Hayashi Laboratory

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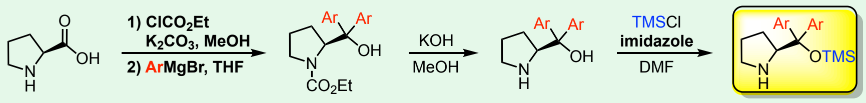
Hayashi Lab. Homepage http://www.ykbsc.chem.tohoku.ac.jp/

Development of new reactions

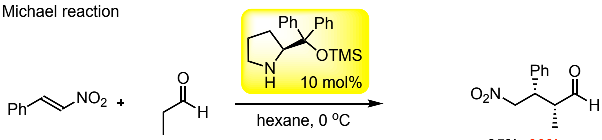
Asymmetric reaction using amino acid or their derivatives as a catalyst,
environmental conscious asymmetric reaction using water as a solvent, and research about origin of chirality

Reaction using diarylprolinol silyl ether derivatives as catalyst



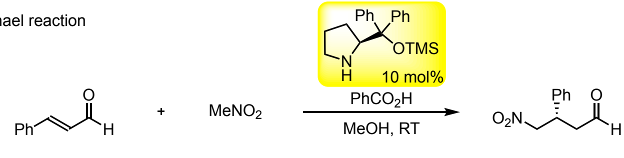
This catalyst is synthesized in short steps from proline.
Substituents on aryl and silyl moiety are easily modified.
Excellent enantioselectivity is obtained

Michael reaction



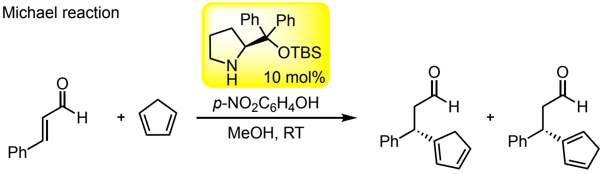
85%, 99% ee
Angew. Chem., Int. Ed., **44**, 4212 (2005).
Org. Synth., **2017**, *94*, 252.

Michael reaction



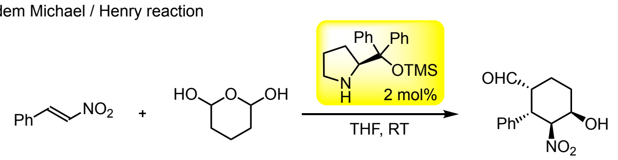
90%, 95% ee
Org. Lett., **9**, 5307 (2007).

Michael reaction



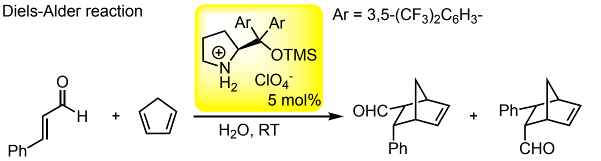
84%, 92% ee
Angew. Chem., Int. Ed., **45**, 6853 (2006).

Tandem Michael / Henry reaction



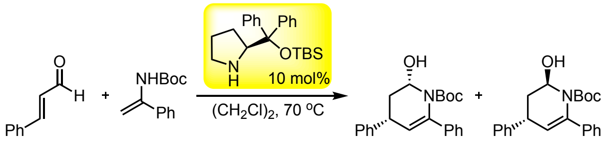
66%, 99% ee
Angew. Chem., Int. Ed., **46**, 4922 (2007).

Diels-Alder reaction



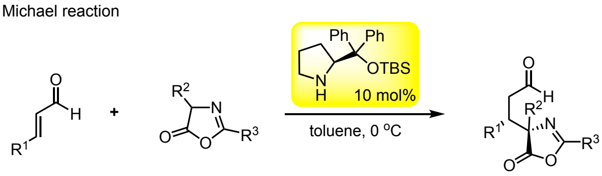
***exo* : *endo* = 80 : 20, 97% ee (*exo*)**
Org. Lett, **9**, 2859 (2007).
Angew. Chem., Int. Ed., **47**, 6634 (2008).

Formal aza [3+3] cycloaddition



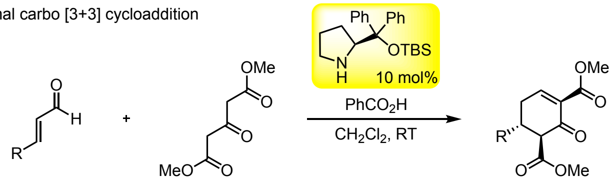
90%, 94% ee, α : β = 34 : 66
Angew. Chem., Int. Ed., **47**, 4012 (2008).

Michael reaction



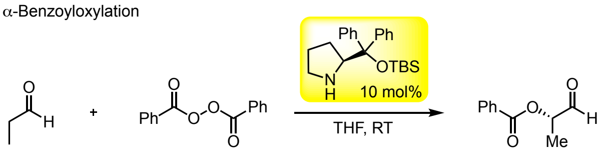
up to 99% ee
up to >90% de
Chem. Asian. J., **4**, 246 (2009).

Formal carbo [3+3] cycloaddition



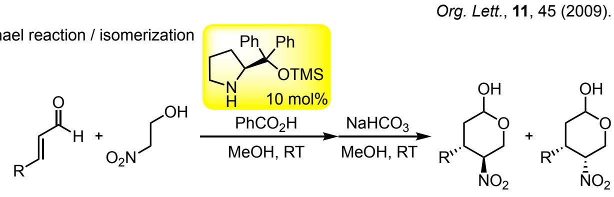
up to 99% ee
Org. Lett., **11**, 45 (2009).

α-Benzoyloxylation



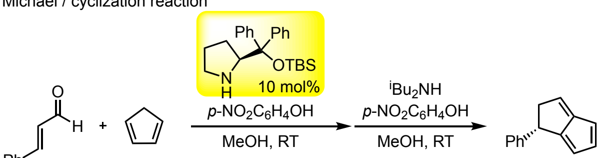
78%, 92% ee
Chem. Commun,, 3083 (2009).

Michael reaction / isomerization



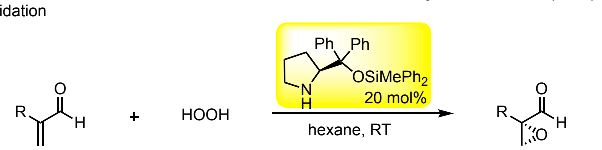
up to 99% ee, a : b = 9 : 1
Org. Lett., **11**, 4056 (2009).

Michael / cyclization reaction



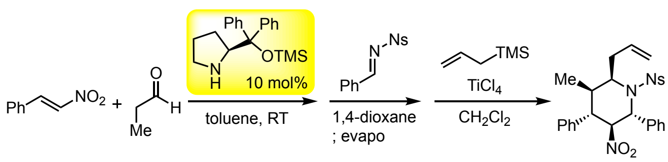
63%, 95% ee
Tetrahedron, **66**, 4894 (2010).

epoxidation



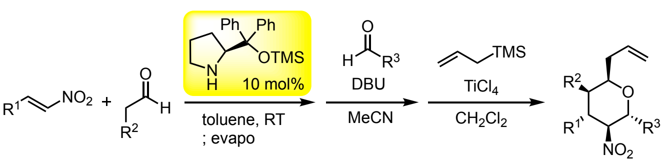
up to 95% ee
Org. Lett., **12**, 5434 (2010).

Michael / aza Henry / aminal formation / additional reaction



up to 99% ee
Single diastereomer
Org.Lett., **12**, 4588 (2010).

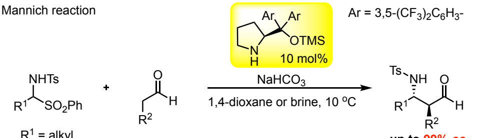
Michael / Henry / acetal formation / additional reaction



up to 99% ee
Single diastereomer
Angew. Chem., Int. Ed., **50**, 3774 (2011).

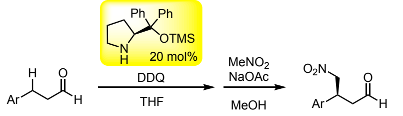
Reaction using diarylprolinol silyl ether derivatives as catalyst

Mannich reaction



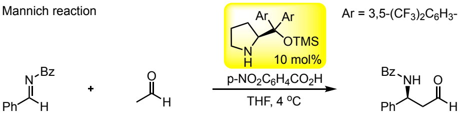
up to 99% ee
Chem. Eur. J., **17**, 8273 (2011).

Formal C-H insertion



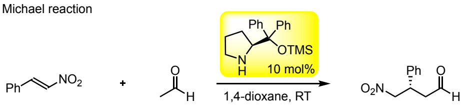
up to 95% ee
Angew. Chem., Int. Ed., **50**, 3920 (2011).
Adv. Synth. Catal. **355**, 3661 (2013).

Mannich reaction



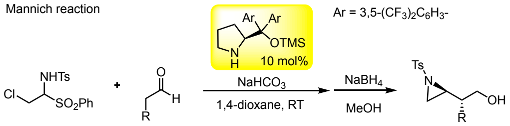
87%, 98% ee
Angew. Chem., Int. Ed., **47**, 9053 (2008).

Michael reaction



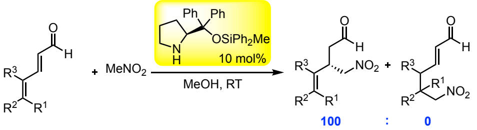
75%, 96% ee
Angew. Chem., Int. Ed., **47**, 4722 (2008).

Mannich reaction



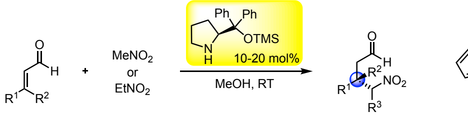
up to 99% ee
Chem. Eur. J., **17**, 8273 (2011).
<Account for Mannich reaction>
J. Synth. Org. Chem., Jpn., **2014,** 72, 1228.

Michael reaction (1,4-Addition versus 1,6-Addition)



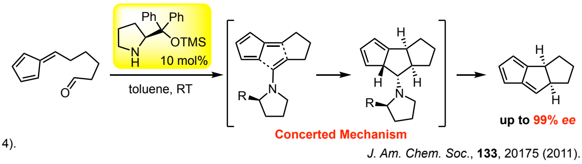
up to 95% ee
ChemCatChem, **4**, 959 (2012).
<Review>
ChemCatChem, **5**, 3499 (2013).

Michael reaction



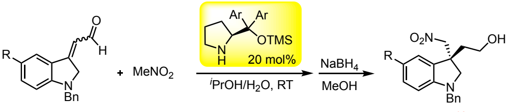
R^3 = H or Me **up to 94% ee**
Chem. Eur. J. **20**, 12072 (2014).

[6+2] cycloaddition reaction



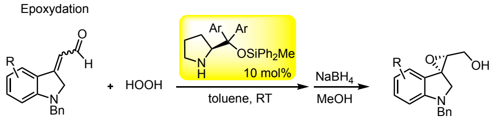
up to 99% ee
J. Am. Chem. Soc., **133**, 20175 (2011).

Michael reaction



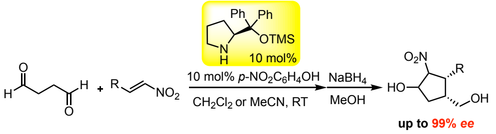
up to 94% ee
Chem. Eur. J. **20**, 13583 (2014).

Epoxydation



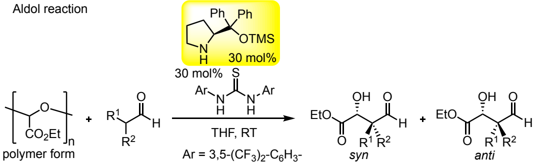
up to 98% ee
ChemCatChem, **7**, 155 (2015).

Formal [3+2] cycloaddition



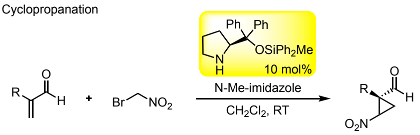
up to 99% ee
Eur. J. Org. Chem. **2015**, 4320.

Aldol reaction



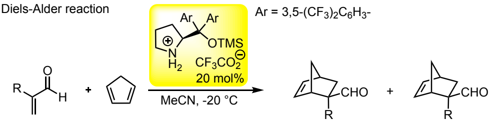
($R^1 < R^2$)
up to *syn* : *anti* = 1 : 2.9
up to 91% ee
Eur. J. Org. Chem. **2015**, 4316.

Cyclopropanation



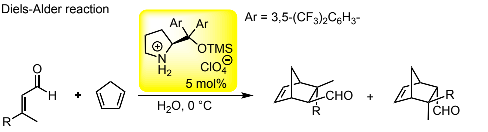
up to 99% ee
Eur. J. Org. Chem. **2015**, 5747.

Diels-Alder reaction



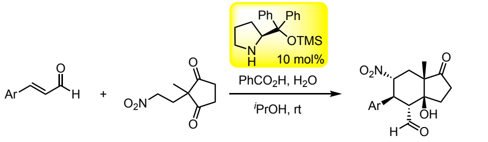
up to *exo* : *endo* = 99 : 1
up to 91% ee
Chem. Eur. J. **2016**, *22*, 15874.

Diels-Alder reaction



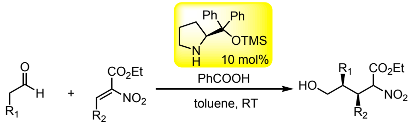
up to *exo* : *endo* = 88 : 12
up to 99% ee
Chem. Eur. J. **2016**, *22*, 15874.

Domino Michael-aldol reaction



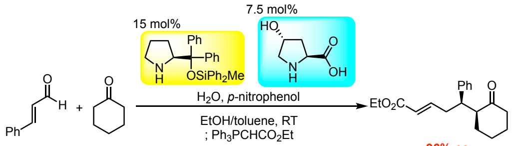
up to >99% ee
dr = >95 : 5
Angew. Chem. Int. Ed. **2017**, *56*, 11812.

Michael reaction



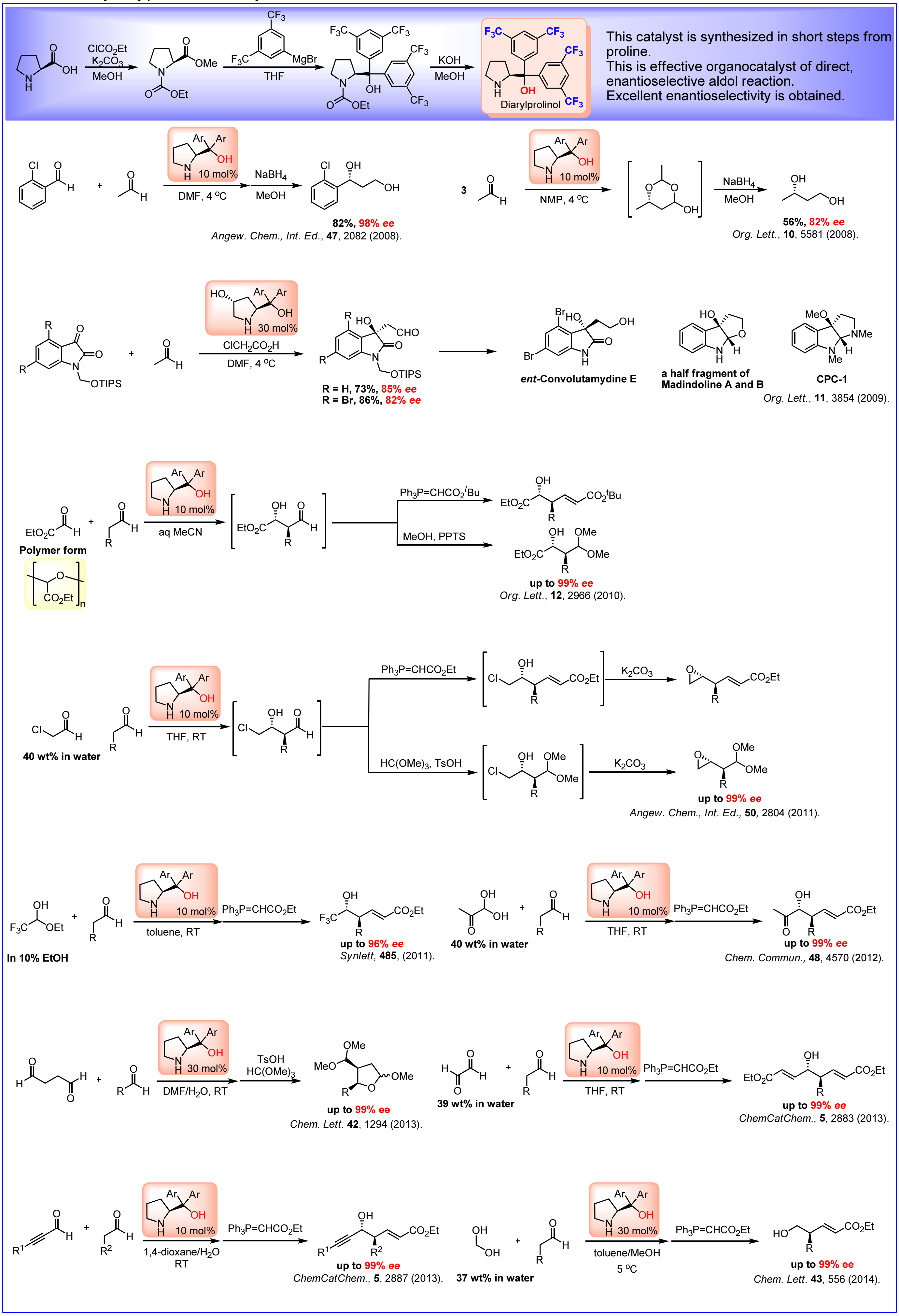
up tp 99% ee
Chem. Lett., **2018**, *47*, 833.

Michael reaction

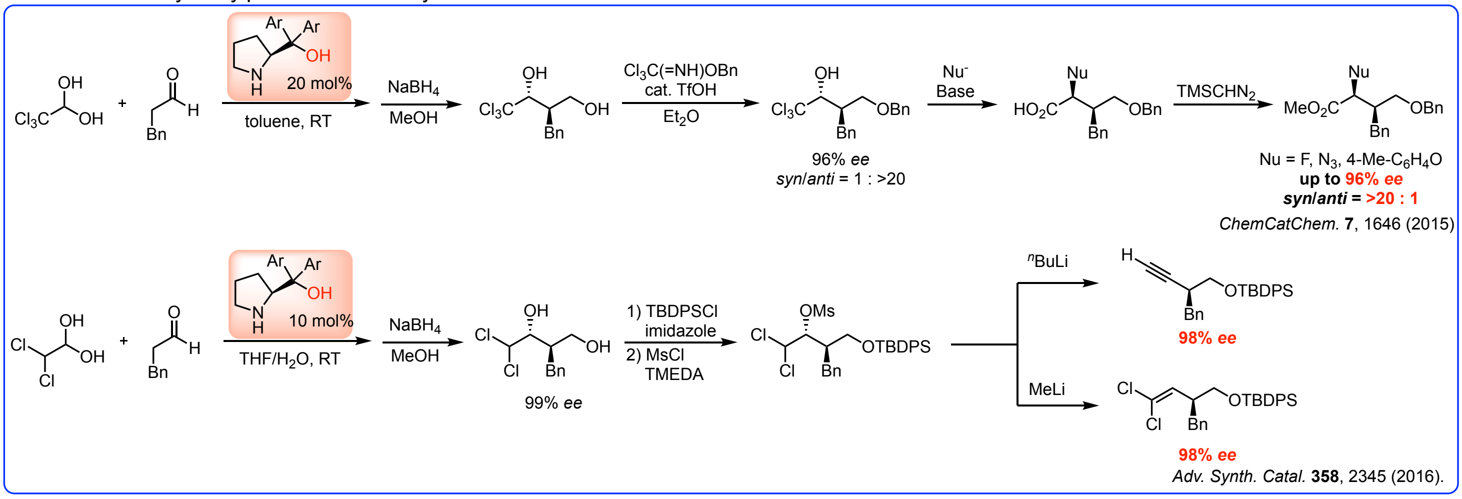


96% ee
***syn* : *anti* = 15 : 1**
Angew. Chem. Int. Ed. **57**, 1958 (2018).

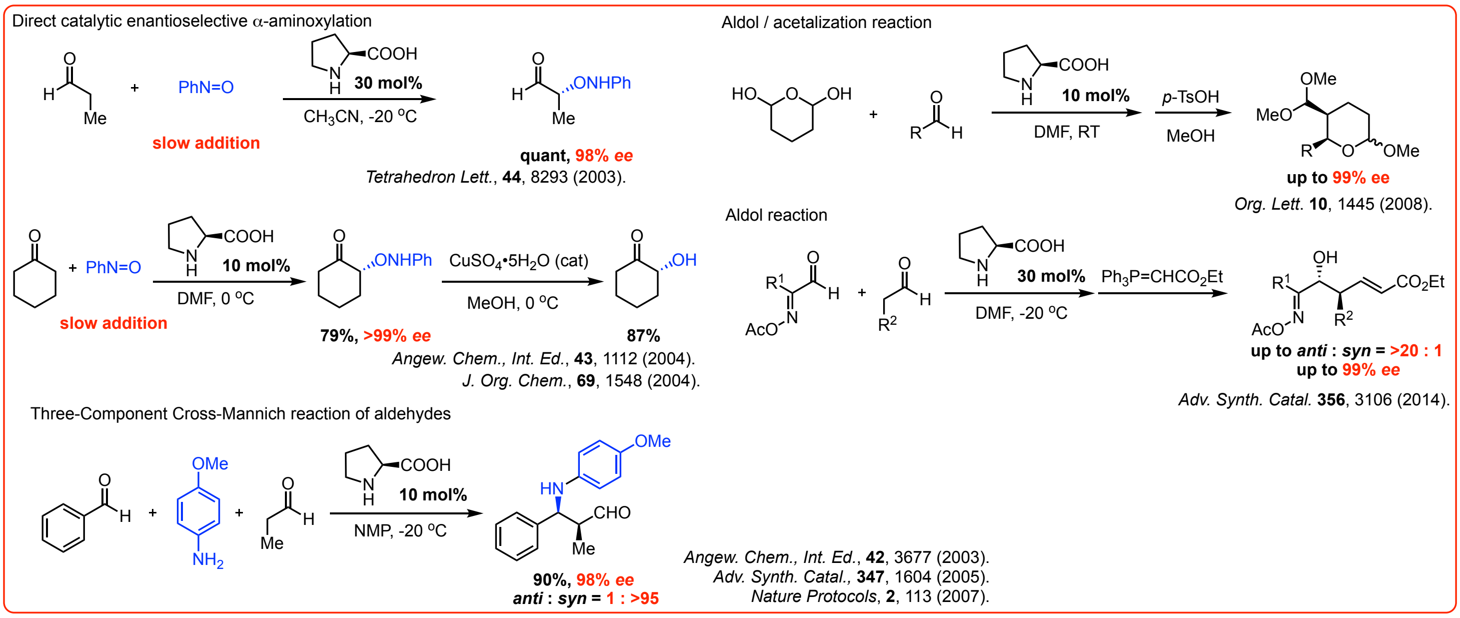
Aldol reaction by diarylprolinol as a catalyst



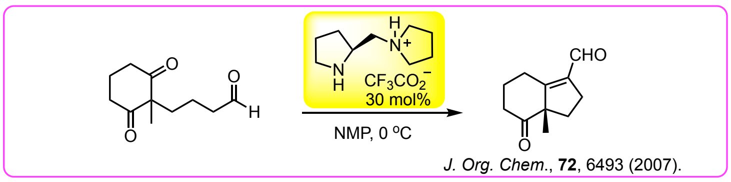
Aldol reaction by diarylprolinol as a catalyst



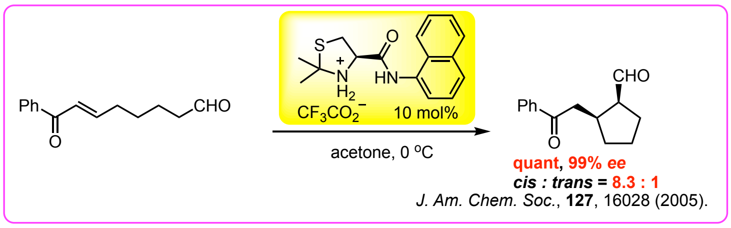
Reaction catalyzed by proline



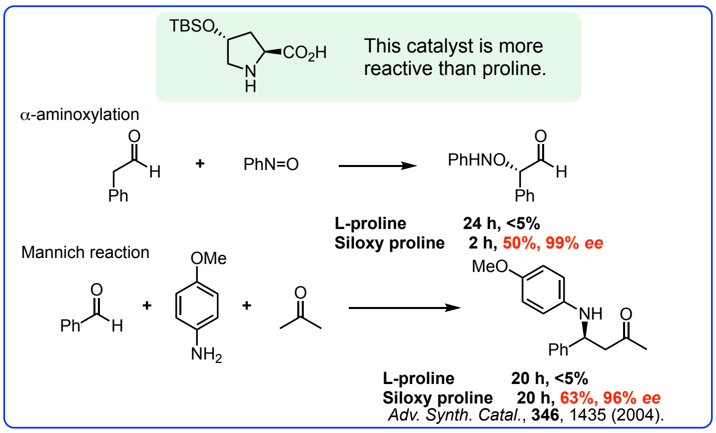
Reaction by proline-derived catalyst



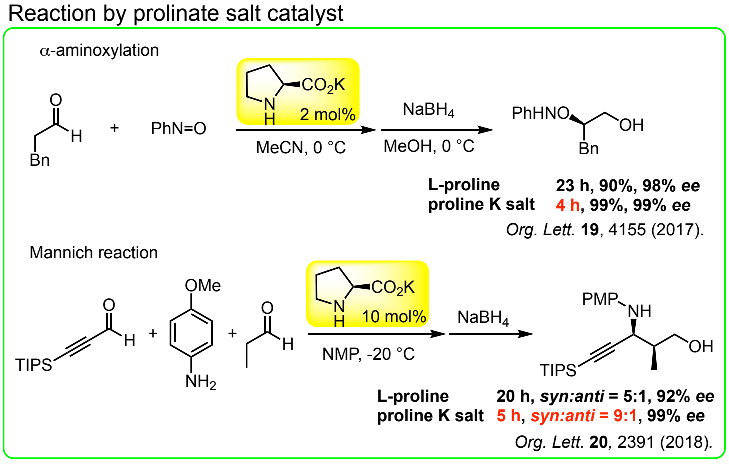
Reaction by cystein-derived catalyst



Reaction by siloxyproline catalyst

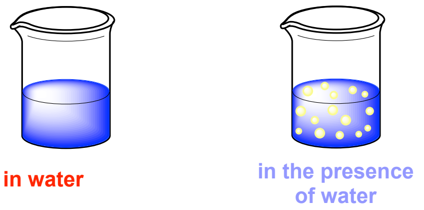


Reaction by prolinate salt catalyst



Organic solvent free reaction

·"in the water" or "in the presence of water" ?

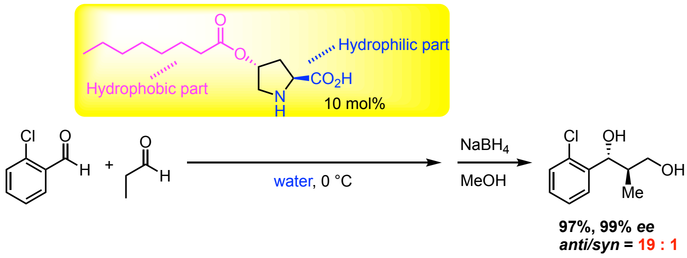


"in water" : The participating reactions are dossplved homogeneously in water.

"in the presence of water" : The reaction proeeds in a concentrated organic phase with water present as a second phase that influences the reactoin in the former.

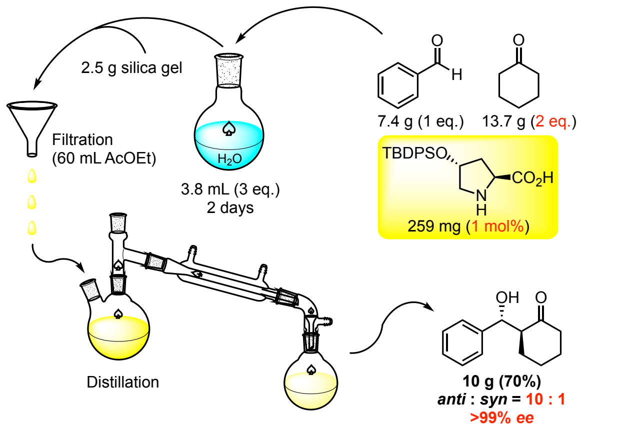
Angew. Chem. Int. Ed. **45**, 8103 (2006).

·Intermolecular aldol reaction between aldehydes in the presence of water



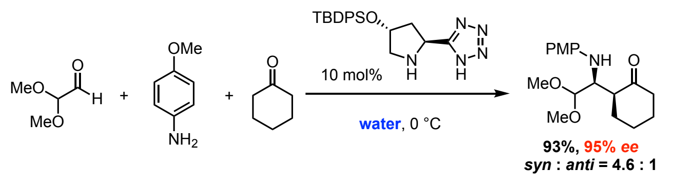
Angew. Chem. Int. Ed. **45**, 5527 (2006).

·Organic solvent free asymmetrric aldol reaction between ketone and aldehyde



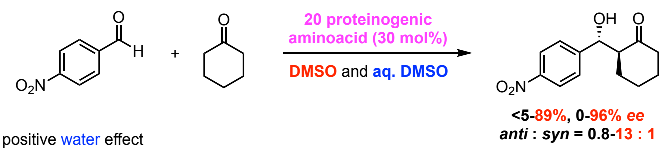
Angew. Chem. Int. Ed. **45**, 958 (2006).
Chem. Eur. J. **13**, 10246 (2007).

·Organic solvent free asymmetrric Mannich reaction with proline catalyst



Org. Lett. **10**, 21 (2008).

·Effect of water on aldol reaction with 20 proteinogenic amino acid



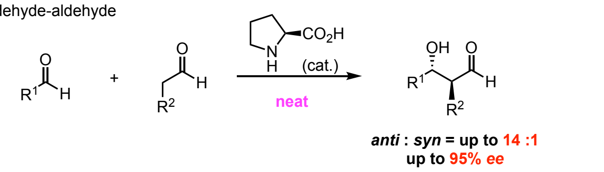
positive water effect

Gly, Ala, Val, Leu, Ile, Phe, Trp, Pro, Ser, Thr, Tyr, Cys, Met, His, Lys, Arg, Asp, Asn, Glu, Gln

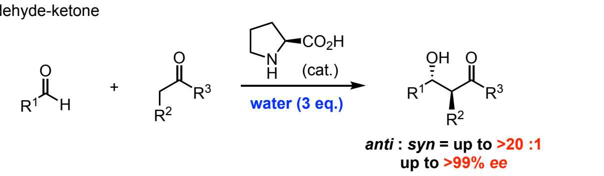
Synlett 1565 (2006).

·Organic solvent free Dry and Wet condition asymetric aldol reaction with proline catalyst

aldehyde-aldehyde

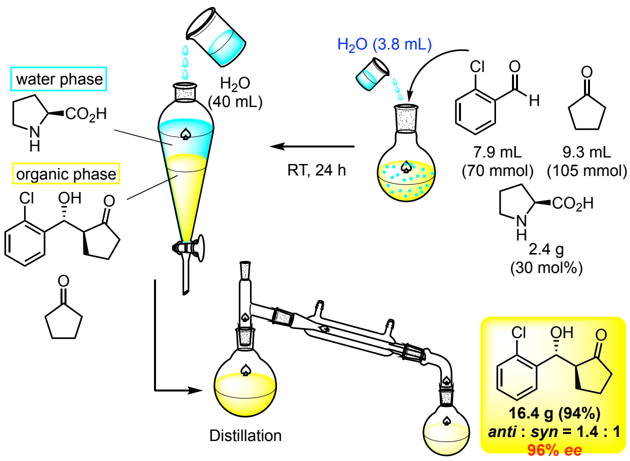


aldehyde-ketone

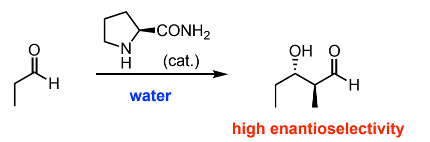


Chem. Commun. 957 (2007).

Organic solvent-free aldol reaction

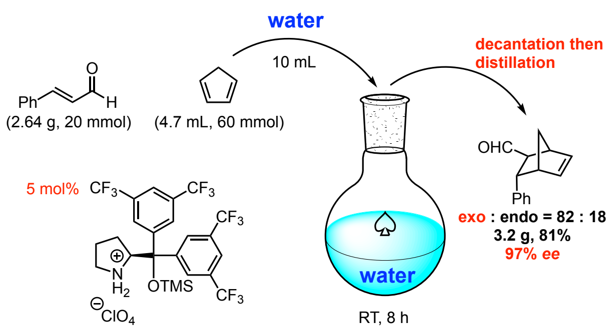


·Self aldol reaction of propanal in water - reaction in water with proline-amide catalyst



Chem. Commun. 2524 (2007).

·Organic solvent free asymmetric Diels-Alder reaction with proline derived catalyst



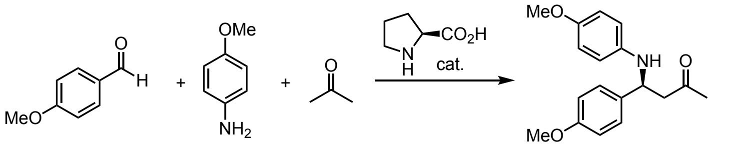
Angew. Chem. Int. Ed. **47**, 634 (2008).

Application of High Pressure Induced by Water-Freezing to the direct catalytic asymmetric reaction

The novel method of high pressure by water-freezing:

The high pressre (cat. 200 MaPa) is easilly is essily achieved simply by freesing water (-20 °C) in a sealed autoclave.

·Mannich reaction



1 atm, RT	**0%, -% ee**	
200 atm, -20 °C	**99%, 96% ee**	

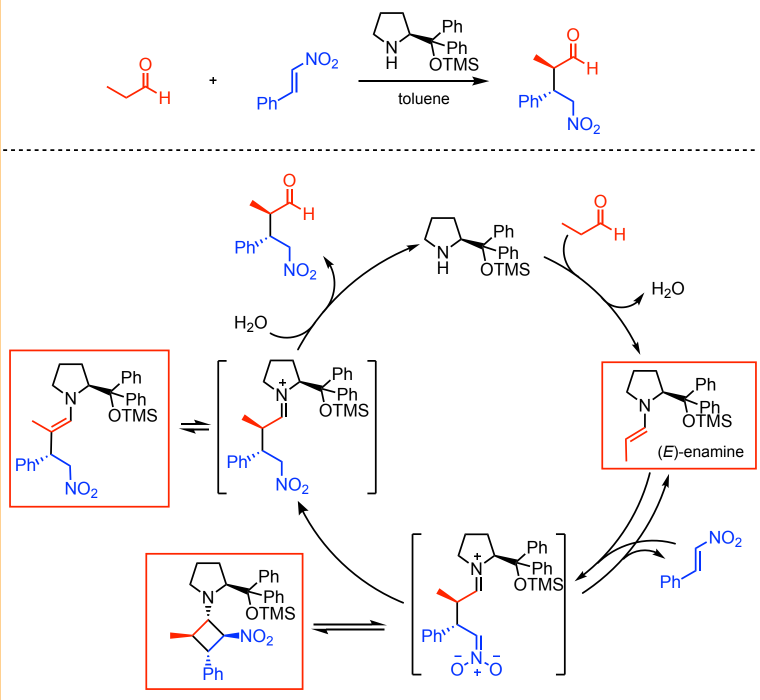
J. Am. Chem. Soc., **125**, 11208 (2003).

·Aldol reaction *Tetrahedron Lett.*, **45**, 4353 (2004).

·Michael reaction *Chem. Lett.*, 296 (2002).

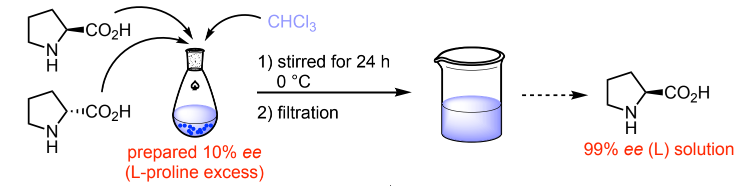
·Baylis-Hillman reaction *Tetrahedron Lett.*, **43**, 8683 (2004).

Proposed mechanism of Michael reaction



Helv. Chim. Acta, **94**, 719 (2011).
Helv. Chim. Acta, **96**, 799, (2013).

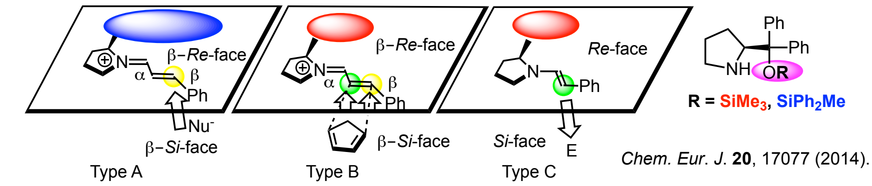
Research about of chirality



Amplification of *ee* from initial low *ee* ⟹ The key to find out origin of chirality

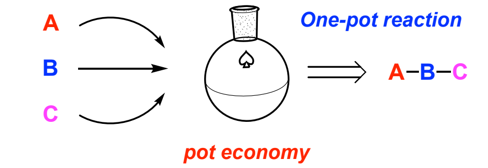
Angew. Chem., Int. Ed. **45**, 4593 (2006).

The effect of silyl substituents of diphenylprolinol silyl ether



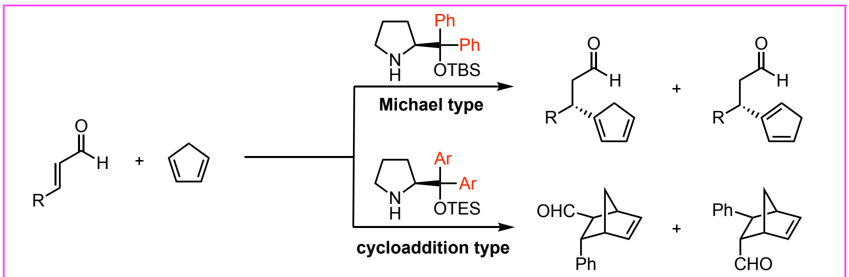
Chem. Eur. J. **20**, 17077 (2014).

Pot ecomomy : Review



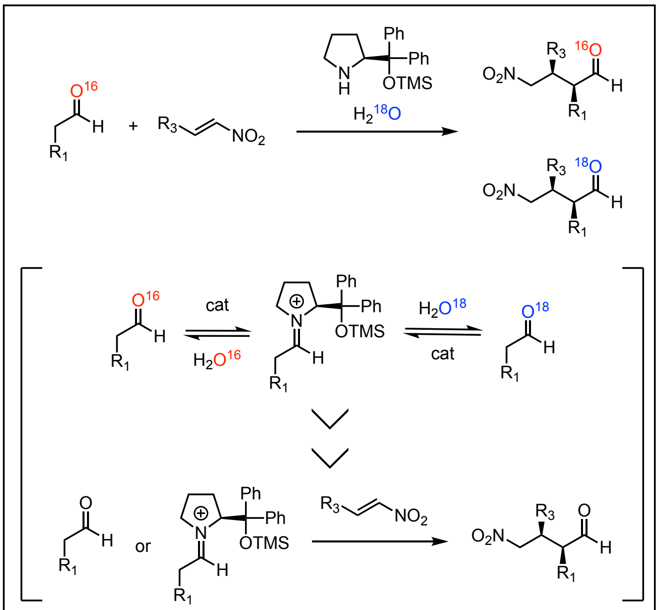
Chem. Sci. **7**, 866 (2016).

The different reactivity of diphenylprolinol silyl ether and diarylprolinol silyl ether



Chem. Eur. J. **21**, 12337 (2015).

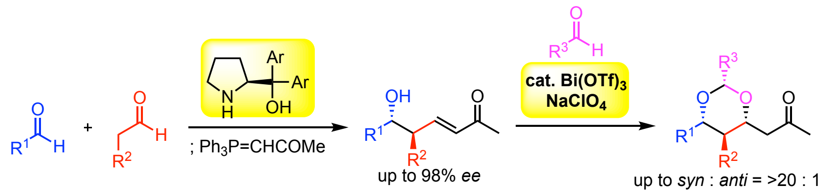
The $^{16}O/^{18}O$ exchanges existance in secondary amine catalyzed reactions



exchenge of oxygen is greatly faster than Michael reaction. So, it is impossible to determine the reaction proceeds with enol or enamine by containing of ^{18}O of TM.

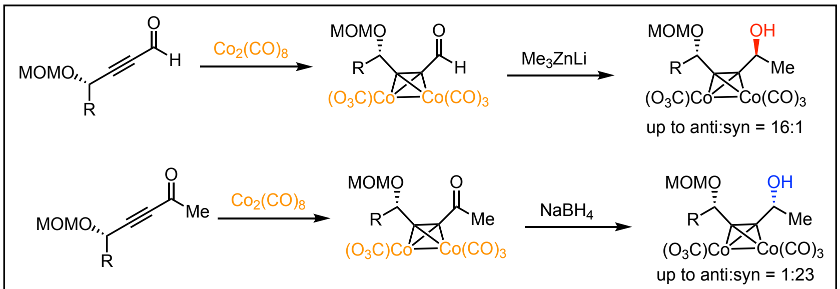
Chem. Eur. J. **2016**, *22*, 5868.

Two-Pot Synthesis of Chiral 1,3-syn-Diols



Chem. Eur. J. **2018**, *24*,4909.

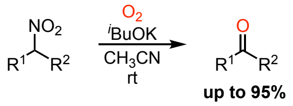
1,4-asymmetric induction using Cobalt alkyne complex



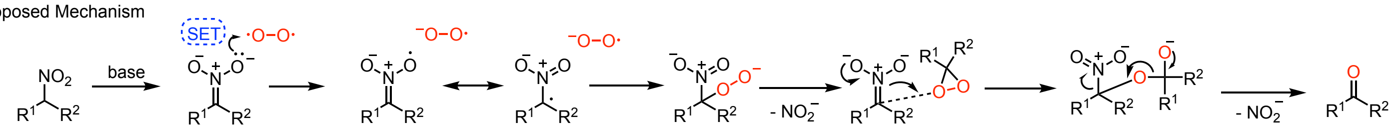
Organometallics **2008**, *27*, 163.

Metal-free oxidative transformations using O_2

Nef reaction using molecular O_2

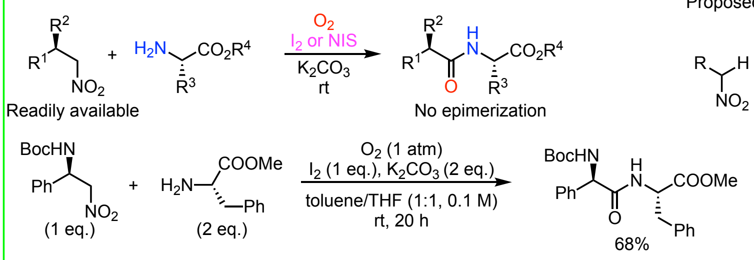


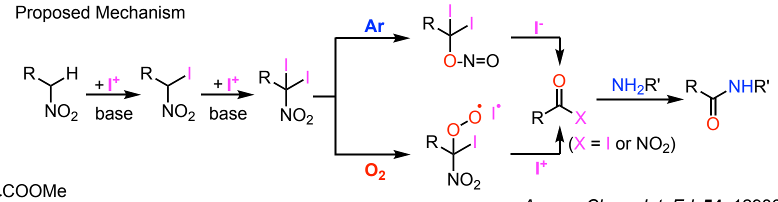
Proposed Mechanism



Chem. Eur. J. **20**, 15753 (2014).

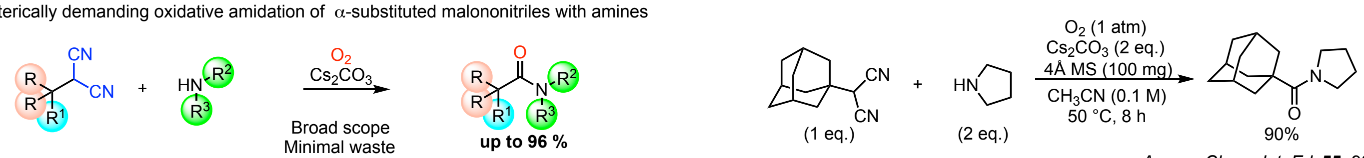
Oxidative amidation of primary nitroalkane and amine





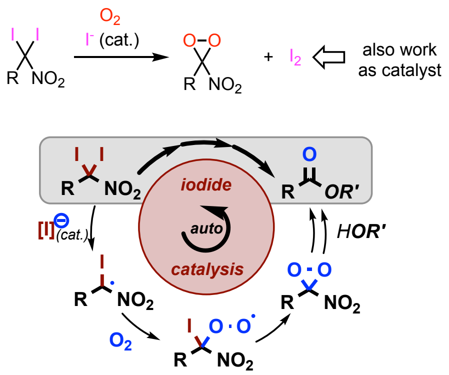
Angew. Chem. Int. Ed. **54**, 12986 (2015).
Chem. Eur. J. **22**, 5538 (2016).

Sterically demanding oxidative amidation of α-substituted malononitriles with amines



Angew. Chem. Int. Ed. **55**, 9060 (2016).

Autoinductive oxidation of α,α-diiodonitroalkanes



Chem. Commun., **2018**, *54*, 6360.