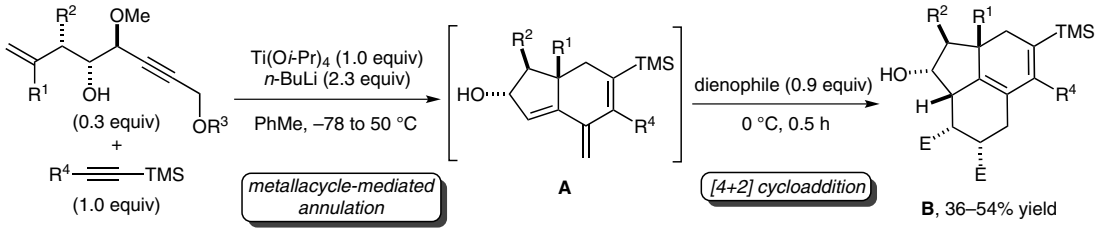
X. CHENG, G. C. MICALIZIO* (DARTMOUTH COLLEGE, HANOVER, USA)

An Annulation Reaction for the Synthesis of Cross-Conjugated Triene-Containing Hydroindanes from Acyclic Precursors
Org. Lett. **2014**, *16*, 5144–5147.

Category
Metal-Mediated Synthesis

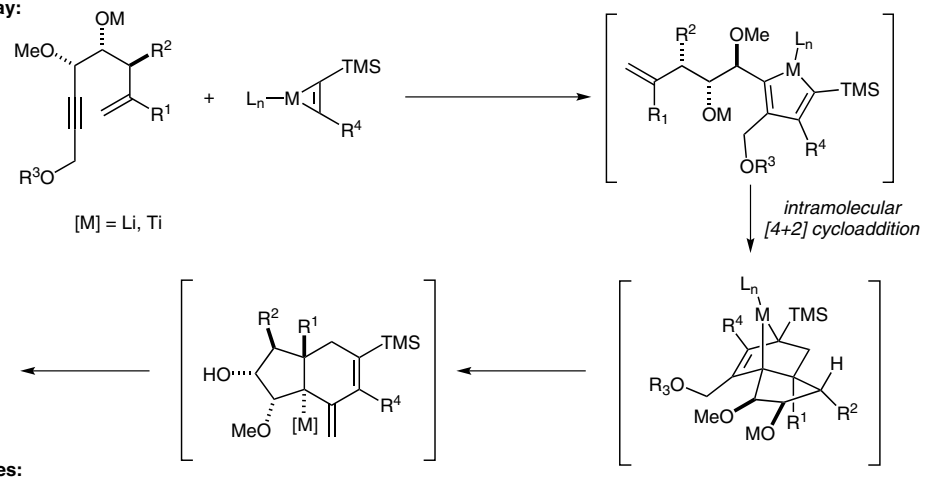
Key words
titanium
annulation
hydroindanes

Metallacycle-Mediated Annulation for the Synthesis of Hydroindanes

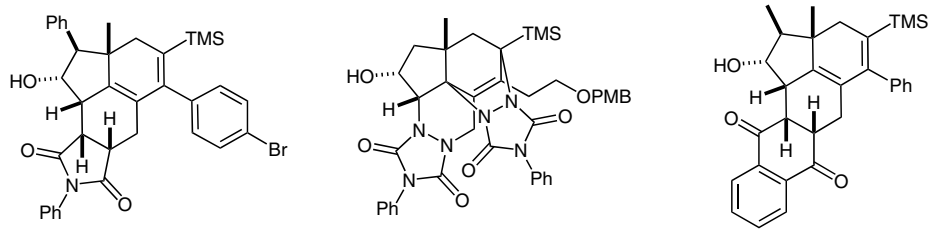


R^1 = Me, Bn
R^2 = H, Me, Ph
R^3 = Me, PMB
R^4 = Me, Ph, 4-BrC_6H_4, CH_2CH_2OPMB, *i*-propenyl

Proposed pathway:



Selected examples:



45% yield 36% yield 54% yield

Significance: Cheng and Micalizio report a stereoselective annulation reaction to afford cross-conjugated triene-containing hydroindanes that are subsequently trapped by a dienophile in a [4+2]-cycloaddition reaction to obtain highly functionalized carbo- and heterocyclic systems.

Comment: The tendency of products of type **A** to undergo Diels–Alder-based dimerization upon standing was harnessed to accomplish this reaction cascade of annulation and intermolecular cycloaddition.

SYNFACTS Contributors: Paul Knochel, Diana Haas
Synfacts 2015, 11(1), 0071 Published online: 15.12.2014
DOI: 10.1055/s-0034-1379649; **Reg-No.:** P15414SF

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Category

Metal-Mediated Synthesis

Key words

boronic acids

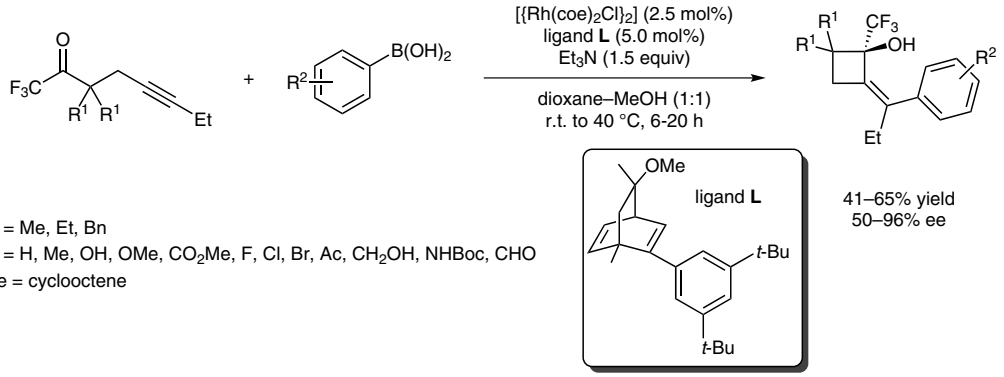
cyclization

rhodium

T. JOHNSON, K.-L. CHOO, M. LAUTENS* (UNIVERSITY OF TORONTO, CANADA)

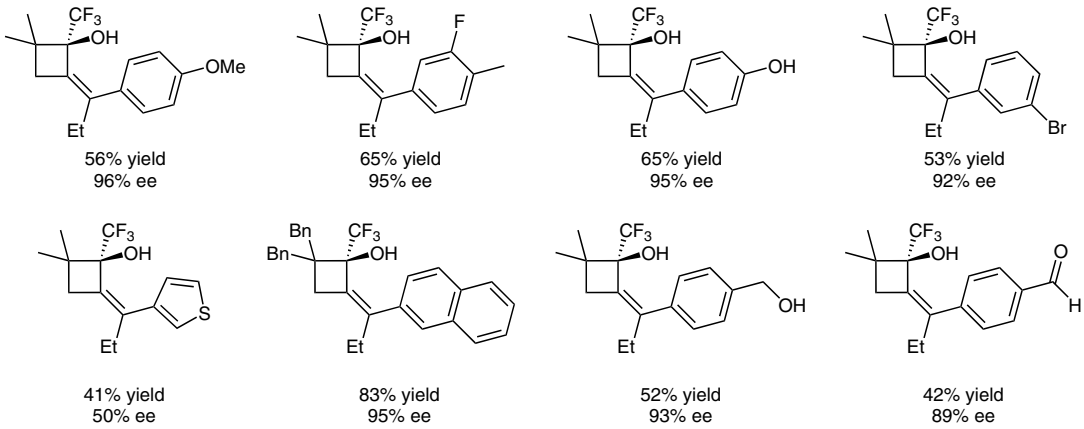
Rhodium-Catalyzed Arylative Cyclization for the Enantioselective Synthesis of (Trifluoromethyl)cyclobutanols
Chem. Eur. J. **2014**, *20*, 14194–14197.

Cyclization of 1-(Trifluoromethyl)-4-alkyn-1-ones with Arylboronic Acids



R^1 = Me, Et, Bn
R^2 = H, Me, OH, OMe, CO_2Me, F, Cl, Br, Ac, CH_2OH, NHBoc, CHO
coe = cyclooctene

Selected examples:



Significance: Lautens and co-workers report a rhodium-catalyzed cyclization of 1-(trifluoromethyl)-4-alkyn-1-ones with variously substituted arylboronic acids to obtain (trifluoromethyl)cyclobutanols bearing an exocyclic double bond.

Comment: The reactivity of the newly formed exocyclic double bond was explored by subjecting a (trifluoromethyl)cyclobutanol to an epoxidation reaction using MCPBA and an ozonolysis.

SYNFACTS Contributors: Paul Knochel, Diana Haas
Synfacts 2015, 11(1), 0072 Published online: 15.12.2014
DOI: 10.1055/s-0034-1379646; **Reg-No.:** P15114SF

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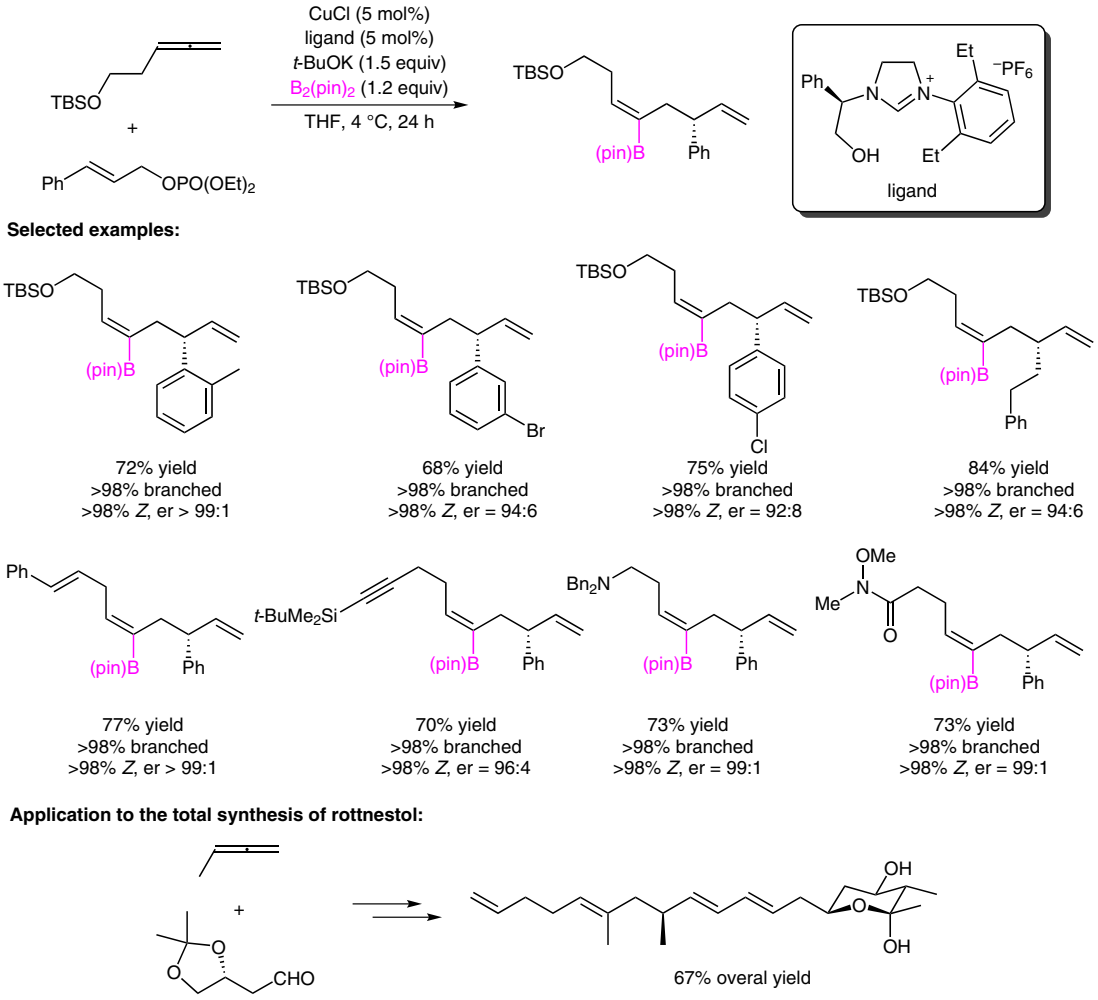
F. MENG, K. P. MCGRATH, A. H. HOVEYDA* (BOSTON COLLEGE, CHESTNUT HILL, USA)
Multifunctional Organoboron Compounds for Scalable Natural Product Synthesis
Nature **2014**, *513*, 367–374.

Category
Metal-Mediated Synthesis

Key words
boron
multicomponent reaction
copper

An Efficient, Practical, and Selective Multicomponent Copper-Catalyzed Process



Significance: The authors demonstrate the generation of multifunctional alkenylboron fragments starting from two simple unsaturated organic molecules and a commercially available diboron reagent. These fragments were shown to carry several advantageous properties. The catalyst used is generated in situ by the reaction of inexpensive CuCl with a chiral ligand which was prepared on multigram scale in good yield.

Comment: The practical protocol can be performed on large scale and makes gram quantities of a variety of complex organic molecules easily available. The products, which contain a stereogenic carbon center, a monosubstituted alkene, and an easily functionalizable *Z*-trisubstituted alkenylboron group, are obtained in good yields and excellent selectivities.

SYNFACTS Contributors: Paul Knochel, Thomas Klatt
Synfacts 2015, 11(1), 0073 Published online: 15.12.2014
DOI: 10.1055/s-0034-1379656; **Reg-No.:** P16014SF

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Category

Metal-Mediated Synthesis

Key words

boron

cross-coupling

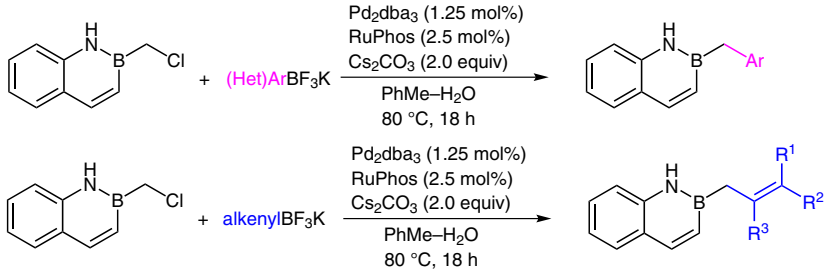
borazaronaphthalenes

G. A. MOLANDER,* J. AMANI, S. R. WISNIEWSKI (UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA, USA)

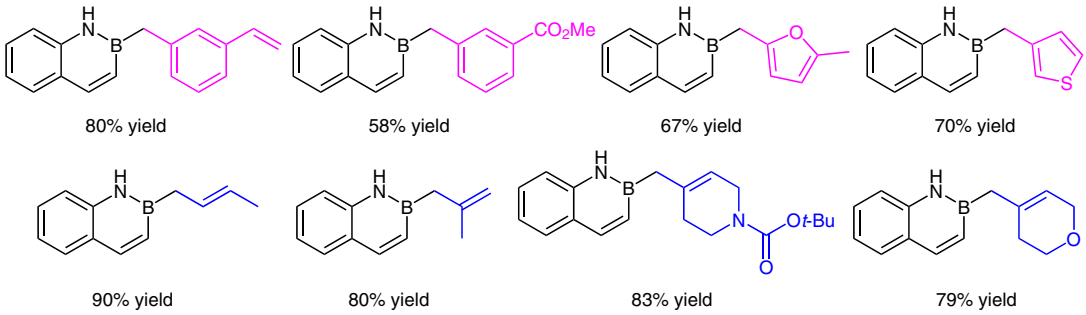
Accessing 2-(Hetero)arylmethyl-, -allyl-, and -propargyl-2,1-borazaronaphthalenes: Palladium-Catalyzed Cross-Couplings of 2-(Chloromethyl)-2,1-borazaronaphthalenes

Org. Lett. **2014**, *16*, 6024–6027.

Accessing 2-(Hetero)arylmethyl-, -allyl-, and -propargyl-2,1-borazaronaphthalenes



Selected examples:



Significance: The authors expanded the electrophilic nature of 2-(chloromethyl)-2,1-borazaronaphthalene. In addition to substitution reactions, now also several metal-catalyzed reactions were performed. Potassium (hetero)aryl and alkenyl trifluoroborates as well as terminal alkynes were successfully used as nucleophiles.

Comment: Impressively, a wide variety of substituted azaborines were prepared starting from one common azaborinyl building block. This new methodology gives access to a whole library of pseudobenzylic-substituted azaborines.

SYNFACTS Contributors: Paul Knochel, Thomas Klatt
Synfacts 2015, 11(1), 0074 Published online: 15.12.2014
DOI: 10.1055/s-0034-1379655; **Reg-No.:** P15914SF

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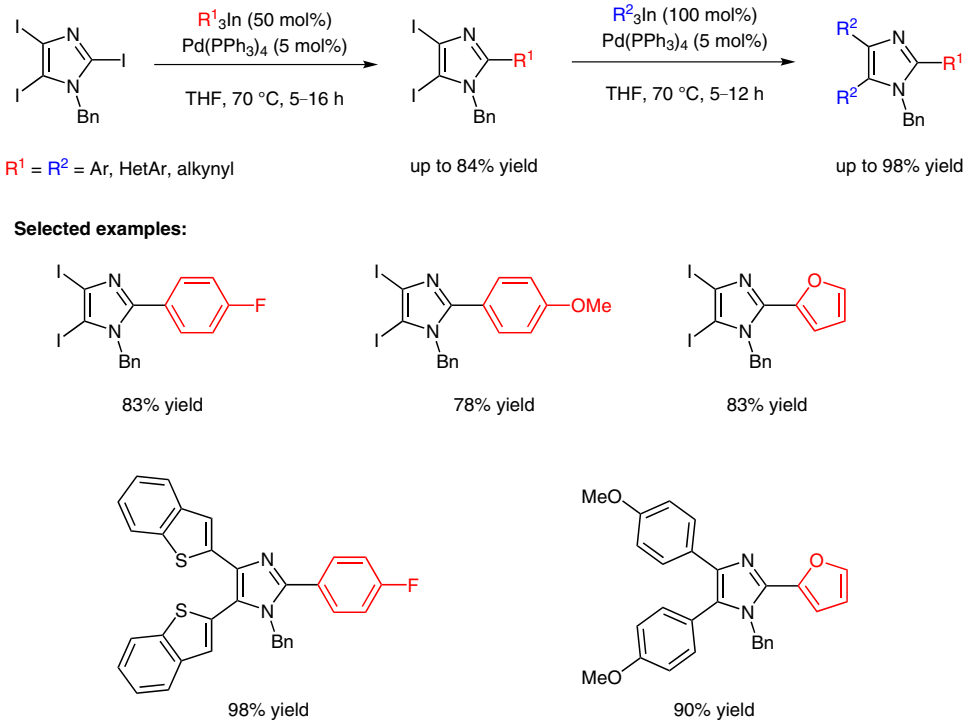
C. PÉREZ-CAAVEIRO, J. P. SESTELO, M. M. MARTÍNEZ,* L. A. SARANDESES*
(UNIVERSIDADE DE CORUÑA, SPAIN)
Triorganoindium Reagents in Selective Palladium-Catalyzed Cross-Coupling with Iodoimidazoles: Synthesis of Neurodazine
J. Org. Chem. **2014**, *79*, 9586–9593.

Category
Metal-Mediated Synthesis

Key words
indium
palladium
imidazoles

Palladium-Catalyzed Cross-Coupling of Triorganoindium Reagents



Significance: The authors demonstrate that triorganoindium reagents react selectively with *N*-benzyl-2,4,5-triiodoimidazole under palladium catalysis to give the corresponding C-2-arylated coupling products in good yields. These products can further be used in a subsequent double cross-coupling to afford trisubstituted imidazoles in good yields.

Comment: This methodology was further applied to the synthesis of neurodazine, a biologically active compound which is able to specifically induce neurogenesis of non-pluripotent myoblasts and the cells derived from mature human skeletal muscle.

SYNFACTS Contributors: Paul Knochel, Jeffrey M. Hammann
Synfacts 2015, 11(1), 0075 Published online: 15.12.2014
DOI: 10.1055/s-0034-1379660; **Reg-No.:** P16414SF

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Category

Metal-Mediated Synthesis

Key words

nickel

cyclization

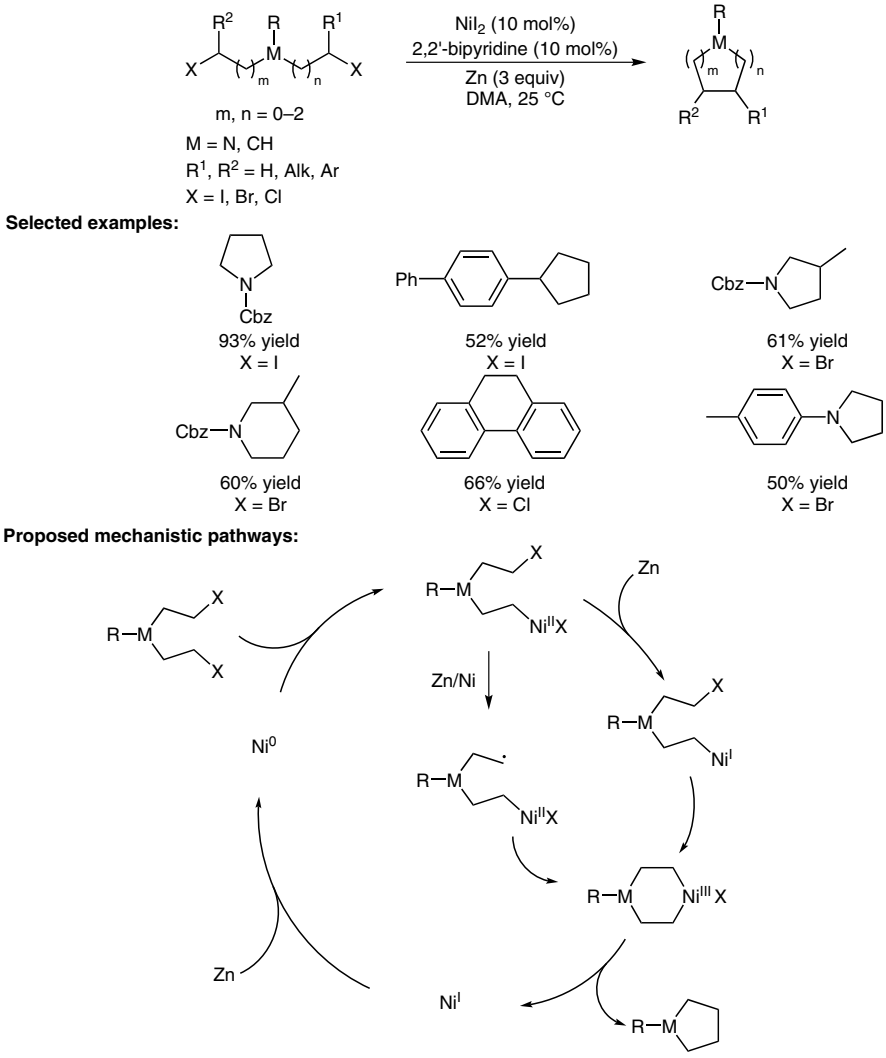
zinc

W. XUE, H. XU, Z. LIANG, Q. QIAN,* H. GONG* (SHANGHAI UNIVERSITY AND ZHENGZHOU UNIVERSITY, P. R. OF CHINA)

Nickel-Catalyzed Reductive Cyclization of Alkyl Dihalides

Org. Lett. **2014**, *16*, 4984–4987.

Nickel-Catalyzed Intramolecular Cyclization of Dihaloalkanes



Significance: The authors have developed an intramolecular cyclization of nitrogen- and carbon-tethered dihaloalkanes. The protocol is especially effective for five-membered rings and only moderately for six-membered rings. The reactions were performed under mild reactions conditions.

Comment: The coupling involving secondary alkyl halides appears to be more efficient than the cyclization of primary/primary alkyl dihalides. Interestingly, the construction of a seven-membered ring is less efficient. Side-reactions are intermolecular oligomerization and hydrodehalogenation of the substrate.

SYNFACTS Contributors: Paul Knochel, Thomas Klatt
Synfacts 2015, 11(1), 0076 Published online: 15.12.2014
DOI: 10.1055/s-0034-1379653; **Reg-No.:** P15714SF

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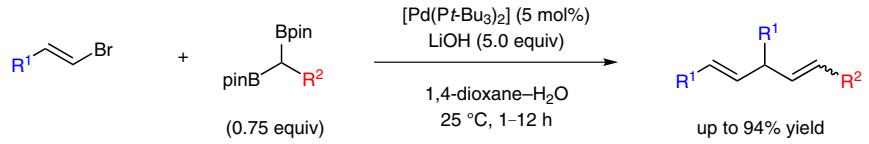
H. LI, Z. ZHANG, X. SHANGGUAN, S. HUANG, J. CHEN, Y. ZHANG, J. WANG* (BEIJING INSTITUTE OF MICROCHEMISTRY AND PEKING UNIVERSITY, BEIJING, P. R. OF CHINA)
Palladium(0)-Catalyzed Cross-Coupling of 1,1-Diboronates with Vinyl Bromides and 1,1-Dibromoalkenes
Angew. Chem. Int. Ed. **2014**, *53*, 11921–11925.

Category
Metal-Mediated Synthesis

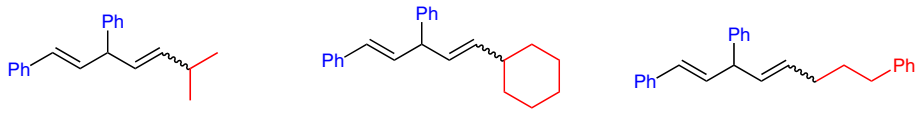
Key words
palladium
cross-coupling

Palladium-Catalyzed Cross-Coupling of 1,1-Diboronates

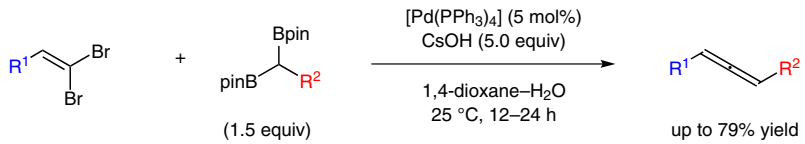


R^1 = Ar, Alk
R^2 = CH_2Bn, *i*-Pr, Cy

Selected examples:

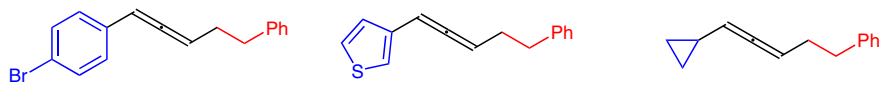


45% yield, *E*/*Z* > 20:1 57% yield, *E*/*Z* > 20:1 80% yield, *E*/*Z* = 11:1



R^1 = Ar, Alk
R^2 = CH_2Bn, Alk, Cy

Selected examples:



74% yield 79% yield 76% yield

Significance: The authors demonstrate a palladium(0)-catalyzed reaction of 1,1-diboronates with substituted vinyl bromides or dibromoalkenes to give 1,4-dienes or allenes in good yields while showing good functional group tolerance.

Comment: When using 1,1-dibromoalkenes bearing a terminal alkynyl group as the substrate, the palladium(0)-catalyzed coupling described above can be followed by a CuI-catalyzed allenation with *N*-tosylhydrazones to give unsymmetrical diallenes.

SYNFACTS Contributors: Paul Knochel, Jeffrey M. Hammann
Synfacts 2015, 11(1), 0077 Published online: 15.12.2014
DOI: 10.1055/s-0034-1379661; **Reg-No.:** P16514SF

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Category

Metal-Mediated Synthesis

Key words

zirconium

nitriles

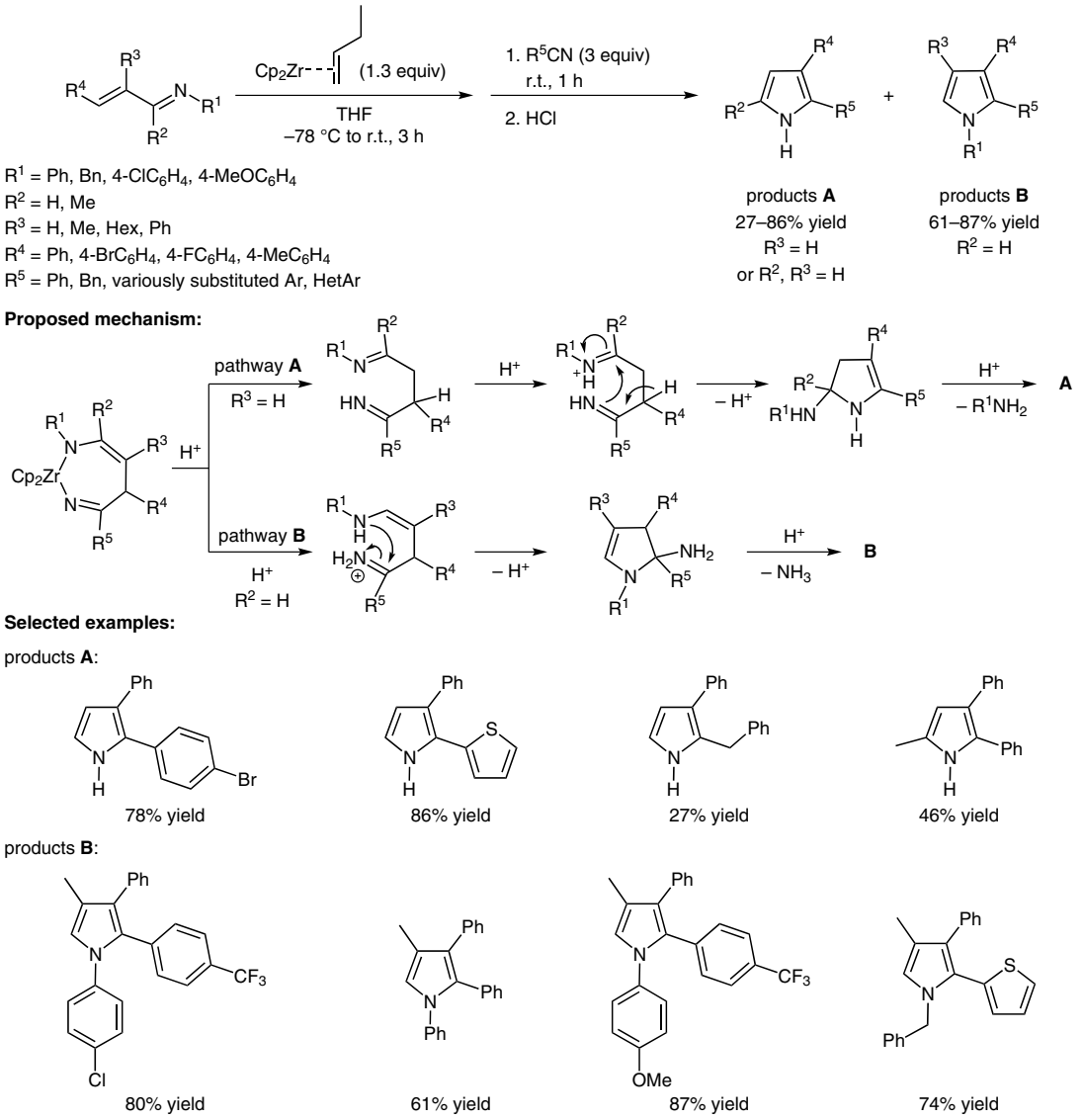
cyclization

S. YU, M. XIONG, X. XIE, Y. LIU* (SHANGHAI INSTITUTE OF ORGANIC CHEMISTRY, P. R. OF CHINA)

Insertion of Nitriles into Zirconocene 1-aza-1,3-diene Complexes: Chemoselective Synthesis of N–H and N-Substituted Pyrroles

Angew. Chem. Int. Ed. **2014**, *53*, 11596–11599.

Zirconium-Mediated Synthesis of Pyrroles



Significance: Liu and co-workers report the direct insertion of nitriles into zirconocene-1-aza-1,3-diene complexes for the synthesis of variously substituted N–H and N-substituted pyrroles in high yields.

Comment: The outcome of the reaction is determined by different cyclization patterns that depend on the relative stability and reactivity of the enamine–imine tautomers that are formed upon hydrolysis of the diazazirconacycles.

SYNFACTS Contributors: Paul Knochel, Diana Haas
Synfacts 2015, 11(1), 0078 Published online: 15.12.2014
DOI: 10.1055/s-0034-1379648; **Reg-No.:** P15314SF

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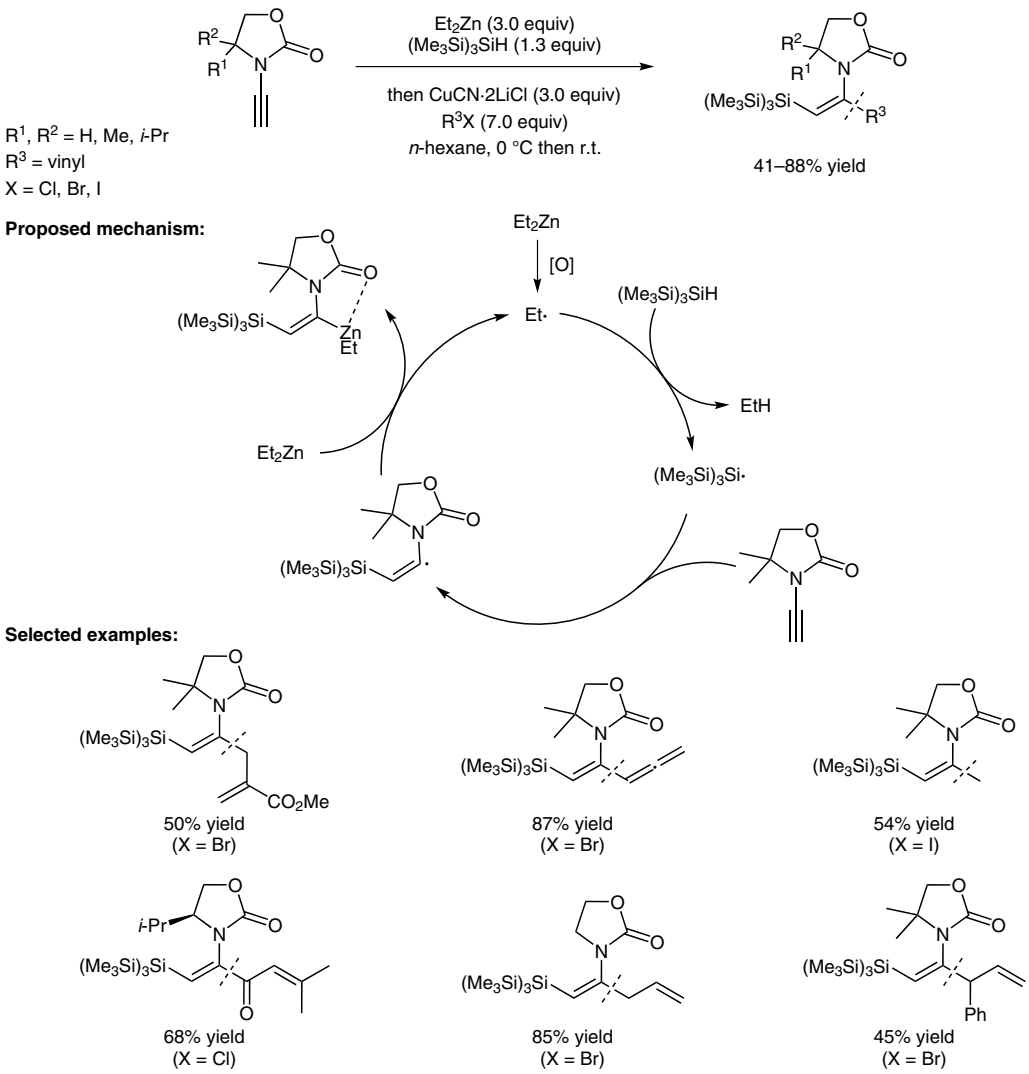
E. ROMAIN, C. FOPP, F. CHEMLA, F. FERREIRA, O. JACKOWSKI, M. OESTREICH,*
A. PEREZ-LUNA* (UNIVERSITÉ PIERRE ET MARIE CURIE, PARIS, FRANCE AND TECHNICAL UNIVERSITY OF BERLIN, GERMANY)
Trans-Selective Radical Silylzincation of Ynamides
Angew. Chem. Int. Ed. **2014**, *53*, 11333–11337.

Category
Metal-Mediated Synthesis

Key words
zinc
copper
silylation

Trans-Selective Silylzincation of Terminal Ynamides



Significance: The authors report a regio- and stereoselective silylzincation reaction of terminal ynamides using $(Me_3Si)_3SiH$ and diethyl zinc. The resulting vinylzinc intermediates are trapped by a copper(I)-mediated substitution reaction to obtain *Z*-β-silylenamides in high yields.

Comment: The radical-chain process involves an addition of the $(Me_3Si)_3Si$ radical to the ynamide to provide a *Z*-configured α-amino vinylic radical which reacts with the dialkylzinc reagent by homolytic substitution to afford a α-zincated β-silylenamide.

SYNFACTS Contributors: Paul Knochel, Diana Haas
Synfacts 2015, 11(1), 0079 Published online: 15.12.2014
DOI: 10.1055/s-0034-1379647; **Reg-No.:** P15214SF

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Category

Metal-Mediated Synthesis

Key words

titanium

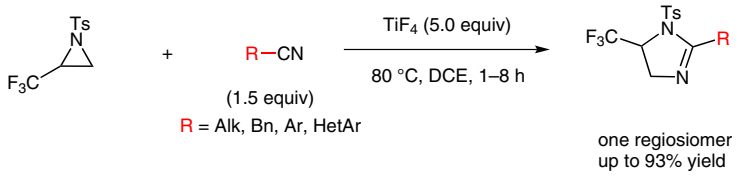
cycloaddition

M. YOSHIKAI, R. ISHIBASHI, Y. YAMADA, T. HANAMOTO* (SAGA UNIVERSITY, JAPAN)

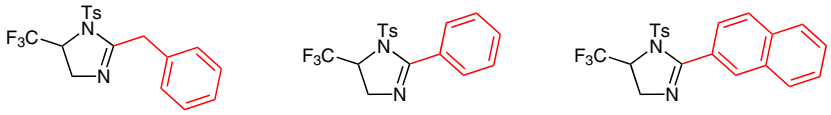
TiF_4-Mediated Regioselective Cycloaddition of 2-(Trifluoromethyl)-*N*-tosylaziridine to Nitriles

Org. Lett. **2014**, *16*, 5509–5511.

Titanium-Mediated Cycloaddition



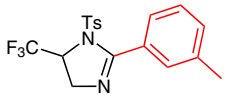
Selected examples:



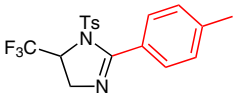
80% yield

85% yield

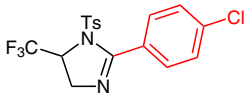
93% yield



81% yield



91% yield



69% yield

Significance: The authors describe a mild and efficient [3+2] cycloaddition of 2-(trifluoromethyl)-*N*-tosylaziridine to various nitriles using TiF_4 as a Lewis acid, to give the corresponding 4-(trifluoromethyl)-1,3-imidazolines in good yields and excellent regioselectivity.

Comment: From a mechanistic point of view, the authors assume that the aziridine is activated by TiF_4, which is then attacked by the nitrile to afford the betaine intermediate, which collapses to form the 1,3-imidazole.

SYNFACTS Contributors: Paul Knochel, Jeffrey M. Hammann
Synfacts 2015, 11(1), 0080 Published online: 15.12.2014
DOI: 10.1055/s-0034-1379659; **Reg-No.:** P16314SF

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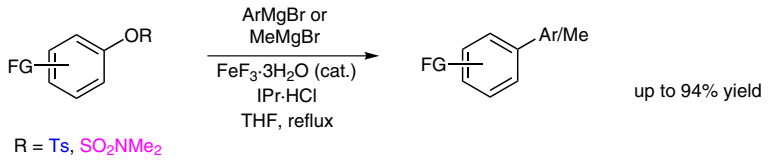
T. AGRAWAL, S. P. COOK* (INDIANA UNIVERSITY, BLOOMINGTON, USA)
Iron-Catalyzed Coupling of Aryl Sulfamates and Aryl/Vinyl Tosylates with Aryl Grignards
Org. Lett. **2014**, *16*, 5080–5083.

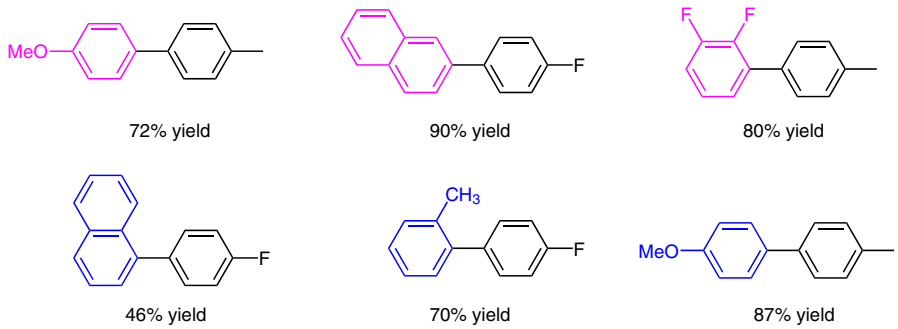
Category
Metal-Mediated Synthesis

Key words
iron
cross-coupling
Grignard reagents

Aryl Sulfamate and Tosylate Cross-Coupling with Aryl Grignard Reagents



Selected examples:



Significance: The authors report the first iron-catalyzed direct coupling of aryl sulfamates and tosylates with aryl Grignard reagents. Interestingly, fluoride counterions were found to increase the yields of the desired products. FeF_3 does not need to be reduced before the reaction, and in fact, reactions performed without the pre-reduction proceed better in almost all cases.

Comment: The reaction was shown to tolerate a number of iron pre-catalysts with no significant homocoupling of the aryl Grignard. Studies to understand the reaction mechanism better are underway.

SYNFACTS Contributors: Paul Knochel, Thomas Klatt
Synfacts 2015, 11(1), 0081 Published online: 15.12.2014
DOI: 10.1055/s-0034-1379654; **Reg-No.:** P15814SF

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Category

Metal-Mediated Synthesis

Key words

nickel

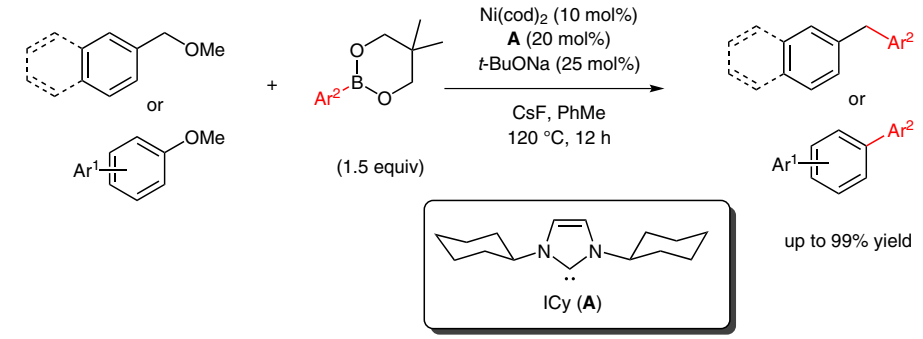
Suzuki–Miyaura cross-coupling

M. TOBSIU,* A. YASUTOME, H. KINUTA, K. NAKAMURA, N. CHATANI* (OSAKA UNIVERSITY, JAPAN)

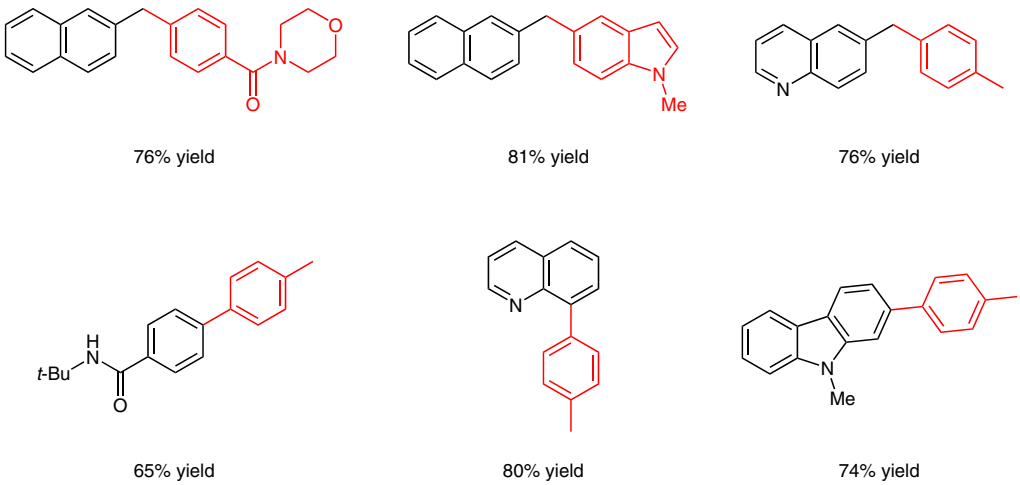
1,3-Dicyclohexylimidazole-2-ylidene as a Superior Ligand for the Nickel-Catalyzed Cross-Coupling of Aryl and Benzyl Methyl Ethers with Organoboron Reagents

Org. Lett. **2014**, *16*, 5572–5575.

Nickel-Catalyzed Suzuki–Miyaura Cross-Coupling



Selected examples:



Significance: The authors developed a novel nickel-based catalyst for the cross-coupling of aryl and benzyl methyl ethers with organoboron reagents. The use of $Ni(cod)_2$ and 1,3-dicyclohexylimidazol-2-ylidene (**A**) gave the expected products in good yields while showing good functional group tolerance.

Comment: Notably, when using **A** instead of Cy_3P, heteroaryl ethers were coupled in good yields (up to 96%), while the same reaction with Cy_3P led to no product.

SYNFACTS Contributors: Paul Knochel, Jeffrey M. Hammann
Synfacts 2015, 11(1), 0082 Published online: 15.12.2014
DOI: 10.1055/s-0034-1379657; **Reg-No.:** P16114SF

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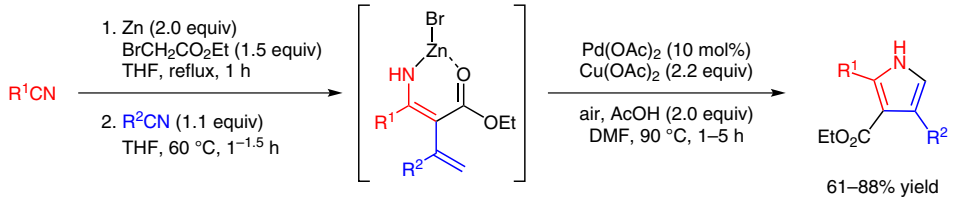
J. H. KIM, S. Y. CHOI, J. BOUFFARD, S.-G. LEE* (EWHA WOMANS UNIVERSITY, SEOUL, REPUBLIC OF KOREA)

Tandem One-Pot Synthesis of Polysubstituted NH-Pyrroles Involving the Palladium-Catalyzed Intramolecular Oxidative Amination of the Zinc Bromide Complex of β-Enamino Esters
J. Org. Chem. **2014**, *79*, 9253–9261.

Category
Metal-Mediated Synthesis

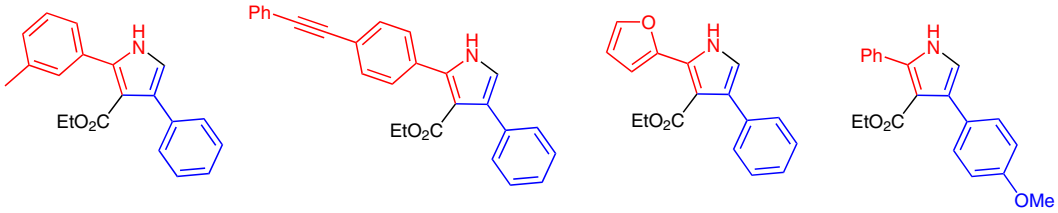
Key words
amination
zinc
pyrroles

Oxidative Amination of the Zinc Bromide Complex of β-Enamino Esters

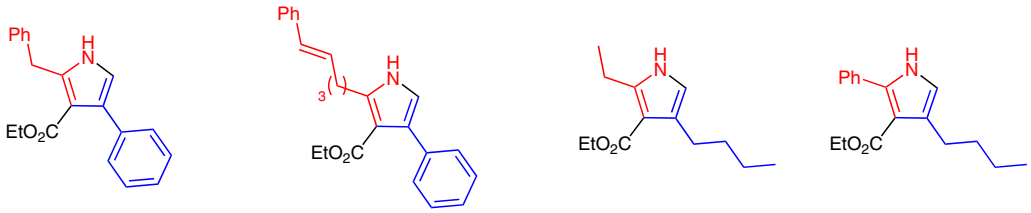


R^1 = Alk, Ar, HetAr, Bn
R^2 = Alk, Ar, CH_2CH_2Ph

Selected examples:



82% yield | 65% yield | 70% yield | 61% yield



79% yield | 77% yield | 64% yield | 73% yield

Significance: Lee and co-workers report a tandem palladium-catalyzed intramolecular oxidative olefin amination of the zinc bromide complex of α-vinylated β-amino esters to afford various 2,3,4-trisubstituted pyrroles in good yields.

Comment: The synthetic utility of this efficient and atom-economical procedure is shown by the synthesis of pyrrolophenanthrenes and pyranopyrrolones through selective palladium- and copper-catalyzed C–C and C–O bond-forming reactions.

SYNFACTS Contributors: Paul Knochel, Diana Haas
Synfacts 2015, 11(1), 0083 Published online: 15.12.2014
DOI: 10.1055/s-0034-1379650; **Reg-No.:** P15514SF

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Category

Metal-Mediated Synthesis

Key words

copper

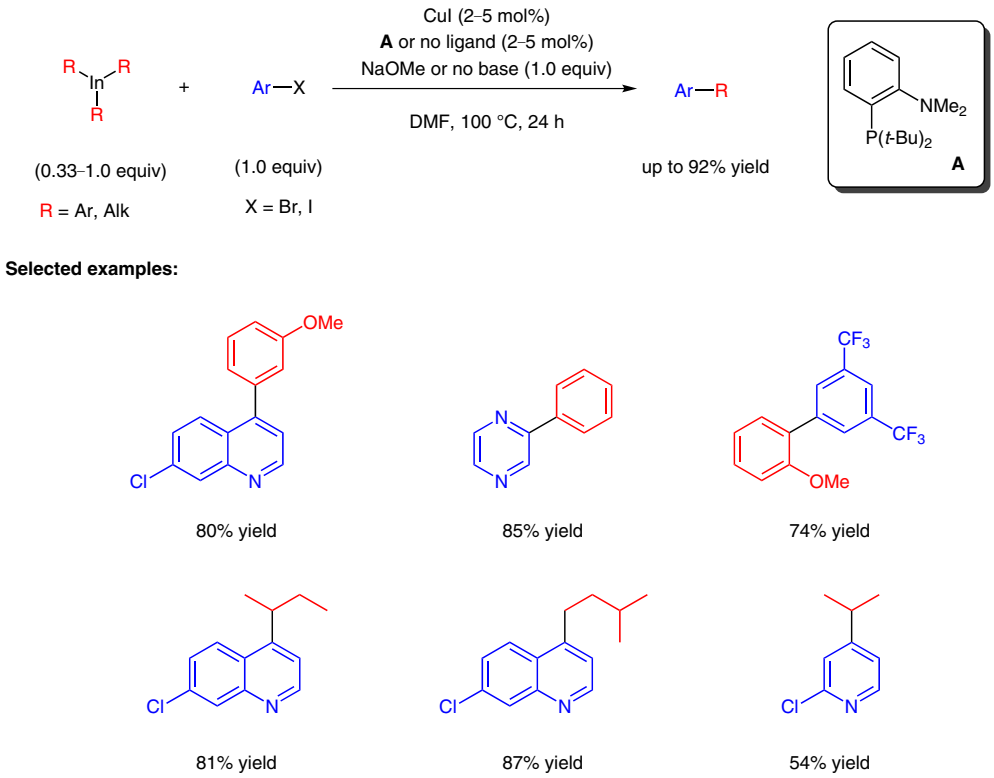
indium

S. THAPA, S. K. GURUNG, D. A. DICKIE, R. GIRI* (UNIVERSITY OF NEW MEXICO, ALBUQUERQUE, USA)

Copper-Catalyzed Coupling of Triaryl- and Trialkylindium Reagents with Aryl Iodides and Bromides through Consecutive Transmetalations

Angew. Chem. Int. Ed. **2014**, *53*, 11620–11624.

Copper-Catalyzed Coupling of Indium Reagents



Significance: Giri and co-workers describe a copper(I)-catalyzed coupling of triorganoindium reagents with aryl iodides and bromides. This reaction shows high functional group tolerance, while being compatible with sterically hindered substrates, leading to the expected products in good yield.

Comment: The reaction can be performed with low catalyst loadings (2 mol%) and only requires 0.33 equivalents of the triorganoindium reagent with respect to the aryl halide.

SYNFACTS Contributors: Paul Knochel, Jeffrey M. Hammann
Synfacts 2015, 11(1), 0084 Published online: 15.12.2014
DOI: 10.1055/s-0034-1379658; **Reg-No.:** P16214SF

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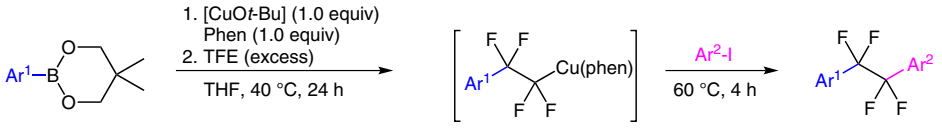
H. SAIJO, M. OHASHI, S. OGOSHI* (OSAKA UNIVERSITY AND JAPAN SCIENCE AND TECHNOLOGY AGENCY, OSAKA, JAPAN)

Fluoroalkylcopper(I) Complexes Generated by the Carbocupration of Tetrafluoroethylene: Construction of a Tetrafluoroethylene-Bridging Structure
J. Am. Chem. Soc. **2014**, *136*, 15158–15161.

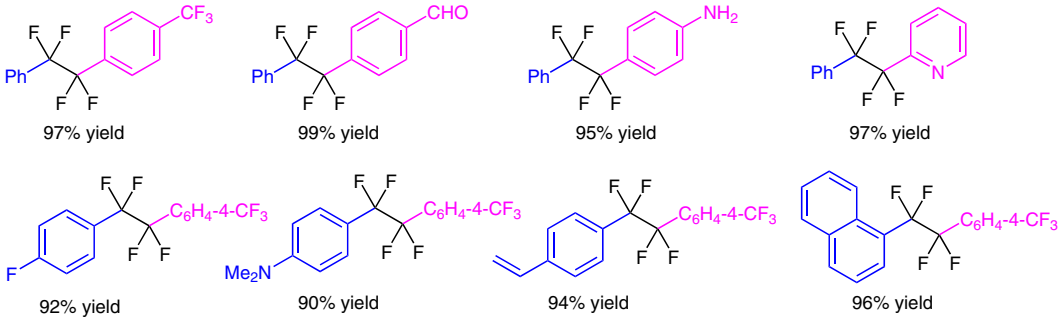
Category
Metal-Mediated Synthesis

Key words
copper
tetrafluoroethylene
aryl groups

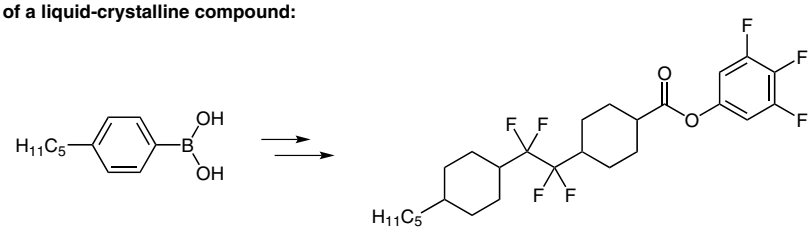
Construction of a Tetrafluoroethylene-Bridging Structure via Carbocupration



Selected examples:



Synthesis of a liquid-crystalline compound:



64% yield over 6 steps

Significance: The authors report the synthesis, characterization, and synthetic application of 2-aryl-1,1,2,2-tetrafluoroethylcopper complexes. Starting with a carbocupration of tetrafluoroethylene (TFE), a variety of 1,2-difunctionalized 1,1,2,2-tetrafluoroethanes were prepared in high yields.

Comment: The molecular structure of the aryl–TFE–copper species was determined by X-ray crystallography and NMR analysis. Furthermore, the synthetic utility for liquid-crystalline compounds bearing a tetrafluoroethylene-bridging structure was demonstrated.

SYNFACTS Contributors: Paul Knochel, Thomas Klatt
Synfacts 2015, 11(1), 0085 Published online: 15.12.2014
DOI: 10.1055/s-0034-1379651; **Reg-No.:** P15614SF

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