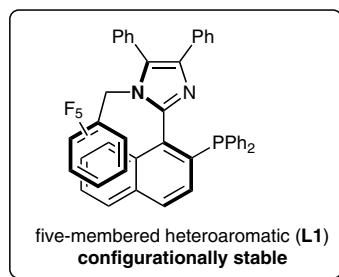
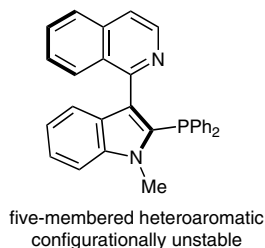
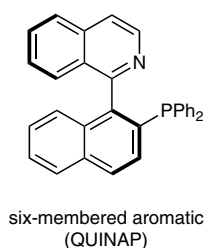
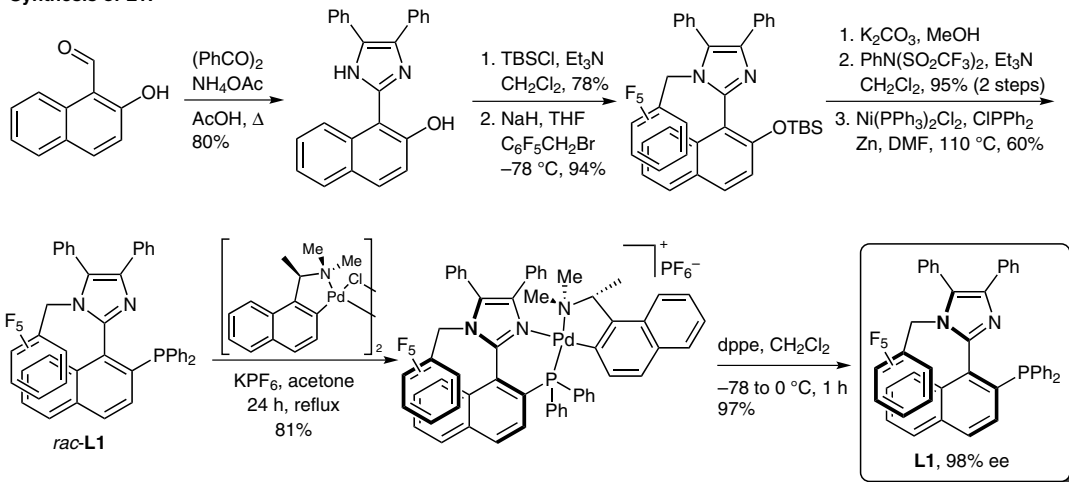


# A Chiral Biaryl P,N-Ligand for Asymmetric Catalysis

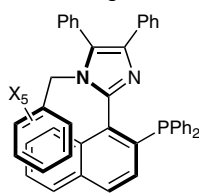
## Concept:



## Synthesis of L1:

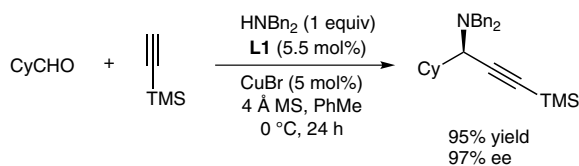


## Importance of $\pi$ -stacking:



L1 (X = F) half-life: 8.7 h at  $75^\circ\text{C}$  in DCE  
 L1-H<sub>5</sub> (X = H) half-life: 22 min

## Selected example:

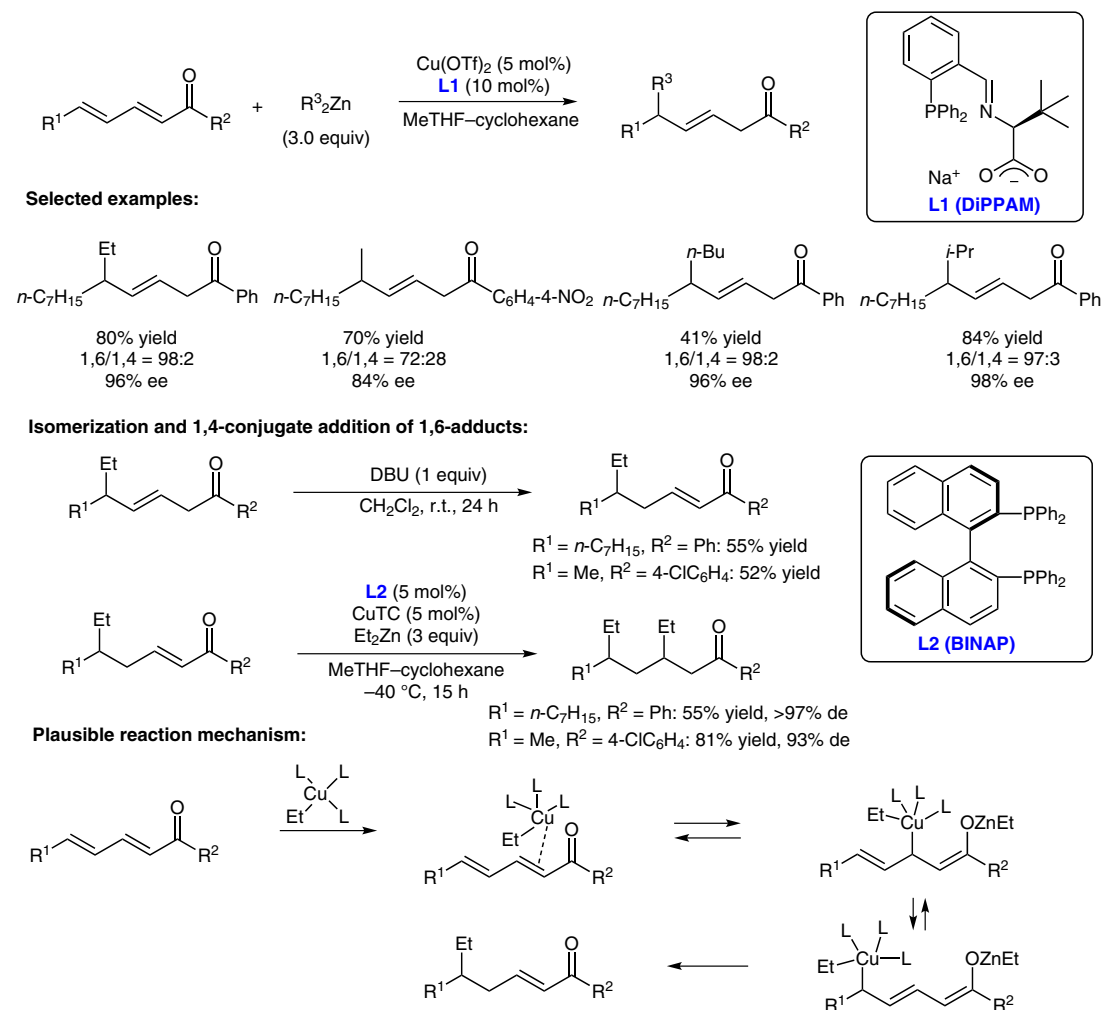


**Significance:** The authors reported the preparation of a new chiral biaryl P,N-ligand incorporating a five-membered electron-rich heteroaromatic. This ligand is easy to prepare and an effective catalyst for the enantioselective alkyne-alkene coupling.

**Comment:** In contrast to the six-membered P,N-ligands, five-membered P,N-ligands are configurationally unstable. The authors have succeeded in preparing a configurationally stable five-membered P,N-ligand involving  $\pi$ -stacking interaction, which would offer a new, unexplored chemical diversity.

M. MAGREZ-CHIQUET, M. S. T. MORIN, J. WENCEL-DELORD, S. D. AMRAOUI, O. BASLÉ, A. ALEXAKIS, C. CRÉVISY,\* M. MAUDUIT\* (ECOLE NATIONALE SUPÉRIEURE DE CHIMIE DE RENNES, FRANCE AND UNIVERSITÉ DE GENÈVE, SWITZERLAND)  
Enantioselective 1,6-Conjugate Addition of Dialkylzinc Reagents to Acyclic Dienones Catalyzed by Cu-DiPPAM  
Complex–Extension to Asymmetric Sequential 1,6/1,4-Conjugate Addition  
*Chem. Eur. J.* **2013**, *19*, 13663–13667.

## Cu-Catalyzed Asymmetric 1,6-Conjugate Addition of Dialkylzinc



**Significance:** The authors reported the asymmetric 1,6-conjugate addition of dialkylzinc to acyclic dienones catalyzed by copper/phosphinoazomethine salt (DiPPAM). After the isomerization of the conjugate adducts, stereoselective sequential 1,4-conjugate addition of diethylzinc was also demonstrated.

**Comment:** The control of regioselectivity of the 1,6-conjugate addition is difficult due to many parameters. Using copper and the DiPPAM ligand, a highly enantio- and regioselective 1,6-conjugate addition was achieved. With the BINAP ligand, unprecedented highly stereoselective induction is noteworthy.

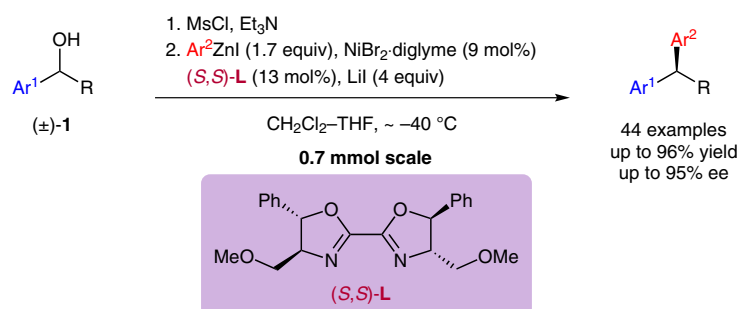
**SYNFACTS Contributors:** Hisashi Yamamoto, Yasushi Shimoda  
Synfacts 2014, 10(1), 0042 Published online: 13.12.2013  
DOI: 10.1055/s-0033-1340436; Reg-No.: H15713SF

2014 © THIEME STUTTGART • NEW YORK

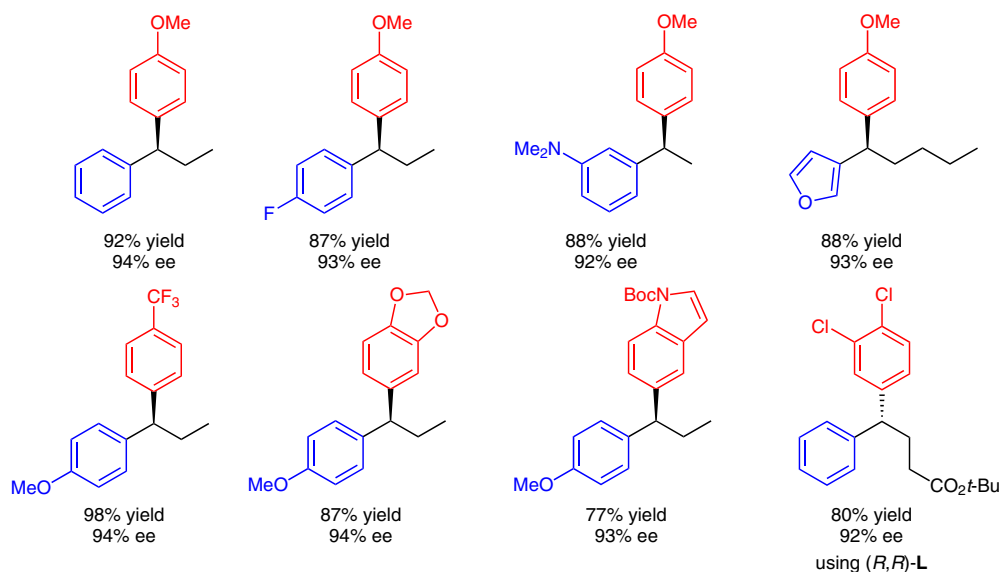
H.-Q. DO, E. R. R. CHANDRASHEKAR, G. C. FU\* (CALIFORNIA INSTITUTE OF TECHNOLOGY, PASADENA AND MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE, USA)

Nickel/Bis(oxazoline)-Catalyzed Asymmetric Negishi Arylations of Racemic Secondary Benzylic Electrophiles to Generate Enantioenriched 1,1-Diarylalkanes  
*J. Am. Chem. Soc.* **2013**, *135*, 16288–16291.

# Arylation of Racemic Secondary Benzylic Electrophiles by Nickel Catalysis



## Selected examples:

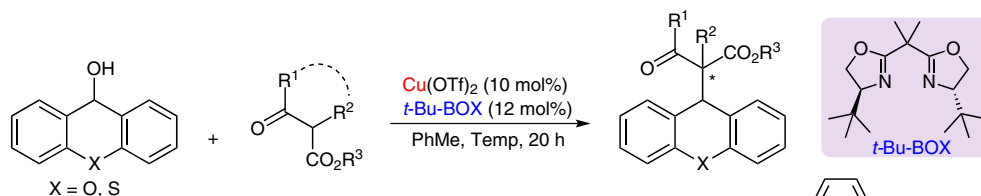


**Significance:** The 1,1-diarylalkane motif is found in a number of the top-selling pharmaceuticals. Therefore, the development of stereoselective methods to access this motif is a worthwhile pursuit. The authors report a two-step stereoconvergent synthesis of 1,1-diarylalkanes starting from racemic benzylic alcohols, which proceeds in excellent yields and with excellent enantioselectivities.

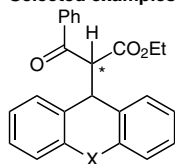
**Comment:** A previous report by the same group disclosed a nickel-catalyzed enantioconvergent Negishi arylation of propargylic carbonates that was not applicable to the use of racemic benzylic carbonates (*J. Am. Chem. Soc.* **2012**, *134*, 2966). The current method generates a benzylic mesylate in situ. The authors propose that the lithium iodide additive transforms the mesylate into an alkyl iodide, which can then participate in the Negishi cross-coupling.

**SYNFACTS Contributors:** Mark Lautens, Christine M. Le  
Synfacts 2014, 10(1), 0043 Published online: 13.12.2013  
DOI: 10.1055/s-0033-1340452; Reg-No.: L16213SF

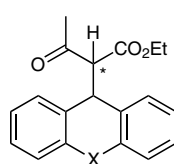
P. TRILLO, A. BAEZA,\* C. NÁJERA\* (UNIVERSIDAD DE ALICANTE, SPAIN)

Copper-Catalyzed Asymmetric Alkylation of  $\beta$ -Keto Esters with Xanthydrols*Adv. Synth. Catal.* **2013**, 355, 2815–2821.Enantioselective Alkylation of  $\beta$ -Keto Esters

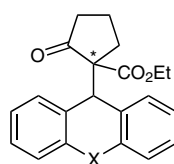
Selected examples:



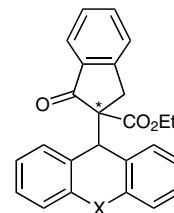
$\text{X} = \text{O}$ ,  $-50^\circ\text{C}$   
82% yield, 80% ee  
 $\text{X} = \text{S}$ ,  $0^\circ\text{C}$   
45% yield, >99% ee



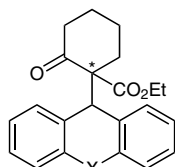
$\text{X} = \text{O}$ ,  $-50^\circ\text{C}$   
91% yield, 0% ee  
 $\text{X} = \text{S}$ ,  $-20^\circ\text{C}$   
75% yield, 69% ee



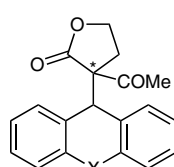
$\text{X} = \text{O}$ ,  $-50^\circ\text{C}$   
87% yield, 73% ee  
 $\text{X} = \text{S}$ ,  $-20^\circ\text{C}$   
37% yield, 90% ee



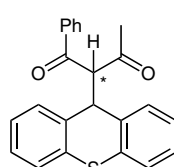
$\text{X} = \text{O}$ ,  $-50^\circ\text{C}$   
89% yield, 82% ee  
 $\text{X} = \text{S}$ ,  $0^\circ\text{C}$   
71% yield, 63% ee



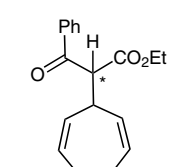
$\text{X} = \text{O}$ ,  $-50^\circ\text{C}$   
90% yield, 16% ee  
 $\text{X} = \text{S}$ ,  $0^\circ\text{C}$   
42% yield, 34% ee



$\text{X} = \text{O}$ ,  $-78^\circ\text{C}$   
87% yield, 56% ee  
 $\text{X} = \text{S}$ ,  $0^\circ\text{C}$   
38% yield, 71% ee

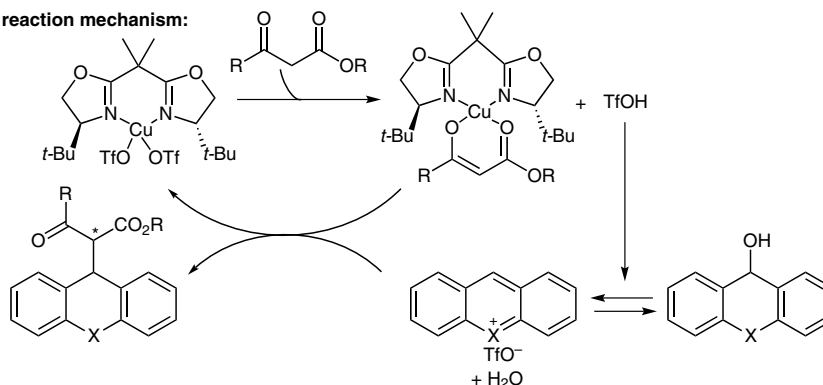


$-50^\circ\text{C}$   
37% yield, 85% ee



$0^\circ\text{C}$   
92% yield, 30% ee

Proposed reaction mechanism:



**Significance:** The  $\text{Cu}(\text{OTf})_2$ /*tert*-butyl-bis-oxazoline catalyst system allows the asymmetric alkylation of  $\beta$ -keto esters with free benzylic alcohols, for example, xanthydrols as alkylating agents. The reaction is environmentally benign as it generates only water as by-product.

**Comment:** The reaction between the asymmetric  $\text{Cu}(\text{II})$ - $\beta$ -keto ester derivative and the in situ generated carbocation proceeds via an  $\text{S}_{\text{N}}1$  mechanism. Albeit unknown, the water produced has a specific role to facilitate the reaction.

SYNFACTS Contributors: Hisashi Yamamoto, Sukalyan Bhadra

Synfacts 2014, 10(1), 0044 Published online: 13.12.2013

DOI: 10.1055/s-0033-1340437; Reg-No.: H15813SF

2014 © THIEME STUTTGART • NEW YORK

# $\text{Rh}_2(R\text{-TPCP})_4$ -Catalyzed Enantioselective Syntheses of 2,5-Dihydroisoxazoles

Category

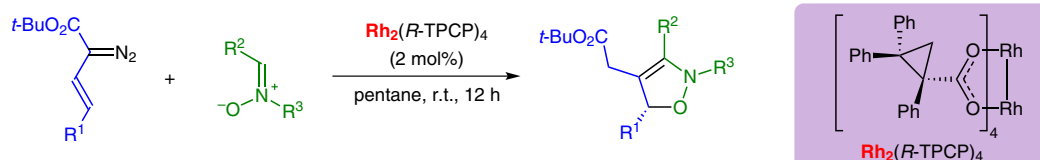
Metal-Catalyzed  
Asymmetric  
Synthesis and  
Stereoselective  
Reactions

Key words

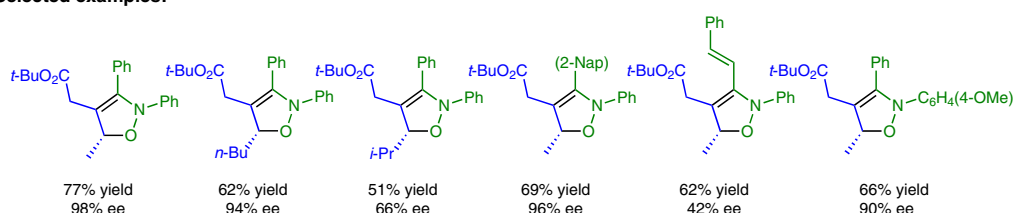
[3+2] cycloaddition

nitrones

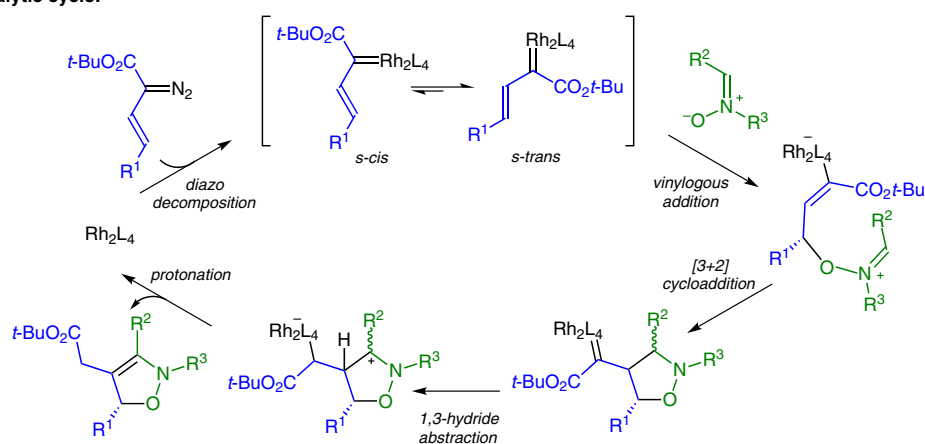
vinyldiazoacetates



## Selected examples:



## Proposed catalytic cycle:



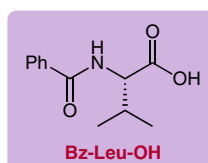
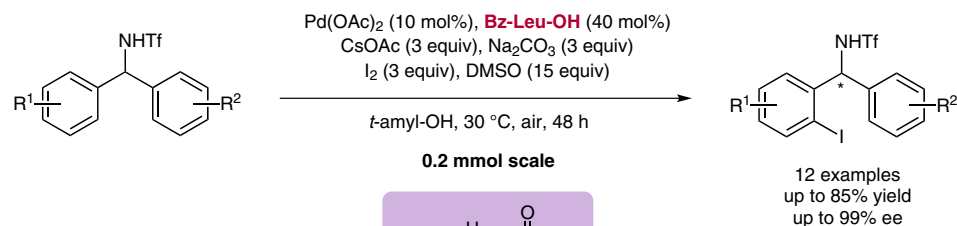
**Significance:** Exploring the vinyllogous reactivity of vinyl rhodium carbenoids, the authors report the  $\text{Rh}_2(R\text{-TPCP})_4$ -catalyzed enantioselective formal [3+2] cycloaddition between nitrones and vinyldiazoacetates. With only 2 mol% of the bulky rhodium catalyst, the 2,5-dihydroisoxazoles were obtained in good yields and moderate to excellent enantioselectivities.

**Comment:** Doyle and colleagues previously reported a dirhodium complex catalyzed synthesis of 3,6-dihydro-1,2-oxazines via an asymmetric formal [3+3] cycloaddition between nitrones and vinyldiazo compounds (*J. Am. Chem. Soc.* **2011**, *133*, 16402). The highlight of this work is the product divergence from [3+3] to [3+2] cycloaddition leading to 2,5-dihydroisoxazoles with clinical choice of substrate and catalyst.

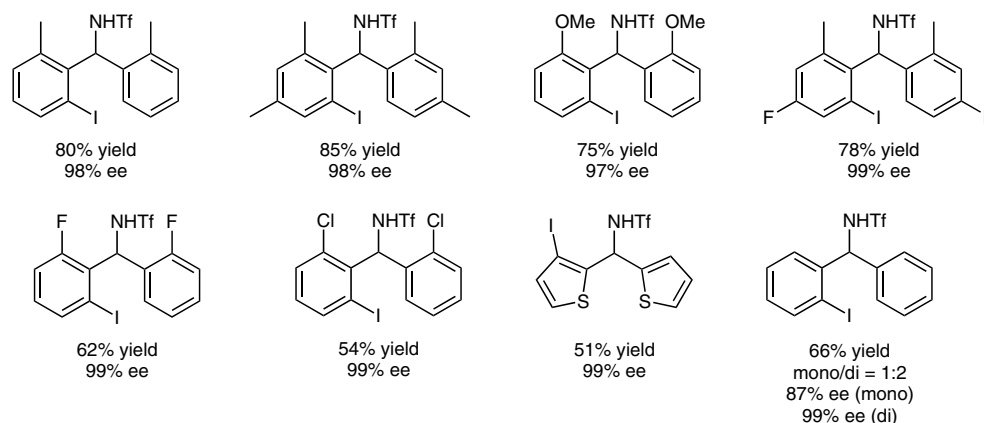
L. CHU, X.-C. WANG, C. E. MOORE, A. L. RHEINGOLD, J.-Q. YU\* (THE SCRIPPS RESEARCH INSTITUTE, LA JOLLA AND THE UNIVERSITY OF CALIFORNIA, SAN DIEGO, LA JOLLA, USA)

Pd-Catalyzed Enantioselective C–H Iodination: Asymmetric Synthesis of Chiral Diarylmethylamines  
*J. Am. Chem. Soc.* **2013**, *135*, 16344–16347.

## Palladium-Catalyzed Enantioselective C–H Iodination



### Selected examples:



**Significance:** The diarylmethylamine motif is present in a range of biologically active compounds. Methods aimed at the enantioselective synthesis of diarylmethylamines include 1,2-addition of organometallic species to aldimines (see Review) and asymmetric hydrogenation of the corresponding imines (*J. Am. Chem. Soc.* **2010**, *132*, 2124). Here, the authors report the asymmetric synthesis of diarylmethylamines via palladium-catalyzed desymmetrizing C–H iodination. This report is the first example of an asymmetric C–H iodination in the absence of a chiral auxiliary.

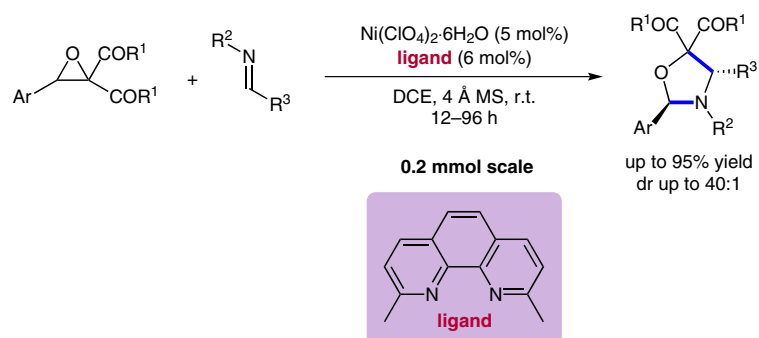
**Comment:** The iodination of *ortho*-substituted substrates proceeds with good yields and excellent enantioselectivities. However, in the absence of *ortho* substituents, a significant amount of the diiodinated product is obtained. Interestingly, the enantioselectivity of the di-iodinated product remains consistently higher than that of the mono-iodinated product.

**Review:** M. T. Robak, M. A. Herbage, J. A. Ellman  
*Chem. Rev.* **2010**, *110*, 3600–3740.

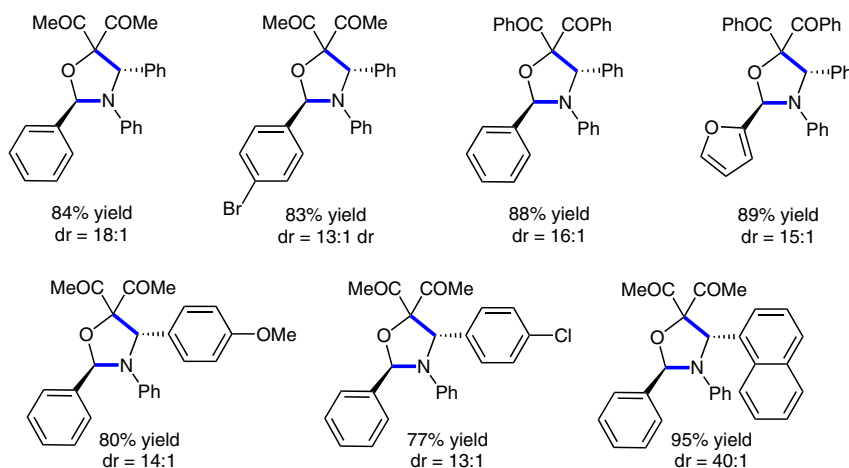
**SYNFACTS Contributors:** Mark Lautens, Christine M. Le  
Synfacts 2014, 10(1), 0046 Published online: 13.12.2013  
**DOI:** 10.1055/s-0033-1340453; **Reg-No.:** L16313SF

2014 © THIEME STUTTGART • NEW YORK

## Ni-Catalyzed Annulation of Donor–Acceptor Oxiranes with Imines



### Selected examples:



**Significance:** The use of donor–acceptor oxiranes as 1,3-dipole equivalents in cycloaddition reactions is a useful strategy for the construction of highly substituted heterocycles in a stereoselective fashion. The authors report a diastereoselective synthesis of 2,4-*trans*-oxazolidines via a nickel-catalyzed [3+2] cycloaddition of donor–acceptor oxiranes and imines.

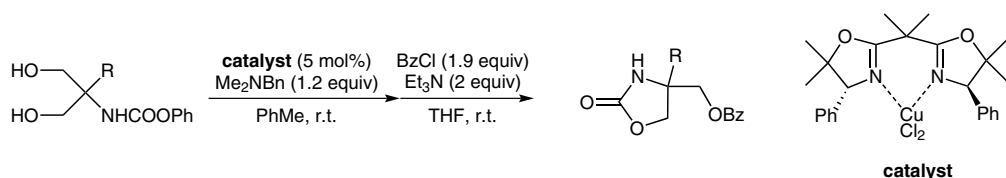
**Comment:** A previous report demonstrated that donor–acceptor aziridines and aldehydes can undergo a [3+2] cycloaddition using a nickel catalyst, which furnishes 2,5-*cis*-oxazolidines (A. Hennig, A. Hoffmann, H. Borchertding, T. Thiele, U. Schedler, U. Resch-Genger *Chem. Commun.* **2011**, 47, 7842). The current report represents a complementary approach towards oxazolidine scaffolds. The authors demonstrate that two electron-withdrawing groups on the oxirane are required for reactivity, suggesting that chelation to the nickel catalyst is crucial for C–C bond cleavage.

Y. S. YOU, T. W. KIM, S. H. KANG\* (KOREA ADVANCED INSTITUTE OF SCIENCE AND TECHNOLOGY, DAEJEON, KOREA)

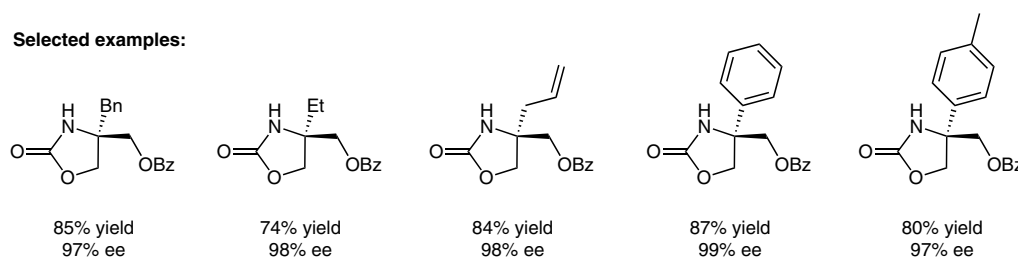
Asymmetric Formation of *tert*-Alkylamines from Serinols by a Dual Function Catalyst

*Chem. Commun.* **2013**, 49, 9669–9671.

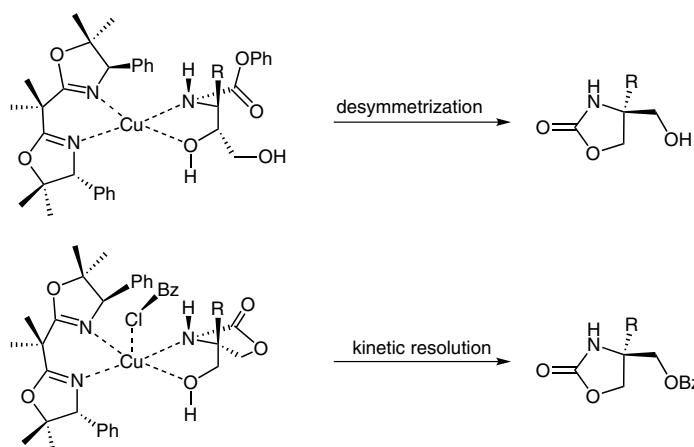
## Consecutive Intramolecular Desymmetrization and Kinetic Resolution



Selected examples:



Proposed intermediates in desymmetrization and kinetic resolution:



**Significance:** This paper describes the consecutive intramolecular desymmetrization and kinetic resolution of 2-substituted *N*-phenoxyserinols by using bisoxazoline- $\text{CuCl}_2$ . The reaction products are obtained in good yield and excellent enantioselectivities (94–99% ee).

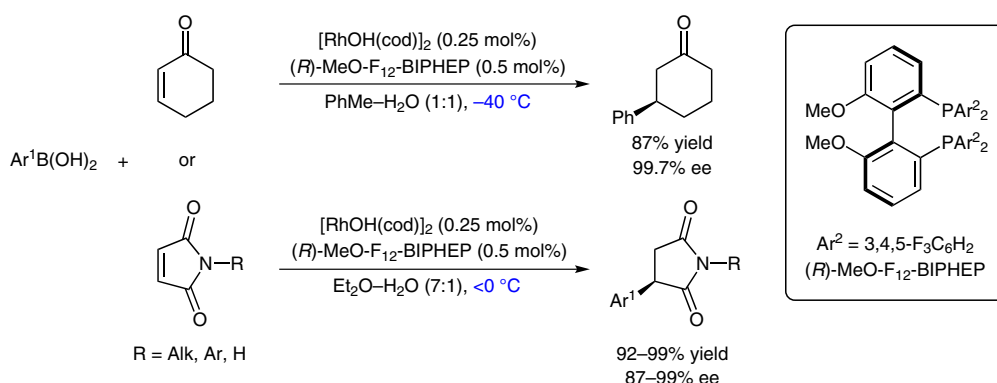
**Comment:** The authors developed a unique asymmetric catalysis system using a single chiral Lewis acid catalyst, which steers two consecutive asymmetric reactions of intramolecular desymmetrization and kinetic resolution. The two successive chemical conversions became unusually enantioselective, resulting in the production of the oxazolidinone benzoates with excellent enantioselectivities, which signifies a powerful and synergistic dual function catalyst effect by a chiral catalyst.

**SYNFACTS Contributors:** Hisashi Yamamoto, Atsuto Izumiseki  
Synfacts 2014, 10(1), 0048 Published online: 13.12.2013  
**DOI:** 10.1055/s-0033-1340432; **Reg-No.:** H15313SF

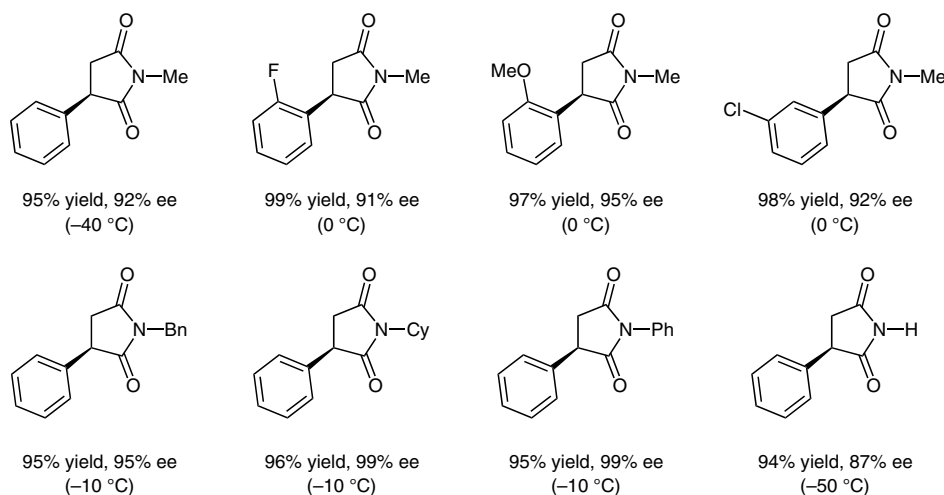
2014 © THIEME STUTTGART • NEW YORK



# Enantioselective Low-Temperature 1,4-Addition of Arylboronic Acids



## Selected examples:



**Significance:** Although various chiral rhodium catalysts have been developed, the rhodium-catalyzed asymmetric conjugate addition of arylboronic acids to  $\alpha,\beta$ -unsaturated carbonyl compounds below  $0\text{ }^\circ\text{C}$  has not been achieved. This paper describes the rhodium-catalyzed enantioselective 1,4-addition of arylboronic acids at low temperature. The use of the highly electron-poor  $(R)\text{-MeO-F}_{12}\text{-BIPHEP}$  ligand can retain the activity of the rhodium catalyst, which can serve to improve enantioselectivities.

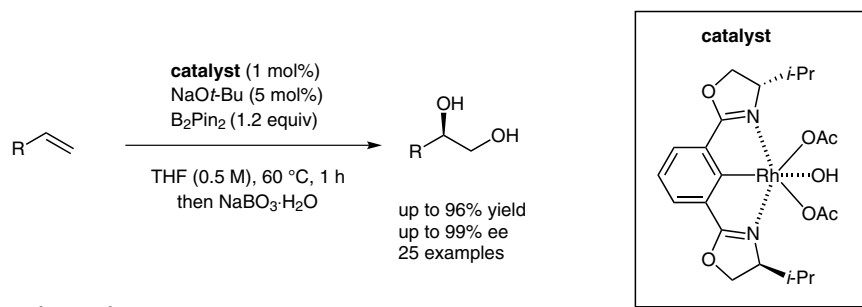
**Comment:** A variety of *N*-substituted maleimides are applicable to this method, affording the corresponding chiral succinimides in excellent yields and enantioselectivities. Notably, the enantioselective 1,4-addition to *N*-H-maleimide, which has been reported as an inactive substrate for rhodium-catalyzed asymmetric 1,4-addition, is also successful. When the reaction is performed at  $-50\text{ }^\circ\text{C}$ , the enantioselectivity is improved to up to  $87\%$  ee.

K. TORIBATAKE, H. NISHIYAMA\* (NAGOYA UNIVERSITY, JAPAN)

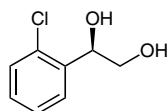
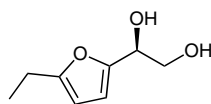
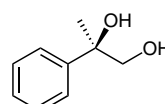
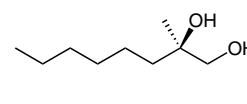
Asymmetric Diboration of Terminal Alkenes with a Rhodium Catalyst and Subsequent Oxidation: Enantioselective Synthesis of Optically Active 1,2-Diols

*Angew. Chem. Int. Ed.* **2013**, 52, 11011–11015.

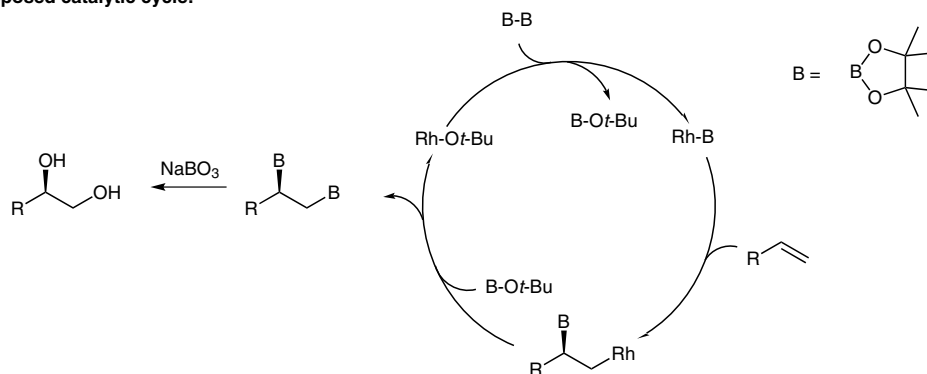
# Rhodium-Catalyzed Enantioselective Synthesis of 1,2-Diols



## Selected examples:

96% yield  
99% ee71% yield  
95% ee71% yield  
76% ee69% yield  
93% ee

## Proposed catalytic cycle:

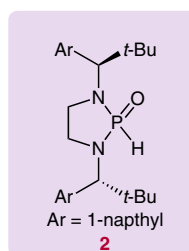
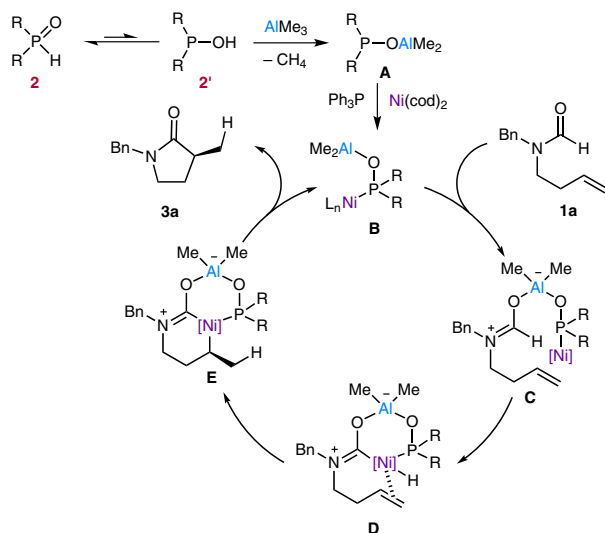
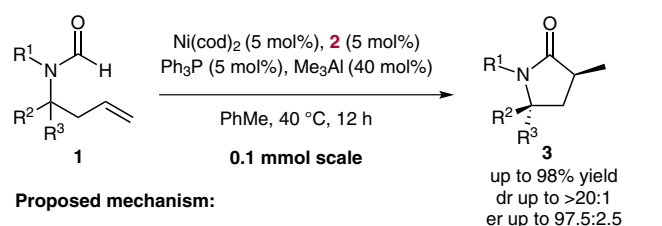


**Significance:** Chiral diols are useful synthetic motifs in organic synthesis. Common methods for their synthesis include dihydroxylation, hydrogenation of hydroxyketones, and hydrolysis of epoxides. The authors report an enantioselective 1,2-diboration of alkenes leading to optically active diols after oxidation.

**Comment:** Morken showed a similar diboration of terminal alkenes with a platinum catalyst with enantioselectivities up to 94% (*J. Am. Chem. Soc.* **2009**, 131, 13210). The authors present a rhodium-catalyzed diboration–oxidation of terminal alkenes providing enantioselectivities up to 99%. However, disubstituted alkenes proved to be more difficult. 1-Methylstyrene gave the diol with a moderate 76% ee, whereas  $\beta$ -methylstyrene, 1,2-dihydronaphthalene, and *trans*-stilbene did not react.

**SYNFACTS Contributors:** Mark Lautens, Zafar Qureshi  
Synfacts 2014, 10(1), 0050 Published online: 13.12.2013  
**DOI:** 10.1055/s-0033-1340442; **Reg-No.:** L15213SF

## Asymmetric Nickel-Catalyzed Hydrocarbamoylation of Alkenes



**Significance:** Secondary phosphine oxides (SPO's) have demonstrated to be versatile and robust preligands in a variety of transition-metal-catalyzed transformations due to their stability to air and moisture (see Review below). The authors report the development of a heterobimetallic catalyst system consisting of aluminum and nickel scaffolded on a chiral SPO tether, which enables the enantioselective intramolecular hydrocarbamoylation of alkenes. This method provides access to enantio-enriched pyrrolidones.

**Review:** N. V. Dubrovina, A. Börner *Angew. Chem. Int. Ed.* **2004**, *43*, 5883–5886.

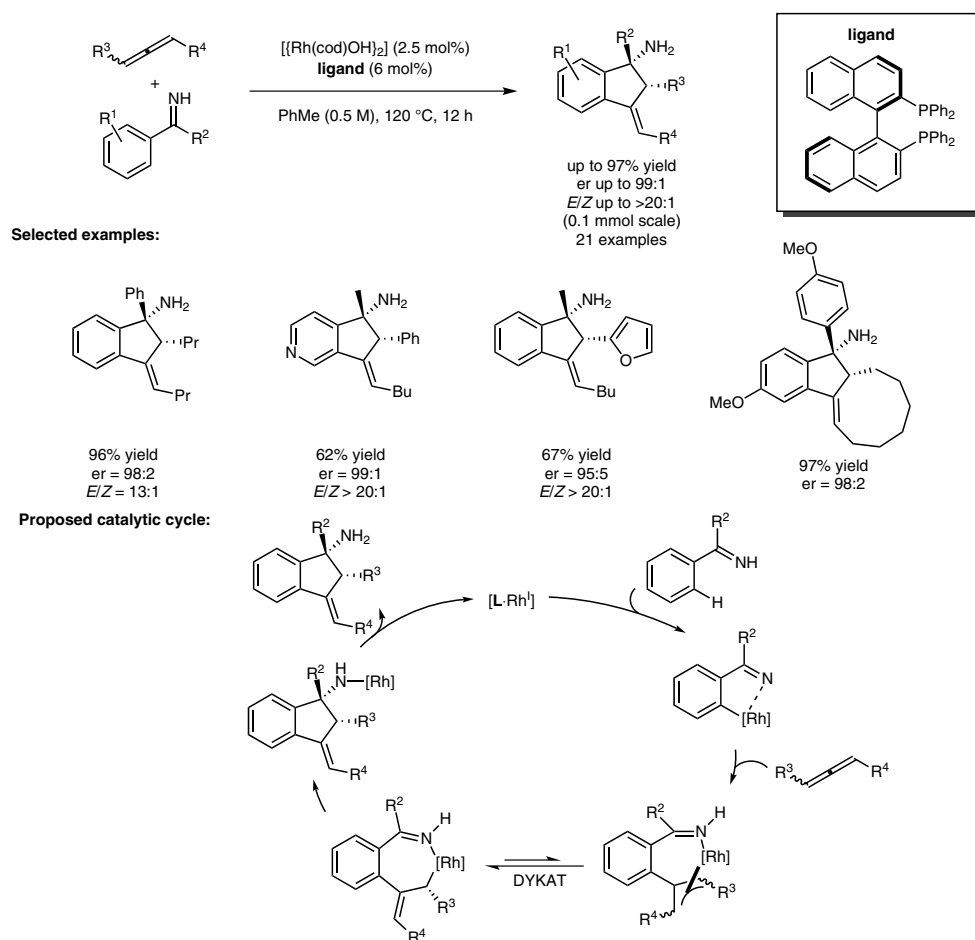
**Comment:** The reaction is believed to initiate via tautomerization of pentavalent phosphine oxide **2** to its trivalent phosphinous acid form, **2'**, which can react with  $\text{Me}_3\text{Al}$  and form complex **A**. Coordination to nickel(0) generates the active heterobimetallic catalyst **B**, which complexes to substrate **1a** via the Lewis acidic aluminum center, activating the formyl group towards insertion. Following oxidative addition of nickel into the C–H bond, migratory insertion of the pendent olefin and reductive elimination regenerate the catalyst and furnish pyrrolidone **3a**.

D. N. TRAN, N. CRAMER\* (ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE, SWITZERLAND)

Rhodium-Catalyzed Dynamic Kinetic Asymmetric Transformations of Racemic Allenes by the [3+2] Annulation of Aryl Ketimines

*Angew. Chem. Int. Ed.* **2013**, 52, 10630–10634.

## Enantioselective Rhodium-Catalyzed DYKAT of Racemic Allenes



**Significance:** Chiral amines are present in numerous biologically active compounds (see Book below). Starting from readily accessible racemic allenes, the authors were able to access indane structures containing chiral amines via a dynamic kinetic asymmetric transformation (DYKAT) in a [3+2] cycloaddition.

**Book:** *Chiral Amine Synthesis*: T. C. Nugent, Ed.; Wiley-VCH: Weinheim, **2010**.

**Comment:** The rhodium hydride, formed by the initial directed C–H activation, adds across the racemic allene forming a rhodium allyl species. The rhodium allyl species can then interconvert via  $\sigma$ - $\pi$ - $\sigma$  isomerization leading to a chiral intermediate which adds to the imine (see below for a Review on axis-to-center chirality transfer).

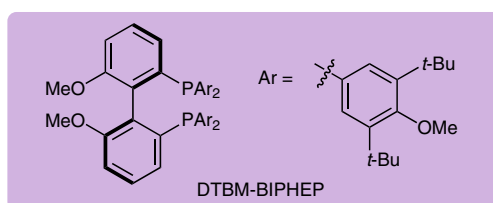
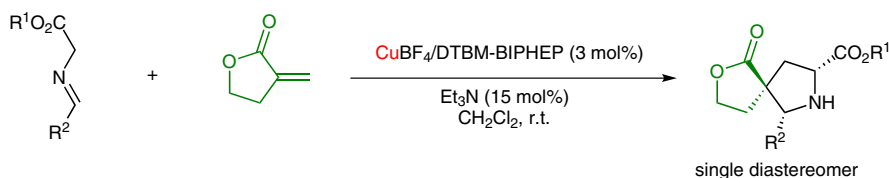
**Review:** N. Krause, C. Winter *Chem. Rev.* **2011**, 111, 1994–2009.

**SYNFACTS Contributors:** Mark Lautens, Zafar Qureshi  
Synfacts 2014, 10(1), 0052 Published online: 13.12.2013  
**DOI:** 10.1055/s-0033-1340440; **Reg-No.:** L15013SF

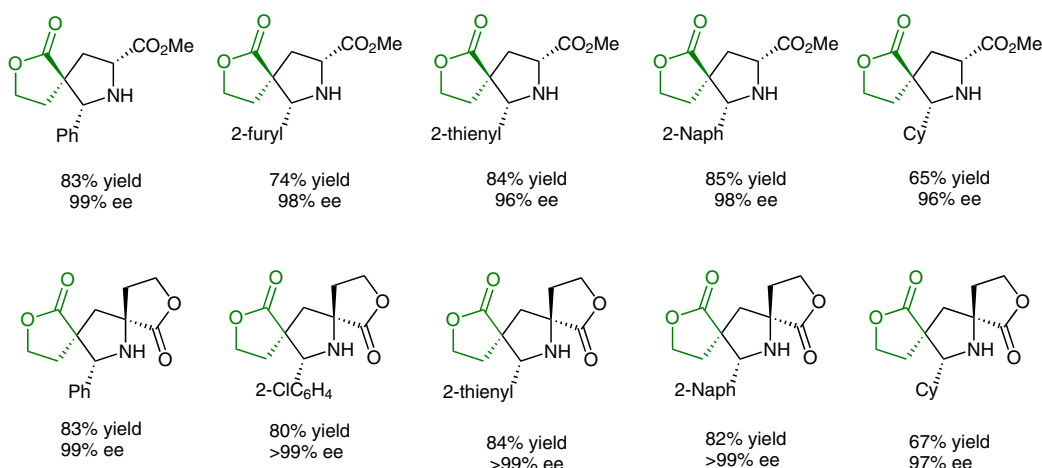
2014 © THIEME STUTTGART • NEW YORK

Q.-H. LI, T.-L. LIU, L. WEI, X. ZHOU, H.-Y. TAO, C.-J. WANG\* (WUHAN UNIVERSITY AND SHANGHAI INSTITUTE OF ORGANIC CHEMISTRY, P. R. OF CHINA)  
*exo*-Selective Construction of Spiro-[Butyrolactone-Pyrrolidine] via 1,3-Dipolar Cycloaddition of Azomethine Ylides with  $\alpha$ -Methylene- $\gamma$ -butyrolactone Catalyzed by Cu(I)/DTBM-BIPHEP  
*Chem. Commun.* **2013**, 49, 9642–9644.

## Synthesis of Spiro-[Butyrolactone-Pyrrolidine]



### Selected examples:



**Significance:** The authors developed an asymmetric synthesis of spiro-[butyrolactone-pyrrolidine] catalyzed by Cu(I)-DTBM-BIPHEP delivering *exo*-selective 1,3-dipolar cycloadducts of azomethine ylides and  $\alpha$ -methylene- $\gamma$ -butyrolactone. In all cases excellent chemical yields and stereo-selectivities were achieved.

**Comment:** Several natural alkaloids and important biological compounds contain spiro-[butyrolactone-pyrrolidine] as core structure making them very attractive targets in the synthetic community. Thus, this finding for the syntheses of bicyclic and tricyclic skeletons with multiple quaternary stereogenic centers is very attractive.

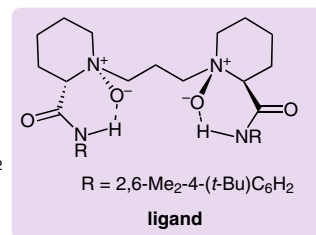
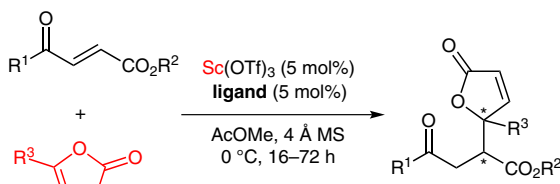
**SYNFACTS Contributors:** Hisashi Yamamoto, Biplab Maji  
 Synfacts 2014, 10(1), 0053 Published online: 13.12.2013  
 DOI: 10.1055/s-0033-1340434; Reg-No.: H15513SF

J. JI, L. LIN, L. ZHOU, Y. ZHANG, Y. LIU, X. LIU, X. FENG\* (SICHUAN UNIVERSITY, CHENGDU, P. R. OF CHINA)

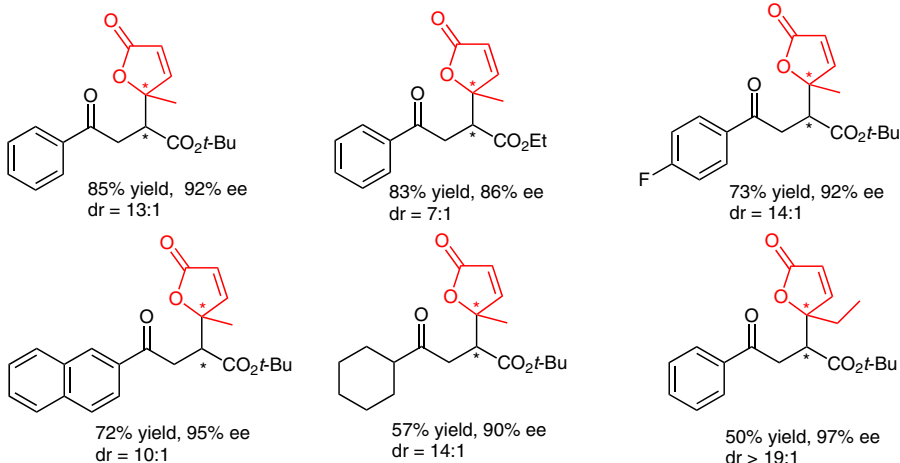
$N,N'$ -Dioxide–Scandium(III)-Catalyzed Asymmetric Michael Addition of  $\beta,\gamma$ -Unsaturated Butenolides to  $\alpha,\beta$ -Unsaturated  $\gamma$ -Keto Esters

*Adv. Synth. Catal.* **2013**, 355, 2764–2768.

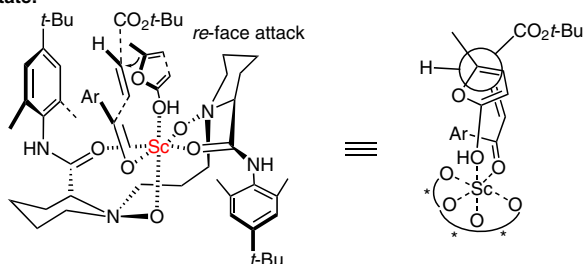
## $N,N'$ -Dioxide–Scandium(III)-Catalyzed Asymmetric Michael Addition



### Selected examples:



### Proposed transition state:

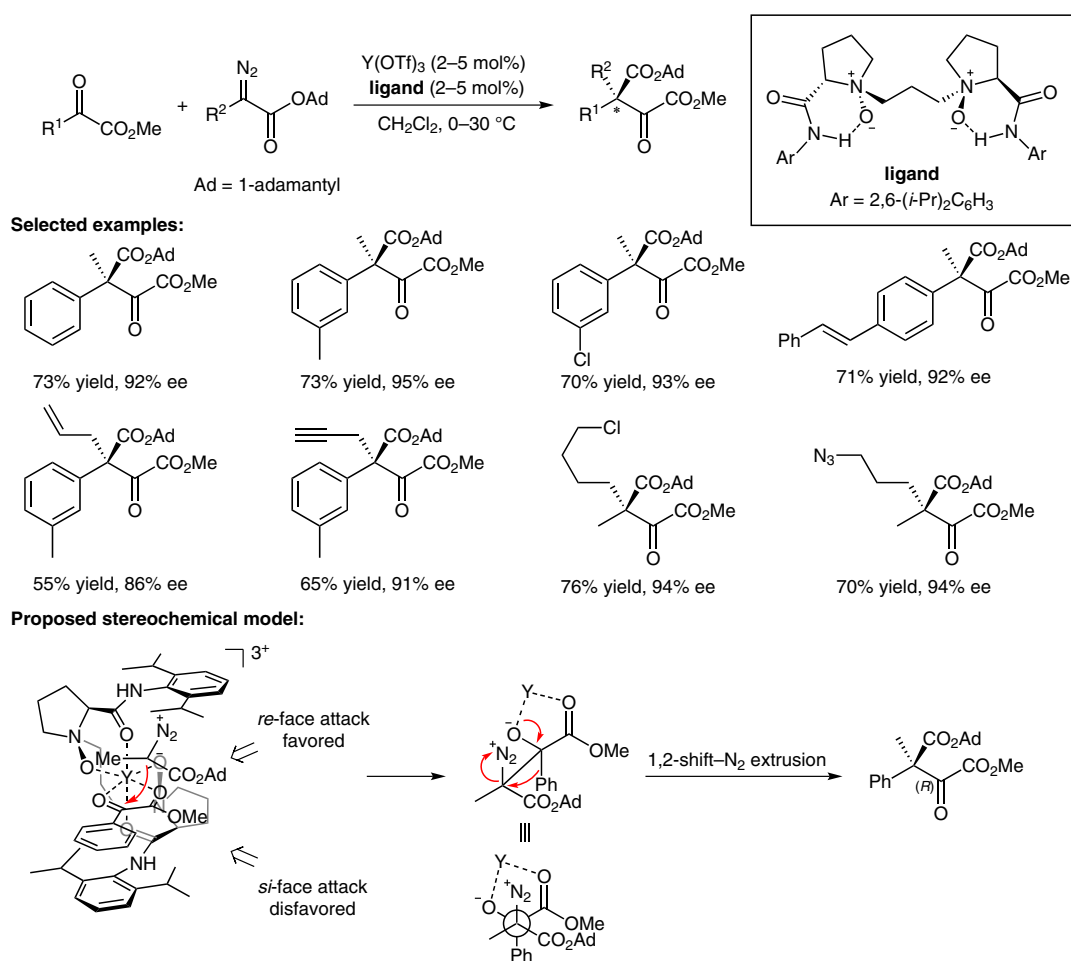


**Significance:** Butenolide derivatives represent an important structural motif in natural products and pharmaceuticals. The authors develop a highly efficient catalytic system for the asymmetric vinylogous Michael addition of  $\gamma$ -substituted butenolides to  $\alpha,\beta$ -unsaturated  $\gamma$ -keto esters, leading to  $\gamma,\gamma$ -disubstituted butenolides in good yield and excellent enantioselectivities.

**SYNFACTS Contributors:** Hisashi Yamamoto, Fengtao Zhou  
Synfacts 2014, 10(1), 0054 Published online: 13.12.2013  
**DOI:** 10.1055/s-0033-1340455; **Reg-No.:** H16213SF

**Comment:** The substrate scope of this reaction is well investigated. The ester groups of the  $\alpha,\beta$ -unsaturated  $\gamma$ -keto esters display an influence on both diastereo- and enantioselectivity. The bulkier  $\gamma$ -substituted groups in the butenolides lead to the increase of diastereo- and enantioselectivity, but the reactivities decrease obviously. Aromatic and aliphatic unsaturated  $\gamma$ -keto esters are well tolerated.

# Enantioselective Homologation of $\alpha$ -Keto Esters with $\alpha$ -Diazo Esters



**Significance:** The Lewis acid catalyzed homologation of carbonyl compounds with diazo compounds can realize synthetically useful carbon chain extension. The authors achieve the asymmetric homologation of acyclic  $\alpha$ -keto esters with  $\alpha$ -diazo esters by using chiral  $N,N'$ -dioxide-ylttrium(III) complexes. Both aryl- and alkyl-substituted  $\alpha$ -keto esters are applicable, providing the corresponding succinate derivatives in good yields and enantioselectivities.

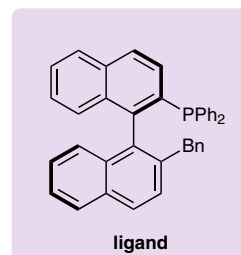
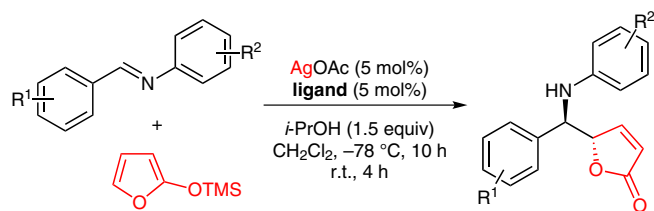
**SYNFACTS Contributors:** Hisashi Yamamoto, Yusuke Ano  
Synfacts 2014, 10(1), 0055 Published online: 13.12.2013

**DOI:** 10.1055/s-0033-1340454; **Reg-No.:** H16113SF

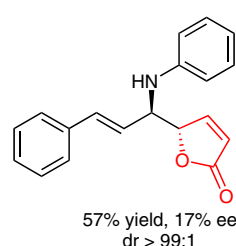
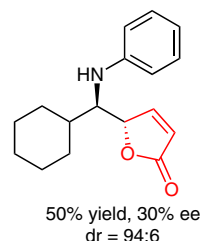
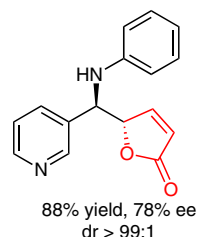
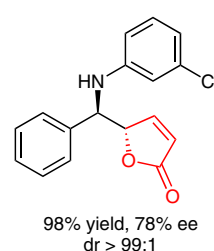
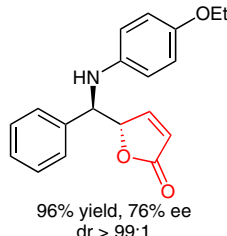
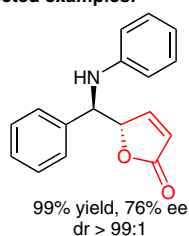
**Comment:** The use of bulky adamantyl  $\alpha$ -diazo esters can suppress the formation of undesired by-products. Steric hindrance on the 2,6-positions of the phenyl ring in the ligand is also essential to improve both enantioselectivity and reactivity. The attack of  $\alpha$ -diazo ester occurs from  $re$ -face of the coordinating  $\alpha$ -keto ester preferably due to the obstruction of  $si$ -face by the aryl group in the  $N,N'$ -dioxide ligand.

L.-S. ZHENG, L. LI, K.-F. YANG, Z.-J. ZHENG, X.-Q. XIAO, L.-W. XU\* (HANGZHOU NORMAL UNIVERSITY AND LANZHOU INSTITUTE OF CHEMICAL PHYSICS, P. R. OF CHINA)  
New Silver(I)–Monophosphine Complex Derived from Chiral Ar-BINMOL: Synthesis and Catalytic Activity in Asymmetric Vinyllogous Mannich Reaction  
*Tetrahedron* **2013**, *69*, 8777–8784.

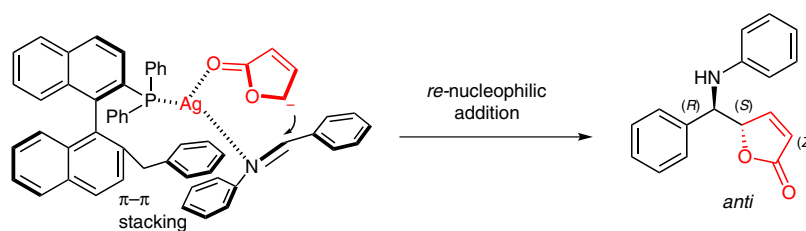
## Silver(I)–Monophosphine-Catalyzed Asymmetric Mannich Reaction



### Selected examples:



### Proposed transition state:



**Significance:** The authors developed a new class of axially chiral monophosphine ligands for silver-catalyzed asymmetric reactions. This catalytic system shows good catalytic activities and good enantioselectivities in an asymmetric vinyllogous Mannich reaction.

**SYNFACTS Contributors:** Hisashi Yamamoto, Fengtao Zhou  
Synfacts 2014, 10(1), 0056 Published online: 13.12.2013  
**DOI:** 10.1055/s-0033-1340456; **Reg-No.:** H16313SF

**Comment:** These air-stable ligands can be synthesized easily on gram scale in good yields from available starting materials. The benzyl group of the chiral monophosphine not only offers weak silver- $\pi/\pi$  stacking, but also provides steric repulsion to favor the diastereoselective *re*-nucleophilic addition of siloxyfuran to the imine.

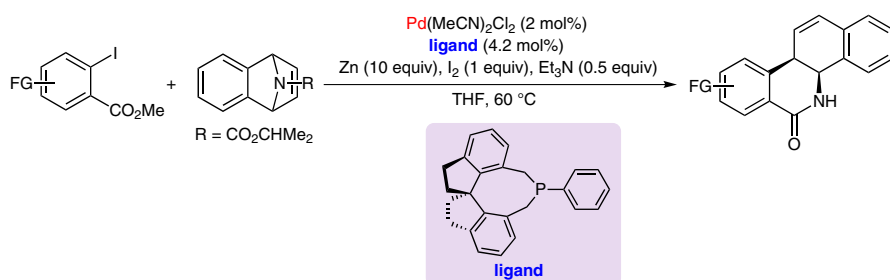


K.-L. HUANG, C. GUO, L.-J. CHENG, L.-G. XIE, Q.-L. ZHOU, X.-H. XU,\* S.-F. ZHU\* (NANKAI UNIVERSITY, TIANJIN, P. R. OF CHINA)

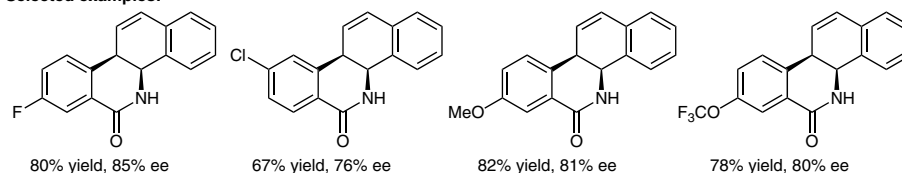
Enantioselective Palladium-Catalyzed Ring-Opening Reaction of Azabenzonorbornadienes with Methyl 2-Iodobenzoate: An Efficient Access to *cis*-Dihydrobenzo[*c*]phenanthridinones

*Adv. Synth. Catal.* **2013**, 355, 2833–2838.

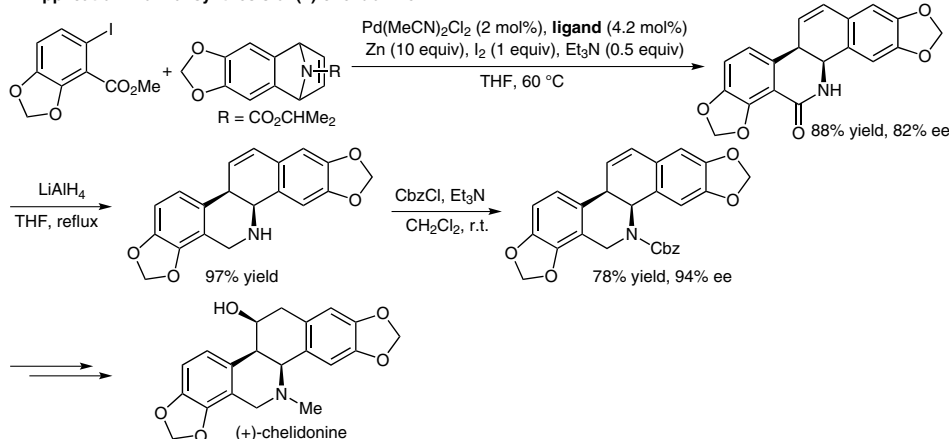
## Pd-Catalyzed Asymmetric Ring Opening of Azabenzonorbornadienes



Selected examples:



Application: Formal synthesis of (+)-chelidonine:



**Significance:** In the presence of electron-rich chiral spirophosphine ligands,  $I_2$  as key additive, and zinc powder as reducing agent,  $Pd(MeCN)_2Cl_2$  efficiently catalyzes the ring opening of azabenzonorbornadiene with various 2-iodobenzoates. The resulting enantioenriched *cis*-dihydrobenzo[*c*]phenanthridinones serve as core structure of numerous optically active natural products.

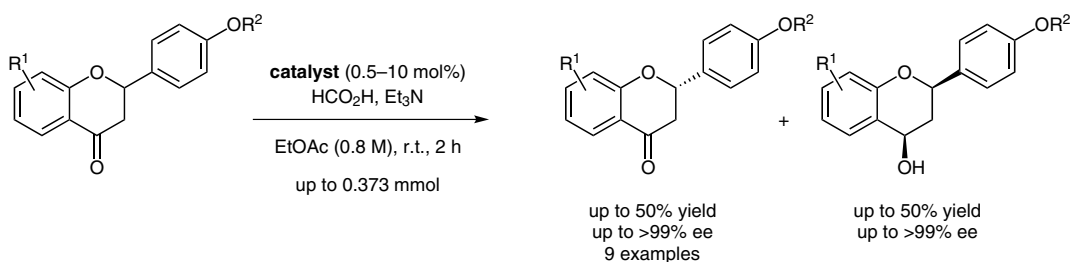
**Comment:** The use of easily available organic halides instead of organometallic reagents and the construction of fused ring systems with multiple stereocenters via the tandem asymmetric ring-opening–cyclization process make the strategy remarkably efficient. A direct application of the present methodology was demonstrated via the concise total synthesis of (+)-chelidonine.

**SYNFACTS Contributors:** Hisashi Yamamoto, Sukalyan Bhadra  
Synfacts 2014, 10(1), 0057 Published online: 13.12.2013

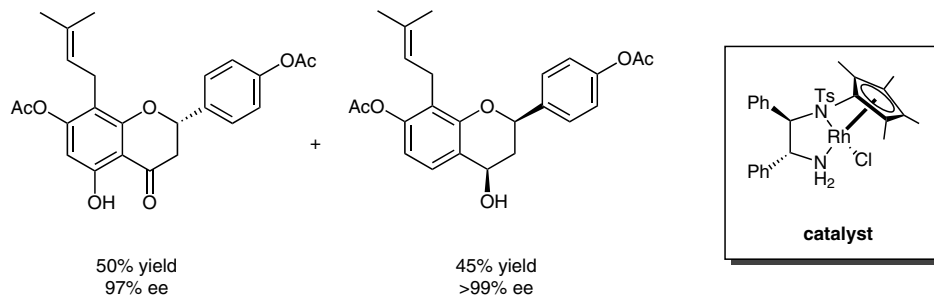
DOI: 10.1055/s-0033-1340438; Reg-No.: H15913SF

M.-K. LEMKE, P. SCHWAB, P. FISCHER, S. TISCHER, M. WITT, L. NOEHRINGER, V. ROGACHEV, A. JÄGER, O. KATAEVA, R. FRÖHLICH, P. METZ\* (TECHNISCHE UNIVERSITÄT DRESDEN UND WESTFÄLISCHE WILHELMS-UNIVERSITÄT MÜNSTER, GERMANY; TOMSK POLYTECHNIC UNIVERSITY, RUSSIA)  
A Practical Access to Highly Enantiomerically Pure Flavanones by Catalytic Asymmetric Transfer Hydrogenation  
*Angew. Chem. Int. Ed.* **2013**, 52, 11651–11655.

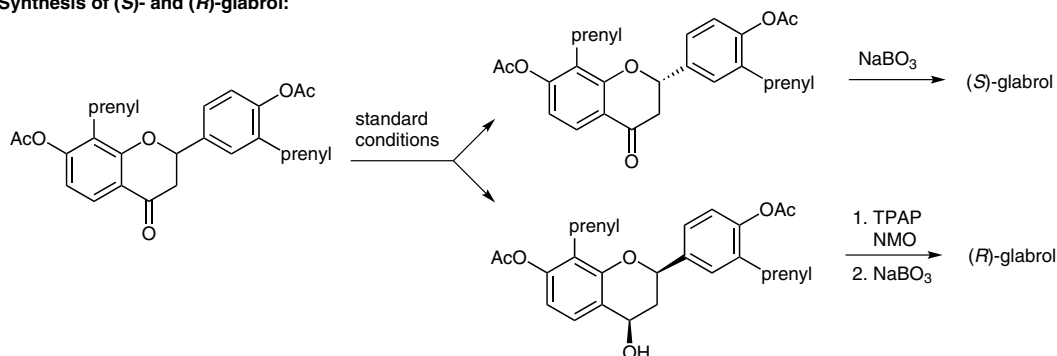
## Rhodium-Catalyzed Asymmetric Transfer Hydrogenation



### Selected examples:



### Synthesis of (*S*)- and (*R*)-glabrol:



**Significance:** Chiral flavanone moieties are among the largest secondary metabolites in plants. As such, they have been known for their antifungal, antibacterial, and antiviral effects. The authors present a practical and convenient method for the synthesis of both enantiomers of this class of molecules.

**Comment:** The catalytically active rhodium hydride species was generated in situ prior to the addition of the substrate. This method allowed the authors to reduce catalyst loading to 0.5 mol% while retaining high enantioselectivities. They were able to synthesize both enantiomers of the natural product glabrol.

**SYNFACTS Contributors:** Mark Lautens, Zafar Qureshi  
Synfacts 2014, 10(1), 0058 Published online: 13.12.2013  
DOI: 10.1055/s-0033-1340441; Reg-No.: L15113SF

2014 © THIEME STUTTGART • NEW YORK

B. FAN,\* S. LI, H. CHEN, Z. LU, S. LIU, Q. YANG, L. YU, J. XU, Y. ZHOU, J. WANG\*  
 (YUNNAN UNIVERSITY OF NATIONALITIES, KUNMING AND SOUTH UNIVERSITY OF  
 SCIENCE AND TECHNOLOGY OF CHINA, SHENZHEN, P. R. OF CHINA)  
 Palladium/Copper Complexes Co-Catalyzed Highly Enantioselective Ring Opening Reaction of  
 Azabenzonorbornadienes with Terminal Alkynes  
*Adv. Synth. Catal.* **2013**, 355, 2827–2832.

Category

Metal-Catalyzed  
 Asymmetric  
 Synthesis and  
 Stereoselective  
 Reactions

Key words

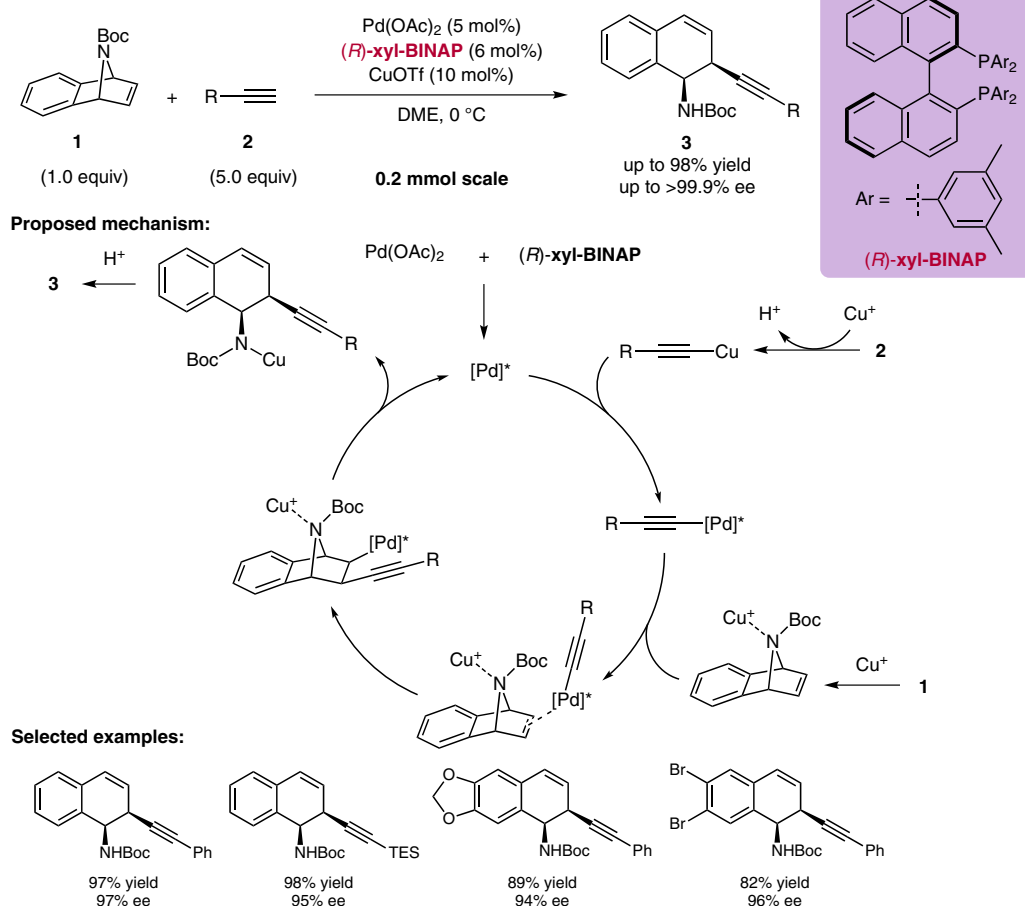
desymmetrization

asymmetric ring  
 opening

palladium

copper

# Ring Opening of Azabicyclic Alkenes Co-Catalyzed by Palladium and Copper



**Significance:** The ring opening of strained meso-heterobicyclic alkenes with different nucleophiles serves as a useful strategy for setting multiple stereocenters in a single transformation. Previous methods for this particular ring opening were limited to the use of bulky terminal acetylenes. Here, the authors report the development of a palladium and copper co-catalyzed system that exhibits broad substrate scope.

**Comment:** The authors propose that the copper(I) catalyst plays two distinct roles in the mechanism: (1) Copper facilitates transmetalation of the acetylene to palladium via the copper acetylide; (2) Copper behaves as a Lewis acid to activate the azabicyclic alkene. In addition to demonstrating wide functional group tolerance, the yields and enantioselectivities observed are excellent across the series of substrates tested.

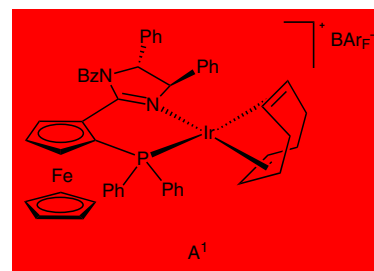
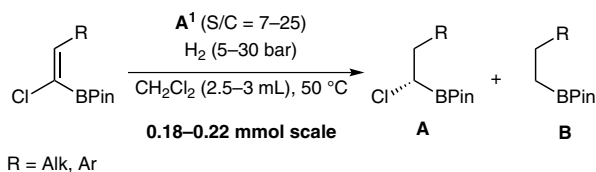
**SYNFACTS Contributors:** Mark Lautens, Christine M. Le  
*Synfacts* 2014, 10(1), 0059 Published online: 13.12.2013  
 DOI: 10.1055/s-0033-1340451; Reg-No.: L16113SF

S. J. ROSEBLADE, E. CASAS-ARCÉ, U. NETTEKOVEN, I. G. SMILOVIĆ, A. ZANOTTI-GEROSA, Z. ČASAR\* (JOHNSON MATTHEY, CAMBRIDGE, UK; SOLVIAS AG, KAISERAUGST, SWITZERLAND; LEK PHARMACEUTICALS, MENGEŠ, SOLVENIA; SANDOZ GMBH, KUNDL, AUSTRIA; UNIVERSITY OF LJUBLJANA, SOLVENIA)

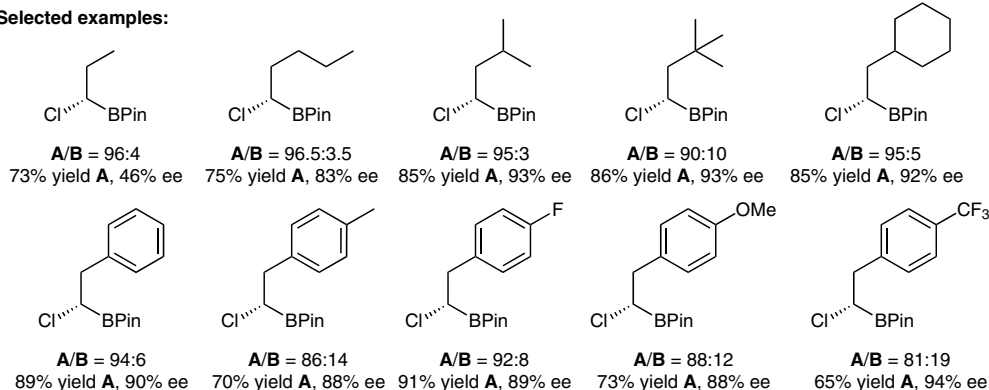
A Practical Synthetic Approach to Chiral ( $\alpha$ -Chloroalkyl)boronic Esters via Iridium-Catalyzed Chemoselective Hydrogenation of Chloro-Substituted Alkenyl Boronates  
*Synthesis* **2013**, 45, 2824–2831.

## Enantioselective Hydrogenation of Chloro-Substituted Alkenyl Boronates

Overall transformation:



Selected examples:



**Significance:** Enantioenriched ( $\alpha$ -chloroalkyl)boronic esters represent an important class of building blocks frequently used in organic synthesis. These chiral halogenated compounds are most commonly synthesized via Matteson-type rearrangements which use stoichiometric lithiated reagents, leading to stoichiometric waste streams. Transition-metal-catalyzed asymmetric hydrogenation has become the premier method for setting diversely substituted stereocenters with high enantiomeric excess under more environmentally friendly conditions. The authors report the synthesis of enantioenriched ( $\alpha$ -chloroalkyl)boronic esters via the iridium-catalyzed asymmetric hydrogenation of chloro-substituted alkenyl boronates.

**SYNFACTS Contributors:** Mark Lautens, David A. Petrone  
Synfacts 2014, 10(1), 0060 Published online: 13.12.2013  
**DOI:** 10.1055/s-0033-1340445; **Reg-No.:** L15513SF

**Comment:** The authors present a protocol for the enantioselective iridium-catalyzed hydrogenation of chloro-substituted alkenyl boronates using a ferrocenyl phosphinoimidazoline ligand. Good to excellent yields and enantioselectivities were obtained for both alkyl- and aryl-bearing substrates. Substrate-to-catalyst ratios (S/C) of up to 25 and hydrogen pressures as low as 5 bar are reported. This catalytic system benefits from a low amount of dechlorinated products resulting from over-reduction.

X. LIU, X. MA, Y. HUANG, Z. GU\* (UNIVERSITY OF SCIENCE AND TECHNOLOGY OF CHINA, HEFEI, P. R. OF CHINA)

Pd-Catalyzed Heck-Type Cascade Reactions with *N*-Tosyl Hydrazones: An Efficient Way to Alkenes via in Situ Generated Alkylpalladium

*Org. Lett.* **2013**, *15*, 4814–4617.

## Category

**Metal-Catalyzed Asymmetric Synthesis and Stereoselective Reactions**

## Key words

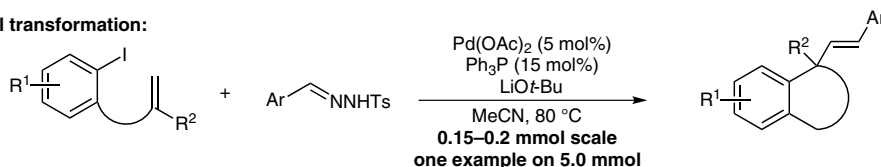
palladium

Heck reaction

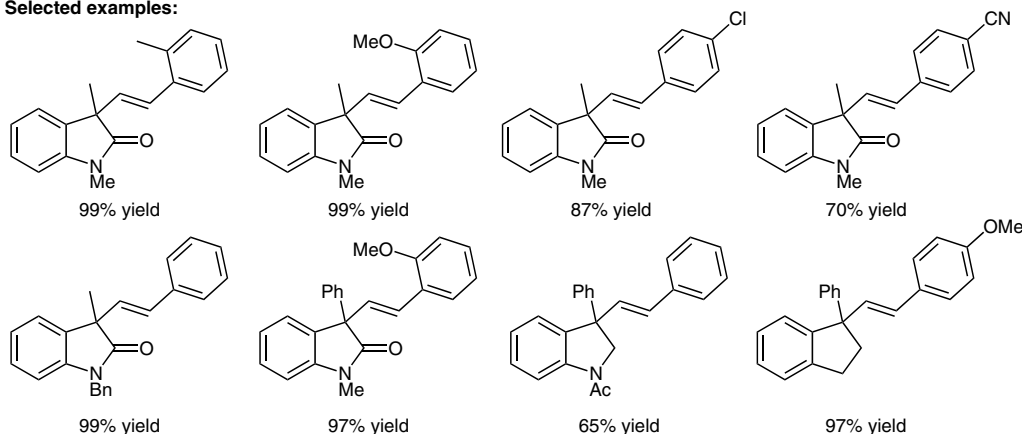
*N*-tosyl hydrazones

# Catalytic Alkenylation of Neopentyl Palladium Species Using *N*-Tosyl Hydrazones

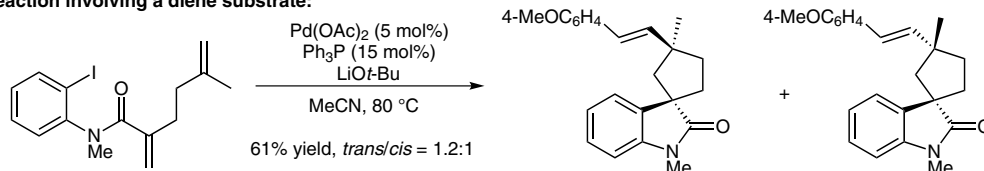
### Overall transformation:



### Selected examples:



### Reaction involving a diene substrate:



**Significance:** Palladium-catalyzed Heck-type cascades have long been used to install molecular complexity in a single transformation. In early pioneering work, Negishi and Grigg have reported cascade processes involving carbonylation sequences, Stille and Suzuki couplings, as well as C–H functionalization as terminating steps. However, despite these advances, terminations involving palladium carbenes have been far less explored. Gu and co-workers report the combination of *N*-tosyl hydrazone derived carbenes and in situ generated alkyl palladiums in a new alkenylation reaction.

**Comment:** The authors present a palladium-catalyzed Heck-type cascade reaction en route to alkene products. By terminating the cyclization sequence with a reaction with *N*-tosyl hydrazones, products can be obtained with high *E/Z* ratios. The method benefits from the ability to generate diverse hetero- and carbocycles in good to excellent yields under relatively mild conditions, using a simple palladium(II) pre-catalyst. Cyclization onto electron-deficient alkenes was shown to be preferred in a competition experiment involving a diene substrate.

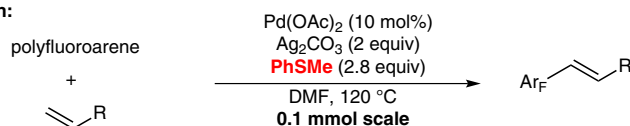
**SYNFACTS Contributors:** Mark Lautens, David A. Petrone  
Synfacts 2014, 10(1), 0061 Published online: 13.12.2013

**DOI:** 10.1055/s-0033-1340447; **Reg-No.:** L15713SF

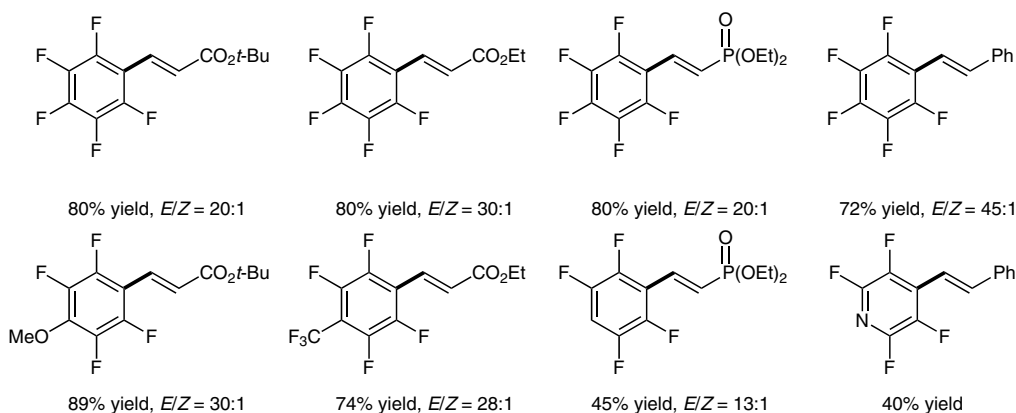
C.-Z. WU, C.-Y. HE, Y. HUANG, X. ZHANG\* (DONGHUA UNIVERSITY, SHANGHAI AND SHANGHAI INSTITUTE OF ORGANIC CHEMISTRY, P. R. OF CHINA)  
Thioether-Promoted Direct Olefination of Polyfluoroarenes Catalyzed by Palladium  
*Org. Lett.* **2013**, *15*, 5266–5269.

## Oxidative Olefination of Polyfluoroarenes Catalyzed by Palladium

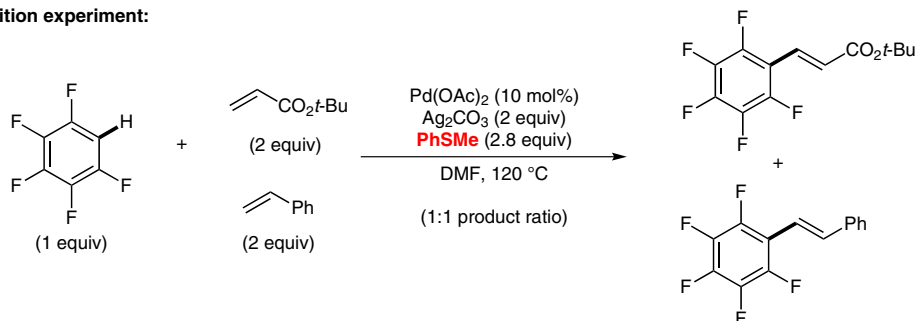
### Overall transformation:



### Selected examples:



### Competition experiment:

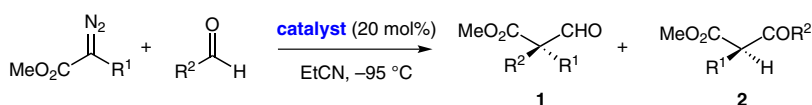


**Significance:** The dehydrogenative Heck reaction represents a more environmentally friendly variant of the classic Nobel prize winning transformation, as it makes use of non-prefunctionalized substrates. Polyfluoroarenes are important structural motifs, and the development of new methods to incorporate them in an efficient manner is an important endeavor. The report represents a rare example of a thioether promoted C–H functionalization of electron-deficient arenes.

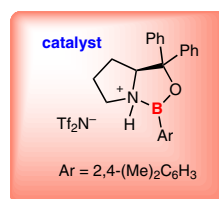
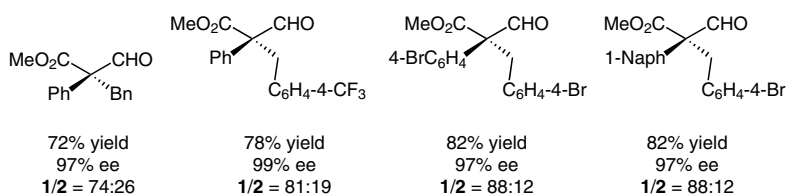
**SYNFACTS Contributors:** Mark Lautens, David A. Petrone  
Synfacts 2014, 10(1), 0062 Published online: 13.12.2013  
**DOI:** 10.1055/s-0033-1340448; **Reg-No.:** L15813SF

**Comment:** The authors report a palladium-catalyzed methyl phenyl sulfide promoted direct olefination of polyfluoroarenes. These previously ‘unreactive’ substrates undergo facile transformation with the specifically chosen sulfur-containing ligand. Products are obtained in good to excellent yields and with high E/Z selectivities. A competition reaction between pentafluorobenzene and both styrene and *tert*-butyl acrylate show that there is no bias between electron-rich and electron-deficient olefins under the reported conditions.

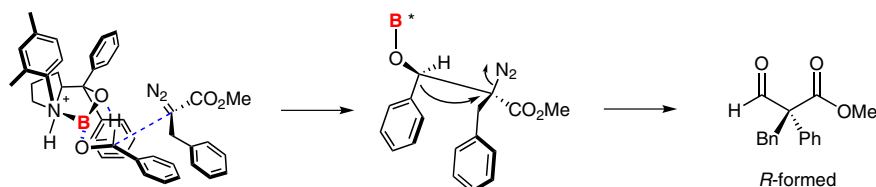
# Asymmetric Formal Insertion of Diazo Esters into Aryl-CHO Bonds



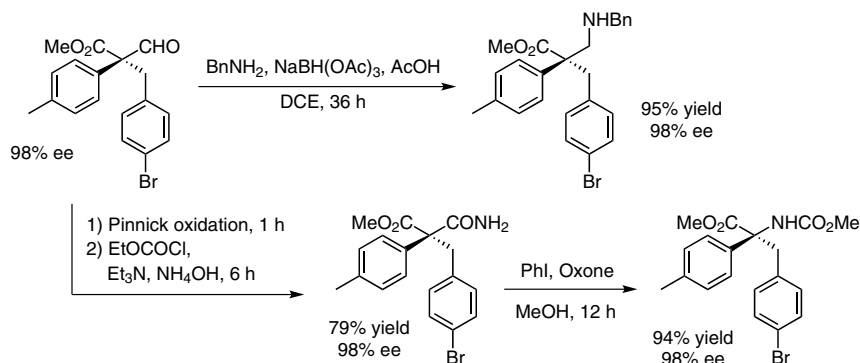
## Selected examples:



## Transition-state model:



## Applications:



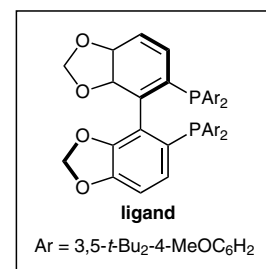
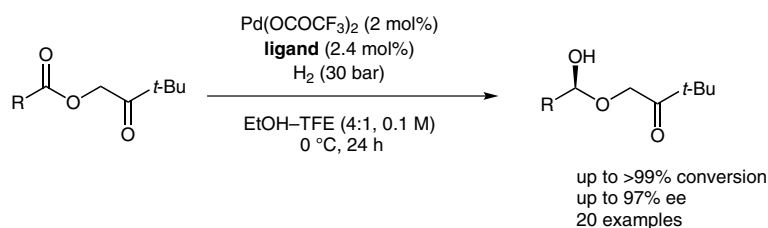
**Significance:** The authors developed an oxazaborolidinium ion catalyzed asymmetric formal C–C bond insertion of diazo esters into aryl-CHO bonds to give functionalized acyclic all-carbon  $\alpha$ -quaternary aldehydes in good yields (up to 83%) and excellent enantioselectivities (up to 99%). The products were transformed into synthetically useful  $\alpha$ - and  $\beta$ -amino esters with ease.

**Comment:** Contrary to the Roskamp reaction, the 1,2-aryl shift is preferred over the 1,2-hydride shift. It is the first catalytic asymmetric report of such a reaction. A variety of diazo esters and aldehydes were explored emphasizing synthetic flexibility. However, the regioselectivities are rather moderate (up to 88:12). Recently, Feng and co-workers reported a similar 1,2-aryl shift for the asymmetric homologation of  $\alpha$ -keto esters (*Angew. Chem. Int. Ed.* **2013**, *52*, 10883).

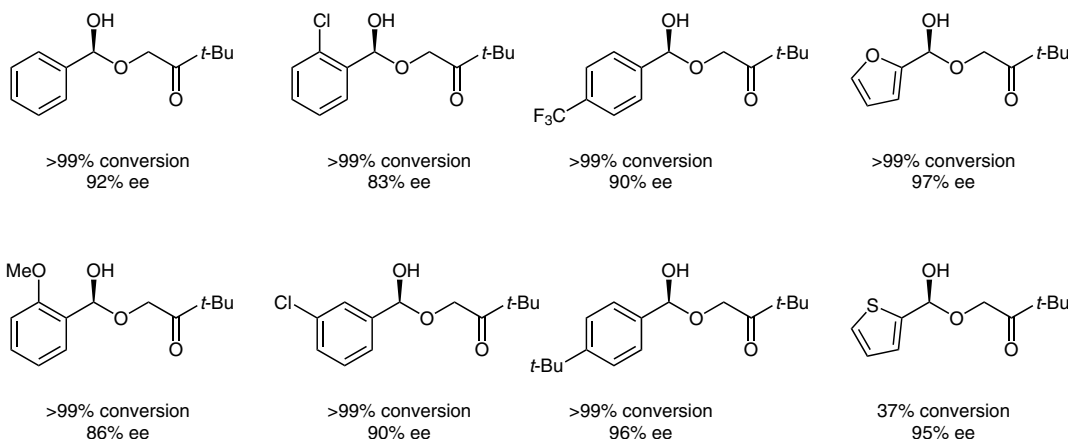
J. CHEN, D. LIU, N. BUTT, C. LI, D. FAN, Y. LIU, W. ZHANG\* (SHANGHAI JIAO TONG UNIVERSITY, P. R. OF CHINA)

Palladium-Catalyzed Asymmetric Hydrogenation of  $\alpha$ -Acyloxy-1-arylethanones  
*Angew. Chem. Int. Ed.* **2013**, 52, 11632–11636.

## Enantioselective Palladium-Catalyzed Allylic Dearomatization



### Selected examples:



**Significance:** Chiral  $\alpha$ -acyloxy-1-arylethanols are an important class of useful structural motifs (R. S. Bhondwea et al. *Bioorg. Med. Chem. Lett.* **2012**, 22, 3656). The authors report a palladium catalyzed enantioselective reduction of  $\alpha$ -acyloxy-1-arylethanones to access  $\alpha$ -acyloxy-1-arylethanols in high enantioselectivities.

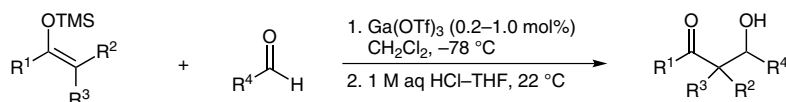
**Comment:** The first synthesis of  $\alpha$ -acyloxy-1-arylethanols was achieved using a chiral diamine ligand and SnCl<sub>2</sub> (T. Mukaiyama, K. Tomimori, T. Oriyama *Chem. Lett.* **1985**, 1359). Then, the use of enzymatic methods for their synthesis with excellent enantioselectivities but moderate regioselectivity was reported (A. Manzocchi, A. Fiecchi, E. Santaniello *J. Org. Chem.* **1988**, 53, 4405; T. Ema, Y. Sugiyama, M. Fukumoto, H. Moriya, J.-N. Cui, T. Sakai, M. Utaka *J. Org. Chem.* **1988**, 63, 4996; R. Hayakawa, M. Shimizu, T. Fujisawa *Tetrahedron Asymmetry* **1997**, 8, 3201). With a palladium catalyst and a bisphosphine ligand, the authors were able to show excellent selectivities for a variety of substrates. In addition, catalyst loadings could be lowered to 0.2 mol% without affecting enantioselectivity.

**SYNFACTS Contributors:** Mark Lautens, Zafar Qureshi  
Synfacts 2014, 10(1), 0064 Published online: 13.12.2013  
**DOI:** 10.1055/s-0033-1340444; **Reg-No.:** L15413SF

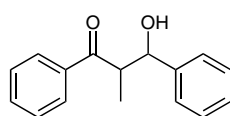
2014 © THIEME STUTTGART • NEW YORK



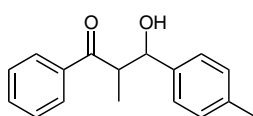
# Mukaiyama Aldol Reaction Catalyzed by Gallium(III) Triflate



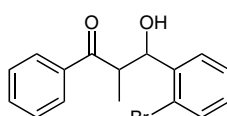
## Selected examples:



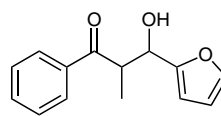
80% yield  
*syn/anti* = 85:15  
 90% yield  
*syn/anti* = 70:30  
 Ga(OTf)<sub>3</sub> (0.01 mol%)



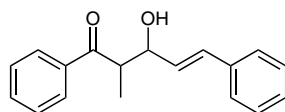
76% yield  
*syn/anti* = 80:20



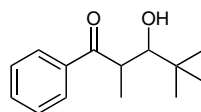
76% yield  
*syn/anti* = 18:82



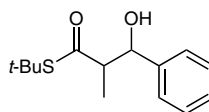
56% yield  
*syn/anti* = 87:13



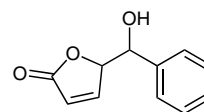
66% yield  
*syn/anti* = 82:18



46% yield  
*syn/anti* = 96:4



75% yield  
*syn/anti* = 66:34



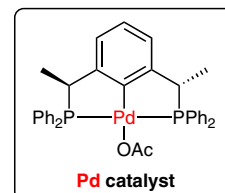
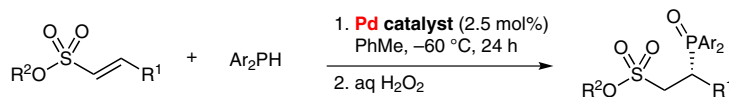
70% yield  
*syn/anti* = 69:31

**Significance:** The authors report a mild method for the diastereoselective Mukaiyama aldol reaction. The process is catalyzed by gallium(III) triflate yielding to the corresponding  $\beta$ -hydroxy ketones in up to 92% yield.

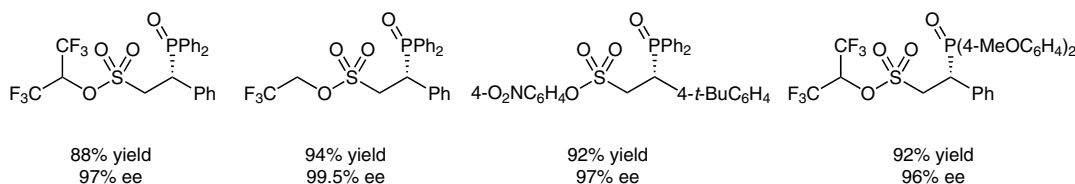
**Comment:** The developed method is an efficient aldol reaction under mild conditions with a very low catalyst loading of gallium(III) triflate (0.01–1.0 mol%). This is the first example of a metal triflate acting as a safe and stable slow-releasing source of triflic acid in the Mukaiyama aldol reaction. Gallium(III) triflate is a stable, easy-to-handle white solid.

J. LU, J. YE, W.-L. DUAN\* (SHANGHAI INSTITUTE OF ORGANIC CHEMISTRY AND EAST CHINA UNIVERSITY OF SCIENCE AND TECHNOLOGY, SHANGHAI, P. R. OF CHINA)  
Palladium-Catalyzed Asymmetric Addition of Diarylphosphines to  $\alpha,\beta$ -Unsaturated Sulfonic Esters for the Synthesis of Chiral Phosphine Sulfonate Compounds  
*Org. Lett.* **2013**, *15*, 5016–5019.

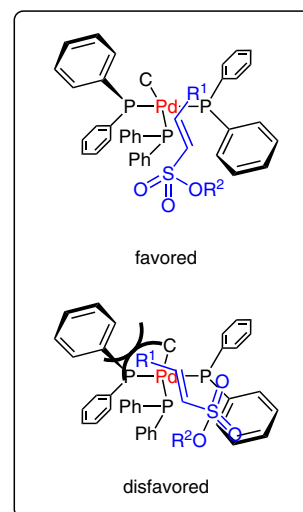
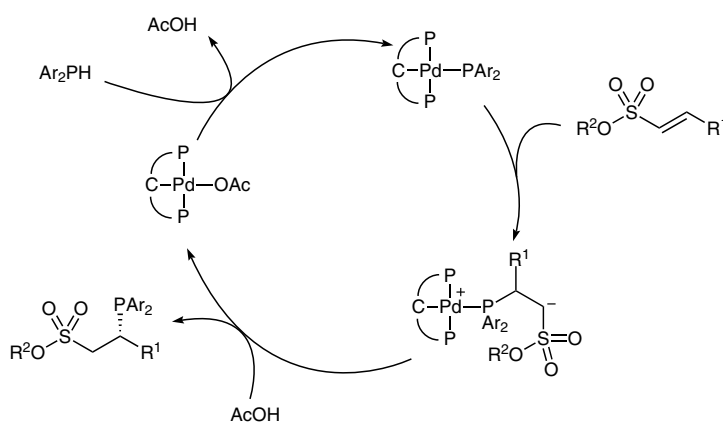
## Palladium-Catalyzed Asymmetric Synthesis of Phosphine Sulfonates



Selected examples:



Proposed catalytic cycle:



**Significance:** The authors reported the asymmetric conjugate addition of diarylphosphines to sulfonic esters catalyzed by a pincer-palladium complex. In the presence of an electron-withdrawing group in the sulfonic esters, phosphine sulfonates were obtained in high yields.

**Comment:** Introducing of heteroatoms into phosphine compounds is interesting since they can be used as ligands in metal-catalyzed transformations. Using this system, a highly enantioselective synthesis of phosphine sulfonates was achieved. The transformation of the product into the palladium complex was also demonstrated.

**SYNFACTS Contributors:** Hisashi Yamamoto, Yasushi Shimoda  
Synfacts 2014, 10(1), 0066 Published online: 13.12.2013  
DOI: 10.1055/s-0033-1340435; Reg-No.: H15613SF

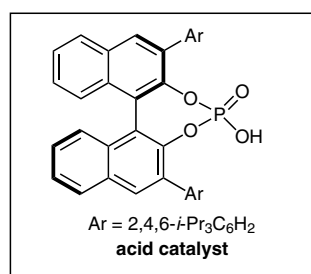
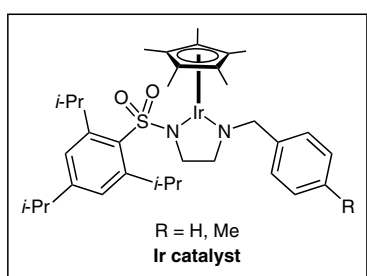
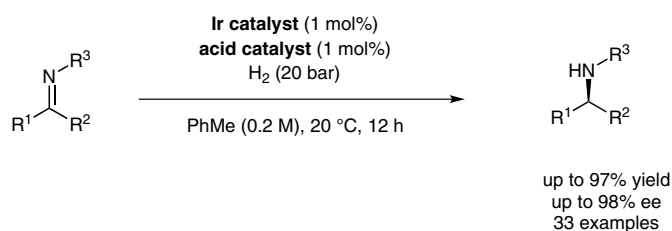
2014 © THIEME STUTTGART • NEW YORK

W. TANG, S. JOHNSTON, C. LI, J. A. IGGO, J. BACSA, J. XIAO\* (UNIVERSITY OF LIVERPOOL, UK)

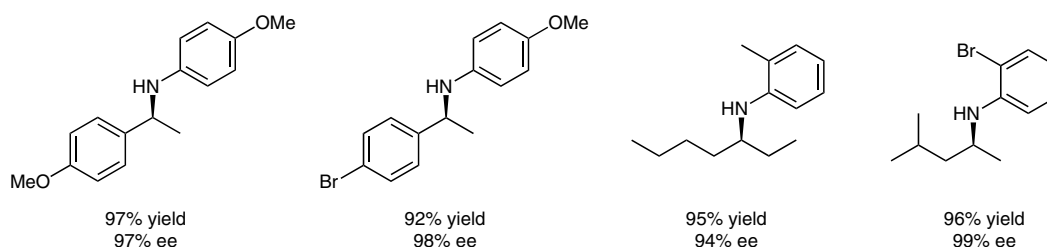
Cooperative Catalysis: Combining an Achiral Metal Catalyst with a Chiral Brønsted Acid Enables Highly Enantioselective Hydrogenation of Imines

*Chem. Eur. J.* **2013**, *19*, 14187–14193.

# Enantioselective Hydrogenation of Imines Using Cooperative Catalysis



## Selected examples:



**Significance:** Optically active amines are common in many fine chemicals, agrochemicals, and pharmaceuticals. The authors report a cooperative metal-organocatalytic system utilizing a chiral Brønsted acid and an achiral iridium catalyst (see below for a Review on transfer hydrogenation).

**Review:** C. Zheng, S.-L. You *Chem. Soc. Rev.* **2012**, *41*, 2498–2518.

**Comment:** The authors have reported the cooperative use of a chiral iridium catalyst with a chiral phosphoric acid in the asymmetric hydrogenation of acyclic imines with H<sub>2</sub> (*J. Am. Chem. Soc.* **2008**, *130*, 14450). Here, they report an achiral iridium catalyst with a chiral phosphoric acid in a similar reaction. Alkyl imines, which are known to be difficult substrates for asymmetric hydrogenation, were shown to be excellent substrates in this system, giving enantioselectivities up to 97%.

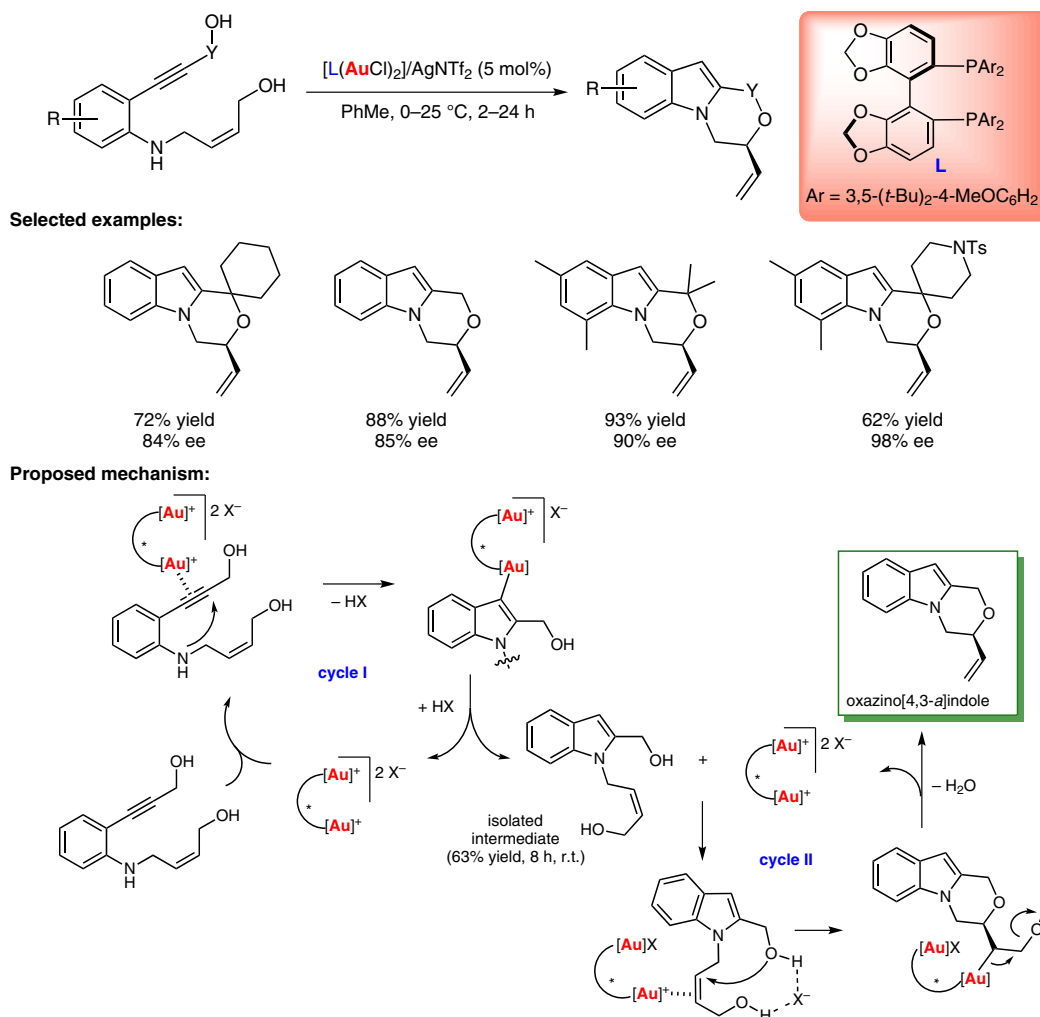
**SYNFACTS Contributors:** Mark Lautens, Zafar Qureshi  
Synfacts 2014, 10(1), 0067 Published online: 13.12.2013  
DOI: 10.1055/s-0033-1340443; Reg-No.: L15313SF

M. CHIARUCCI, R. MOCCI, L.-D. SYNTRIVANIS, G. CERA, A. MAZZANTI, M. BANDINI\*  
(UNIVERSITY OF BOLOGNA, ITALY)

Merging Synthesis and Enantioselective Functionalization of Indoles by a Gold-Catalyzed Asymmetric Cascade Reaction

*Angew. Chem. Int. Ed.* **2013**, *52*, 10850–10853.

## Oxazinoindoles via Gold-Catalyzed Stereoselective Cascade Reaction



**Significance:** The authors developed a gold-catalyzed hydroamination followed by an asymmetric nucleophilic allylic substitution cascade to access oxazino[4,3-*a*]indoles in good yields and enantioselectivities. Owing to pharmacologically active indole alkaloids, this rapid synthesis and asymmetric decoration of the polycyclic indolyl core is highly important.

**SYNFACTS Contributors:** Hisashi Yamamoto, Mahiuddin Baidya  
Synfacts 2014, 10(1), 0068 Published online: 13.12.2013  
**DOI:** 10.1055/s-0033-1340458; **Reg-No.:** H16513SF

**Comment:** Amazingly, the stereodifferentiating event in this gold-catalyzed asymmetric domino process takes place at the late stage, which is somewhat unusual and more challenging. Extensive mechanistic studies support the stepwise S<sub>N</sub>2'-type mechanism for the final allylic alkylation ring closure (cycle II).

W. DAI, J. LI, G. LI, H. YANG, L. WANG, S. GAO\* (DALIAN INSTITUTE OF CHEMICAL PHYSICS, DALIAN NATIONAL LABORATORY FOR CLEAN ENERGY AND UNIVERSITY OF CHINESE ACADEMY OF SCIENCES, BEIJING, P. R. OF CHINA)

Asymmetric Epoxidation of Alkenes Catalyzed by a Porphyrin-Inspired Manganese Complex

*Org. Lett.* **2013**, *15*, 4138–4141.

# Manganese-Catalyzed Enantioselective Alkene Epoxidation

Category

Metal-Catalyzed  
Asymmetric  
Synthesis and  
Stereoselective  
Reactions

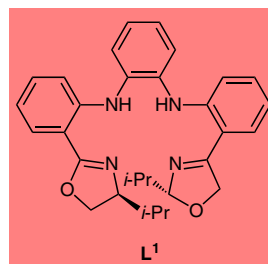
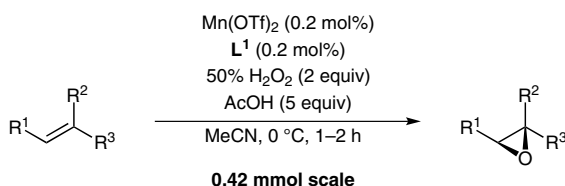
Key words

epoxidation

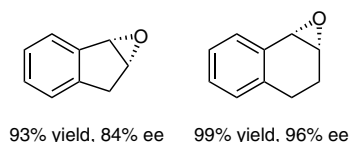
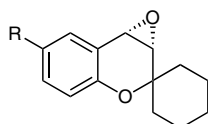
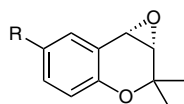
manganese

hydrogen peroxide

Overall transformation:

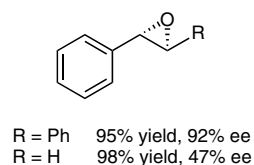


Selected examples:

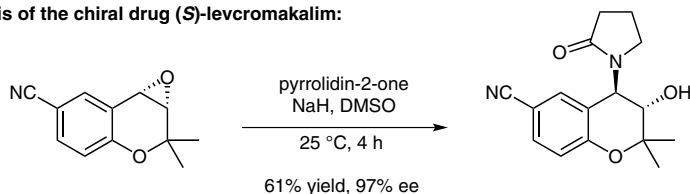


R = CN	95% yield, 95% ee
Cl	93% yield, 96% ee
Br	90% yield, 96% ee
NO <sub>2</sub>	93% yield, 94% ee
CO <sub>2</sub> Me	95% yield, 96% ee
Ph	98% yield, 94% ee
CH <sub>2</sub> OH	96% yield, >99% ee

R = CN	98% yield, 90% ee
Br	91% yield, 94% ee
NO <sub>2</sub>	92% yield, 92% ee
CO <sub>2</sub> Me	97% yield, 90% ee
Ph	99% yield, 96% ee
NHAc	99% yield, 98% ee



Gram-scale synthesis of the chiral drug (S)-levcromakalim:



**Significance:** Epoxides are an important class of molecules and serve frequently as intermediates in complex molecule synthesis. Many highly effective protocols have been developed for the generation of enantioenriched epoxides by way of transition-metal and organocatalysis. However, not all classes of substrates proceed smoothly with high levels of enantioselectivity under the published methods, and therefore the development of new and robust epoxidation methods is of great interest.

**Comment:** Gao and co-workers report the use of Jacobsen-type manganese-catalyzed epoxidation of chromenes, indenenes, styrenes, and dihydronaphthalenes using a porphyrin-inspired tetradentate ligand. Products are obtained in excellent yields and enantioselectivities using a low catalyst loading (0.2 mol%). This environmentally friendly method makes use of two equivalents of H<sub>2</sub>O<sub>2</sub> as the terminal oxidant. The authors were able to extend their methodology to the synthesis of the chiral drug (S)-levcromakalim.

**SYNFACTS Contributors:** Mark Lautens, David A. Petrone  
Synfacts 2014, 10(1), 0069    Published online: 13.12.2013  
DOI: 10.1055/s-0033-1340446; Reg-No.: L15613SF

2014 © THIEME STUTTGART • NEW YORK