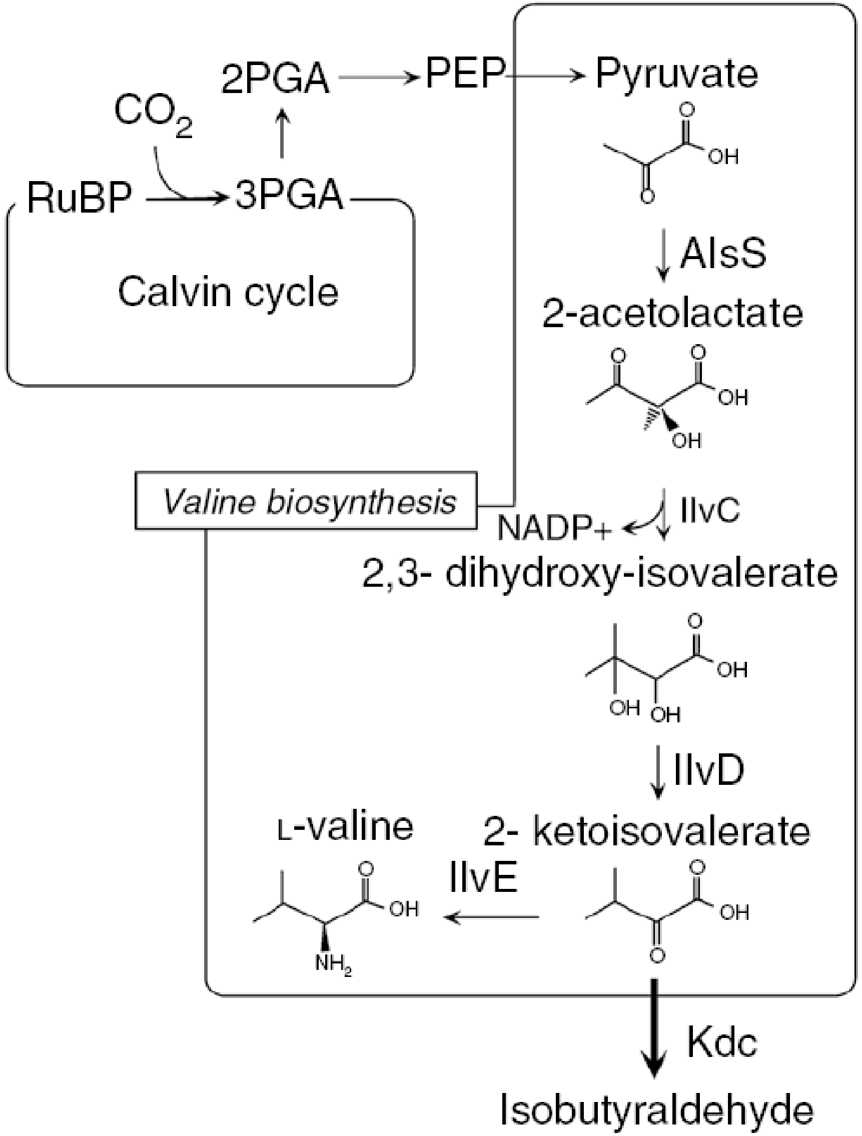
Prof. J. C. Liao
(UCLA and Easel Biotechnologies)

Biochemical recycling of CO_2 to higher alcohols

Nature Biotech. **2009**, *27*, 1177

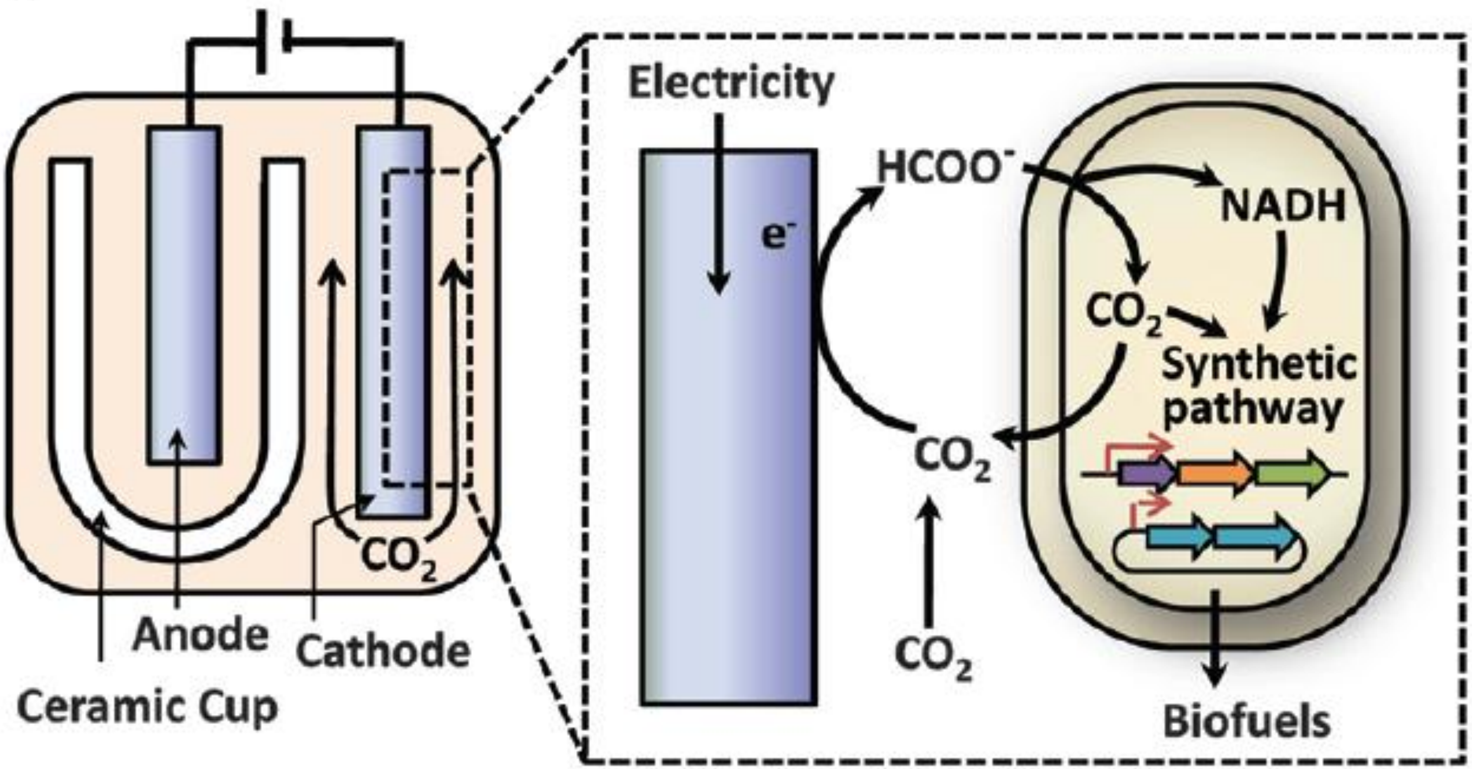
genetically engineered *Synechococcus elongatus* PCC7942

60 billion gal higher alcohols = 8.3% total CO_2 emission in US/yr



Prof. J. C. Liao (UCLA and Easel Biotechnologies)

An integrated electromicrobial process to convert CO_2 to higher alcohols



Science **2012**, *335*, 1596

LS9, Inc.

Genetically engineered a variety of microorganisms to act like refineries

Engineered microorganisms

Fermentable sugars → alkanes, olefins, fatty alcohols, or fatty esters

- Eliminates benzene, sulfur, and the heavy metals found in petroleum-based diesel
- 85 percent decrease in greenhouse gas (GHG) emissions
- Competitive price

C&EN

Volume 90 Issue 38 | p. 16 | Concentrates
Issue Date: September 17, 2012

LS9 Starts Up Florida Demonstration Plant

By Melody M. Bomgardner

Department: Business
Keywords: fatty acids, biobased chemicals, biofuels, LS9

Biobased chemicals and fuels firm LS9 has begun producing fatty alcohols from sugar at its first scale-up plant, in Okeechobee, Fla. The facility will be used to generate large commercial samples for testing and qualification by partners and prospective customers. The long-carbon-chain alcohols are used in surfactants for detergents and other applications. LS9 also plans to demonstrate its ability to produce diesel fuel and esters at the plant.

[+]Enlarge

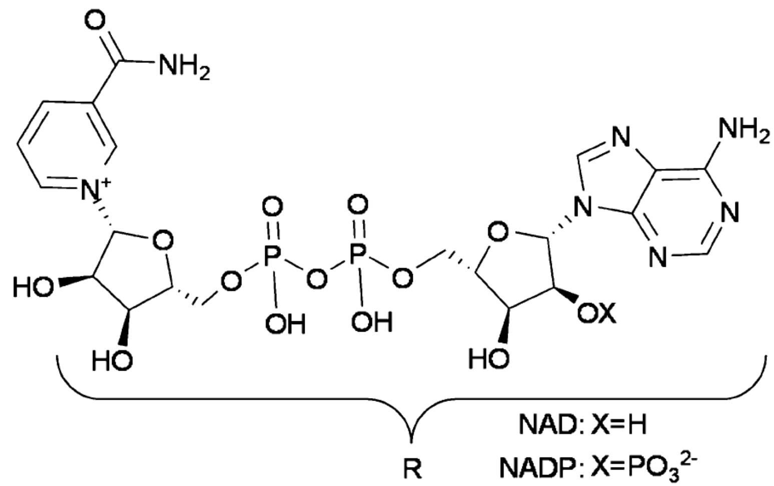
LS9 makes fatty alcohols at this plant in Florida.

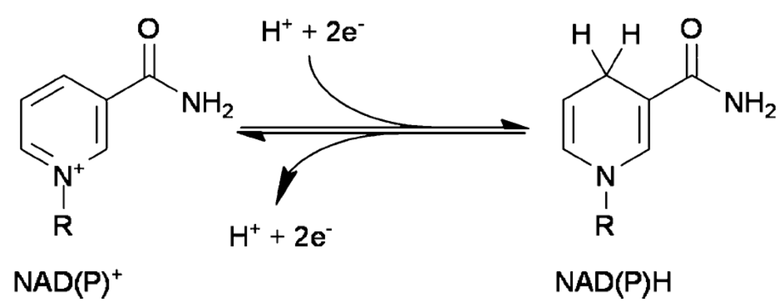
Credit: LS9

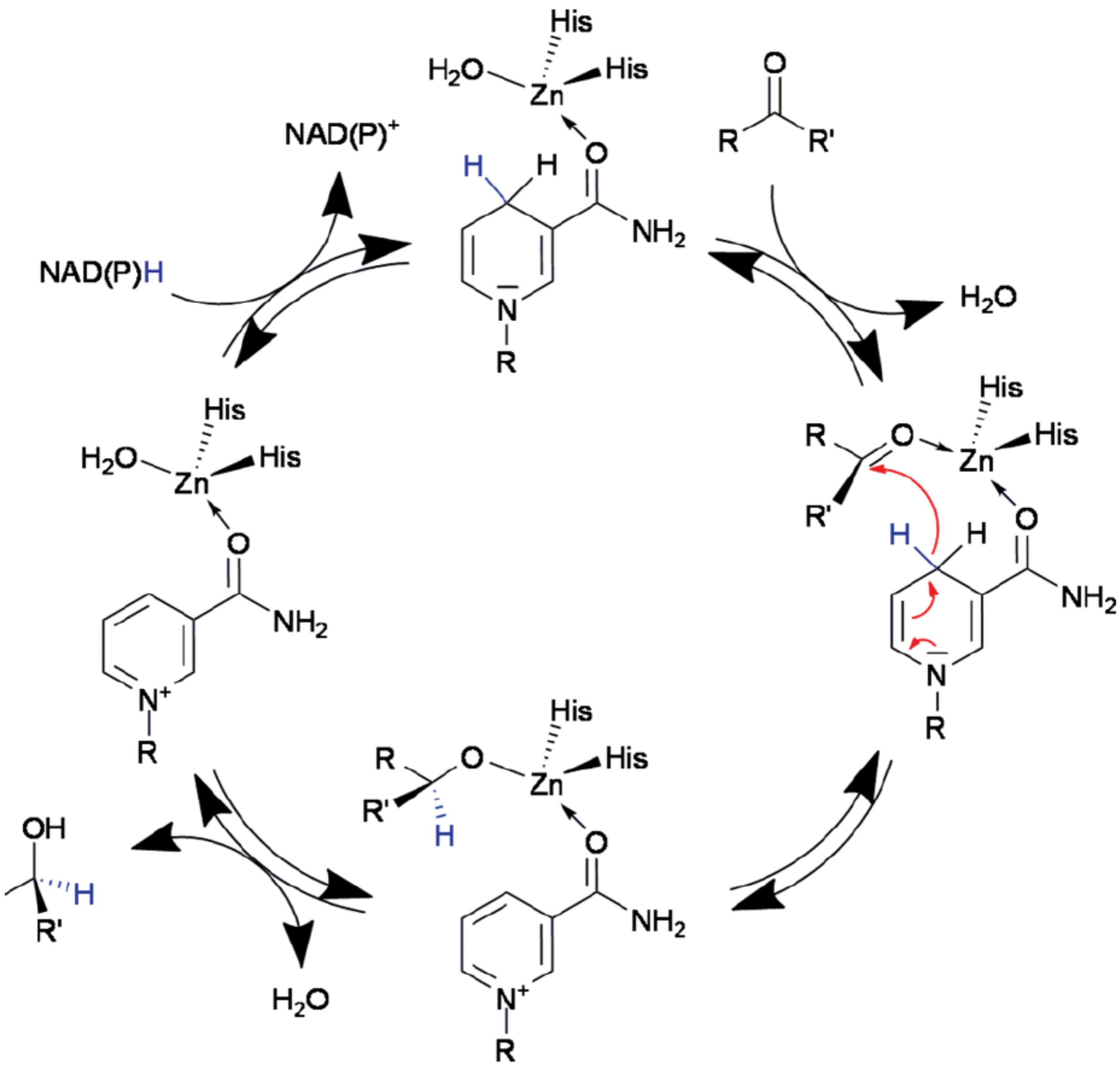
Enzymatic reductions

Hollmann, F.; Arends, I. W. C. E.; Holtmann, D. *Green Chem.*, **2011**, *13*, 2285

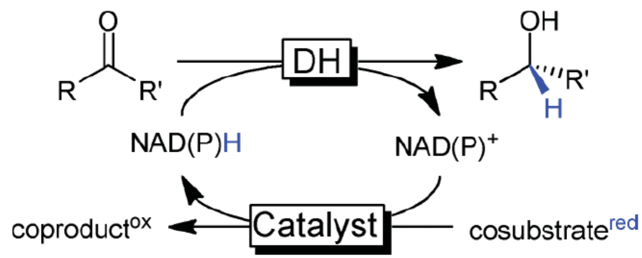
Alcohol dehydrogenases for carbonyl reductions







His
H_2O
Zn
His
O
NAD(P)$^+$
H
H
NH_2
N
R
R
R'
NAD(P)H
H_2O
His
R
O
Zn
His
R'
O
H
H
NH_2
N
R
His
H_2O
Zn
His
O
NH_2
N$^+$
R
His
R
O
Zn
His
R'
H
O
NH_2
N$^+$
R
OH
H
R'
H_2O



Cosubstrate	Coproduct	Catalyst	g (coproduct) mol (NAD(P)H)$^{-1}$	ΔG′ [kcal mol^{-1}]
Glucose	Gluconic acid	GDH	196	–6.9
Isopropanol	Acetone	DH	58	–6.1
Ethanol	Acetic acid	ADH/AldDH	30	–12.9
Formic acid	CO_2	FDH Rh	44	–5.2
H_3PO_3	H_3PO_4	PDH Rh	98	–15
H_2	H_2O	Hase	18	–4.35
Cathode	—	Rh Hase/diaphorase	0	Variable

GDH: glucose DH; ADH: alcohol DH (general); AldDH: aldehyde DH; FDH: formate DH; Rh: $[Cp^*Rh(bpy)(H_2O)]^{2+}$; Hase: hydrogenase.

Whole cells or isolated enzymes?

Whole cells

Advantage
No enzyme purification
No external cofactor regeneration

Disadvantage
Dependence on metabolic activity
Often low productivity
Reactant metabolization
Sometimes low selectivity

Isolated enzymes

Advantage
High volumetric productivities
Less side reactions

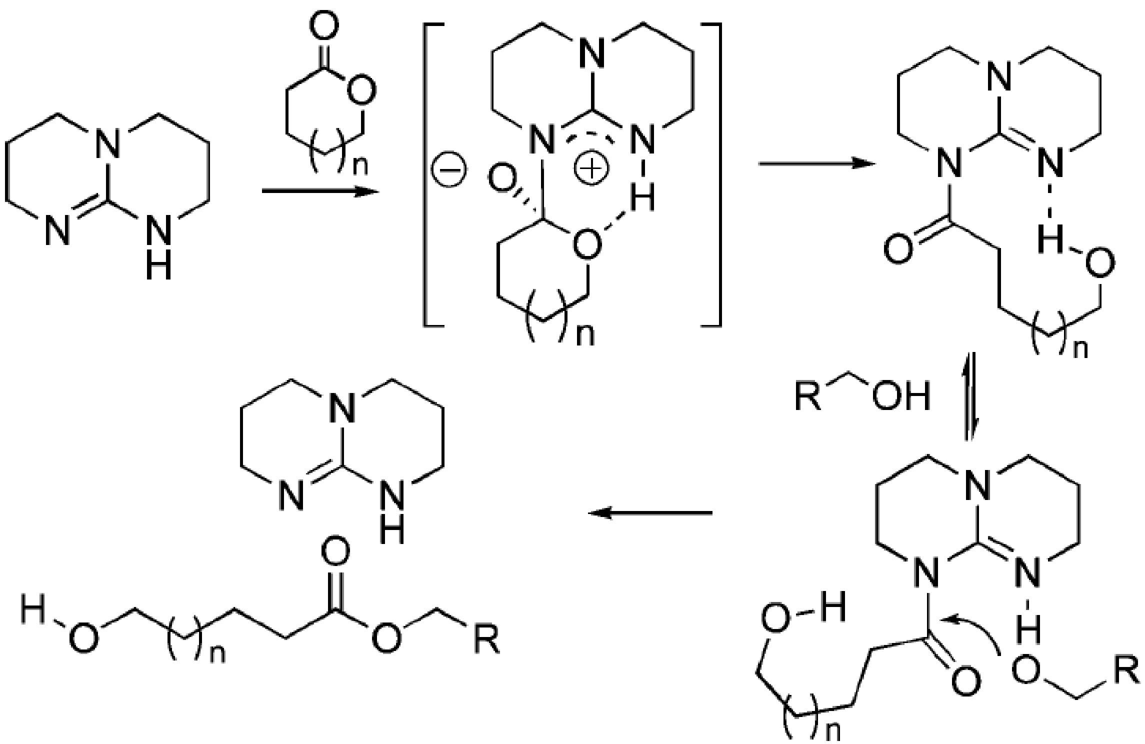
Disadvantage
Purification can be costly
Cofactor regeneration required
Stability can be an issue

Organocatalysts

2012 Academic Award

Prof. R. M. Waymouth (Stanford), Dr. J. L. Hedrick (IBM)

Discovered metal-free catalysts that are highly active and able to make a wide variety of plastics

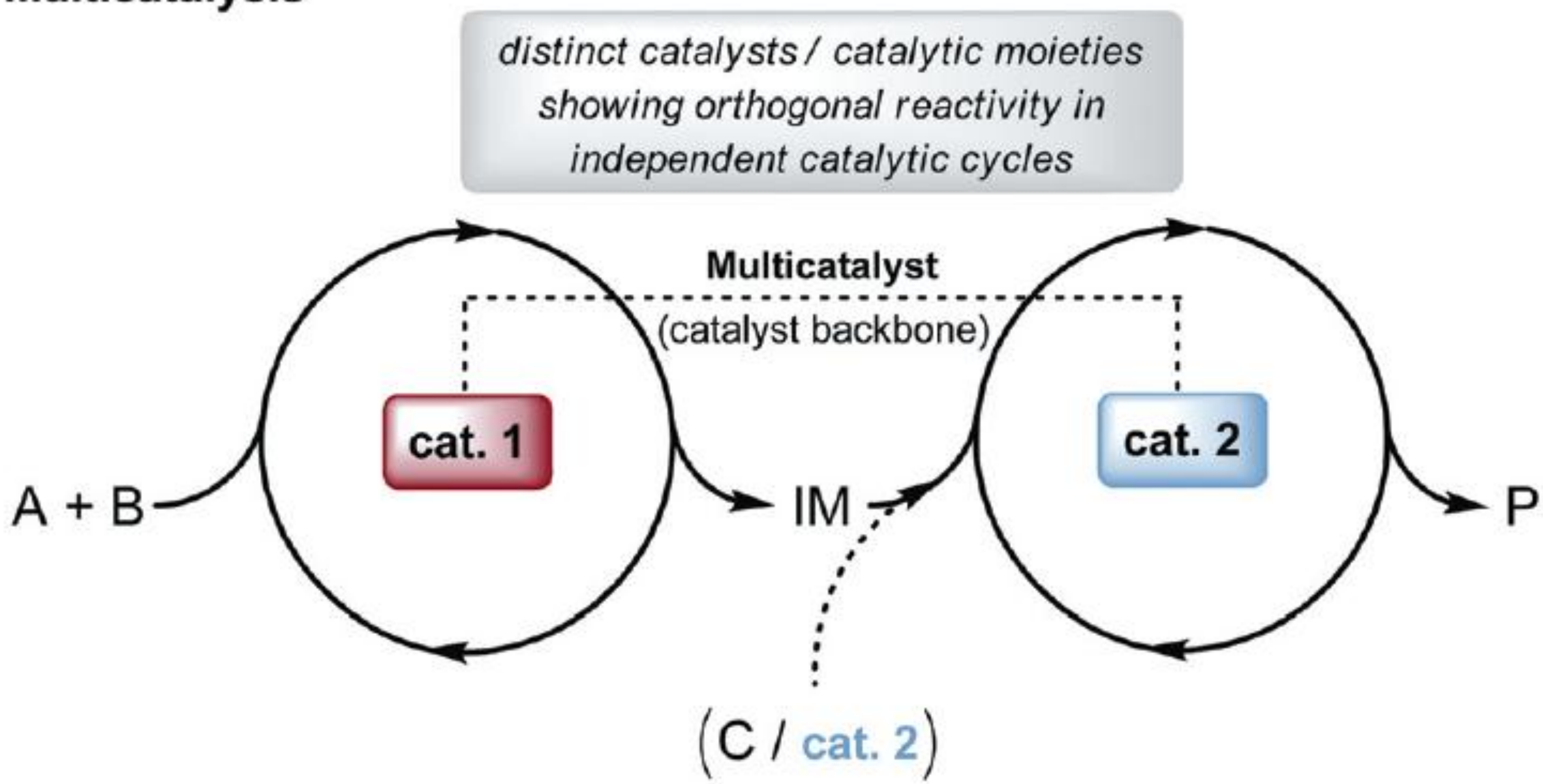


J. Am. Chem. Soc. **2006**, *128*, 4556

Organomulticatalysis

Wende, R. C.; Schreiner, P. R. *Green Chem*. **2012**, *14*, 1821

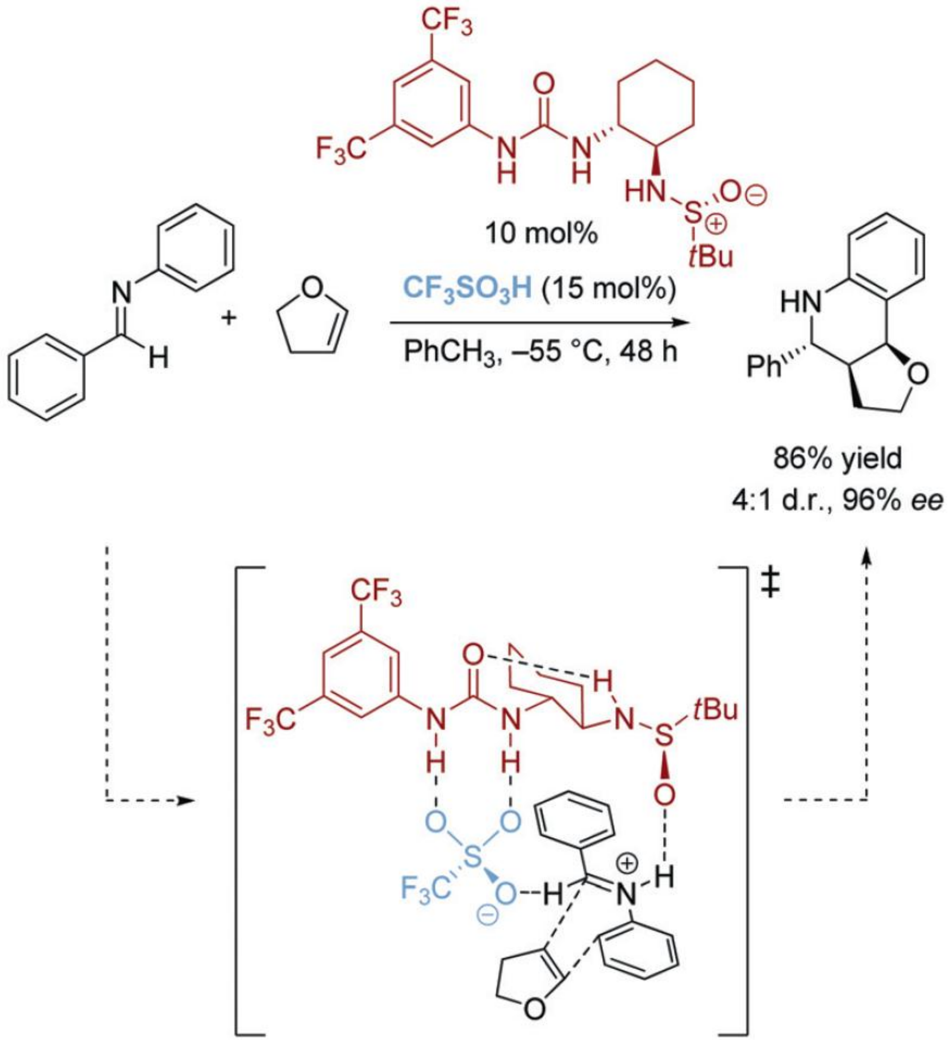
Multicatalysis



1.) Sequential multicatalysis: addition of cat. 2, reagents, or change in reaction conditions after completion of the 1st catalytic cycle

2.) Tandem / Relay catalysis: no change in reaction conditions required

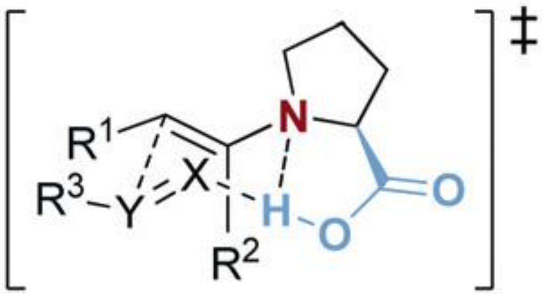
Cooperative catalysis



Xu, H.; Zuend, S. J.; Woll, M. G.; Tao, Y.; Jacobsen, E. N. *Science*, **2010**, *327*, 986.

Multifunctional catalyst

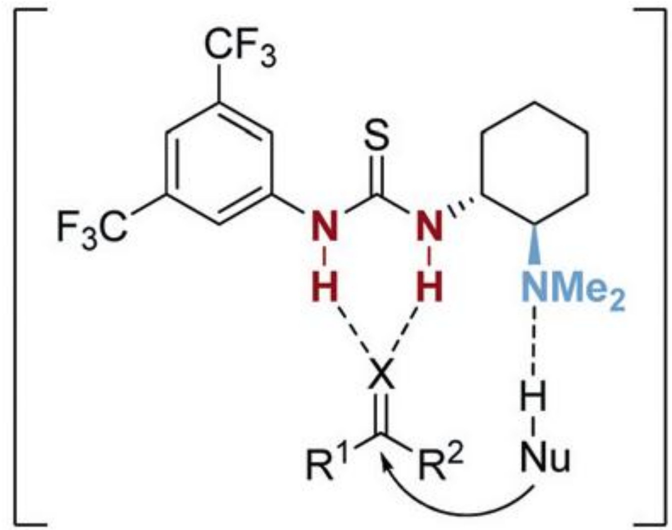
L-Proline



R^1, R^2, R^3 = H, alkyl, aryl
X = O, NR; Y = C, N, O, S
Nu = nucleophile

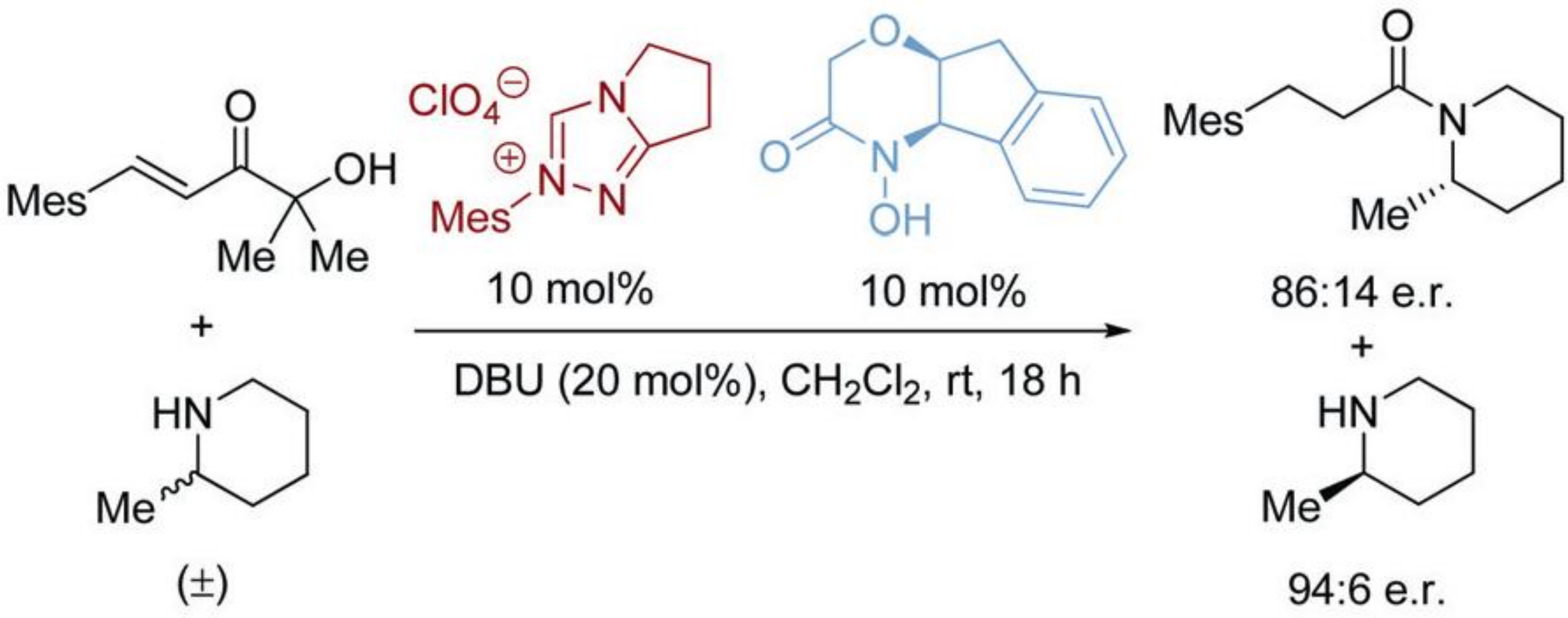
List, B. *Tetrahedron* **2002**, *58*, 5573

Takemoto's catalyst

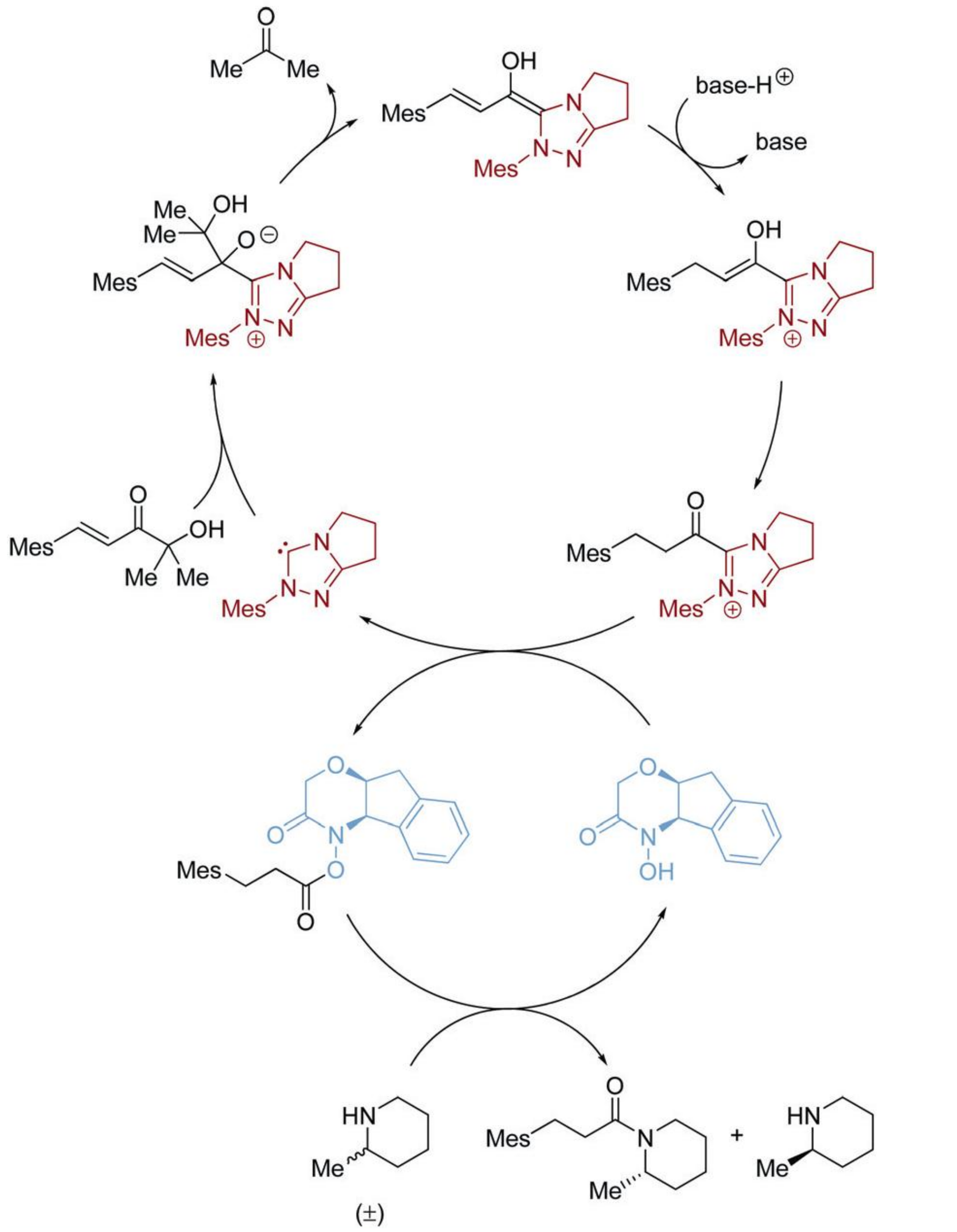


Panday, S. K. *Tetrahedron: Asymmetry* **2011**, *22*, 1817

Dual catalysis / Synergistic catalysis

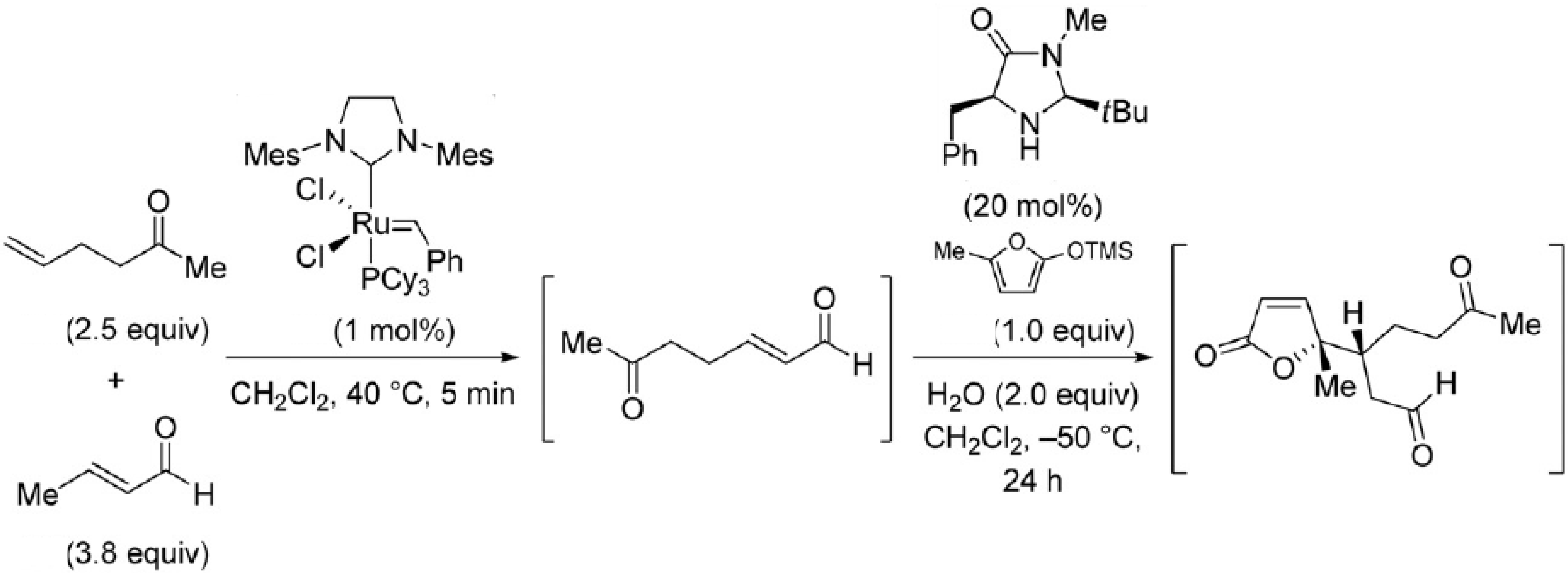


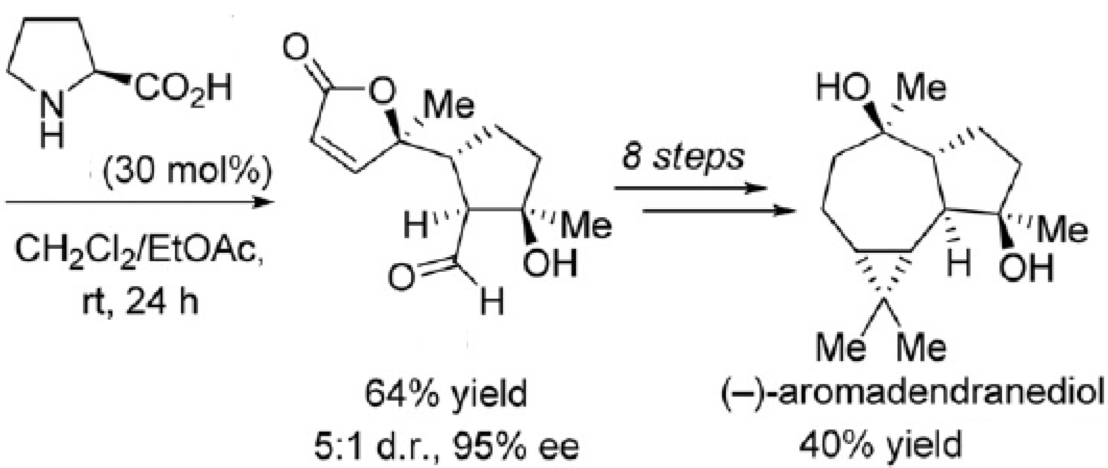
Binanzer, M.; Hsieh, S.-Y.; Bode, J. W. *J. Am. Chem. Soc.* **2011**, *133*, 19698



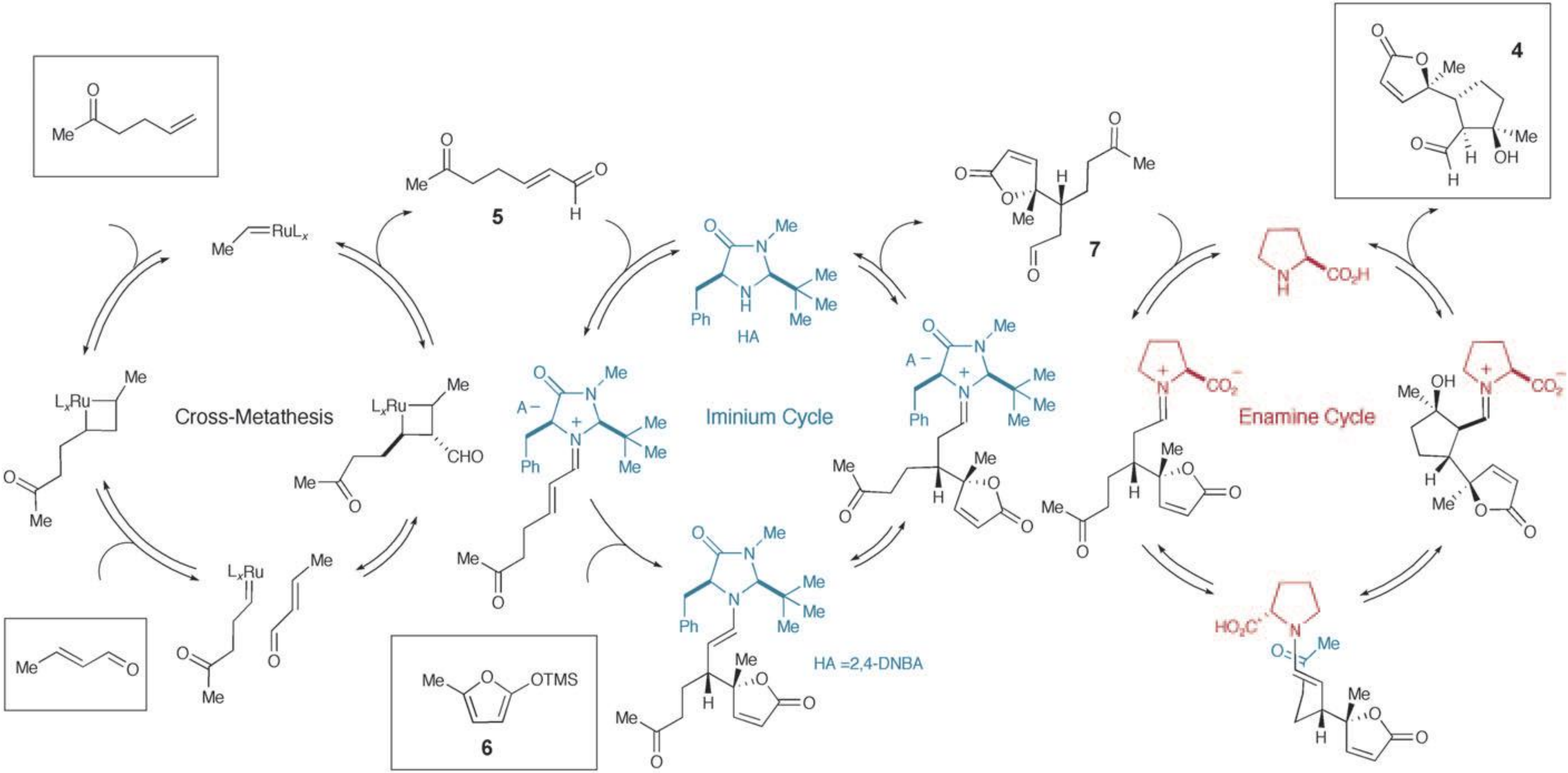
O
Me
Me
OH
Mes
N
N
N
Mes
base-H⊕
base
Me
OH
Me
O⊖
Mes
N
N
N
Mes
⊕
OH
Mes
N
N
N
Mes
⊕
O
Mes
OH
Me
Me
N
N
N
Mes
O
Mes
N
N
N
Mes
⊕
O
O
N
O
Mes
O
O
O
N
OH
HN
Me
(±)
O
Mes
N
Me
+
HN
Me

Multicatalysis

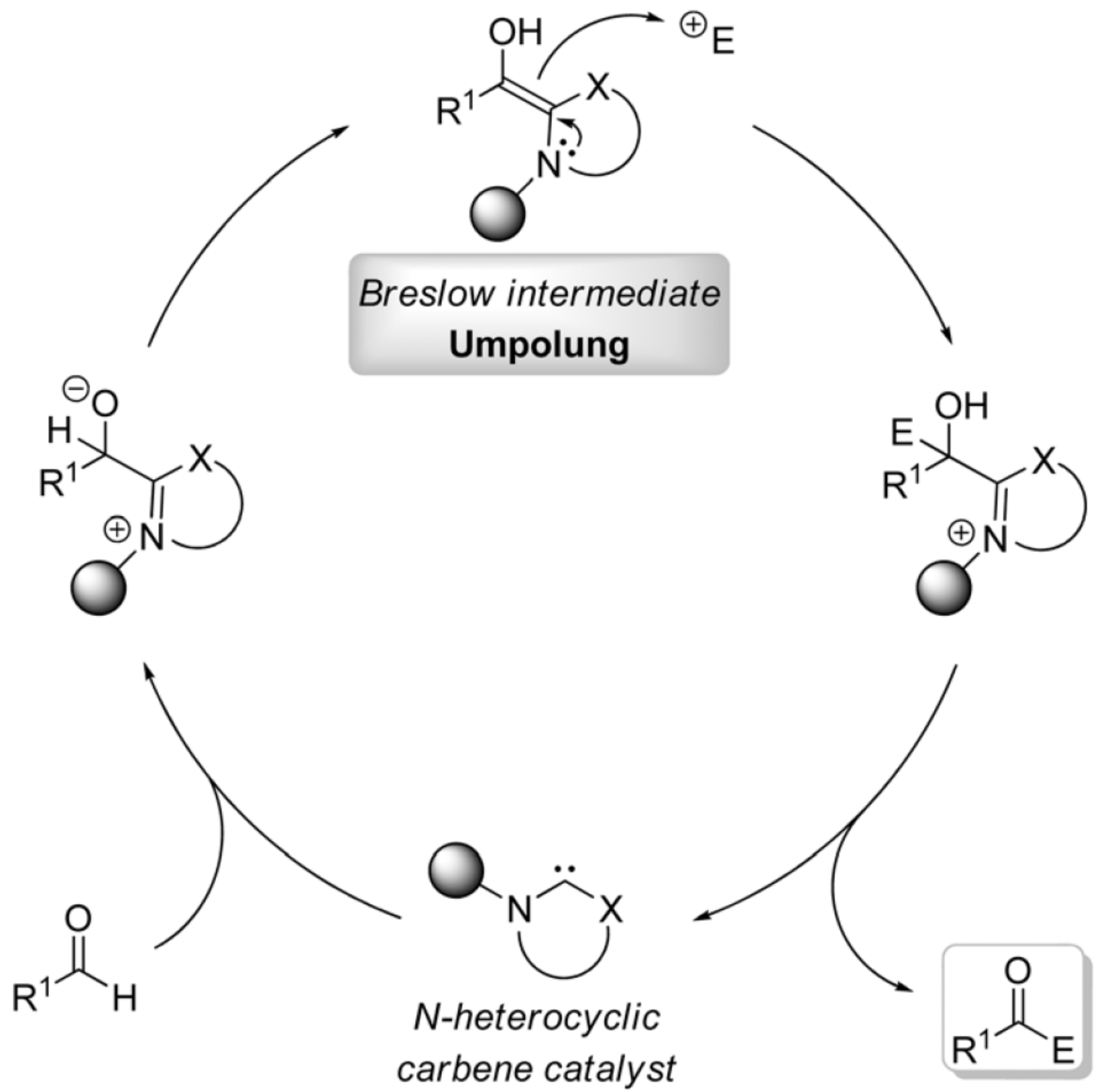




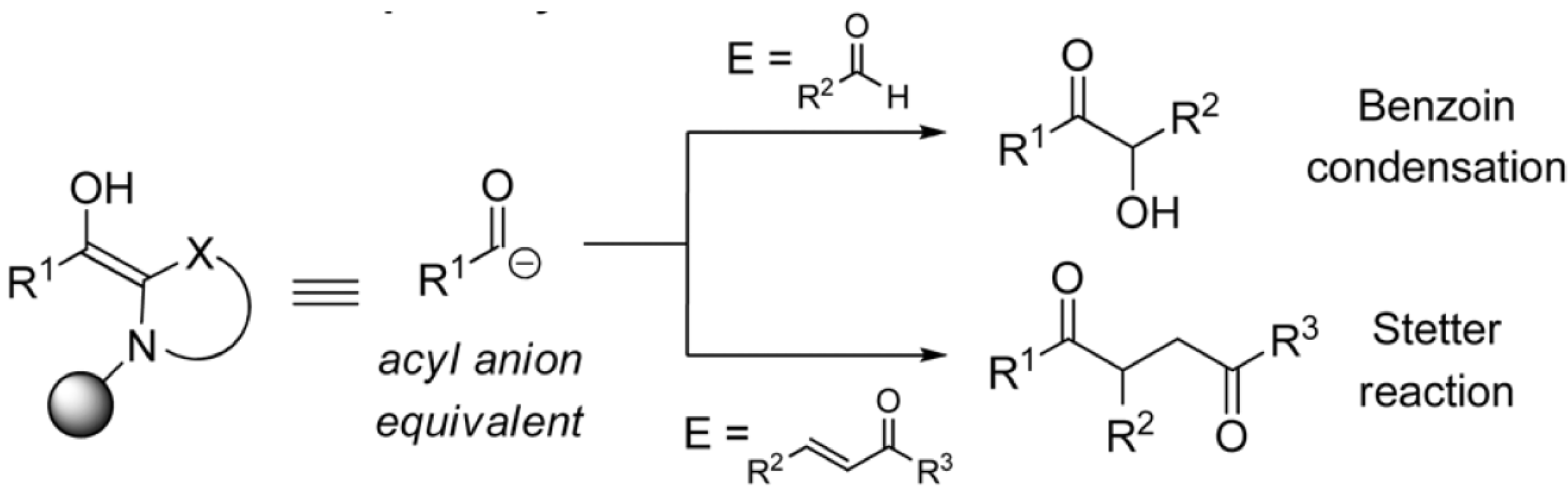
Simmons, B.; Walji, A. M.; MacMillan, D. W. C. *Angew. Chem., Int. Ed.* **2009**, *48*, 4349


Cross-Metathesis
Iminium Cycle
Enamine Cycle
HA
HA =2,4-DNBA
5
6
7
4

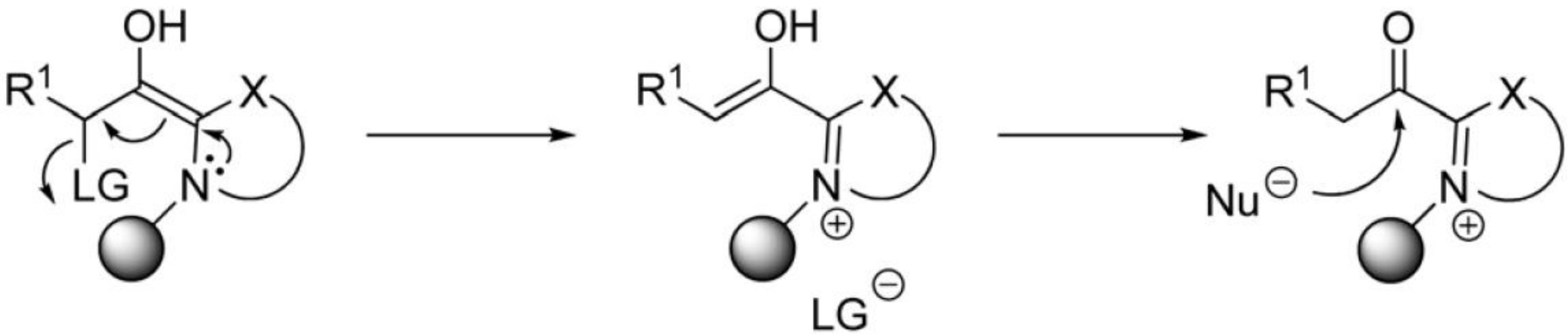
N-Heterocyclic carbene catalysts



Two possibilities



Extended Umpolung



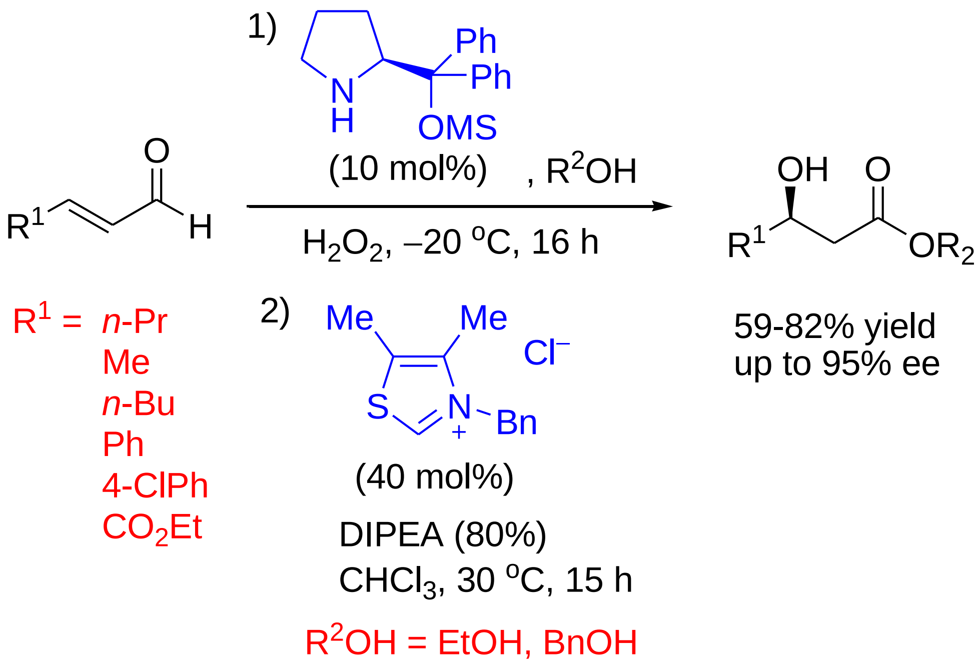
intramolecular redox reaction (extended Umpolung)

X = NR, S

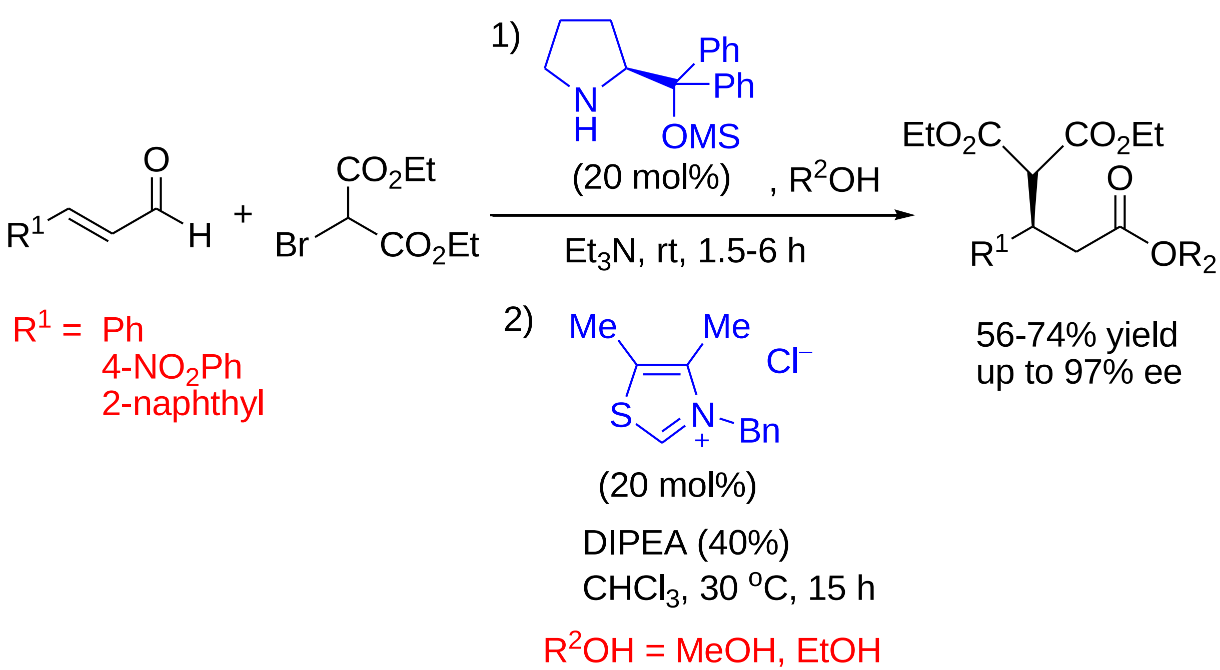
R^1, R^2, R^3 = alkyl, aryl

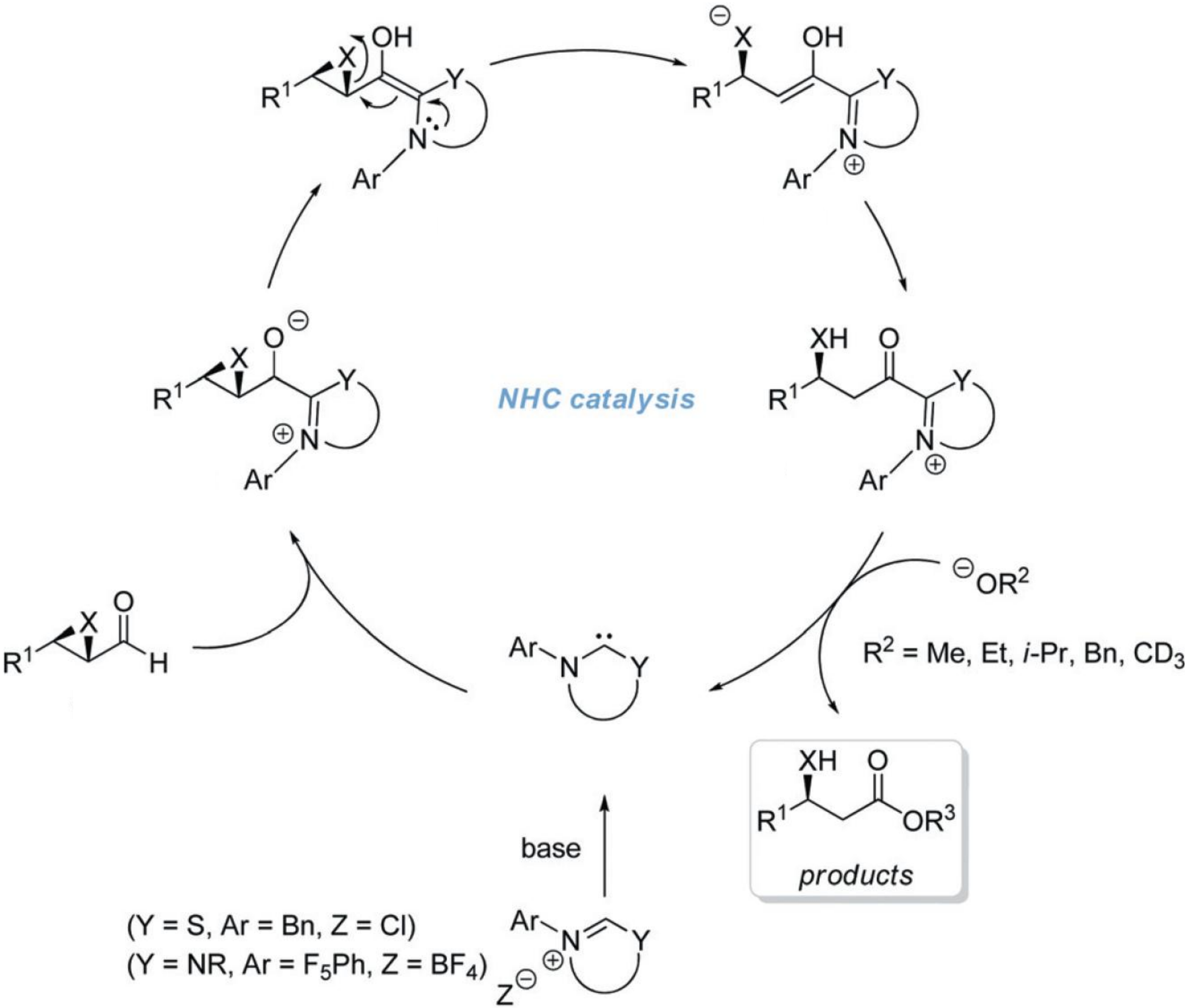
LG = leaving group

E = electrophile; Nu = nucleophile

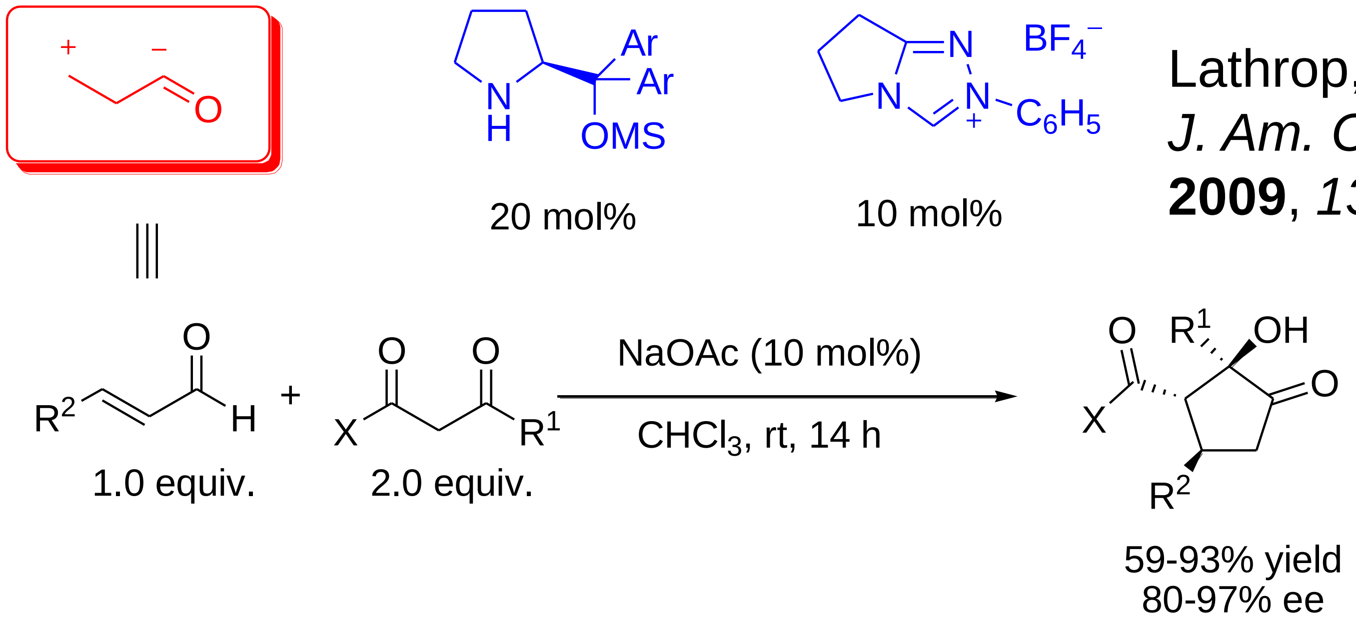


Zhao, G.-L.; Córdova, A.
Tetrahedron Lett.,
2007, 48, *5976*

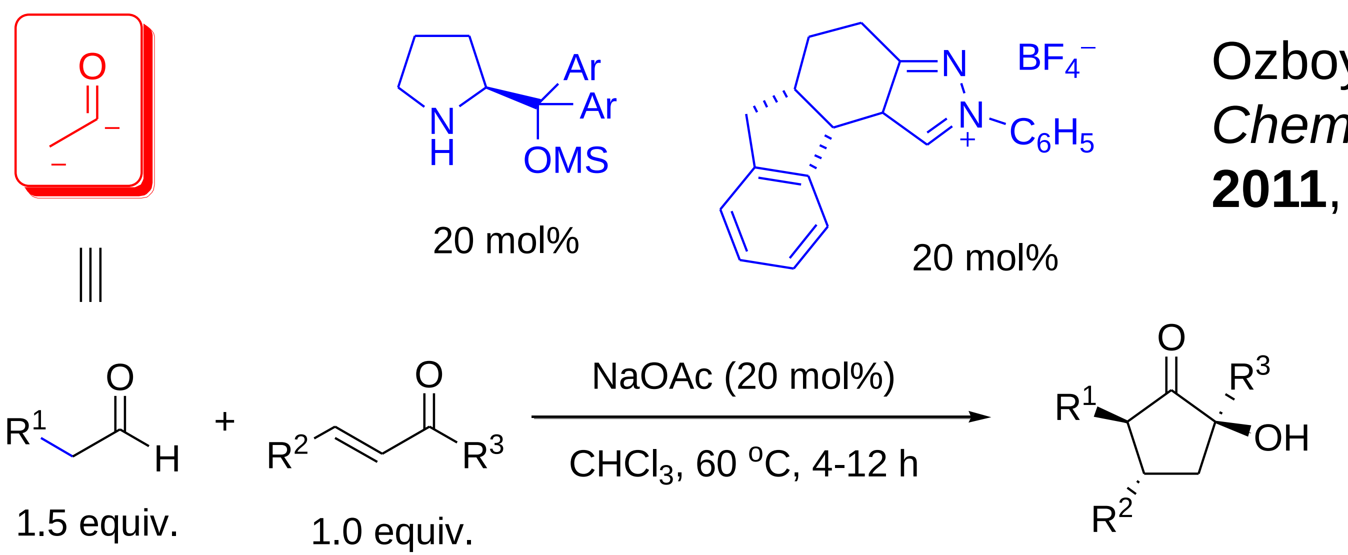




NHC catalysis
$^{\ominus}OR^2$
R^2 = Me, Et, *i*-Pr, Bn, CD_3
base
(Y = S, Ar = Bn, Z = Cl)
(Y = NR, Ar = F_5Ph, Z = BF_4)
products



Lathrop, S. P.; Rovis, T.
J. Am. Chem. Soc.
2009, *131*, 13628



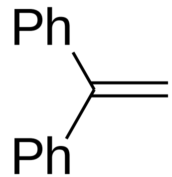
Ozboya, K. E.; Rovis, T.
Chem. Sci.
2011, **2**, 1835

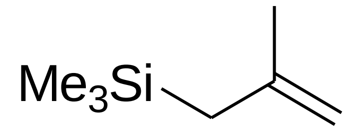
Catalytic hydrogenation: using organocatalyst

Frustrated Lewis Pairs (FLP)

$$(C_6F_5)Ph_2P + B(C_6F_5)_3 \underset{}{\overset{H_2}{\rightleftharpoons}} [(C_6F_5)Ph_2PH][HB(C_6F_5)_3]$$

20 mol%, 5 bar H_2, CH_2Cl_2, rt





	99% (24 h)	95% (12 h)
(*p*-Tol)$_2$NMe 5 mol%	87% (40 h)	99% (12 h)

Greb, L.; OCa-Burgos, P.; Schirmer, B.; Grimme, S.; Stephan, D. W.; Paradies, J. *Angew. Chem. Int. Ed.* **2012**, *51*, 10164

Stephan, D. W.; Erker, G. *Angew. Chem. Int. Ed.* **2010**, *49*, 46

Catalytic hydrogenation: using Pd

Silia*Cat* Pd^{o}
Made of highly dispersed Pd nanoparticles (4.0−6.0 nm)
encapsulated within an organosilica matrix
via an alcohol-free sol−gel process

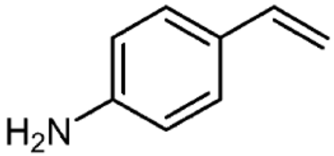
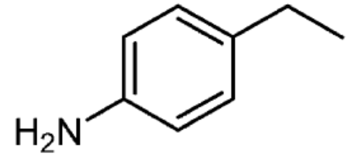
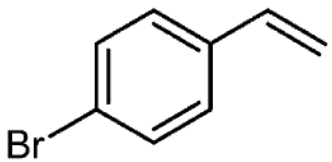
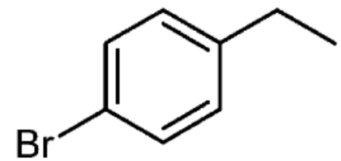
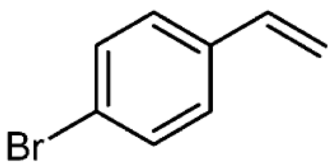
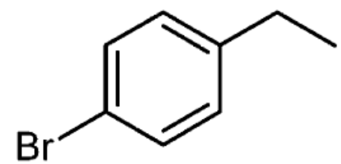
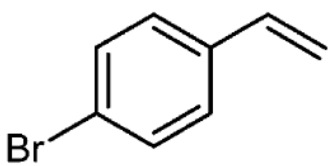
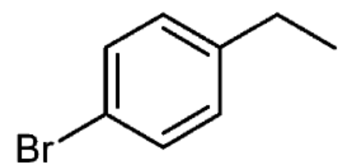
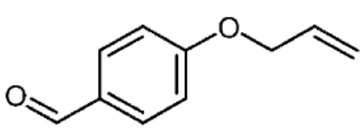
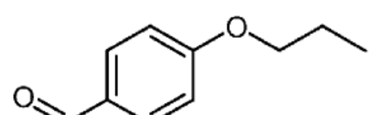
Conditions:

- 0.1 mol % catalyst
- hydrogen balloon, rt
- MeOH, EtOH, and THF
- complete after 0.5−3 h

Leaching of Pd and Si: in general <5 ppm

Selective and reusable

Pandarus, V.; Gingras, G.; Béland, F.; Ciriminna, R.; Pagliaro, M.
Org. Process Res. Dev. **2012**, *16*, 1230

Entry	Substrate	Catalyst (mol%)	Solvent (M)	Time (h)	Product	Conv(Yield)[b] (%)	Select[b] (%)
1		0.1	MeOH (0.25 M)	0.5 1		92 100 (99.1)	100
2		0.1	MeOH (0.25 M)	1 3		22 35	
3		0.25	MeOH (0.25 M)	1		100	99
4		0.5	MeOH (0.25 M)	0.5		100 (98.5)	100
10		0.1	EtOH (0.25 M)	0.5 1		92 100	95

Green oxidation reagent: O_2 catalyzed by transition metals

Traditional oxidation methods:

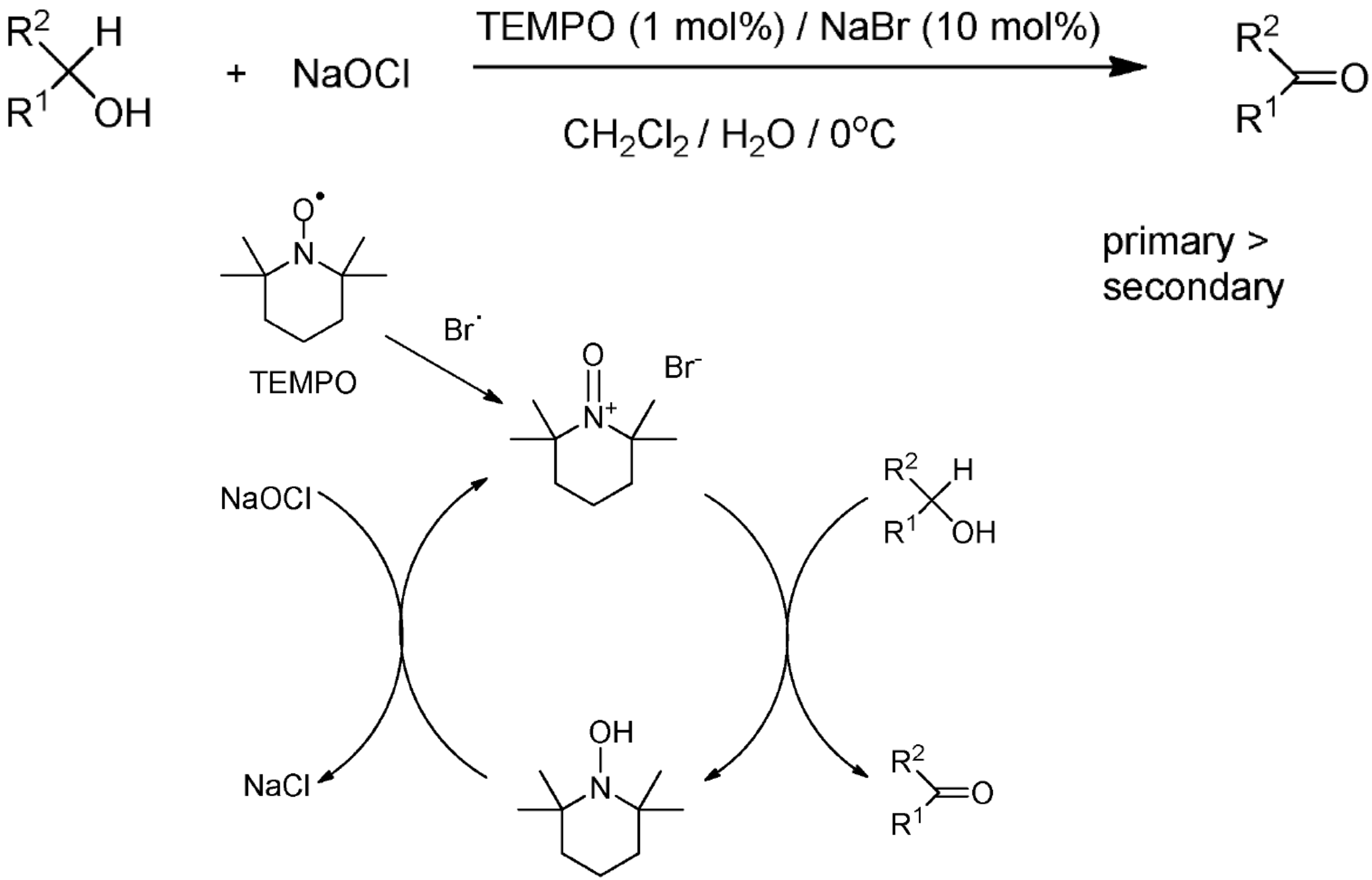
- Stoichiometric metal oxidation
- Nitric acid
- Swern oxidation
- Dess-Martin periodinane
- IBX
- TPAP/NMO

Problems:

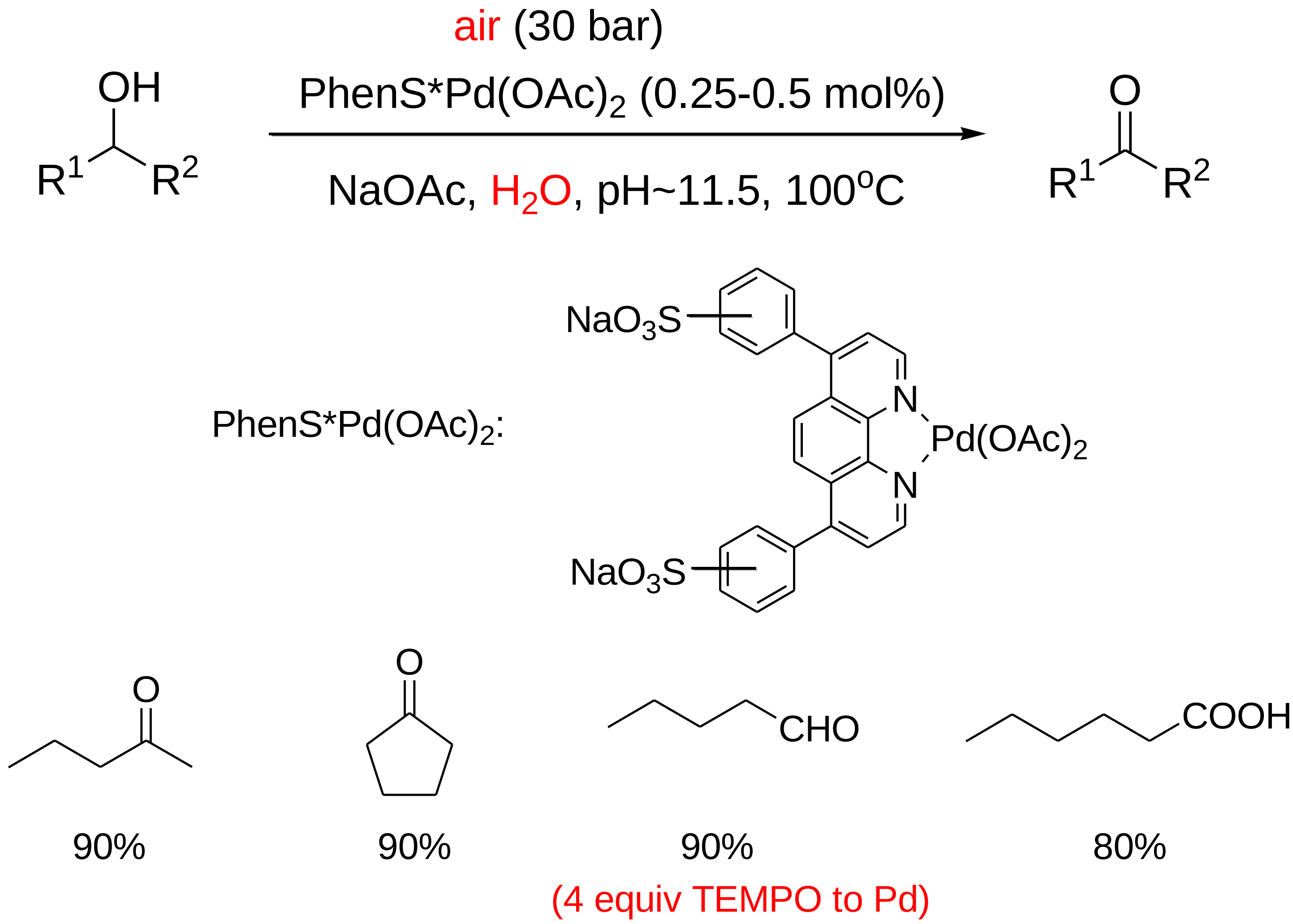
Heavy metal waste
Nitrogen oxides
Poor atom efficiencies
Difficult to scale-up

Parmeggiani, C.; Cardona, F. *Green Chem*., **2012**, *14*, 547

TEMPO catalysed oxidations with NaOCl

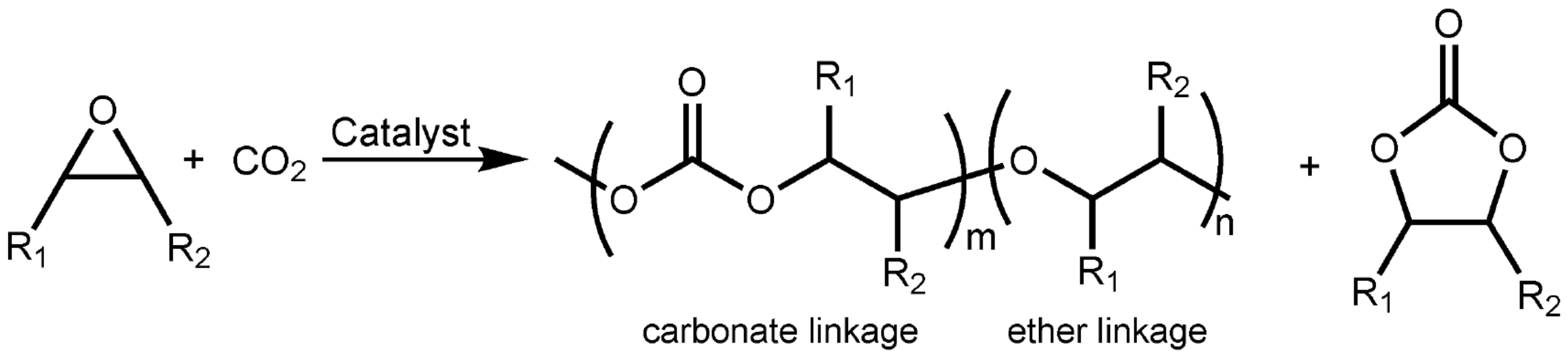


Anelli, L.; Biffi, C.; Montanari, F.; Quici, S. *J. Org. Chem*. **1987**, *52*, 2559
See also: Sheldon, R. A. *Chem. Soc. Rev*. **2012**, *41*, 1437

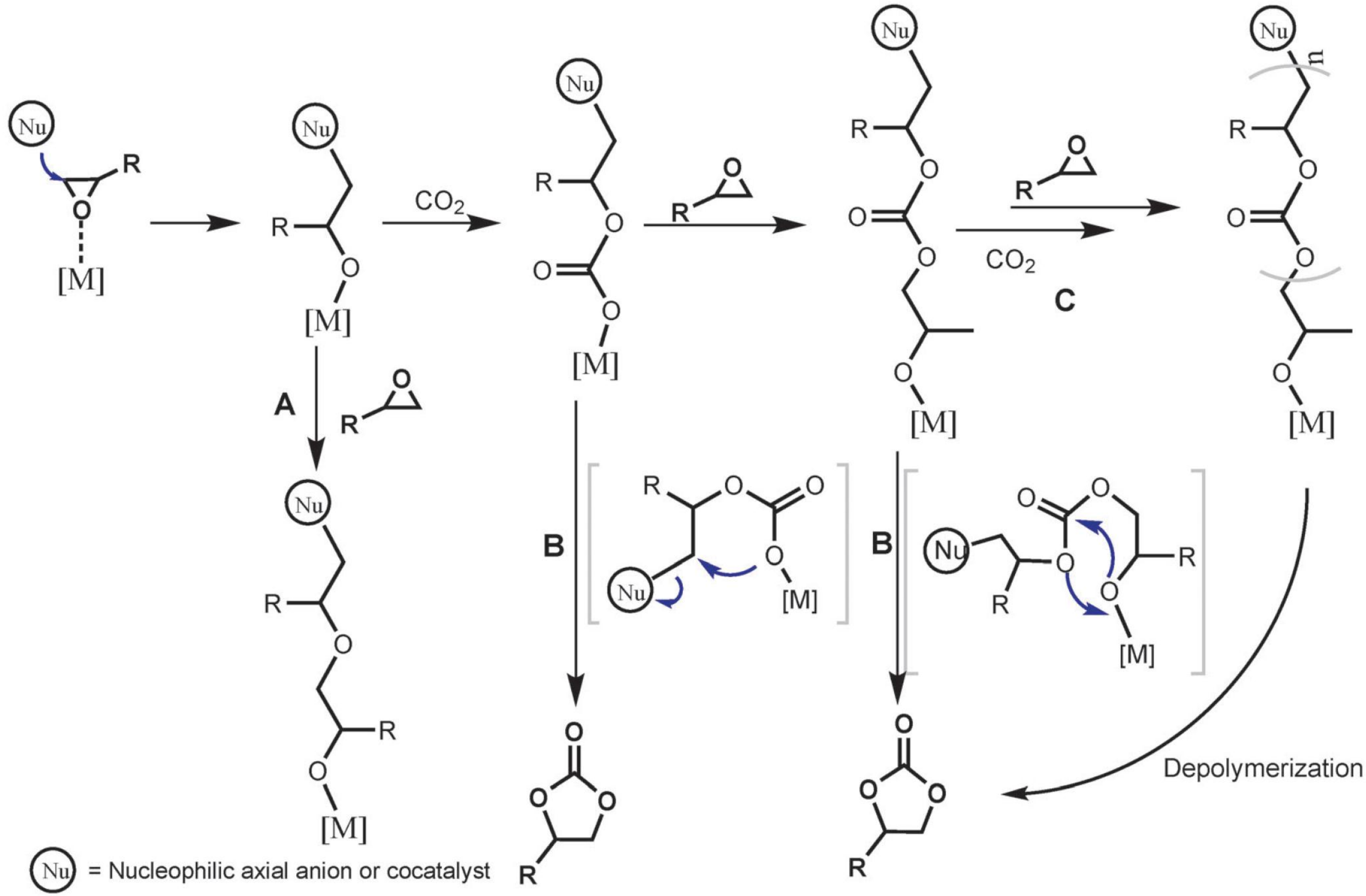


Ten Brink, G.-J.; Arends, I. W. C. E.; Sheldon, R. A. *Science* **2000**, *287*, 1636

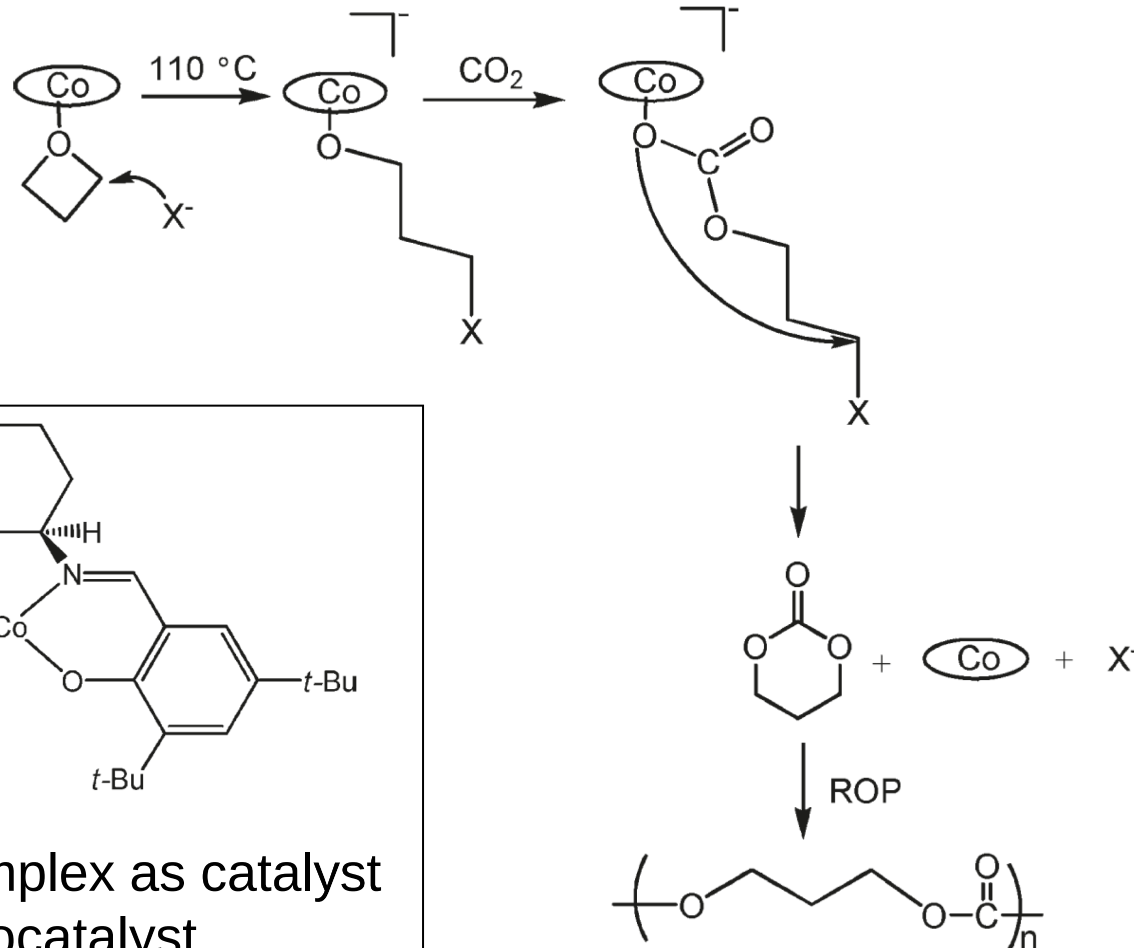
CO_2 and Carbonates

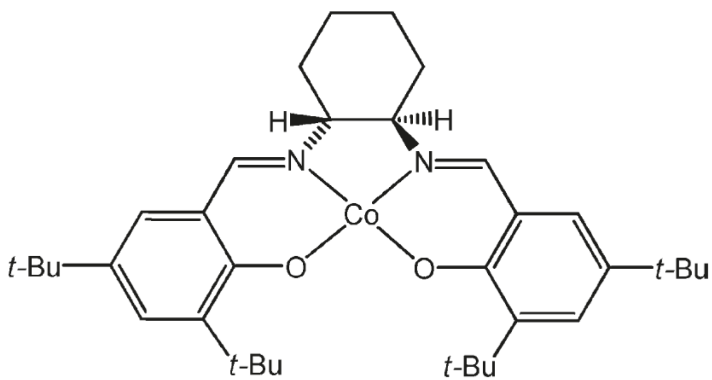


Lu, X.-B.; Darensbourg, D. J. *Chem. Soc. Rev.*, **2012**, *41*, 1462



The reaction pathways are dependent on the nature of the epoxide, the metal complex and cocatalyst employed, as well as reaction conditions (such as temperature, CO_2 pressure)





salenCo(II) complex as catalyst
\+ Bu_4NBr as cocatalyst

Darensbourg, D. J.; Moncada, A. I. *Macromolecules* **2009**, *42*, 4063

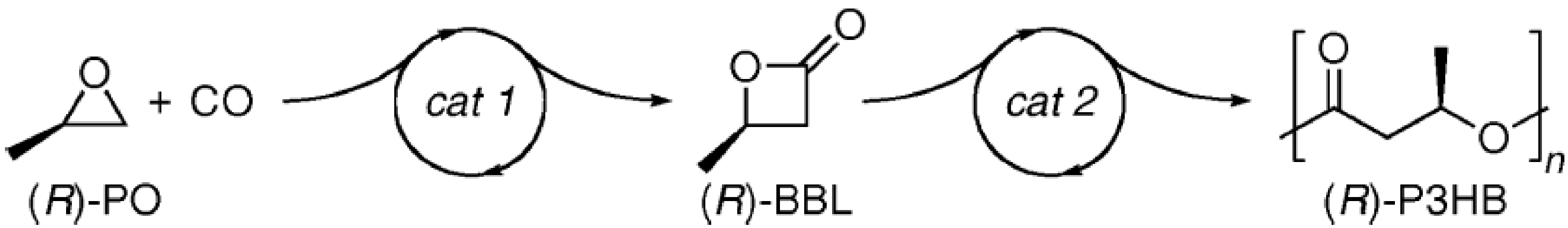
One-Pot Carbonylative Polymerization

2012 **US Presidential Green Chemistry Challenge Awards**

Academic Award

Prof. G. W. Coates (Cornell)

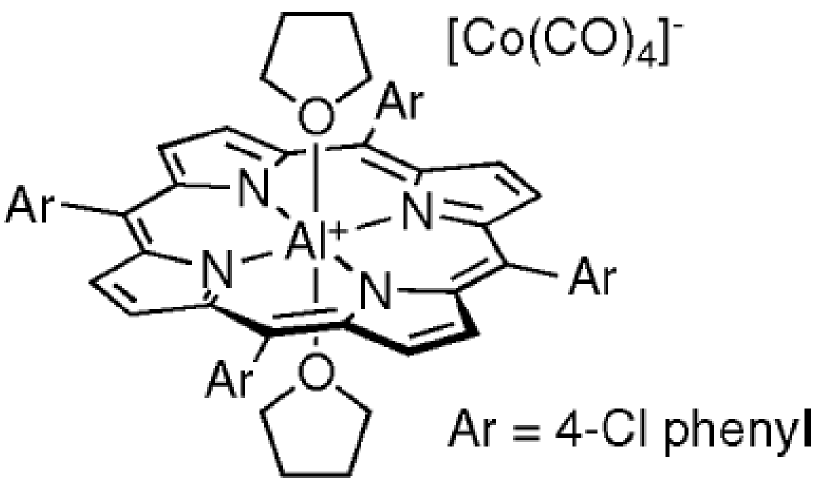
Developed catalysts that convert CO_2 and CO into polymers



J. Am. Chem. Soc. **2010**, *132*, 11412

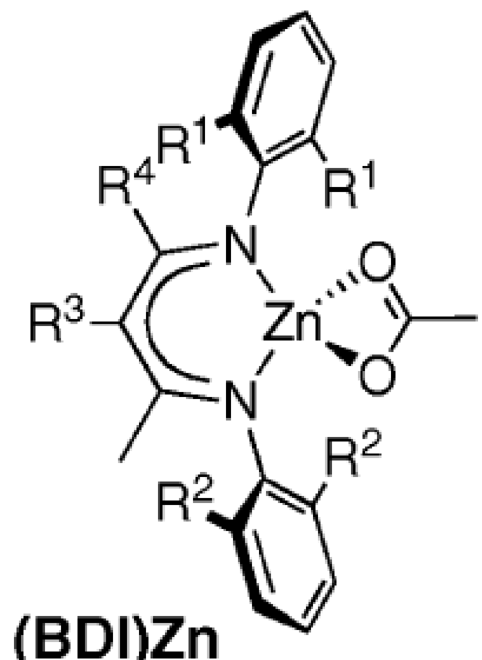
Carbonylation catalyst

0.05 mol %



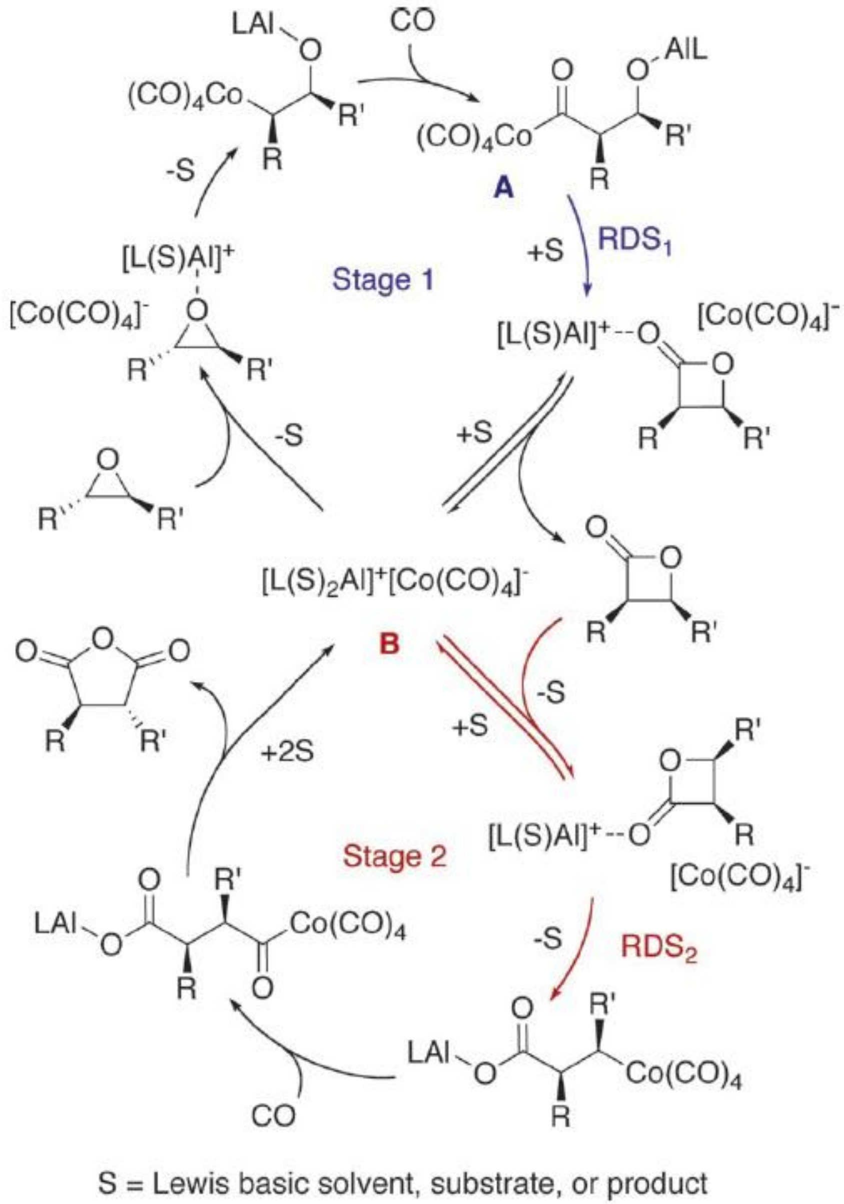
Polymerization catalyst

0.5 mol %

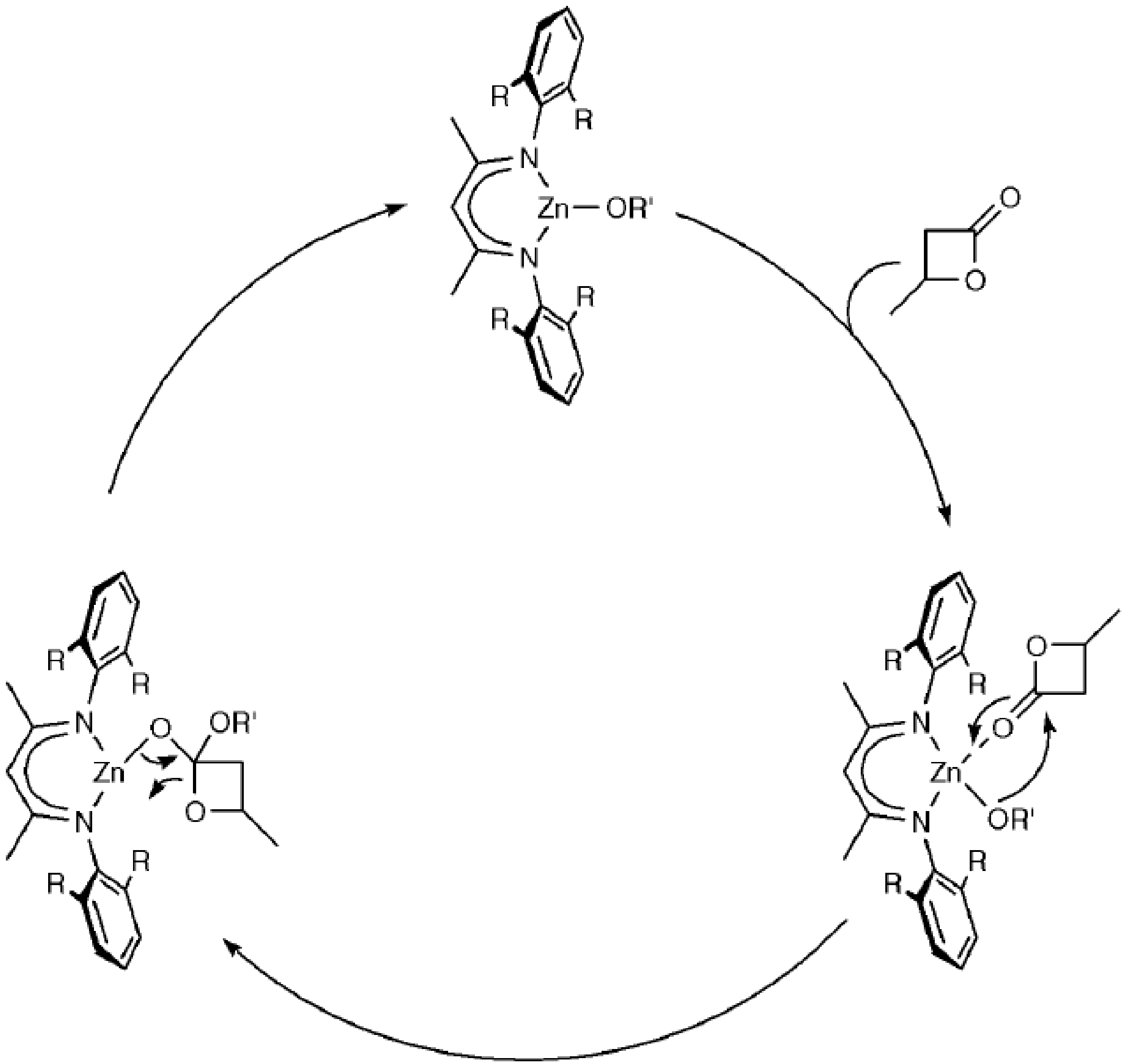


$R^1 = R^2 = {}^iPr$, $R^3 = H$, $R^4 = Me$

J. Am. Chem. Soc. **2007**, *129*, 4948

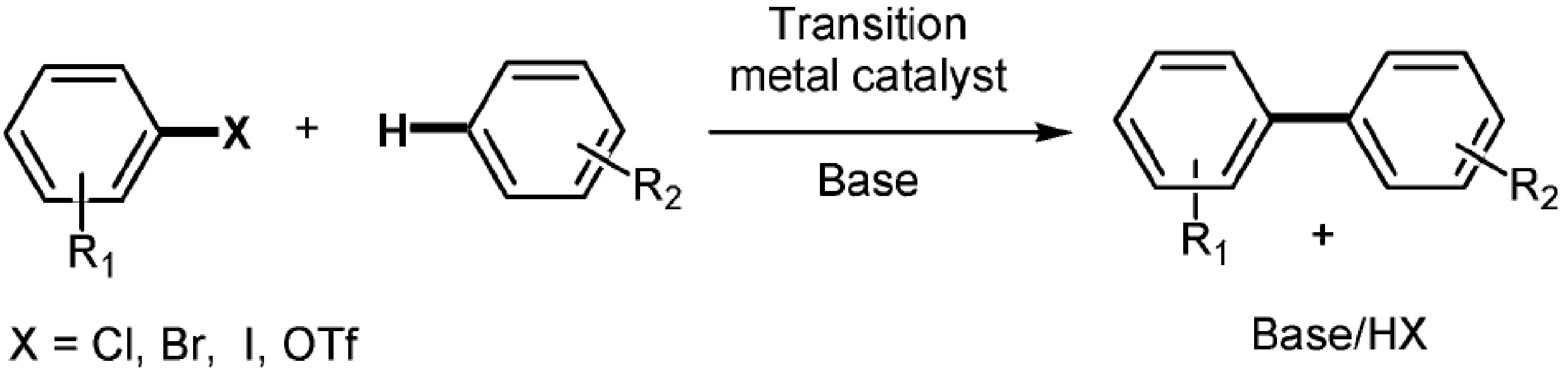


J. Am. Chem. Soc. **2002**, *124*, 15239

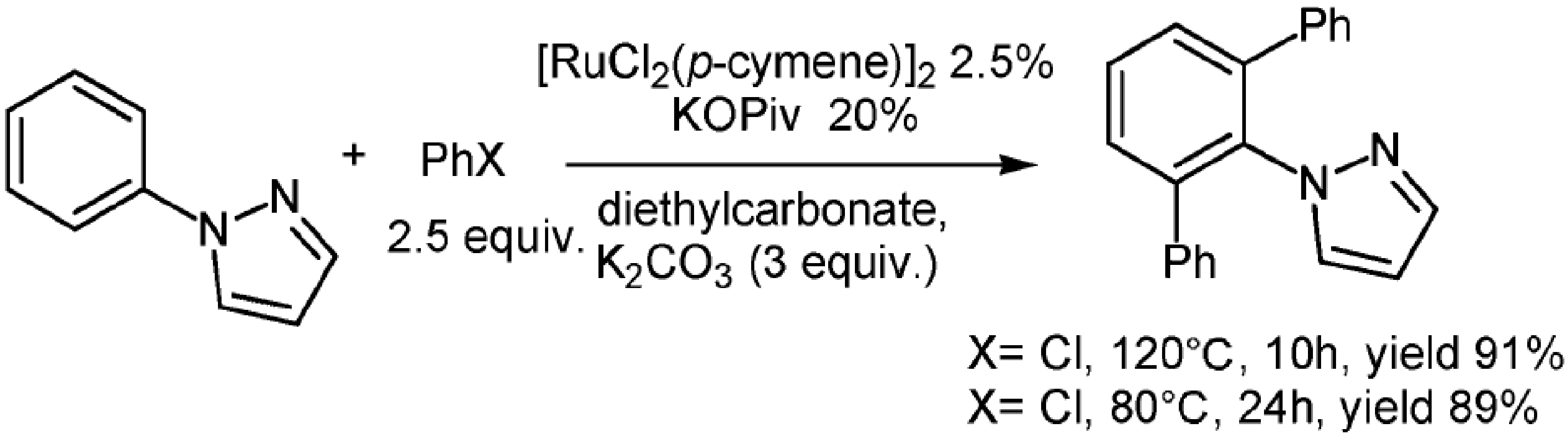


Greener solvents for biaryl couplings

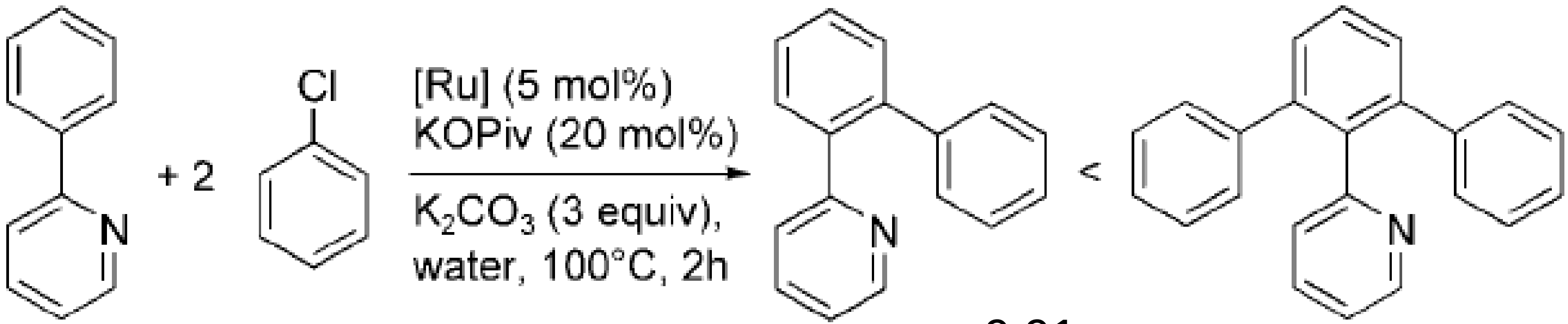
Fischmeister, C.; Doucet, H. *Green Chem.*, **2011**, *13*, 741



Solvents: DMF
NMP
DMAC

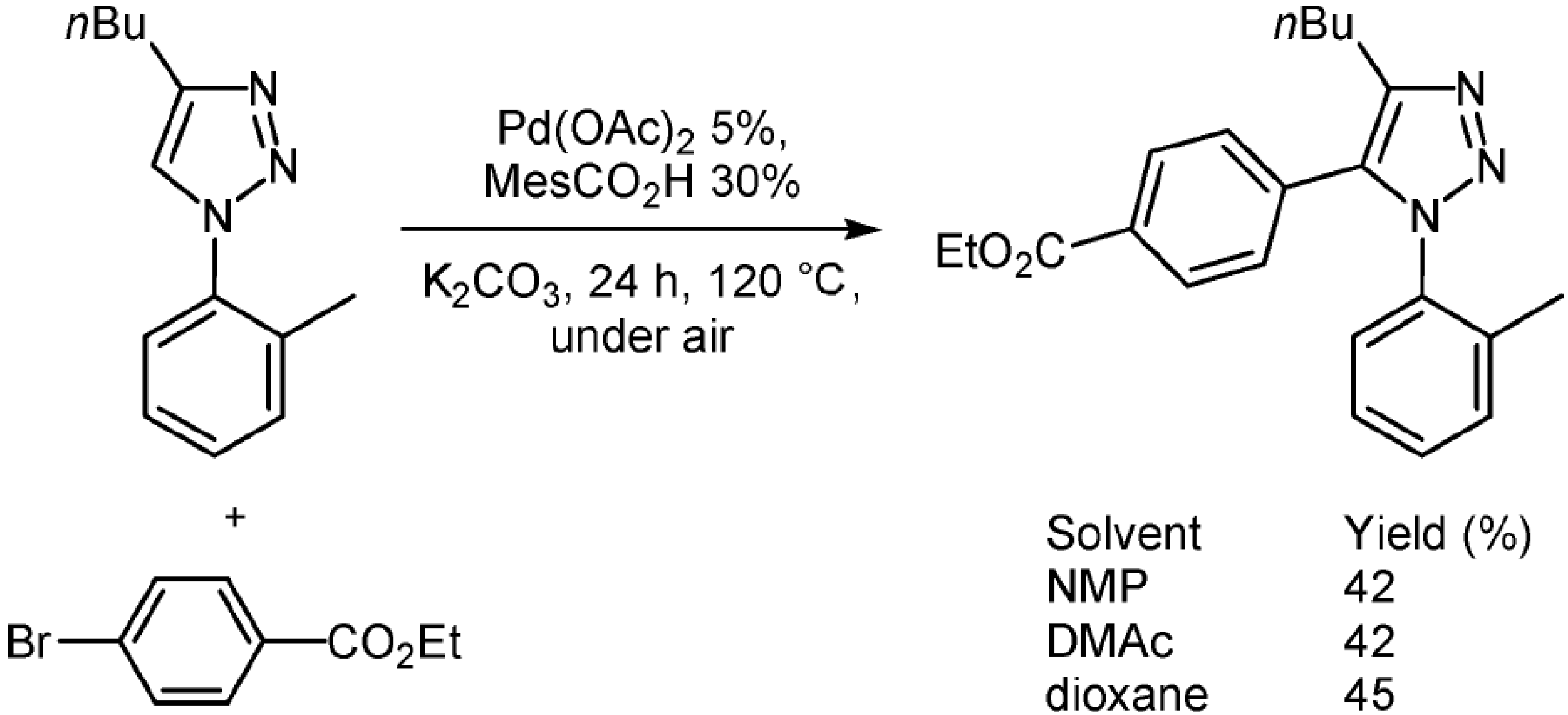


Arockiam, P.; Poirier, V.; Fischmeister, C.; Bruneau, C.; Dixneuf, P. H. *Green Chem.*, **2009**, *11*, 1871



9:91

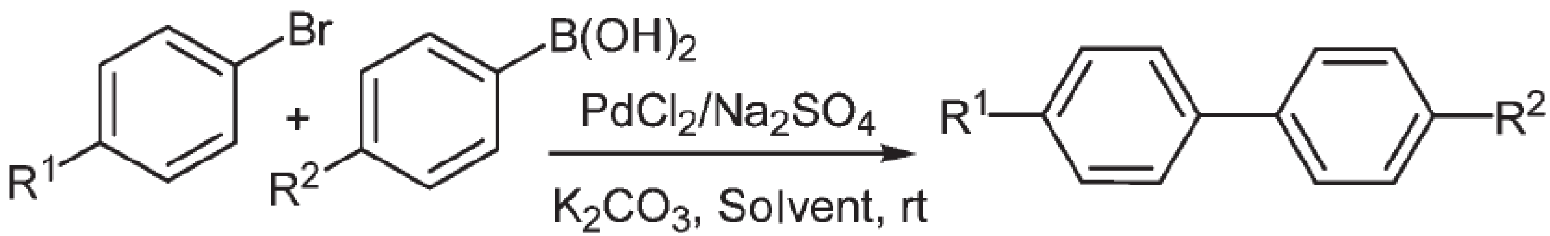
Arockiam, P. B.; Fischmeister, C.; Bruneau, C.; Dixneuf, P. H.
Angew. Chem. Int. Ed. **2010**, *49*, 6629



Solvent	Yield (%)
NMP	42
DMAc	42
dioxane	45
PEG-2000	39
PEG-20000	74

Ackermann, L.; Vicente, R. *Org. Lett.*, **2009**, *11*, 4922

Pd-catalyzed ligand-free Suzuki–Miyaura coupling in water



R^1	R^2	Solvent	Time (h)	Yield (%)
NO_2	H	i-PrOH	5	90
CHO	H	i-PrOH	7	98
$COCH_3$	H	i-PrOH	5	96
OCH_3	H	i-PrOH	7	98
H	H	i-PrOH	3	100
CH_3	OCH_3	i-PrOH	1	90
CH_3	OCH_3	H_2O	1	97
CHO	OCH_3	H_2O	3	95
OCH_3	OCH_3	H_2O	2	90
H	OCH_3	H_2O	6	94
CHO	H	H_2O	5	95
H	H	H_2O	1	98
CH_3	H	H_2O	2	97
OCH_3	H	H_2O	5	97

ArBr (0.5 mmol)
$ArB(OH)_2$ (0.55 mmol)
$PdCl_2$ (2 mol%),
Additive (8 mol%)
Base (1.5 mmol),
Solvent (4 mL)
25 °C, in air.

Mondal, M.; Bora, U. *Green Chem*. **2012**, *14*, 1873

Summary

Green chemistry technologies provide a number of benefits, including:

- Reduced waste, eliminating costly end-of-the-pipe treatments
- Safer products
- Reduced use of energy and resources
- Improved competitiveness of chemical manufacturers and their customers