DOI: 10.1002/ejoc.201000231

Copper-Catalyzed Multicomponent Coupling of Organoindium Reagents with Nitrogen-Containing Aromatic Heterocycles

Ramsay E. Beveridge,[a,b] Daniel A. Black,[a] and Bruce A. Arndtsen*[a]

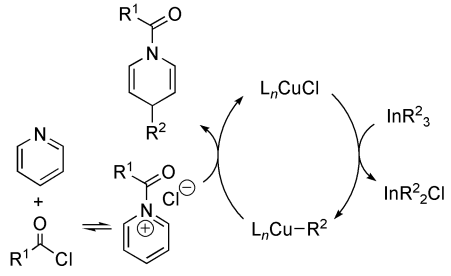
Keywords: Nitrogen heterocycles / Organoindium reagents / Copper / Multicomponent reactions / Pyridinium salts

A mild, copper-catalyzed coupling of organoindium reagents with nitrogen-containing aromatic heterocycles and chloroformates is described. This reaction proceeds with a range of organoindium reagents, yielding predominately or exclusively the 1,4-addition products with pyridine. In addition, a range of other nitrogen-containing heterocycles can be employed in this reaction (e.g. benzoxazole, benzothiazole, phthalazine). As an illustration of the utility of this reaction, this heterocycle functionalization is coupled with a subsequent oxidation to achieve the one-pot synthesis of functionalized pyridine and benzothiazole derivatives.

Introduction

The addition of organometallic nucleophiles to pyridinium salts provides a useful route to functionalized pyridine derivatives.[1,2] A variety of nucleophiles have been used in this chemistry, including Grignard reagents,[3] organozinc compounds,[4] organostannanes,[5] and others.[6,7] The products of these reactions, 1,2- or 1,4-dihydropyridine derivatives, are of interest as biologically active molecules (e.g. NADH mimics),[8] and useful synthetic intermediates in the synthesis of pyridines[2] and natural products.[9–11] Whereas this synthetic approach is effective, the reactivity of many of the nucleophiles employed in this chemistry can result in significant functional-group incompatibility, as well as limit the availability of many substituted variants of these substrates. In addition, extension of this reaction to other C=N-containing azaaromatic compounds (e.g. benzoxazole, benzothiazole, phthalazine) through N-activation and functionalization with organometallic reagents has not seen widespread use, due in part to the sensitivity of many of these heterocycles to ring opening and/or deprotonation.[12,13] The use of more mild organometallic reagents, such as organostannanes, has been reported to demonstrate better functional-group tolerance and compatibility in these reactions, but these are often restricted to the transfer of allyl, benzyl or alkynyl units.[5,13] For these reasons, it could be advantageous to develop a milder and more general method to access these and related functionalized heterocycles.

Recently, organoindium reagents have been found to be useful organometallic coupling partners in a wide range of metal-catalyzed carbon–carbon bond-forming reactions.[14] These substrates can be prepared with a range of organic fragments, demonstrate high functional-group compatibility, transfer all of their organic groups upon reaction (providing high atom economy), and generate low-toxicity $InCl_3$ as a by-product. Although organoindium reagents are typically not reactive toward pyridines and related heterocycles,[15] we have recently reported that copper complexes can catalyze the multicomponent coupling of imines, acyl chlorides and organoindium reagents to generate α-substituted amides.[16] Considering the resonance structure similarity of imines to pyridines, we have undertaken a study of the potential use of organoindium reagents in the reductive functionalization of pyridines, by the postulated mechanism shown in Scheme 1. As described below, this can provide a mild route to reductively functionalized pyridines and a range of other nitrogen-containing heterocycles.



Scheme 1. Proposed mechanism of the copper-catalyzed coupling of pyridine, chloroformate and organoindium reagents.

Results and Discussion

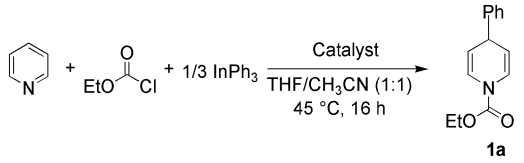
Our initial efforts focused on the reaction of triphenylindium with pyridines in the presence of ethyl chloroformate.

[a] Department of Chemistry, McGill University
801 Sherbrooke St. W., Montreal, QC H3A2K6, Canada
Fax: +1-514-398-3797
E-mail: bruce.arndtsen@mcgill.ca
[b] Pfizer Global Research and Development,
Groton, CT 06320, USA

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201000231.

As shown in Table 1, triphenylindium is essentially unreactive towards in situ generated pyridinium salts in the absence of a catalyst, yielding only traces of **1a** (Entry 1). In a similar fashion to that observed with imines, the addition of copper salt catalysts significantly improves the efficiency of this reaction (Entries 2–5). In all cases, the reaction is highly 1,4-regioselective, with <5% of any other isomer observed. In the case of CuCl, the addition is both regioselective and high-yielding, providing **1** in 85% yield (Entry 5).

Table 1. Catalyst for coupling of Ph_3In with pyridine and ethyl chloroformate.[a]



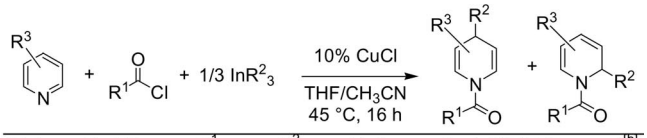
Entry	Catalyst	Yield of **1a**
1	–	8%
2	10% CuI	46%
3	10% CuBr	48%
4	10% $Cu(OTf)_2$	57%
5	10% CuCl	85%

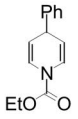
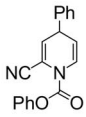
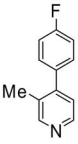
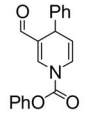
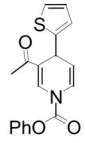
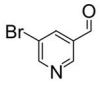
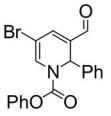
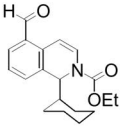
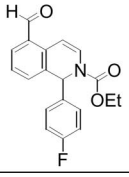
[a] Pyridine (40 mg, 0.50 mmol), chloroformate (61 mg, 0.60 mmol) in CH_3CN (2 mL) added to CuCl (5 mg, 0.05 mmol) in CH_3CN (1 mL), followed by $InPh_3$ (0.18 mmol) in THF (3 mL), 45 °C, 16 h.

In addition to simple pyridine, this copper-catalyzed coupling is compatible with a variety of functionalized pyridine derivatives (Table 2). This includes 2- or 3-alkyl-, cyano-, as well as more reactive halogen- and carbonyl-substituted pyridines. The latter can be sensitive to the use of more potent nucleophiles in additions.[9a] In this case, selective carbon–carbon bond formation is observed on the pyridine ring, likely arising from the lower nucleophilicity of the organoindium reagent. A range of organic groups can be transferred from the indium reagent, including aryl, heteroaryl, and alkyl units. In the case of the *para*-fluoroaryl-substituted product (Entry 3), the heterocycle spontaneously aromatizes upon isolation (vide infra).

These reactions yield 1,4-addition products, either exclusively with pyridine, or as the major product with sterically more encumbered 2- and 3-substituted pyridines. The exception to this is the sterically blocked 3-bromo-5-carbonyl-substituted derivative (Entry 6). This preferred 1,4-addition is similar to that noted in related copper-catalyzed additions to in situ generated pyridinium salts,[1,3] but contrasts with our results using terminal alkynes, which are postulated to generate analogous organocuprate derivatives as intermediates.[2b,17] Whereas the reason for this latter difference is at present unclear, it may result from interaction of the indium reagent with the organocuprate (or *N*-acylpyridinium intermediate) after transmetallation. In contrast to these results with pyridine, isoquinoline derivatives have only a single site of activation upon chloroformate addition, and yield exclusively 1,2-addition products in good yield (Entries 7, 8).[18]

Table 2. Copper-catalyzed coupling of pyridines and organoindium reagents.[a]



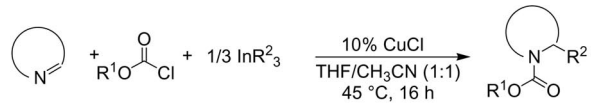
Entry	Pyridine	R^1	R^2	Major product	Yield (isomer)[b]
1		OEt			85%
2[c]		OPh			71% (3:1)
3		OEt			48%
4		OPh			55% (2:1)
5[d]		OPh			62% (1.3:1:1)
6		OPh			31%[e]
7		OEt			63%
8		OEt			84%

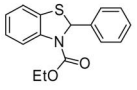
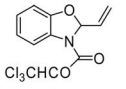
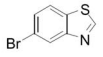
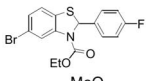
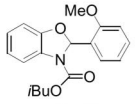
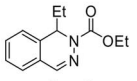
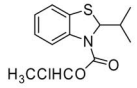
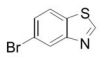
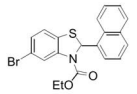
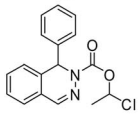
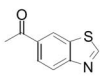
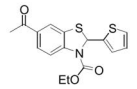
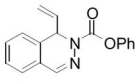
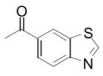
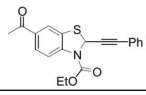
[a] Conditions of Table 1. [b] Combined yield of isomers [ratio of 4-substituted isomer to 2- or 6-substituted]. [c] 72 h. [d] 45 °C, 24 h. [e] 55 °C, 48 h.

The results with isoquinoline suggested to us the potential application of this approach to a broader scope of heterocycles than pyridine derivatives. In principle, this copper-catalyzed carbon–carbon bond formation can be employed with any heterocycle that can be activated with chloroformates according to the mechanism in Scheme 1. The latter is illustrated in Table 3, where this same copper-catalyzed organoindium coupling can be used to derivatize a number of heterocycles, including phthalazine, benzoxazole, benzothiazole. Each of these reactions leads to the formation of the 2-substituted heterocycle. In general, ethyl chloroformate leads to the highest product yields in these sys-

tems. In addition to aromatic groups, alkyl or vinyl units can also be transferred from the organoindium reagent in these reactions. It is notable that stronger nucleophilic reagents often react with these substrates to lead to ring-opened products rather than derivatization.[12,13] As with pyridines, these reactions are compatible with various substituents on the heterocycle, including bromo and carbonyl units. Whereas general with benzo-fused heterocycles, it was found that this reaction is not compatible with simple oxazoles or thiazoles.[19]

Table 3. Coupling of organoindium reagents with nitrogen heterocycles.[a]

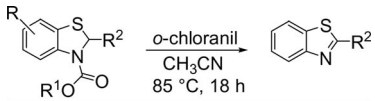


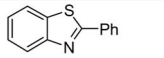
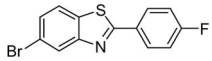
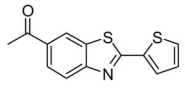
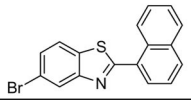
Entry	Substrate	R^1	R^2	Product(s)	Yield[b]
1		Et			91%
2		CH_2CCl_3			61%
3		Et			61%
4		*i*Bu			51%
5		Et			65%
6		$CHClCH_3$			39%
7		Et			84%
8		$CHClCH_3$			38%
9		Et			72%
10		Ph			85%
11		Et			64%

[a] Conditions of Table 1. [b] Isolated.

As an illustration of further potential utility in this reaction, it was noted that dihydropyridine derivatives can be oxidized to substituted pyridines.[2] As such, we envisioned that incorporating oxidative conditions with this copper-catalyzed organoindium coupling could provide a one-pot route to generate substituted aromatic heterocycles. As shown in Table 4, treatment of benzothiazole derivatives with *o*-chloranil can allow the straightforward formation of a range of 2-substituted benzothiazoles in good to excellent yield. Overall, this provides a straightforward approach to derivatize heterocycles directly from the parent structure with good functional-group compatibility.

Table 4. Synthesis of 2-substituted benzothiazoles.



Entry	Product	Yield[b]
1		87[c]
2		63
3		65
4		54

[a] Heterocycle in MeCN, 1 equiv. of *o*-chloranil (3,4,5,6-tetrachloro-1,2-benzoquinone), 85 °C, 18 h. [b] . Isolated yield. [c] 45 °C, 4 h.

Conclusions

This study has shown that the copper-catalyzed coupling of organoindium reagents with nitrogen-containing heterocycles, in the presence of a chloroformate activator, can provide an approach to generate partially reduced heterocycle derivatives. This provides a mild method to directly functionalize heterocycles without strong nucleophiles or the initial pre-derivatization of the heterocycle (e.g. halogenation). The reaction displays good functional-group compatibility, transfers a variety of organic groups from indium, and generates low-toxicity $InCl_3$ as the only by-product. Investigations towards the use of this coupling to derivatize other reagents are underway.

Experimental Section

General Methods: Unless otherwise noted, all manipulations were performed under an inert gas in a Vacuum Atmospheres 553-2 dry box or by using standard Schlenk or vacuum-line techniques. All reagents were purchased from Aldrich® and used as received. Acetonitrile was distilled from CaH_2 under nitrogen. Deuterated acetonitrile was dried like its protonated analogue, but was transferred under vacuum from the drying agent, and stored over molecular sieves (4 Å). Deuterated chloroform was dried with molecular sieves (3 Å). All organoindium reagents were prepared from commercially available Grignard reagents and $InCl_3$ by standard literature procedures[20] and used fresh. All compounds were characterized by ^1H and ^{13}C NMR and HRMS and by comparison to literature data.[21] Regioselectivity assignments for dihydropyridine compounds (Table 2) were determined by ^1H NMR, 1D NOESY

and 2D ^{1}H-^{13}C HMQC and HMBC experiments. ^{1}H and ^{13}C NMR spectra were recorded with Varian Mercury 200 MHz, 300 MHz, 400 MHz, Unity 500 MHz, and JEOL 270 MHz spectrometers. 1D NOESY spectra were recorded with a Varian Mercury 400 MHz spectrometer, 2D ^{1}H-^{13}C HMQC and HMBC were recorded with a Varian Mercury 400 MHz or Unity 500 MHz spectrometer. Mass spectra were obtained from the McGill University and Pfizer Global Research and Development mass spectral facilities.

Preparation of Triorganoindium Reagents: The appropriate organomagnesium reagent (0.50 mmol) was added to a Schlenk flask under N_2 containing $InCl_3$ (0.18 mmol, 39 mg) in THF at –78 °C over a period of 30 min (total volume: 3 mL of THF). The solution was then warmed to room temperature and stirred for an additional 30–60 min until the solution became homogeneous. The solution was then transferred by syringe to the reaction mixture.

Representative Procedure for Heterocycle Functionalization: Pyridine (0.5 mmol, 40 mg), ethyl chloroformate (0.6 mmol, 62 mg) and CuCl (0.05 mmol, 5 mg) were combined in CH_3CN (3 mL) in a screw cap vial in a glove box. To this solution was added a Ph_3In solution (0.18 mmol Ph_3In) in THF (3 mL). The mixture was stirred at 45 °C for 16 h. The solvent was removed in vacuo, then the product dissolved in Et_2O (30 mL), washed with satd. aq. $NaHCO_3$ (15 mL), which was then washed with Et_2O (15 mL). The organic layers were combined, dried ($MgSO_4$), filtered, and the product was purified by flash column chromatography on silica gel by using 10% EtOAc/hexanes as eluent. Isolated Yield: 97 mg, 85%.

Representative Procedure for the Synthesis of 2-Substituted Benzothiazoles: Purified 5-bromo-2-(4-fluorophenyl)benzo[*d*]thiazole (61 mg, 0.2 mmol) was dissolved in MeCN (5 mL), *o*-chloranil (3,4,5,6-tetrachloro-1,2-benzoquinone, 49 mg, 0.2 mmol) added, and the mixture was placed in a 85 °C heating bath for 18 h. The solvent was removed in vacuo, and the crude residue purified by flash column chromatography on silica gel by using EtOAc/hexanes as eluent. Isolated yield: 39 mg, 63%.

Ethyl 4-Phenylpyridine-1(4*H*)-carboxylate (1a): Table 2, Entry 1. Isolated yield: 97 mg, 85%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.39–7.22 (m, 5 H, Ph), 7.03–6.80 (m, 2 H), 5.07–4.85 (m, 2 H), 4.29 (q, J = 7 Hz, 2 H, CH_2CH$_3$), 4.18 (br. s, 1 H, C*H*Ph), 1.32 (t, J = 7 Hz, 3 H, CH$_2$CH_3) ppm. ^{13}C NMR (67.9 MHz, $CDCl_3$): δ = 151.5, 145.9, 128.7, 127.8, 127.2, 126.7, 109.5, 62.6, 39.2, 14.4 ppm. HRMS: calcd. for for $C_{14}H_{15}NO_2$ [M + Na] 252.1003, found 252.0998.

Phenyl 2-Cyano-4-phenylpyridine-1(4*H*)-carboxylate: Table 2, Entry 2. Isolated yield: 80 mg, 53%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.48–7.24 (m, 10 H), 7.11 (d, J = 8 Hz, 1 H, NC*H*=CH), 6.07–6.03 [m, 1 H, (CN)C=C*H*], 5.20–5.13 [m, 1 H, (Ph)CHC*H*], 4.34 (t, J = 5 Hz, 1 H, C*H*Ph) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 150.6, 148.9, 142.6, 129.7, 129.4, 129.3, 127.9, 127.8, 126.5, 123.6, 121.4, 114.0, 111.5, 110.1, 40.4 ppm. HRMS: calcd. for $C_{19}H_{14}N_2O_2$ [M + Na] 325.0955, found 325.0947.

Phenyl 6-Cyano-2-phenylpyridine-1(2*H*)-carboxylate: Table 2, Entry 2. Isolated yield: 27 mg, 18%. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.42–7.25 (m, 10 H), 6.43 [d, J = 6 Hz, 1 H, (CN)C=C*H*], 6.32–6.28 (m, 2 H), 6.14 [d, J = 6 Hz, 1 H, (Ph)CHC*H*] ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 151.8, 150.9, 137.7, 130.8, 129.6, 129.0, 127.3, 127.1, 126.3, 125.8, 121.5, 121.3, 115.0, 110.6, 55.6 ppm. HRMS: calcd. for $C_{19}H_{14}N_2O_2$ [M + Na] 325.0955, found 325.0947.

4-(4-Fluorophenyl)-3-methylpyridine: Table 2, Entry 3. Isolated yield: 45 mg, 48%. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.49–8.45 (m, 2 H), 7.30–7.11 (m, 5 H), 2.25 (s, 3 H, CH_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.8, 161.8, 151.5, 148.5, 147.5, 135.2, 130.5, 124.3, 115.8–115.6 (d, $J_{C,F}$ = 20 Hz), 17.4 ppm. HRMS: calcd. for $C_{12}H_{10}FN$ [M + H] 188.0896, found 188.0869.

Phenyl 3-Formyl-4-phenylpyridine-1(4*H*)-carboxylate: Table 2, Entry 4. Isolated yield: 58 mg, 38%. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.41 [s, 1 H, C(O)*H*], 7.91 [s, 1 H, NC*H*=C(CHO)], 7.48–7.20 (m, 10 H), 7.10 (d, J = 12 Hz, 1 H, NC*H*=CH), 5.40–5.35 [m, 1 H, (Ph)CH-C*H*], 4.58 (t, J = 3 Hz, 1 H, C*H*Ph) ppm. ^{13}C NMR (67.9 MHz, $CDCl_3$): δ = 189.8, 150.5, 149.4, 143.5, 139.4, 129.7, 128.6, 128.1, 127.0, 126.6, 123.8, 121.2, 121.0, 113.8, 37.0 ppm. HRMS: calcd. for $C_{19}H_{15}NO_3$ [M + Na] 328.0952, found 328.0942.

Phenyl 3-Formyl-6-phenylpyridine-1(6*H*)-carboxylate: Table 2, Entry 4. Isolated yield: 26 mg, 17%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 9.39 [s, 1 H, C(O)*H*], 7.82 [s, 1 H, NC*H*=CH(CHO)], 7.43–7.20 (m, 8 H), 7.12–6.89 (m, 2 H), 6.58 [d, J = 12 Hz, 1 H, (CHO)CC*H*], 6.00 (d, J = 8 Hz, 1 H, C*H*Ph), 5.82–5.75 [m, 1 H, (Ph)-CHC*H*=CH] ppm. ^{13}C NMR (67.9 MHz, $CDCl_3$): δ = 187.1, 150.5, 142.0, 129.7, 129.5, 128.9, 128.6, 128.1, 127.0, 126.4, 123.8, 121.1, 119.5, 115.7, 59.6 ppm. HRMS: calcd. for $C_{19}H_{15}NO_3$ [M + Na] 328.0952, found 328.0942.

Phenyl 3-Acetyl-4-(thiophen-2-yl)pyridine-1(4*H*)-carboxylate: Table 2, Entry 5. Isolated yield: 39 mg, 25%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.30 (s, 3 H, CH_3) 3.93 [s, 1 H, (COMe)CC*H*CS] 4.92 [dd, J = 24.00, 4.00 Hz, 1 H, (CS)CHC*H*] 5.29–5.50 (m, 1 H, NC*H*) 6.78–6.83 (m, 1 H) 6.84–6.93 (m, 2 H) 7.06–7.33 (m, 4 H) 7.38–7.46 (m, 1 H) 8.04 [s, 1 H, NC*H*=C(COMe)] ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 25.54, 32.21, 54.66, 112.28, 112.98, 115.54, 120.67, 121.49, 124.61, 125.04, 127.06, 129.93, 132.92, 148.52, 150.51, 156.06, 196.37 ppm. HRMS: calcd. for $C_{18}H_{15}NO_3S$ [M + Na] 348.0659, found 348.0664.

Phenyl 5-Acetyl-2-(thiophen-2-yl)pyridine-1(2*H*)-carboxylate: Table 2, Entry 5. Isolated yield: 30 mg, 19%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.33 (s, 3 H, CH_3) 5.86 [dd, J = 9.76, 5.66 Hz, 1 H, (CS)CHC*H*] 6.26 [br. s, 1 H, NC*H*C(CS)] 6.82 (dd, J = 9.76, 1.17 Hz, 1 H) 6.96 (dd, J = 4.98, 3.61 Hz, 1 H) 7.07–7.17 (m, 3 H) 7.25–7.31 (m, 2 H) 7.37–7.44 (m, 2 H) 7.86 [s, 1 H, NC*H*=C(COMe)] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.98, 50.16, 114.29, 118.33, 120.11, 120.37, 125.45, 125.63, 125.77, 125.90, 126.28, 128.64, 132.72, 141.20, 149.41, 193.03 ppm. HRMS: calcd. for $C_{18}H_{15}NO_3S$ [M + Na] 348.0659, found 348.0665.

Phenyl 3-Acetyl-2-(thiophen-2-yl)pyridine-1(2*H*)-carboxylate: Table 2, Entry 5. Isolated yield: 28 mg, 18%. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.39 (s, 3 H, CH_3) 5.63–5.76 (m, 1 H, N-CH) 6.88–6.96 [m, 1 H, C*H*=C(COMe)] 6.98 [s, 1 H, NC*H*(CS)] 7.08 (d, J = 12.20 Hz, 1 H) 7.13–7.24 (m, 4 H) 7.24–7.31 (m, 2 H) 7.41 (d, J = 6.83 Hz, 2 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 25.37, 49.53, 105.70, 121.74, 125.59, 126.46, 126.82, 129.76, 130.71, 131.19, 131.80, 132.73, 142.61, 150.76, 152.40, 195.20 ppm. HRMS: calcd. for $C_{18}H_{15}NO_3S$ [M + Na] 348.0659, found 348.0687.

Phenyl 5-Bromo-3-formyl-2-phenylpyridine-1(2*H*)-carboxylate: Table 2, Entry 6. Isolated yield: 59 mg, 31%. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.40 [s, 1 H, C(O)*H*], 7.91 (s, 1 H, NC*H*=CBr), 7.50–7.21 (m, 10 H), 7.09–6.98 (m, 1 H), 4.69 [s, 1 H, (Br)CC*H*C(COH)] ppm. ^{13}C NMR (67.9 MHz, $CDCl_3$): δ = 188.6, 150.4, 140.9, 137.4, 129.8, 128.6, 128.5, 127.7, 126.8, 123.5, 122.1, 121.0, 119.3, 11.7, 45.6 ppm. HRMS: calcd. for $C_{19}H_{14}BrNO_3$ [M + Na] 406.0057, found 406.0048.

Ethyl 1-Cyclohexyl-5-formylisoquinoline-2(1*H*)-carboxylate: Table 2, Entry 7. Isolated yield: 99 mg, 63%. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.89–1.16 (m, 5 H) 1.34 (d, J = 7.50 Hz), 1.42–1.52 [m, 1 H, C*H*(CHN)] 1.57–1.79 (m, 5 H) 4.27 (q, J = 7.07 Hz, 2 H, CH_2CH$_3$) 4.92–5.16 (m, 1 H, NC*H*) 7.02–7.15 (m, 2 H) 7.18–7.28 (m, 1 H) 7.29–7.36 (m, 1 H) 7.66–7.74 [m, 1 H, C*H*C(COH)] 10.22 [s, 1 H, C(O)*H*] ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 14.74, 26.16, 29.42, 41.44, 60.31, 61.19, 62.80, 105.37, 126.17, 128.85, 129.24, 129.62, 131.84, 132.64, 132.99, 153.43, 193.08 ppm. HRMS: calcd. for $C_{19}H_{23}NO_3$ [M + H] 314.1756, found 314.1750.

Ethyl 1-(4-Fluorophenyl)-5-formylisoquinoline-2(1*H*)-carboxylate: Table 2, Entry 8. Isolated yield: 136 mg, 84%. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.33 (t, J = 7.07 Hz, 3 H, CH$_2$CH_3), 4.18–4.38 (m, 2 H, CH_2CH$_3$), 6.55 (br. s, 1 H, NC*H*Ar), 6.94 (t, J = 8.66 Hz, 2 H), 7.01–7.14 (m, 2 H), 7.21–7.38 (m, 4 H), 7.72 [d, J = 6.83 Hz, 1 H, C*H*C(COH)], 10.24 [s, 1 H, C(O)*H*] ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 14.69, 57.34, 63.15, 104.06, 115.52, 115.69, 127.30, 128.46, 129.26, 129.59, 131.39, 132.93, 137.43, 153.24, 161.62, 163.58, 192.87 ppm. HRMS: calcd. for $C_{19}H_{16}FNO_3$ [M + H] 326.1178, found 326.1186.

Ethyl 2-Phenyl-1,3-benzothiazole-3(2*H*)-carboxylate: Table 3, Entry 1. Isolated yield: 130 mg, 91%. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.83 (d, J = 15 Hz, 1 H), 7.35–7.22 (m, 5 H), 7.18–7.10 (m, 2 H), 7.01 (t, J = 9 Hz, 1 H), 6.97 (s, 1 H, C*H*Ph), 4.23 (q, J = 7 Hz, 2 H, CH_2CH$_3$), 1.23 (t, J = 7 Hz, 3 H, CH$_2$CH_3) ppm. ^{13}C NMR (68.0 MHz, $CDCl_3$): δ = 153.0, 142.6, 138.4, 128.8, 128.5, 127.4, 125.6, 125.4, 124.5, 122.4, 117.4, 66.9, 62.6, 14.4 ppm. HRMS: calcd. for $C_{16}H_{15}NO_2S$ [M + Na] 308.0723, found 308.0714.

2,2,2-Trichloroethyl 2-Vinyl-1,3-benzoxazole-3(2*H*)-carboxylate: Table 3, Entry 2. Isolated yield: 98 mg, 61%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.63–7.47 (m, 1 H), 7.02–6.81 (m, 3 H), 6.53 (d, J = 8 Hz, 1 H, C*H*CH=CH$_2$), 6.11–5.92 (m, 1 H, C*H*=CH$_2$), 5.62 (d, J = 14 Hz, 1 H), 5.43 [d, J = 8 Hz, 1 H, (H)C*H*=CH], 4.88–4.82 (br. s, 2 H, Cl$_3$CCH_2) ppm. ^{13}C NMR (67.9 MHz, $CDCl_3$): δ = 150.3, 149.8, 132.0, 128.2, 124.5, 121.6, 120.1, 114.8, 109.2, 94.9, 93.3, 75.4 ppm. HRMS: calcd. for $C_{12}H_{10}Cl_3NO_3$ [M + H] 321.9825, found 321.9799.

Ethyl 5-Bromo-2-(4-fluorophenyl)benzo[*d*]thiazole-3(2*H*)-carboxylate: Table 3, Entry 3. Isolated yield: 117 mg, 61%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.18–1.27 (m, 3 H, CH$_2$CH_3), 4.17–4.26 (m, 2 H, CH_2CH$_3$), 6.68 (s, 1 H, C*H*Ar), 6.92–7.01 (m, 2 H), 7.18–7.29 (m, 4 H), 7.66 (br. s, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.51, 62.96, 66.65, 115.81, 116.02, 116.94, 118.43, 124.98, 127.38, 127.46, 128.64, 137.86, 152.63, 161.68, 164.15 ppm. HRMS: calcd. for $C_{16}H_{13}BrFNO_2S$ [M + H] 381.9898, found 381.9907.

Isobutyl 2-(2-Methoxyphenyl)benzo[*d*]oxazole-3(2*H*)-carboxylate: Table 3, Entry 4. Isolated yield: 83 mg, 51%. ^{1}H NMR (400 MHz, CD_3OD): δ = 0.58–0.87 [m, 6 H, (CH_3)$_2$CH(CH$_2$)] 0.89–1.07 [m, 2 H, CH_2CH(Me)$_2$] 3.80 (s, 3 H, OCH_3) 3.87 (br. s, 1 H, C*H*Ar) 6.68–6.73 (m, 1 H) 6.85–6.93 (m, 3 H) 7.02 (d, J = 8.20 Hz, 1 H) 7.15–7.21 (m, 1 H) 7.24–7.29 (m, 1 H) 7.30–7.37 (m, 1 H) 7.54 (br. s, 1 H) ppm. ^{13}C NMR (101 MHz, CD_3OD): δ = 17.87, 27.86, 54.95, 71.97, 90.11, 106.53, 108.34, 111.27, 113.40, 120.42, 120.86, 123.57, 124.37, 124.99, 126.64, 130.96, 150.48, 157.75 ppm. HRMS: calcd. for $C_{19}H_{21}NO_4$ [M + H] 328.1543, found 328.1545.

Ethyl 1-Ethylphthalazine-2(1*H*)-carboxylate: Table 3, Entry 5. Isolated yield: 75 mg, 65%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.67–7.61 (br. s, 1 H, C*H*=N), 7.44–7.21 (m, 3 H), 7.10 (d, J = 14 Hz, 1 H), 5.37 (t, J = 6 Hz, 1 H, C*H*Et), 4.35 (q, J = 7 Hz, 2 H, OCH_2CH$_3$), 1.75–1.60 (m, 2 H, CHCH_2CH$_3$), 1.36 (t, J = 6 Hz, 3 H, OCH$_2$CH_3), 0.79 (t, J = 7 Hz, 3 H, CHCH$_2$CH_3) ppm. ^{13}C NMR (67.9 MHz, $CDCl_3$): δ = 154.3, 142.9, 133.7, 131.3, 128.1, 126.4, 125.7, 124.0, 62.8, 54.9, 27.9, 14.7, 9.6 ppm. HRMS: calcd. for $C_{13}H_{16}N_2O_2$ [M + H] 233.1311, found 233.1281.

1-Chloroethyl 2-Isopropyl-1,3-benzothiazole-3(2*H*)-carboxylate: Table 3, Entry 6. Isolated yield: 56 mg, 39%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.84–7.45 (m, 1 H), 7.17–6.97 (m, 3 H), 6.68 [q, J = 9 Hz, 1 H, C(Cl)*H*CH$_3$], 5.67 [d, J = 4 Hz, 1 H, C*H*CH(Me)$_2$], 2.27–2.12 [m, 1 H, (Me)$_2$C*H*CH], 1.92–1.84 [m, 3 H, (Cl)CHCH_3], 0.98–0.86 [m, 6 H, CH(CH_3)$_2$] ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 150.3, 138.4, 129.9, 125.2, 122.2, 118.0, 83.2, 72.9, 35.2, 25.6, 18.4, 16.2 ppm. HRMS: calcd. for $C_{13}H_{16}ClNO_2S$ [M + H] 286.0689, found 286.0660.

Ethyl 5-Bromo-2-(naphthalen-1-yl)benzo[*d*]thiazole-3(2*H*)-carboxylate: Table 3, Entry 7. Isolated yield: 174 mg, 84%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.15–1.28 (m, 3 H, CH$_2$CH_3) 4.11–4.29 (m, 2 H, CH_2CH$_3$) 6.88 (s, 1 H, C*H*Ar) 7.20–7.28 (m, 2 H) 7.37 (dd, J = 8.59, 1.95 Hz, 1 H) 7.43–7.49 (m, 2 H) 7.66 (s, 1 H) 7.73–7.82 (m, 4 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.51, 62.89, 67.54, 116.89, 118.41, 123.26, 124.18, 125.00, 126.70, 126.75, 127.91, 128.41, 128.60, 129.38, 131.08, 133.08, 133.53, 137.10, 138.90, 152.79 ppm. HRMS: calcd. for $C_{20}H_{16}BrNO_2S$ [M + H] 414.0150, found 414.0157.

1-Chloroethyl 1-Phenylphthalazine-2(1*H*)-carboxylate: Table 3, Entry 8. Isolated yield: 60 mg, 38%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.79–7.86 (m, 1 H), 7.44 (t, J = 7 Hz, 1 H), 7.40–7.31 (m, 2 H), 7.28–7.20 (m, 6 H), 6.67 [q, J = 4 Hz, 1 H, C(Cl)*H*CH$_3$], 6.60 (s, 1 H, C*H*Ph), 1.92–1.85 [m, 3 H, (Cl)CHCH_3] ppm. ^{13}C NMR (67.9 MHz, $CDCl_3$): δ = 152.0, 143.6, 143.4, 142.8, 133.1, 132.1, 128.7, 128.6, 128.0, 127.0, 126.6, 126.3, 83.6, 57.1, 25.4 ppm. HRMS: calcd. for $C_{17}H_{15}ClN_2O_2$ [M + Na] 337.0722, found 337.0712.

Ethyl 6-Acetyl-2-(thiophen-2-yl)benzo[*d*]thiazole-3(2*H*)-carboxylate: Table 3, Entry 9. Isolated yield: 120 mg, 72%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.33 (t, J = 7.03 Hz, 3 H, CH$_2$CH_3) 2.54 [s, 3 H, C(O)-CH_3] 4.31 (q, J = 7.29 Hz, 2 H, CH_2CH$_3$) 6.85–6.90 (m, 1 H) 7.00 (s, 1 H, C*H*Ar) 7.07 (d, J = 3.51 Hz, 1 H) 7.18 (d, J = 5.08 Hz, 1 H) 7.68–7.76 (m, 1 H) 7.80 (d, J = 1.95 Hz, 2 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 13.33, 25.45, 61.96, 115.73, 121.22, 124.40, 124.89, 125.60, 125.98, 126.19, 128.13, 132.60, 139.60, 143.82, 151.08, 195.21 ppm. HRMS: calcd. for $C_{16}H_{15}NO_3S_2$ [M + H] 334.0578, found 334.0566.

Phenyl 1-Vinyl-1*H*-phthalazine-2-carboxylate: Table 3, Entry 10. Isolated yield: 118 mg, 85%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.01 [d, 1 H, (H)C*H*=CH] 5.12–5.19 [m, 1 H, (H)C*H*=CH] 5.90 (ddd, J = 16.98, 10.25, 5.37 Hz, 1 H, C*H*=CH$_2$) 6.07 (d, J = 5.27 Hz, 1 H, C*H*CH=CH$_2$) 7.17–7.26 (m, 4 H) 7.29–7.34 (m, 1 H) 7.34–7.43 (m, 3 H) 7.44–7.52 (m, 1 H) 7.74 (s, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 56.10, 117.00, 121.99, 123.81, 126.02, 126.38, 126.86, 128.86, 129.57, 132.17, 132.19, 134.80, 143.53, 151.41, 152.99 ppm. HRMS: calcd. for $C_{17}H_{14}N_2O_2$ [M + H] 279.1128, found 279.1137.

Phenyl 6-Acetyl-2-(2-phenylethynyl)benzo[*d*]thiazole-3(2*H*)-carboxylate: Table 3, Entry 11. Isolated yield: 128 mg, 64%. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.59 [s, 3 H, C(O)CH_3] 6.82 [s, 1 H, C*H*C(CPh)] 7.24–7.37 (m, 6 H) 7.41–7.49 (m, 4 H) 7.75–7.82 (m, 1 H) 7.87 (s, 1 H) 7.99 (br. s, 1 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 26.74, 55.74, 85.71, 86.68, 115.59, 117.09, 121.69, 121.81, 122.65, 126.66, 127.61, 128.60, 129.42, 129.89, 132.15, 132.30, 134.20, 140.62, 150.58, 196.40 ppm. HRMS: calcd. for $C_{24}H_{17}NO_3S$ [M + H] 400.0999, found 400.1001.

2-Phenylbenzo[*d*]thiazole: Table 4, Entry 1. Isolated yield: 37 mg, 87%. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.13–8.07 (m, 3 H), 7.91

(d, J = 9 Hz, 1 H), 7.54–7.45 (m, 4 H), 7.38 (t, J = 6 Hz, 1 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 168.3, 154.4, 135.3, 133.9, 131.2, 129.2, 127.8, 126.5, 125.4, 123.5, 121.8 ppm. HRMS: calcd. for $C_{13}H_9NS$ [M + H] 212.0529, found 212.0528.

5-Bromo-2-(4-fluorophenyl)benzo[*d*]thiazole: Table 4, Entry 2. Isolated yield: 39 mg, 63%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.18 (t, J = 8.59 Hz, 2 H) 7.58 (dd, J = 8.59, 1.95 Hz, 1 H) 7.89 (d, J = 8.98 Hz, 1 H) 7.99–8.10 (m, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 116.39, 116.61, 119.01, 124.37, 124.46, 129.75, 130.16, 136.86, 153.15, 163.58, 166.09 ppm. HRMS: calcd. for $C_{13}H_7BrFNS$ [M + H] 307.9535, found 307.9539.

1-[2-(Thiophen-2-yl)benzo[*d*]thiazol-6-yl]ethanone: Table 4, Entry 3. Isolated yield: 34 mg, 65%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.67 [s, 3 H, C(O)CH_3] 7.15 (dd, J = 5.08, 3.90 Hz, 1 H) 7.55 (dd, J = 4.98, 1.07 Hz, 1 H) 7.70 (dd, J = 3.71, 1.17 Hz, 1 H) 8.04 (dd, J = 2.54, 1.17 Hz, 2 H) 8.47 (dd, J = 1.56, 0.78 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 27.03, 122.56, 122.88, 126.98, 128.53, 129.82, 130.64, 134.15, 135.23, 137.08, 156.88, 165.20, 197.12 ppm. HRMS: calcd. for $C_{13}H_9NOS_2$ [M + H] 260.0200, found 260.0198.

5-Bromo-2-(naphthalen-1-yl)benzo[*d*]thiazole: Table 4, Entry 4. Isolated yield: 37 mg, 54%. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.57–7.61 (m, 2 H) 7.63 (dd, J = 8.78, 1.46 Hz, 1 H) 7.88–7.93 (m, 1 H) 7.96–8.02 (m, 3 H) 8.09 (d, J = 1.95 Hz, 1 H) 8.21 (dd, J = 8.66, 1.59 Hz, 1 H) 8.57 [s, 1 H, (Br)CCH] ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 119.05, 124.44, 124.52, 124.54, 127.26, 127.92, 128.00, 128.15, 129.10, 129.19, 130.17, 130.80, 133.40, 134.98, 137.00, 153.35, 168.87 ppm. HRMS: calcd. for $C_{17}H_{10}BrNS$ [M + H] 339.9787, found 339.9790.

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra.

Acknowledgments

The authors would like to thank the National Sciences and Engineering Research Council of Canada and the Canadian Foundation for Innovation for financial support. R. E. B. and D. A. B. would like to thank McGill University for providing graduate student fellowships, and R. E. B. thanks Pfizer Global Research for the use of their facilities and resources towards the completion of this manuscript.

[1] For reviews on the chemistry of dihydropyridines including their synthesis by nucleophilic additions to pyridinium salts, see: a) R. Lavilla, *J. Chem. Soc. Perkin Trans. 1* **2002**, 1141–1156; b) A. I. Meyers, D. Stout, *Chem. Rev.* **1982**, *82*, 223–243; c) U. Eisner, J. Kuthan, *Chem. Rev.* **1972**, *72*, 1–42.

[2] a) For a review on the regioselective synthesis of pyridines by nucleophilic additions to pyridinium salts, see: D. L. Comins, S. O'Connor, *Adv. Heterocycl. Chem.* **1988**, *44*, 199; for some recent examples, see: b) R. E. Beveridge, B. A. Arndtsen, *Synthesis* **2010**, 1000–1008; c) N. A. O. Williams, C. Masdeu, J. L. Diaz, R. Lavilla, *Org. Lett.* **2006**, *8*, 5789; d) M.-L. Bennasar, E. Zulaica, T. Roca, Y. Alonso, M. Monerris, *Tetrahedron Lett.* **2003**, *44*, 4711; e) P. A. Krapcho, D. J. Waterhouse, A. Hammach, R. D. Domenico, E. Menta, A. Oliva, S. Spinelli, *Synth. Commun.* **1997**, *27*, 781; f) A. Lemire, M. Grenon, M. Pourashraf, A. B. Charett, *Org. Lett.* **2004**, *6*, 3517; g) C. Chen, B. Wang, B. Munoz, *Synlett* **2003**, 2404.

[3] For selected examples, see: a) D. L. Comins, A. H. Abdullah, *J. Org. Chem.* **1982**, *47*, 4315; b) R. Yamaguchi, Y. Matsuki, E.-I. Hata, M. Kawanisi, *Bull. Chem. Soc. Jpn.* **1987**, *60*, 215; c) B. Guilloteau-Bertin, D. Compere, L. Gil, C. Marazano, B. C. Das, *Eur. J. Org. Chem.* **2000**, 1391; d) D. Barbier, C. Marazano, C. Riche, B. C. Das, P. Poitier, *J. Org. Chem.* **1998**, *63*, 1767; e) A. Ohno, S. Oda, N. Yamazaki, *Tetrahedron Lett.* **2001**, *42*, 399; f) J. Pabel, G. Hofman, K. T. Wanner, *Bioorg. Med. Chem. Lett.* **2000**, *10*, 1377.

[4] a) M. A. Fernandez-Ibanez, B. Macia, M. G. Pizzuti, A. J. Minnaard, B. J. Feringa, *Angew. Chem. Int. Ed.* **2009**, *48*, 1–4; b) A. P. Krapcho, D. J. Waterhouse, *Heterocycles* **1999**, *51*, 737; c) for mixed zinc/copper examples, see: E. Le Gall, C. Gosmini, J.-Y. Nedelec, J. Perichon, *Tetrahedron* **2001**, *57*, 1923.

[5] a) R. Yamaguchi, M. Moriyasu, M. Yoshioka, M. Kawanisi, *J. Org. Chem.* **1985**, *50*, 287; b) R. Yamaguchi, M. Moriyasu, M. Kawanisi, *Tetrahedron Lett.* **1986**, *27*, 211; c) R. Yamaguchi, E.-I. Hata, K. Utimoto, *Tetrahedron Lett.* **1988**, *29*, 1785; d) R. Yamaguchi, M. Moriyasu, M. Yoshioka, M. Kawinisi, *J. Org. Chem.* **1988**, *53*, 3507.

[6] For some organocuprate examples, see: a) M. L. Bennasar, C. Juan, J. Bosch, *Tetrahedron Lett.* **1998**, *39*, 9275; b) M. L. Bennasar, C. Juan, J. Bosch, *Tetrahedron Lett.* **2001**, *42*, 585; c) K.-S. Shih, C. W. Liu, Y.-J. Hsieh, S.-F. Chen, H. Ku, L. T. Liu, Y.-C. Lin, H.-L. Huang, C.-L. Wang, *Heterocycles* **1999**, *51*, 2439.

[7] a) For an organotitanium example, see: L.-L. Gundersen, F. Rise, K. Undheim, *Tetrahedron* **1992**, *48*, 5647; b) for an organocadmium example, see ref.[3a]

[8] a) A. I. Meyers, T. Oppenlaender, *J. Am. Chem. Soc.* **1986**, *108*, 1989; b) V. A. Burgess, S. G. Davies, R. T. Skerlj, *Tetrahedron: Asymmetry* **1991**, *2*, 299; c) S. Obika, T. Nishiyama, S. Tatematsu, K. Miyashita, T. Imanishi, *Tetrahedron* **1997**, *53*, 3073.

[9] a) For a review on using *N*-acylpyridinium salts for the synthesis of alkaloids, see: D. L. Comins, S. Joseph, *Adv. Nitrogen Heterocycl.* **1996**, *2*, 251; for selected examples, see: b) R. W. Bates, S. E. Kanicha, *Tetrahedron* **2002**, *58*, 5957; c) M. Buffat, *Tetrahedron* **2004**, *60*, 1701.

[10] For reviews of the synthetic utility of asymmetric additions to 3-TIPS-4-methoxypyridines towards natural product synthesis, see: a) S. Joseph, D. L. Comins, *Curr. Opin. Drug Disc.* **2002**, *5*, 870; b) D. L. Comins, *J. Heterocycl. Chem.* **1999**, *36*, 1491.

[11] For examples of natural product or bio-active compound synthesis from organometallic additions to pyridinium salts, see: a) A. Lemire, A. B. Charette, *Org. Lett.* **2005**, *7*, 2747; b) T. Focken, A. B. Charette, *Org. Lett.* **2006**, *8*, 2985; c) J. T. Kuethe, D. L. Comins, *J. Org. Chem.* **2004**, *69*, 5219; d) M.-L. Bennasar, E. Zulaica, Y. Alsonso, J. Bosch, *Tetrahedron: Asymmetry* **2003**, *14*, 469.

[12] a) F. Babudri, S. Florio, G. Inguscio, *Synthesis* **1985**, 522; b) F. Babudri, G. Bartolli, S. Florio, G. Ingrosso, *Tetrahedron Lett.* **1984**, *25*, 2047.

[13] For Organotin functionalization of these substrates, see: a) T. Itoh, H. Hasegawa, K. Nagata, A. Ohsawa, *J. Org. Chem.* **1994**, *59*, 1319; b) T. Itoh, H. Hiroshi, O. Kazuhiro, O. Mamiko, A. Ohsawa, *Tetrahedron Lett.* **1992**, *33*, 5399; c) J.-Y. Zhou, Z.-G. Chen, S.-H. Wu, *Synlett* **1995**, 1117; d) T. Itoh, H. Hasegawa, K. Nagata, M. Okada, A. Ohsama, *Tetrahedron* **1994**, *50*, 13089–13100.

[14] For selected examples, see: a) I. Perez, J. P. Sestelo, L. A. Sarandeses, *J. Am. Chem. Soc.* **2001**, *123*, 4155 and references cited therein; b) D. Rodriguez, J. P. Sestelo, L. A. Sarandeses, *J. Org. Chem.* **2004**, *69*, 8136; c) R. Riveiros, D. Rodríguez, J. P. Sestelo, L. A. Sarandeses, *Org. Lett.* **2006**, *8*, 1403; d) C.-J. Li, T.-H. Chan, *Tetrahedron* **1999**, *55*, 11149; e) K. K. Chauhan, C. G. Frost, *J. Chem. Soc. Perkin Trans. 1* **2000**, 3015; f) B. C. Ranu, *Eur. J. Org. Chem.* **2000**, 2347; g) B. W. Fausett, L. S. Liebeskind, *J. Org. Chem.* **2005**, *70*, 4851; h) K. Takami, H. Yorimitsu, H. Shinokubo, S. Matsubara, K. Oshima, *Org. Lett.* **2001**, *3*, 1997; i) S. W. Lee, K. Lee, D. Seomoon, S. Kim, H. Kim, H. Kim, E. Shim, M. Lee, S. Lee, M. Kim, P. H. Lee, *J. Org. Chem.* **2004**, *69*, 4852; j) P. H. Lee, S. W. Lee, D. Seomoon, *Org. Lett.* **2003**, *5*, 4963.

[15] The indium-mediated regioselective allylation of *N*-acylpyridinium salts has been reported previously: T.-P. Loh, P.-L. Lye, R.-B. Wang, K.-Y. Sim, *Tetrahedron Lett.* **2000**, *41*, 7779.
[16] D. A. Black, B. A. Arndtsen, *Org. Lett.* **2006**, *8*, 1991.
[17] a) D. A. Black, R. E. Beveridge, B. A. Arndtsen, *J. Org. Chem.* **2008**, *73*, 1906; b) D. A. Black, B. A. Arndtsen, *Org. Lett.* **2004**, *6*, 1107.
[18] Quinoline can also participate in this reaction, but leads to a mixture of 1,2- and 1,4-addition products.
[19] Results not shown. Oxazole and thiazole in this copper-catalyzed organoindium addition reaction did not generate product as observed by LC-MS or NMR analysis of the crude reaction mixtures.
[20] I. Pérez, J. P. Sestelo, L. A. Sarandeses, *J. Am. Chem. Soc.* **2001**, *123*, 4155 and references cited therein.
[21] References for known compounds are as follows: a) compound **1** (Table 2, Entry 1): (i) D. L. Comins, M. O. Killpatrick, *Heterocycles* **1990**, *31*, 2025; (ii) K. Akiba, Y. Iseki, M. Wada, *Bull. Chem. Soc. Jpn.* **1984**, *57*, 1994; b) phenyl 3-formyl-4-phenylpyridine-1(4*H*)-carboxylate (Table 2, Entry 4): D. L. Comins, J. J. Herrick, *Heterocycles* **1987**, *26*, 2159; c) 2-phenylbenzo[*d*]-thiazole (Table 4, Entry 1): Q. Ding, X.-G. Huang, J. Wu, *J. Comb. Chem.* **2009**, *11*, 1047.

Received: February 19, 2010
Published Online: May 14, 2010

