A General Approach to the Coupling of Organoindium Reagents with Imines via Copper Catalysis

Daniel A. Black and Bruce A. Arndtsen*

801 Sherbrooke St. W., Department of Chemistry, McGill University
Montreal, Quebec H3A 2K6 Canada

Supporting Information

	Page
I General Procedures	S2
II Synthesis and Spectroscopic Data	S2-S6
III References	S6
IV ¹ H NMR Spectra of 1 and 2	S7-S32

General Procedures

Unless otherwise noted, all manipulations were performed under an inert atmosphere 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 CaH₂ under nitrogen. THF was distilled over sodium benzophenone ketyl. Deuterated acetonitrile was dried as its protonated analogue, but was transferred under vacuum from the drying agent, and stored over 4 Å molecular sieves. Deuterated DMSO and chloroform were dried over 3 Å molecular sieves. Imines were prepared as per standard literature procedures.¹ Tetraorganoindium reagents were prepared by the slow addition (10 minutes) of the appropriate Grignard reagent to a solution of InCl₃ (0.25 equiv) in 1 mL of THF at -78°C, allowed to stir for 30 min. at -78°C, followed by warming to room temperature.² ¹H and ¹³C NMR were recorded on JEOL 270, Varian Mercury 300 MHz, and Mercury 400 MHz spectrometers. Mass spectra were obtained from the McGill University mass spectral facilities.

Typical Procedure for Catalytic Synthesis of α -Substituted Amides

(4-CH₃C₆H₄)HC=N(CH₂C₆H₅) (105 mg, 0.50 mmol) and p-anisoyl chloride (111 mg, 0.65 mmol) were mixed in 3 mL of acetonitrile. This was added to a solution of CuCl (4.4 mg, 0.05 mmol) in 2 mL of dry acetonitrile. The reaction mixture was transferred to a 25 mL reaction bomb. The in situ generated organoindium reagent (Ph)₄InMgBr (0.0166 mmol) in 1 mL of THF was added into the reaction mixture, which was then heated at 45 °C for 16 hours. The reaction mixture was then concentrated in vacuo and redissolved in 50 mL of diethyl ether. The organic layer was washed with 50 mL of sat. NaHCO₃ (aq), and this was extracted with 2 x 50 mL of diethyl ether. The organic layers were combined and dried over anhydrous MgSO₄. The drying agent was then filtered away, the solvent removed in vacuo, and the residual crude product was purified by column chromatography using ethyl acetate / hexanes as eluent. All compounds characterized by ¹H and ¹³C NMR, and HRMS. Compounds 1c, 1f, 1k, and 1l, and 2l are previously reported compounds.³

Spectroscopic Data

N-Benzyl-4-methoxy-N-(phenyl-p-tolyl-methyl)-benzamide (1a) Isolated Yield: 95 % with triorganoindium, 96 % with tetraorganoindate. ¹H NMR (300 MHz, 55 °C, CDCl₃): δ 7.40 (m, 2H), 7.33-7.14 (m, 6H), 7.14-6.98 (m, 6H), 6.94-6.76 (m, 4H), 6.53 (s, 1H), 4.75 (s, 2H), 3.80 (s, 3H), 2.32 (s, 3H). ¹³C NMR (75.5 MHz, 55 °C, CDCl₃): δ 173.2, 160.8, 139.9, 138.5, 137.5, 136.6, 129.5, 129.3, 129.1, 128.6, 128.6, 127.9, 127.8, 127.7, 127.3, 126.4, 114.0, 66.2, 55.6, 49.0, 21.3. HRMS for C₂₉H₂₇NO₂, calculated: 421.2042, found: 421.2029.

(1-Benzo[1,3]dioxol-5-yl-propyl)-ethyl-carbamic acid benzyl ester (1b) Isolated Yield: 92 % with triorganoindium, 94 % with tetraorganoindate. ¹H NMR (300 MHz, 55 °C, CDCl₃): δ 7.42-7.23 (m, 5H), 6.84-6.71 (m, 3H), 5.93 (s, 2H), 5.26-5.09 (m, 3H), 3.10 (q, *J* = 6.9 Hz, 2H), 1.90 (m, 2H), 1.02-0.85 (m, 6H). ¹³C NMR (68.0 MHz, 55 °C, CDCl₃): δ 156.5, 147.8, 146.8, 137.2, 134.7, 128.4, 127.8, 127.8, 121.0, 108.5, 107.9, 100.9, 67.0, 60.2, 38.0, 24.3, 14.8, 11.1. HRMS for C₂₀H₂₃NO₄Na⁺, calculated: 364.1525, found: 364.1519.

Benzyl-(1-p-tolyl-allyl)-carbamic acid benzyl ester (1c) Isolated Yield: 89 % with triorganoindium, 91 % with tetraorganoindate. ¹H NMR (270 MHz, 90 °C, d⁶-DMSO): δ 7.40-7.04 (m, 14H), 6.15 (m, 1H), 5.76 (br, 1H), 5.23-5.05 (m, 4H), 4.59 (d, *J* = 9.2 Hz, 1H), 4.40 (d, *J* = 9.2 Hz, 1H), 2.27 (s, 3H). ¹³C NMR (68.0 MHz, 90 °C, d⁶-DMSO): δ 155.2, 138.3, 136.2, 136.0, 135.9, 135.5, 128.3, 127.6, 127.4, 127.1, 126.9, 126.8, 126.6, 126.0, 117.3, 66.0, 62.2, 48.3, 19.9. HRMS for C₂₅H₂₅NO₂, calculated: 371.1885, found: 371.1879. This compound is identical to compound **1e** from reference 3.

N-[(4-Bromo-phenyl)-(4-fluoro-phenyl)-methyl]-N-ethyl-4-iodo-benzamide (1d) Isolated Yield: 81 % with triorganoindium, 87 % with tetraorganoindate. ¹H NMR (300 MHz, 55 °C, CDCl₃): δ 7.80 (m, 2H), 7.57 (m, 2H), 7.24 (m, 2H), 7.16 (m, 6H), 6.38 (s, 1H), 3.46 (m, 2H), 0.73 (t, *J* = 6.9 Hz, 3H). ¹³C NMR (75.5 MHz, 55 °C, CDCl₃): δ 171.0, 164.2, 160.6, 138.4, 137.7, 136.4, 134.7, 134.7, 131.9, 130.5, 130.4, 130.1, 127.9, 122.0, 115.9, 115.5, 95.5, 63.9, 40.4, 14.0. HRMS for C₂₂H₁₈⁷⁹BrFINO, calculated: 536.9601, found: 536.9617. HRMS for C₂₂H₁₈⁸¹BrFINO, calculated: 538.9580, found: 538.9598.

Furan-2-carboxylic acid ethyl-{[1-(toluene-4-sulfonyl)-1H-indol-2-yl]-o-tolyl-methyl}-amide (1e)

Isolated Yield: 79 % with triorganoindium, 84 % with tetraorganoindate. ¹H NMR (270 MHz, 75 °C, CD₃CN): δ 8.02 (d, *J* = 8.4 Hz, 1H), 7.72 (m, 2H), 7.51 (s, 1H), 7.40-7.20 (m, 6H), 7.19-6.92 (m, 5H), 6.84 (s, 1H), 6.47 (s, 1H), 3.66 (m, 2H), 2.34 (s, 3H), 2.19 (s, 3H), 0.60 (t, *J* = 3.9 Hz, 3H). ¹³C NMR (68.0 MHz, 75 °C, CD₃CN): δ 160.6, 148.6, 146.1, 144.5, 137.7, 136.8, 136.2, 135.2, 131.0, 130.3, 130.2, 128.4, 128.4, 127.0, 126.3, 126.1, 125.6, 124.0, 123.6, 120.5, 115.5, 114.4, 111.4, 54.6, 41.0, 20.8, 18.5, 14.4. HRMS for C₃₀H₂₈N₂O₄S, calculated: 512.1770, found: 512.1783.

N-Benzyl-N-(1-tert-butyl-allyl)-acetamide (1f) Isolated Yield: 89 % with triorganoindium, 95 % with tetraorganoindate. ¹H NMR (270 MHz, 130 °C, d⁶-DMSO): δ 7.35-7.12 (m, 5H), 6.06 (m, 1H), 5.06 (m, 2H), 4.57 (s, 2H), 1.94 (s, 3H), 0.96 (s, 9H). ¹³C NMR (68.0 MHz, 130 °C, d⁶-DMSO): δ 170.2, 138.5, 133.8, 127.3, 125.7, 125.6, 118.2, 48.9, 35.0, 26.9, 24.8, 21.5. HRMS for C₁₆H₂₃NO, calculated: 245.1780, found: 245.1777. This compound is identical to compound **1c** from reference 3.

(4-Methoxy-phenyl)-(2-methyl-1-p-tolyl-butyl)-carbamic acid ethyl ester (1g) Isolated Yield: 77 % with triorganoindium, 75 % with tetraorganoindate. ¹H NMR (270 MHz, 75 °C, CD₃CN): δ 7.00 (m, 2H), 6.88 (m, 2H), 6.73 (m, 2H), 6.60 (m, 2H), 5.07 (br, 1H), 4.09 (m, 2H), 3.78 (s, 3H), 2.34 (s, 3H), 2.10 (m, 2H), 1.29 (m, 3H), 1.12 (m, 4H), 0.82 (t, *J* = 5.4 Hz, 1H), 0.73 (d, *J* = 6.9 Hz, 2H). ¹³C NMR (68.0 MHz, 75 °C, CD₃CN): δ 158.5, 158.5, 156.6, 156.6, 136.9, 136.8, 136.5, 136.4, 132.5, 132.2, 131.0, 130.9, 129.5, 129.4, 128.6, 128.5, 113.6, 113.5, 67.5, 67.2, 61.3, 61.3, 55.3, 35.3, 35.3, 26.5, 26.3, 21.0, 16.5, 16.5, 14.6, 11.3, 10.8. HRMS calculated for C₂₂H₂₉NO₃, calculated: 355.2147, found: 355.2151.

Allyl-[1-(4-methoxy-phenyl)-propyl]-carbamic acid phenyl ester (1h) Isolated Yield: 84% with triorganoindium, 84% with tetraorganoindate. ¹H NMR (270 MHz, 75 °C, CD₃CN): δ 7.44-7.29 (m, 4H), 7.22-7.11 (m, 3H), 6.90 (d, *J* = 6.9 Hz, 2H), 6.71 (m, 1H), 5.27 (m, 1H), 5.04 (m, 2H), 3.83 (s, 3H), 3.70 (br, 1H), 2.06 (t, *J* = 6.7 Hz, 2H), 1.09 (br, 3H). ¹³C NMR (68.0 MHz, 75 °C, CD₃CN): δ 159.2, 155.1, 151.8, 135.1, 132.1, 131.9, 129.2, 125.0, 121.7, 116.5, 114.0, 60.9, 55.3, 46.5, 24.4, 11.3. HRMS calculated for C₂₀H₂₃NO₃, calculated: 325.1678, found: 325.1677.

N-Benzyl-N-[(2,6-dimethyl-phenyl)-p-tolyl-methyl]-4-methoxy-benzamide (1i) Isolated Yield: 84 % with triorganoindium, 94% with tetraorganoindate. ¹H NMR (270 MHz, 55 °C, CDCl₃): δ 7.36 (m, 2H), 7.13-6.90 (m, 8H), 6.88-6.62 (m, 7H), 5.00 (d, *J* = 10.9 Hz, 1H), 4.51 (d, *J* = 10.9 Hz, 1H), 3.75 (s, 3H), 2.33 (s, 3H), 2.01 (s, 6H). ¹³C NMR (68.0 MHz, 55 °C, CDCl₃): δ 177.0, 164.4, 142.5, 142.4, 142.2, 140.2, 140.1, 133.5, 133.4, 133.1, 132.4, 131.6, 131.5, 131.0, 130.9, 130.2, 117.4, 65.9, 59.1, 53.8, 25.7, 24.7. HRMS for C₃₁H₃₁NO₂, calculated: 449.2355, found: 449.2366.

N-Benzyl-4-methoxy-N-[(2-methoxy-phenyl)-p-tolyl-methyl]-benzamide (1j) Isolated Yield: 86 % with triorganoindium, 90% with tetraorganoindate. ¹H NMR (270 MHz, 55 °C, CDCl₃): δ 7.36 (m, 2H), 7.10 (m, 2H), 7.07-6.99 (m, 5H), 6.92-6.70 (m, 6H), 6.62 (s, 1H), 6.50 (m, 1H), 5.18 (d, *J* = 15.1 Hz, 1H), 4.30 (d, *J* = 15.1 Hz, 1H), 3.76 (s, 3H), 3.55 (s, 3H), 2.35 (s, 3H). ¹³C NMR (68.0 MHz, 55 °C, CDCl₃): δ 173.5, 160.5, 157.9, 138.6, 137.5, 136.6, 131.0, 130.6, 129.9, 129.2, 129.1, 128.3, 128.2, 127.7, 127.5, 125.9, 120.0, 113.4, 110.1, 60.9, 55.3, 54.8, 48.3, 21.0. HRMS for C₃₀H₂₉NO₃, calculated: 451.2147, found: 451.2152.

[Isobutyryl-(1-p-tolyl-allyl)-amino]-acetic acid methyl ester (1k) Isolated Yield: 74 %. ¹H NMR (270 MHz, 20 °C, CDCl₃): δ 7.20-7.09 (m, 4H), 6.45 (d, *J* = 7.2 Hz, 0.3H, minor isomer), 6.08 (m, 1H), 5.69 (d, *J* = 7.2 Hz, 0.7H, major isomer), 5.44-5.23 (m, 2H), 4.03-3.79 (m, 2H), 3.60 (s, 2.1H, major isomer), 3.50 (s, 0.9H, minor isomer), 2.92 (q, 0.7H, major isomer), 2.60 (q, 0.3H, minor isomer), 2.34-2.30 (m, 3H), 1.21 (m, 6H). ¹³C NMR (68.0 MHz, 20 °C, CDCl₃): for major and minor isomers, δ 178.0, 177.8, 170.0, 169.6, 137.8, 137.4, 135.7, 135.1, 134.8, 134.6, 129.3, 129.0, 128.6, 127.8, 118.6, 117.6, 62.4, 58.2, 52.0, 51.8, 45.9, 45.3, 31.2, 30.4, 21.0, 21.0, 19.8, 19.7, 19.5, 19.4. HRMS for C₁₇H₂₃NO₃, calculated: 289.1678, found: 289.1675. This compound is identical to compound **1b** from reference 3.

N-Ethyl-4-methyl-N-(3-phenyl-1-vinyl-allyl)-benzamide (1l) Isolated Yield: 73 % (optimal). ¹H NMR (270 MHz, 75 °C, CD₃CN): δ 7.43-7.08 (m, 9H), 6.42 (d, *J* = 6.9 Hz, 1H), 6.29 (dd, *J* = 0.7, 6.9 Hz, 1H), 6.04 (m, 1H), 5.22-5.00 (m, 3H), 3.58-3.21 (m, 2H), 2.27 (s, 3H), 1.07 (t, *J* = 6.9 Hz, 3H). ¹³C NMR (68.0 MHz, 75 °C, CD₃CN): δ 171.7, 139.6, 137.3, 137.0, 135.4, 132.7, 129.2, 128.9, 128.1, 126.7, 126.6, 115.5, 115.3, 61.8, 39.8, 20.6, 14.8. HRMS calculated for C₂₁H₂₃NO, calculated: 305.1780, found: 305.1775. This compound is identical to compound **2** from reference 3.

N-Ethyl-4-methyl-N-(3-phenyl-penta-1,4-dienvyl)-benzamide (2l) Isolated Yield: 81 % with triorganoindium, 88% with tetraorganoindate. ¹H NMR (270 MHz, 75 °C, CD₃CN): δ 7.42-7.23 (m, 9H), 6.52 (m, 1H), 6.10 (m, 1H), 5.90 (m, 1H), 5.04-4.89 (m, 2H), 3.91 (t, *J* = 6.9 Hz, 1H), 3.70 (q, *J* = 6.7 Hz, 2H), 2.47 (s, 3H), 1.26 (t, *J* = 4.9 Hz, 3H). ¹³C NMR (68.0 MHz, 75 °C, CD₃CN): δ 170.0, 143.8, 141.3, 141.3, 140.5, 133.8, 129.7, 129.1, 128.8, 128.1, 127.8, 126.6, 114.5, 114.0, 103.6, 50.3, 39.2, 20.6, 12.0. HRMS calculated for C₂₁H₂₃NO, calculated: 305.1780, found: 305.1776. This compound is identical to compound **3** from reference 3.

References

1. Layer, R. *Chem. Rev.* **1963**, 63, 489.
2. Runge, F.; Zimmermann, W.; Pfeiffer, H. I. *Z. Anorg. Allg. Chem.* **1951**, 267, 39.
3. Black, D.A.; Arndtsen, B. A. *J. Org. Chem.* **2005**, 70, 5133.

Compound **1a**, ^1H spectrum

Compound **1a**, ^{13}C spectrum

Compound **1b**, ^1H spectrum

Compound **1b**, ^{13}C spectrum

Compound **1c**, ^1H spectrum

Compound **1c**, ^{13}C spectrum

Compound **1d**, ^1H spectrum

Compound **1d**, ^{13}C spectrum

Compound **1e**, ^1H spectrum

Compound **1e**, ^{13}C spectrum

Compound **1f**, ^1H spectrum

Compound **1f**, ^{13}C spectrum

Compound **1g**, ^1H spectrum

Compound **1g**, ^{13}C spectrum

Compound **1h**, ^1H spectrum

Compound **1h**, ^{13}C spectrum

Compound **1i**, ^1H and ^{13}C spectrum

Compound **1i**, ^{13}C spectrum

Compound **1j**, ^1H spectrum

Compound **1j**, ^{13}C spectrum

Compound **1k**, ^1H spectrum

Compound **1k**, ^{13}C spectrum

Compound 11, ^1H spectrum

Compound **11**, ^{13}C spectrum

Compound **2l**, ^1H spectrum

Compound **2l**, ^{13}C spectrum