Category

Metal-Mediated Synthesis

Key words

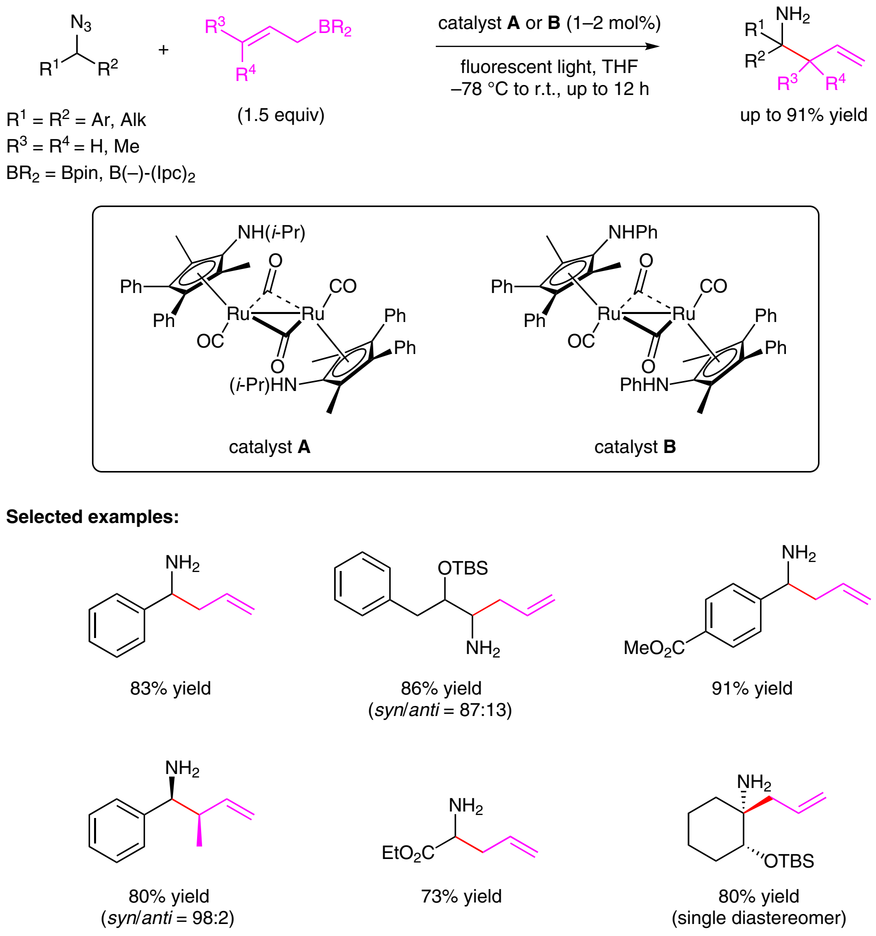
allylation

azides

ruthenium

J. H. LEE, S. GUPTA, W. JEONG, Y. H. RHEE,* J. PARK* (POHANG UNIVERSITY OF SCIENCE AND TECHNOLOGY, REPUBLIC OF KOREA)
Characterization and Utility of N-Unsubstituted Imines Synthesized from Alkyl Azides by Ruthenium Catalysis
Angew. Chem. Int. Ed. **2012**, *51*, 10851–10855.

Ruthenium-Catalyzed Generation of N-Unsubstituted Imines



Significance: The authors report, that N-unsubstituted imines can be efficiently generated from alkyl azides using a ruthenium catalyst and fluorescent light. Furthermore, an allylation reaction in a one-pot fashion was achieved, leading to homoallylic imines.

Comment: The mild reaction conditions allow an asymmetric allylation of in situ generated benzaldimine from benzyl azide. Using the chiral allyl bis(isopinocampheyl)borane reagent at –78 °C furnishes the homoallylic amine in 87% yield with an enantiomeric excess of 89%.

SYNFACTS Contributors: Paul Knochel, Andreas K. Steib
Synfacts 2013, 9(1), 0079
DOI: 10.1055/s-0032-1317740; **Reg-No.:** P16212SF

Category

Metal-Mediated Synthesis

Key words

palladium

zinc

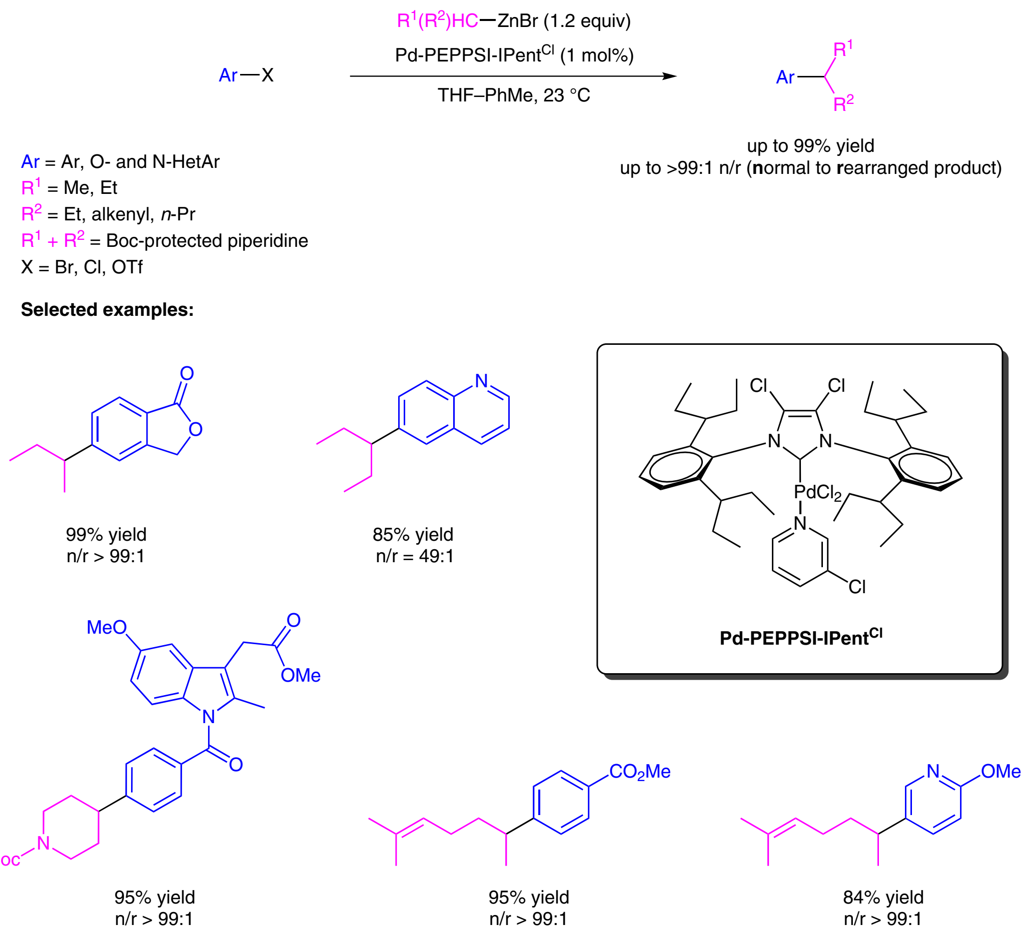
PEPPSI

organcozinc reagents

M. POMPEO, R. D. J. FROESE, N. HADEI, M. G. ORGAN* (YORK UNIVERSITY, TORONTO, CANADA)

Pd-PEPPSI-IPent^{Cl}: A Highly Effective Catalyst for the Selective Cross-Coupling of Secondary Organozinc Reagents
Angew. Chem. Int. Ed. **2012**, *51*, 11354–11357.

Pd-PEPPSI-IPent^{Cl} – Selective Coupling of Secondary Organozinc Nucleophiles



Significance: The authors report the new catalyst Pd-PEPPSI-IPent^{Cl}, which highly efficiently couples secondary alkylzinc reagents to (hetero)aryl bromides, chlorides and triflates. The corresponding alkylated aromatics are obtained in excellent yield and with high regioselectivity.

Comment: β-Hydride elimination (BHE) constitutes one of the main drawbacks for the cross-coupling of secondary alkyl reagents, especially if they react with electron-rich coupling partners. These problems are overcome by the new palladium-catalyst, which bears bulkier substituents and additionally, is characterized by a decreased electron density, thus favoring reductive elimination instead of BHE. Density functional theory (DFT) calculations support the theoretical selectivities.

SYNFACTS Contributors: Paul Knochel, Nadja M. Barl
Synfacts 2013, 9(1), 0080
DOI: 10.1055/s-0032-1317731; **Reg-No.:** P15312SF

S. ASPIN, A.-S. GOUTIERRE, P. LARINI, R. JAZZAR, O. BAUDOIN* (UNIVERSITÉ CLAUDE BERNARD LYON 1, FRANCE)
Synthesis of Aromatic α-Aminoesters: Palladium-Catalyzed Long-Range Arylation of Primary Csp^3–H Bonds
Angew. Chem. Int. Ed. **2012**, *51*, 10808–10811.

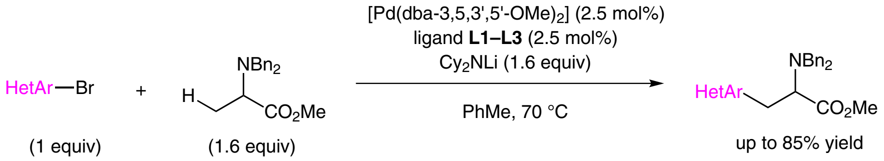
Category

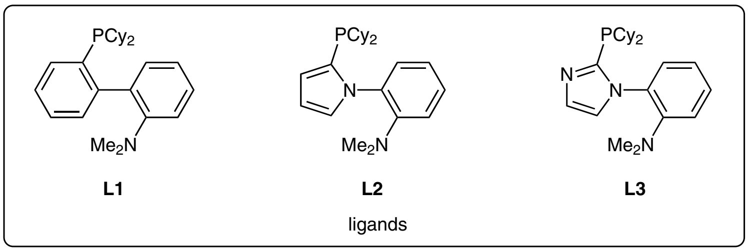
Metal-Mediated Synthesis

Key words

arylation
palladium
C–C coupling

Palladium-Catalyzed β-Arylation of α-Amino Esters





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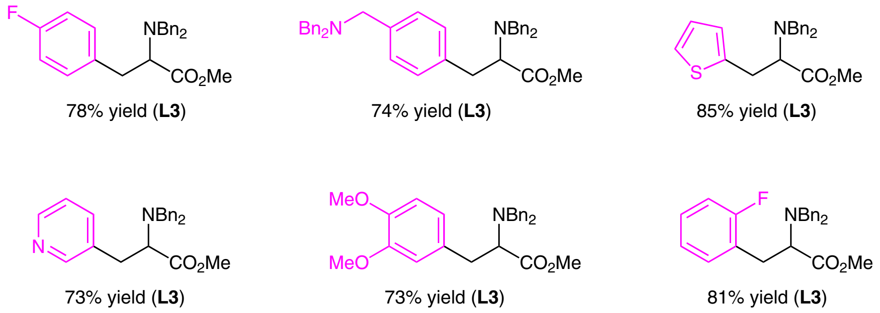


Significance: A novel general β-arylation of protected alanine esters to yield synthetically useful (hetero)aryl alanine building blocks has been disclosed. The protocol utilizes a lithium amide to form an enolate that undergoes a palladium-catalyzed C–C coupling with various aromatic bromides.

Comment: Interestingly, the reaction could be extended to α-amino acids bearing other linear alkyl chains. Arylation occurs preferentially at the terminal Csp^3–H bond, thus providing δ-, ε- and even ζ-arylated products. All products could be deprotected via hydrogenolysis to give the respective amines.

SYNFACTS Contributors: Paul Knochel, Andreas K. Steib
Synfacts 2013, 9(1), 0081 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317739; **Reg-No.:** P16112SF

Category

Metal-Mediated Synthesis

Key words

enantioselective fluoroallylboration

aldehydes

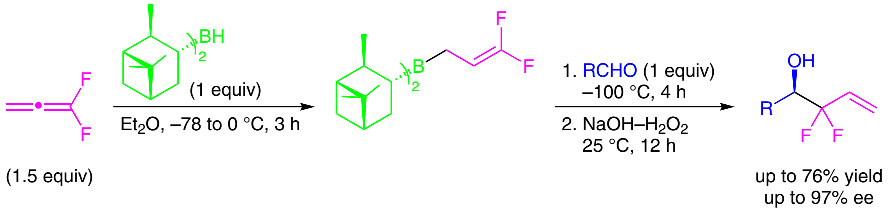
2,2-*gem*-difluorinated homoallylic alcohols

P. V. RAMACHANDRAN,* A. TAFELSKA-KACZMAREK, A. CHATTERJEE (PURDUE UNIVERSITY, WEST LAFAYETTE, USA)

B-(3,3-Difluoroallyl)diisopinocampheylborane for the Enantioselective Fluoroallylboration of Aldehydes

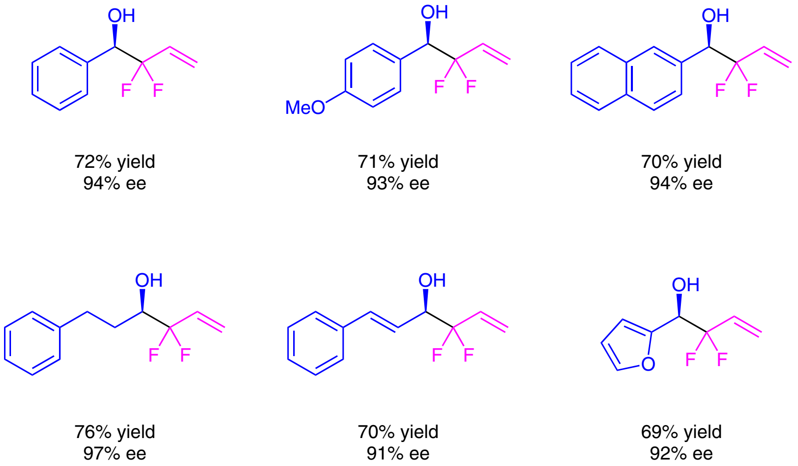
J. Org. Chem. **2012**, *77*, 9329–9333.

Enantioselective Fluoroallylboration of Aldehydes



R = Ph, PMP, Naph, $(CH_2)_2$Ph, (*E*)-CH=CHPh, 2-furyl

Selected examples:



Significance: An enantioselective fluoroallylboration of a variety of aldehydes with *B*-(3,3-difluoroallyl)diisopinocampheylborane has been disclosed. The resulting 2,2-*gem*-difluorinated homoallylic alcohols have been obtained in good yield and high enantioselectivity.

Comment: The described reaction proceeds in one pot. After the synthesis of *B*-(3,3-difluoroallyl)diisopinocampheylborane out of freshly prepared 1,1-difluoroallene, the aldehyde is added directly to the reaction mixture, followed by an oxidative workup.

SYNFACTS Contributors: Paul Knochel, Christoph Sämann
Synfacts 2013, 9(1), 0082 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317738; **Reg-No.:** P16012SF

W.-J. YOO, M. G. CAPDEVILA, X. DU, S. KOBAYASHI* (THE UNIVERSITY OF TOKYO, JAPAN)
Base Mediated Carboxylation of Unprotected Indole Derivatives with Carbon Dioxide
Org. Lett. **2012**, *14*, 5326–5329.

Category

Metal-Mediated Synthesis

Key words

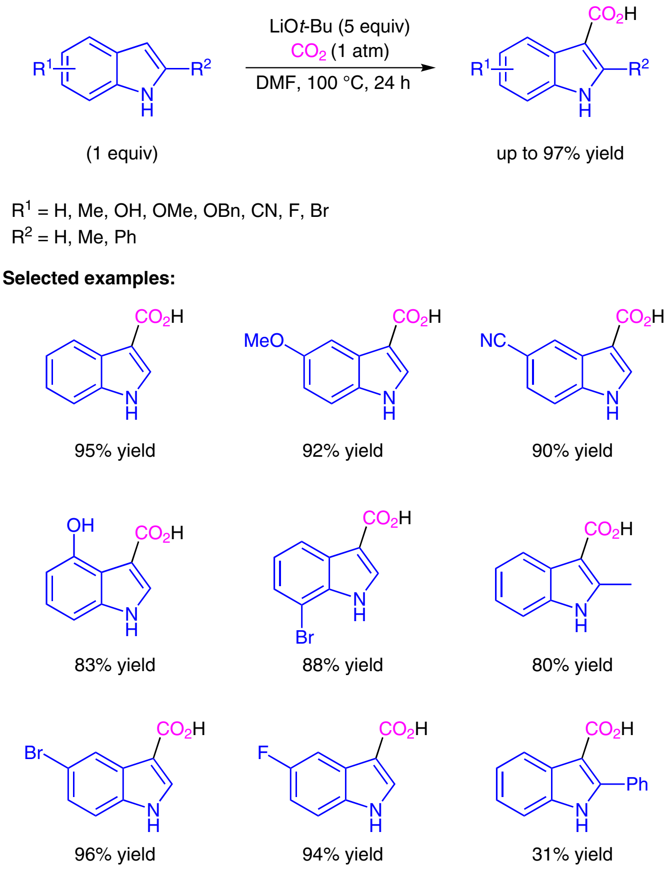
carboxylation

indoles

carbon dioxide

lithium

Carboxylation of Unprotected Indole Derivatives with Carbon Dioxide



Significance: A practical and straight-forward method for the preparation of indole-3-carboxylic acids has been reported. Deprotonation with LiO*t*-Bu under an atmospheric pressure of carbon dioxide furnishes a variety of indole-3-carboxylic acids in high yield.

Comment: The described reaction is very versatile since it tolerates various functional groups and has therefore a broad substrate scope. According to the authors, the large excess of LiO*t*-Bu suppresses the undesired decarboxylation side reaction.

SYNFACTS Contributors: Paul Knochel, Christoph Sämann
Synfacts 2013, 9(1), 0083

DOI: 10.1055/s-0032-1317734; **Reg-No.:** P15612SF

Category

Metal-Mediated Synthesis

Key words

boron

copper

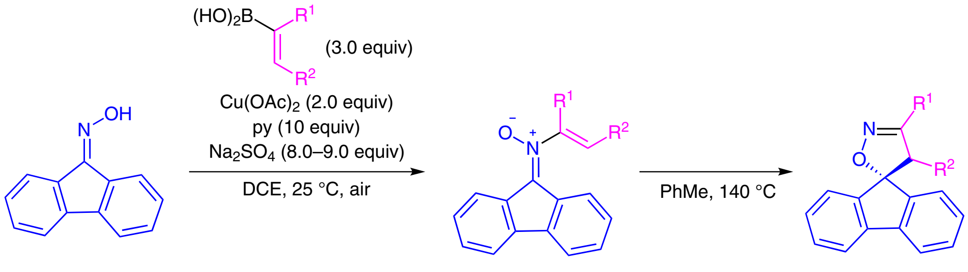
fluorenone oxime

***N*-vinyl nitrones**

[3+2] cycloaddition

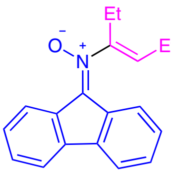
D.-L. MO, D. A. WINK, L. L. ANDERSON* (UNIVERSITY OF ILLINOIS AT CHICAGO, USA)
Preparation and Rearrangement of *N*-Vinyl Nitrones: Synthesis of Spiroisoxazolines and Fluorene-Tethered Isoxazoles
Org. Lett. **2012**, *14*, 5180–5183.

Preparation and Rearrangement of *N*-Vinyl Nitrones

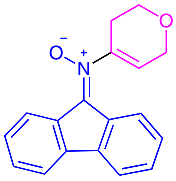


R^1 = Et, Me, H, Ph, 4-$O_2NC_6H_4$, 4-FC_6H_4, 4-$F_3CC_6H_4$
R^2 = Et, Me, *n*-Bu, Ph
R^1 + R^2 = 1-cyclohexene derivatives, 1-cyclopentene, 1-cycloheptene, dihydropyran

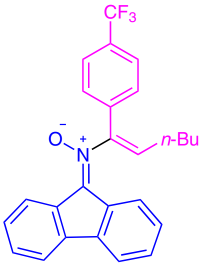
Selected examples:



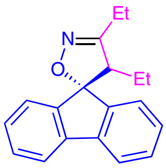
61% yield



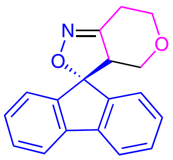
81% yield



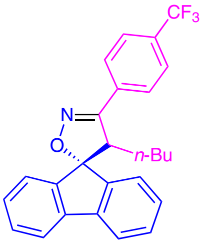
54% yield



81% yield



75% yield



68% yield

Significance: Herein, the authors disclose the single-step, copper-mediated coupling of fluorene oximes and vinyl boronic acids, which undergo thermal rearrangement via [3+2] cycloaddition to form spiroisoxazolines. The corresponding *N*-vinyl nitrones and spiroisoxazolines are obtained in good yield.

Comment: In addition, this methodology may be applied to the synthesis of fluorene-tethered isoxazoles by treatment of *N*-vinyl nitrones with terminal or internal electron-deficient alkynes. The mechanism is supposed to proceed via [3+2] cycloaddition and subsequent elimination.

SYNFACTS Contributors: Paul Knochel, Nadja M. Barl
Synfacts 2013, 9(1), 0084 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317732; **Reg-No.:** P15412SF

M. Tobisu,* K. Koh, T. Furukawa, N. Chatani* (Osaka University, Japan)
Modular Synthesis of Phenanthridine Derivatives by Oxidative Cyclization of 2-Isocyanobiphenyls with Organoboron Reagents
Angew. Chem. Int. Ed. **2012**, *51*, 11363–11366.

Synthesis of Phenanthridine Derivatives via Oxidative Cyclization

Category

Metal-Mediated Synthesis

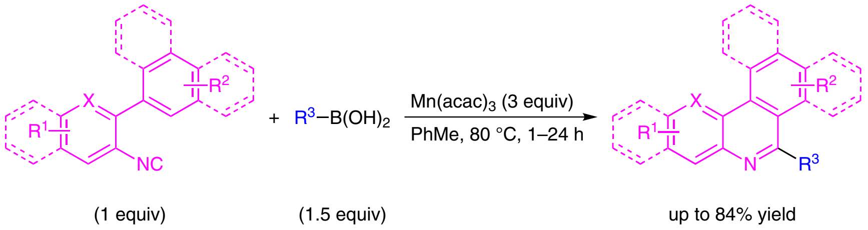
Key words

phenanthridine derivatives

organoboron reagents

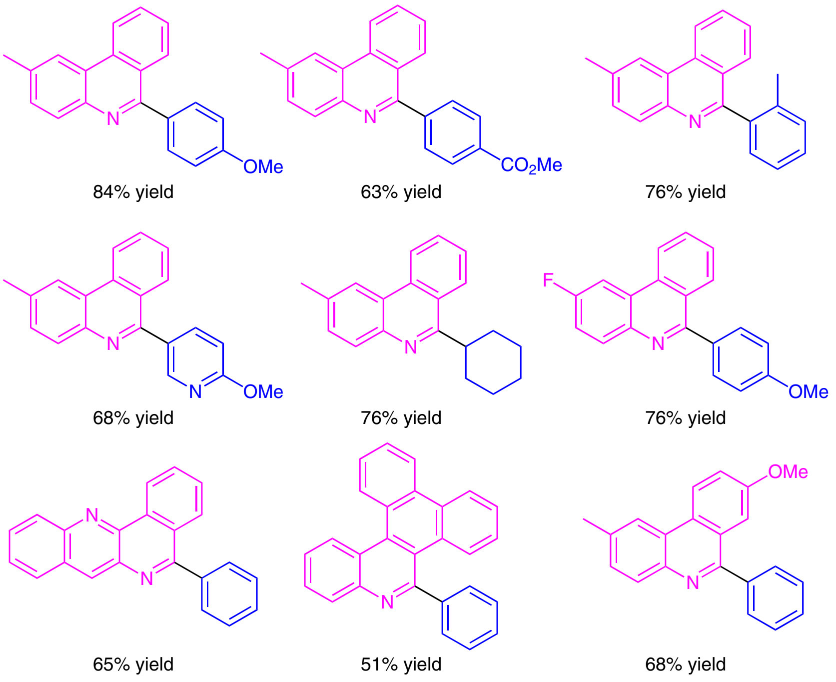
oxidative cyclization

manganese



X = CH, N
R^1 = H, Me, F, Cl
R^2 = H, F, OMe
R^3 = Ar, HetAr, Alk

Selected examples:



Significance: A straight-forward synthesis of a broad range of phenanthridine derivatives via a manganese-mediated annulation of 2-isocyanobiaryls with organoboronic acids has been disclosed. This rapid and divergent reaction furnishes the corresponding phenanthridine derivatives in good yield.

Comment: The reported reaction shows a simple pathway for the synthesis of phenanthridine frameworks out of readily accessible starting materials. Furthermore, mechanistic studies indicate that the reaction proceeds by the intramolecular homolytic aromatic substitution of an imidoyl radical intermediate.

SYNFACTS Contributors: Paul Knochel, Christoph Sämann
Synfacts 2013, 9(1), 0085 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317737; **Reg-No.:** P15912SF

Category

Metal-Mediated Synthesis

Key words

boron

lithium

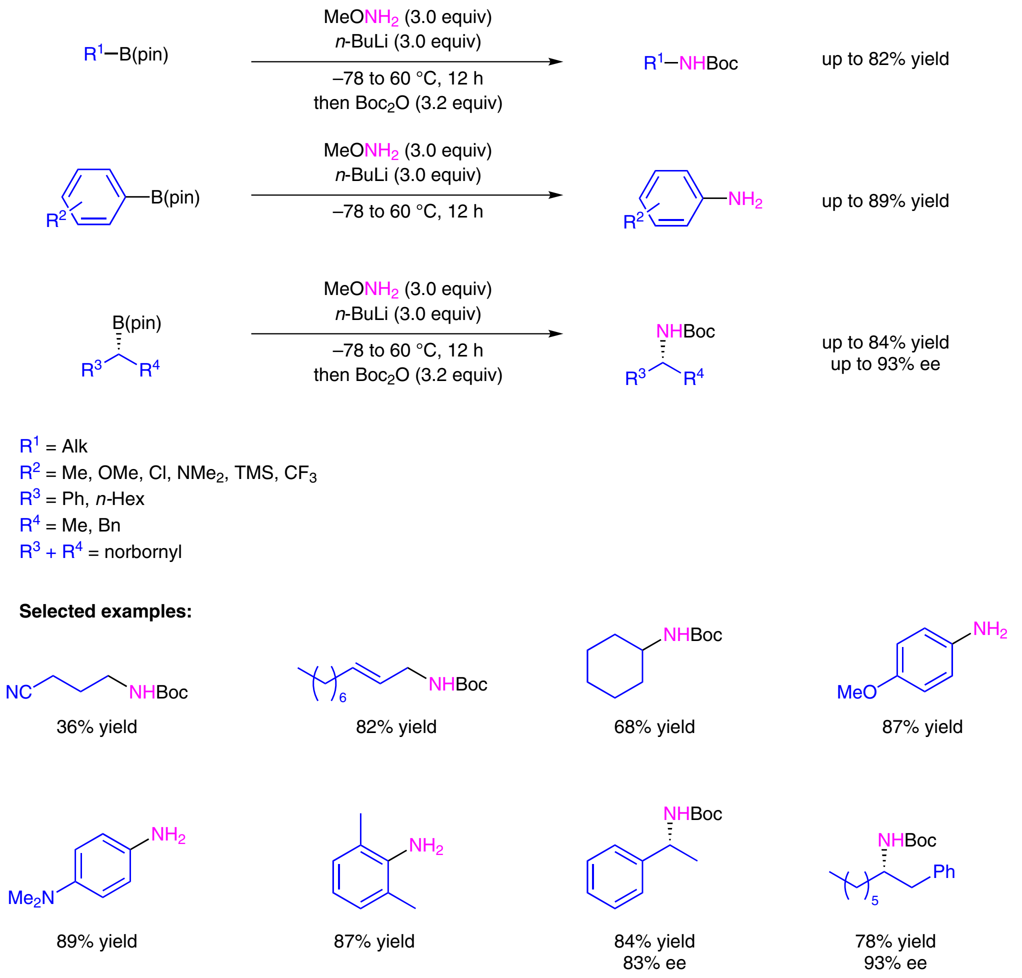
direct amination

pinacol boronates

S. N. MLYNARSKI, A. S. KARNS, J. P. MORKEN* (BOSTON COLLEGE, CHESTNUT HILL, USA)

Direct Stereospecific Amination of Alkyl and Aryl Pinacol Boronates
J. Am. Chem. Soc. **2012**, *134*, 16449–16451.

Direct Amination of Alkyl and Aryl Pinacol Boronates



R^1 = Alk
R^2 = Me, OMe, Cl, NMe_2, TMS, CF_3
R^3 = Ph, *n*-Hex
R^4 = Me, Bn
R^3 + R^4 = norbornyl

Significance: Herein, the direct and stereospecific amination of various aryl and alkyl pinacol boronates with lithiated methoxyamine is disclosed. The corresponding (un)protected amines are obtained in very good yield and, in case of chiral compounds, with high enantiomeric excess.

Comment: Sensitive functional groups such as CN, OMe and CF_3 moieties are well tolerated with this methodology. In addition, this strategy might even be applied to gram-scale reactions without any further drawbacks.

SYNFACTS Contributors: Paul Knochel, Nadja M. Barl
Synfacts 2013, 9(1), 0086 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317730; **Reg-No.:** P15212SF

M. ARISAWA,* T. ICHIKAWA, M. YAMAGUCHI* (TOHOKU UNIVERSITY, SENDAI, JAPAN)
Rhodium-Catalyzed Synthesis of Diaryl Sulfides Using Aryl Fluorides and Sulfur/Organopolysulfides
Org. Lett. **2012**, *14*, 5318–5321.

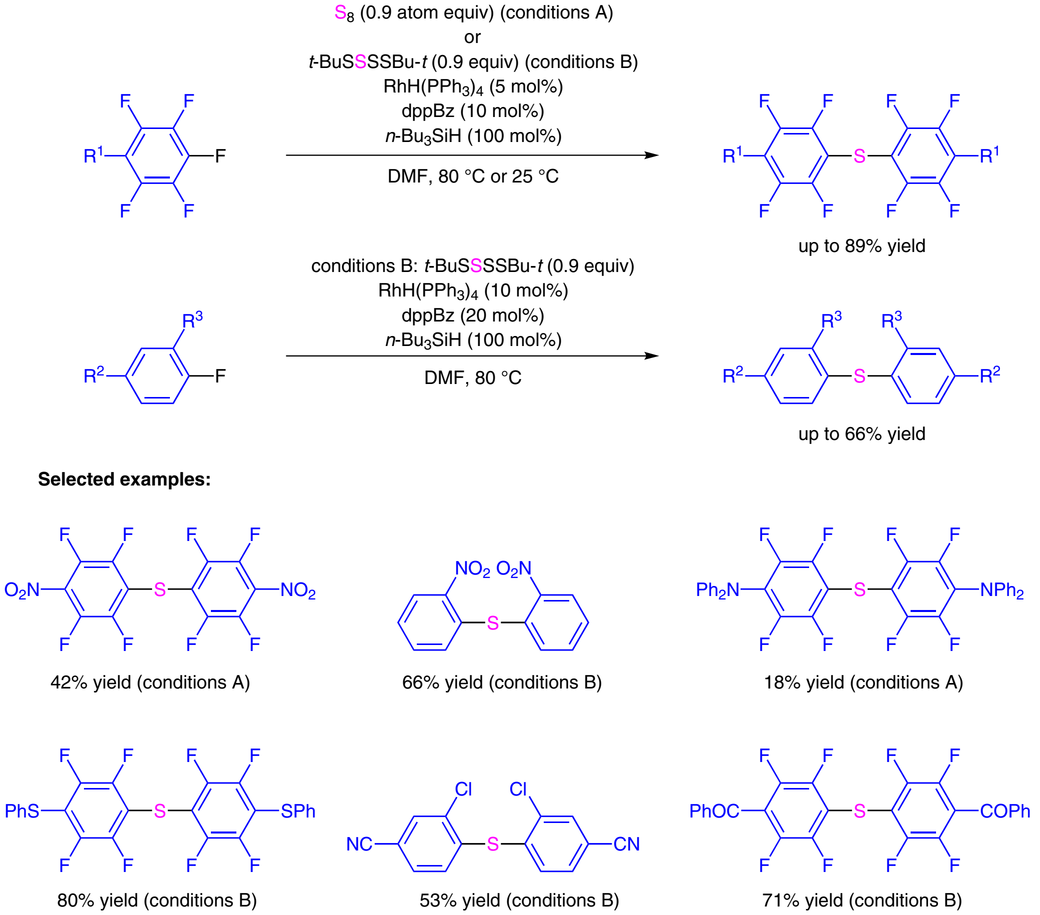
Category

Metal-Mediated Synthesis

Key words

rhodium
sulfur
aryl fluorides
diaryl sulfides

Rhodium-Catalyzed Synthesis of Diaryl Sulfides Using S_8/Organopolysulfides



Significance: The rhodium-catalyzed reaction of sulfur or organopolysulfides with aryl penta- and monofluorides in the presence of tributylsilane is disclosed. The corresponding diaryl sulfides are obtained in moderate to good yield.

Comment: The mechanism is proposed to proceed via oxidative addition of the rhodium complex to the aryl fluoride and the SS–SS bond. After insertion of one sulfur atom, di-*tert*-butyl trisulfide is expelled and the rhodium–fluoride–aryl sulfide complex reacts with another aryl fluoride. The fluoride atoms are trapped with tributylsilane or triphenylphosphine and the corresponding diaryl sulfides are obtained after reductive elimination.

SYNFACTS Contributors: Paul Knochel, Nadja M. Barl
Synfacts 2013, 9(1), 0087
DOI: 10.1055/s-0032-1317733; **Reg-No.:** P15512SF

Category

Metal-Mediated Synthesis

Key words

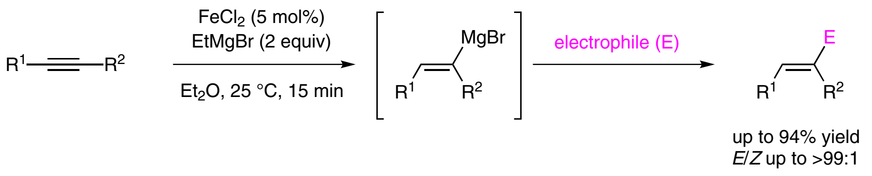
iron

magnesium

alkynes

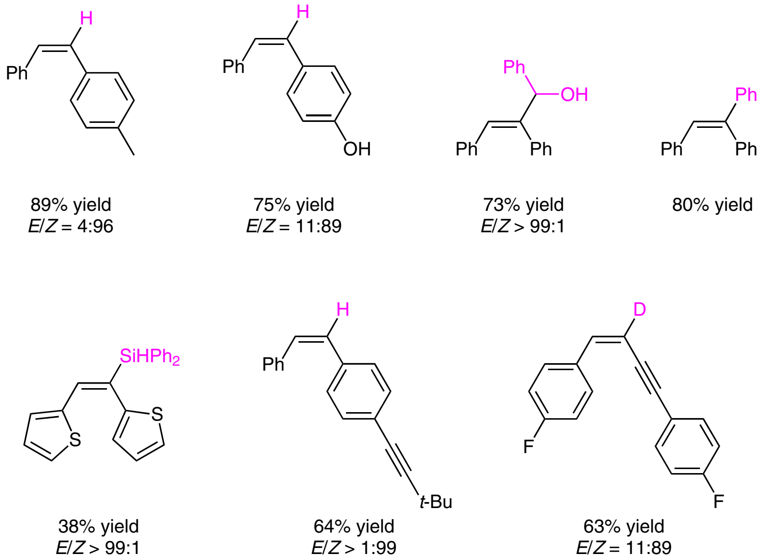
L. ILIES, T. YOSHIDA, E. NAKAMURA* (THE UNIVERSITY OF TOKYO, JAPAN)
Iron-Catalyzed Chemo- and Stereoselective Hydromagnesiation of Diarylalkynes and Diynes
J. Am. Chem. Soc. **2012**, *134*, 16951–16954.

Iron-Catalyzed Hydromagnesiation of Diarylalkynes and Diynes



R^1 = Ph, 2-thienyl, 4-FC_6H_4, Tol, PMP
R^2 = Ar, HetAr, Alk, alkene, and alkyne substituents
E = H_2O, D_2O, allyl bromide, DMF, PhCHO, Ph_2SiHCl, PhI, *N*-ethyl-*N*-(2-iodobenzyl)ethanamine

Selected examples:



Significance: The authors report a novel iron-catalyzed hydromagnesiation of diarylalkynes in high yield with high stereoselectivity. Furthermore, alkenyl-magnesium compounds can be synthesized from diynes in a chemo-, regio- and stereoselective way.

Comment: The alkenylmagnesium intermediates can further be functionalized in a one-pot sequence. Reactions with allyl bromide, *N*,*N*-dimethylformamide and even nickel-catalyzed cross-couplings have been disclosed. The authors suggest a radical mechanism instead of a pure anionic mechanism.

SYNFACTS Contributors: Paul Knochel, Andreas K. Steib
Synfacts 2013, 9(1), 0088 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317741; **Reg-No.:** P16312SF

P. ZHANG, C. WOLF* (GEORGETOWN UNIVERSITY, WASHINGTON, D.C., USA)
Synthesis of Pentafluorinated β-Hydroxy Ketones
J. Org. Chem. **2012**, *77*, 8840–8844.

Category

Metal-Mediated Synthesis

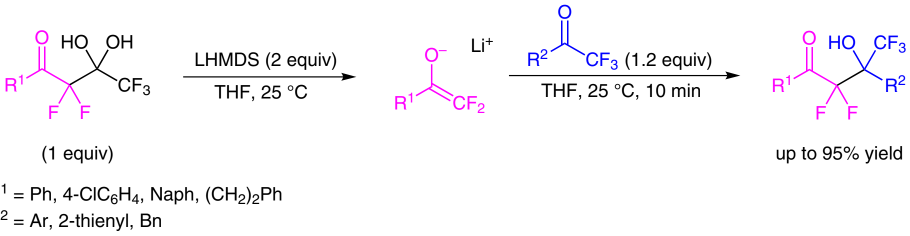
Key words

pentafluorinated β-hydroxy ketones

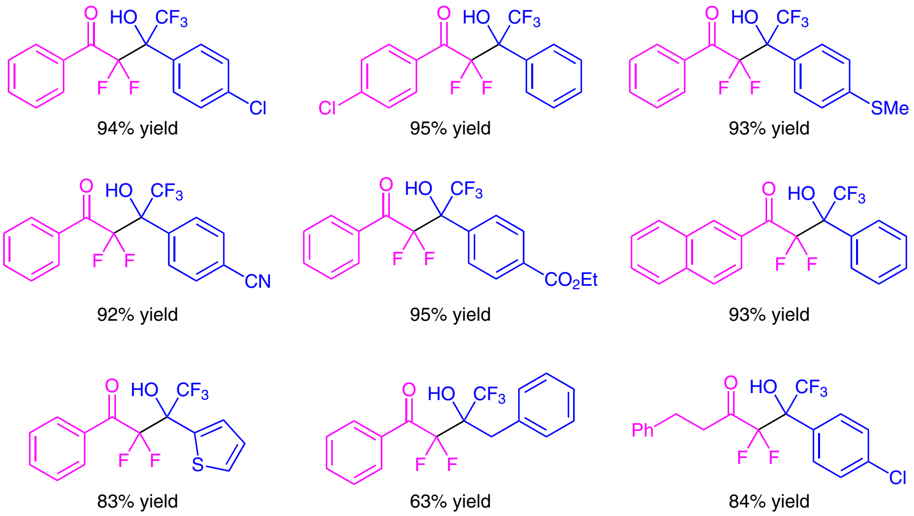
aldol reaction

lithium

Pentafluorinated β-Hydroxy Ketone Synthesis via Lithium-Mediated Aldol Reaction



Selected examples:



Significance: A fast and mild synthesis of pentafluorinated β-hydroxy ketones has been disclosed. The reaction proceeds via a lithium-promoted aldol reaction of readily available difluoroenolate precursors with trifluoromethyl ketones furnishing the corresponding pentafluorinated β-hydroxy ketones in good to excellent yield.

Comment: The described reaction is very versatile since it proceeds under ambient temperature and tolerates a broad range of functional groups. Furthermore, the authors show that the reduction of the pentafluorinated β-hydroxy ketones furnishes quantitatively the corresponding 1,3-diols favoring the *syn*-isomer.

SYNFACTS Contributors: Paul Knochel, Christoph Sämann
Synfacts 2013, 9(1), 0089 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317735; **Reg-No.:** P15712SF

Category

Metal-Mediated Synthesis

Key words

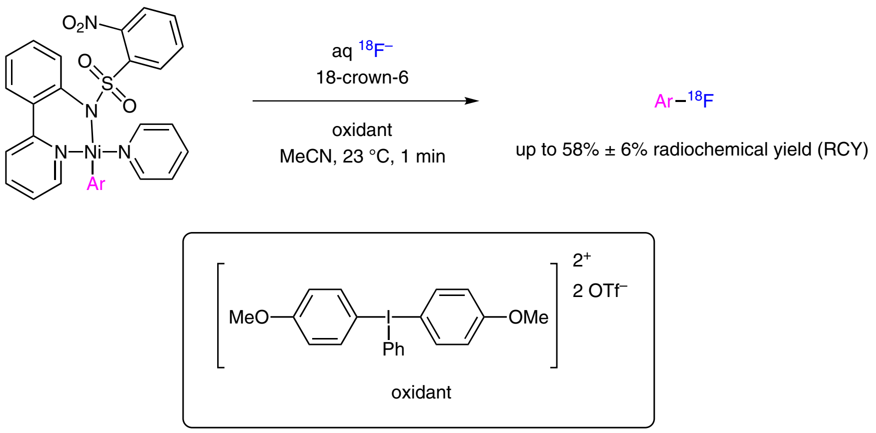
nickel

fluorination

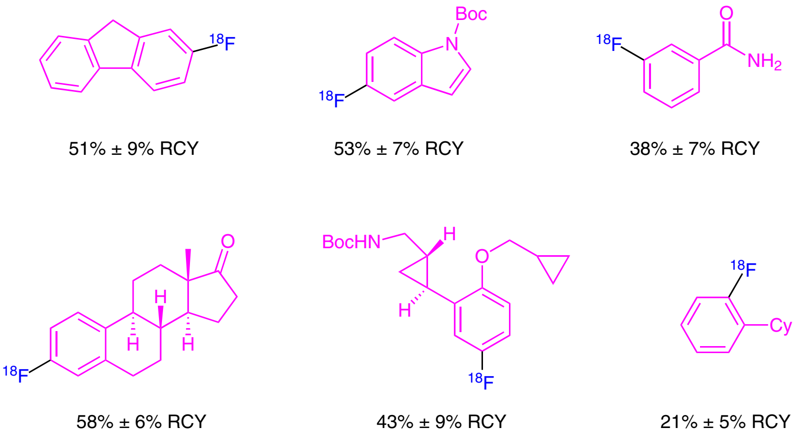
palladium

E. LEE, J. M. HOOKER, T. RITTER* (HARVARD UNIVERSITY, CAMBRIDGE, GENERAL HOSPITAL AND HARVARD MEDICAL SCHOOL, CHARLESTOWN AND MASSACHUSETTS GENERAL HOSPITAL, BOSTON, USA)
Nickel-Mediated Oxidative Fluorination for PET with Aqueous [^{18}F]Fluoride
J. Am. Chem. Soc. **2012**, *134*, 17456–17458.

Fluorination of Nickel(II)–Aryl Complexes with [^{18}F]Fluoride



Selected examples:



Significance: The authors report a one-step oxidative fluorination of arylnickel complexes which enables a straight-forward and practical ^{18}F late-stage fluorination of molecules. Therefore, ^{18}F-labeled substances of high specific activity for PET imaging can be synthesized.

Comment: As the protocol can be performed using aqueous fluoride solutions, extensive drying procedures of fluoride, which are typical for radiochemistry, are not required. Furthermore, direct use of aqueous fluoride solutions increases the yield and prevents radioactive decay.

SYNFACTS Contributors: Paul Knochel, Andreas K. Steib
Synfacts 2013, 9(1), 0090 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317742; **Reg-No.:** P16412SF

R. K. CHINNAGOLLA, M. JEGANMOHAN* (INDIAN INSTITUTE OF SCIENCE EDUCATION AND RESEARCH, PUNE, INDIA)
Regioselective *Ortho*-Arylation and Alkenylation of *N*-Alkyl Benzamides with Boronic Acids via Ruthenium-Catalyzed C–H Bond Activation: An Easy Route to Fluorenones Synthesis
Org. Lett. **2012**, *14*, 5246–5249.

Category

Metal-Mediated Synthesis

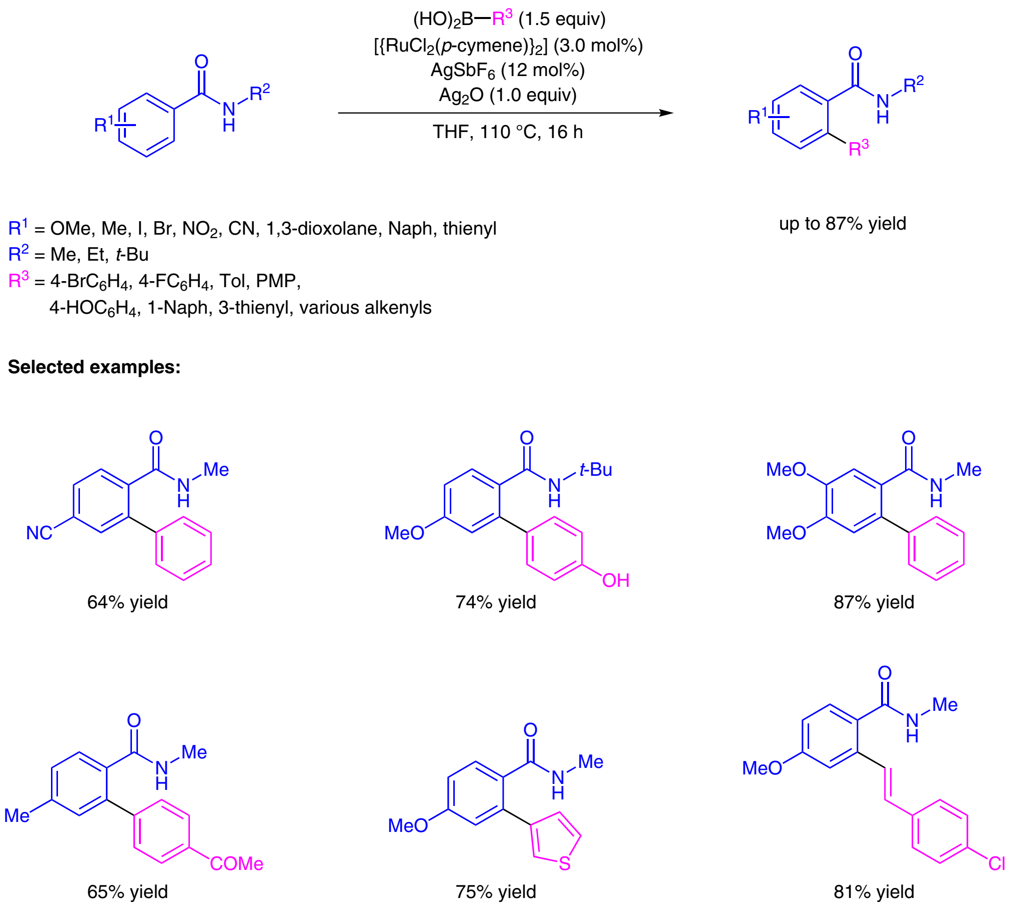
Key words

ruthenium

boronic acids

***ortho*-arylation**

Ruthenium-Catalyzed *ortho*-Arylation and Alkenylation of *N*-Alkyl Benzamides



R^1 = OMe, Me, I, Br, NO_2, CN, 1,3-dioxolane, Naph, thienyl
R^2 = Me, Et, *t*-Bu
R^3 = 4-BrC_6H_4, 4-FC_6H_4, Tol, PMP,
4-HOC_6H_4, 1-Naph, 3-thienyl, various alkenyls

up to 87% yield

Selected examples:

64% yield

74% yield

87% yield

65% yield

75% yield

81% yield

Significance: The authors report a highly regioselective ruthenium-catalyzed *ortho*-arylation and alkenylation of various *N*-alkyl benzamides with different (hetero)aromatic and alkenyl boronic acids in the presence of silver salts. The corresponding benzamides are obtained in good to very good yield.

Comment: Noteworthy, this methodology may be applied to the synthesis of fluorenones by treatment of the biarylic coupling products with trifluoroacetic anhydride and hydrogen chloride.

SYNFACTS Contributors: Paul Knochel, Nadja M. Barl
Synfacts 2013, 9(1), 0091 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317729; **Reg-No.:** P15112SF

Category

Metal-Mediated Synthesis

Key words

amination

silyl ketene acetals

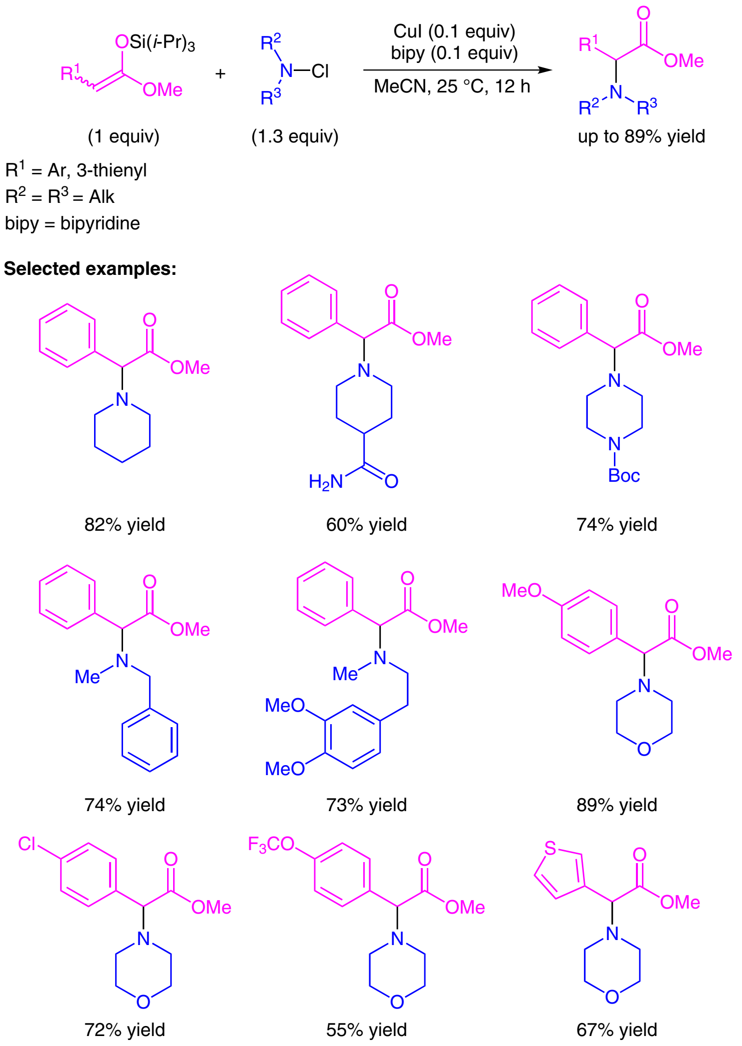
α-amino esters

copper

T. MIURA, M. MORIMOTO, M. MURAKAMI* (KYOTO UNIVERSITY, JAPAN)

Copper-Catalyzed Amination of Silyl Ketene Acetals with *N*-Chloroamines
Org. Lett. **2012**, *14*, 5214–5217.

Copper-Catalyzed Amination of Silyl Ketene Acetals with *N*-Chloroamines



Significance: A copper-catalyzed amination reaction of silyl ketene acetals with *N*-chloroamines under mild reaction conditions has been developed. The formation of the corresponding α-amino esters is catalyzed by a copper(I)–2,2′-bipyridyl complex which furnishes them in high yield.

Comment: According to the authors, the bulky silyl group disfavors the formation of unwanted byproducts and improves the yield of the desired α-amino ester. Furthermore, the facile availability of *N*-chloroamines from secondary amines with NCS permits a one-pot, two-step synthesis, especially if the *N*-chloroamine is too unstable for isolation.

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Category

Metal-Mediated Synthesis

Key words

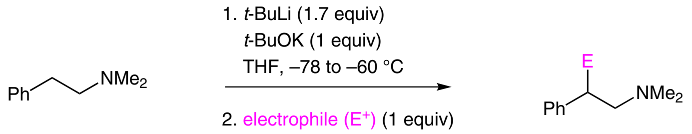
lithium

benzylic metalation

potassium

C. UNKELBACH, H. S. ROSENBAUM, C. STROHMANN* (TECHNISCHE UNIVERSITÄT DORTMUND, GERMANY)
Direct Benzylic Metalation of a Phenethylamine Derivative: Potassium as the Key to Both Generation and Stabilization of a 'Labile Anion'
Chem. Commun. **2012**, *48*, 10612–10614.

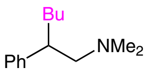
Metalation of 2-Phenylethyldimethylamine under Mild Conditions



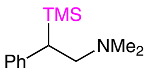
E = Bu, TMS, SiMePh$_2$, CPh$_2$OH, C(C$_5$H$_{10}$)OH

up to 92% yield

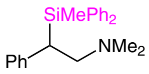
Selected examples:



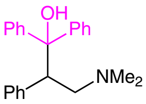
92% yield



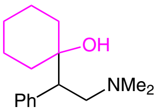
84% yield



60% yield



74% yield



84% yield

Significance: The direct benzylic metalation of 2-phenylethylamine derivatives suffers from β-elimination. The authors found that benzylic metalation of 2-phenylethyldimethylamine can be performed at –78 °C with a mixture of *t*-BuLi and *t*-BuOK. The metalated species was found to be stable up to –40°C.

Comment: Interestingly, the metalation cannot be performed with a mixture of *t*-BuLi and *t*-BuOLi. Therefore, the potassium cation seems to be crucial for an efficient conversion. Theoretical and structural studies reveal that potassium is important for the lowering of the barrier of the initial deprotonation, as well as for stabilization of the labile anion.

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