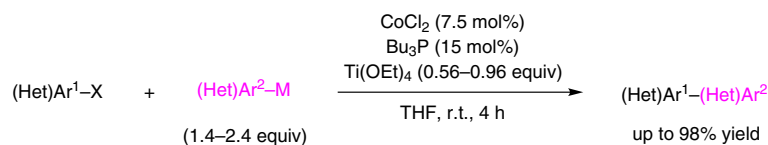


# Co/Ti Cooperative C(sp<sup>2</sup>)-C(sp<sup>2</sup>) Cross-Coupling Reactions

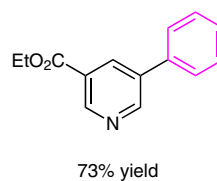
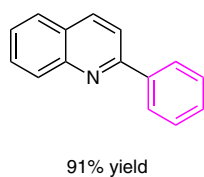
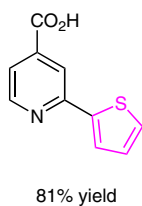
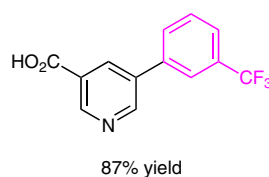
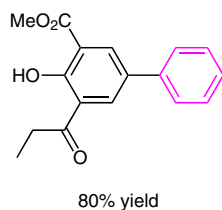
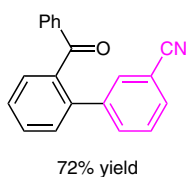
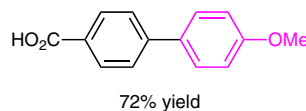
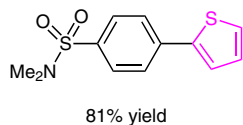
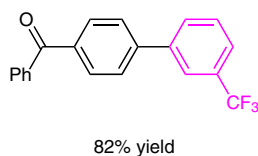


(Het)Ar<sup>1/2</sup> = various substituted (hetero)aromatics

X = F, Cl, Br

M = MgBr, MgCl, Li

## Selected examples:



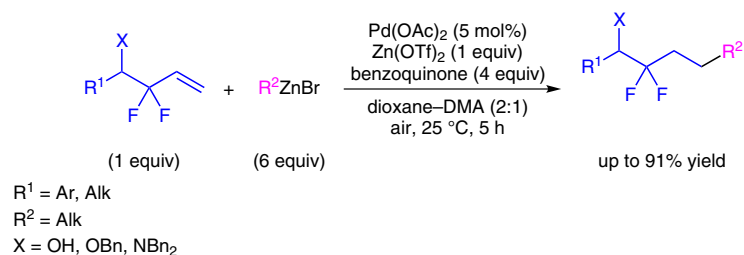
**Significance:** A novel method for cobalt-catalyzed cross-coupling reactions between aryl chlorides or bromides and aromatic magnesium or lithium reagents is reported by Duan and co-workers. The presence of 40 mol% of Ti(OEt)<sub>4</sub> suppresses undesired homocoupling side-products resulting from the organometallic reagent.

**Comment:** Interestingly, the reaction can also take place in the presence of a free carboxylic acid, a hydroxyl, or an amide residue. Therefore, this protocol allows an efficient arylation of highly functionalized aryl halides without protection-deprotection sequences.

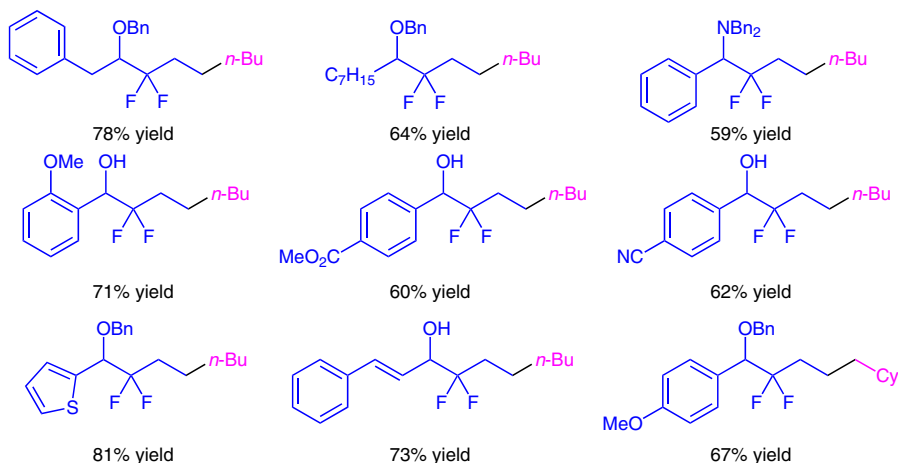
X. LIN, F.-L. QING\* (SHANGHAI INSTITUTE OF ORGANIC CHEMISTRY AND DONGHUA UNIVERSITY, SHANGHAI, P. R. OF CHINA)

Palladium-Catalyzed Anti-Markovnikov Hydroalkylation of Homoallylic Alcohols Bearing  $\beta$ -Fluorines  
*Org. Lett.* **2013**, *15*, 4478–4481.

## Palladium-Catalyzed Anti-Markovnikov Hydroalkylation of Homoallylic Alcohols



### Selected examples:

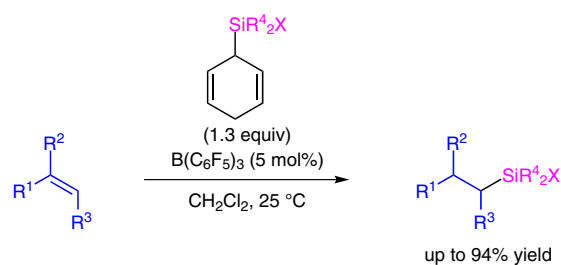


**Significance:** Lin and Qing report a mild and convenient protocol for the anti-Markovnikov hydroalkylation of  $\beta,\beta$ -difluorinated homoallylic alcohols. The palladium-catalyzed reaction with alkylzinc reagents furnishes the products in good to excellent yields.

**Comment:** The reported protocol affords a wide range of synthetically useful *gem*-difluorinated compounds with good functional-group compatibility. Moreover, the results show that the transposition of  $\text{CH}_2$  into  $\text{CF}_2$  at the allylic position of homoallylic alcohols can modify the electronic and steric environment of the alkene.

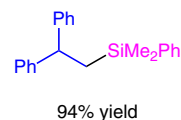
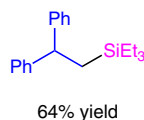
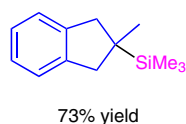
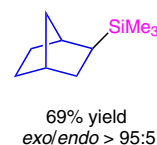
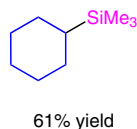
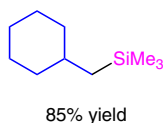
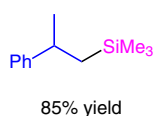
A. SIMONNEAU, M. OESTREICH\* (TECHNISCHE UNIVERSITÄT BERLIN, GERMANY)  
 3-Silylated Cyclohexa-1,4-dienes as Precursors for Gaseous Hydrosilanes: The  $B(C_6F_5)_3$ -Catalyzed Transfer  
 Hydrosilylation of Alkenes  
*Angew. Chem. Int. Ed.* **2013**, 52, 11905–11907.

## $B(C_6F_5)_3$ -Catalyzed Transfer Hydrosilylation of Alkenes



$R^1$  = H, Hex, Ph, Hept  
 $R^2$  = H, Me, Ph  
 $R^3$  = H, Me  
 $R^1, R^2$  = Cy  
 $R^1, R^3$  = indenyl derivatives, dihydronaphthalenyl, cyclohexenyl, cycloheptenyl, norbornenyl  
 $R^4$  = Me, Et  
 $X$  = H, Me, Ph (if  $R^4$  = Me)

### Selected examples:



**Significance:** Herein, the easy-to-handle  $B(C_6F_5)_3$ -catalyzed ionic transfer hydrosilylation of various alkenes using 3-silylated cyclohexa-1,4-dienes is described. The corresponding hydrosilylated alkenes are obtained in high yields.

**Comment:** Often, work in the laboratory with  $Me_3SiH$  and  $Me_2SiH_2$  is prohibited because of safety considerations. Since the silylated cyclohexadienes are precursors for the analogous gaseous hydrosilanes, which are generated in situ by a  $B(C_6F_5)_3$ -catalyzed release of these hydrosilanes, this protocol is a safe alternative for the hydrosilylation of alkenes.

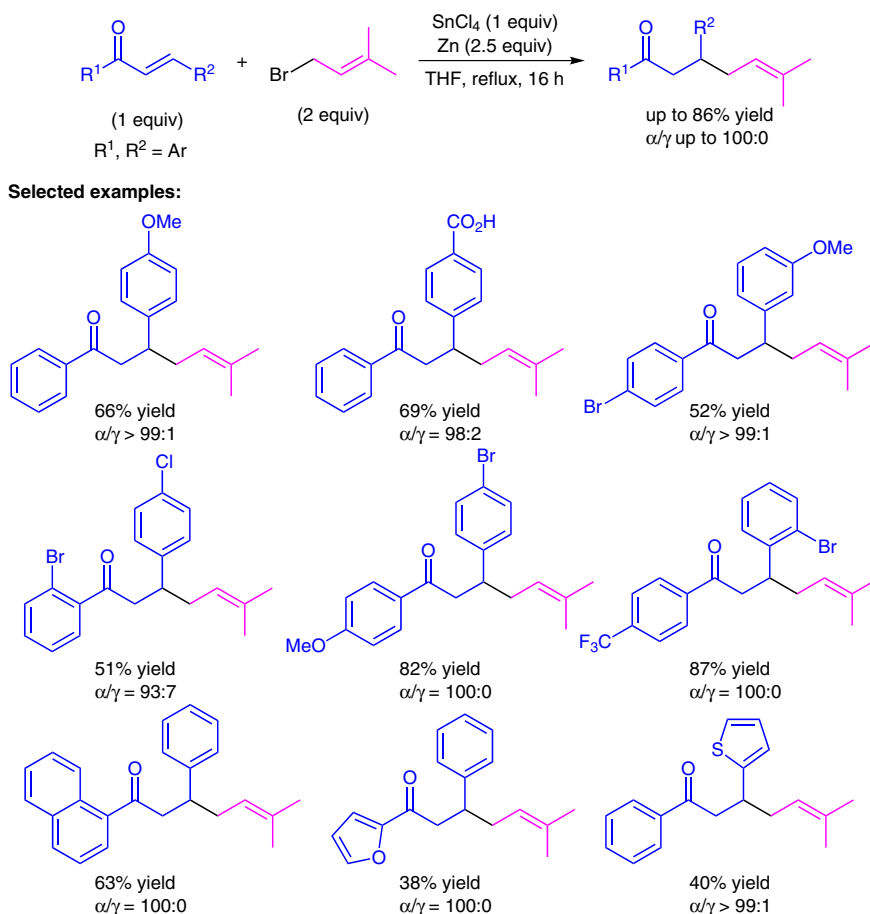
**SYNFACTS Contributors:** Paul Knochel, Nadja M. Barl  
 Synfacts 2014, 10(1), 0073 Published online: 13.12.2013  
 DOI: 10.1055/s-0033-1340372; Reg-No.: P16213SF

L.-M. ZHAO,\* S.-Q. ZHANG, F. DOU, R. SUN (JIANGSU NORMAL UNIVERSITY, XUZHOU, P. R. OF CHINA)

Zinc-Mediated Highly  $\alpha$ -Regioselective 1,4-Addition of Chalcones with Prenyl Bromide in THF

*Org. Lett.* **2013**, *15*, 5154–5157.

## Highly $\alpha$ -Regioselective 1,4-Addition of Chalcones with Prenyl Bromide



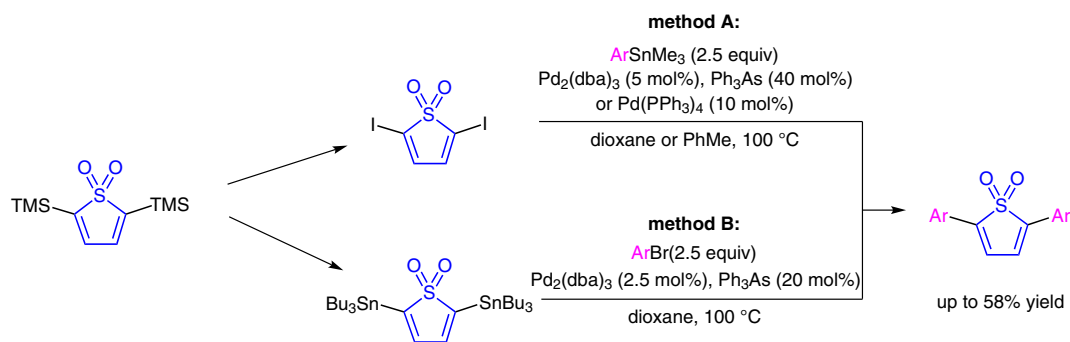
**Significance:** An efficient method for the introduction of a prenyl group onto the  $\beta$ -position of chalcones by zinc-mediated conjugate addition in the presence of tin(IV) chloride ( $\text{SnCl}_4$ ) is reported. The corresponding products are obtained in high yields and excellent  $\alpha/\gamma$ -selectivities.

**Comment:** The reaction has proven to be highly  $\alpha$ -regioselective in a 1,4-manner. Moreover, the  $\alpha$ -regioselectivity of these additions is higher than that of the corresponding addition of allylic barium, lithium, and copper reagents.

**SYNFACTS Contributors:** Paul Knochel, Christoph Sämann  
Synfacts 2014, 10(1), 0074 Published online: 13.12.2013  
**DOI:** 10.1055/s-0033-1340363; **Reg-No.:** P15313SF

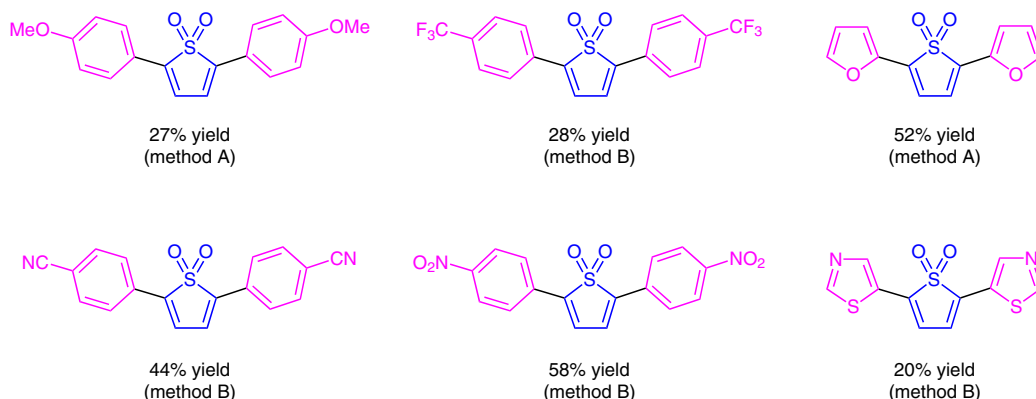
2014 © THIEME STUTTGART • NEW YORK

# Synthesis of 2,5-Diarylated Thiophene 1,1-Dioxides



Ar = Ph, 4-MeOC<sub>6</sub>H<sub>4</sub>, 4-F<sub>3</sub>CC<sub>6</sub>H<sub>4</sub>, 4-NCC<sub>6</sub>H<sub>4</sub>, 4-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>, 2-thienyl, 2-furyl, 5-thiazolyl

## Selected examples:



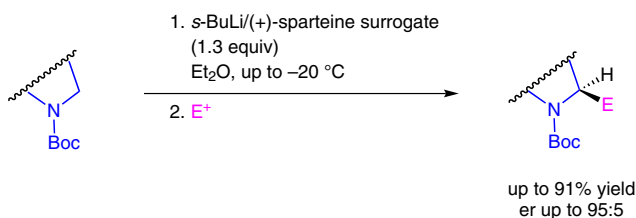
**Significance:** The authors disclose the palladium-catalyzed diarylation of distannylated thiophene 1,1-dioxide (electron-poor aryl coupling partners) and diiodo thiophene 1,1-dioxide (electron-rich aryl coupling partners) by Stille cross-coupling reactions to synthesize various 2,5-bis(aryl)thiophene 1,1-dioxides in moderate yields. Furthermore, the electrochemical and photophysical properties of these diarylated thiophene dioxides were investigated using cyclic voltammetry and fluorescence spectroscopy.

**Comment:** The corresponding distannylated thiophene 1,1-dioxides are obtained by treatment of 2,5-bis(trimethylsilyl)thiophene 1,1-dioxide with tetrabutylammonium fluoride (TBAF) and bis(tributyltin) oxide. A wide range of these diarylated thiophene dioxides show significant quantum yields, and their appropriate reduction and oxidation potentials may easily be tuned by the use of electron-donating and -withdrawing aryl groups.

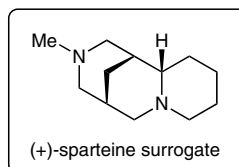
**SYNFACTS Contributors:** Paul Knochel, Nadja M. Barl  
 Synfacts 2014, 10(1), 0075 Published online: 13.12.2013  
 DOI: 10.1055/s-0033-1340375; Reg-No.: P16513SF

G. GELARDI, G. BARKER, P. O'BRIEN,\* D. C. BLAKEMORE (UNIVERSITY OF YORK AND PFIZER WORLDWIDE RESEARCH AND DEVELOPMENT, CAMBRIDGE, UK)  
Asymmetric Lithiation Trapping of *N*-Boc Heterocycles at Temperatures above  $-78^{\circ}\text{C}$   
*Org. Lett.* **2013**, *15*, 5424–5427.

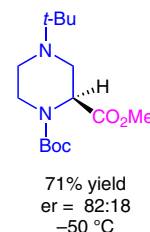
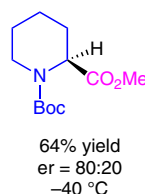
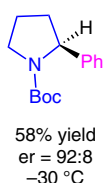
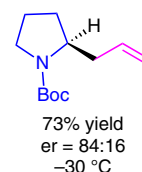
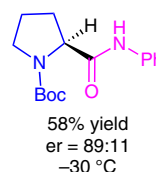
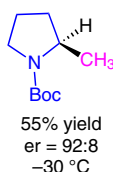
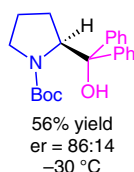
## Asymmetric Lithiation Trapping of *N*-Boc Heterocycles



$\text{E}^+$  = PhCHO,  $\text{MeO}_2\text{CCl}$ ,  $\text{Ph}_2\text{CO}$ ,  $\text{Me}_2\text{SO}_4$ ,  $\text{PhNCO}$ , allyl bromide, PhBr



### Selected examples:



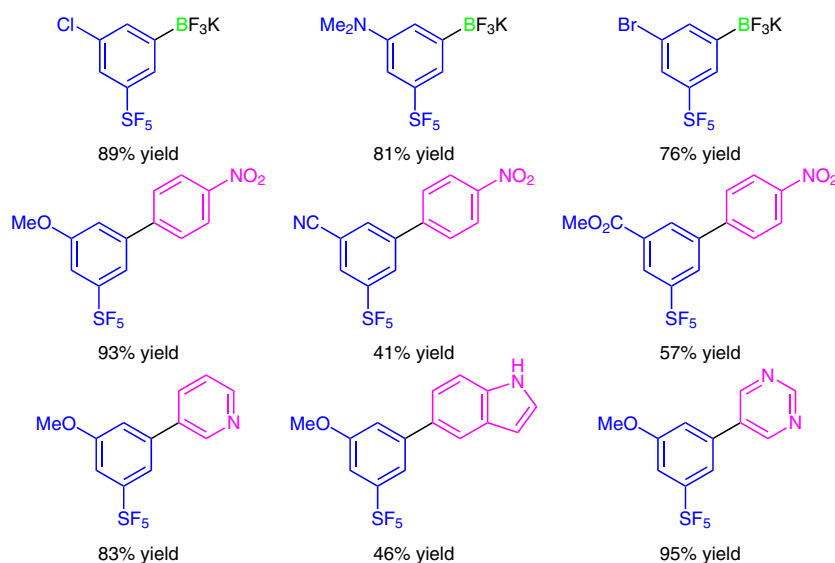
**Significance:** The asymmetric lithiation trapping of various *N*-Boc heterocycles is disclosed, using *s*-BuLi and chiral diamines such as (–)-sparteine and (+)-sparteine surrogate at temperatures above  $-78^{\circ}\text{C}$ . The corresponding chiral heterocycles are obtained in high yields and with good enantiomeric ratios.

**Comment:** The experiments can be conveniently performed, since asymmetric lithiation trappings of, for example, *N*-Boc pyrrolidine may be conducted at  $-30^{\circ}\text{C}$ , still furnishing the chiral heterocycles with a high enantiomeric ratio of about 9:1.

**SYNFACTS Contributors:** Paul Knochel, Nadja M. Barl  
Synfacts 2014, 10(1), 0076 Published online: 13.12.2013  
**DOI:** 10.1055/s-0033-1340374; **Reg-No.:** P16413SF

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# Iridium-Catalyzed Preparation of SF<sub>5</sub>-Substituted Aryl Trifluoroborates



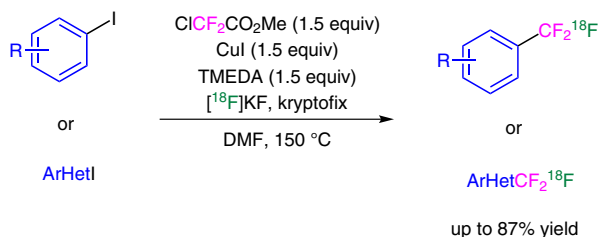
**Comment:** The described protocol is very versatile since the prepared compounds are potential important building blocks for drug discovery and agrochemicals. Moreover, the reaction proceeds under relatively mild conditions and tolerates various functional groups.

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M. HUIBAN, M. TREDWELL, S. MIZUTA, Z. WAN, X. ZHANG, T. L. COLLIER, V. GOUVERNEUR,\* J. PASSCHIER\* (IMPERIAL COLLEGE LONDON AND UNIVERSITY OF OXFORD, UK; GLAXOSMITHKLINE, SHANGHAI, P. R. OF CHINA; ADVION BIOSYSTEMS, ITHACA, USA)

A Broadly Applicable  $[^{18}\text{F}]$ Trifluoromethylation of Aryl Iodides and Heteroaryl Iodides for PET Imaging  
*Nature Chem.* **2013**, *5*, 941–944.

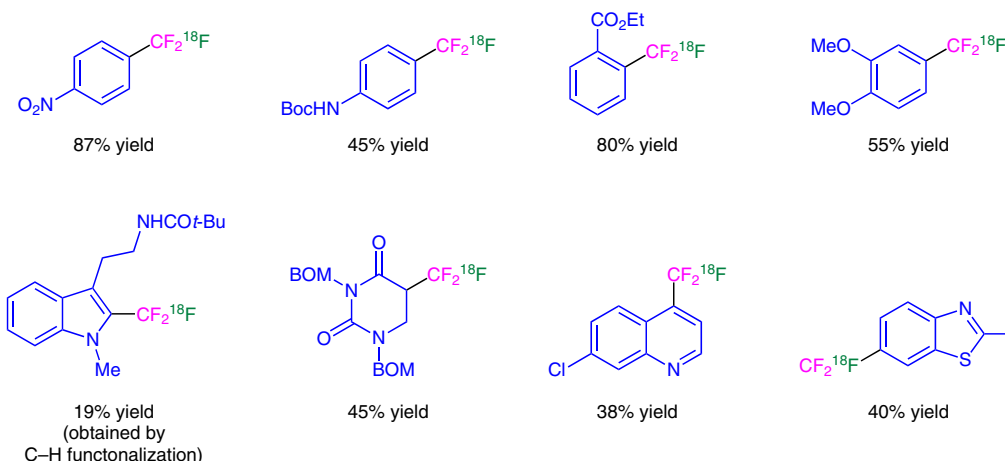
## $[^{18}\text{F}]$ Trifluoromethylation of Aryl and Heteroaryl Iodides



R =  $\text{NO}_2$ ,  $\text{CO}_2\text{Et}$ , CHO, Ac,  $\text{CO}_2\text{H}$ , CN, Br, Ph, OAc, OPiv, OH, OBn, OMe,  $\text{CONH}_2$ ,  $\text{NH}_2$ ,  $\text{NHC(O)Me}$ ,  $\text{NHBoc}$ , chiral dipeptide, chiral carbohydrate

HetAr = pyridyl, pyrazyl, quinolyl, benzothiazolyl, thienyl, uracilyl and indolyl derivatives

### Selected examples:



**Significance:** The authors disclose the easy and broadly applicable late-stage  $[^{18}\text{F}]$ trifluoromethylation of various aryl and heteroaryl iodides using methyl chlorodifluoroacetate,  $\text{CuI}$ ,  $\text{TMEDA}$ , and  $[^{18}\text{F}]$ fluoride. The  $[^{18}\text{F}]$ trifluoromethylated (hetero)aryls, which serve as  $[^{18}\text{F}]$ -PET (positron emission tomography) tracers, are obtained in good yields.

**Comment:** Usually, access to  $[^{18}\text{F}]$ -labelled probes is limited by the short half-life of  $^{18}\text{F}$  and the small availability of parent  $^{18}\text{F}$  sources that show a suitable reactivity, such as  $[^{18}\text{F}]\text{F}^-$  and  $[^{18}\text{F}]\text{F}_2$ . Furthermore, this operational simple  $[^{18}\text{F}]\text{CuCF}_3$ -based strategy excludes the tedious preparation of complex organometallic precursors and may be performed on air. The active  $[^{18}\text{F}]\text{CF}_3\text{Cu}$  is generated in situ.

**SYNFACTS Contributors:** Paul Knochel, Nadja M. Barl  
Synfacts 2014, 10(1), 0078 Published online: 13.12.2013  
**DOI:** 10.1055/s-0033-1340373; **Reg-No.:** P16313SF

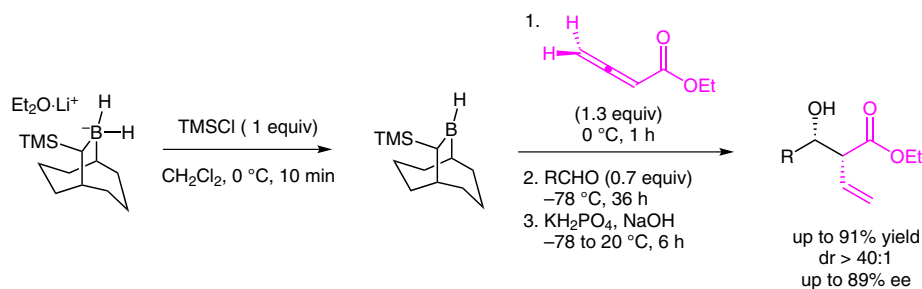
2014 © THIEME STUTTGART • NEW YORK

J. KISTER, D. H. ESS, W. R. ROUSH\* (SCRIPPS FLORIDA, JUPITER AND BRIGHAM YOUNG UNIVERSITY, PROVO, USA)

Enantio- and Diastereoselective Synthesis of *syn*- $\beta$ -Hydroxy- $\alpha$ -vinyl Carboxylic Esters via Reductive Aldol Reactions of Ethyl Allenecarboxylate with 10-TMS-9-Borabicyclo[3.3.2]decane and DFT Analysis of the Hydroboration Pathway

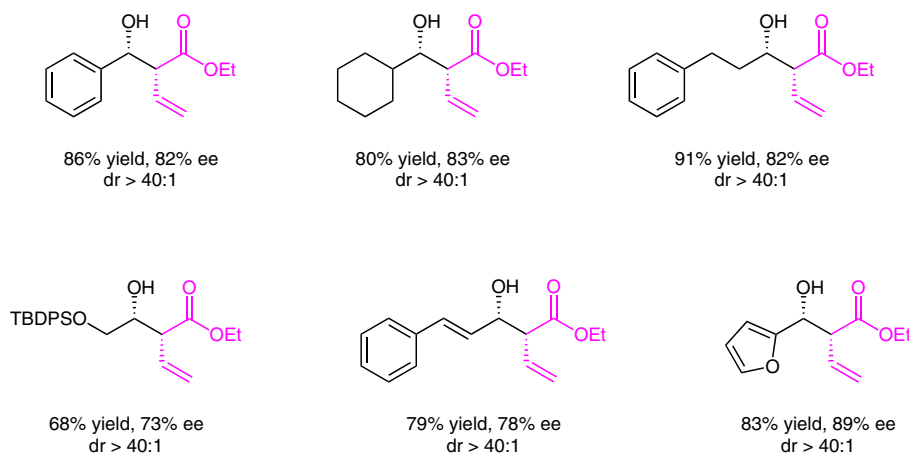
*Org. Lett.* **2013**, *15*, 5436–5439.

## Stereoselective Synthesis of *syn*- $\beta$ -Hydroxy- $\alpha$ -vinyl Carboxylate Esters



R = Ph, Cy,  $(\text{CH}_2)_2\text{Ph}$ ,  $\text{CH}_2\text{OTBDPS}$ ,  $\text{CHCHPh}$ , 3-pyridyl, 2-furyl

### Selected examples:



**Significance:** The authors report a novel enantio- and diastereoselective synthesis of *syn*- $\beta$ -hydroxy- $\alpha$ -vinyl carboxylate esters. The reaction proceeds via a reductive aldol reaction of an ethyl allene carboxylate with 10-TMS-9-borabicyclo[3.3.2]decane.

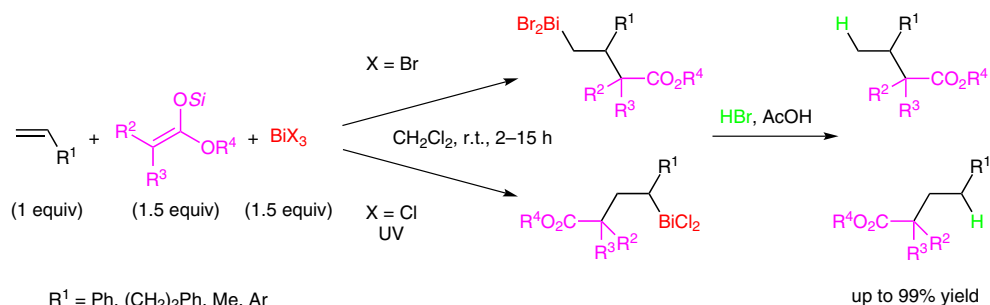
**Comment:** The exclusive formation of *syn*- $\beta$ -hydroxy- $\alpha$ -vinyl carboxylate esters can be explained by an aldol reaction via a chair-like transition state. DFT calculations suggest that the allene hydroboration involves a 1,4-reduction of the ethyl allene carboxylate with 10-TMS-9-borabicyclo[3.3.2]decane.

**SYNFACTS Contributors:** Paul Knochel, Andreas K. Steib  
Synfacts 2014, 10(1), 0079 Published online: 13.12.2013

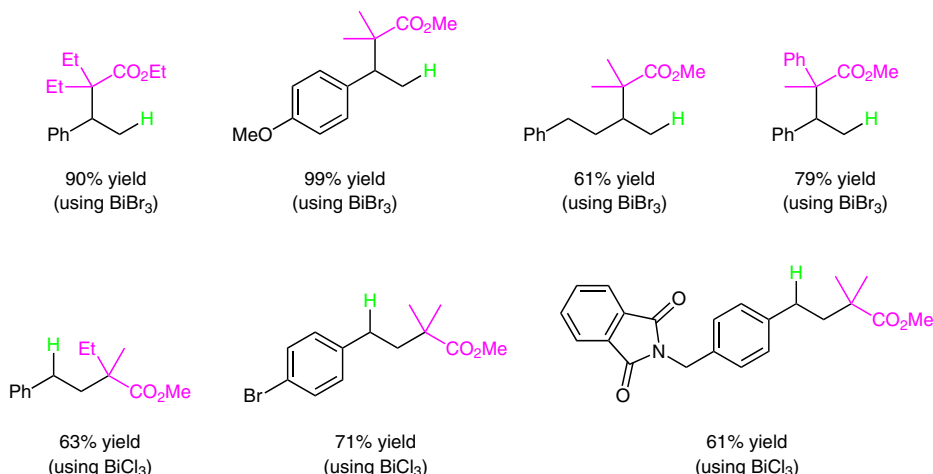
DOI: 10.1055/s-0033-1340369; Reg-No.: P15913SF

Y. NISHIMOTO, M. TAKEUCHI, M. YASUDA, A. BABA\* (OSAKA UNIVERSITY, JAPAN)  
 Synthesis of Alkylbismuths by Regiodivergent Carbobismuthination of Simple Alkenes  
*Chem. Eur. J.* **2013**, *19*, 14411–14415.

## Bismuth-Mediated Switchable Regioselective Carbometalation



### Selected examples:



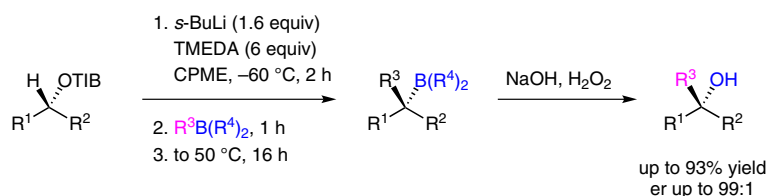
**Significance:** Baba and co-workers report a novel carbobismuthination reaction of alkenes using bismuth trihalides and ketene silyl acetals. Furthermore, in this protocol, the first switch in regioselectivity of the carbometalation using  $\text{BiCl}_3$  instead of  $\text{BiBr}_3$  is reported.

**Comment:** The resultant alkylbismuth compounds react with a range of reagents in order to give functionalized aliphatics. Therefore, reaction with *N*-bromosuccinimide furnishes the bromide, reaction with AIBN and  $\text{PhSSPh}$  introduces a thiophenyl group, and  $\text{PhI}(\text{OAc})_2$  in combination with  $\text{TMSOAc}$  gives the acetate.

**SYNFACTS Contributors:** Paul Knochel, Andreas K. Steib  
 Synfacts 2014, 10(1), 0080 Published online: 13.12.2013  
 DOI: 10.1055/s-0033-1340367; Reg-No.: P15713SF

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# Lithiation–Borylation of Secondary Alkyl Benzoates



TIB = 2,4,6-triisopropyl benzoate

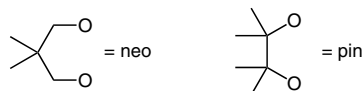
CPME = cyclopentyl methyl ether

R<sup>1</sup> = CH<sub>2</sub>Bn, (CH<sub>2</sub>)<sub>2</sub>CHCH<sub>2</sub>, (CH<sub>2</sub>)<sub>3</sub>OTHP

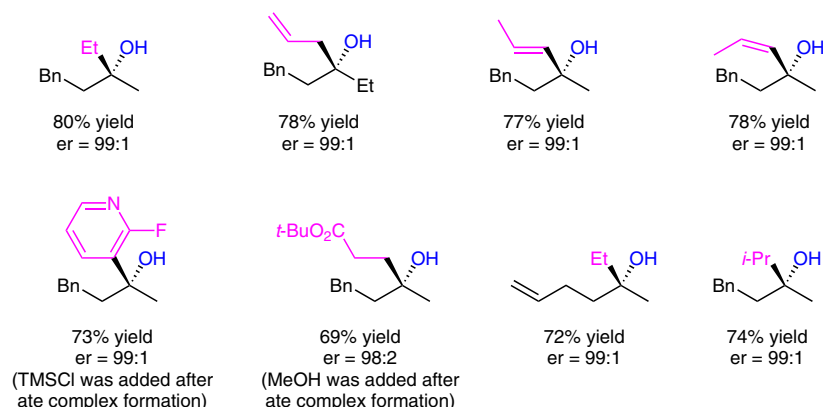
R<sup>2</sup> = Me, Et

R<sup>3</sup> = Et, *i*-Pr, Ph, allyl, 3-(2-fluoropyridyl), (CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>*t*-Bu, CHCHCH<sub>3</sub>

(R<sup>4</sup>)<sub>2</sub> = pin, neo, Et<sub>2</sub>



## Selected examples:

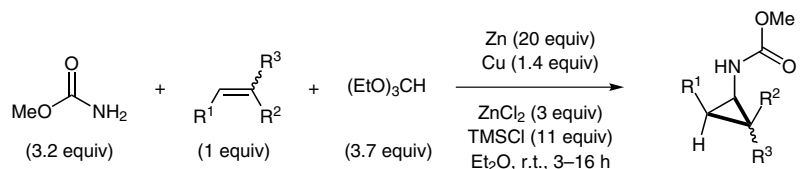


**Significance:** Against common wisdom, Aggarwal and co-workers have now shown that secondary 2,4,6-triisopropyl benzoates (TIP esters) can be deprotonated at –60 °C using a combination of *s*-BuLi and TMEDA in cyclopentyl methyl ether (CPME). The resulting lithium reagents were allowed to react with various neopentyl boronic esters which after 1,2-metalate rearrangement and oxidation furnished a range of tertiary alcohols in good enantioselectivity.

**Comment:** This lithiation reaction cannot be performed in THF. Simply switching from THF to diethyl ether increased the yield of the lithiated benzoate. The extent of lithiation was increased further by using CPME. Interestingly, the subsequent borylation reaction occurs with complete retention of configuration.

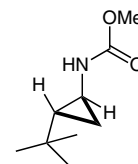
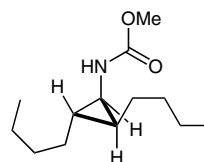
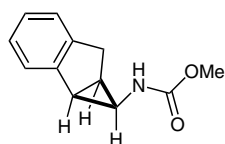
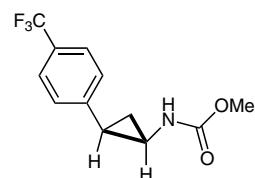
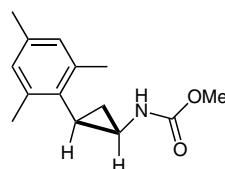
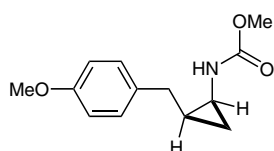
S. ISHIKAWA, T. D. SHEPPARD, J. M. D'OYLEY, A. KAMIMURA, W. B. MOTHERWELL\*  
(UNIVERSITY COLLEGE LONDON, UK AND YAMAGUCHI UNIVERSITY, UBE, JAPAN)  
A Rapid Route to Aminocyclopropanes via Carbamatoorganozinc Carbenoids  
*Angew. Chem. Int. Ed.* **2013**, 52, 10060–10063.

## Zn/Cu-Mediated Aminocyclopropanation



$\text{R}^1 = \text{Alk, Ar}$   
 $\text{R}^2, \text{R}^3 = \text{Alk, Ar}$

### Selected examples:

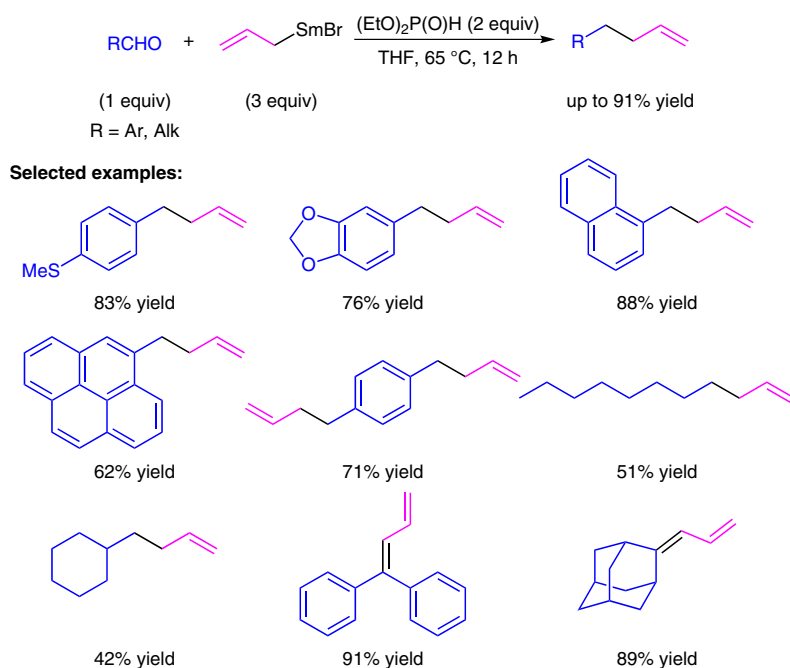


**Significance:** The authors report a novel method for the preparation of carbamate-protected aminocyclopropanes. The reaction proceeds via aminocyclopropanation of alkenes using carbamates in the presence of metallic zinc and copper. The conditions are very mild (room temperature) using only 3.2 equivalents of carbamate.

**Comment:** The prepared cyclopropane carbamates can be deprotected using iodotrimethylsilane in chloroform and methanol. Subsequent isolation furnishes the corresponding aminocyclopropanes as their crystalline HI salts in high yields.

Y. LI, Y.-Y. HU, S.-L. ZHANG\* (SOOCHOW UNIVERSITY, SUZHOU, P. R. OF CHINA)  
 Dual Role of Allylsamarium Bromide as a Grignard Reagent and a Single Electron Transfer Reagent in the One-Pot  
 Synthesis of Terminal Olefins  
*Chem. Commun.* **2013**, 49, 10635–10637.

## Terminal Olefin Synthesis via Reaction of Aldehydes with Allylsamarium Bromide



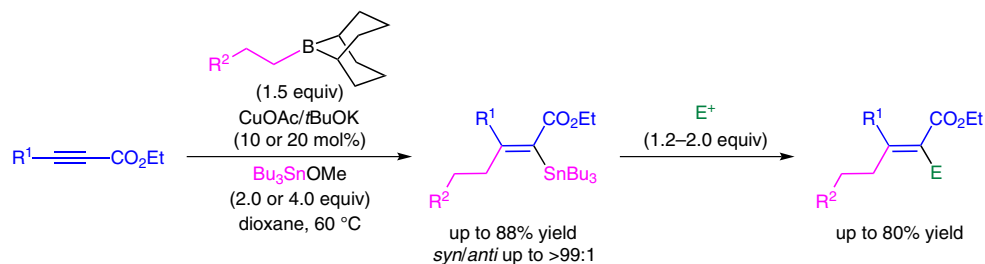
**Significance:** A simple and efficient one-pot protocol for the synthesis of terminal alkenes has been reported. The reaction of carbonyl compounds with allylsamarium bromide in the presence of diethyl phosphate furnishes the corresponding olefins in good to excellent yields.

**Comment:** Allylsamarium bromide acts in the reported reaction as both, a nucleophilic reagent and a single electron transfer reagent. Moreover, the described methodology is very versatile since several functional groups are tolerated.

T. WAKAMATSU, K. NAGAO, H. OHMIYA,\* M. SAWAMURA\* (HOKKAIDO UNIVERSITY, SAPPORO, JAPAN)

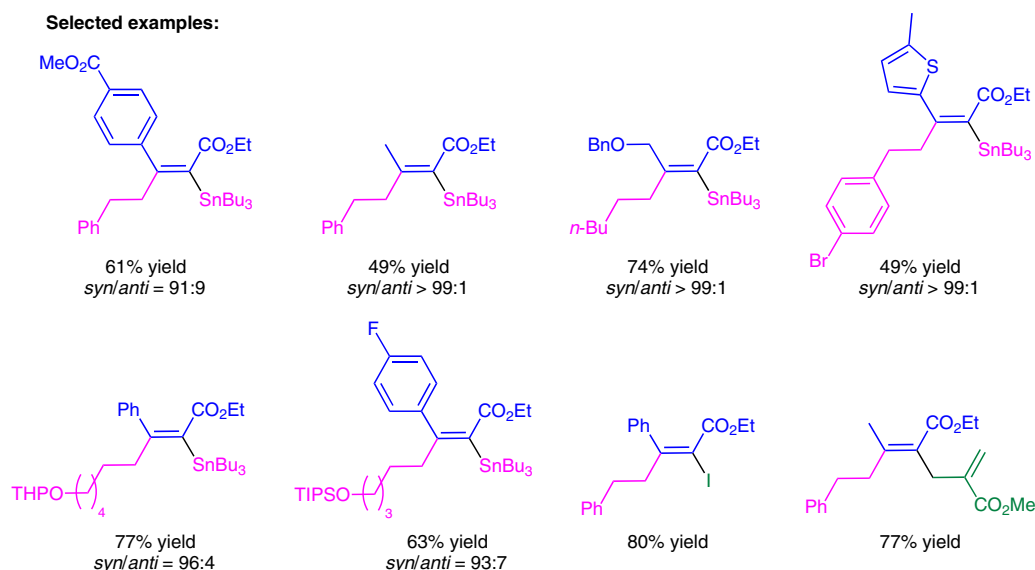
Synthesis of Trisubstituted Alkenylstannanes through Copper-Catalyzed Three-Component Coupling of Alkylboranes, Alkynoates and Tributyltin Methoxide  
*Angew. Chem. Int. Ed.* **2013**, 52, 11620–11623.

## Synthesis of Trisubstituted Alkenylstannanes Starting from Alkynoates



R<sup>1</sup> = Ph, *n*-Bu, *n*-Pent, (CH<sub>2</sub>)<sub>3</sub>phthalimide, (CH<sub>2</sub>)<sub>4</sub>OTHP, C(Me)<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Me, 4-BrC<sub>6</sub>H<sub>4</sub>, (CH<sub>2</sub>)<sub>3</sub>OTIPS  
R<sup>2</sup> = Ph, 4-MeOC<sub>6</sub>H<sub>4</sub>, 4-MeO<sub>2</sub>CC<sub>6</sub>H<sub>4</sub>, 2-MeC<sub>6</sub>H<sub>4</sub>, Me, CH<sub>2</sub>OTHP, CH<sub>2</sub>OBn, 4-FC<sub>6</sub>H<sub>4</sub>, 2-thienyl derivative

### Selected examples:



**Significance:** The authors report a highly regio-selective copper-catalyzed synthesis of trisubstituted alkenylstannanes. Through a three-component coupling of alkylboranes, alkynoates and tributyltin methoxide, these trisubstituted alkenylstannanes are obtained in good yields and with high *syn* selectivity. The appropriate alkylboranes are easily accessible by hydroboration of the corresponding alkenes with the 9-borabicyclo[3.3.1]nonane (9-BBN-H) dimer.

**Comment:** Standard methods for the synthesis of alkenylstannanes described by Shirakawa and Hiyama include the palladium- or nickel-catalyzed carbostannylation of internal alkynes with organostannanes which are somewhat difficult to prepare.

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