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]。

Recent Advances in Green Catalysis
觸媒反應新趨勢

Chun-Chen Liao

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Chungli 32023, TAIWAN

綠色/永續合成化學講習會
化學會年會，台灣大學
2010. 12. 03

主辦單位：化學會化學與環境委員會
協辦單位：中央研究院化學研究所
台灣大學化學系
贊助廠商：台灣神隆股份有限公司

第七次全國科學技術會議

討論議題一：發展特色研究領域

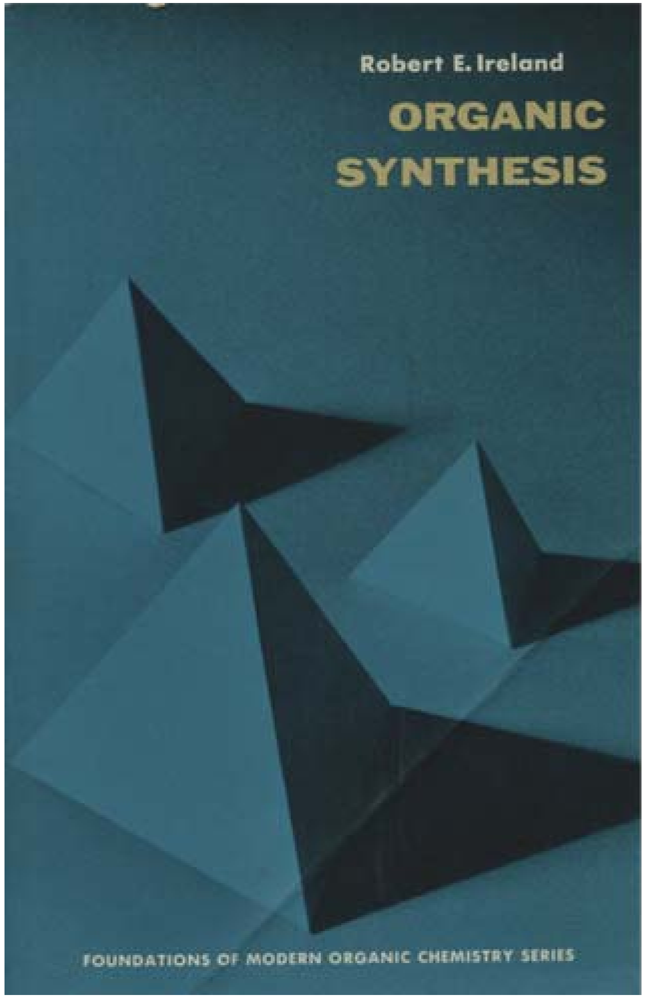
(一) 強化海洋科技研究
(二) 發展綠色科技研究
(三) 強化跨領域尖端研究能力

Molecular Design and Synthesis

Molecular design is the application of all techniques leading to the discovery of new chemical entities with specific properties required for the intended application. IUPAC Gold-Book

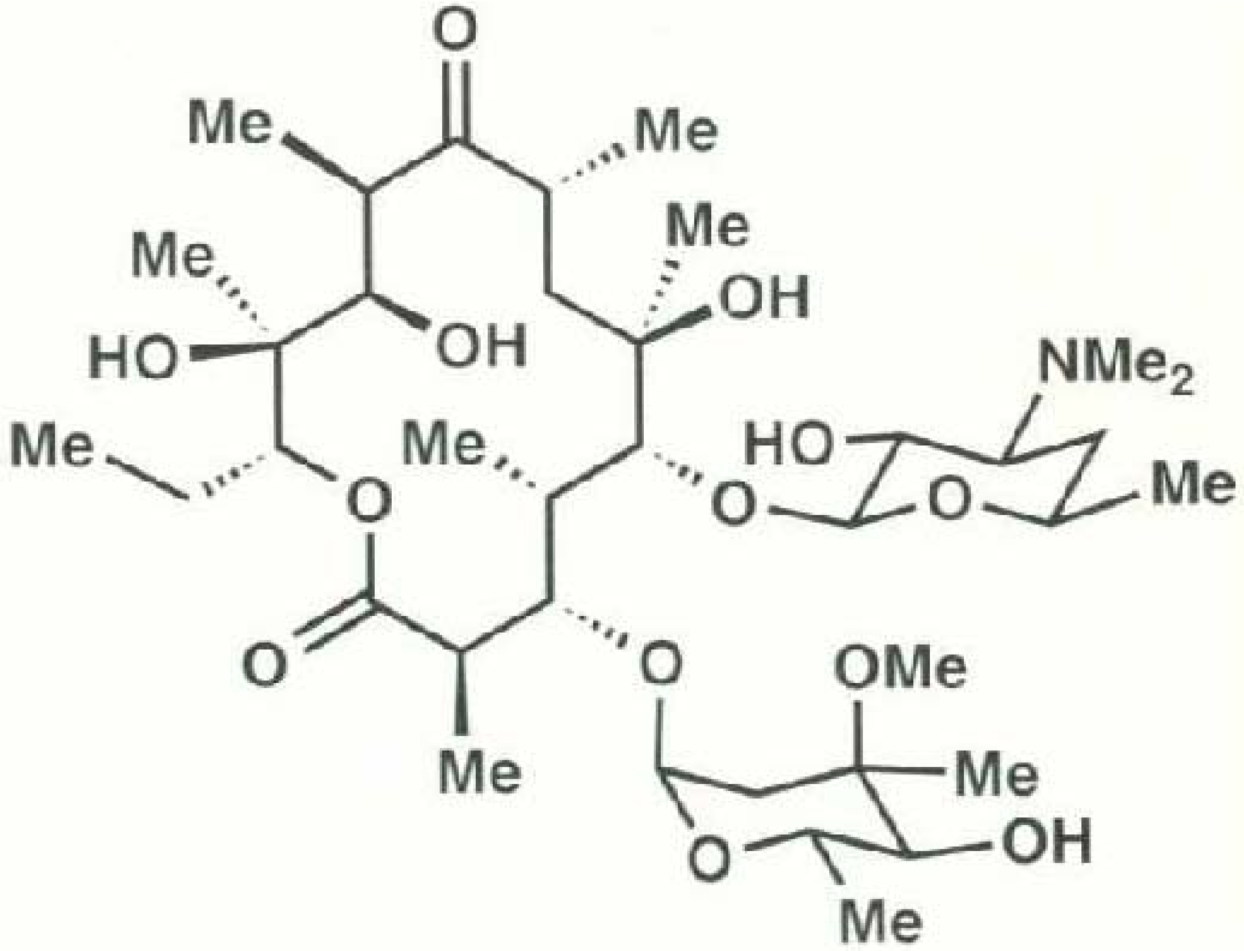
Organic Synthesis

- C-C bond formation
- Transformation of functional groups
- Stereochemistry



Robert E. Ireland
ORGANIC
SYNTHESIS
FOUNDATIONS OF MODERN ORGANIC CHEMISTRY SERIES

Stereochemistry raises its ugly head



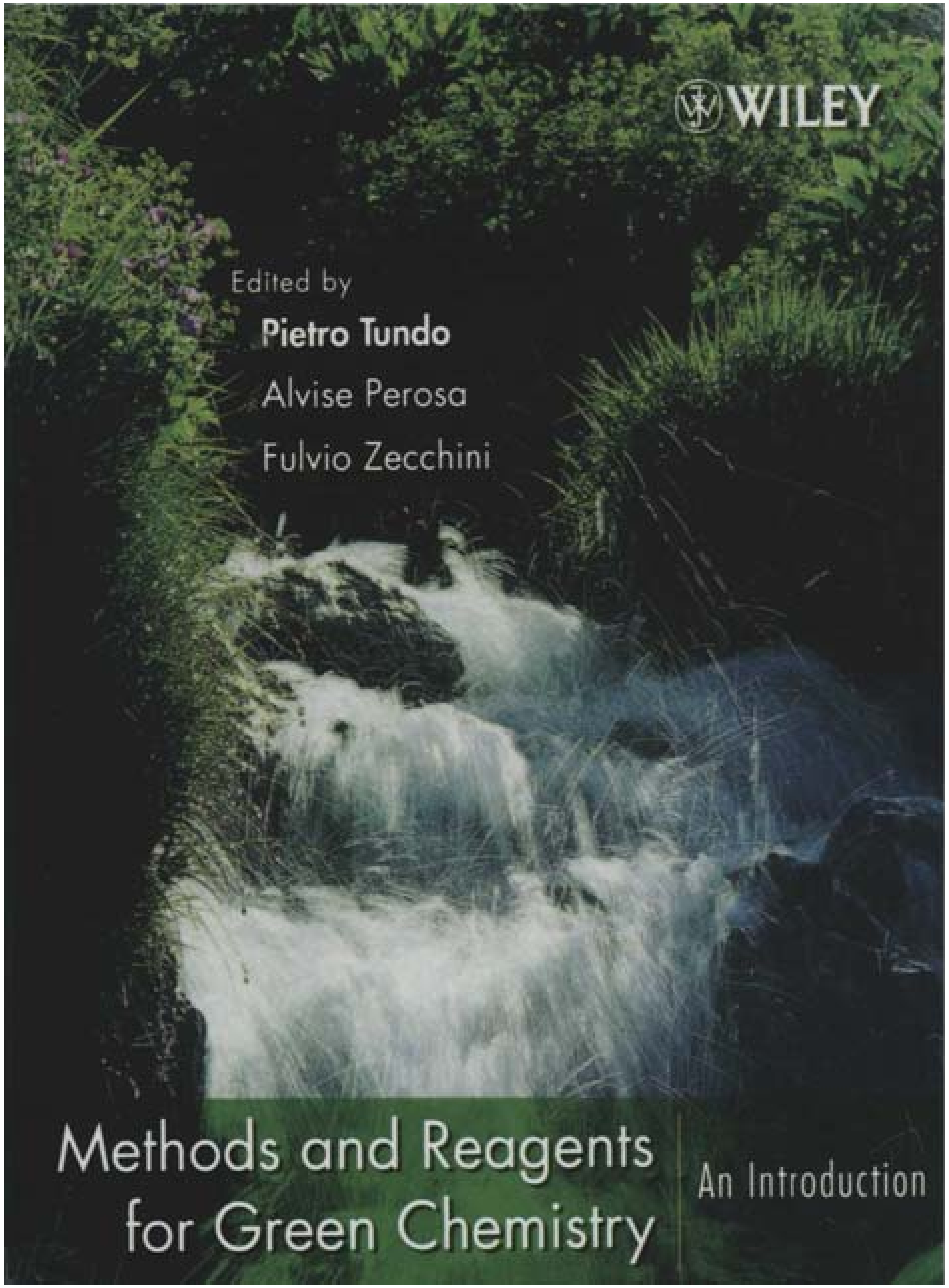
Erythromycin A

Stereocenters = 18

Stereoisomers = 262,144

Green Chemistry

Technologies that efficiently utilize energy and raw materials and reduce, or preferably, eliminate, the generation of waste and avoid the use of toxic and /or hazardous reagents, and solvents.



Condensed Principles of Green Chemistry

Twelve principles of green chemistry written in the form of a mnemonic: PRODUCTIVELY

P – Prevent wastes
R – Renewable materials
O – Omit derivatization steps
D – Degradable chemical products
U – Use safe synthetic methods
C – Catalytic reagents
T – Temperature, Pressure ambient
I – In–Process Monitoring
V – Very few auxiliary substances
E – E-factor, maximize feed in product
L – Low toxicity of chemical products
Y – Yes, it is safe

S. L. Y. Tang, R. L. Smith, M. Poliakoff, *Green Chem.*, 2005, *7*, 761-762

Nature of Green Solvents

having…

- **Low toxicity**
- **Easy recyclability (No disposal)**
- **Further desirable characteristics :**

  easy removal from the product and low reactivity.

Water as a Solvent

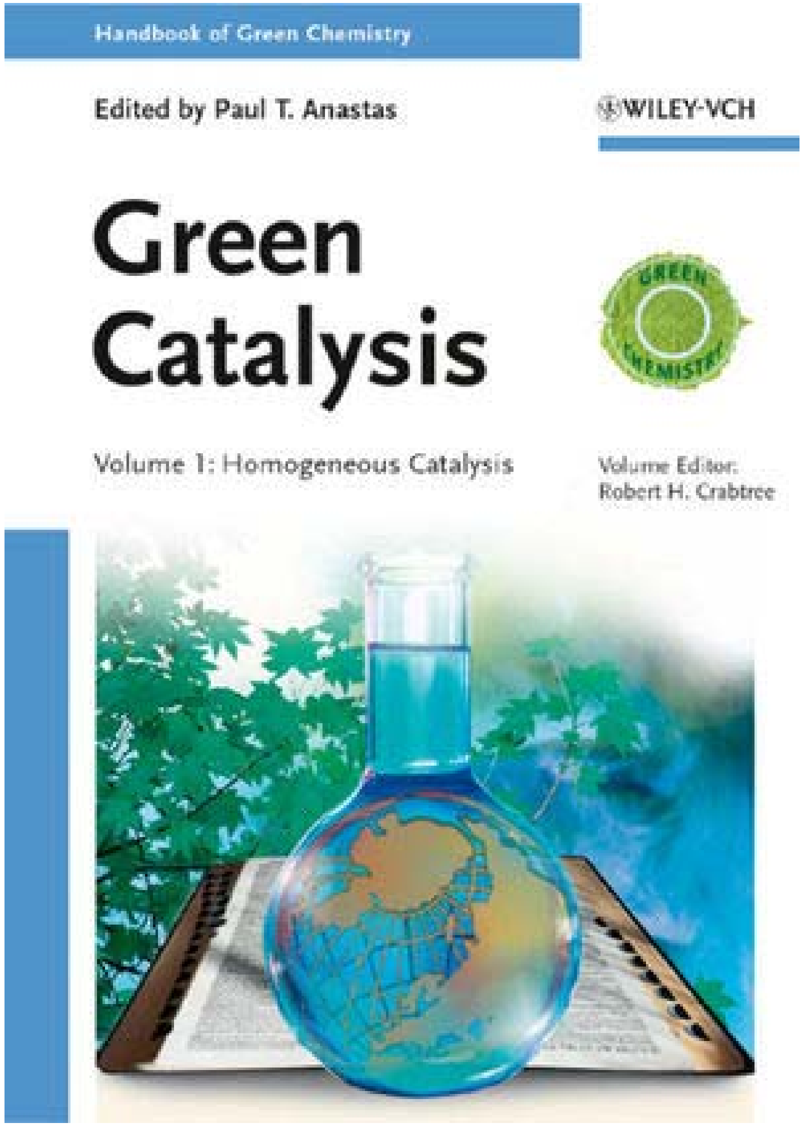
Advantages

- Economically & Environmentally attractive
- Inexpensive and abundantly available
- Non-inflammable and non-toxic
- Odorless & colorless
- Highly polar reaction medium
- Novel reactivity of organometallic complexes
- Facile product separation/catalyst recycling
- Reduced product contamination

I. T. Horvath, *Green Chem.*, 2008, *10*, 1024-1028.

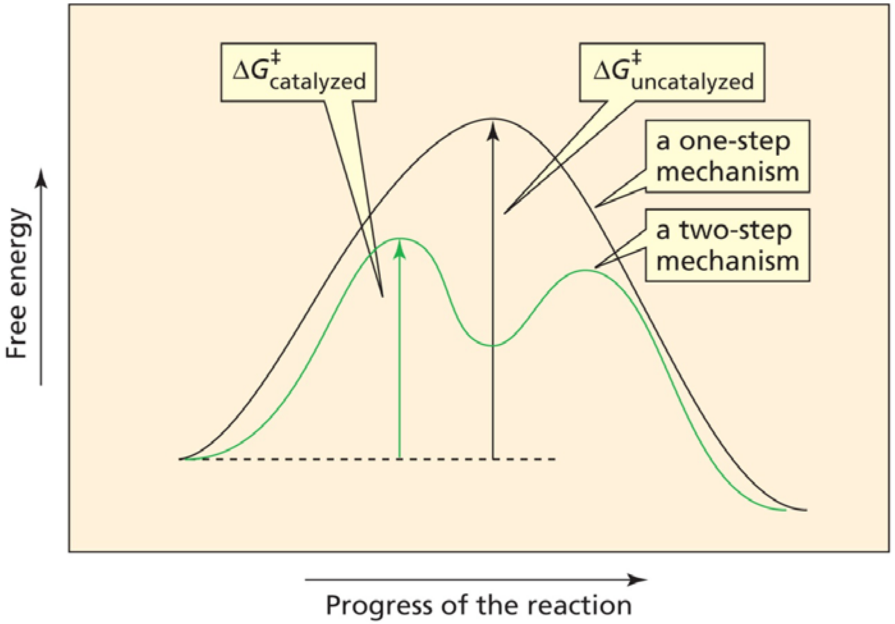
Catalysis

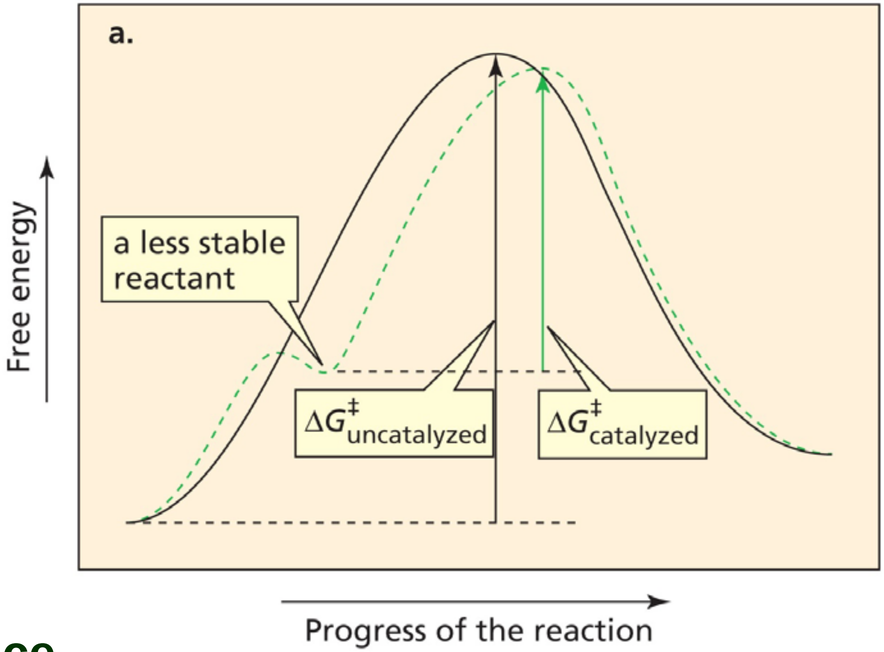
Brønsted Acid-Base Catalysis
Lewis Acid-Base Catalysis
Transition-metal catalysis
Organocatalysis
Asymmetric Catalysis
Biocatalysis
Photocatalysis



Catalysis in Organic Reactions

- It can provide a new reaction route.
- It can increase the stability of a transition state.
- It can increase the reactivity of a nucleophile.
- It can increase the susceptibility of an electrophile to nucleophilic attack.
- It can increase the leaving ability of a group by converting it into a weaker base.





adapted from Organic chemistry by P. Y. Bruice

Homogeneous vs.
Heterogeneous Catalysis

	Homogeneous	**Heterogeneous**
Advantages	- Mild reaction conditions - High reactivity and selectivity - Efficient heat transfer	- Facile separation of catalyst and products - Continuous processing
Disadvantages	- Cumbersome separation and recycling of catalyst - Product contamination	- Heat transfer problems - Low reactivity and selectivity

The Role of Green Catalysis

The increasing use of catalytic processes can substantially reduce waste at the source, resulting in primary pollution prevention.

Stoichiometric vs. Catalytic Oxidation

Stoichiometric: (The Jones oxidation)

$$3\ PhCH(OH)CH_3 + 2\ CrO_3 + 3\ H_2SO_4 \longrightarrow 3\ PhCOCH_3 + Cr_2(SO_4)_3 + 6\ H_2O$$

Atom efficiency = 120 x 3/122 x 3 + 100 x 2 + 98 x 3 = 360 / 860 = 42 %

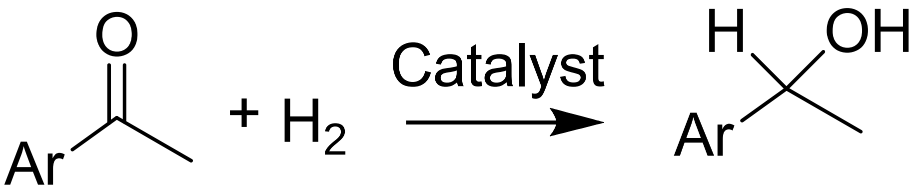
Catalytic: $PhCH(OH)CH_3 + 1/2\ O_2 \longrightarrow PhCOCH_3 + H_2O$

Atom efficiency = 120 / 122 + 16 = 120 / 138 = 87%

$$\%\ \text{Atom Economy} = \left(\frac{\text{molecular weight of desired product}}{\text{molecular weight of all reactants}} \right) \text{x } 100$$

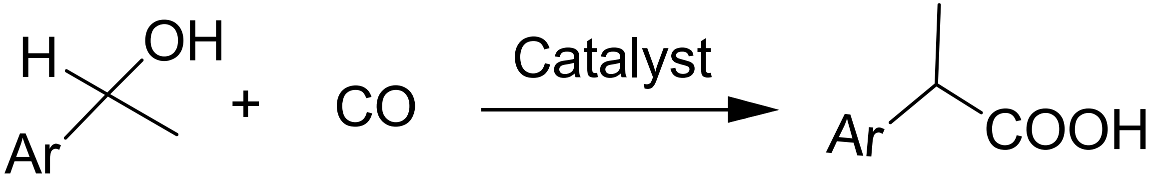
Atom-efficient Catalytic Processes

Hydrogenation:



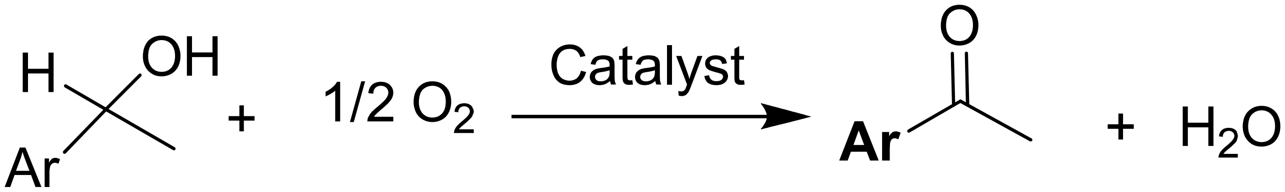
100 % atom efficient

Carbonylation:



100 % atom efficient

Oxidation:

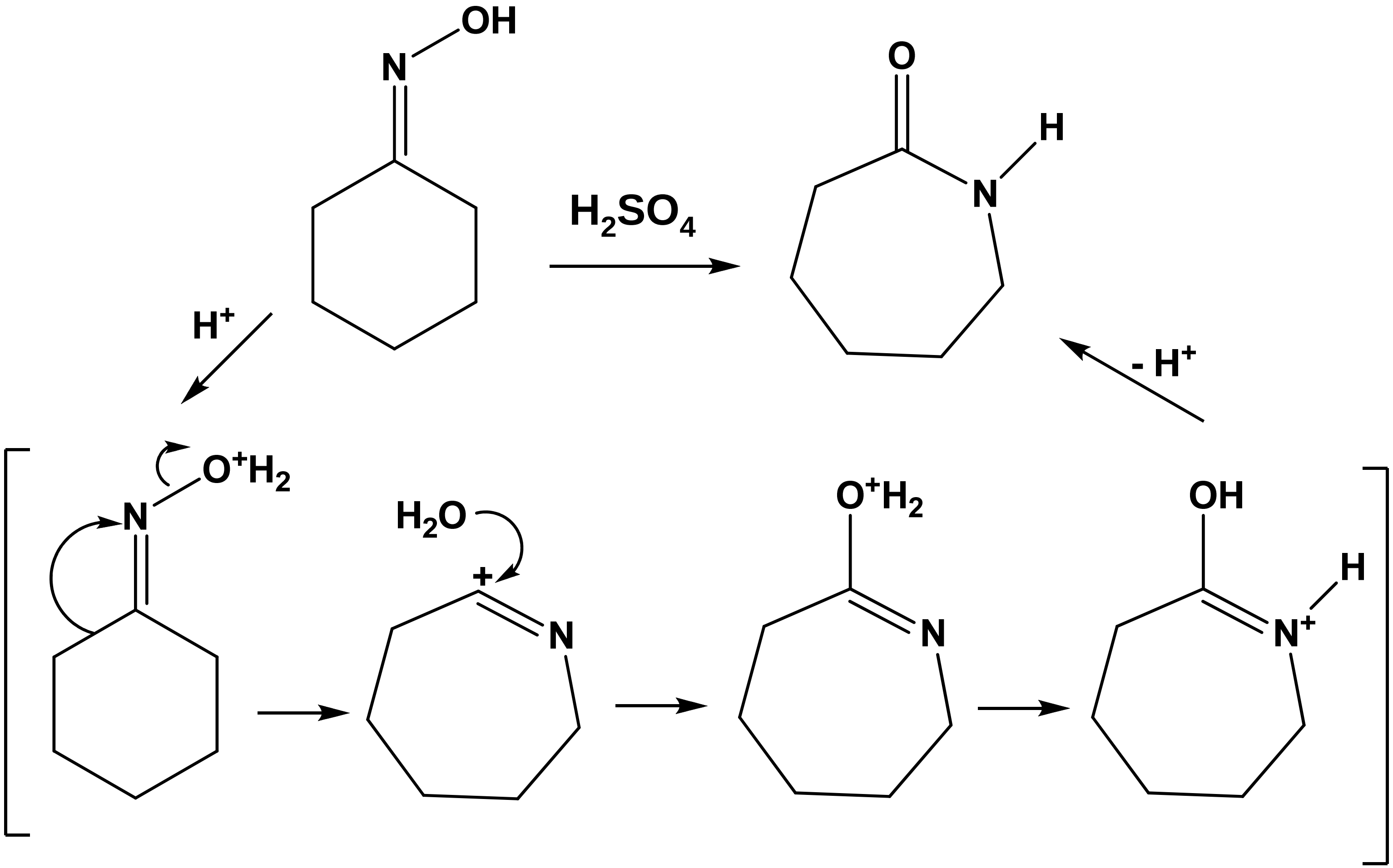


87 % atom efficient

Ar = Phenyl

Brønsted-Acid Catalysis

Caprolactam Formation; Beckmann Rearrangement



Lewis-acid Catalysis

-Initial coordination of a Lewis acid occurs to the basic site of the substrate.

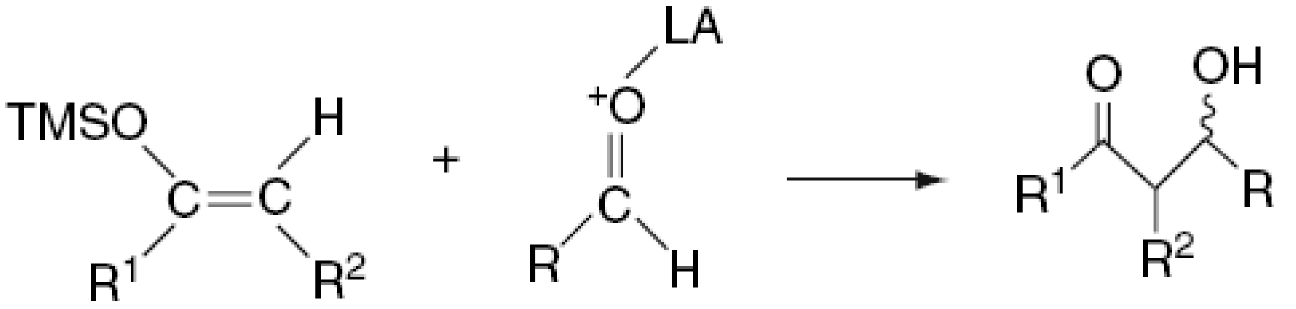
-The Lewis acid plays the key role to determine the overall reaction path by controlling the generation and trapping of the cationic species.

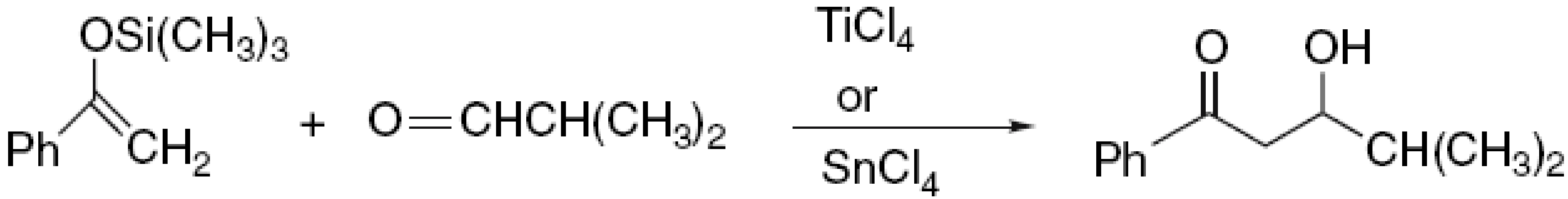
-The Lewis acid decides also the nature of the cationic species generated, an ion pair or a loosely bound covalent species or somewhere in-between.

-Lewis acid-base catalysis reactions are becoming of increasing importance in current organic synthesis.

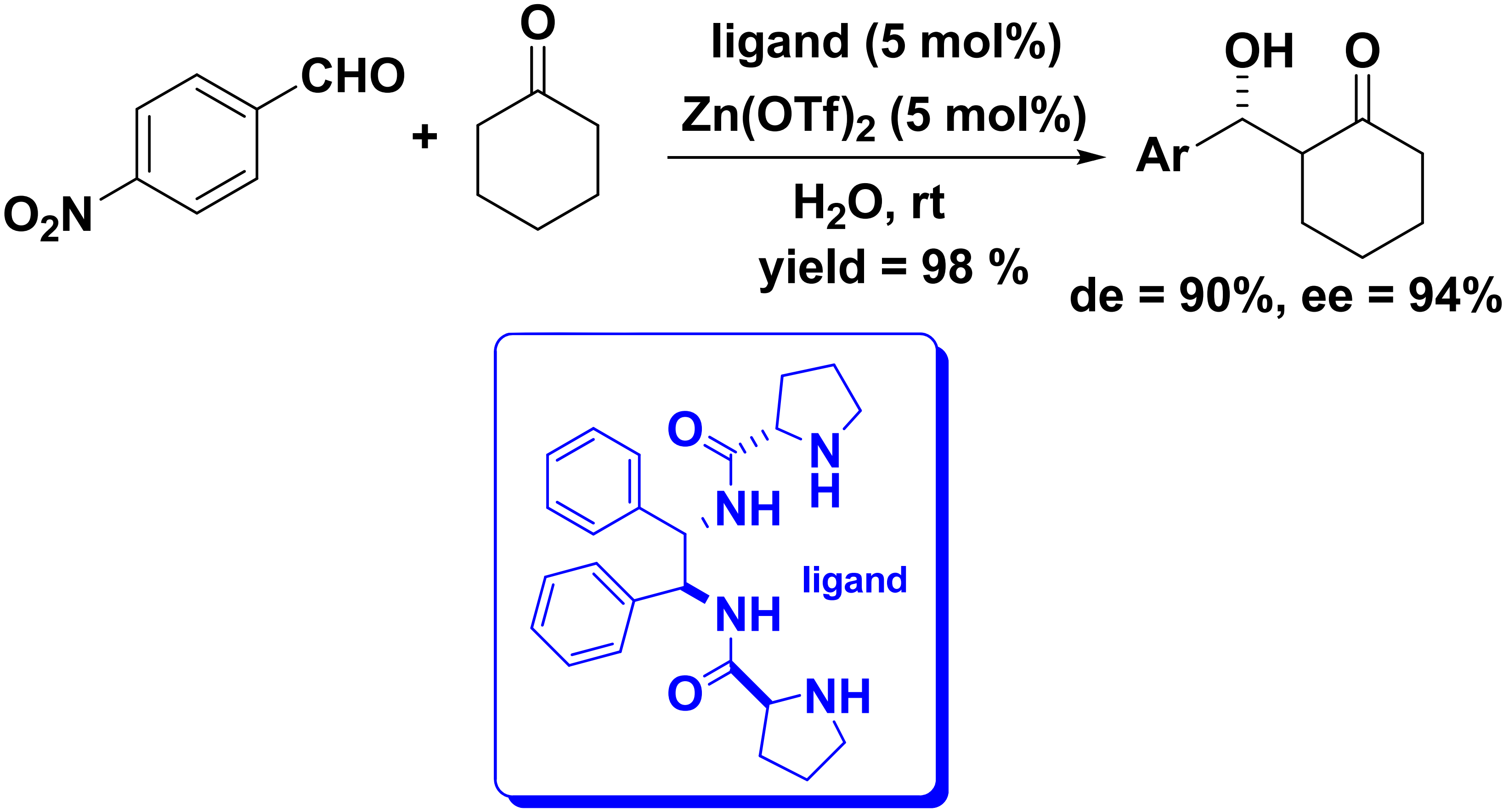
http://www.organic-chemistry.org/topics/lewis acid-base catalysis.shtm

The Mukaiyama Aldol Reaction



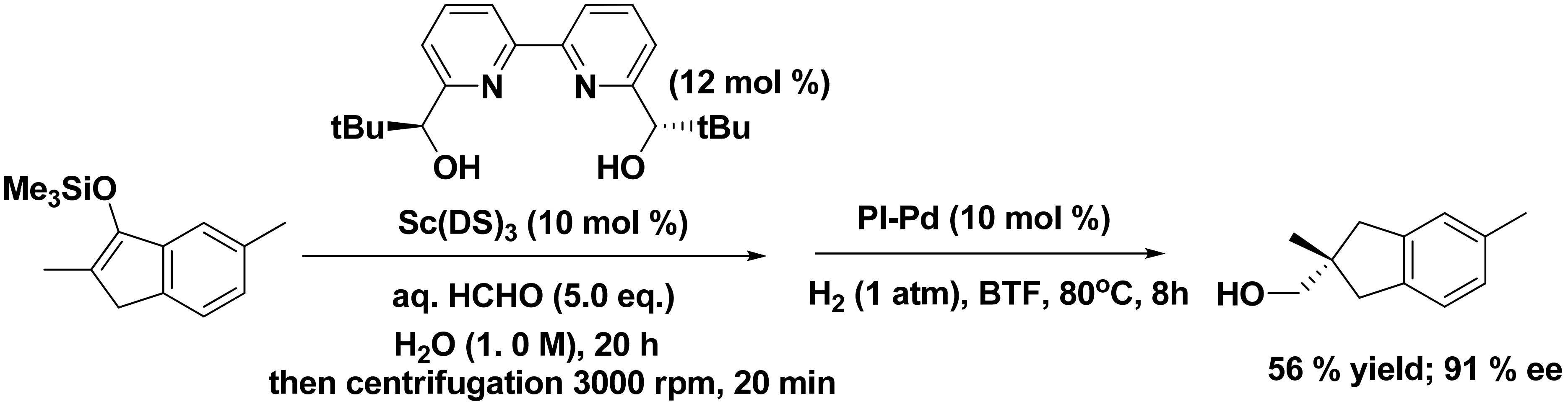


Asymmetric Aldol Reaction in Water



J. Paradowska, M. Stodulski, J. Mlynarski, *Adv. Synth. Catal.*, 2007, 349,1041

Asymmetric Aldol Reaction in Water



$Sc(DS)_3$ (10 mol %)

aq. HCHO (5.0 eq.)

H_2O (1. 0 M), 20 h

then centrifugation 3000 rpm, 20 min

PI-Pd (10 mol %)

H_2 (1 atm), BTF, 80°C, 8h

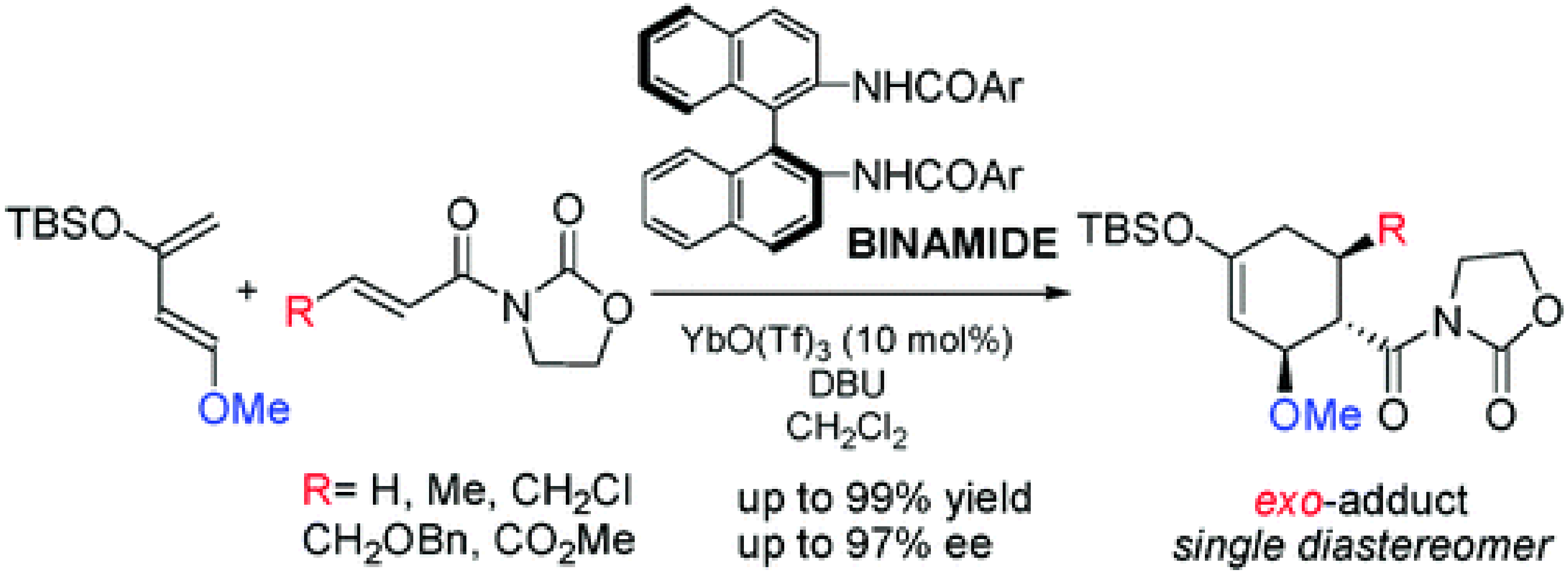
56 % yield; 91 % ee

This reaction does not require any organic solvent

$Sc(DS)_3 = Sc[O_3S(CH_2)_{10}\ CH_3]_3$
PI-Pd = polymer incarcerated palladium; BTF = benzo triffluoride

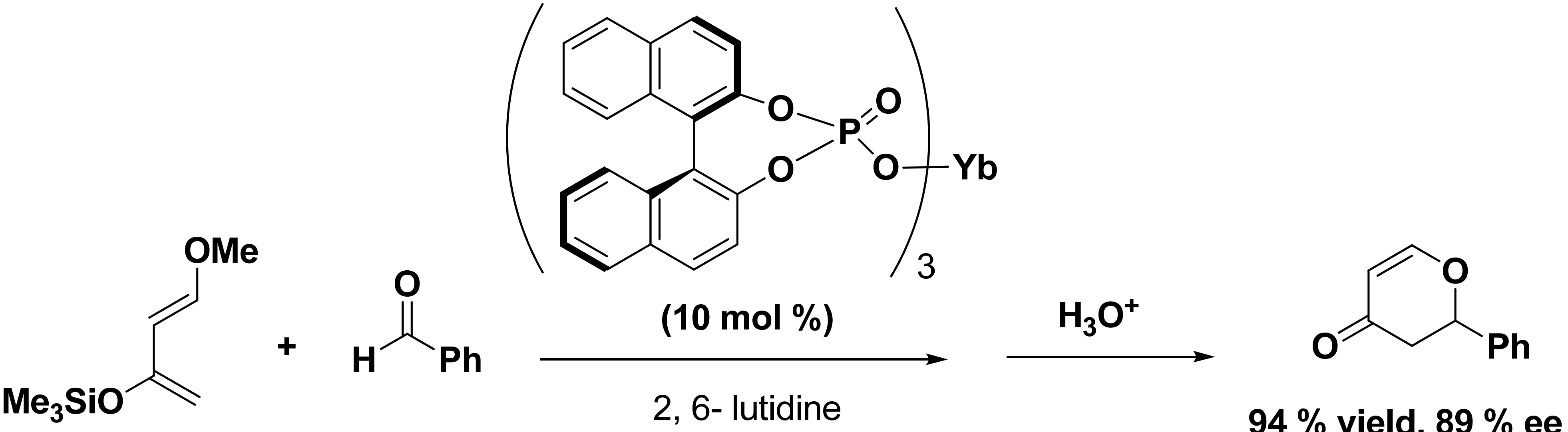
M. Kokubo, C. Ogawa, S. Kobayashi, *Angew. Chem. Int. Ed*. 2008, *47*, 6909-6911.

Asymmetric Diels-Alder Reaction



Y. Sudo, D. Shirasaki, S. Harada, A. Nishida
***J. Am. Chem. Soc.*, 2008, *130*, 12588-12589.**

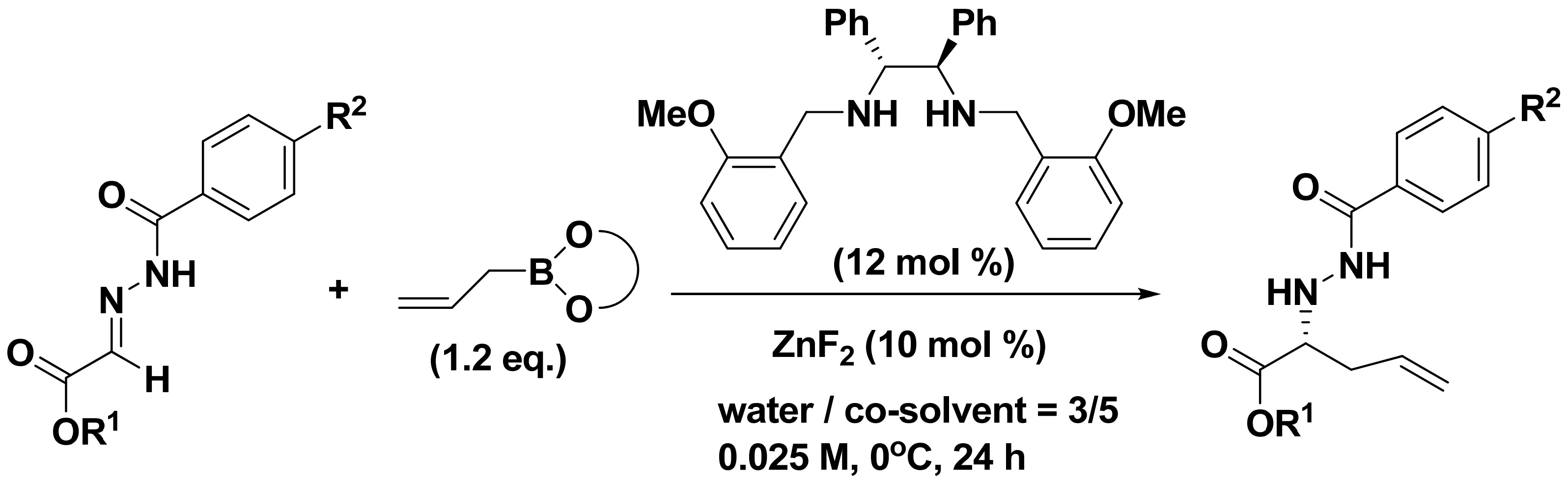
Asymmetric Hetero-Diels-Alder Reaction



94 % yield, 89 % ee

H. Furuno, T. Hanamoto, Y. Sugimoto, J. Inanaga, *Org. Lett*. 2000, *2*, 49-52

Asymmetric Allylation of Hydrazono Esters with Allylboronates in Aqueous Media



(1.2 eq.)

(12 mol %)

ZnF_2 (10 mol %)

water / co-solvent = 3/5
0.025 M, 0°C, 24 h

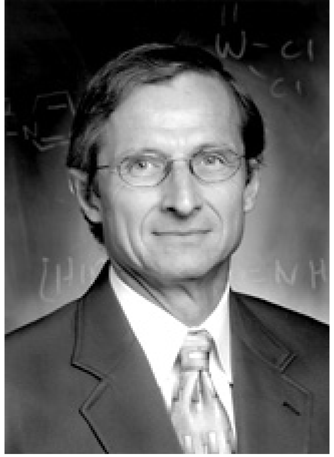
R^1	R^2	co-solvent	yield %	ee %
Et	H	acetone	quant.	79
Et	H	DMSO	71	71
Et	H	CH_3CN	76	62
Me	NMe_2	acetone	quant.	90

M. Fujita, T. Nagano, U. Schnieder, T. Hamada, C. Ogawa, S. Kobayashi, *J. Am. Chem. Soc*. 2008, *130*, 2914-2915

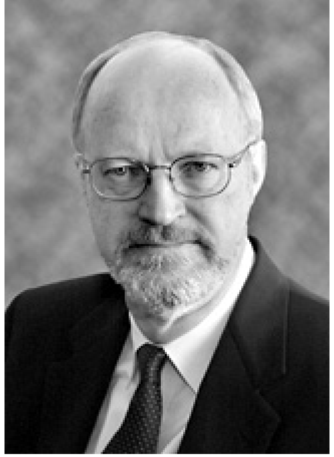
Metathesis

Nobel Laureates in Chemistry, 2005

Yves Chauvin



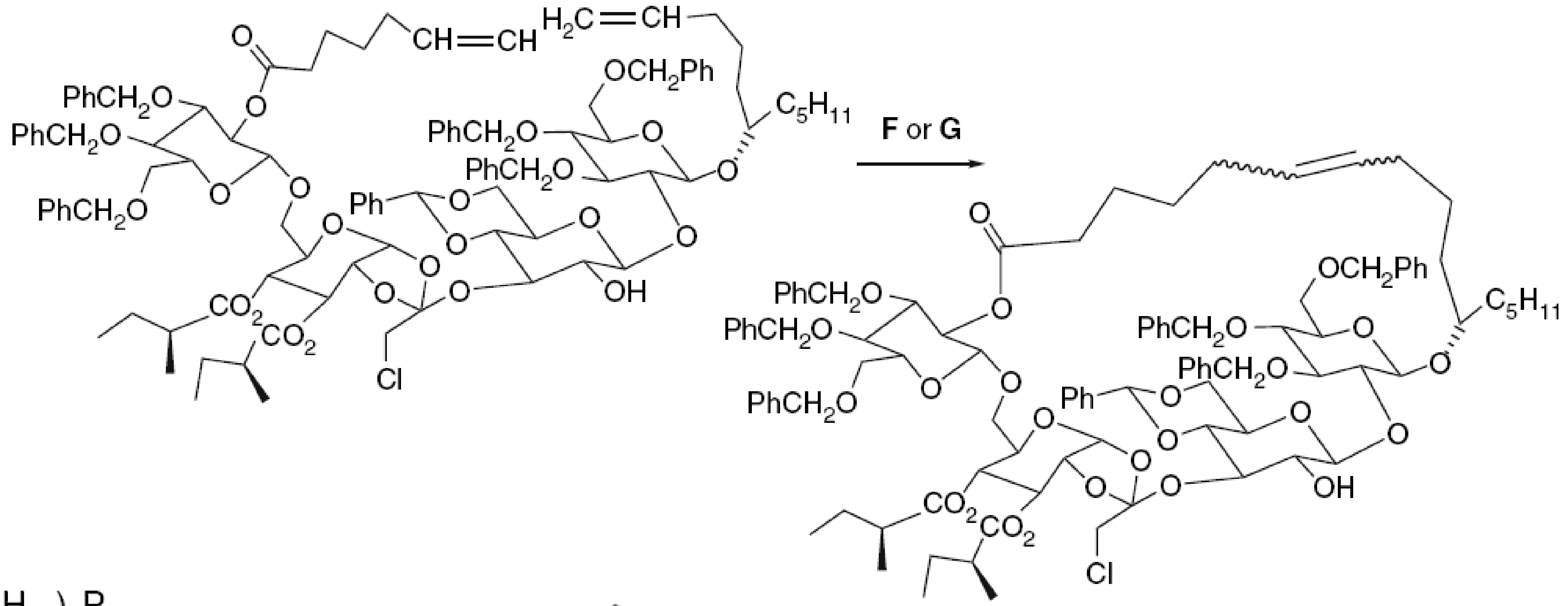
Richard Schrock

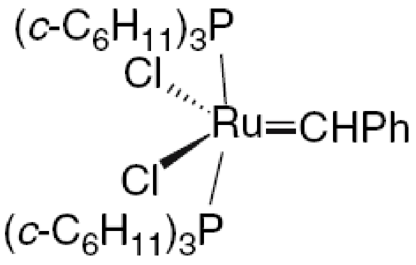


Robert Grubbs

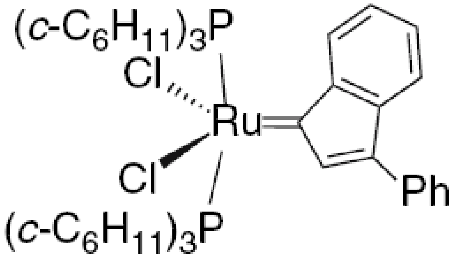
- more efficient (fewer reaction steps, fewer resources required, less wastage),
- simpler to use (stable in air, at normal temperatures and pressures) and
- environmentally friendlier (non-injurious solvents, less hazardous waste products).
- This represents a great step forward for "green chemistry", reducing potentially hazardous waste through smarter production. Metathesis is an example of how important basic science has been applied for the benefit of man, society and the environment.

The Olefin Metathesis Reaction





F

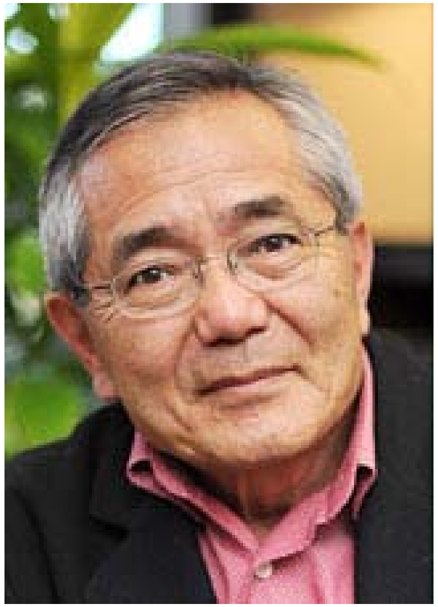


G

Palladium-catalyzed Cross Couplings in Organic Synthesis

Nobel Laureates in Chemistry, 2010

Richard F. Heck

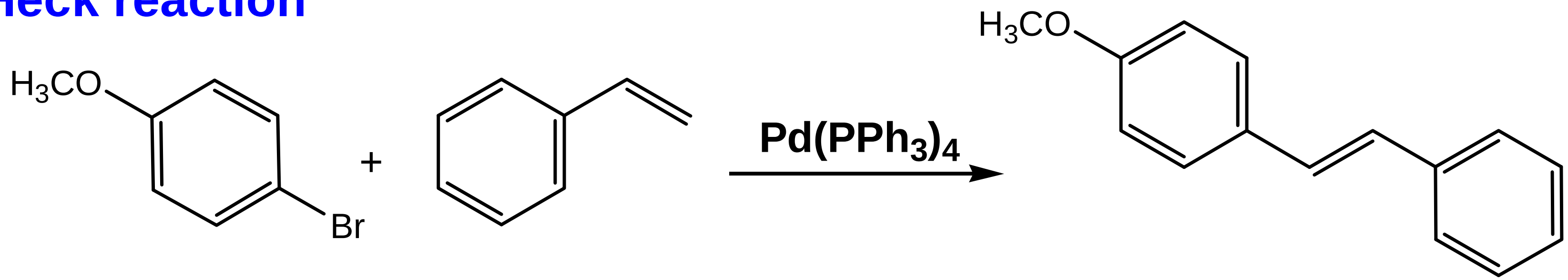


Ei-ichi Negishi

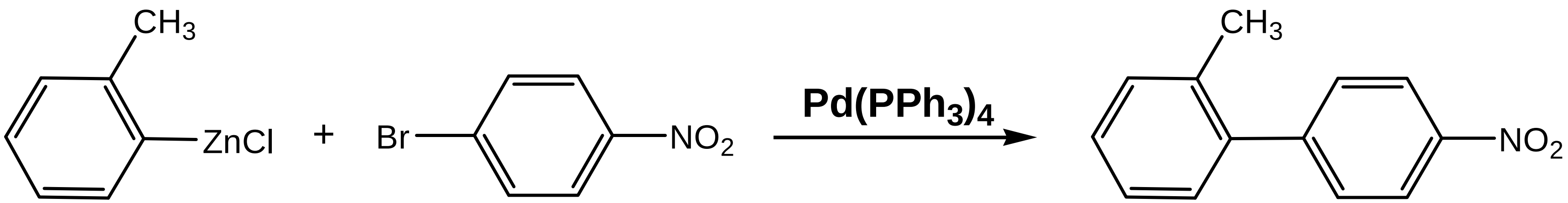
Akira Suzuki

Palladium-catalyzed Cross Couplings

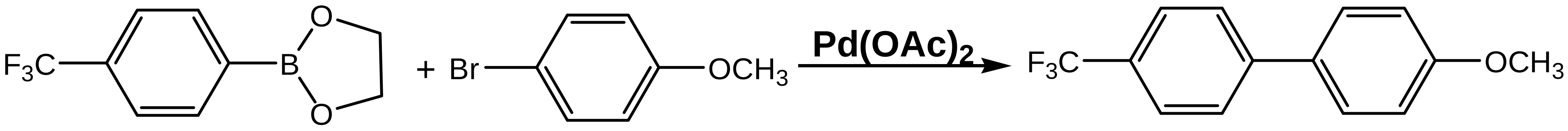
Heck reaction



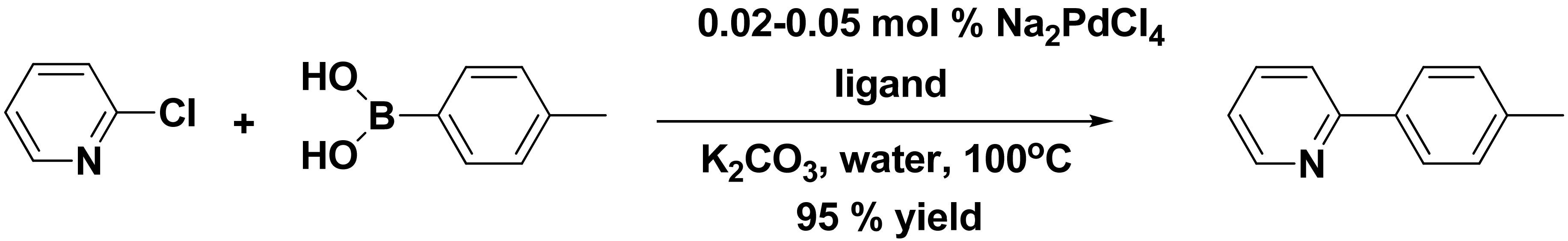
Negishi reaction



Suzuki reaction



Suzuki-Miyaura Coupling in Water

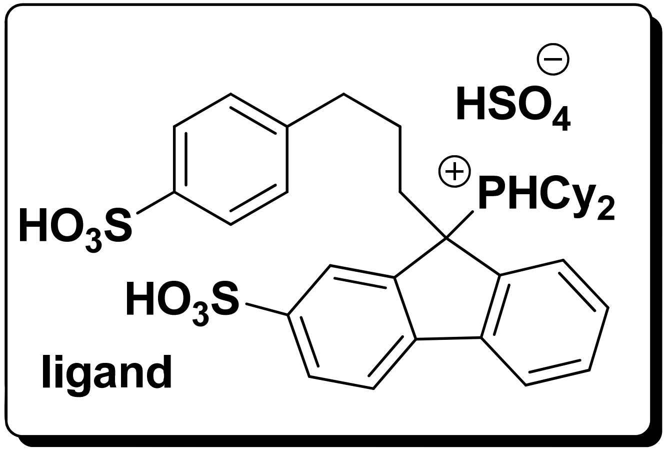


0.02-0.05 mol % Na_2PdCl_4

ligand

K_2CO_3, water, 100°C

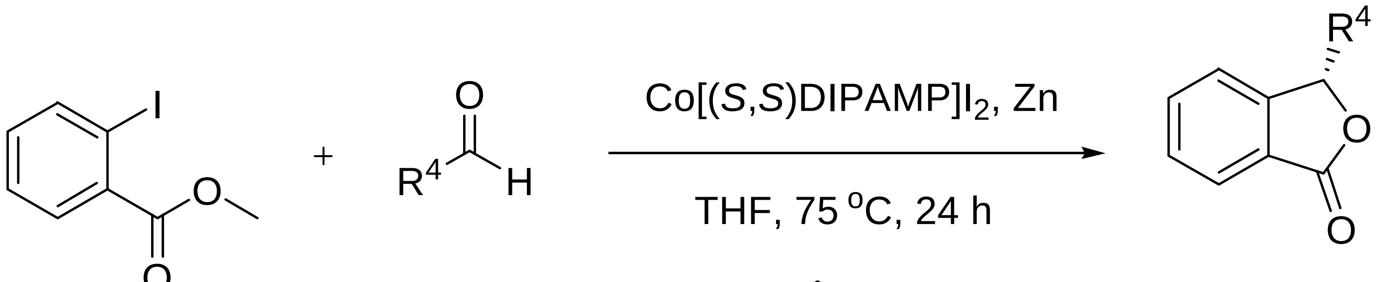
95 % yield



ligand

C. A. Fleckenstien, H. plenio, *Green Chem.*, 2007, *9*, 1287-1291.

Asymmetric Cyclization of *o*-Iodobenzoates with Aldehydes Catalyzed by Cobalt Complexes

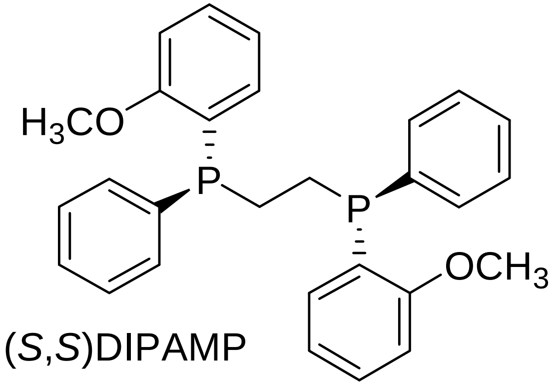


1a

2a-c,f and **g**

4a-e

2a: R^4 = Ph
2b: R^4 = *p*-CH_3-C_6H_4
2c: R4 = *p*-*t*-butyl-C_6H_4
2f: R^4 = *p*-Cl-C_6H_4
2g: R^4 = *p*-CF_3-C_6H_4

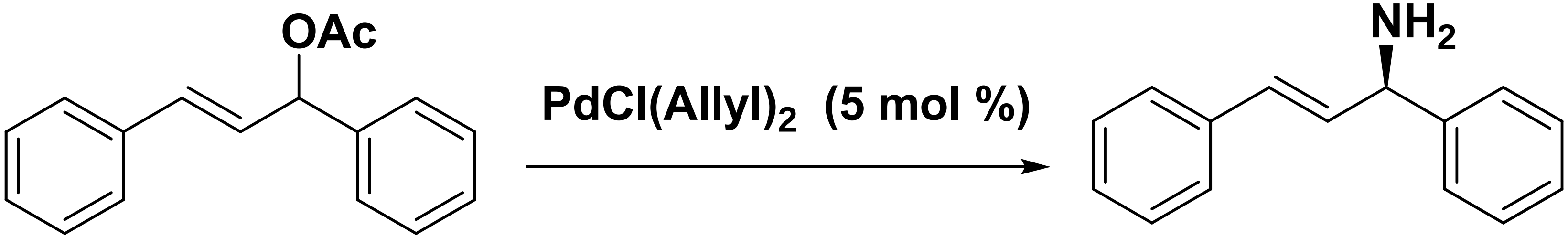


(*S*,*S*)DIPAMP

4a: 89%, 84% ee
4b:80%, 79% ee
4c: 85%, 91% ee
4d: 83%, 98% ee
4e: 81%, 70% ee

Chang, H.T.; Jeganmohan M.; Cheng C.H. *Chem. Eur. J.,* 2007, *15*, 4356.

Palladium-catalized Asymmetric Allylic Amination

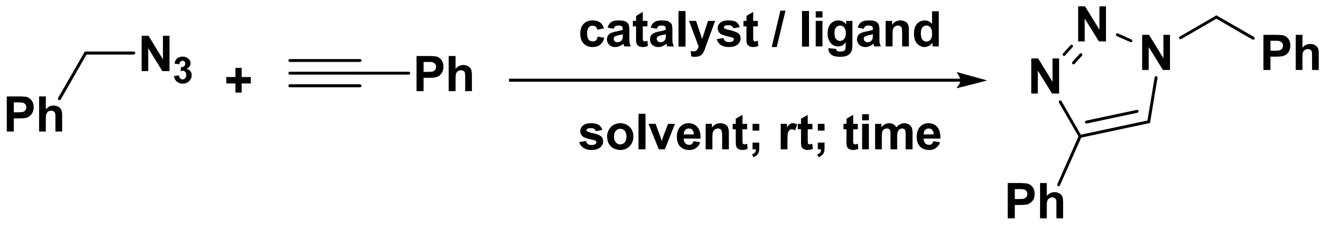


$PdCl(Allyl)_2$ (5 mol %)

***R*-Binap (20 mol%)**
aqueous NH_3 / 1, 4-Dioxane (1/2) 0.04 M,
rt, 18h
71 % yield; 87 % ee

T. Nagano, S. Kobayashi, *J. Am. Chem. Soc*. 2009, *131*, 4200-4201

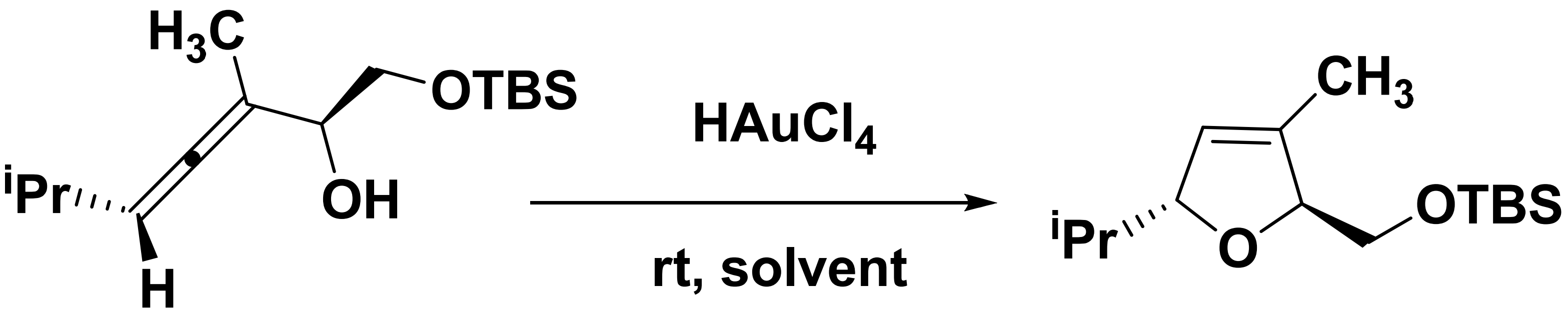
Click Reaction in Water



catalyst / ligand	solvent	time	yield %
5 mol % CuBr / 30 mol % PhSMe	t- BuOH	1 h	< 5
5 mol % CuBr / 30 mol % PhSMe	t- BuOH / H_2O (1:2)	10 min	50
5 mol % CuBr / 30 mol % PhSMe	H_2O	5 min	96
10 mol % CuBr / 30 mol % PhSMe	H_2O	5 min	97

F. Wang, H. Fu, Y. Jiang, Y. Zhao, *Green Chem.*, 2008, *10*, 452-456.

Chloroauric Acid ($HAuCl_4$)-catalyzed Reaction in Water



dr = 85 : 15

dr = 85 : 15

solvent	catalyst loading (mol %)	time	yield %
water (10 mL)	5	2.5 h	78
water (10 mL)	10	1 h	58
water (10 mL)	1	5 h	43

C. Winter, N. Krause, *Green Chem.*, 2009, *11*, 1309-1312.

Production of Acetic Acid from Methanol and Carbon Monoxide

$CH_3OH + CO \rightarrow CH_3COOH$ $\Delta H = -136.6$ kJ/mol

Brønsted Acid Catalysis

$$CH_3OH \xrightarrow{HI} CH_3I + H_2O$$

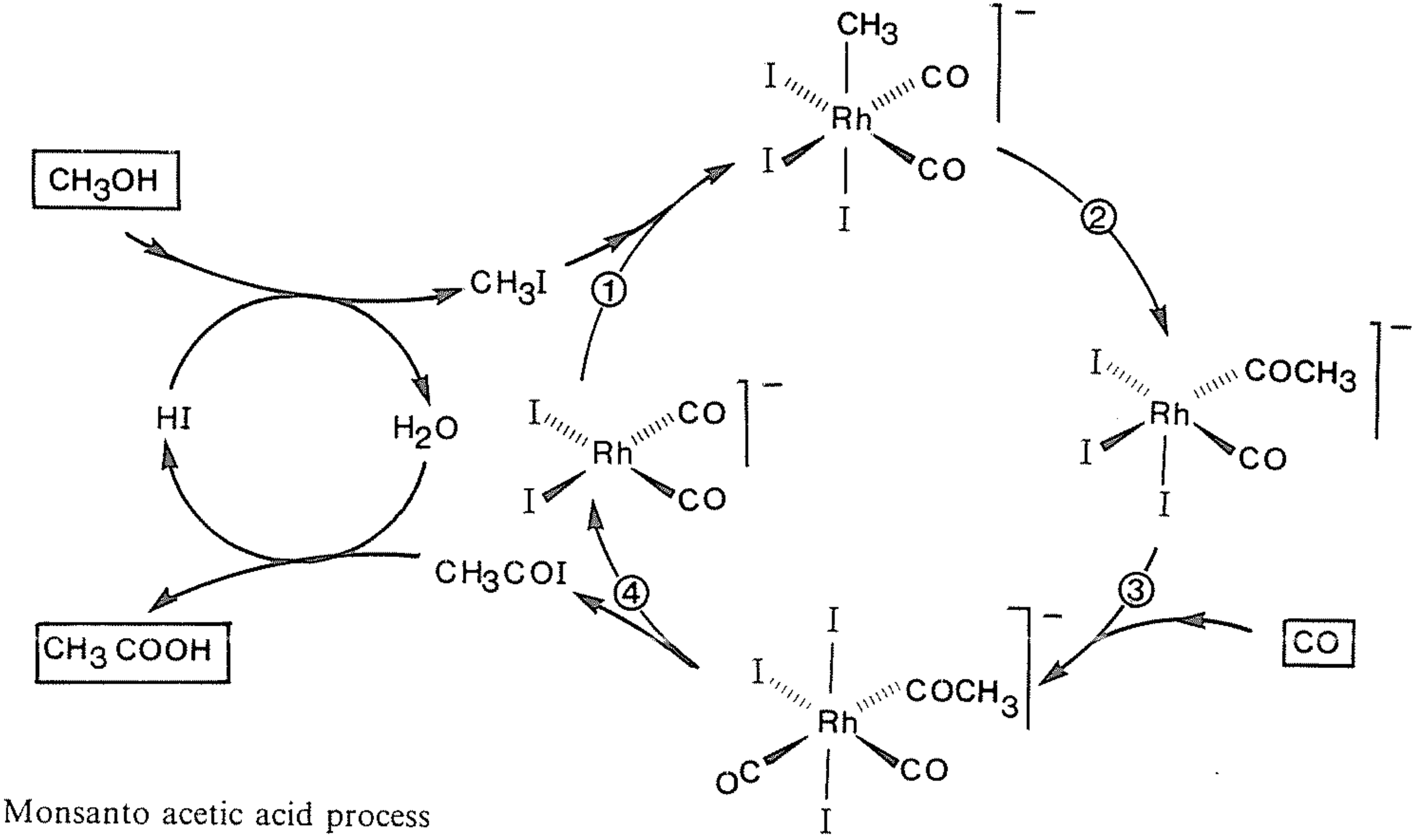
Transition-metal catalysis

$$CH_3I + CO \longrightarrow CH_3COI$$

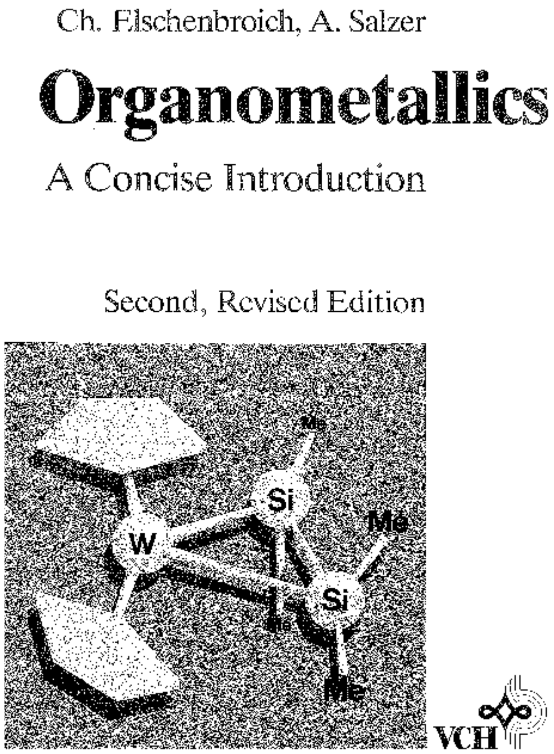
Hydrolysis

$$CH_3COI + H_2O \longrightarrow CH_3CO_2H + HI$$

Monsanto Acetic Acid Process



Monsanto acetic acid process


Ch. Elschenbroich, A. Salzer

Organometallics

A Concise Introduction

Second, Revised Edition

VCH

What is Organocatalysis?

- A concatenation of the terms “organic” and “catalyst”

- In organic chemistry the term Organocatalysis refers to a form of catalysis, whereby the rate of a chemical reaction is increased by an organic catalyst consisting (mainly) of carbon, hydrogen, sulfur, nitrogen, oxygen, and phosphorus.

- Metal free catalysis

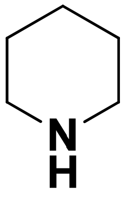
Primary Attractions of Organocatalysis

- Readily available.
- Non-toxic (environmentally benign).
- Inexpensive compared to metal-based catalysts.
- Inertness towards moisture and oxygen demanding reaction conditions (inert atmosphere, low temperatures, absolute solvents, etc,.) are usually not required.
- Absence of transition metals, attractive for synthesis of non-toxic - pharmaceutical and agrochemical products.
- Biomimetic-induce cascade reactions.

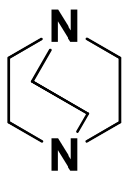
Comparison with Conventional Catalysis

Type	Advantages	Disadvantages
Organometallic Catalysis	Wide substrate scope high catalytic activity	Tedious process, potential heavy metal pollution
Enzyme Catalysis	High selectivity and catalytic activity	Limited substrate scope usually single enantiomer
Organocatalysis	Simple structure, inexpensive, natural molecules, nontoxic	No

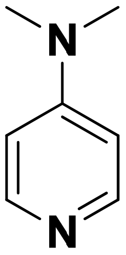
Achiral and Chiral Organocatalysts



Piperidine



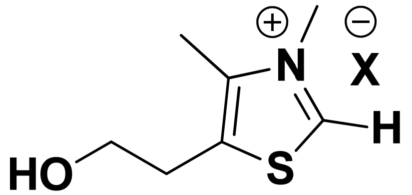
DABCO



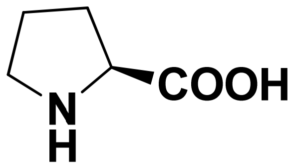
DMAP

$H\text{-}C\equiv N$

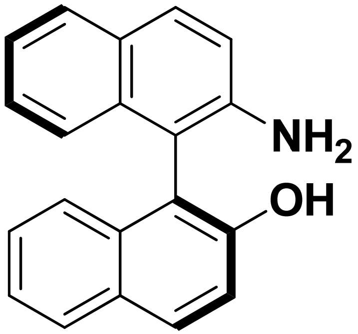
hydroen cynide



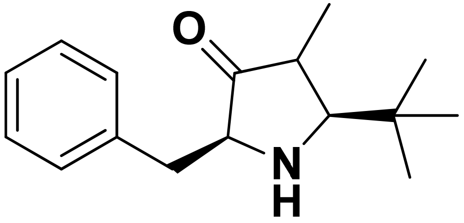
thiazolium salts



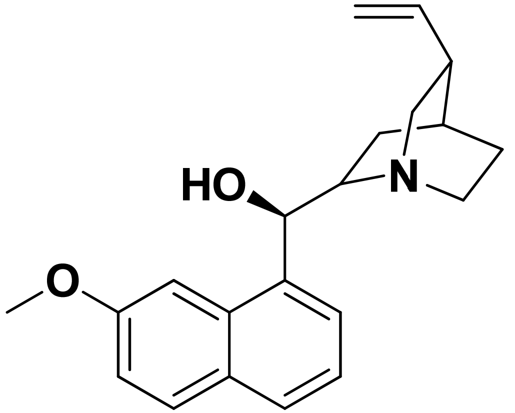
L-Proline



Nobin



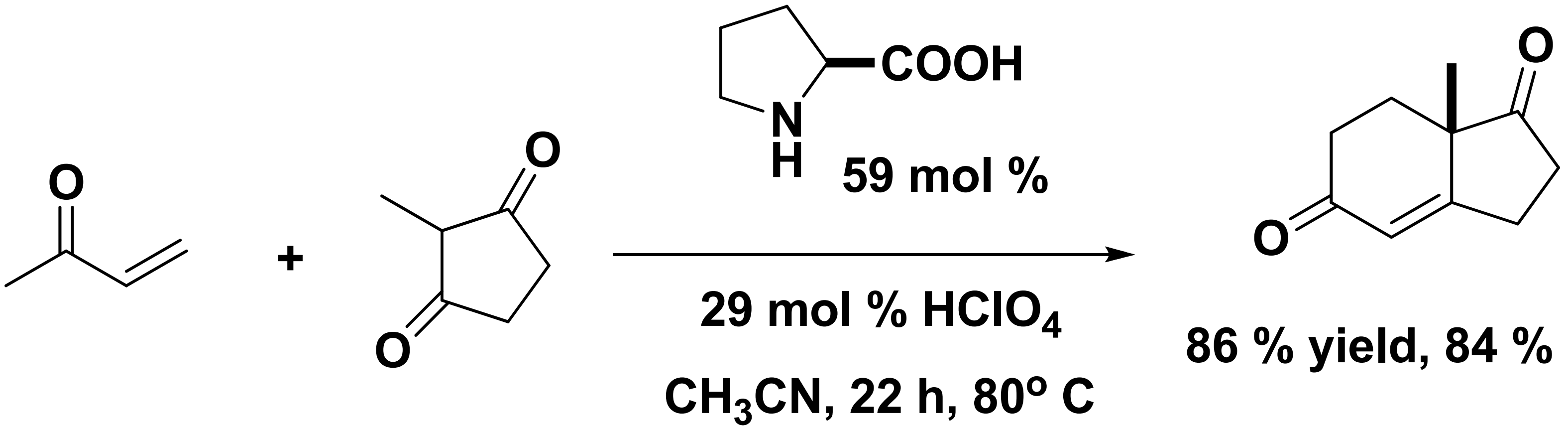
Macmillan's catalyst



Quinine

Robinson Annulation

Early Organocatalysis:



59 mol %

29 mol % $HClO_4$

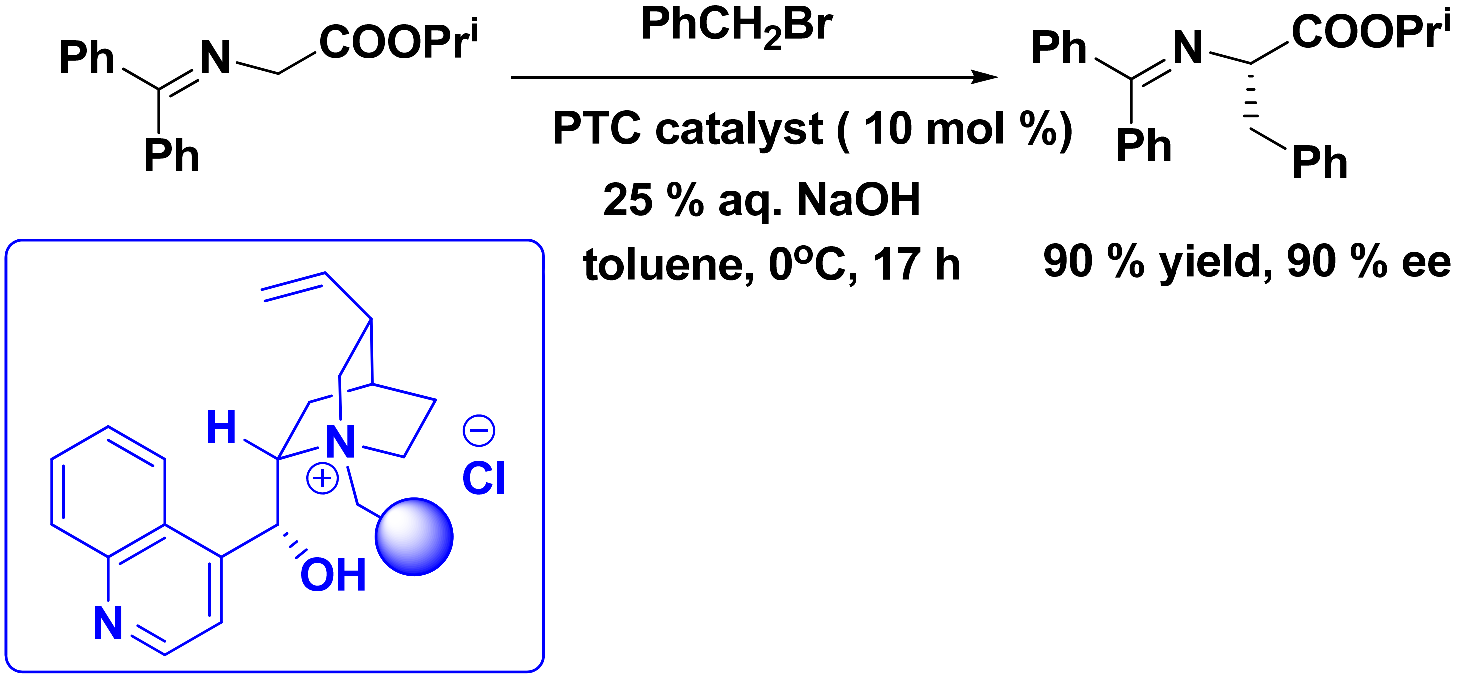
CH_3CN, 22 h, 80° C

86 % yield, 84 % ee

Eder et al. *Angew. Chem. Int. Ed.* 1971, *10*, 496-497

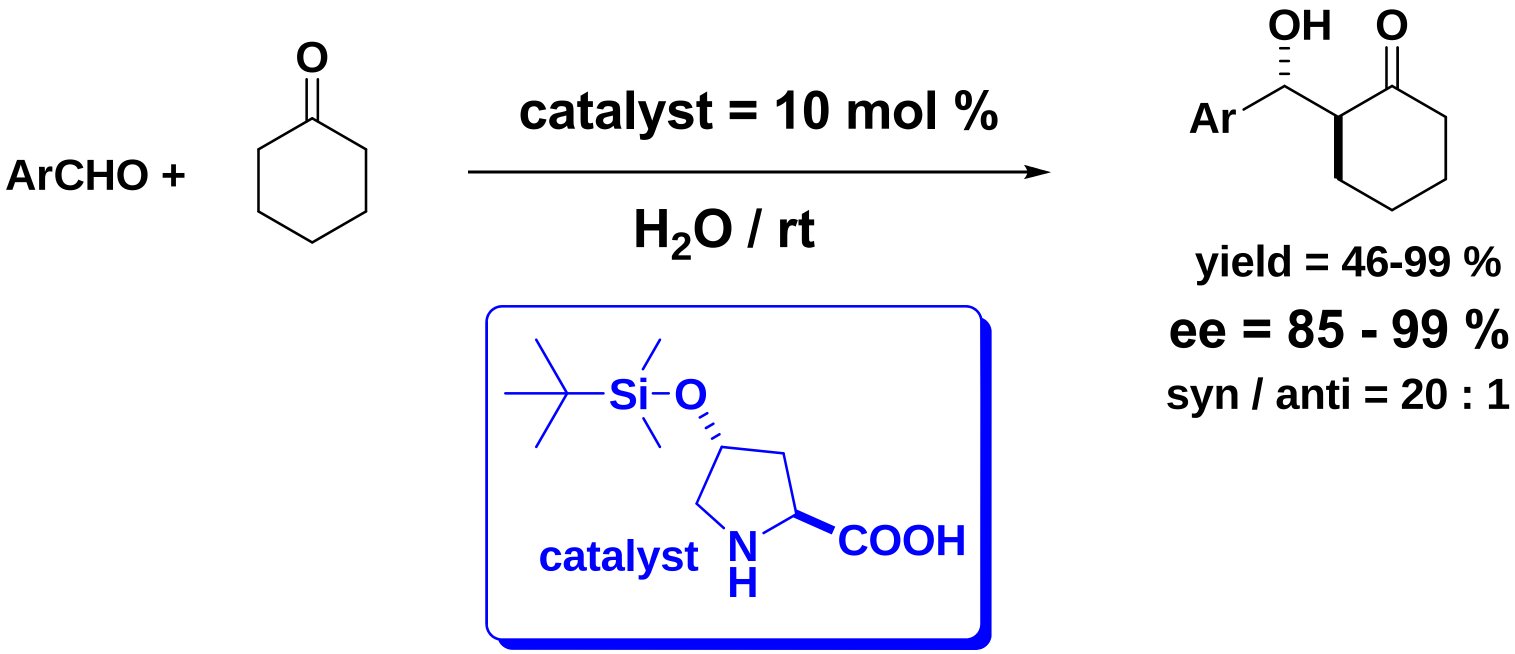
Z. Hajos, D. Parrish, *J. Org. Chem.* 1974, *39*, 1615-1621

Easily Recoverable Phase-Transfer Catalysts for the Asymmetric Synthesis of α-Amino Acids



R. Chinchilla, P. Mazon, C. Najera, *Adv. Synth. Catal*., 2004, *346*, 1186-1194;
A. F. Trindade, P. M. P. Gois, C. A. M. Afonso, *Chem. Rev.*, 2009, *109*, 418-514

Asymmetric Aldol Reaction with Homochiral Organocatalyst in Water



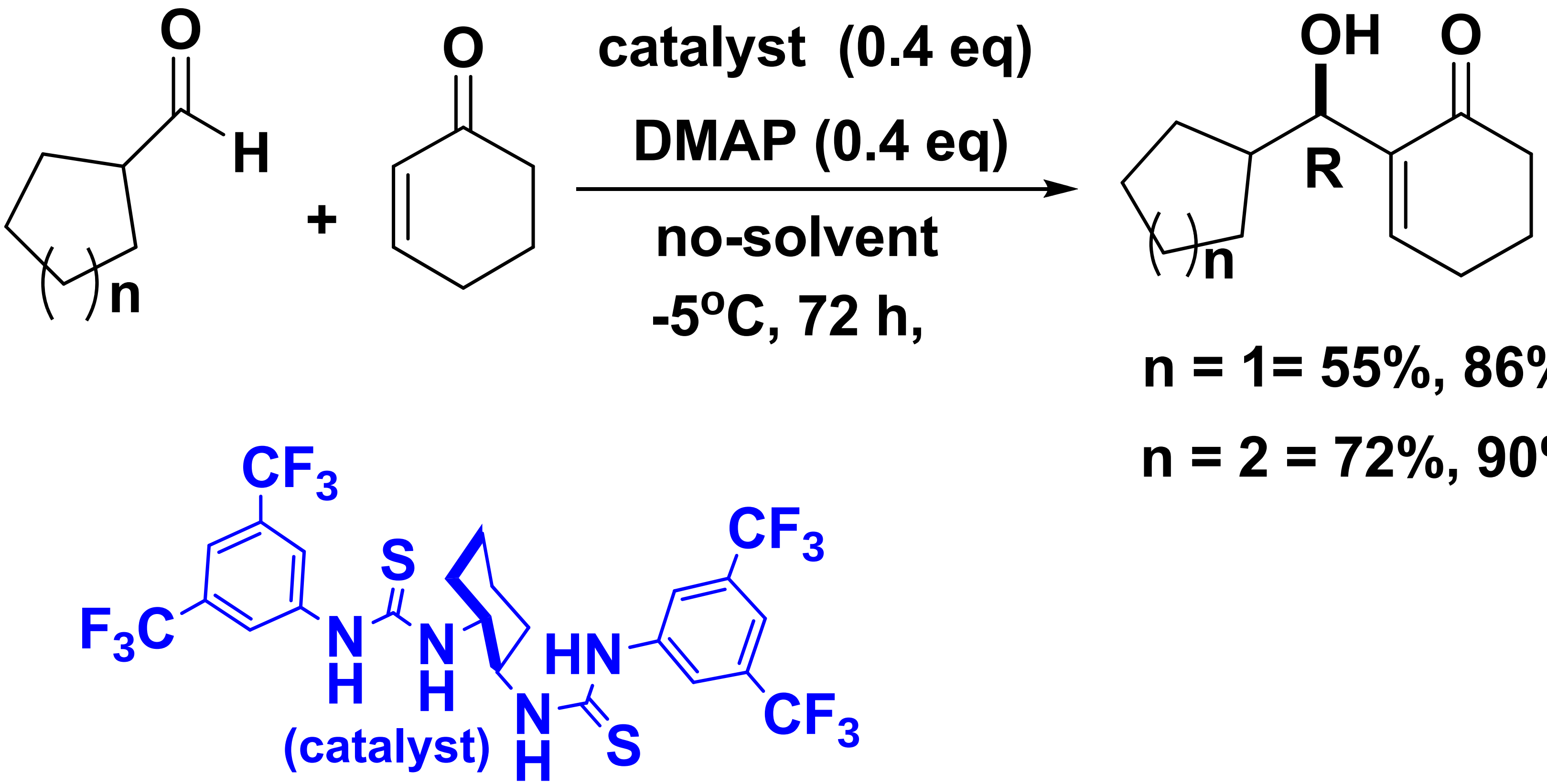
yield = 46-99 %

ee = 85 - 99 %

syn / anti = 20 : 1

N. Mase, Y. Nakai, N. Ohara, H. Yoda, K. Takabe, F. Tanaka, C. F. Barbas III, *J. Am. Chem. Soc.*, 2006, *128*, 734.

Baylis-Hillman Reaction



catalyst (0.4 eq)

DMAP (0.4 eq)

no-solvent

-5°C, 72 h,

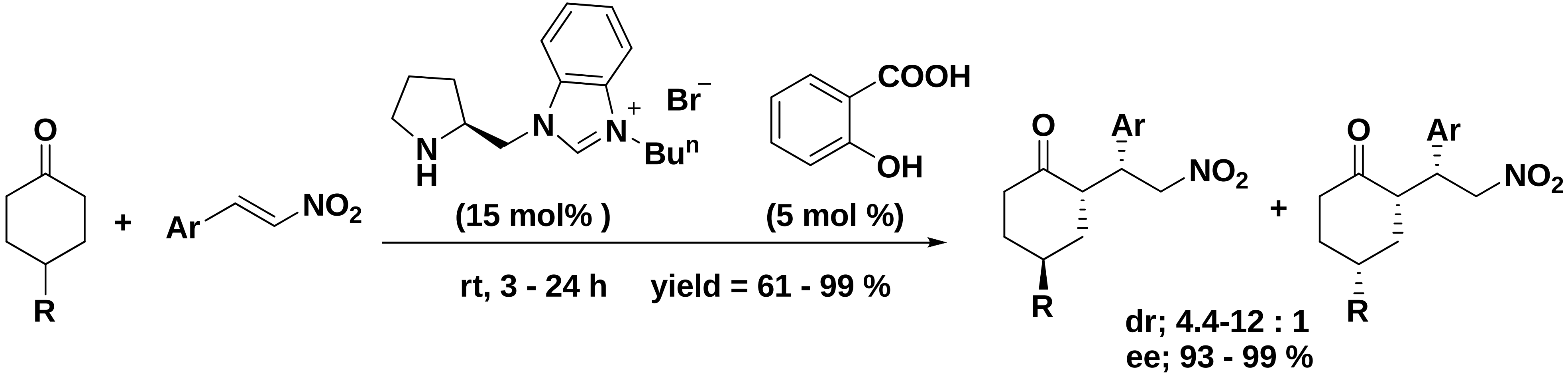
n = 1= 55%, 86%ee

n = 2 = 72%, 90%ee

(catalyst)

Sohtome, Y.; Tanatani, A.; Hashimoto, Y.; Nagasawa, K. *Tetrahedron Lett.* 2004, *45*, 5589.

Michael Addition Reactions in Chiral Ionic Liquids

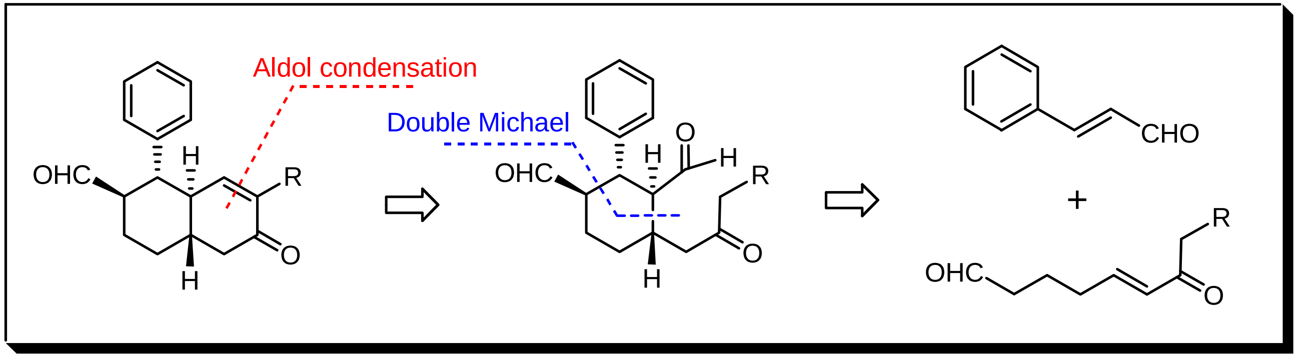


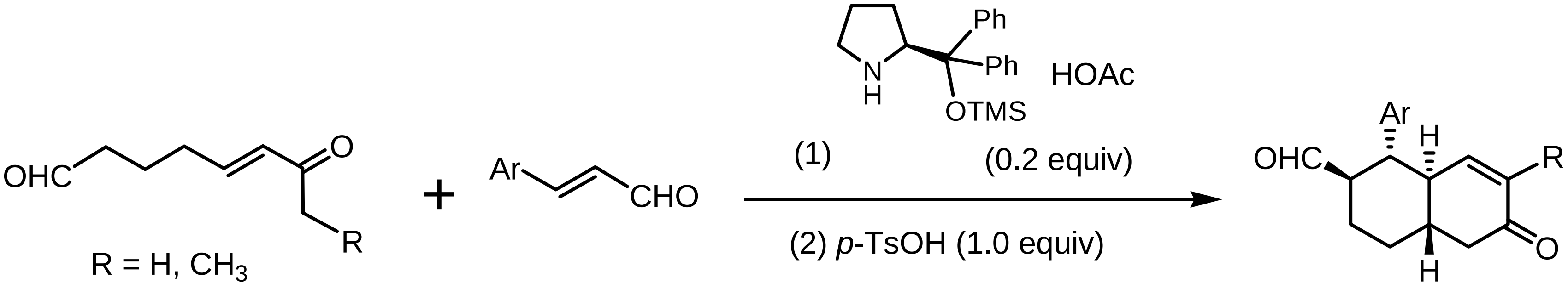
R = Me, Et, t-Bu, Ph, N_3, SAc, OH, Br, CN

Ar = Ph, 4-ClPh, 2-ClPh, 4-MePh, 4-PhPh, 4-MeOPh, 4-NO_2Ph, 2-NO_2Ph, 1-Naph, Piperal

S. Luo, L. Zhang, X. Mi, Y. Qiao, J. –P. Cheng, *J. Org. Chem.*, 2007, 72, 9350-9352.

Enantioselective Synthesis of Highly Functionalized Octahydro-6-oxo-1-phenylnaphthalene-2-carbaldehydes via Organocatalytic Domino Reactions





R = H, CH_3

(1) (0.2 equiv)

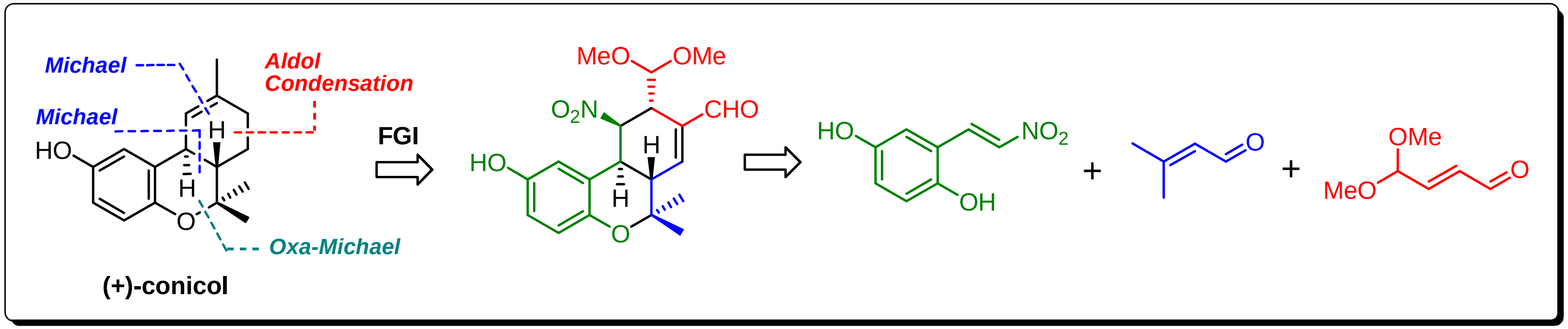
(2) *p*-TsOH (1.0 equiv)

CH_3CN

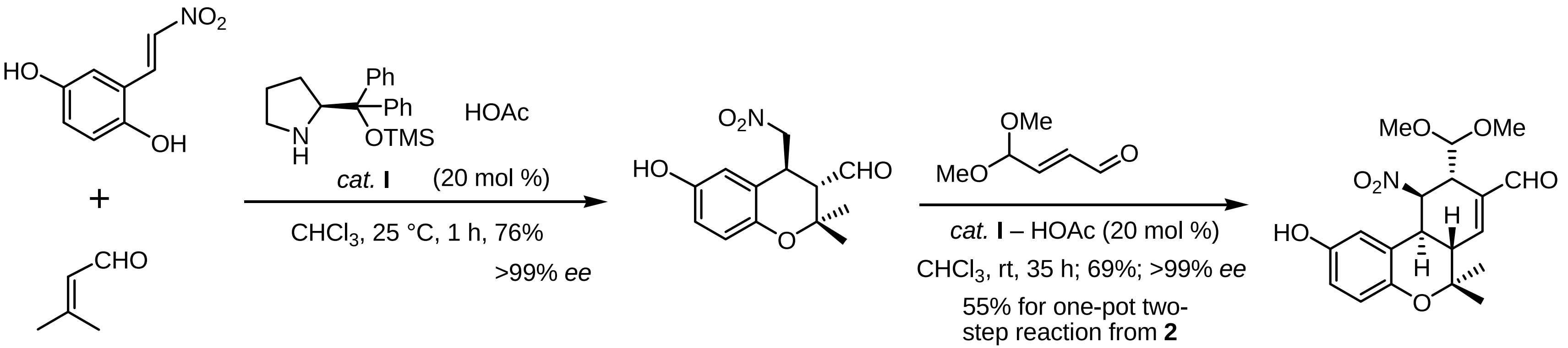
63-86% yield
>99% *ee*

B.-C. Hong,* R. Y. Nimje, J.-H. Liao, *Org. Biomol. Chem.* 2009, 3095–3101.

Enantioselective Total Synthesis of (+)-Conicol via Cascade Three-Component Organocatalysis



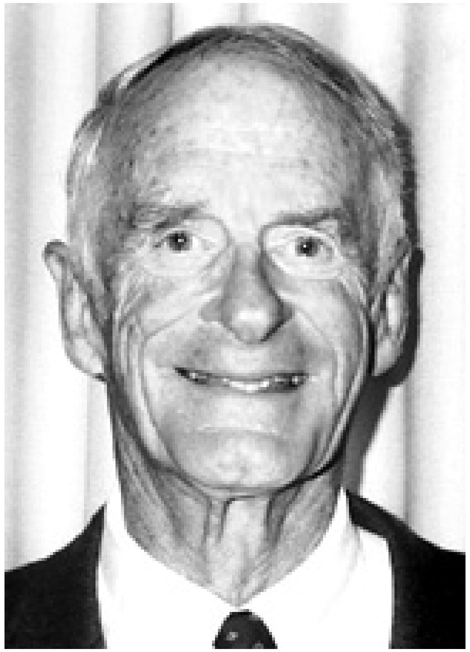
(+)-conicol



**B.-C. Hong,* P. Kotame, C.-W. Tsai, J.-H. Liao *Org. Lett.* 2010, ASAP,
DOI: 10.1021/ol902840x**

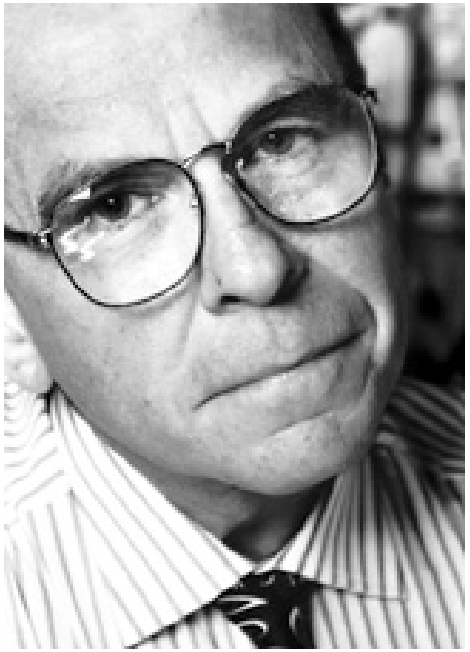
Asymmetric Catalysis

Nobel Laureates in Chemistry, 2001



William S. Knowles

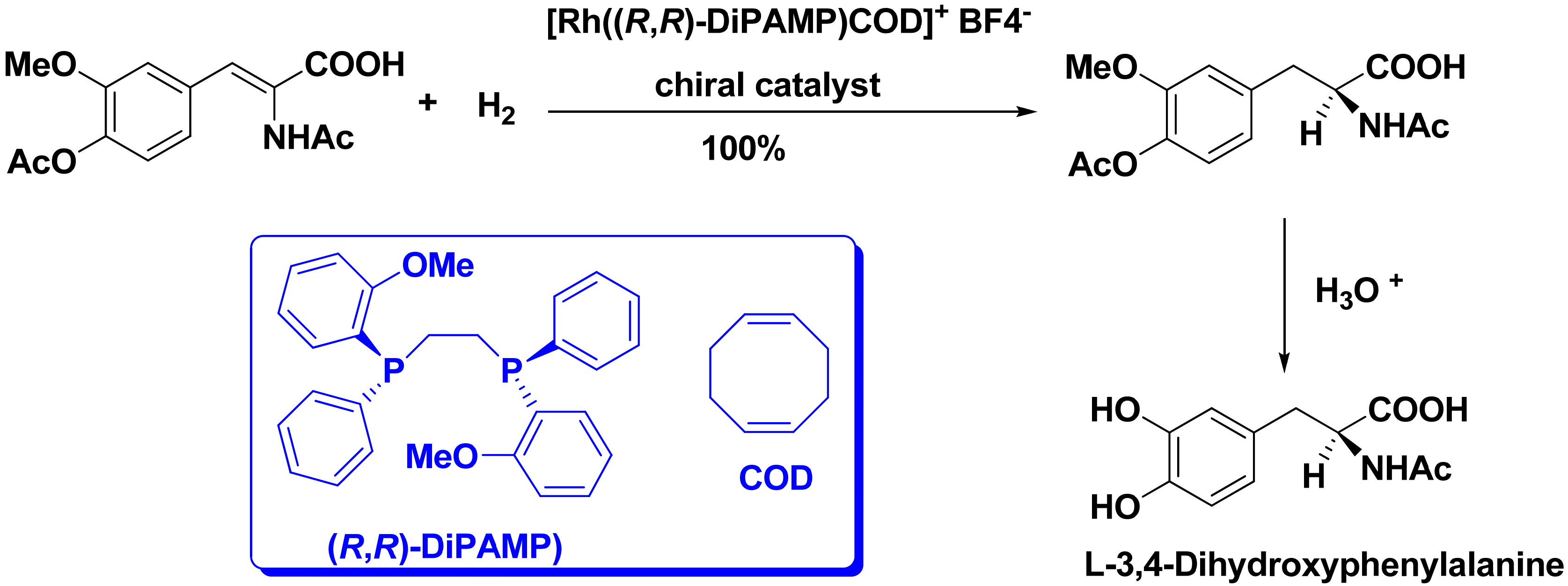
Ryoji Noyori



K. Barry Sharpless

MONOSANTO L-DOPA PROCESS

The first industrial catalytic asymmetric synthesis



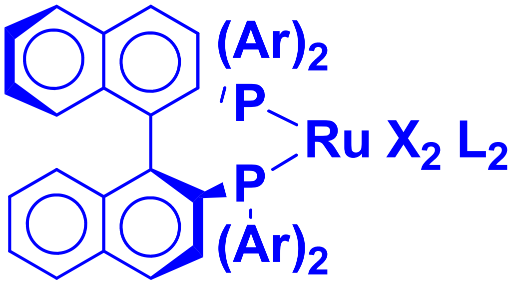
L-3,4-Dihydroxyphenylalanine

(L-DOPA)

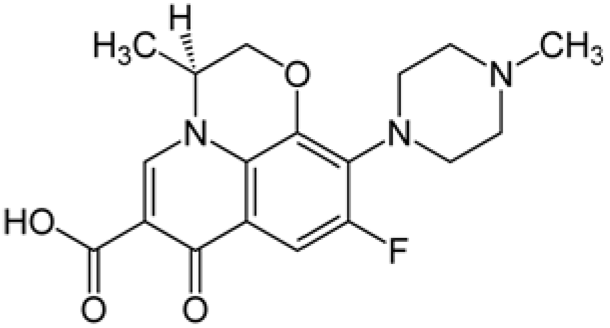
W. S. Knowles, Acc. Chem. Res., 1983, 16, 106-112; J. Chem. Edu., 1986, 63, 222-225

(*R*)-BINAP-Ru-catalyzed Hydrogenation

Ar = aryl, L = ligand, X = Cl, Br, I

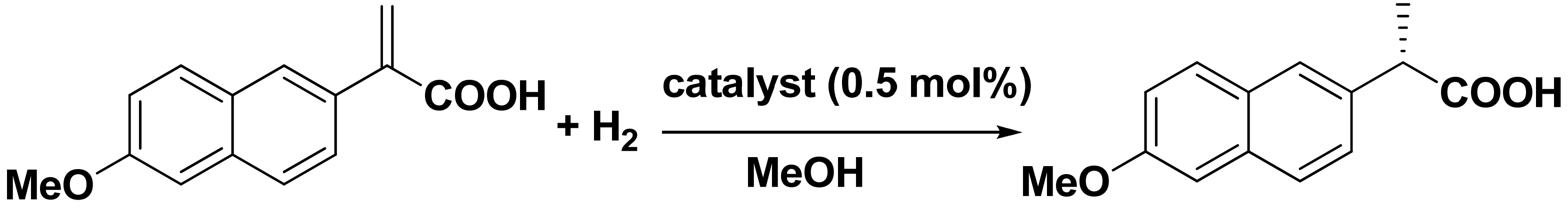


The (*R*)- BINAP-Ru-catalyzed hydrogenation of acetol to (*R*)-1,2-propanediol is currently used for the industrial synthesis of antibacterial levofloxacin



M. Kitamura, T. Ohkuma, S. Inoue, N. Sayo, H. Kumobayashi, S. Akutagawa, T. Otha, H.Takaya, R. Noyori, *J. Am. Chem. Soc.*, 1988, *110*, 629.

Catalytic Asymmetric Synthesis of (S)-Naproxen



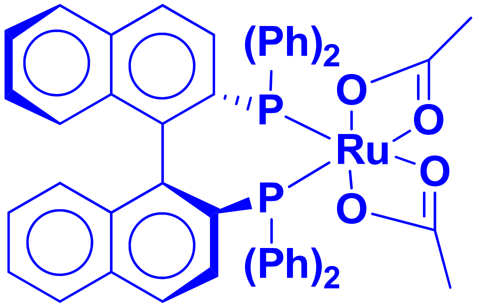
catalyst (0.5 mol%)

MeOH

92 % yield, 97 % ee

(*S*)-Naproxen
an anti-inflammatory agent

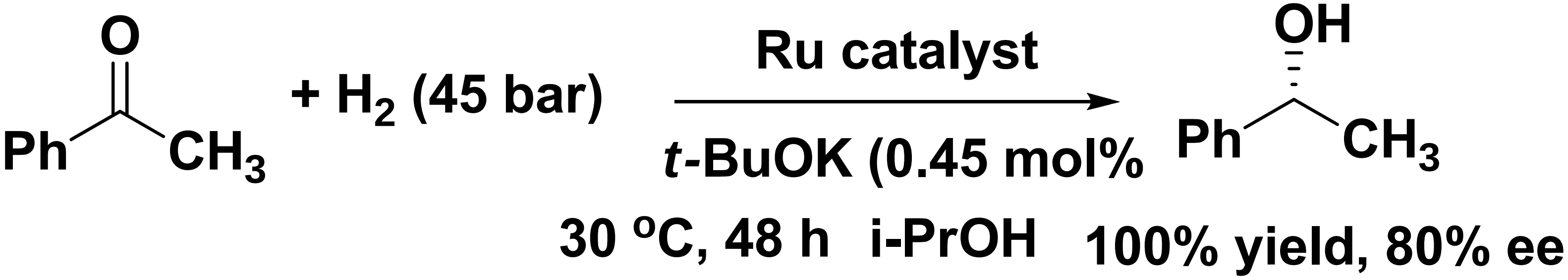
catalyst



(*S*)-BINAP-Ru$(OCOCH_3)_2$

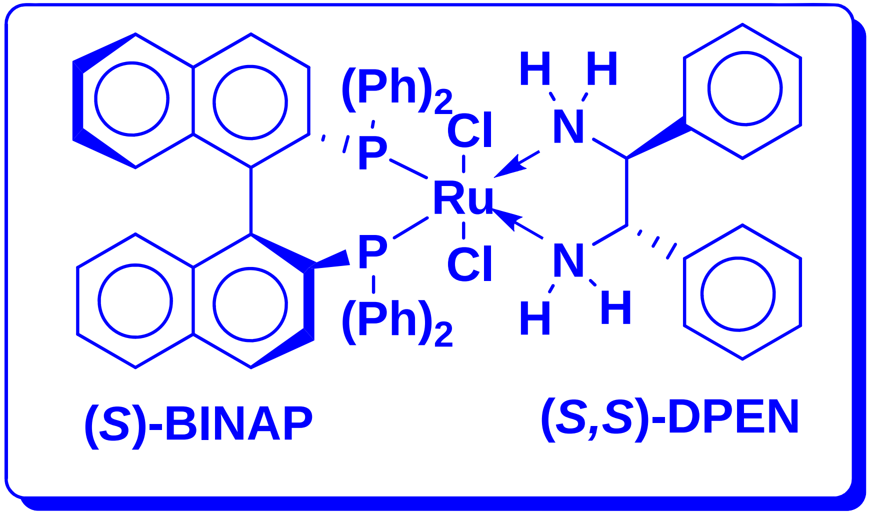
T. Ohta, H. Takaya, R. Noyori, *Inorg. Chem.,* 1988, 27, 566

Asymmetric Hydrogenation of Ketones



100% yield, 80% ee

Turnover number (TON) = 2400000

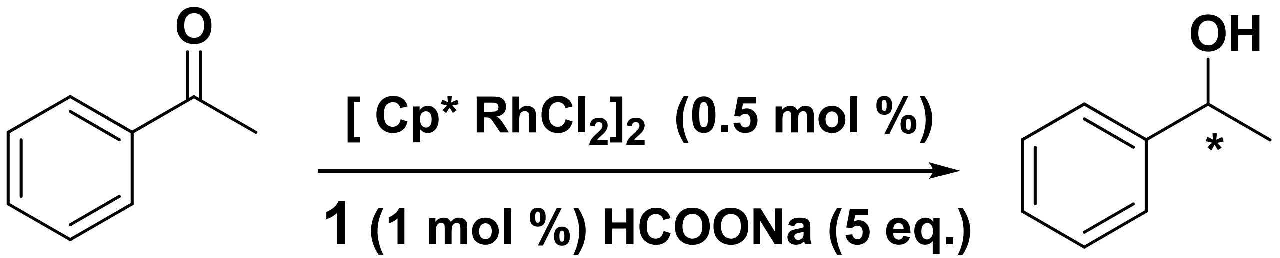


(*S*)-BINAP

(*S*,*S*)-DPEN

R. Noyori et al., *Angew. Chem. Int. Ed.,* 1998, *37*, 1703-1707.

Rhodium-catalyzed Asymmetric Hydrogenation in Water

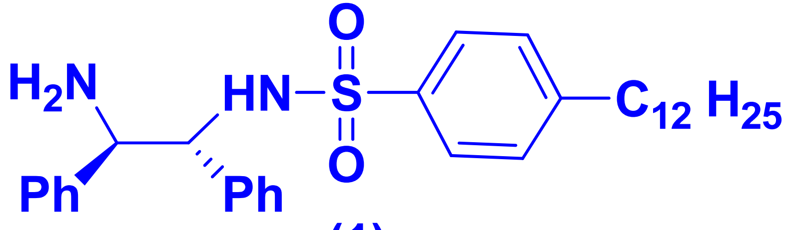


[Cp* $RhCl_2]_2$ (0.5 mol %)

1 (1 mol %) HCOONa (5 eq.)

H_2O, 28 °C, 17 h

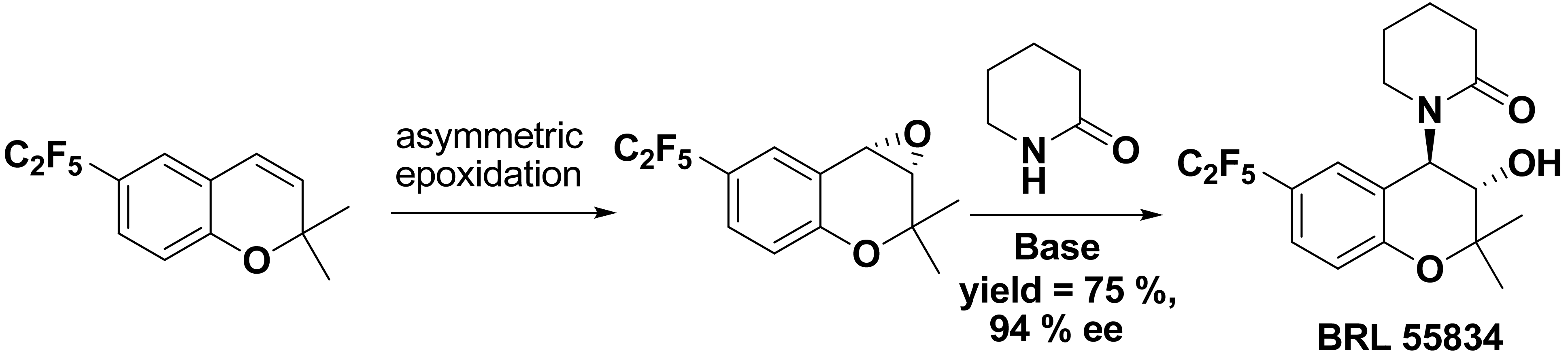
conversion = 97 %;
ee = 97 % (*R*)



(1)

K. Ahlford, J. Lind, L. Maler, H. Adolfsson, *Green Chem.*, 2008, *10*, 832-835.

Asymmetric Epoxidation of Alkenes



BRL 55834
K channel activator

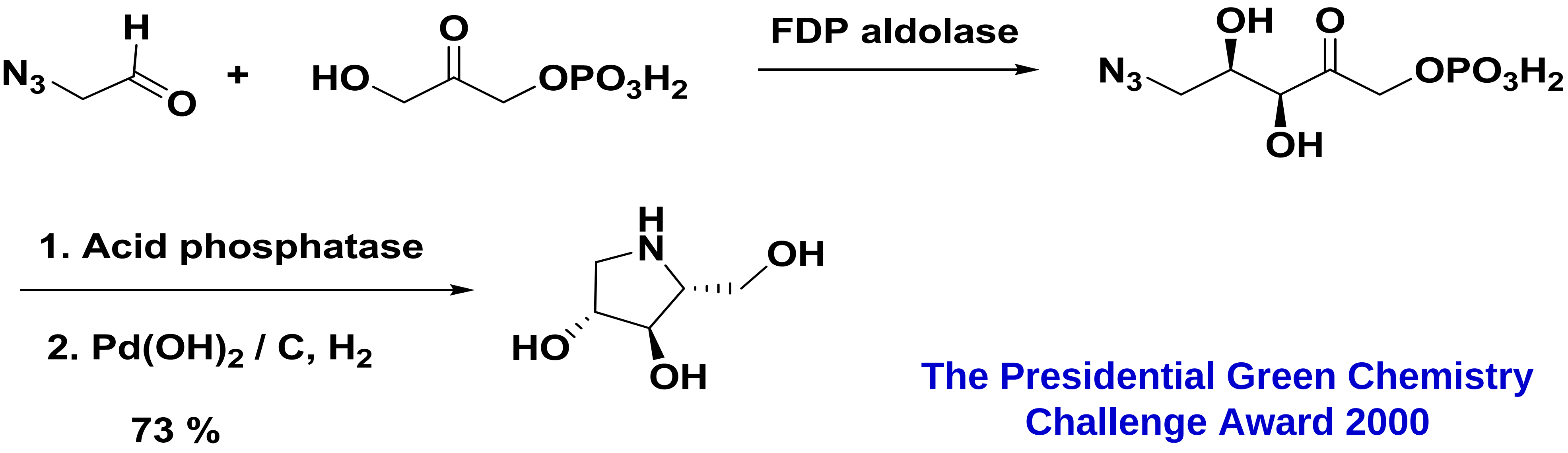
N. H. Lee, A. R. Muci, E. N. Jacobsen, *Tetrahedron Lett.,* 1991, 32, 5055-5058.
D. Bell, M. R. Davies, F. J. L. Finney, *Tetrahedron Lett.,* 1996, 37, 3895-3898.

Industrial Applications of Biocatalysts

Why Biocatalysis….?

- **Mild conditions**
- **Ambient temperature**
- **Pressure and physiological pH**
- **Fewer steps (avoids protection/deprotection steps)**
- **Largely avoids toxic/hazardous reagents & solvents**
- **High chemo-, regio-, and stereoselectivities**

D-Fructose-6-phosphate Aldolase-Catalyzed One-Pot Synthesis of Iminocyclitols



The Presidential Green Chemistry Challenge Award 2000

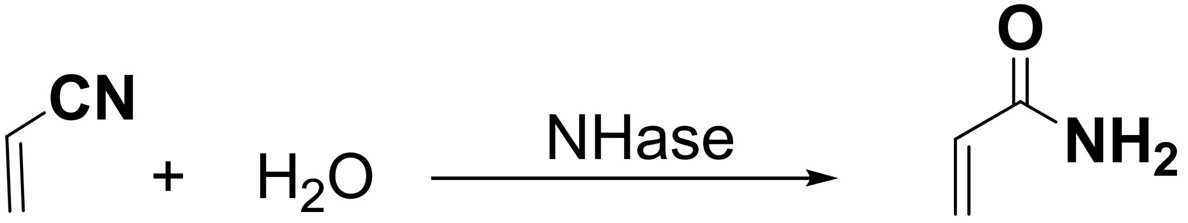
Academic Award

Enzymes in Large-Scale Organic Synthesis

M. Sugiyama, Z. Hong, P. H. Liang, S. M. Dean, L. J. Whalen, W. A. Greenberg, C. -H. Wong, *J. Am. Chem. Soc.*, 2007, *129*, 14811-14817

Biocatalytic production of Acrylamide

Mitsubishi



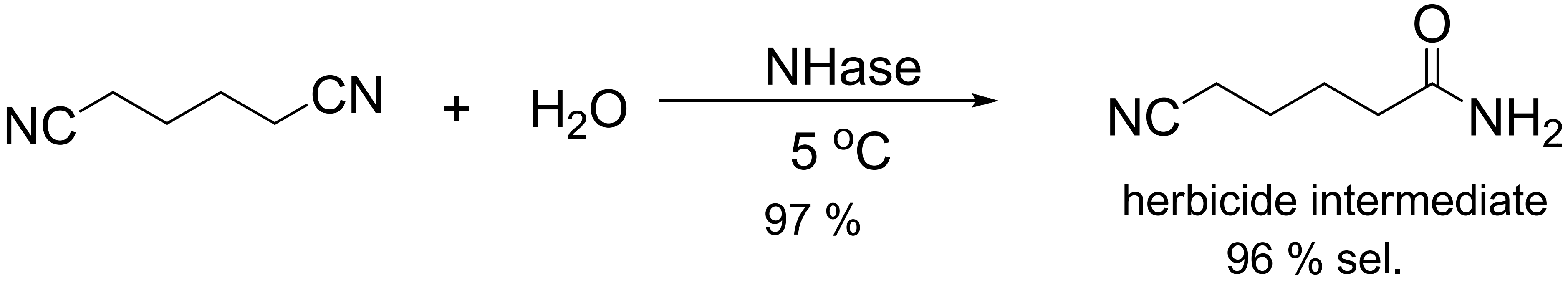
conv. > 99.99 %

sel. 99.99 %

- **100,000 tons per annum and still increasing**
- **Simpler than chemical process (Cu-catalyst)**
- **Immobilized whole cells of *Rh. rhodocrous* J1**
- **Mild conditions (5 °C); no polymerization inhibitor needed**
- **high product quality.**

A. Liese, K. Seelbach, C. Wandrey, *Industrial Biotransfermations,* Wiley-VCH, 2000

Biocatalytic Hydrolysis of Nitriles



- **Immobilized whole cells of *P. chlororaphis* B23**
- **Catalyst consumption 0.006 kg/kg product**
- **Higher conversion/selectivity than chemical process (MnO_2 cat. / 130 °C)**

R. Dicosimo et al., *Bioorg. Med. Chem*. 1999, 7. 2239.

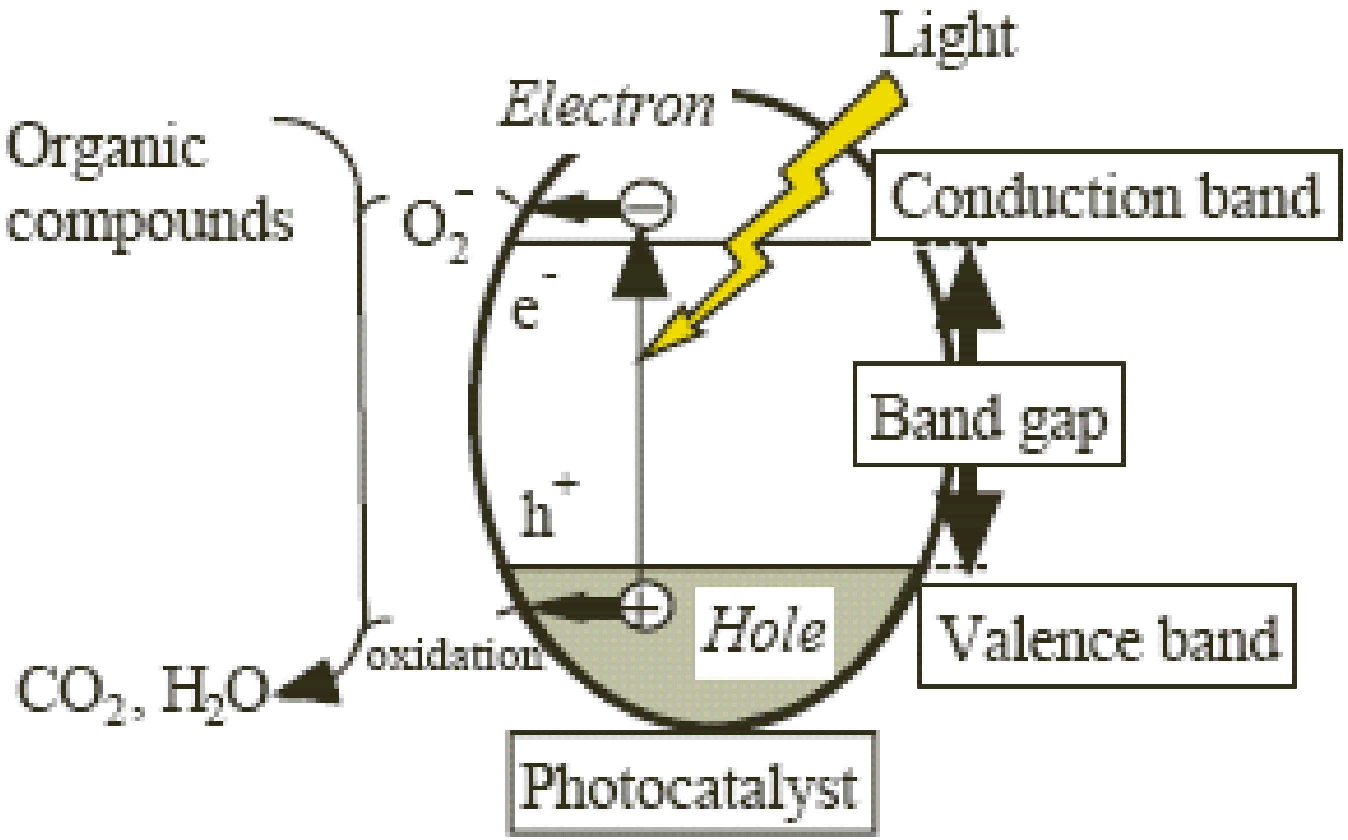
Photocatalysis

The phenomenon by which a relatively small amount of light-absorbing material, called a photocatalyst, changes the rate of chemical reaction without itself being consumed.

Photocatalysis by TiO_2 has been investigated for decades since the first report by Fujishma and Honda in 1972.

A. Fujishima, K.Honda, *Nature*, 1972, 238, 37-38.

Mechanism of Photocatalysis



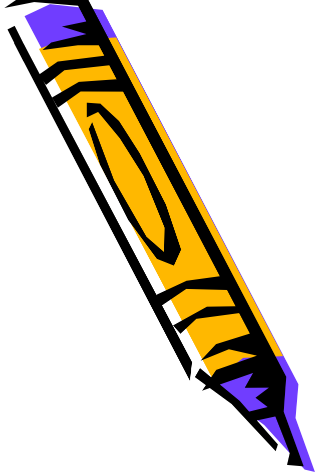
Conclusion

Recent Advances in Green Catalysis

Brønsted Acid-Base Catalysis
Lewis Acid-Base Catalysis
Transition-metal catalysis
Organocatalysis
Asymmetric Catalysis
Biocatalysis

Acknoledgements

劉廣定教授
甘魯生教授
周德璋教授
趙奕姼教授
鄭建鴻教授
洪伯誠教授



Thank You for Your Attention

敬請指正