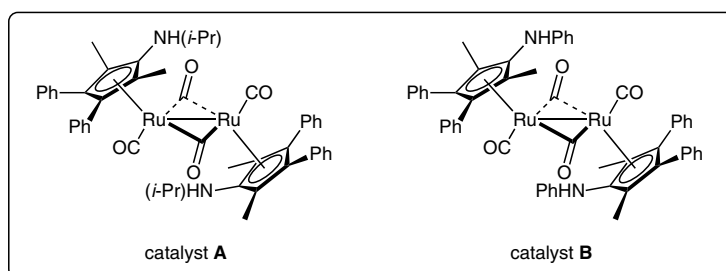
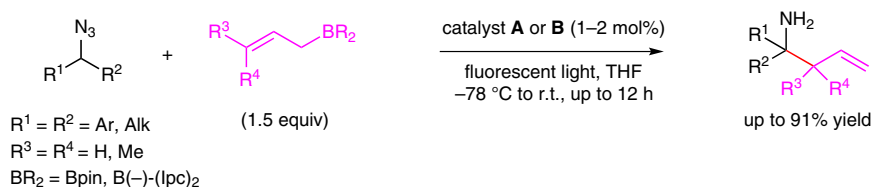
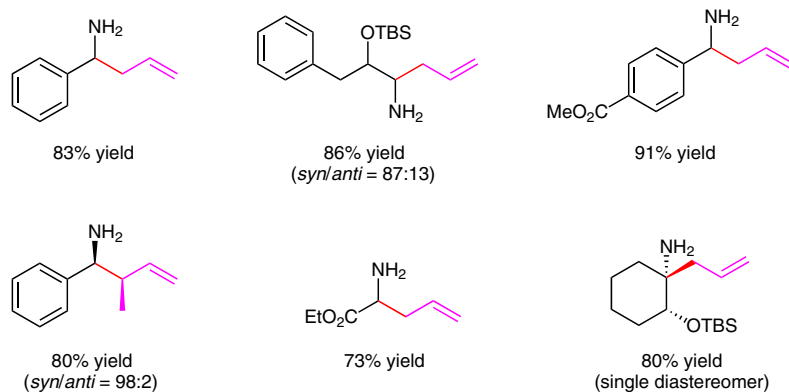


# Ruthenium-Catalyzed Generation of N-Unsubstituted Imines



## Selected examples:



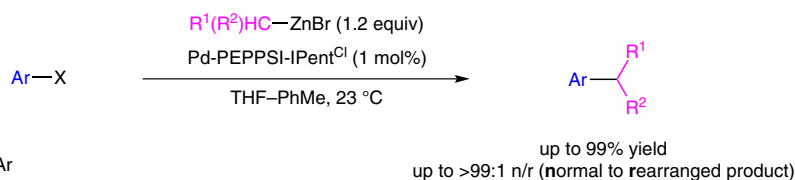
**Significance:** The authors report, that N-unsubstituted imines can be efficiently generated from alkyl azides using a ruthenium catalyst and fluorescent light. Furthermore, an allylation reaction in a one-pot fashion was achieved, leading to homoallylic imines.

**Comment:** The mild reaction conditions allow an asymmetric allylation of in situ generated benzaldehyde from benzyl azide. Using the chiral allyl bis(isopinocampheyl)borane reagent at  $-78\text{ }^\circ\text{C}$  furnishes the homoallylic amine in 87% yield with an enantiomeric excess of 89%.

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

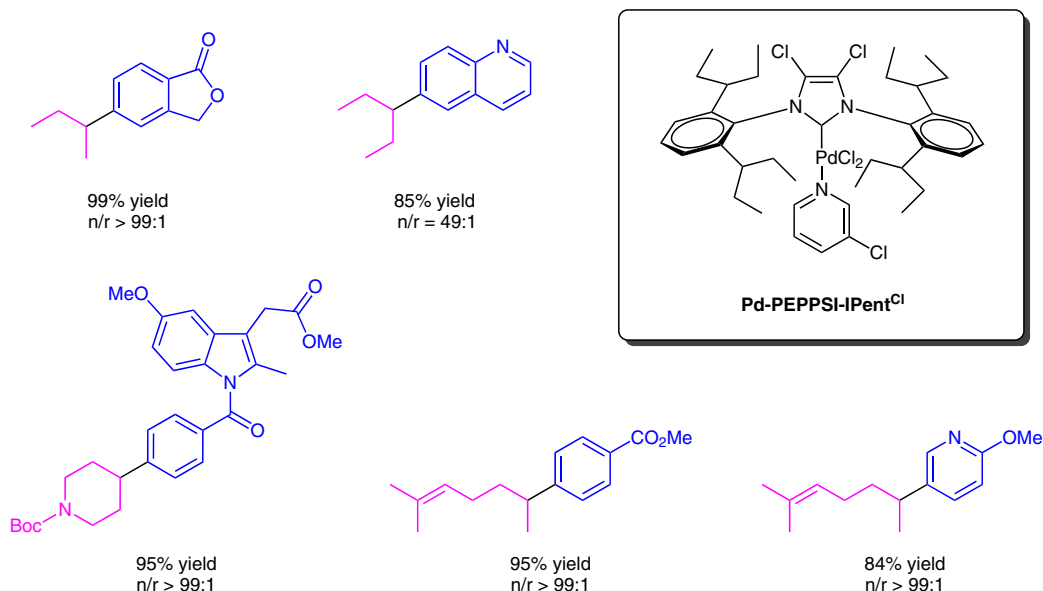
Pd-PEPPSI-IPent<sup>Cl</sup>: A Highly Effective Catalyst for the Selective Cross-Coupling of Secondary Organozinc Reagents  
*Angew. Chem. Int. Ed.* **2012**, *51*, 11354–11357.

## Pd-PEPPSI-IPent<sup>Cl</sup> – Selective Coupling of Secondary Organozinc Nucleophiles



Ar = Ar, O- and N-HetAr  
 R<sup>1</sup> = Me, Et  
 R<sup>2</sup> = Et, alkenyl, *n*-Pr  
 R<sup>1</sup> + R<sup>2</sup> = Boc-protected piperidine  
 X = Br, Cl, OTf

### Selected examples:



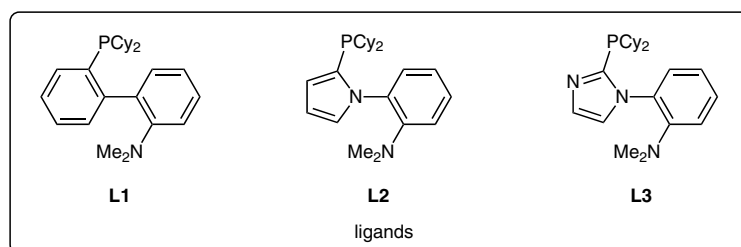
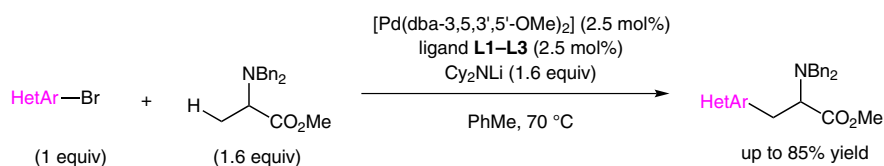
**Significance:** The authors report the new catalyst Pd-PEPPSI-IPent<sup>Cl</sup>, which highly efficiently couples secondary alkylzinc reagents to (hetero)aryl bromides, chlorides and triflates. The corresponding alkylated aromatics are obtained in excellent yield and with high regioselectivity.

**Comment:**  $\beta$ -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.

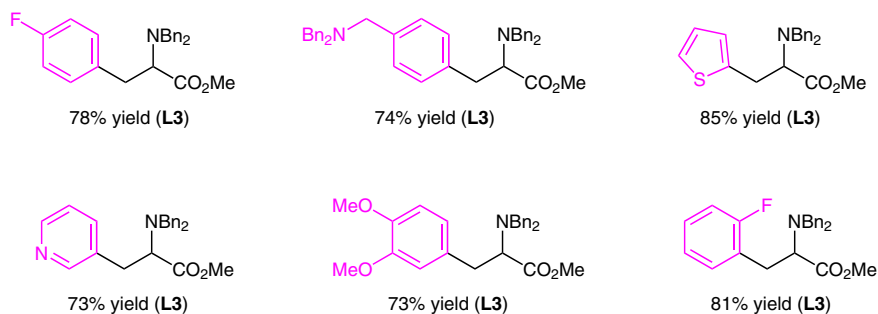
**SYNFACTS Contributors:** Paul Knochel, Nadja M. Barl  
 Synfacts 2013, 9(1), 0080 Published online: 17.12.2012  
 DOI: 10.1055/s-0032-1317731; Reg-No.: P15312SF

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## Palladium-Catalyzed $\beta$ -Arylation of $\alpha$ -Amino Esters



### Selected examples:

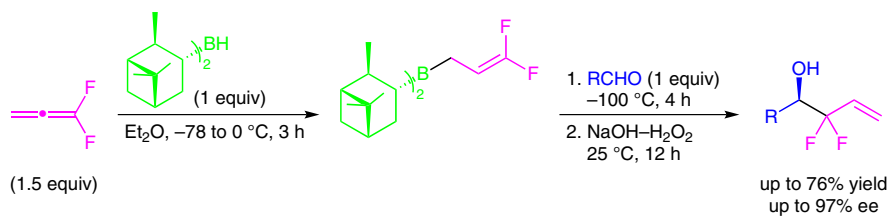


**Significance:** A novel general  $\beta$ -arylation of protected alanine esters to yield synthetically useful (hetero)aryl alanine building blocks has been disclosed. The protocol utilizes a lithium amide to form an enolate that undergoes a palladium-catalyzed C–C coupling with various aromatic bromides.

**Comment:** Interestingly, the reaction could be extended to  $\alpha$ -amino acids bearing other linear alkyl chains. Arylation occurs preferentially at the terminal Csp<sup>3</sup>-H bond, thus providing  $\delta$ -,  $\epsilon$ - and even  $\zeta$ -arylated products. All products could be deprotected via hydrogenolysis to give the respective amines.

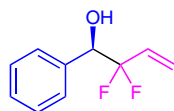
P. V. RAMACHANDRAN,\* A. TAFELSKA-KACZMAREK, A. CHATTERJEE (PURDUE UNIVERSITY, WEST LAFAYETTE, USA)  
*B*-(3,3-Difluoroallyl)diisopinocampheylborane for the Enantioselective Fluoroallylboration of Aldehydes  
*J. Org. Chem.* **2012**, *77*, 9329–9333.

## Enantioselective Fluoroallylboration of Aldehydes

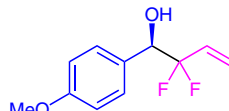


R = Ph, PMP, Naph, (CH<sub>2</sub>)<sub>2</sub>Ph, (*E*)-CH=CHPh, 2-furyl

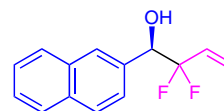
### Selected examples:



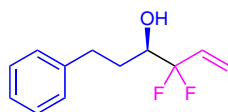
72% yield  
94% ee



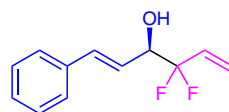
71% yield  
93% ee



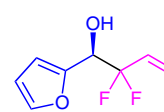
70% yield  
94% ee



76% yield  
97% ee



70% yield  
91% ee

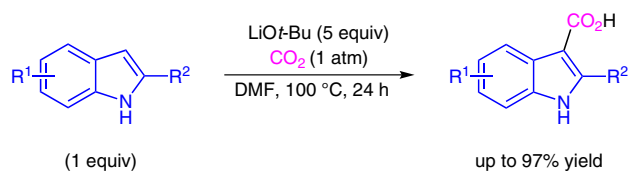


69% yield  
92% ee

**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.

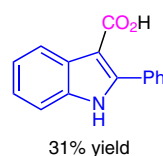
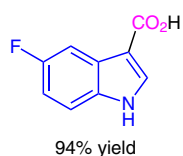
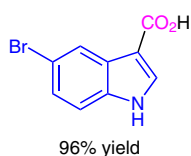
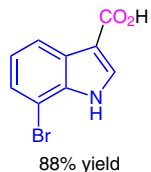
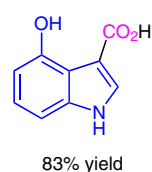
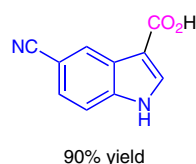
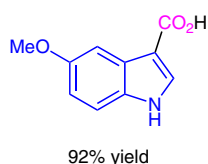
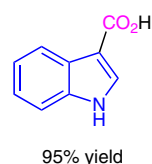
# Carboxylation of Unprotected Indole Derivatives with Carbon Dioxide



R<sup>1</sup> = H, Me, OH, OMe, OBn, CN, F, Br

R<sup>2</sup> = H, Me, Ph

### Selected examples:

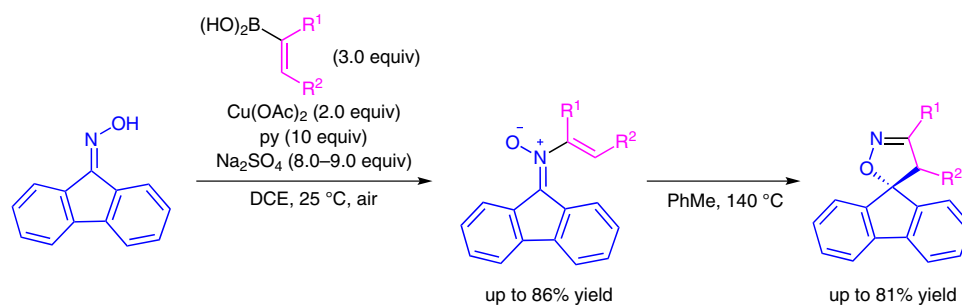


**Significance:** A practical and straight-forward method for the preparation of indole-3-carboxylic acids has been reported. Deprotonation with LiOt-Bu under an atmospheric pressure of carbon dioxide furnishes a variety of indole-3-carboxylic acids in high yield.

**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 LiOt-Bu suppresses the undesired decarboxylation side reaction.

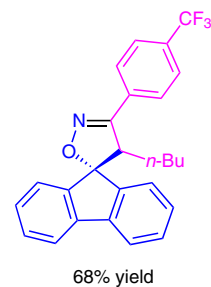
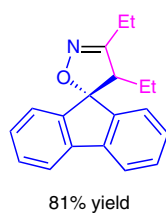
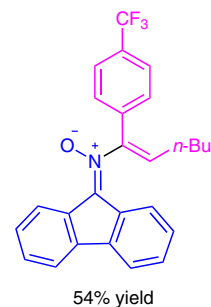
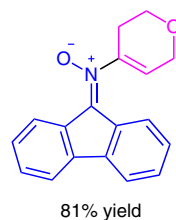
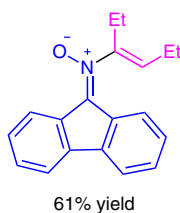
D.-L. MO, D. A. WINK, L. L. ANDERSON\* (UNIVERSITY OF ILLINOIS AT CHICAGO, USA)  
Preparation and Rearrangement of *N*-Vinyl Nitrones: Synthesis of Spiroisoxazolines and Fluorene-Tethered Isoxazoles  
*Org. Lett.* **2012**, *14*, 5180–5183.

## Preparation and Rearrangement of *N*-Vinyl Nitrones



$\text{R}^1 = \text{Et, Me, H, Ph, 4-O}_2\text{NC}_6\text{H}_4, 4\text{-FC}_6\text{H}_4, 4\text{-F}_3\text{CC}_6\text{H}_4$   
 $\text{R}^2 = \text{Et, Me, } n\text{-Bu, Ph}$   
 $\text{R}^1 + \text{R}^2 = 1\text{-cyclohexene derivatives, 1-cyclopentene, 1-cycloheptene, dihydropyran}$

### Selected examples:

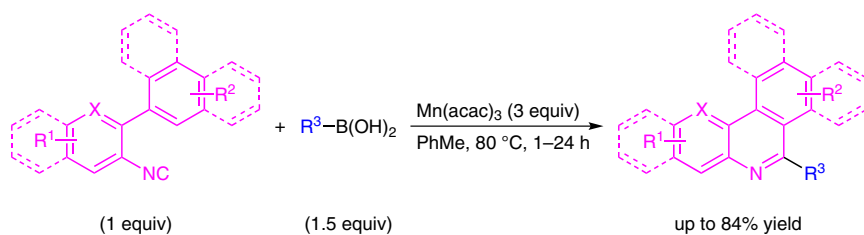


**Significance:** Herein, the authors disclose the single-step, copper-mediated coupling of fluorene oximes and vinyl boronic acids, which undergo thermal rearrangement via [3+2] cycloaddition to form spiroisoxazolines. The corresponding *N*-vinyl nitrones and spiroisoxazolines are obtained in good yield.

**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.

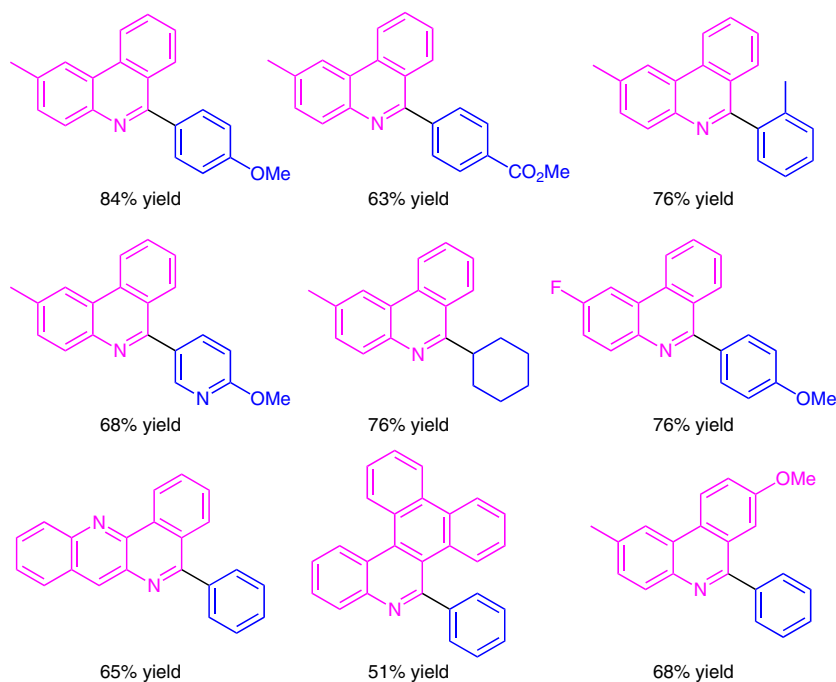
**SYNFACTS Contributors:** Paul Knochel, Nadja M. Barl  
 Synfacts 2013, 9(1), 0084 Published online: 17.12.2012  
**DOI:** 10.1055/s-0032-1317732; **Reg-No.:** P15412SF

# Synthesis of Phenanthridine Derivatives via Oxidative Cyclization



X = CH, N  
R<sup>1</sup> = H, Me, F, Cl  
R<sup>2</sup> = H, F, OMe  
R<sup>3</sup> = Ar, HetAr, Alk

## Selected examples:

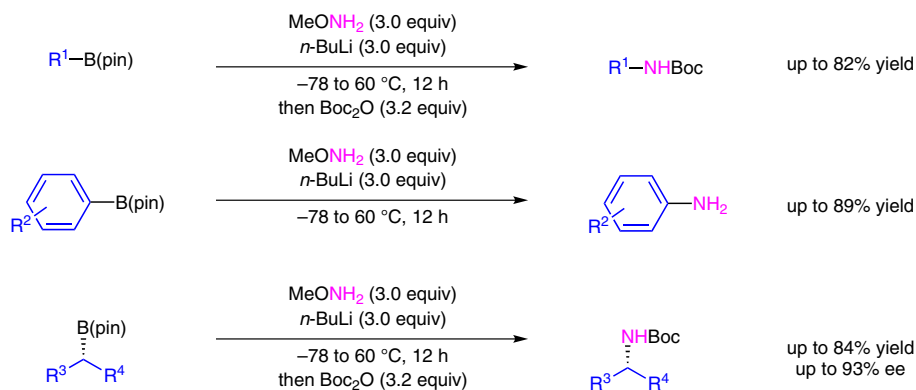


**Significance:** A straight-forward synthesis of a broad range of phenanthridine derivatives via a manganese-mediated annulation of 2-isocyanobiaryls with organoboronic acids has been disclosed. This rapid and divergent reaction furnishes the corresponding phenanthridine derivatives in good yield.

**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.

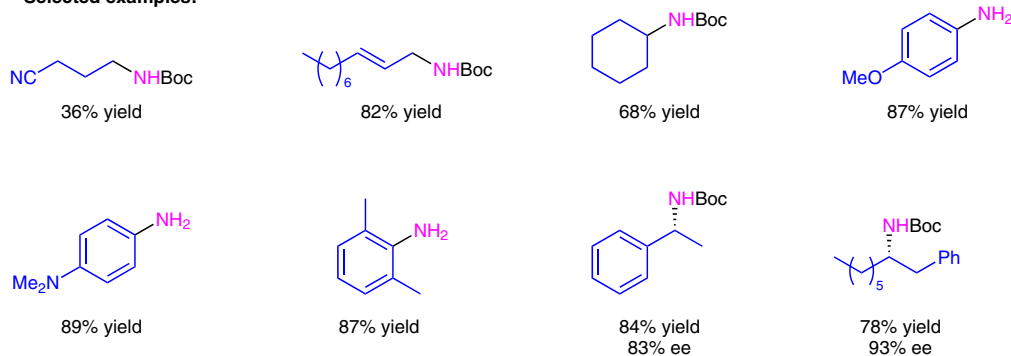
S. N. MLYNARSKI, A. S. KARNs, J. P. MORKEN\* (BOSTON COLLEGE, CHESTNUT HILL, USA)  
Direct Stereospecific Amination of Alkyl and Aryl Pinacol Boronates  
*J. Am. Chem. Soc.* **2012**, *134*, 16449–16451.

## Direct Amination of Alkyl and Aryl Pinacol Boronates



$R^1$  = Alk  
 $R^2$  = Me, OMe, Cl, NMe<sub>2</sub>, TMS, CF<sub>3</sub>  
 $R^3$  = Ph, *n*-Hex  
 $R^4$  = Me, Bn  
 $R^3 + R^4$  = norbornyl

### Selected examples:



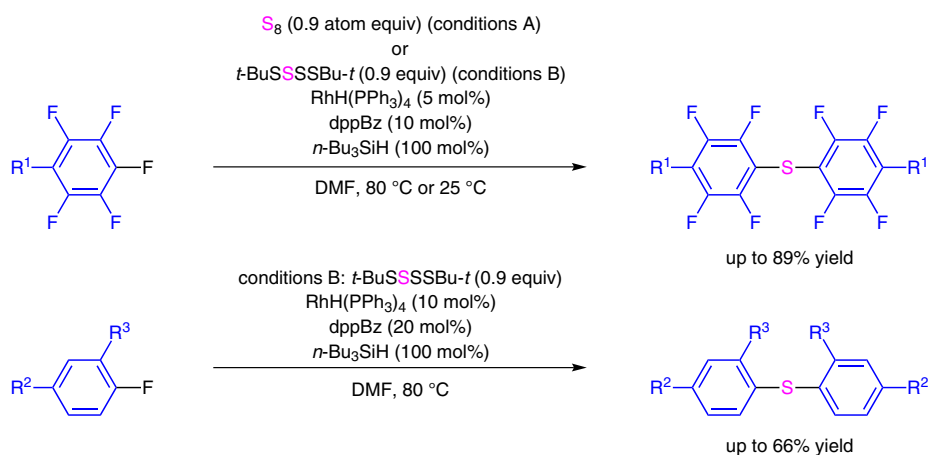
**Significance:** Herein, the direct and stereospecific amination of various aryl and alkyl pinacol boronates with lithiated methoxyamine is disclosed. The corresponding (un)protected amines are obtained in very good yield and, in case of chiral compounds, with high enantiomeric excess.

**Comment:** Sensitive functional groups such as CN, OMe and CF<sub>3</sub> moieties are well tolerated with this methodology. In addition, this strategy might even be applied to gram-scale reactions without any further drawbacks.

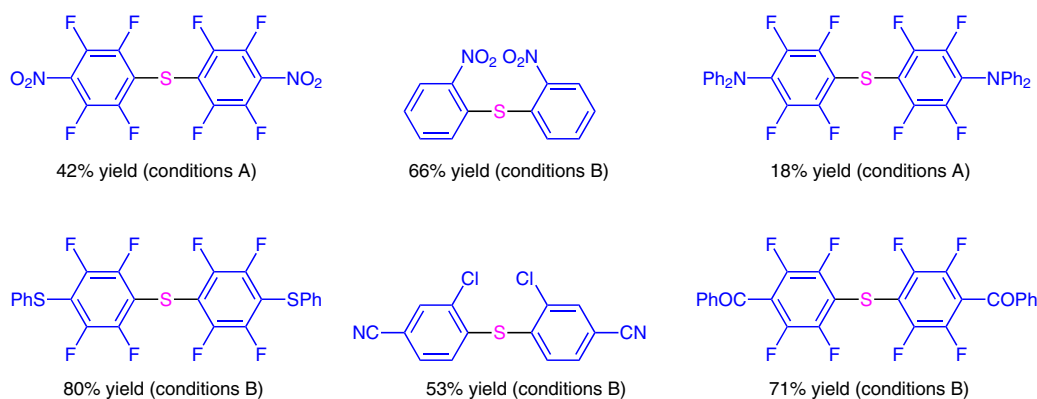
**SYNFACTS Contributors:** Paul Knochel, Nadja M. Barl  
 Synfacts 2013, 9(1), 0086 Published online: 17.12.2012  
 DOI: 10.1055/s-0032-1317730; Reg-No.: P15212SF



# Rhodium-Catalyzed Synthesis of Diaryl Sulfides Using S<sub>8</sub>/Organopolysulfides



## Selected examples:

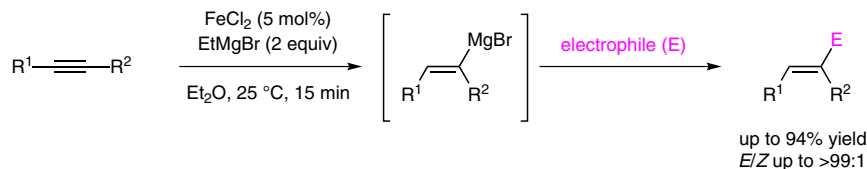


**Significance:** The rhodium-catalyzed reaction of sulfur or organopolysulfides with aryl penta- and monofluorides in the presence of tributylsilane is disclosed. The corresponding diaryl sulfides are obtained in moderate to good yield.

**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.

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

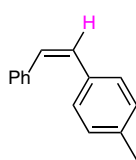


R<sup>1</sup> = Ph, 2-thienyl, 4-FC<sub>6</sub>H<sub>4</sub>, Tol, PMP

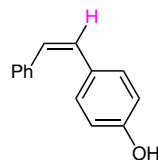
R<sup>2</sup> = Ar, HetAr, Alk, alkene, and alkyne substituents

E = H<sub>2</sub>O, D<sub>2</sub>O, allyl bromide, DMF, PhCHO, Ph<sub>2</sub>SiHCl, PhI, *N*-ethyl-*N*-(2-iodobenzyl)ethanamine

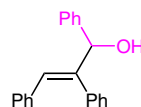
### Selected examples:



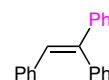
89% yield  
E/Z = 4:96



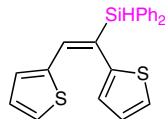
75% yield  
E/Z = 11:89



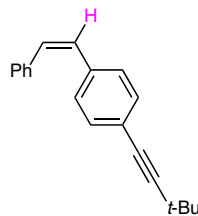
73% yield  
E/Z > 99:1



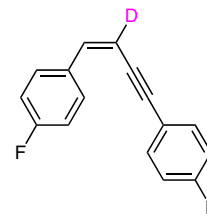
80% yield



38% yield  
E/Z > 99:1



64% yield  
E/Z > 1:99



63% yield  
E/Z = 11:89

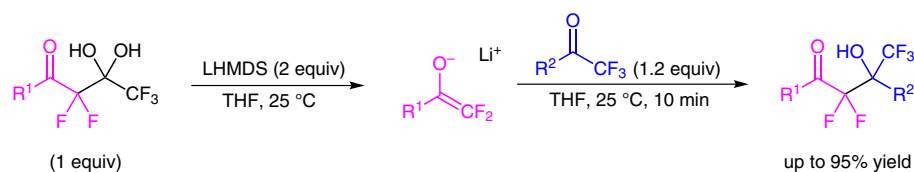
**Significance:** The authors report a novel iron-catalyzed hydromagnesiation of diarylalkynes in high yield with high stereoselectivity. Furthermore, alkenyl-magnesium compounds can be synthesized from diynes in a chemo-, regio- and stereoselective way.

**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

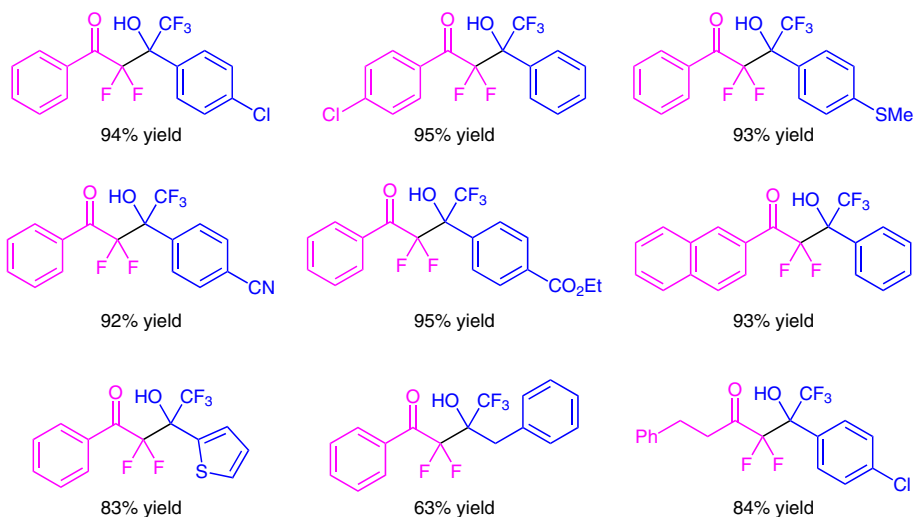
# Pentafluorinated $\beta$ -Hydroxy Ketone Synthesis via Lithium-Mediated Aldol Reaction



$R^1$  = Ph, 4-ClC<sub>6</sub>H<sub>4</sub>, Naph, (CH<sub>2</sub>)<sub>2</sub>Ph

$R^2$  = Ar, 2-thienyl, Bn

## Selected examples:



**Significance:** A fast and mild synthesis of pentafluorinated  $\beta$ -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  $\beta$ -hydroxy ketones in good to excellent yield.

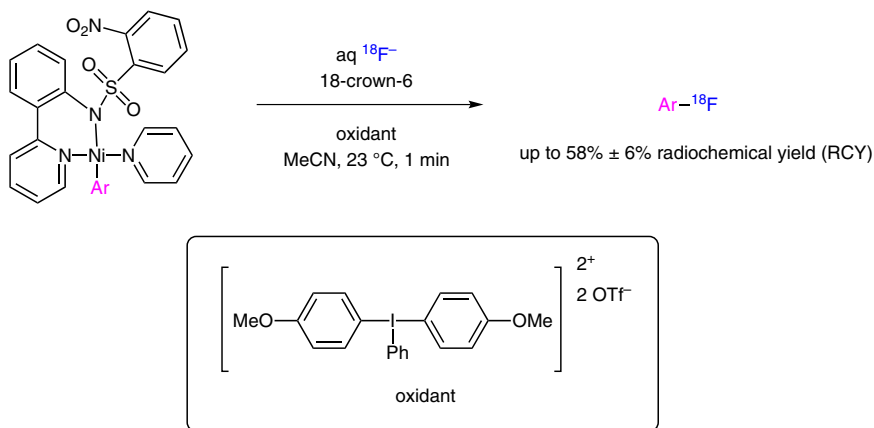
**Comment:** The described reaction is very versatile since it proceeds under ambient temperature and tolerates a broad range of functional groups. Furthermore, the authors show that the reduction of the pentafluorinated  $\beta$ -hydroxy ketones furnishes quantitatively the corresponding 1,3-diols favoring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

E. LEE, J. M. HOOKER, T. RITTER\* (HARVARD UNIVERSITY, CAMBRIDGE, GENERAL HOSPITAL AND HARVARD MEDICAL SCHOOL, CHARLESTOWN AND MASSACHUSETTS GENERAL HOSPITAL, BOSTON, USA)

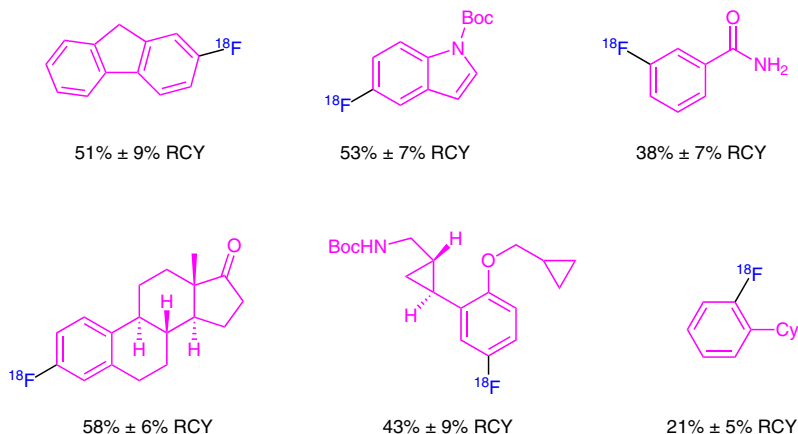
Nickel-Mediated Oxidative Fluorination for PET with Aqueous [ $^{18}\text{F}$ ]Fluoride

*J. Am. Chem. Soc.* **2012**, *134*, 17456–17458.

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



### Selected examples:



**Significance:** The authors report a one-step oxidative fluorination of arylnickel complexes which enables a straight-forward and practical  $^{18}\text{F}$  late-stage fluorination of molecules. Therefore,  $^{18}\text{F}$ -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

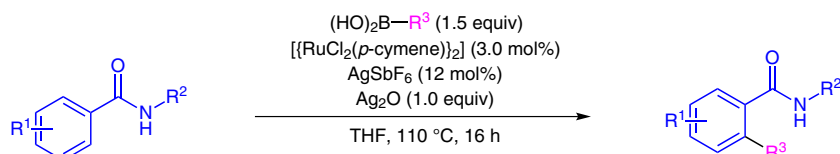
**DOI:** 10.1055/s-0032-1317742; **Reg-No.:** P16412SF

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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.

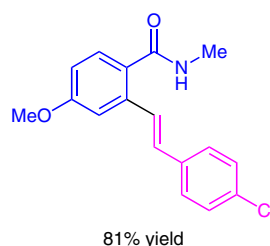
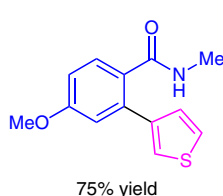
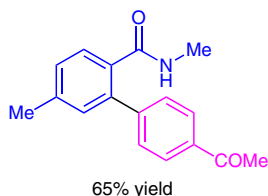
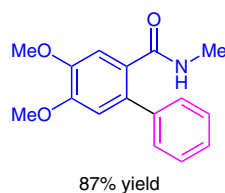
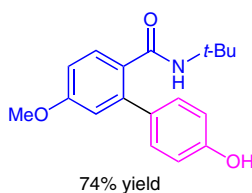
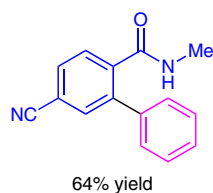
## Ruthenium-Catalyzed *ortho*-Arylation and Alkenylation of *N*-Alkyl Benzamides



R<sup>1</sup> = OMe, Me, I, Br, NO<sub>2</sub>, CN, 1,3-dioxolane, Naph, thienyl  
R<sup>2</sup> = Me, Et, *t*-Bu  
R<sup>3</sup> = 4-BrC<sub>6</sub>H<sub>4</sub>, 4-FC<sub>6</sub>H<sub>4</sub>, Tol, PMP,  
4-HOC<sub>6</sub>H<sub>4</sub>, 1-Naph, 3-thienyl, various alkenyls

up to 87% yield

### Selected examples:



**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 biaryllic 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

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Category

Metal-Mediated  
Synthesis

Key words

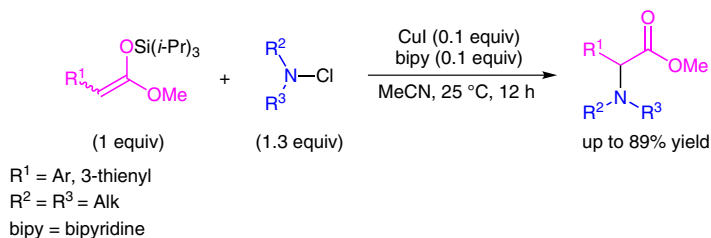
ruthenium

boronic acids

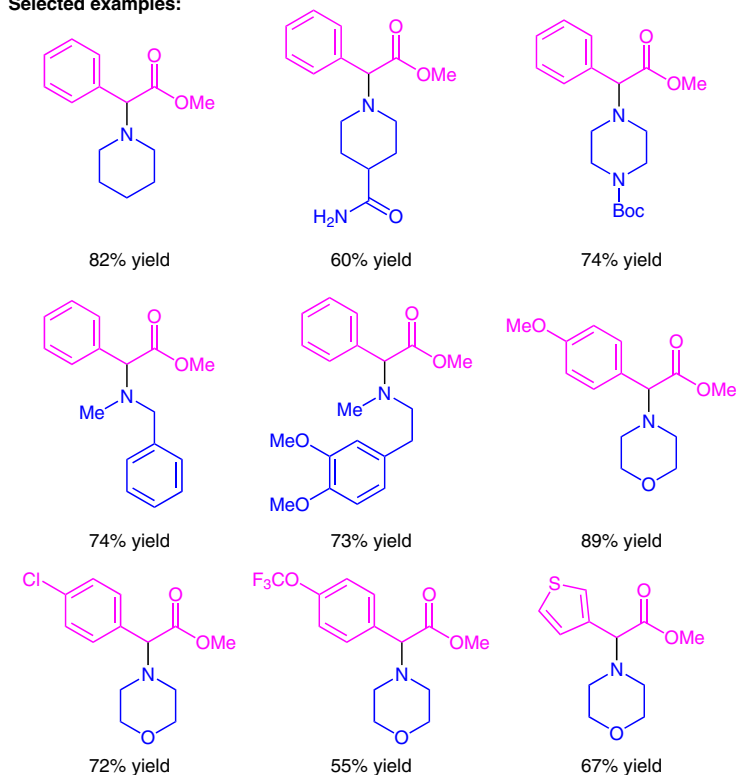
*ortho*-arylation

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



### Selected examples:



**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  $\alpha$ -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 by-products and improves the yield of the desired  $\alpha$ -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.

**SYNFACTS Contributors:** Paul Knochel, Christoph Sämann  
*Synfacts* 2013, 9(1), 0092 Published online: 17.12.2012  
**DOI:** 10.1055/s-0032-1317736; **Reg-No.:** P15812SF

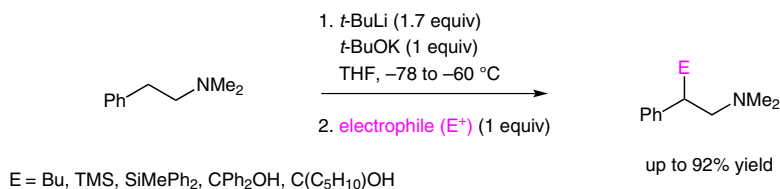
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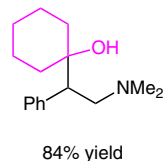
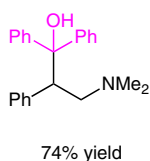
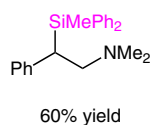
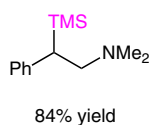
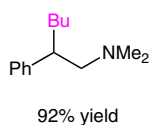
Direct Benzylic Metalation of a Phenethylamine Derivative: Potassium as the Key to Both Generation and Stabilization of a 'Labile Anion'

*Chem. Commun.* **2012**, 48, 10612–10614.

## Metalation of 2-Phenylethyldimethylamine under Mild Conditions



### Selected examples:



**Significance:** The direct benzylic metalation of 2-phenylethylamine derivatives suffers from  $\beta$ -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.

**SYNFACTS Contributors:** Paul Knochel, Andreas K. Steib  
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Category

Metal-Mediated  
Synthesis

Key words

lithium

benzylic metalation

potassium