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

Enantioselective Baeyer–Villiger Oxidation: Desymmetrization of Meso Cyclic Ketones and Kinetic Resolution of Racemic 2-Arylcyclohexanones

J. Am. Chem. Soc. **2012**, *134*, 17023–17026.

Category

Metal-Catalyzed Asymmetric Synthesis and Stereoselective Reactions

Key words

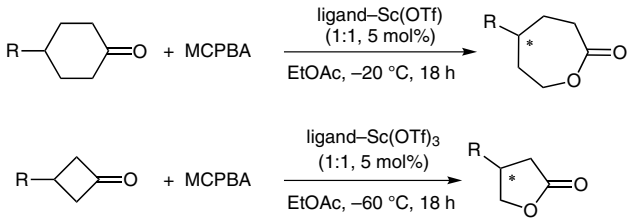
Baeyer–Villiger oxidation

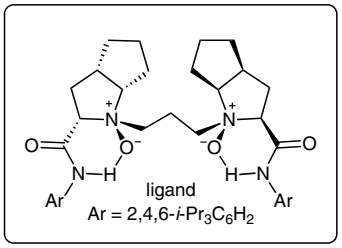
scandium

desymmetrization

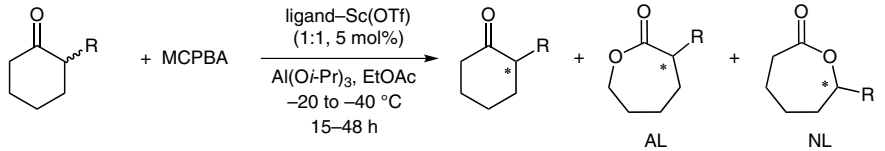
Enantioselective Baeyer-Villiger Oxidation

Desymmetrization of *meso*-cyclic ketones:

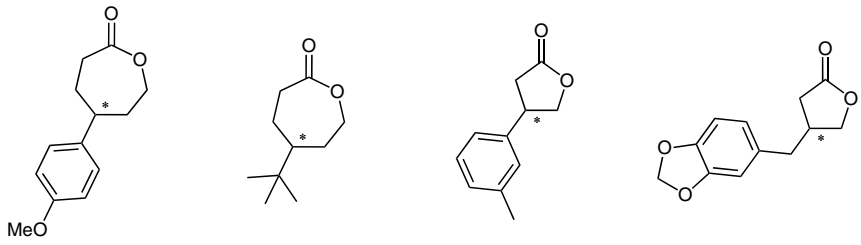




Kinetic resolution of racemic cyclohexanones:

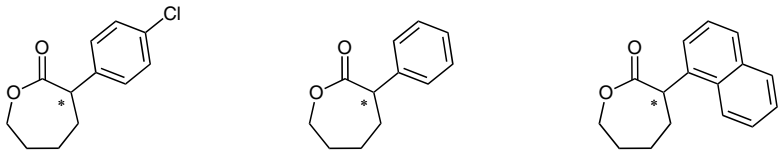


Selected examples of desymmetrization:



81% yield, 95% ee | 81% yield, 94% ee | 80% yield, 91% ee | 99% yield, 80% ee

Selected examples of kinetic resolution:



AL/NL > 19:1
93% ee (AL)

AL/NL = 16.5:1
90% ee (AL)

AL/NL > 19/1
99% ee (AL)

Significance: The asymmetric Baeyer–Villiger oxidation of prochiral and racemic cyclic ketones effectively synthesized optically active ε- and γ-lactones. The desymmetrization of racemic cyclohexanones interestingly showed a reversal of migratory aptitude with high levels of enantioselectivity.

Comment: The authors continued their use of chiral *N*,*N*′-dioxide-metal catalysts for the Baeyer–Villiger oxidation reaction. During the desymmetrization of *meso*-cyclohexanones and *meso*-cyclobutanones, the electronic and steric nature of the substituents appeared to have no effect on enantioselectivity; the opposite was true for the kinetic resolution of racemic cyclohexanones.

SYNFACTS Contributors: Hisashi Yamamoto, Kimberly Griffin
Synfacts 2013, 9(1), 0049 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317774; **Reg-No.:** H15412SF

Key words

palladium

bis(oxazoline) ligands

alkylazaarenes

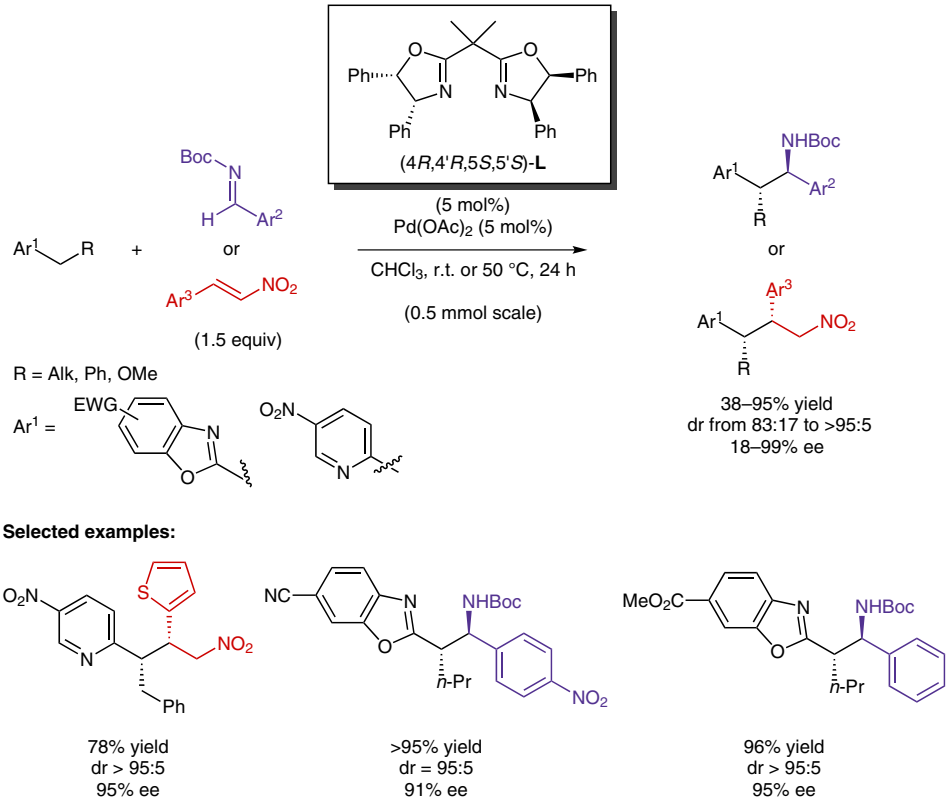
nitroalkenes

N-Boc imines

D. BEST, S. KUJAWA, H. W. LAM* (UNIVERSITY OF EDINBURGH, UK)

Diastereo- and Enantioselective Pd(II)-Catalyzed Additions of 2-Alkylazaarenes to *N*-Boc Imines and Nitroalkenes
J. Am. Chem. Soc. **2012**, *134*, 18193–18196.

Palladium-Catalyzed Asymmetric Addition of Alkylazaarenes to Imines and Nitroalkenes



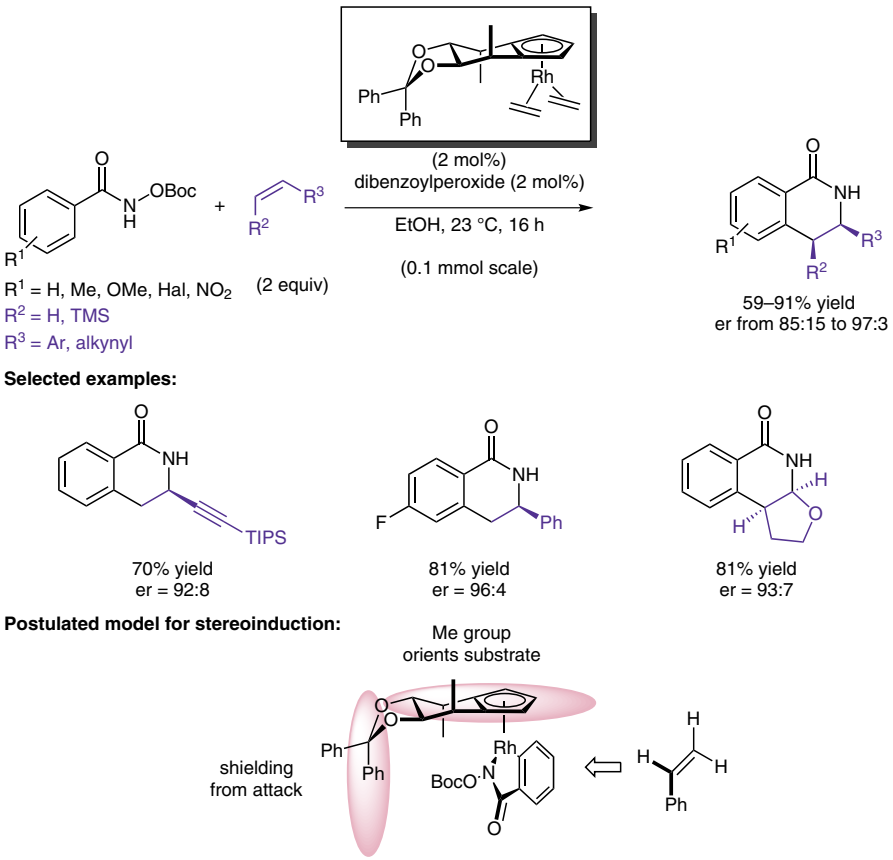
Significance: While precedence of the direct addition of alkylazaarenes to imines and nitroalkenes in a racemic manner exists, the authors report the use of a chiral palladium(II)–bis(oxazoline) catalyst that can render this reaction highly diastereo- and enantioselective. The reaction proceeds under practical conditions, employing undried solvent at mild temperatures and under an air atmosphere.

Comment: The use of electron-withdrawing groups on the azaarene facilitates the deprotonation of the benzylic position at lower temperatures, which allows the catalyst to exert high stereocontrol. The corollary is, that the scope is limited to electron-poor azaarenes. However, the authors demonstrate the utility of these products with functionalization of the nitro group on the azaarenes. Treatment of the imine-addition products with mild acid readily deprotects the Boc group.

SYNFACTS Contributors: Mark Lautens, Lei Zhang
Synfacts 2013, 9(1), 0050 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317750; **Reg-No.:** L15212SF

B. YE, N. CRAMER* (ECOLE POLYTECHNIC FÉDÉRALE DE LAUSANNE, SWITZERLAND)
Chiral Cyclopentadienyl Ligands as Stereocontrolling Element in Asymmetric C–H Functionalization
Science **2012**, *338*, 504–506.

Chiral Cp Ligands in Rhodium-Catalyzed Asymmetric C–H Functionalization



Significance: A rhodium complex with a chiral Cp ligand that catalyzes an enantioselective synthesis of isoquinolones via a directed C–H bond functionalization is reported. Often, in half-sandwich transition-metal-catalyzed reactions, Cp remains the sole permanent ligand on the metal. Thus, despite the challenges, the development of chiral Cp ligands for inducing enantioselectivity is a powerful approach.

Comment: The highly effective Cp ligand reported is postulated to control the spatial orientation of the coupling partners. For instance, the ligand is C_2-symmetric to avoid diastereomeric coordination of the metal. The benzophenone ketal shields one face of the substrate and the equatorial methyl group pushes the bulky Boc group away. The controlled trajectory of the attacking alkene gives rise to the stereo-configuration of the product.

SYNFACTS Contributors: Mark Lautens, Lei Zhang
Synfacts 2013, 9(1), 0051 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317747; **Reg-No.:** L14912SF

Category

Metal-Catalyzed Asymmetric Synthesis and Stereoselective Reactions

Key words

rhodium

chiral cyclopentadienyl ligands

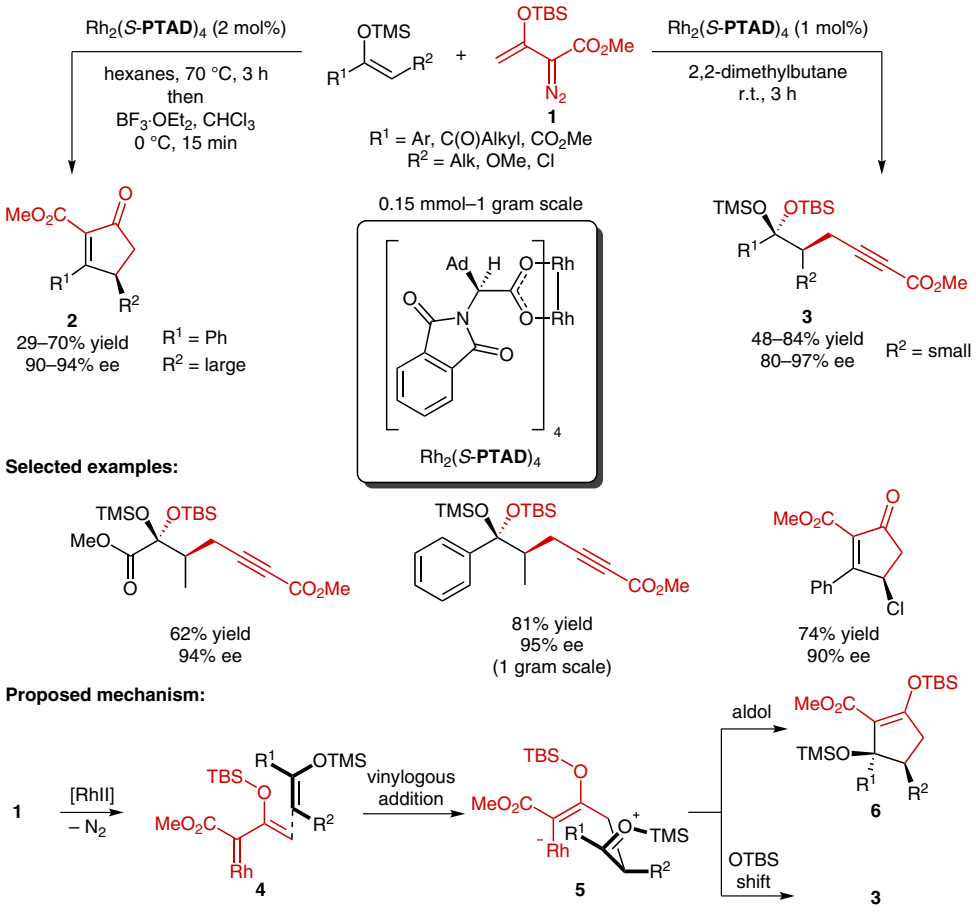
isoquinolones

asymmetric C–H functionalization

A. G. SMITH, H. M. L. DAVIES* (EMORY UNIVERSITY, ATLANTA, USA)

Rhodium-Catalyzed Enantioselective Vinylogous Addition of Enol Ethers to Vinyldiazoacetates
J. Am. Chem. Soc. **2012**, *134*, 18241–18244.

Rhodium-Catalyzed Asymmetric Vinylogous Addition to Vinyldiazoacetates



Significance: A rhodium-catalyzed asymmetric vinylogous addition of silyl enol ethers to siloxy-vinyldiazoacetates is reported. Depending on the sterics of the substituents on the substrate, this method can access cyclopentenones **2** or alkynoates **3** with high yield and excellent enantioselectivity.

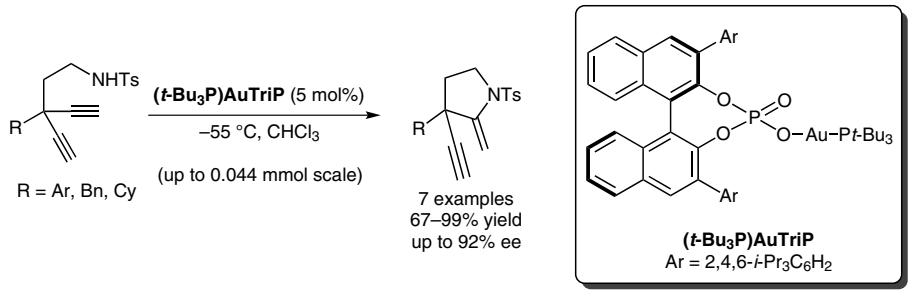
Comment: The use of (*Z*)-silyl enol ethers is critical in achieving the observed enantioselectivity. In the proposed mechanism, vinylogous adduct **5** can undergo a stereoselective 1,4-silyoxy shift to form **3**. Bulkier R^1 groups favor the aldol reaction to form formal [3+2] adduct **6**, which in one pot, in acid, can afford **2.**

SYNFACTS Contributors: Mark Lautens, Lei Zhang
Synfacts 2013, 9(1), 0052 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317749; **Reg-No.:** L15112SF

A. K. MOURAD, J. LEUTZOW, C. CZEKELIUS* (FREIE UNIVERSITÄT BERLIN, GERMANY AND FAYOUM UNIVERSITY, EGYPT)

Anion-Induced Enantioselective Cyclization of Diynamides to Pyrrolidines Catalyzed by Cationic Gold Complexes
Angew. Chem. Int. Ed. **2012**, *51*, 11149–11152.

Cationic Gold-Catalyzed Cyclization of Diynamides



Significance: The authors report an enantioselective cycloisomerization of diynamides to methylene pyrrolidines catalyzed by cationic gold with optically active binol phosphates as counteranions. This work was inspired by Toste and coworkers' application of chiral counterions in gold-catalyzed functionalization of allenes (*Science* **2007**, *317*, 462). The chiral pyrrolidine products formed are highly valuable as they contain an all-carbon-substituted quaternary stereocenter and are difficult to prepare in enantiomerically pure form by other conventional methods.

Comment: Czekelius and co-workers had previously demonstrated that cationic gold complexes cyclize diynols and diynamides to the corresponding unsaturated heterocycles in good yield (*Chem. Eur. J.* **2009**, *15*, 13323). However, optically active phosphine and carbene ligands gave poor enantioselectivity due to the linear coordination geometry in gold(I)–alkyne complexes. The use commercially available binol phosphates as chiral counterions overcomes this problem and allows for high enantioselectivity in the cyclization. The best results were obtained in chlorinated solvents at low temperatures, which is in line with the contact ion pair model of the cationic gold–alkyne complex and the anionic chiral phosphate.

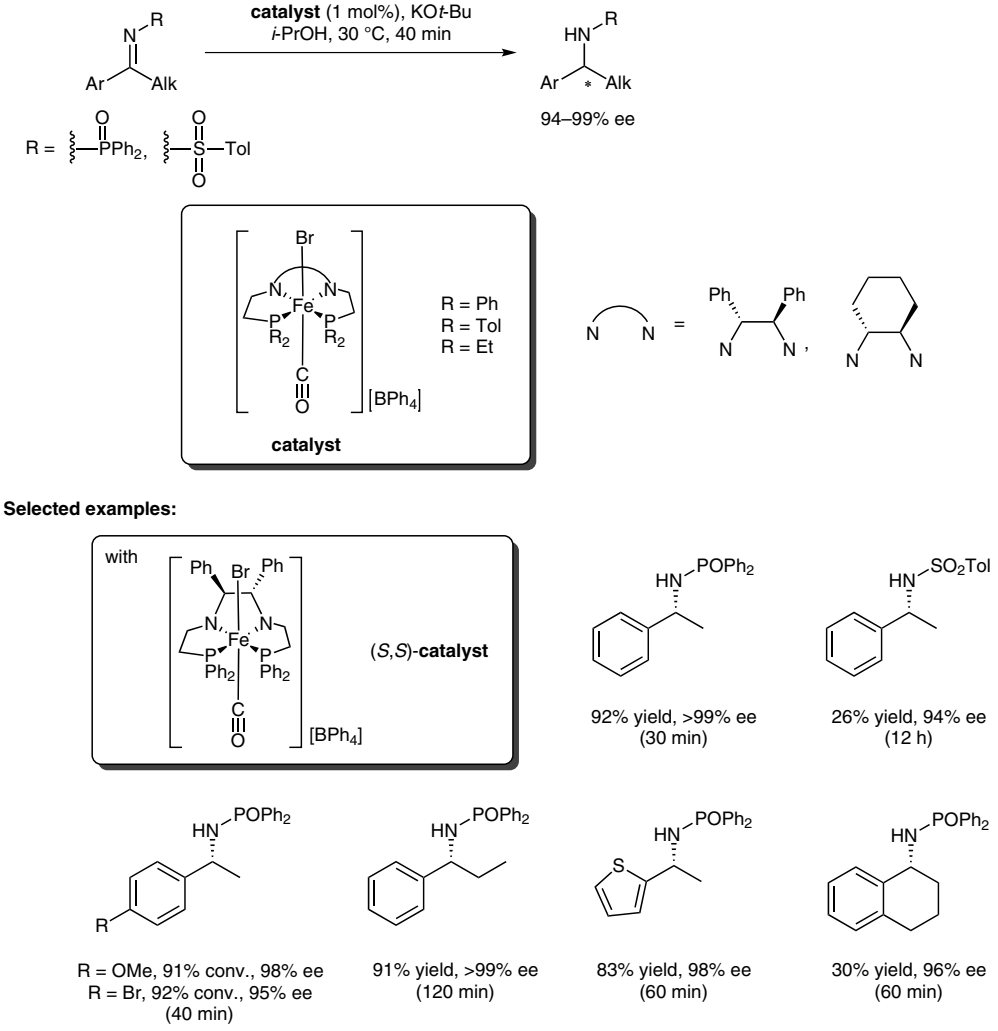
SYNFACTS Contributors: Mark Lautens, Jennifer Tsoung
Synfacts 2013, 9(1), 0053 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317753; **Reg-No.:** L15512SF

A. A. MIKHAILINE, M. I. MAISHAN, R. H. MORRIS* (UNIVERSITY OF TORONTO, CANADA)

Asymmetric Transfer Hydrogenation of Ketimines Using Well-Defined Iron(II)-Based Precatalysts Containing a PNNP Ligand

Org. Lett. **2012**, *14*, 4638–4641.

Iron-Catalyzed Asymmetric Transfer Hydrogenation of Ketimines



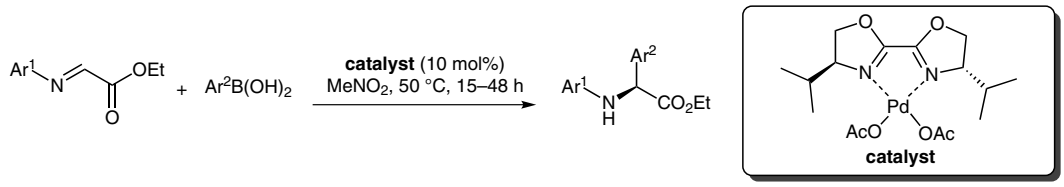
Significance: The authors report an iron-catalyzed asymmetric transfer hydrogenation under mild conditions that gives chiral amines with high enantioselectivity (94–99% ee). The system provides a solution to the challenging C=N bond reduction and proceeds with 2-propanol as the reducing agent.

Comment: Iron(II)–PNNP complexes that catalyze the asymmetric reduction of *N*-(diphenylphosphinoyl)- and *N*-(4-tolylsulfonyl)ketimines were developed. The (*R*,*R*)-diamine catalyst produces the (*S*)-amine. (*S*,*S*)-**3** are found to be the most active and stereoselective catalyst. The reaction outcome is influenced mainly by the sterics around the imine carbon but is insensitive to its electronic character.

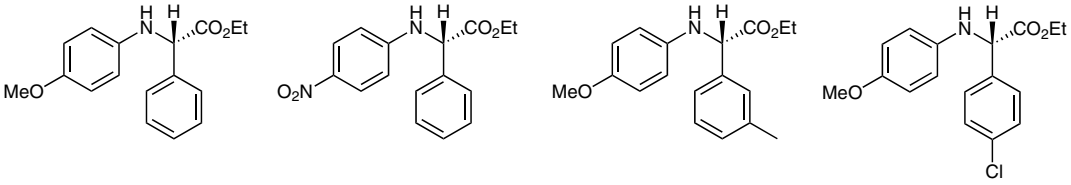
SYNFACTS Contributors: Hisashi Yamamoto, Lan Luo
Synfacts 2013, 9(1), 0054 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317846; **Reg-No.:** H16512SF

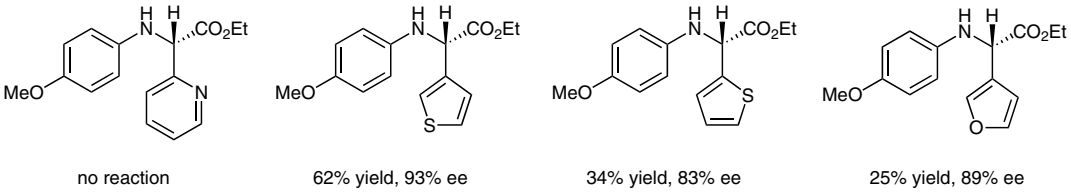
J. CHEN, X. LU, W. LOU, Y. YE, H. JIANG, W. ZENG* (SOUTH CHINA UNIVERSITY OF TECHNOLOGY, GUANGZHOU AND CHENGDU INSTITUTE OF BIOLOGY, P. R. OF CHINA)
Palladium(II)-Catalyzed Enantioselective Arylation of α-Imino Esters
J. Org. Chem. **2012**, *77*, 8541–8548.

Palladium-Catalyzed Enantioselective Arylation of α-Imino Esters

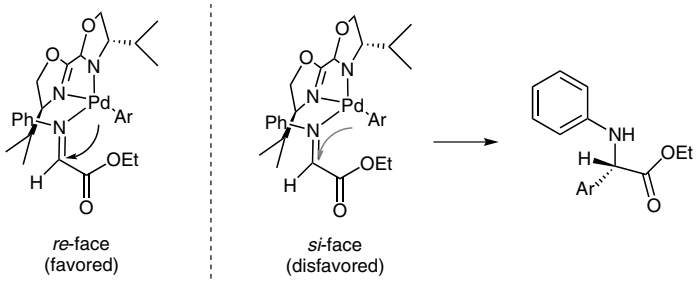


Substrate scope:





Proposed transition state:



Significance: This protocol provides a practical and direct route to chiral arylglycines with high enantioselectivity (up to 99% ee). These derivatives can be easily converted into optically active α-amino acids, which are commonly used as chiral auxiliaries in asymmetric catalysis.

Comment: A palladium(II)-catalyzed asymmetric arylation of *N*-aryl-α-imino esters using a chiral BOX ligand was developed. This method is applicable to various aromatic boronic acids. A stereochemical model, consistent with experimental results, suggests a *re*-face attack of the aryl group onto the *N*-arylimine carbon.

SYNFACTS Contributors: Hisashi Yamamoto, Lan Luo
Synfacts 2013, 9(1), 0055 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317845; **Reg-No.:** H16412SF

Category

Metal-Catalyzed Asymmetric Synthesis and Stereoselective Reactions

Key words

palladium

asymmetric arylation

arylglycine derivatives

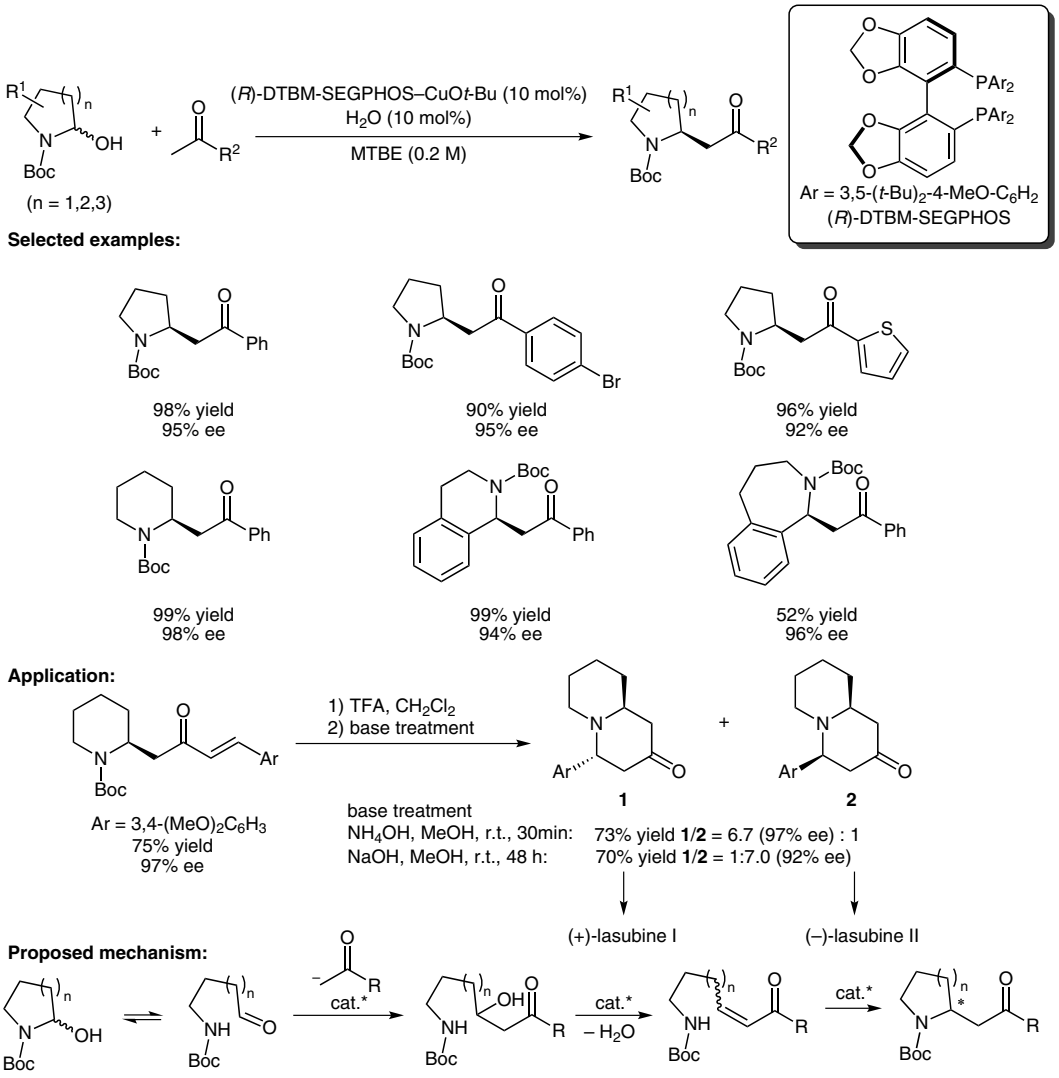
α-amino acids

S. L. SHI, X. F. WEI, Y. SHIMIZU, M. KANAI* (THE UNIVERSITY OF TOKYO AND JAPAN SCIENCE AND TECHNOLOGY AGENCY, KAWAGUCHI-SHI, JAPAN)

Copper(I)-Catalyzed Enantioselective Incorporation of Ketones to Cyclic Hemiaminals for the Synthesis of Versatile Alkaloid Precursors

J. Am. Chem. Soc. **2012**, *134*, 17019–17022.

Copper-Catalyzed Enantioselective Incorporation of Ketones to Hemiaminals



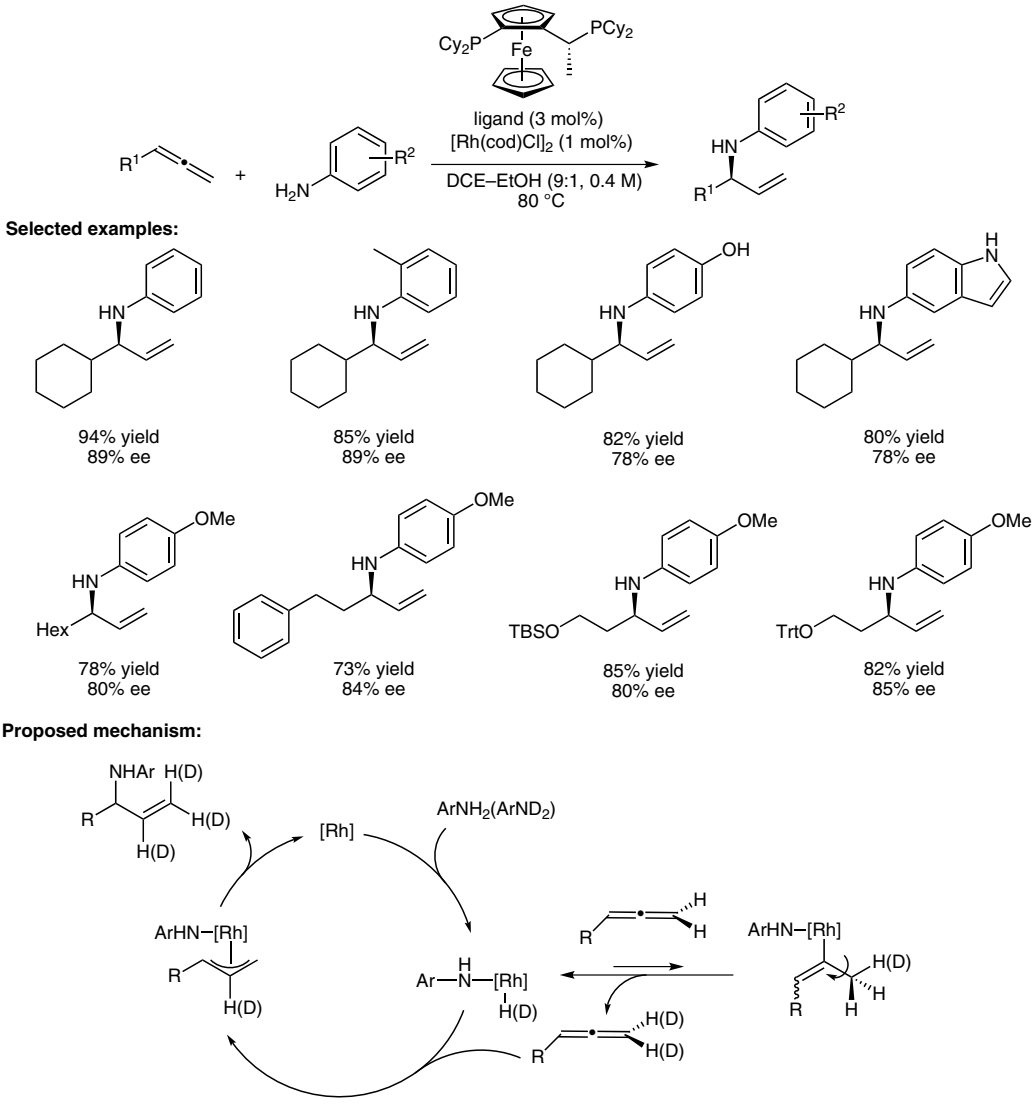
Significance: The authors developed a copper-catalyzed enantioselective incorporation of ketones to cyclic hemiaminals. A series of hemiaminals, including five-, six- and seven-membered rings, were applicable to provide versatile alkaloid precursors in high yield with excellent enantioselectivity.

Comment: This reaction proceeds through three successive steps: aldol reaction, dehydration and intramolecular enantioselective aza-Michael reaction. Employment of this pathway contributed to improve the reaction conditions and expand the substrate scope. Synthetic utility was demonstrated by the preparation of alkaloid and drug precursors.

SYNFACTS Contributors: Hisashi Yamamoto, Susumu Oda
Synfacts 2013, 9(1), 0056 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317777; **Reg-No.:** H15712SF

M. L. COOKE, K. XU, B. BREIT* (ALBERT-LUDWIGS-UNIVERSITÄT FREIBURG, GERMANY)
Enantioselective Rhodium-Catalyzed Synthesis of Branched Allylic Amines by Intermolecular Hydroamination of Terminal Allenes
Angew. Chem, Int. Ed. **2012**, *51*, 10876–10879.

Rhodium-Catalyzed Enantioselective Hydroamination of Allenes



Significance: Despite the versatility of α-chiral allylic amines, synthetic methods to access them have been underdeveloped. The authors reported the first example of the enantioselective intermolecular hydroamination of mono-substituted allenes.

Comment: A variety of substituted anilines, even bearing unprotected alcohol and indole moieties, were employed to give good yields and high enantioselectivities. Further mechanistic study is desirable to explain the regioselectivity of the hydrometalation step.

SYNFACTS Contributors: Hisashi Yamamoto, Susumu Oda
Synfacts 2013, 9(1), 0057 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317778; **Reg-No.:** H15812SF

Category
Metal-Catalyzed Asymmetric Synthesis and Stereoselective Reactions

Key words
rhodium
hydroamination
allenes

Key words

palladium

bis(imidazoline) ligands

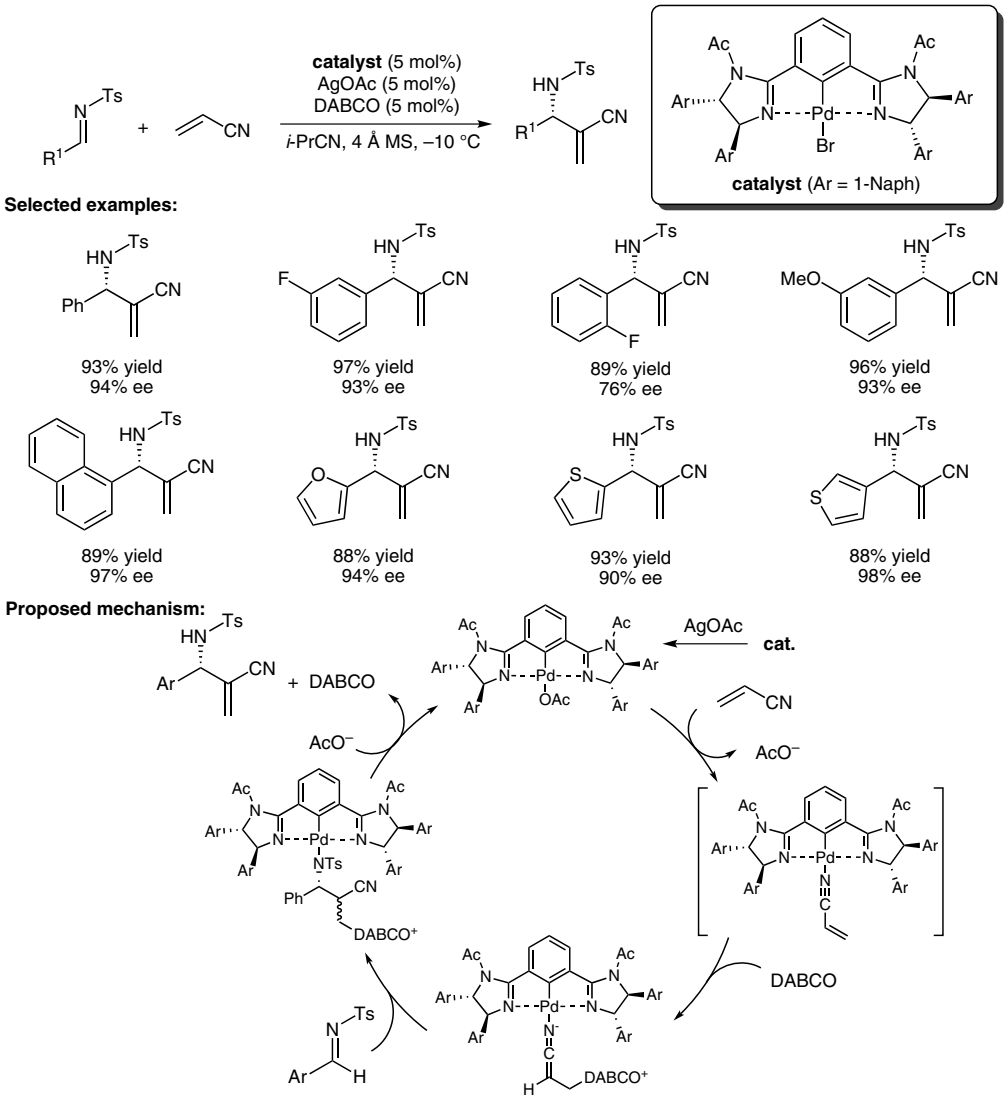
aza-Morita–Baylis–Hillman reaction

K. HYODO, S. NAKAMURA,* N. SHIBATA* (NAGOYA INSTITUTE OF TECHNOLOGY, JAPAN)

Enantioselective Aza-Morita–Baylis–Hillman Reactions of Acrylonitrile Catalyzed by Palladium(II) Pincer Complexes having C_2-Symmetric Chiral Bis(imidazoline) Ligands

Angew. Chem. Int. Ed. **2012**, *51*, 10337–10341.

Palladium-Catalyzed Enantioselective Aza-Morita–Baylis–Hillman Reaction



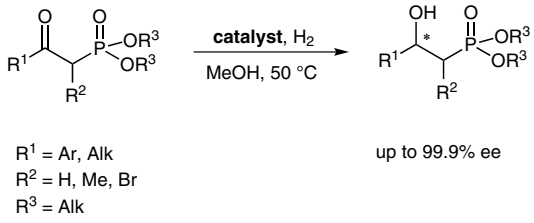
Significance: This paper describes the palladium-catalyzed enantioselective aza-Morita–Baylis–Hillman reaction of acrylonitriles with imines. The bulky pincer ligand enabled the synthesis of enantioenriched α-methylene-β-aminonitriles in high yield.

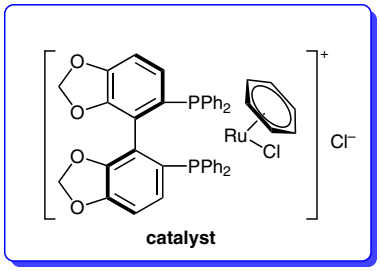
Comment: The palladium–pincer complex preferably activates acrylonitrile, even in the presence of ethyl acrylate. The palladium ketenimide is a key intermediate for the asymmetric induction. The palladium complex may promote other Lewis acid catalyzed reactions.

SYNFACTS Contributors: Hisashi Yamamoto, Susumu Oda
Synfacts 2013, 9(1), 0058 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317779; **Reg-No.:** H15912SF

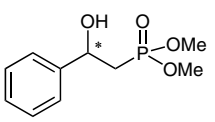
X. TAO, W. LI, X. MA, X. LI, W. FAN, L. ZHU, X. XIE, Z. ZHANG* (SHANGHAI JIAO TONG UNIVERSITY AND SHANGHAI INSTITUTE OF ORGANIC CHEMISTRY, P. R. OF CHINA)
Enantioselective Hydrogenation of β-Ketophosphonates with Chiral Ru(II) Catalysts
J. Org. Chem. **2012**, *77*, 8401–8409.

Ruthenium-Catalyzed Asymmetric Hydrogenation of β-Ketophosphonates





Selected examples: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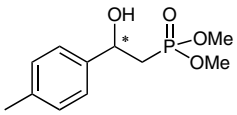
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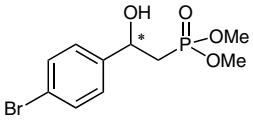
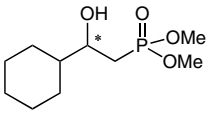
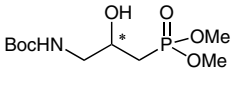
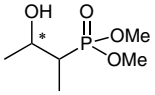
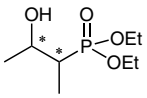
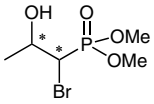

>99% conv., 99.9% ee


>99% conv., 96.4% ee


>99% conv., 97.3% ee


>99% conv., 98.6% ee
syn/*anti* > 94:6


>99% conv., 99.5% ee
syn/*anti* > 94:6


>99% conv., 99.7% ee
syn/*anti* = 96:4

Significance: The current work represents an efficient protocol for the enantioselective hydrogenation of β-ketophosphonate derivates catalyzed by a ruthenium–(*S*)-Sunphos complex. Good to excellent enantioselectivity and yield were obtained for a variety of substrates.

Comment: Hydroxyphosphonate motifs are known to be mimics of hydroxy carboxylic acids or amino acids. Given their medicinal importance, many synthetic methodologies have been developed. The protocol described herein was even used for the reduction of α-substituted β-ketophosphonates, providing the desired products with good *syn* diastereoselectivity.

SYNFACTS Contributors: Hisashi Yamamoto, Jiajing Tan
Synfacts 2013, 9(1), 0059 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317784; **Reg-No.:** H16112SF

Category

Metal-Catalyzed Asymmetric Synthesis and Stereoselective Reactions

Key words

ruthenium

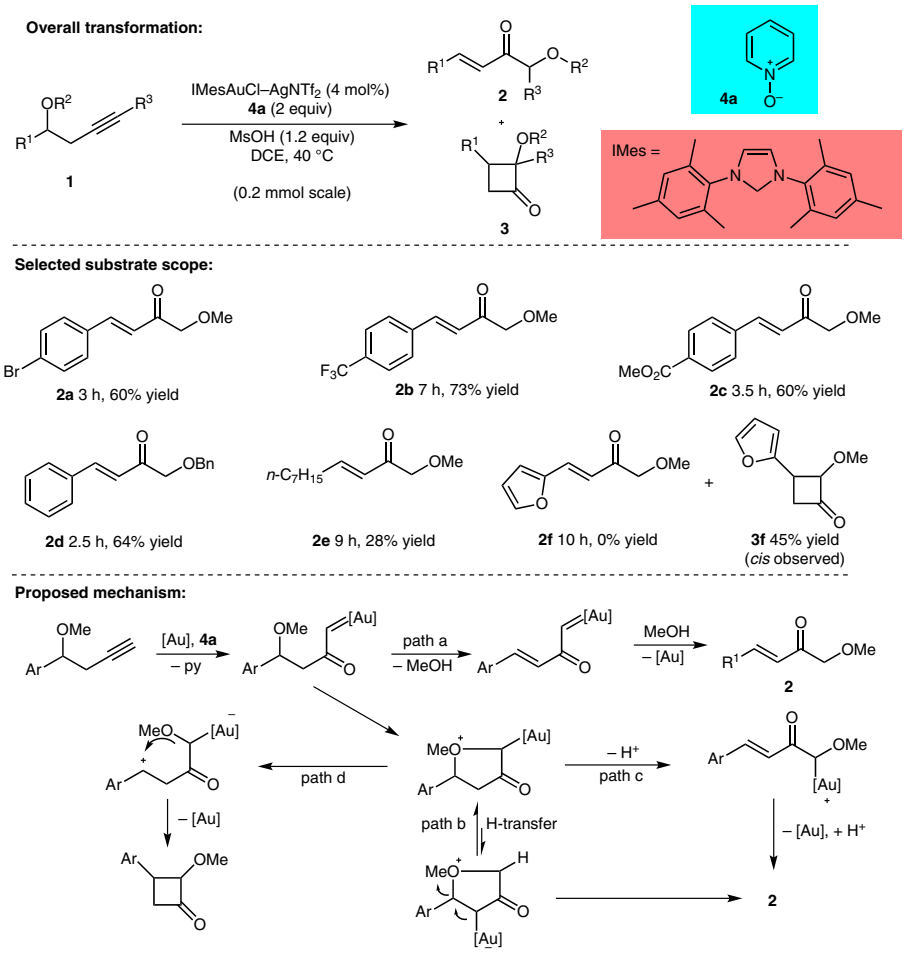
hydrogenation

ketophosphonates

M. XU, T.-T. REN, C.-Y. LI* (ZHEJIANG SCI-TECH UNIVERSITY, HANGZHOU, P. R. OF CHINA)

Gold-Catalyzed Oxidative Rearrangement of Homopropargylic Ether via Oxonium Ylide
Org. Lett. **2012**, *14*, 4902–4905.

Homopropargylic Ether Rearrangement via Gold Catalysis



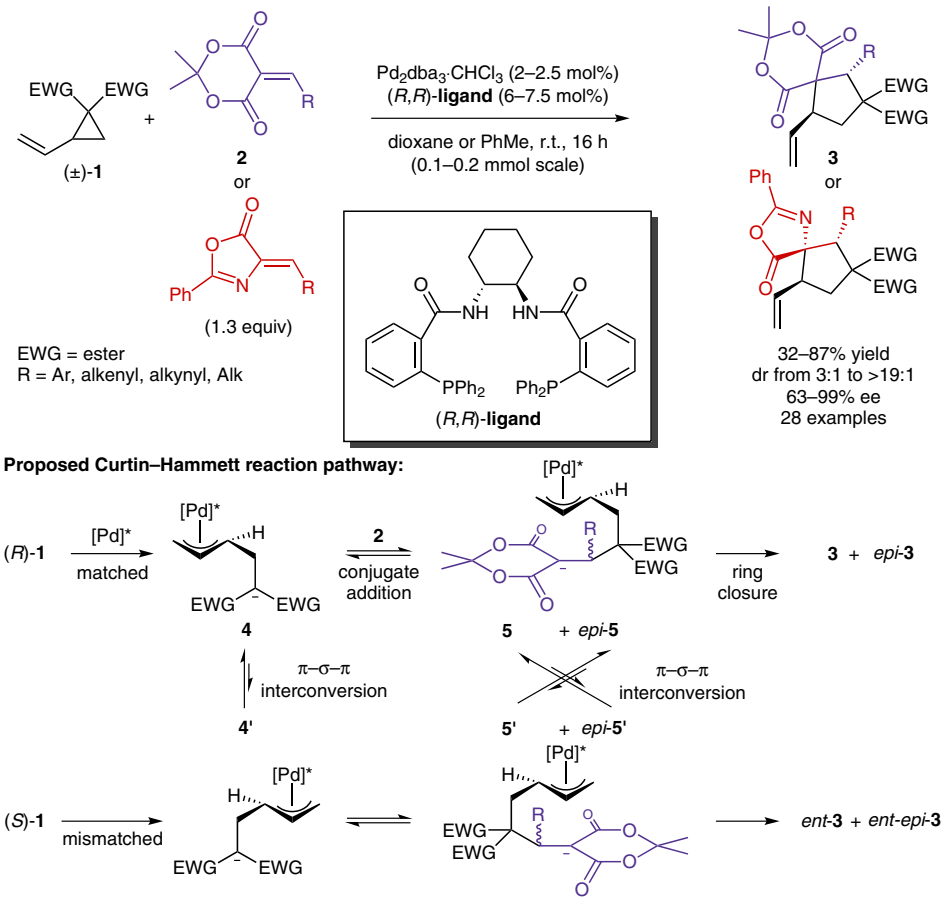
Significance: Gold catalysis has emerged as a powerful platform to conduct complex organic transformations. Specifically, the implementation of gold carbenoids has shown great promise in synthetic planning. These useful intermediates offer a convenient alternative to generate metal carbenes which are traditionally obtained from diazo compounds. The authors utilize these intermediates to synthesize α,β-unsaturated carbonyl compounds from homopropargylic ethers.

Comment: The authors report a silver-assisted gold(I)-catalyzed carbonyl synthesis. In an effort to obtain cyclobutanes **3** via a [1,2]-shift mechanism (path d), the authors unexpectingly obtained the corresponding α,β-unsaturated carbonyl compounds **2**. Control experiments show that neither IMesAuCl, nor $AgNTf_2$ or $HNTf_2$ alone could catalyze the reaction. The scope of the reported reaction is quite broad; however, yields are generally moderate to good. In some instances cyclobutanones are obtained as the major product.

SYNFACTS Contributors: Mark Lautens, David A. Petrone
Synfacts 2013, 9(1), 0060 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317758; **Reg-No.:** L16012SF

B. M. TROST,* P. J. MORRIS, S. J. SPRAGUE (STANFORD UNIVERSITY, USA)
Palladium-Catalyzed Diastereo- and Enantioselective Formal [3 + 2]-Cycloadditions of Substituted Vinylcyclopropanes
J. Am. Chem. Soc. **2012**, *134*, 17823–17831.

Palladium-Catalyzed Asymmetric Formal [3+2] Cycloaddition



Significance: A palladium-catalyzed asymmetric formal [3+2] cycloaddition of vinylcyclopropanes to electron-poor olefins is reported using the Trost ligand. The developed method can access highly substituted cyclopentanes with high diastereo- and enantioselectivity with moderate to high yield.

Comment: As the vinylcyclopropanes **1** used are racemic, the authors propose that the reaction occurs under Curtin–Hammett conditions for this stereo-convergent reaction. Notably, the effects of π–σ– π interconversion and the reversibility of the conjugate addition establish pre-equilibria of diastereomeric reactive intermediates **4** and **5**, consequently favoring the formation of **3**.

SYNFACTS Contributors: Mark Lautens, Lei Zhang
Synfacts 2013, 9(1), 0061 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317751; **Reg-No.:** L15312SF

Category

Metal-Catalyzed Asymmetric Synthesis and Stereoselective Reactions

Key words

palladium

Trost ligand

vinylcyclopropanes

formal [3+2] cycloaddition

cyclopentanes

Category

Metal-Catalyzed Asymmetric Synthesis and Stereoselective Reactions

Key words

ruthenium

transfer hydrogenation

tridentate N-ligands

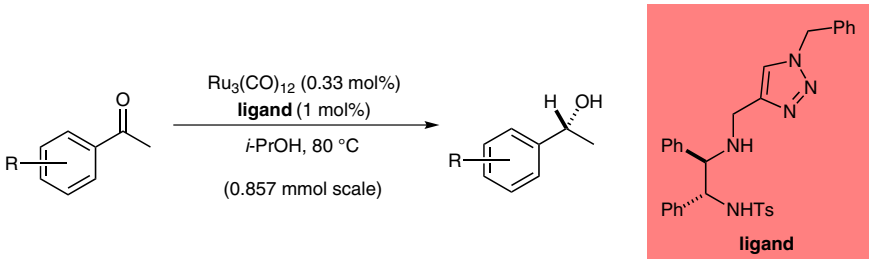
T. C. JOHNSON, W. G. TORRY, M. WILLS* (THE UNIVERSITY OF WARWICK, COVENTRY, UK)

Application of Ruthenium Complexes of Triazole-Containing Tridentate Ligands to Asymmetric Transfer Hydrogenation of Ketones

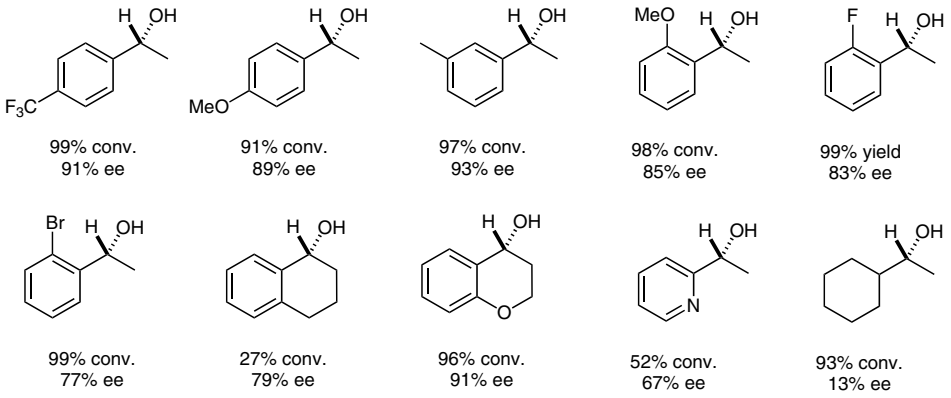
Org. Lett. **2012**, *14*, 5230–5233.

Asymmetric Ruthenium-Catalyzed Transfer Hydrogenation of Ketones

Overall transformation:



Selected substrate scope:



Significance: Transition-metal-catalyzed asymmetric transfer hydrogenation (ATH) has become a leading reduction method, which can be credited to its broad scope and relatively mild conditions. Additionally, the development of more general methods to synthesize chiral secondary alcohol is a useful endeavor. Specifically, the ATH reduction of *ortho*-substituted aryl ketones is considered a more challenging transformation than that of related *meta*- and *para*-substituted substrates.

Comment: The authors report a ruthenium-catalyzed ATH of substituted aryl methyl ketones using a novel tridentate triazole containing ligand. The scope of this transformation is quite broad, and conversions and enantioselectivities range from moderate to excellent. Notably, tetralone and 4-chromanone can be reduced efficiently with synthetically useful enantioselectivity. The reduction of cyclohexyl methyl ketone proceeds with excellent conversion, yet enantioselectivity remains low (13% ee).

SYNFACTS Contributors: Mark Lautens, David A. Petrone
Synfacts 2013, 9(1), 0062 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317759; **Reg-No.:** L16112SF

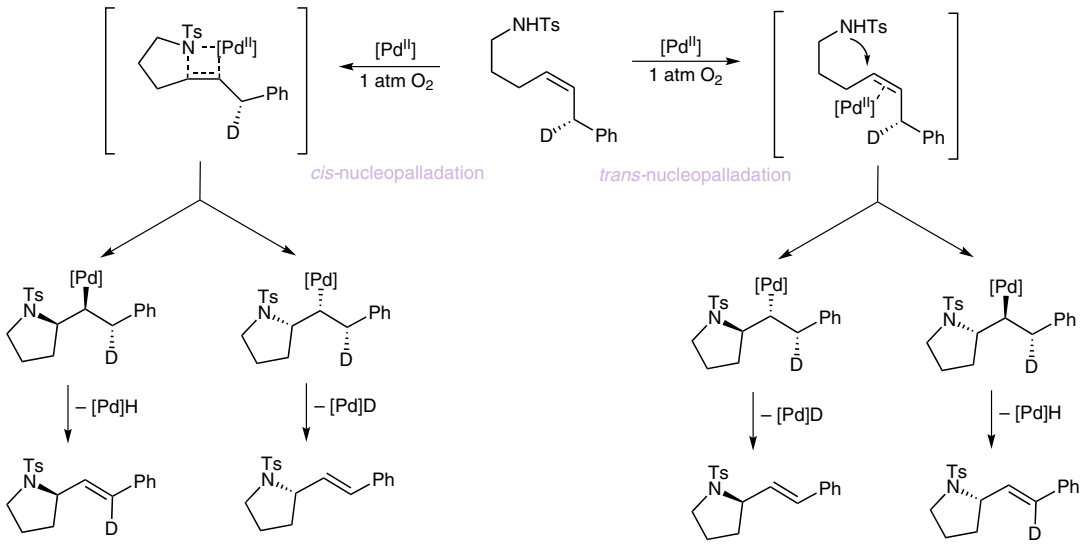
A. B. WEINSTEIN, S. S. STAHL* (UNIVERSITY OF WISCONSIN-MADISON, USA)

Reconciling the Stereochemical Course of Nucleopalladation with the Development of Enantioselective Wacker-Type Cyclizations

Angew. Chem. Int. Ed. **2012**, *51*, 11505–11509.

Mechanistic Study of Palladium-Catalyzed Wacker-Type Cyclizations

Stereochemical pathways:



Significance: Recently, Stahl and co-workers had shown that a Pd(II) catalyst with a chiral pyridine–oxazoline (pyrox) ligand allowed preparation of pyrrolidines in high yield and enantioselectivity (*Org. Lett.* **2011**, *13*, 2830). In the enantioselective cyclization of γ-alkenyl tosylamides, the anionic ligand (TFA vs OAc) was found to have a significant impact on the reaction outcome, where the use of [Pd(pyrox)$(OAc)_2$] gave significantly diminished yield and enantioselectivity. Through a series of mechanistic investigations with a chiral, deuterated substrate probe, the authors showed the significant effect the anionic ligand has in selecting the nucleopalladation (NP) pathway of the Wacker-type cyclization, which in course determines the ancillary neutral donor's ability to alter the stereochemical course of the pathway. This data provides the first direct correlation between NP stereoselectivity and the enantioselectivity of the transformation.

Comment: By using ^{1}H NMR spectroscopy and HPLC analyses to determine H/D ratios and enantiomeric excesses, the authors were able to determine the yields of the four possible products from the reaction of a deuterated acyclic substrate under different conditions (see above). They showed that only in the *trans* pathway does the pyrox ligand play a significant role, thus the *trans*-amidopalladation (AP) pathway proceeds with high enantioselectivity, while the *cis*-AP pathway exhibits low enantioselectivity. The authors suggest that the carboxylate ligand acts as a Brønsted base to mediate Pd–amidate bond formation in the *cis*-AP pathway, whereas the TFA anionic ligand is substituted by the substrate alkene and favors the *trans*-AP pathway.

SYNFACTS Contributors: Mark Lautens, Jennifer Tsoung
Synfacts 2013, 9(1), 0063 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317755; **Reg-No.:** L15712SF

Category

Metal-Catalyzed Asymmetric Synthesis and Stereoselective Reactions

Key words

Wacker-type cyclization

palladium

pyrrolidines

Key words

palladium

dehydrogenative olefination

1,3-enynes

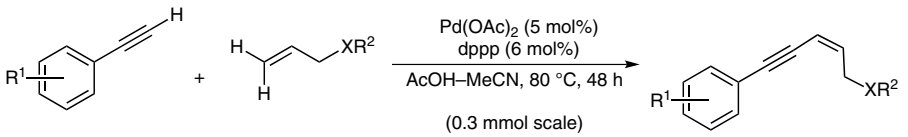
Y.-L. SHAO, X.-H. ZHANG,* J.-S. HAN, P. ZHONG* (WENZHOU UNIVERSITY, P. R. OF CHINA)

Pd(II)-Catalyzed Dehydrogenative Olefination of Terminal Arylalkynes with Allylic Ethers: General and Selective Access to Linear (*Z*)-1,3-Enynes

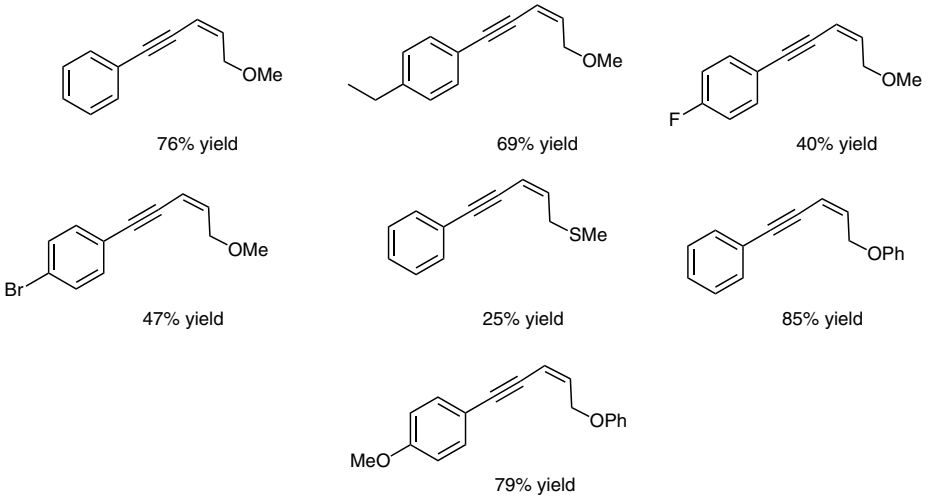
Org. Lett. **2012**, *14*, 5242–5245.

Access to 1,3-Enynes by Pd(II)-Catalyzed Dehydrogenative Olefination

Overall transformation:



Selected substrate scope:



Significance: 1,3-enynes are important motifs found in pharmaceutically active compounds and natural products. For this reason, efficient methods which easily access these structures are desirable to synthetic chemists. Despite advances made using copper and iron catalysis, which commonly require alkene pre-activation, palladium-catalyzed dehydrogenative cross-coupling has shown promise as a more benign strategy in this regard.

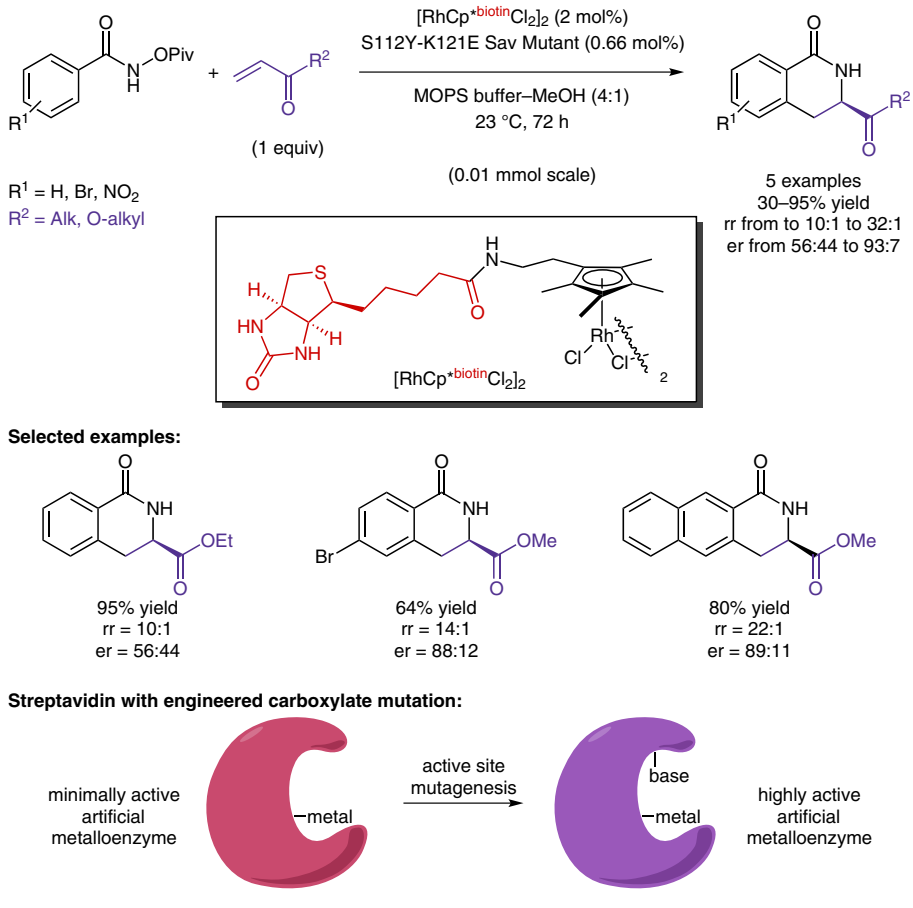
Comment: The authors report the first example of a $Pd(OAc)_2$-catalyzed direct dehydrogenative olefination of terminal aryl alkynes and allylic ethers to exclusively access (*Z*)-1,3-enyne derivatives. The reaction exhibits good scope with respect to arylalkynes, however, only allylic ethers and thioethers were used as coupling partners, thus limiting the applicability. Nonetheless, this method appears to be an interesting application of dehydrogenative cross-coupling which accesses these important compounds in a step-efficient manner.

SYNFACTS Contributors: Mark Lautens, David A. Petrone
Synfacts 2013, 9(1), 0064 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317763; **Reg-No.:** L16312SF

T. K. HYSTER, L. KNÖRR, T. R. WARD,* T. ROVIS* (COLORADO STATE UNIVERSITY, FORT COLLINS, USA AND UNIVERSITY OF BASEL, SWITZERLAND)

Biotinylated Rh(III) Complexes in Engineered Streptavidin for Accelerated Asymmetric C–H Activation
Science **2012**, *338*, 500−503.

Artificial Rh(III)–Metalloenzyme-Catalyzed Asymmetric C–H Activation



Significance: A highly active, artificial rhodium(III) metalloenzyme that catalyzes an asymmetric synthesis of dihydroisoquinolones through C–H activation is reported. A biotinylated rhodium(III) complex is successfully incorporated into streptavidin. With active-site mutagenesis, the engineered enzyme displayed up to 100-fold reaction rate increase compared to the activity of the unbound rhodium complex.

Comment: As Cp is the only permanently bound ligand on rhodium in the catalytic cycle, it has been difficult to render this reaction enantioselective until recently. This report provides an alternative solution for this problem. Based on the concerted metalation–deprotonation mechanism, the authors used docking modeling and introduced a basic carboxylate moiety in the active site. With kinetic isotope effect experiments, the importance of this mutation in accelerating the catalysis is demonstrated.

SYNFACTS Contributors: Mark Lautens, Lei Zhang
Synfacts 2013, 9(1), 0065 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317748; **Reg-No.:** L15012SF

Category

Metal-Catalyzed Asymmetric Synthesis and Stereoselective Reactions

Key words

rhodium

streptavidin

biotin

artificial metallo-enzymes

benzamides

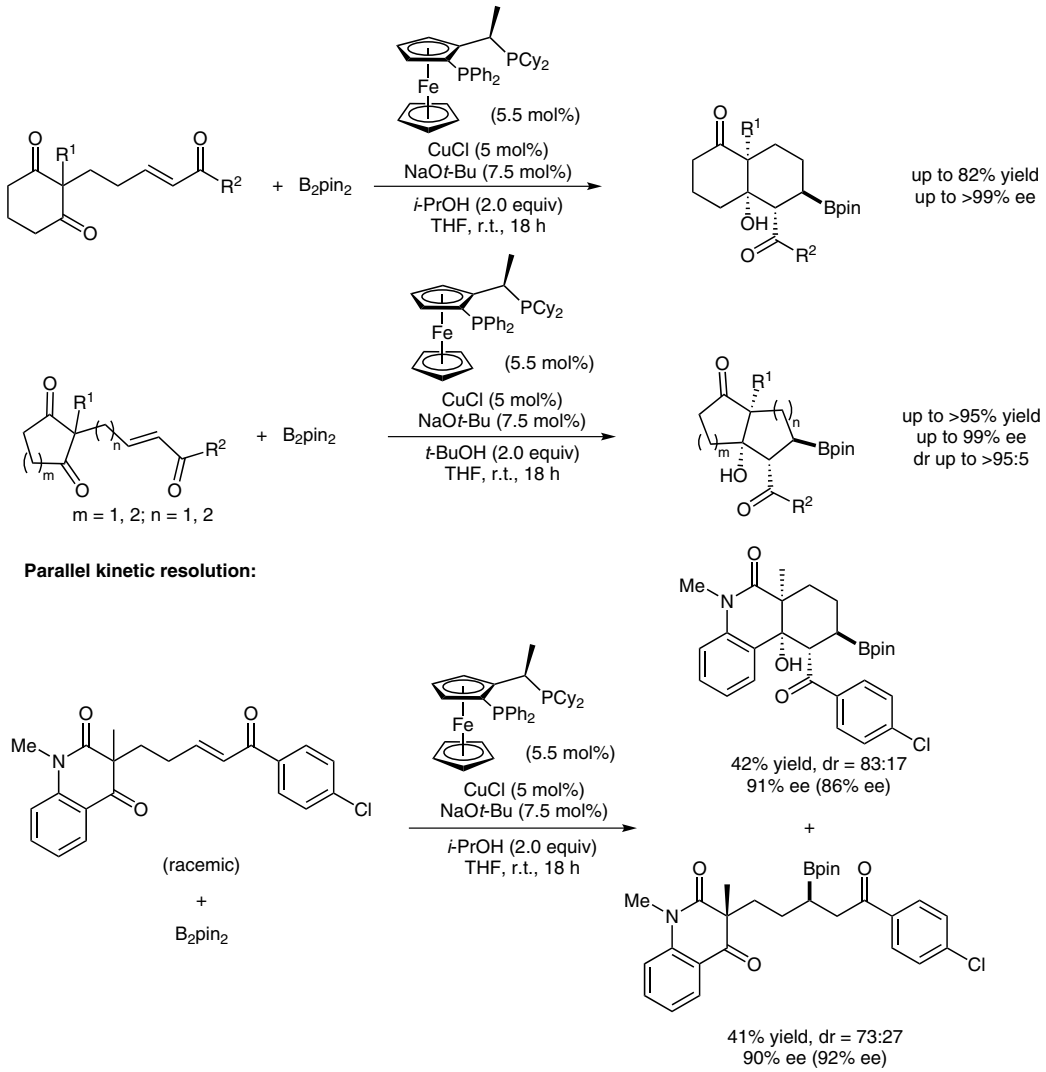
dihydroiso-quinolines

asymmetric C–H activation

A. R. BURNS, J. S. GONZÁLEZ, H. W. LAM* (UNIVERSITY OF EDINBURGH, UK)

Enantioselective Copper(I)-Catalyzed Borylative Aldol Cyclizations of Enone Diones
Angew. Chem. Int. Ed. **2012**, *51*, 10827–10831.

Enantioselective Copper-Catalyzed Borylative Aldol Cyclizations



Significance: The formation of metal enolates allows for precise enolization, as well as potential enantio- and diastereoselective enolization. In this report, the authors apply this idea to a copper-catalyzed conjugate boration–aldol cyclization sequence to produce enantioenriched decalin-, hydrindane- and diquinone-based products.

Comment: The copper–bisphosphine catalyst system developed, produces decalins as well as [5,6]-, [6,5]-, and [5,5]-bicyclic ring products with high levels of diastereo- and enantioselectivity. Kinetic resolution of a racemic chiral enone also afforded the cyclization product with good diastereo- and enantioselectivity.

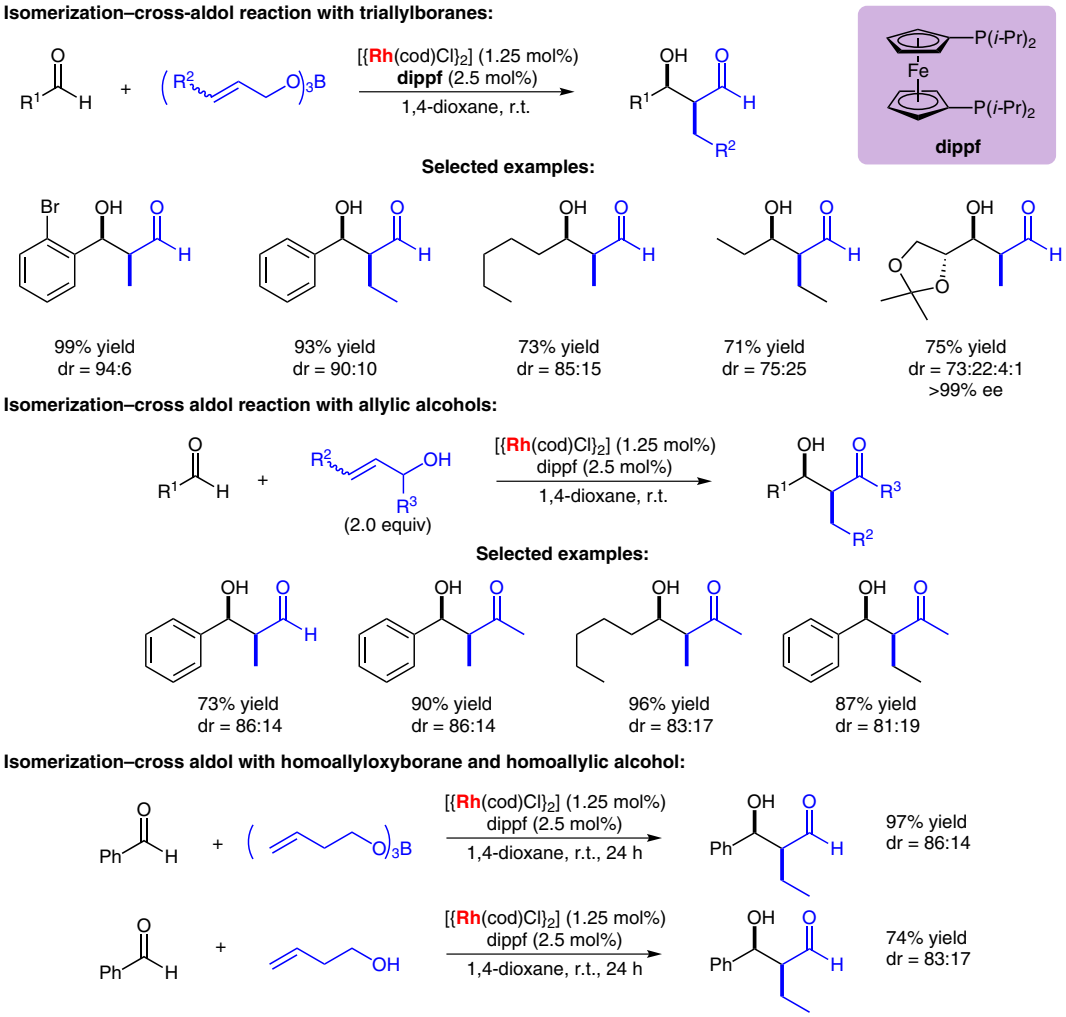
SYNFACTS Contributors: Hisashi Yamamoto, Kimberly Griffin
Synfacts 2013, 9(1), 0066 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317775; **Reg-No.:** H15512SF

L. LIN, K. YAMAMOTO, S. MATSUNAGA,* M. KANAI* (THE UNIVERSITY OF TOKYO AND ERATO JAPAN SCIENCE AND TECHNOLOGY AGENCY, TOKYO, JAPAN)

Rhodium-Catalyzed Cross-Aldol Reaction: In Situ Aldehyde-Enolate Formation from Allyloxyboranes and Primary Allylic Alcohols

Angew. Chem. Int. Ed. **2012**, *51*, 10275–10279.

In Situ Aldehyde Enolate Formation by Rhodium-Catalyzed Isomerization



Significance: Aldol reactions in which the aldol donor is derived from an aldehyde, are particularly challenging. This report describes a strategy in which aldehyde enolates are generated in situ by rhodium-catalyzed isomerization of triallylboroxanes. High *syn*-selectivity is obtained for a variety of aldehyde-donor and -acceptor partners.

Comment: Remarkably, the use of triallyloxyboranes is not required; simple primary and secondary allylic alcohols also undergo the isomerization–cross-aldol sequence with similar levels of reactivity and selectivity, presumably through a rhodium-enolate or -enol mechanism.

SYNFACTS Contributors: Hisashi Yamamoto, Patrick Brady
Synfacts 2013, 9(1), 0067 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317772; **Reg-No.:** H15212SF

Category

Metal-Catalyzed Asymmetric Synthesis and Stereoselective Reactions

Key words

rhodium

aldol reaction

aldehydes

allylic alcohols

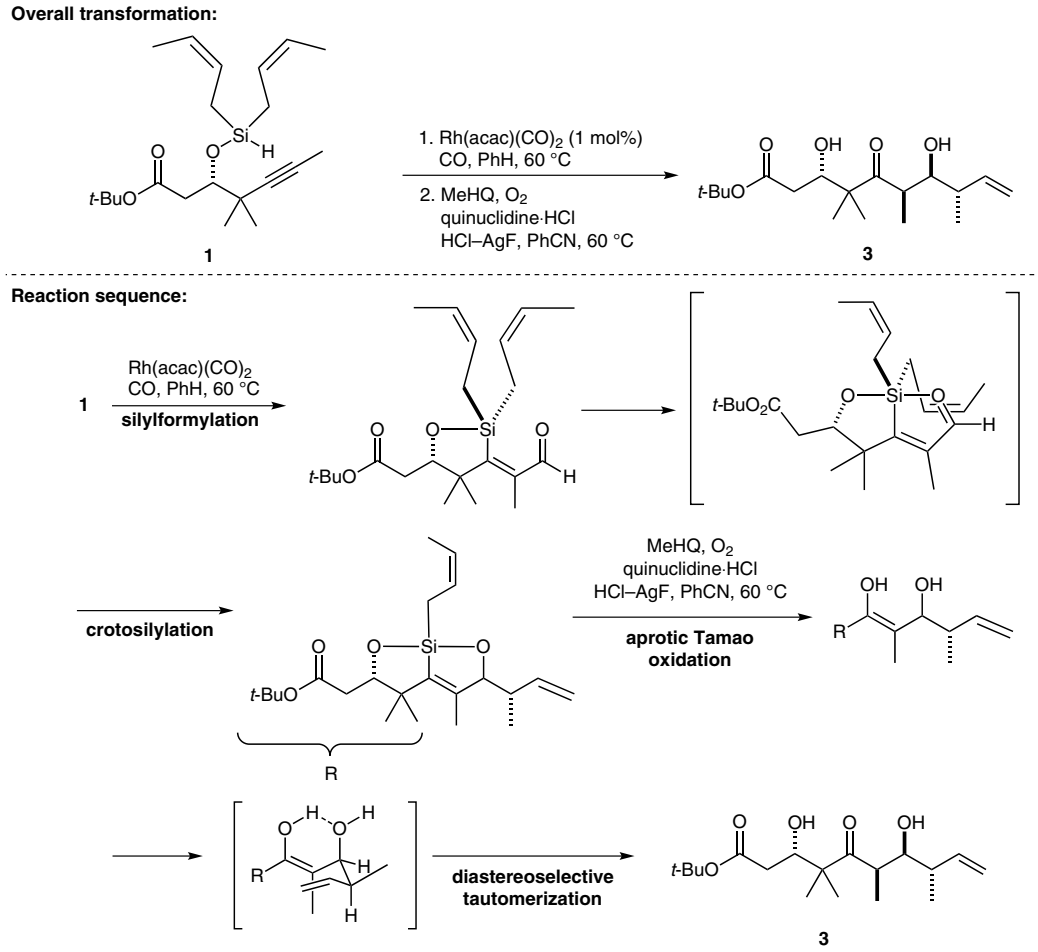
allyloxyboranes

T. J. HARRISON, P. M. A. RABBAT, J. L. LEIGHTON* (COLUMBIA UNIVERSITY, NEW YORK, USA)

An 'Aprotic' Tamao Oxidation/*Syn*-Selective Tautomerization Reaction for the Efficient Synthesis of the C(1)–C(9) Fragment of Fludelone

Org. Lett. **2012**, *14*, 4890–4893.

A Rhodium(I)-Catalyzed Silylformylation–Crotosilylation–Tamao Oxidation



Significance: Access to complex polyketide fragments typically consists of complex stepwise syntheses. Recent advances, including asymmetric crotylation and aldol cascades, have allowed chemists to synthesize extremely complex polyketide fragments with good step- and redox-economy, as well as minimal use of protecting groups. In this regard, silylformylation and silylcrotylation have emerged as complementary methods towards this end.

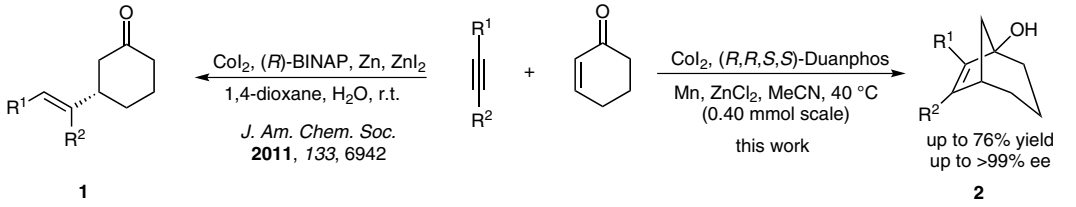
Comment: The authors report the synthesis of the C1–C9 fragment of fludelone, a polyketide natural product. The authors elegantly utilize their silylformylation–crotosilylation chemistry (*J. Am. Chem. Soc.* **2000**, *122*, 8587) in conjunction with this newly developed aprotic Tamao oxidation–diastereoselective tautomerization methodology to access this ketone containing four stereocenters, three of which are contiguous.

SYNFACTS Contributors: Mark Lautens, David A. Petrone
Synfacts 2013, 9(1), 0068 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317757; **Reg-No.:** L15912SF

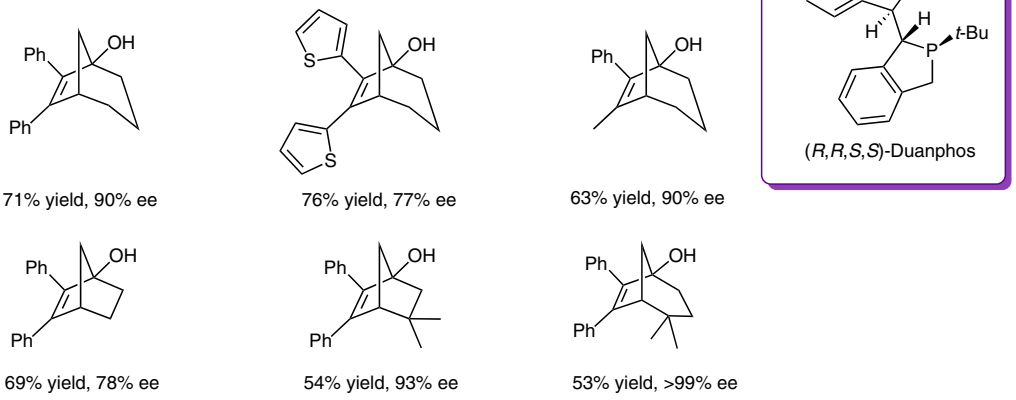
C.-H. WEI, S. MANNATHAN, C.-H. CHENG* (NATIONAL TSING HUA UNIVERSITY, HSINCHU, TAIWAN)

Regio- and Enantioselective Cobalt-Catalyzed Reductive [3+2] Cycloaddition Reaction of Alkynes with Cyclic Enones: A Route to Bicyclic Tertiary Alcohols
Angew. Chem. Int. Ed. **2012**, *51*, 10592–10595.

Cobalt-Catalyzed [3+2] Cycloaddition of Alkynes with Cyclic Enones



Selected examples:



Significance: Cheng and co-workers describe a cobalt-catalyzed [3+2]-cycloaddition reaction that provides an atom-economic method for the synthesis of bicyclic tertiary alcohols from alkynes and cyclic enones with regioselectivity. During their previous studies of enantioselective reductive coupling of alkynes with cyclic enones to synthesize β-substituted ketones **1**, they found that the use of a $CoBr_2$/dppe–Mn–$ZnCl_2$ system gave the bicyclic product **2** instead in high yield. With the use of a chiral ligand such as Duanphos, moderate to high enantioselectivity was also obtained.

Comment: This reported system is remarkable in that it allows for the reductive cycloaddition of various alkynes and cyclic enones to occur with good regio- and stereoselectivity using an air-stable cobalt catalyst, a mild reducing agent and water as the hydrogen source. Unsymmetrical alkynes also undergo reductive cycloaddition with good to high regioselectivity, though terminal alkynes and silyl-protected alkynes were unsuitable.

SYNFACTS Contributors: Mark Lautens, Jennifer Tsoung
Synfacts 2013, 9(1), 0069 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317752; **Reg-No.:** L15412SF

Category

Metal-Catalyzed Asymmetric Synthesis and Stereoselective Reactions

Key words

cobalt

cycloaddition

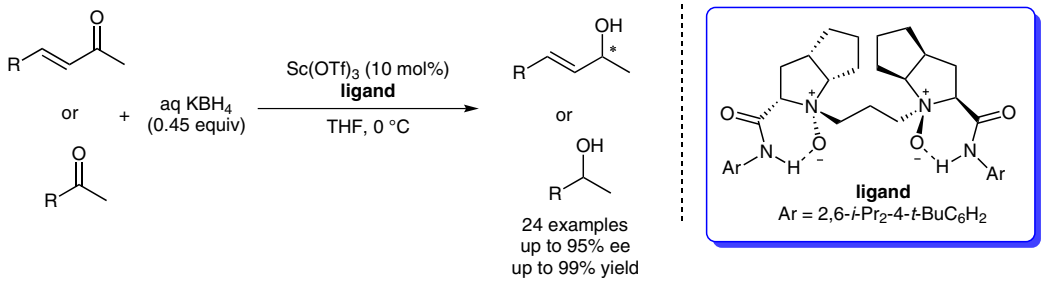
tertiary alcohols

P. HE, X. LI, H. ZHENG, W. LI, L. LIN, X. FENG* (SICHUAN UNIVERSITY, CHENGDU, P. R OF CHINA)

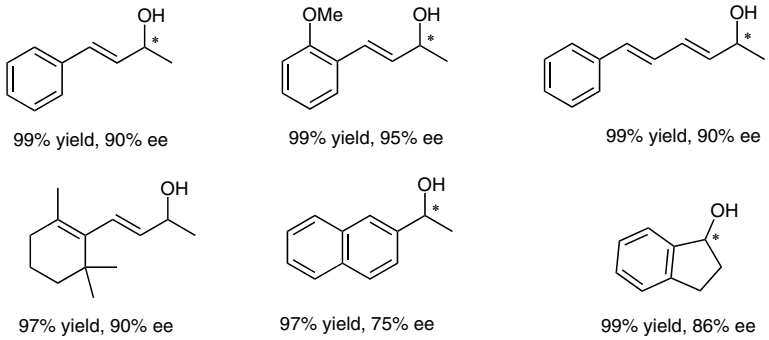
Asymmetric 1,2-Reduction of Enones with Potassium Borohydride Catalyzed by Chiral *N,N′*-Dioxide–Scandium(III) Complexes

Org. Lett. **2012**, *14*, 5134–5137.

Scandium-Catalyzed Asymmetric Reduction with Potassium Borohydride



Selected examples:



Significance: As an extension on previous work using chiral *N,N′*-dioxide–metal complexes for asymmetric catalysis (see Review), the authors now describe the scandium-catalyzed asymmetric reaction of enones and ketones with KBH_4. The resulting chiral alcohols are obtained with good yield and enantioselectivity.

Review: X. Liu, L. Lin, X. Feng *Acc. Chem. Res.* **2011**, *44*, 574–587.

Comment: Chiral allylic alcohols are important motifs widely present in natural products and biologically active molecules. The enantioselective reduction of enones is known as the most straightforward access to such motifs. Herein, the first example of catalytic enantioselective reduction of enones and ketones by using KBH_4 is reported. The utilization of an aqueous solution of KBH_4 was found to be crucial for obtaining high yield and enantioselectivity as the presence of water is believed to benefit proton transfer to accelerate the catalytic cycle. In this case, the reaction was performed in a homogeneous catalyst system. The HRMS spectra experiments indicated that the initial reducing species is KBH_3OH.

SYNFACTS Contributors: Hisashi Yamamoto, Jiajing Tan
Synfacts 2013, 9(1), 0070 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317785; **Reg-No.:** H16212SF

N. GAO, X.-W. GUO, S.-C. ZHENG, W.-K. YANG, X.-M. ZHAO* (TONGJI UNIVERSITY, SHANGHAI AND DALIAN UNIVERSITY OF TECHNOLOGY, P. R OF CHINA)

Iridium-Catalyzed Enantioselective Allylation of Sodium 2-Aminobenzenethiolate: An Access to Chiral Benzo-Fused N,S-Heterocycles
Tetrahedron **2012**, *68*, 9413–9418.

Category

Metal-Catalyzed Asymmetric Synthesis and Stereoselective Reactions

Key words

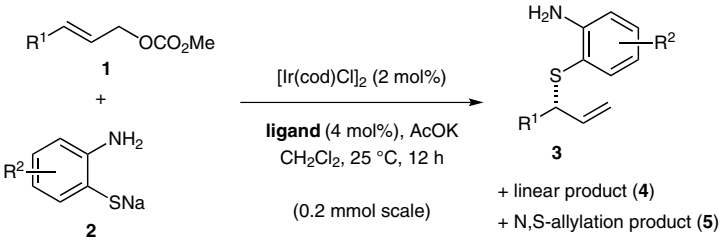
iridium

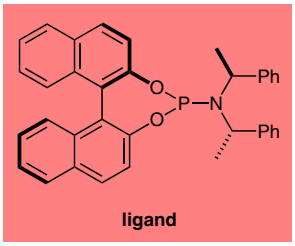
allylation

N,S-heterocycles

Enantioselective Iridium(I)-Catalyzed Allylation of Sodium 2-Aminobenzenethiolates

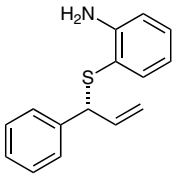
Overall transformation:



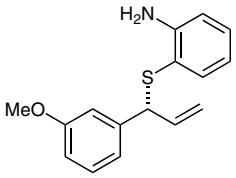


ligand

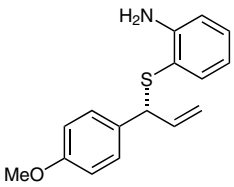
Selected substrate scope:



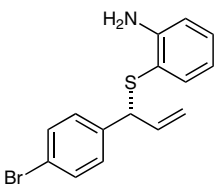
83% yield (**3**), 96% ee
3/**4**/**5** = 96:4 trace



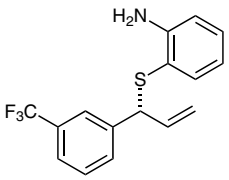
74% yield (**3**), 96% ee
3/**4**/**5** = 94:8:8:trace



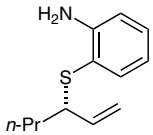
70% yield (**3**), 96% ee
3/**4**/**5** = 90:10:trace



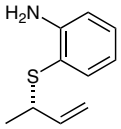
67% yield (**3**), 93% ee
3/**4**/**5** = 96:4:trace



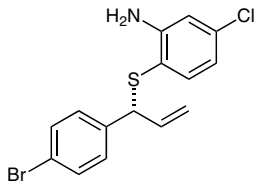
75% yield (**3**), 97% ee
3/**4**/**5** = 96:4:trace



75% yield (**3**), 94% ee
3/**4**/**5** = 96:4:trace



54% yield (**3**), 94% ee
3/**4**/**5** = 98:2:trace



52% yield (**3**), 96% ee
3/**4**/**5** = 85:15:trace

Significance: Iridium-catalyzed enantioselective allylation has emerged as a powerful method to synthesize structurally diverse, chiral molecules. Despite much progress in the area of enantioselective carbon–sulfur bond formation using iridium, there have been no reports on the use of sodium 2-aminobenzenethiolate as a nucleophile in this class of reaction. Despite, the potential of this substrate class to encounter detrimental '*ortho*-substituent effects' on stereoselectivity, Zhao accomplishes selective and highly enantioselective S-allylation.

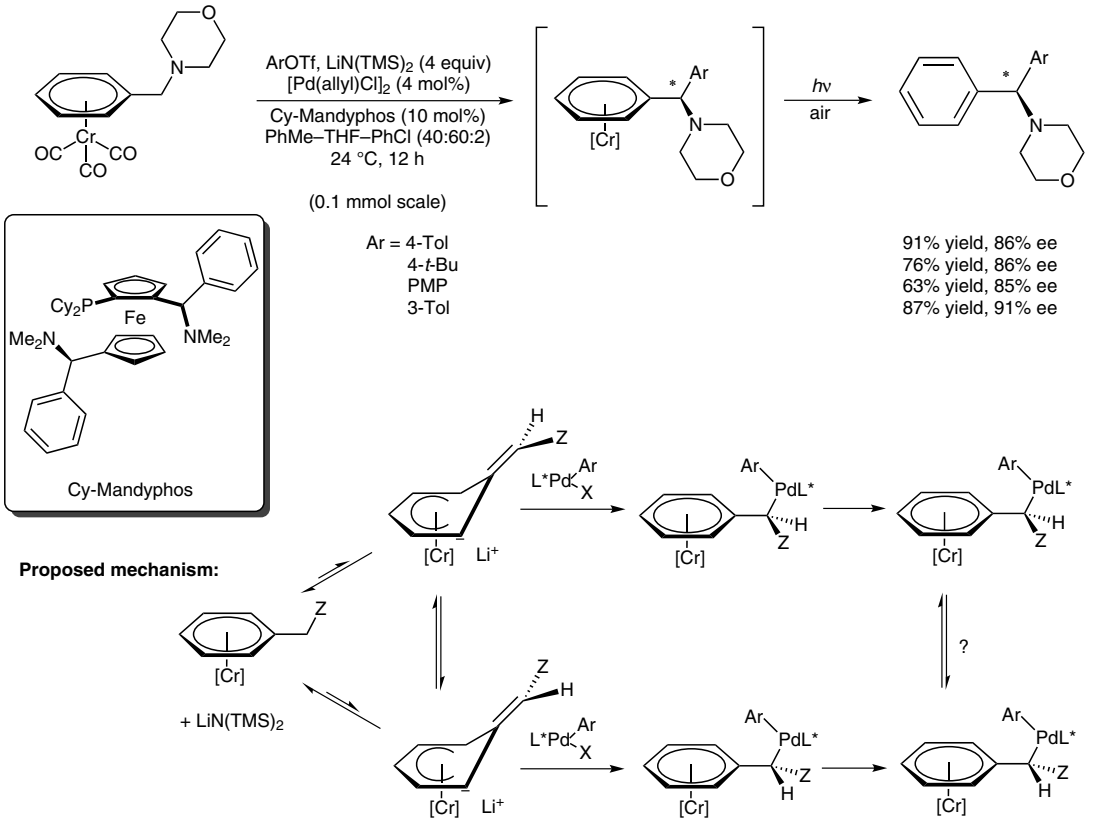
Comment: The authors report an iridium-catalyzed asymmetric S-allylation reaction using chiral phosphoramidite ligands. The method is highly regio- and enantioselective for a variety of aryl- and alkyl-substituted allyl carbonates. Yields range from moderate to good with excellent enantiocontrol. In most cases, the authors are able to completely inhibit bisallylation and maintain high levels of branched-to-linear selectivity. The author use the products to synthesize enantioenriched N,S-heterocycles via an N-allylation/ring-closing metathesis sequence.

SYNFACTS Contributors: Mark Lautens, David A. Petrone
Synfacts 2013, 9(1), 0071 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317762; **Reg-No.:** L16212SF

G. I. MCGREW, C. STANCIU, J. ZHANG, P. J. CARROLL, S. D. DREHER,* P. J. WALSH* (UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA AND MERCK AND CO. INC., RAHWAY, USA)

Asymmetric Cross-Coupling of Aryl Triflates to the Benzylic Position of Benzylamines
Angew. Chem. Int. Ed. **2012**, *51*, 11510–11513.

Palladium-Catalyzed Direct Arylation of Chromium-Activated Benzylic C–H Groups



Significance: The authors previously described the application of (η^6-$C_6H_5CH_2R$)$Cr(CO)_3$ complexes as nucleophile precursors in Pd-catalyzed allylic substitution reactions (*J. Am. Chem. Soc.* **2011**, *133*, 20552). They now report the first catalytic asymmetric cross-coupling of benzyllithiums α to tertiary amines using [$Cr(CO)_3$] activation of benzylic C–H bonds. The stabilized organolithium undergoes Pd-catalyzed coupling with aryl triflates by dynamic kinetic resolution to yield enantioenriched Cr-coordinated diarylmethylamines in good to high yield, which can be de-complexed by exposure to sunlight and air.

Comment: Development of an enantioselective version of the previously reported transformation is challenging as it requires the enantioenriched palldium catalyst to select for one of the chromium adducts faster than the other, and also requires the products to be impervious to racemization. High-throughput screening identified the chiral ligand Cy-Mandyphos, and that the addition of PMDETA and toluene as co-solvents increased the yield. The authors report future plans to close the catalytic cycle by focusing on an arene exchange between the chromium-complexed product and the free arene to liberate the product and regenerate the substrate.

SYNFACTS Contributors: Mark Lautens, Jennifer Tsoung
Synfacts 2013, 9(1), 0072 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317756; **Reg-No.:** L15812SF

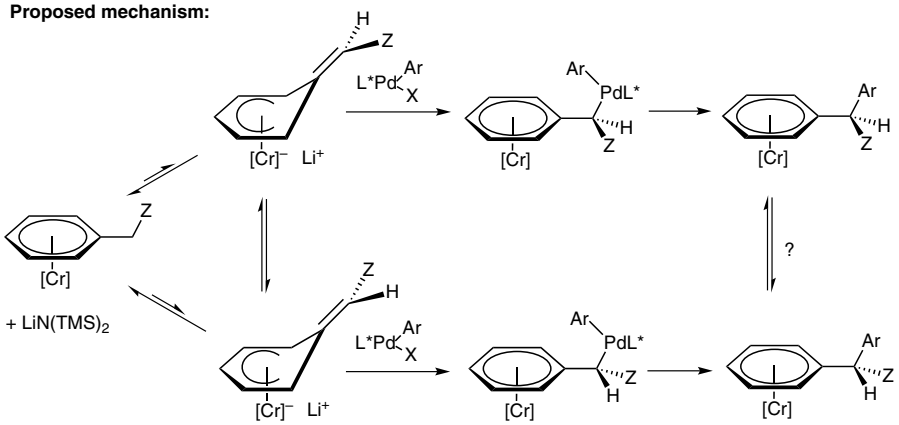
Erratum

Palladium-Catalyzed Direct Arylation of Chromium-Activated Benzylic C–H Groups

G. I. McGrew, C. Stanciu, J. Zhang, P. J. Carroll, S. D. Dreher,* P. J. Walsh* *Synfacts* **2013**, *9*, 72.

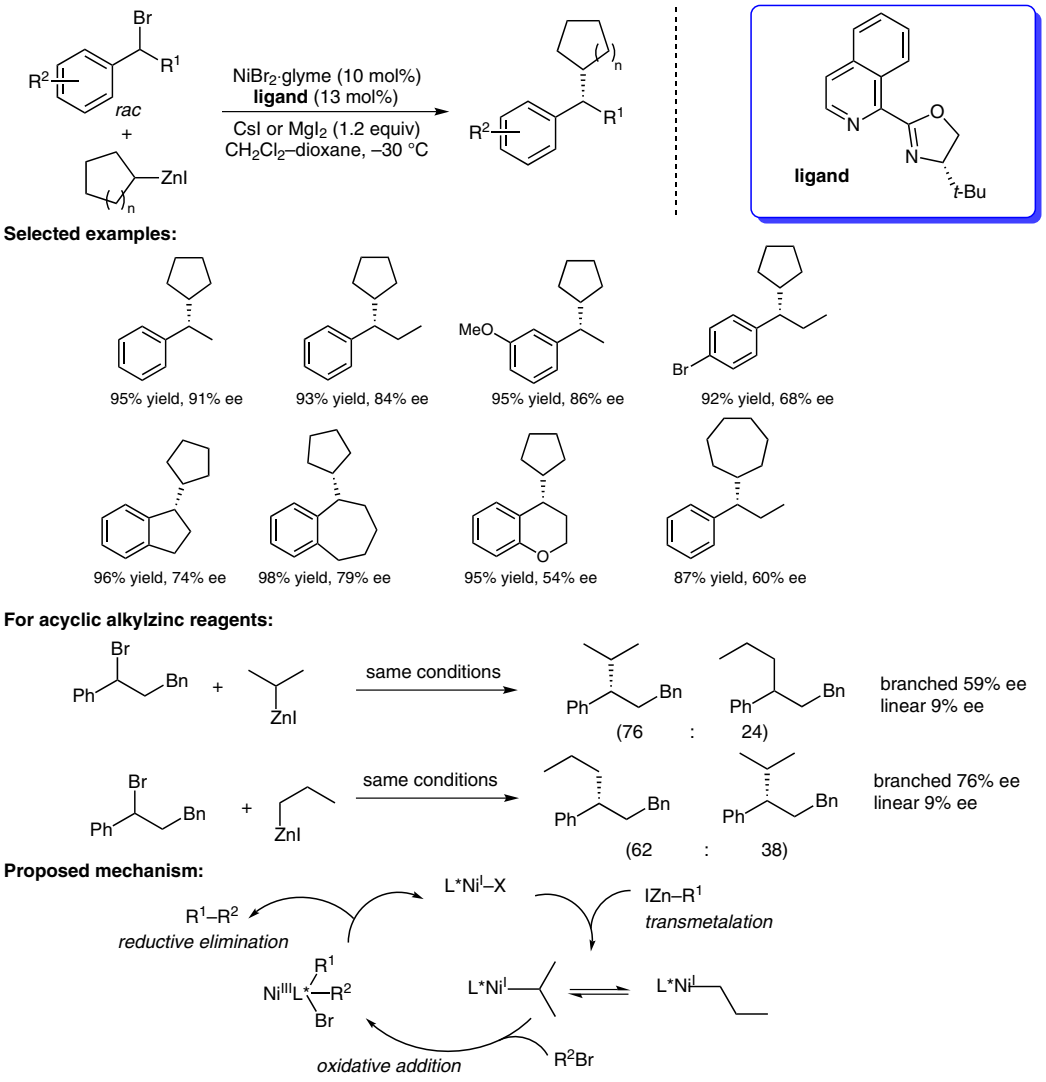
The keywords were incorrect. The correct keywords are palladium, enantioselective cross-coupling, diarylmethylamines. In addition, in the proposed mechanism, the two structures on the right should not contain palladium. The correct scheme is shown below. We apologize for this mistake.

Proposed mechanism:



J. T. BINDER, C. J. CORDIER, G. C. FU* (MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE AND CALIFORNIA INSTITUTE OF TECHNOLOGY, PASADENA, USA)
Catalytic Enantioselective Cross-Couplings of Secondary Alkyl Electrophiles with Secondary Alkylmetal Nucleophiles: Negishi Reactions of Racemic Benzylic Bromides with Achiral Alkylzinc Reagents
J. Am. Chem. Soc. **2012**, *134*, 17003–17006.

Negishi Reaction of Racemic Benzylic Bromides and Alkylzinc Reagents



Significance: Reported here is an enantioselective cross-coupling of racemic benzylic bromides with achiral alkylzinc reagents. A novel bidentate oxazoline-type ligand was developed, leading to the desired products in good yield and enantioselectivity.

Comment: It is surprising that both reagents are achiral. For acyclic alkylzinc reagents, an usual isomerization was observed and a substantial amount of a branched product was generated from an unbranched nucleophile.

SYNFACTS Contributors: Hisashi Yamamoto, Jiajing Tan
Synfacts 2013, 9(1), 0073 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317780; **Reg-No.:** H16012SF

Category
Metal-Catalyzed Asymmetric Synthesis and Stereoselective Reactions

Key words
nickel
Negishi coupling
oxazoline ligands

Key words

rhodium

diazo compounds

sulfur

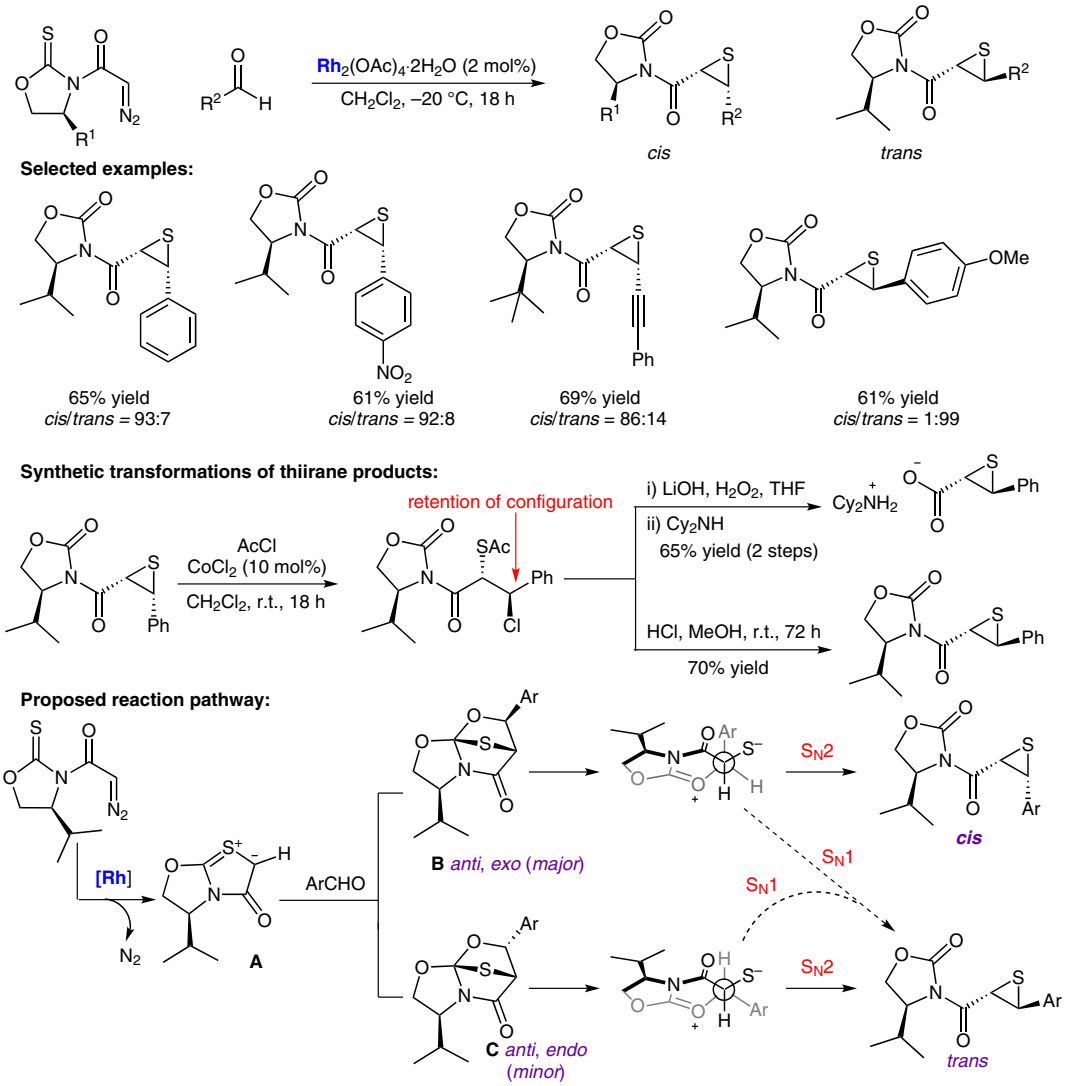
thiiranes

ylides

I. CANO, E. GÓMEZ-BENGOA, A. LANDA, M. MAESTRO, A. MIELGO, I. OLAIZOLA, M. OIARBIDE, C. PALOMO* (UNIVERSIDAD DEL PAÍS VASCO, SAN SEBASTIÁN AND UNIVERSIDADE DA CORUÑA, SPAIN)

N-(Diazoacetyl)oxazolidin-2-thiones as Sulfur-Donor Reagents: Asymmetric Synthesis of Thiiranes from Aldehydes
Angew. Chem. Int. Ed. **2012**, *51*, 10856–10860.

Asymmetric Synthesis of α,β-Thioepoxy Carbonyls by Rhodium Catalysis



Significance: Stereoselective formation of C–S bonds is a difficult yet important challenge. This report describes the use of diazo thiianes as intramolecular sulfur-donor reagents. Under rhodium catalysis, reaction with aldehydes forms thiiranes with high selectivity.

Comment: Computational studies indicate formation of thiocarbonyl ylide intermediate **A**. Reaction with an aldehyde yields a tricyclic adduct, with preferential formation of *anti*,*exo*-product **B** by 0.8–1.2 kcal/mol, which collapses to the *cis* product by an S_N2 reaction. However, when the aryl substituent is anisyl, the *trans* product forms by an S_N1 mechanism.

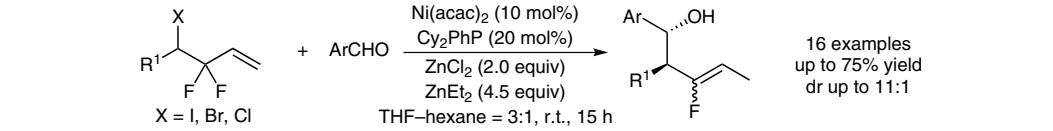
SYNFACTS Contributors: Hisashi Yamamoto, Patrick Brady
Synfacts 2013, 9(1), 0074 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317773; **Reg-No.:** H15312SF

X. LIN, F. ZHENG, F.-L. QING* (SHANGHAI INSTITUTE OF ORGANIC CHEMISTRY AND DONGHUA UNIVERSITY, SHANGHAI, P. R. OF CHINA)

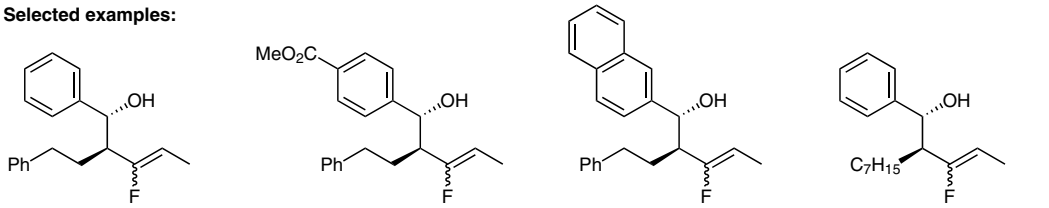
Regio- and Diastereoselective Nickel-Catalyzed Allylation of Aromatic Aldehydes with α-Halo-β,β-difluoropropene Derivatives

J. Org. Chem. **2012**, *77*, 8696–8704.

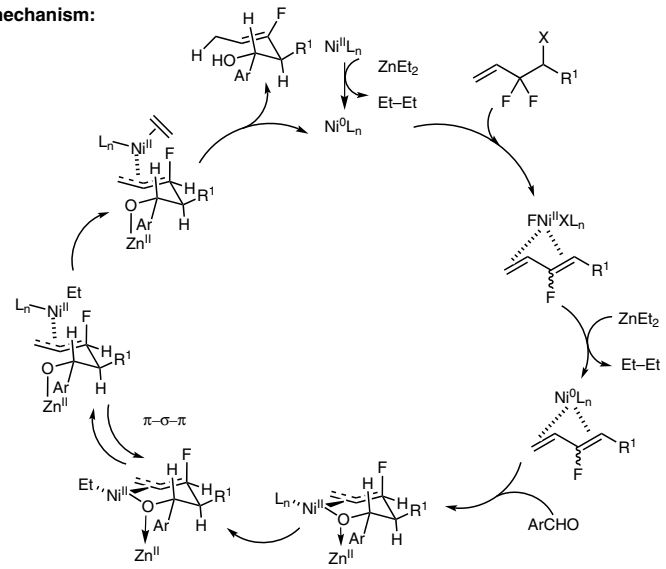
Nickel-Catalyzed Synthesis of γ-Fluorinated Homoallylic Alcohols



Selected examples:



Proposed mechanism:



Significance: Functionalized fluoro olefins have been synthetic targets due to the ability of fluorine to alter the biological activity of organic compounds. In response to the high demand of fluorinated olefins, the authors developed a nickel-catalyzed reductive coupling of fluorinated dienes and carbonyl compounds to synthesize fluoro olefinic alcohols.

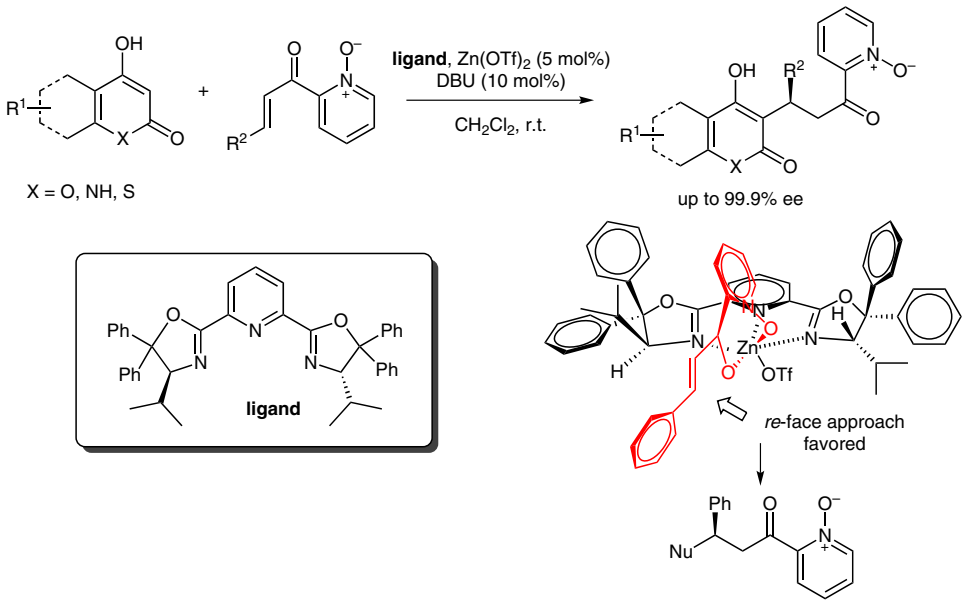
Comment: Both electron-rich and electron-deficient aromatic aldehydes undergo allylation, albeit with lower regioselectivity for electron-deficient aldehydes. The authors rationalize the *Z*/*E*-selectivity by the coordination ability of the aldehyde to $ZnCl_2$: for electron-rich aldehydes, the coupling reaction proceeds faster than diene isomerization, and the *Z*/*E*-ratio remains unchanged in the product.

SYNFACTS Contributors: Hisashi Yamamoto, Kimberly Griffin
Synfacts 2013, 9(1), 0075 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317776; **Reg-No.:** H15612SF

S. K. RAY, P. K. SINGH, N. MOLLETI, V. K. SINGH* (INDIAN INSTITUTE OF TECHNOLOGY KANPUR AND INDIAN INSTITUTE OF SCIENCE EDUCATION AND RESEARCH BHOPAL, INDIA)

Enantioselective Synthesis of Coumarin Derivatives by PYBOX–DIPH–Zn(II) Complex Catalyzed Michael Reaction
J. Org. Chem. **2012**, *77*, 8802–8808.

Zink-Catalyzed Synthesis of Coumarin Derivatives by Asymmetric Michael Reaction



Significance: Coumarin derivatives are a broad class of biological interesting molecules. The zinc-catalyzed system presented provides an efficient access to the direct precursors of such compounds with excellent yield (up to 99%) and enantioselectivity (up to 97%).

Comment: The authors report a PYBOX–DIPH–Zn(II) catalyzed asymmetric Michael reaction and its successful application in the synthesis of coumarin derivatives. This method can tolerate a wide range of cyclic 1,3-dicarbonyl compounds. The resulting products can be easily converted into bioactive molecules such as warfarin and acenocoumarol without loss of enantiopurity.

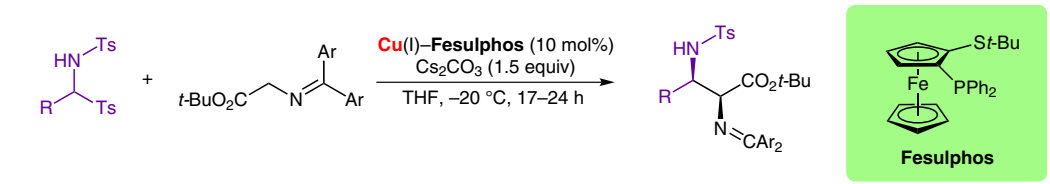
SYNFACTS Contributors: Hisashi Yamamoto, Lan Luo
Synfacts 2013, 9(1), 0076 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317844; **Reg-No.:** H16312SF

E. HERNANDO, R. G. ARRAYÁS,* J. C. CARRETERO* (UNIVERSIDAD AUTONÓMA DE MADRID, SPAIN)

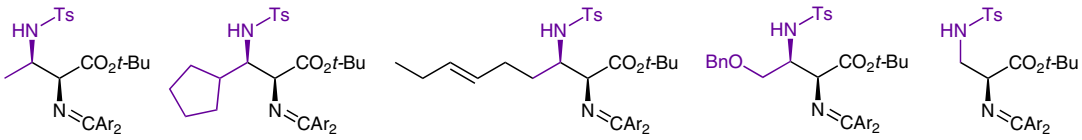
Catalytic Asymmetric Mannich Reaction of Glycine Schiff Bases with α-Amido Sulfones as Precursors of Aliphatic Imines

Chem. Commun. **2012**, *48*, 9622–9624.

Copper-Catalyzed Asymmetric Mannich Reaction of Glycine Imines



Selected examples:



74% yield
dr > 98:2
>99% ee
Ar = 4-F-C_6H_4

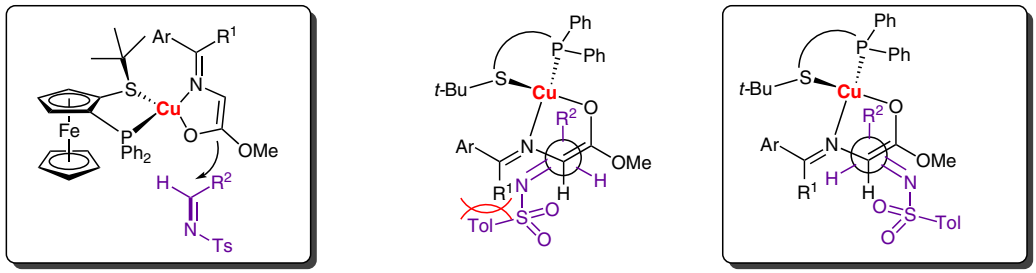
83% yield
dr > 99:1
>99% ee
Ar = Ph

78% yield
dr = 90:10
>99% ee
Ar = 4-F-C_6H_4

50% yield
dr = 95:5
93% ee
Ar = 4-F-C_6H_4

80% yield
83% ee
Ar = 4-F-C_6H_4

Proposed transition-state model:



(2*S*)-configured products

anti-(2*S*,3*S*)
(minor)

syn-(2*S*,3*R*)
(major)

Significance: α,β-Diamino acids are valuable due to their presence in peptide-based drugs and other bioactive compounds. In this report, the authors have extended their copper-catalyzed Mannich reaction of glycine Schiff bases to imines derived from aliphatic aldehydes, which previously performed poorly.

Comment: α-Amido sulfones are employed as imine precursors, due to the instability of imines derived from aliphatic aldehydes. Excellent enantioselectivity and *syn*-selectivity is obtained for a variety of imines. The products have high synthetic applicability due to the orthogonal protection of the amines.

SYNFACTS Contributors: Hisashi Yamamoto, Patrick Brady
Synfacts 2013, 9(1), 0077 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317771; **Reg-No.:** H15112SF

Category

Metal-Catalyzed Asymmetric Synthesis and Stereoselective Reactions

Key words

***C*-glycosides**

cobalt

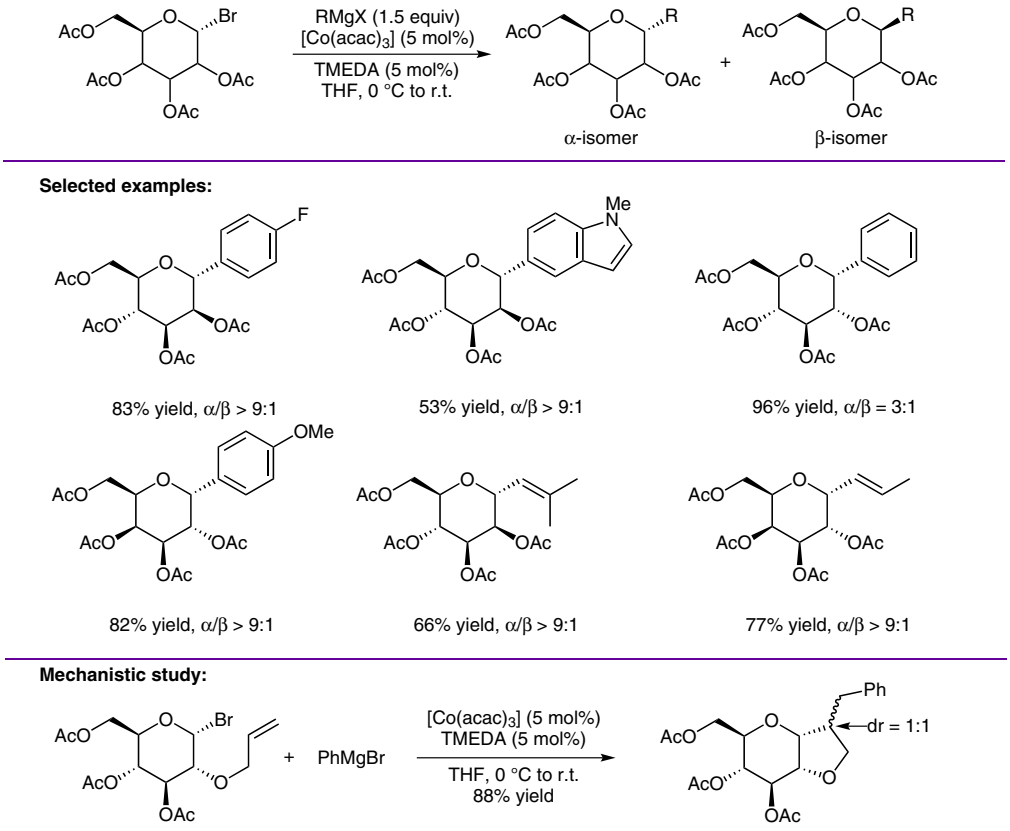
Grignard reagents

L. NICOLAS, P. ANGIBAUD, I. STANSFIELD, P. BONNET, L. MEERPOEL, S. REYMOND,* J. COSSY* (ESCPI PARISTECH, JANSSEN RESEARCH & DEVELOPMENT, VAL DE REUIL, FRANCE AND BEERSE, BELGIUM)

Diastereoselective Metal-Catalyzed Synthesis of *C*-Aryl and *C*-Vinyl Glycosides

Angew. Chem. Int. Ed. **2012**, *51*, 11101–11104.

Cobalt-Catalyzed Cross-Coupling of 1-Bromo Glycosides and Grignard Reagents



Significance: Numerous metal-catalyzed cross-coupling methods to form anomeric C–C bonds exist, which are important for the synthesis of carbohydrate analogues such as *C*-glycosides (see Review below). However, β-elimination is a major drawback of these reactions. The authors report a new diastereoselective cobalt-catalyzed cross-coupling between 1-bromo glycosides and aryl and alkenyl Grignard reagents with moderate to good α-selectivity.

Review: L. Somsák *Chem. Rev*. **2001**, *101,* 81–136.

Comment: The authors report that there was good α-selectivity for the cross-coupling reaction with mannose and galatose derivatives, but lower α/β ratios for glucose derivatives. Like most cobalt-catalyzed cross-coupling reactions, the stereoselectivity of this reaction supports a radical pathway. Treatment of a δ-olefinic 1-bromoglycoside produced an epimeric mixture of the bicyclic product, which would result from the formation of an anomeric radical that leads to a 5-*exo*-trig cyclization followed by cross-coupling with PhMgBr.

SYNFACTS Contributors: Mark Lautens, Jennifer Tsoung
Synfacts 2013, 9(1), 0078 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317754; **Reg-No.:** L15612SF