Supporting Information for

Ketone Synthesis under Neutral Conditions. Cu(I)

Diphenylphosphinate-Mediated, Palladium-

Catalyzed Coupling of Thiol Esters and

Organostannanes

*Rüdiger Wittenberg, Jiri Srogl, Masahiro Egi, and Lanny S. Liebeskind**

Emory University, Department of Chemistry, 1515 Pierce Drive, Atlanta, Georgia 30322.

General Experimental. ^1H and ^{13}C NMR spectra were recorded in deuteriochloroform (CDCl_3) with the solvent residual peak (CDCl_3 : ^1H = 7.27 ppm, ^{13}C = 77 ppm) as internal reference unless otherwise stated. Data are reported in the following order: chemical shifts are given (); multiplicities are indicated (br (broadend), s (singlet), d (doublet), t, (triplet), q (quartet), m (multiplet), app (apparent); coupling constants, J , are reported (Hz); integration is provided. Infrared peaks are reported (cm^{-1}) with the following relative intensities: s (strong), m (medium), w (weak), and br (broad). Analytical thin-layer chromatography (TLC) was performed on Merck silica gel glass plates with F-254 indicator. Visualization was accomplished by UV light, or by staining with solutions of $\text{K}_2\text{CO}_3/\text{KMnO}_4$ in water, phosphomolybdic acid in ethanol, or p -anisaldehyde in ethanol. Solvents for reactions and chromatography were reagent grade and used as received. Flash column chromatography was performed by the method of Still¹ with 32-63 μm silica gel 60 (Woelm). Rotary chromatography was performed with a ChromatotronTM from Harrison Research using 4 mm PF-254 silica gel rotors. Solvents used as reaction media were purchased in >99% purity and purged for several minutes with argon or nitrogen then dried and stored over 4Å molecular sieves (water content below 10 ppm

determined with a Fisher Coulomatic K-F titrator). All reactions requiring inert atmospheres were carried out under dry argon or dry nitrogen in oven-dried glassware. Bulb-to-bulb ("Kugelrohr") distillations were done on a Büchi GKR-50 Kugelrohr and boiling points (bp) correspond to uncorrected air bath temperatures. "Brine" refers to a saturated aqueous solution of NaCl. Unless otherwise specified, solutions of NH₄Cl, NaHCO₃ refer to aqueous solutions.

Starting Materials. The following compounds were prepared by literature methods: *p*-tolyltri-*n*-butylstannane,² dodecanethioic acid *S-p*-tolyl ester,³ *E*-cinnamothioic acid *S-p*-tolyl ester,⁴ 4-nitrothiobenzoic acid *S-p*-tolyl ester,⁵ *S*-lauroyl-4-mercaptotoluene,⁶ and 2-methyl-1-propenyl-tri-*n*-butylstannane.⁷ The preparation of 2-*S*-phenylcarbonylpyrazine, 1-*S-p*-tolylcarbonyladamantane and 2-acetoxythioacetic acid *S-p*-tolyl ester were described in previous paper.⁸ *E*-Cinnamoyl chloride, dodecanoyl chloride, *p*-nitrobenzoyl chloride, *p*-tolylmagnesium bromide, 2-tri-*n*-butylstannylthiophene, 2-tri-*n*-butylstannylfuran, tri-*n*-butylstannyl chloride, allyltri-*n*-butylstannane, isatoic anhydride, and tri-2-furylphosphine were purchased from Sigma-Aldrich; *p*-toluenethiol was purchased from Acros; 2-tri-*n*-butylstannylthiazole, 2-tri-*n*-butylstannylpyrimidine, 2-tri-*n*-butylstannylpyridine, 3-tri-*n*-butylstannylpyridine, 1-methyl-2-(tri-*n*-butylstannyl)-1*H*-pyrrole, 2-tri-*n*-butylstannylbenzofuran, and 4-tri-*n*-butylstannylpyridyl-3-carboxaldehyde were purchased from Frontier Scientific, Inc.

Synthesis of Copper(I) diphenylphosphinate (CuDPP).

Diphenylphosphinic acid (21.70 g, 0.100 mol) and Cu₂O (3.33g , 0.025 mol) were refluxed in degassed toluene (250 mL) using a Dean- Stark adaptor under an argon atmosphere for 20 hours (until the original red color of the suspension changed to a tan color). After cooling, the suspension was filtered with exclusion of air and the solid was washed with degassed toluene (100 mL), Et₂O (50 ml) and hexanes (100mL) and then dried under reduced pressure. A light tan product was obtained (11.54 g, 83%). IR (KBr, cm⁻¹): 1593 (m), 1490 (m), 1444 (s). Anal. Calcd for C₈H₇CuO₃: C, 44.76; H, 3.29; Found: C, 44.11; H, 3.36.

2-Methyl Thiobenzoic Acid *S-p*-Tolyl Ester. *o*-Toluoyl chloride (5.64 mL, 0.043 mol, 1.0 equiv) and *p*-thiocresol (5.37 g, 0.043 mol, 1.0 equiv) were dissolved in hexanes (50 mL) and the mixture

¹ Still, W. C.; Kahn, M. Mitra, A. *J. Org. Chem.* **1978**, 43, 2923-2925.

² Wardell, J. L.; Ahmed, S. *J. Organomet. Chem.* **1974**, 78, 395-404.

³ Liebeskind, L. S. Srogl, J. *J. Am. Chem. Soc.* **2000**, 122, 11260-11261.

⁴ Perumal, S.; Vasuki, G.; Vijayabaskar, V.; Selvaraj, S.; Boykin, D. W. *Magn. Reson. Chem.* **1998**, 36, 720-726.

⁵ Grillot, G. F.; Levin, P. M.; Green, R.; Bashford, R. I. *J. Am. Chem. Soc.* **1950**, 72, 1863.

⁶ Liebeskind, L. S.; Srogl, J. *J. Am. Chem. Soc.* **2000**, 122, 11260-11261.

⁷ Labadie, J. W.; Stille, J. K. *J. Am. Chem. Soc.* **1983**, 105, 6129-6137.

⁸ Liebeskind, L. S., Srogl, J. *J. Am. Chem. Soc.*, **2000**, 122, 11260-11261.

was cooled to 0 °C. Triethylamine (6.63 mL, 0.048 mol, 1.1 equiv) dissolved in hexanes (20 mL) was added dropwise over 10 min to the stirred reaction mixture. After stirring at room temperature for 21 h, the reaction mixture was diluted with hexanes (20 mL). The white precipitate was filtered and washed with a 1:1 mixture of hexanes and Et₂O (2 x 20 mL). The filtrate was evaporated under reduced pressure and the residue was recrystallized from hexanes yielding yellow crystals (3.60 g, 35%). M.p. 78–80 °C (hexanes); ¹H NMR (300 MHz, CDCl₃) 7.94 (d, *J* = 7.8 Hz, 1H), 7.46–7.37 (m, 3H), 7.34–7.24 (m, 4H), 2.49 (s, 3H), 2.41 (s, 3H); ¹³C NMR (75.5 MHz, CDCl₃) 192.6, 139.7, 137.4, 136.8, 134.8, 131.9, 131.7, 130.1, 128.6, 125.8, 124.6, 21.4, 20.7; IR (neat, cm⁻¹) 2926, 1695, 1494, 1208; Anal. Calcd for C₁₅H₁₄OS: C, 74.35; H, 5.82; S, 13.23. Found: C, 74.17; H, 5.98; S, 13.18.

3-Phenylthioacrylic acid S-*p*-tolyl ester. *p*-Thiocresol (2.12 g, 17 mmol) was dissolved in hexanes (40 mL) and cooled to 0 °C. *E*-Cinnamoyl chloride (3.40 g, 1.2 equiv. 20.4 mmol) dissolved in 50 mL hexanes was added followed by triethylamine (3.6 mL, 1.5 equiv., 25.5 mmol) in 50 mL hexanes. The mixture was warmed slowly to 25 °C and stirred for an additional 5 h 30 min. The reaction mixture was filtered over Celite™ and silica gel (eluting with hexanes then ether ~500 mL) and then the organics were evaporated to a remaining volume of ~100 mL. The concentrated solution was stored in a refrigerator overnight for crystallisation. Crystallisation afforded 2.129 g (49 %) of the thiol ester as a pale yellow solid: mp = 75 °C. The mother liquor was evaporated and an additional crop was obtained by recrystallisation of the residue from hexanes/ether mixtures: 0.84 g. Total yield: 2.96 g (69 %). TLC (17 % ethyl acetate in hexanes, *R_f* = 0.65); ¹H NMR (300MHz, CDCl₃) 7.69 (d, *J* = 15.8 Hz, 1H), 7.58 (m, 2H), 7.46-7.36 (m, 5H), 7.30-7.24 (m, 2H), 7.69 (d, *J* = 15.8 Hz, 1H), 2.41 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) 188.4, 141.3, 139.7, 134.5, 134.0, 130.6, 130.0, 128.9, 128.4, 124.1, 124.0, 21.3; IR (KBr, cm⁻¹) 3440 (br), 3059 (w), 3024 (w), 2916 (w), 1680 (s), 1618 (s), 1575 (w), 1494 (w), 1448 (w), 1328 (w), 1306 (w), 1032 (s), 1016 (s), 998 (m), 882 (m), 806 (m), 767 (s), 754 (m), 691 (m), 573 (m); Anal. Calcd for C₁₆H₁₄OS: C, 75.55; H, 5.55; S, 12.61. Found: C, 75.50; H, 5.56; S, 12.55.

2-Amino-thiobenzoic acid S-*p*-tolyl ester:⁹ Isatoic anhydride (16.30 g, 0.100 mol) was dissolved in dioxane (100 mL) together with *p*-toluenethiol (12.40 g, 0.100 mol) then NaOH (0.20 g, 0.005) was added. The mixture was stirred at 80 °C for 4 hours under nitrogen. Water (20 mL) was added and the

⁹ Staiger, J., Miller, S. *J. Org. Chem.*, **1959**, 24, 1214-1216

mixture was placed in refrigerator overnight for crystallization. The resulting crystals were collected by filtration giving the desired product in 92% yield (22.36 g) as a yellow needles m.p.: 94-95 °C. (lit.⁹ 96 °C). ¹H NMR (CDCl₃, 400 MHz): 8.01 (dd, *J* = 8.0 Hz, *J* = 1.6 Hz, 1H), 7.40 (app.d., *J* = 8.0 Hz, 2H), 7.36- 7.27 (m, 3H), 6.72 (dt, *J* = 7.4 Hz, *J* = 1.2 Hz, 1H), 6.65(dd, *J* = 8.2 Hz, *J* = 1.2 Hz, 1H), 5.81 (br.s., 2H), 2.41 (s, 3H). IR (CDCl₃, cm⁻¹): 3513 (w), 3376 (w), 1647 (m), 1619 (s), 1587 (vs), 1205 (vs).

Table Entry 1. 1-*p*-Tolyl-dodecan-1-one. *p*-Tolyltri-*n*-butylstannane (133 mg, 1.1 equiv., 0.35 mmol), dodecanethioic acid *S-p*-tolyl ester (98 mg, 0.32 mmol, 1.0 equiv), CuDPP (120 mg, 1.2 equiv., 0.38 mmol), tri-2-furylphosphine (6 mg, 8 mol%, 26 μmol) and Pd₂(dba)₃ (3 mg, 1 mol%, 3.2 μmol) were placed in a Schlenk tube under argon. Dry THF (5.1 mL) was added and the mixture was heated to 50 °C. After 7 h 10:1 hexanes/CH₂Cl₂ (10 mL) was added and the mixture was filtered through a plug of SiO₂ (washed with 15 mL hexanes/CH₂Cl₂ 10:1) and then evaporated. Purification of the residue by silica gel flash chromatography (hexanes hexanes/CH₂Cl₂ 5:1 hexanes/CH₂Cl₂ 3:1) afforded 80 mg (91 %) of the ketone as a white solid. M.p. 47 °C (ether/hexanes); ¹H NMR (400 MHz, CDCl₃) 7.86 (d, *J* = 7.2 Hz, 2H), 7.25 (d, *J* = 7.2 Hz, 2H), 2.93 (t, *J* = 7.4 Hz, 2H), 2.41 (s, 3H), 1.72 (pent, *J* = 7.2 Hz, 2H), 1.40–1.20 (m, 16H), 0.88 (t, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) 200.2, 143.5, 134.6, 129.1, 128.1, 38.5, 31.9, 29.6, 29.5, 29.4, 29.3, 24.4, 22.6, 21.5, 14.1; IR (neat, cm⁻¹) 2918, 2849, 1679, 1610, 1463; Anal. Calcd for C₁₉H₃₀O: C, 83.15; H, 11.02. Found: C, 83.06; H, 11.12.

Table Entry 2. 1-Furan-2-yl-dodecan-1-one. 2-(Tri-*n*-butylstannyl)furan (125 mg, 1.1 equiv., 0.35 mmol), dodecanethioic acid *S-p*-tolyl ester (98 mg, 0.32 mmol, 1.0 equiv), CuDPP (120 mg, 1.2 equiv., 0.38 mmol), tri-2-furylphosphine (6 mg, 8 mol%, 26 μmol) and Pd₂(dba)₃ (3 mg, 1 mol%, 3.2 μmol) were placed in a Schlenk tube under argon. Dry THF (5.1 mL) was added and the mixture was heated to 50 °C. After 7 h 10:1 hexanes/CH₂Cl₂ (10 mL) was added and the mixture was filtered through a plug of SiO₂ (washed with 10:1 15 mL hexanes/CH₂Cl₂) and then evaporated. Purification of the residue by silica gel flash chromatography (hexanes hexanes/CH₂Cl₂ 5:1 hexanes/CH₂Cl₂ 3:1) afforded 63 mg (78 %) of the ketone as a colorless oil. ¹H NMR (400 MHz, CDCl₃) 7.57 (d, *J* = 1.6 Hz, 1H), 7.17 (d, *J* = 3.8 Hz, 1H), 6.52 (dd, *J* = 3.6, 1.9 Hz, 1H), 2.80 (t, *J* = 7.5 Hz, 2H), 1.71 (pent, *J* = 7.5 Hz, 2H), 1.40–1.20 (m, 16H), 0.87 (t, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) 189.9, 152.8, 146.2, 116.8, 112.1, 38.5, 31.9, 29.6, 29.5, 29.4, 29.3, 24.3, 22.7, 14.1; IR (neat, cm⁻¹) 1679, 1571, 1471, 1158, 1085, 1011; Anal. Calcd for C₁₆H₂₆O₂: C, 76.75; H, 10.47. Found: C, 76.59; H, 10.50.

Table Entry 3. 1-Thiophene-2-yl-dodecan-1-one. 2-(Tri-*n*-butylstannyl)thiophene (131 mg, 1.1 equiv., 0.35 mmol), dodecanethioic acid *S*-*p*-tolyl ester (98 mg, 0.32 mmol, 1.0 equiv), CuDPP (120 mg, 1.2 equiv., 0.38 mmol), tri-2-furylphosphine (6 mg, 12 mol%, 26 μ mol) and Pd₂(dba)₃ (3 mg, 1 mol%, 3.2 μ mol) were placed in a Schlenk tube under argon. Dry THF (5.1 mL) was added and the mixture was heated to 50 °C. After 7 h 10:1 hexanes/CH₂Cl₂ (10 mL) was added and the mixture was filtered through a plug of SiO₂ (washed with 15 mL hexanes/CH₂Cl₂ 10:1) and then evaporated. Purification of the residue by preparative TLC 4:1 (hexanes/acetone) afforded 63 mg (73 %) of the ketone as a yellow oil. ¹H NMR (300 MHz, CDCl₃) 6.06 (s, 1H), 2.38 (t, *J* = 7.5 Hz, 2H), 2.13 (s, 3H), 1.86 (s, 3H), 1.56 (pent, *J* = 7.0 Hz, 2H), 1.35–1.18 (m, 16H), 0.86 (t, *J* = 6.8 Hz, 3H); ¹³C NMR (75.5 MHz, CDCl₃) 201.4, 154.7, 123.8, 44.3, 31.9, 29.6, 29.5, 29.3, 27.6, 24.3, 22.7, 20.6, 14.1; IR (neat, cm⁻¹) 2926, 2856, 1691, 1621, 1447; HRMS (EI) Calcd for C₁₆H₃₀O: 238.2297. Found 238.2296 [M⁺].

Table Entry 4. 3-Phenyl-1-pyridin-3-yl-propenone. 3-(Tri-*n*-butylstannyl)pyridine (129 mg, 1.1 equiv., 0.35 mmol), *E*-cinnamothioic acid *S*-*p*-tolyl ester (81 mg, 0.32 mmol, 1.0 equiv), CuDPP (120 mg, 1.2 equiv., 0.38 mmol), tri-2-furylphosphine (6 mg, 8 mol%, 26 μ mol) and Pd₂(dba)₃ (3 mg, 1 mol%, 3.2 μ mol) were placed in a Schlenk tube under argon. Dry THF (5.1 mL) was added and the mixture was heated to 50 °C. After 7 h 10:1 hexanes/CH₂Cl₂ (10 mL) was added and the mixture was filtered through a plug of Celite™ (washed with 15 mL 10:1 hexanes/CH₂Cl₂) and evaporated. Purification of the residue by preparative TLC (1mm, hexanes 4:1 /acetone) afforded 51 mg (76%) of the ketone as a colorless solid: mp 76 °C. TLC (50 % ethyl acetate in hexanes, *R*_f = 0.33); ¹H NMR (400MHz, CDCl₃) 9.25 (br s, 1H), 8.82 (br d, *J* = 3.5 Hz, 1H), 8.30 (dt, *J* = 9.9, 1.9 Hz, 1H), 7.86 (d, *J* = 15.6 Hz, 1H), 7.67 (m, 2H), 7.50 (d, *J* = 15.9 Hz, 1H), 7.49-7.43 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) 189.1, 153.1, 149.7, 146.0, 135.9, 134.4, 131.0, 129.0, 128.6, 123.7, 121.3; IR (KBr, cm⁻¹) 3445 (m), 3063 (w), 3027 (w), 2919 (w), 1668 (s), 1608 (s), 1585 (s), 1449 (m), 1416 (m), 1384 (m), 1331 (m), 1289 (w), 1235 (m), 1049 (m), 1018 (m), 752 (s), 697 (m), 690 (m), 679 (m); MS (low resolution EI), *m/z* (relative intensity) 210 (M+H⁺, 14), 209 (M⁺, 93), 208 (M-H⁺, 100), 180 (23), 106 (10), 103 (41), 78 (11), 77 (15); HRMS (EI) Calcd for C₁₄H₁₁NO: 209.0841. Found: 209.0849.

Table Entry 5. 3-Phenyl-1-pyridin-4-yl-propenone. 4-(Tri-*n*-butylstannyl)pyridine (129 mg, 1.1 equiv., 0.35 mmol), *E*-cinnamothioic acid *S*-*p*-tolyl ester (81 mg, 0.32 mmol, 1.0 equiv), CuDPP (120 mg, 1.2 equiv., 0.38 mmol), tri-2-furylphosphine (6 mg, 8 mol%, 26 μ mol) and Pd₂(dba)₃ (3 mg, 1 mol%, 3.2 μ mol) were placed in a Schlenk tube under argon. Dry THF (5.1 mL) was added and the mixture was heated to 50 °C. After 7 h hexanes/CH₂Cl₂ 10:1 (10 mL) was added and the mixture was filtered through a plug of Celite™ (washed with 15 mL 10:1 hexanes/CH₂Cl₂) and then evaporated. The residue was taken up in 10 mL ether and subsequently washed with aqueous ammonia solution (10%) and brine (10 mL). The organic extracts were dried over MgSO₄ and concentrated. Purification of the residue by silica gel flash chromatography (hexanes hexanes/ethyl acetate 3:1 hexanes/ethyl acetate 1:1) afforded 45 mg (67 %) of the ketone as a yellow solid: mp 85 °C. TLC (25% ethyl acetate in hexanes, R_f = 0.09); ¹H NMR (400MHz, CDCl₃) 8.85 (br s, 2H), 7.83, (d, *J* = 15.6 Hz, 1H), 7.78 (m, 2H), 7.65 (m, 2H), 7.49-7.40 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) 189.8, 150.8, 146.8, 144.3, 134.2, 131.2, 129.0, 128.7, 121.5, 121.1; IR (KBr, cm⁻¹) 3434 (w), 1666 (s), 1604 (s), 1574 (m), 1549 (w), 1448 (w), 1408 (w), 1384 (w), 1342 (m), 1226 (m), 1043 (w), 986 (w), 827 (w), 765 (m), 667 (w); MS (low resolution EI), *m/z* (relative intensity) 210 (M+H⁺, 15), 209 (M⁺, 100), 208 (M-H⁺, 87), 180 (14), 131 (12), 103 (94), 102 (21), 78 (33), 77 (83), 50 (33); HRMS (EI) Calcd for C₁₄H₁₁NO: 209.0841. Found: 209.0837.

Table Entry 6. (4-Nitrophenyl)-pyridin-2-yl-methanone. 2-(Tri-*n*-butylstannyl)pyridine (125 mg, 1.1 equiv., 0.35 mmol), 4-nitrothiobenzoic acid *S*-*p*-tolyl ester (87 mg, 0.32 mmol, 1.0 equiv), CuDPP (120 mg, 1.2 equiv., 0.38 mmol), tri-2-furylphosphine (6 mg, 8 mol%, 26 μ mol) and Pd₂(dba)₃ (3 mg, 1 mol%, 3.2 μ mol) were placed in a Schlenk tube under argon. Dry THF (5.1 mL) was added and the mixture was heated to 50 °C. After 7 h 10:1 hexanes/CH₂Cl₂ (10 mL) was added and the mixture was filtered through a plug of Celite™ (washed with 15 mL hexanes/CH₂Cl₂ 10:1) and then evaporated. Purification of the residue by silica gel flash chromatography (hexanes/acetone 10:1 hexanes/acetone 4:1) afforded 51 mg (70 %) of the ketone as a pale yellow solid: mp 98 °C. TLC (25 % acetone in hexanes, R_f = 0.31); ¹H NMR (400MHz, CDCl₃) 8.72 (br d, *J* = 4.8 Hz, 1H), 8.32 (app d, *J* = 8.9 Hz, 2H), 8.25 (app d, *J* = 8.9 Hz, 2H), 8.17 (d, *J* = 7.6 Hz, 1H), 7.96 (dt, *J* = 7.6, 1.6 Hz, 1H), 7.56 (ddd, *J* = 7.6, 4.8, 1 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) 191.9, 153.6, 149.8, 148.7, 141.5, 137.4, 131.9, 127.0, 124.7, 123.1; IR (KBr, cm⁻¹) 3431 (br), 3101 (w), 3072 (w), 2956 (w), 2923 (w), 2868 (w), 1673 (s), 1600 (m), 1584 (s), 1519 (s), 1437 (m), 1357 (s), 1310 (s), 1289 (s), 1247 (m), 1154 (m), 996 (m), 941 (s), 865 (s), 852 (s), 746 (m), 736 (m), 704 (s), 619 (m); MS (low resolution EI), *m/z* (relative intensity) 228 (M⁺, 31), 227 (M-H⁺, 43), 211 (13), 200 (100), 182 (21), 154 (90), 104 (64), 92 (29), 78 (79), 76 (64); HRMS (EI) Calcd for C₁₂H₈N₂O₃: 228.0535. Found:

228.0538; Anal. Calcd for $C_{12}H_8N_2O_3$: C, 63.16; H, 3.53; N, 12.28. Found: C, 62.78, H, 3.70, N, 11.89.

Table Entry 7. (1-Methyl-1H-pyrrol-2-yl)-(4-nitrophenyl)-methanone. 1-Methyl-2-tri-*n*-butylstannyl-1H-pyrrole (130 mg, 1.1 equiv., 0.35 mmol), 4-nitrothiobenzoic acid *S-p*-tolyl ester (87 mg, 0.32 mmol, 1.0 equiv), CuDPP (120 mg, 1.2 equiv., 0.38 mmol), tri-2-furylphosphine (6 mg, 8 mol%, 26 μ mol) and $Pd_2(dba)_3$ (3 mg, 1 mol%, 3.2 μ mol) were placed in a Schlenk tube under argon. Dry THF (5.1 mL) was added and the mixture was heated to 50 °C. After 7 h 5:1 hexanes/ CH_2Cl_2 (10 mL) was added and the mixture was filtered through a plug of Celite™ (washed with 15 mL 1:1 hexanes/ CH_2Cl_2) and evaporated. Purification of the residue by silica gel flash chromatography (hexanes hexanes/ CH_2Cl_2 3:1 hexanes/ CH_2Cl_2 1:2) afforded 67 mg (91 %) of the ketone as a yellow solid: mp 148 °C. TLC (50 % ethyl acetate in hexanes, R_f = 0.7); 1H NMR (400MHz, $CDCl_3$) 8.30 (m, 2H), 7.91 (m, 2H), 7.00 (m, 1H), 6.68 (dd, J = 1.9 and 4.4 Hz, 1H), 6.19 (dd, J = 2.5 and 4.1 Hz, 1H), 4.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 183.6, 149.2, 145.3, 132.7, 129.8, 123.6, 123.3, 108.8, 37.5; one signal was not observed; IR (KBr, cm^{-1}) 3444 (m), 1628 (s), 1597 (s), 1516 (s), 1409 (s), 1383 (m), 1350 (s), 1331 (m), 1319 (w), 1251 (m), 1109 (w), 1066 (w), 922 (w), 848 (m), 744 (m), 730 (m), 716 (m) 602 (w); MS (low resolution EI), m/z (relative intensity) 231 ($M+H^+$, 14), 230 (M^+ , 90), 229 (66), 213 (31), 184 (15), 183 (68), 108 (100), 80 (24), 50 (10); HRMS (EI) Calcd for $C_{12}H_{10}N_2O_3$: 230.0691. Found: 230.0694.

Table Entry 8. (4-Nitrophenyl)-pyrimidin-2-yl-methanone. 2-(Tri-*n*-butylstannyl)pyrimidine (129 mg, 1.1 equiv., 0.35 mmol), 4-nitrothiobenzoic acid *S-p*-tolyl ester (87 mg, 0.32 mmol, 1.0 equiv), CuDPP (120 mg, 1.2 equiv., 0.38 mmol), tri-2-furylphosphine (14 mg, 20 mol%, 64 μ mol) and $Pd_2(dba)_3$ (7 mg, 2.5 mol%, 8 μ mol) were placed in a Schlenk tube under argon. Dry THF (5.1 mL) was added and the mixture was heated to 50 °C. After 7 h 1:1 hexanes/ CH_2Cl_2 (10 mL) was added and the mixture was filtered through a plug of Celite™ (washed with 15 mL hexanes/ CH_2Cl_2 1:1) and then evaporated. The residue was taken up in 15 mL ethyl acetate and was subsequently washed twice with aqueous ammonia solution (10%) and brine (15 mL each). The organic extracts were dried over $MgSO_4$ and concentrated. Purification of the residue by silica gel flash chromatography (hexanes/acetone 5:1 hexanes/acetone 2:1) afforded 45 mg (61 %) of the ketone as a colorless solid: mp 139 °C. TLC (50% ethyl acetate in hexanes, R_f = 0.18); 1H NMR (400MHz, $CDCl_3$) 9.00 (d, J = 4.8 Hz, 2H), 8.32, (d, J = 8.9 Hz, 2H), 8.25 (d, J = 8.9 Hz, 2H), 7.57 (t, J = 4.8 Hz, 1H); ^{13}C NMR

(100 MHz, CDCl₃) 189.4, 161.0, 157.6, 150.2, 140.1, 131.9, 123.3, 122.9; IR (KBr, cm⁻¹) 3107 (w), 3068 (w), 1687 (m), 1606 (w), 1562 (m), 1521 (s), 1348 (m), 1314 (s), 1192 (m), 949 (m), 875 (w), 854 (m), 828 (w), 716 (m); MS (low resolution EI), *m/z* (relative intensity) 230 (M+H⁺, 13), 229 (M⁺, 99), 201 (19), 183 (27), 182 (27), 150 (100), 120 (18), 104 (59), 92 (28), 79 (26), 76 (55), 53 (40); HRMS (EI) Calcd for C₁₁H₇N₃O₃: 229.0487. Found: 229.0481.

Table Entry 9. (4-Nitrophenyl)-thiazol-2-yl-methanone.¹⁰ 2-(Tri-*n*-butylstannyl)thiazole (131 mg, 1.1 equiv., 0.35 mmol), 4-nitrothiobenzoic acid *S-p*-tolyl ester (87 mg, 0.32 mmol, 1.0 equiv), CuDPP (120 mg, 1.2 equiv., 0.38 mmol), tri-2-furylphosphine (14 mg, 20 mol%, 64 μmol) and Pd₂(dba)₃ (7 mg, 2.5 mol%, 8 μmol) were placed in a Schlenk tube under argon. Dry THF (2.5 mL) and 2.5 mL hexanes sparged with argon were added and the mixture was heated to 40 °C. After 7 h the mixture was filtered through a plug of Celite™ (washed with 15 mL ether) and then evaporated. The residue was taken up in 20 mL ethyl acetate and washed with aqueous NH₃ solution (10 %) and brine (20 mL each). The organic phase was dried over MgSO₄ and concentrated. Purification of the residue by silica gel flash chromatography (hexanes hexanes/CH₂Cl₂ 5:1 hexanes/CH₂Cl₂ 1:1) afforded 52 mg (69 %) of the ketone as a pale yellow solid: mp 121 °C; TLC (50 % dichloromethane in hexanes, R_f = 0.42); ¹H NMR (400MHz, CDCl₃) 8.67 (d, *J* = 8.9 Hz, 2H), 8.37 (d, *J* = 8.9 Hz, 2H), 8.15 (d, *J* = 2.9 Hz, 1H), 7.83 (d, *J* = 2.9 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) 182.5, 150.4, 145.3, 139.9, 132.1, 127.4, 123.4, one signal is not observed; IR (KBr, cm⁻¹) 3125 (w), 3079 (w), 1665 (m), 1600 (w), 1518 (s), 1482 (w), 1384 (m), 1355 (s), 1333 (m), 1295 (m), 899 (w), 882 (w), 841 (s), 758 (m), 710 (m); MS (low resolution EI), *m/z* (relative intensity) 234 (M⁺, 27), 206 (100), 160 (37), 120 (17), 104 (32), 92 (11), 76 (30); HRMS (EI) Calcd for C₁₀H₆N₂O₃S: 234.0099. Found: 234.0105; Anal. Calcd for C₁₀H₆N₂O₃S: C, 51.28; H, 2.58; N, 11.96; S, 13.69. Found: C, 51.05; H, 2.58; N, 11.87; S, 13.65.

Cross-coupling Procedure Applied to Table Entry Examples 10 – 13: Thiol ester (0.50 mmol), organostannane (0.50 mmol), CuDPP (0.65 mmol, 1.3 equivalent), Pd₂dba₃ (0.003 mmol, 0.65 %) and tri-2-furylphosphine (0.024 mmol, 4 equivalents per Pd) were placed in the reaction vessel and the vessel was flushed with argon. THF (3 mL) and hexanes (3 mL) were added and the reaction mixture was magnetically stirred at 40 °C under nitrogen for 18 hours. Then, Et₂O (4 mL) was added and the suspension was filtered through sintered glass funnel. The volatiles were evaporated under reduced pressure and the residue was subjected to rotary chromatography (Chromatotron™ from Harrison Research) using a solvent gradient starting with 100% hexanes and proceeding to 100% Et₂O.

¹⁰ For ¹H, mp., and elemental analysis see: Dondoni, A.; Douglas, A. W.; Shinkai, I. *J. Org. Chem.* **1993**, 58, 3196-3200.

Table Entry 10. Benzofuran-2-yl-pyrazin-2-yl-methanone: 2-Benzofuranyl-tri-*n*-butylstannane (0.50 mmole, 0.203 g), 2-*S*-phenylcarbonylpyrazine (0.50 mmol, 0.108 g) and CuDPP (0.185 mmol, 0.65 g) gave off-white crystals (0.108 g, 96%) m.p.: 144-146 °C. ¹H NMR (CDCl₃, 400 MHz): 9.43 (app.d, *J*= 1.6 Hz 1H), 8.84 (app.d, *J*= 2.0 Hz, 1H), 8.75 (m, 1H), 8.43 (app.d, *J*= 0.8 Hz, 1H), 7.79 (dd, *J*₁= 8.0 Hz, *J*₂= 0.8 Hz, 1H), 7.68 (dd, *J*₁= 8.4 Hz, *J*₂= 0.8 Hz, 1H), 7.54 (dt, *J*₁= 7.8 Hz, *J*₂= 1.2 Hz, 1H), 7.35 (dt, *J*₁=7.6 Hz, *J*₂= 0.8 Hz, 1H). ¹³C NMR (CDCl₃, 100MHz): 179.6, 155.9, 150.4, 148.4, 147.6, 145.5, 143.1, 129.2, 127.3, 124.0, 123.9, 120.5, 112.5. IR (CDCl₃, cm⁻¹): 2251 (w), 1653 (s), 1544 (m), 1329 (w) 1125 (w). Anal. Calcd for C₁₃H₈N₂O₂: C, 69.64 ; H, 3.60 ; N, 12.49; Found: C, 69.38; H, 3.65 ; N, 12.35.

Table Entry 11. 4-(Adamantane-2-carbonyl)-pyridine-3-carbaldehyde: 4-Tri-*n*-butylstannylpyridyl-3-carboxaldehyde (0.50 mmole, 0.198 g), 1-*S*-*p*-tolylcarbonyladamantane (0.50 mmol, 0.143 g) and CuDPP (0.185 mmol, 0.65 g) gave white crystals (0.091 g, 68%) m.p: 100-102 °C. ¹H NMR (CDCl₃, 400 MHz): 10.02 (s, 1H), 9.08 (s, 1H), 8.84 (d, *J*= 4.8 Hz, 1H), 7.18 (d, *J* = 5.2 Hz, 1H), 2.04 (s, 3H), 1.90 (d, *J*= 2.4 Hz, 6H), 1.70 (q, *J*= 11.6 Hz, 6H). ¹³C NMR (CDCl₃, 100MHz): 210.6, 189.7, 154.0, 153.5, 149.1, 128.2, 120.5, 47.1, 38.1, 36.4, 36.2, 29.7, 27.7. IR (CDCl₃, cm⁻¹): 2918 (vs), 2854 (m), 2255 (s) 1704 (s), 1692 (s), 1242 (m). Calcd for C₁₇H₁₉NO₂: C, 75.81; H, 7.11; N, 5.20; Found: C,75.72; H, 7.06; N, 5.24.

Table Entry 12. (2-Aminophenyl)-benzofuran-2-yl-methanone: 2-Benzofuranyl-tri-*n*-butylstannane (0.50 mmole, 0.205 g), 2-aminothiobenzoic acid *S*-*p*-tolyl ester (0.50 mmol, 0.121 g) and CuDPP (0.185 mmol, 0.65 g) gave a yellow oil (0.110 g, 93%). ¹H NMR (CDCl₃, 400 MHz): 8.02 (dd, *J*₁= 6.8 Hz, *J*₂= 1.6 Hz, 1H), 7.72 (app.d, *J*= 8.0 Hz, 1H), 7.63 (dd, *J*₁= 8.2 Hz, *J*₂= 0.4 Hz, 1H), 7.47 (dt, *J*₁= 7.8 Hz, *J*₂= 1.2 Hz, 1H), 7.43 (d, *J*= 1.2 Hz, 1H), 7.37- 7.30 (m, 2H), 6.80- 6.74 (m, 2H). ¹³C NMR (CDCl₃, 100MHz): 185. 3, 155.4, 152.7, 150.1, 134.4, 132.5, 127.7, 127.1, 123.8, 122.9, 118.4, 117.3, 116.4, 115.2, 112.4. IR (CDCl₃, cm⁻¹): 3502 (w), 3372 (w), 2255 (w), 1626 (vs), 1585 (s), 1552 (s). HRMS (EI) Calcd for C₁₅H₁₁NO₂: 237.0789. Found: 237.0797 ([M]).

Table Entry 13. Acetic acid 2-benzofuran-2-yl-2-oxo-ethyl ester:¹¹ 2-Benzofuranyl-tri-*n*-butylstannane (0.50 mmole, 0.203 g), 2-acetoxythioacetic acid *S-p*-tolyl ester (0.50 mmol, 0.112 g) and CuDPP (0.185 mmol, 0.65 g) gave white crystals (0.105, 96%) m.p.: 85-87 °C (lit³ 86-87 °C) . ¹H NMR (CDCl₃, 400 MHz): 7.71 (app.d, *J* = 8.0 Hz, 1H), 7.60 - 7.57 (m, 2H), 7.50 (dt, *J*₁ = 7.8 Hz, *J*₂ = 1.2 Hz, 1H), 7.33 (dt, *J*₁ = 7.6 Hz, *J*₂ = 0.8 Hz, 1H), 5.32 (s, 2H), 2.24 (s, 3H). ¹³C NMR (CDCl₃, 100MHz): 183.7, 170.3, 155.6, 150.3, 128.7, 126.6, 124.1, 123.4, 113.3, 112.4, 65.8, 20.5. IR (CDCl₃, cm⁻¹): 2937 (w), 2256 (w), 1752 (s), 1707 (s), 1565 (s), 1293 (s).

Table Entry 14. 2-Methyl-2-pentadecen-4-one. CuOP(O)Ph₂ (0.185 g, 0.659 mmol, 2.2 equiv), tri-2-furylphosphine (14 mg, 0.060 mmol, 0.2 equiv), and Pd₂dba₃ (7 mg, 0.008 mmol, 0.026 equiv) were added to a solution of dodecanethioic acid *S-p*-tolyl ester (0.092 g, 0.301 mmol, 1.0 equiv) and (2-methyl-1-propenyl)tri-*n*-butylstannane (0.114 g, 0.330 mmol, 1.1 equiv) in THF (3.6 mL). The reaction mixture was stirred at 50 °C for 19 h and then evaporated. The residue was diluted with hexanes/CH₂Cl₂ (10/1, 10 mL) and the suspension was filtered through a plug of Celite™. The organic layer was evaporated and purified by SiO₂ column chromatography with a gradient of 5/1–3/1 hexanes/CH₂Cl₂ to give 2-methyl-2-pentadecen-4-one (66 mg, 92%) as a colorless oil. ¹H NMR (300 MHz, CDCl₃) 6.06 (s, 1H), 2.38 (t, *J* = 7.5 Hz, 2H), 2.13 (s, 3H), 1.86 (s, 3H), 1.56 (pent, *J* = 7.0 Hz, 2H), 1.35–1.18 (m, 16H), 0.86 (t, *J* = 6.8 Hz, 3H); ¹³C NMR (75.5 MHz, CDCl₃) 201.4, 154.7, 123.8, 44.3, 31.9, 29.6, 29.5, 29.3, 27.6, 24.3, 22.7, 20.6, 14.1; IR (neat, cm⁻¹) 2926, 2856, 1691, 1621, 1447; HRMS (EI) Calcd for C₁₆H₃₀O: 238.2297. Found 238.2296 [M⁺].

Table Entry 15. 3-Methyl-1-(2-methylphenyl)-2-buten-1-one. CuOP(O)Ph₂ (0.186 g, 0.663 mmol, 2.2 equiv), tri-2-furylphosphine (14 mg, 0.060 mmol, 0.20 equiv), and Pd₂dba₃ (7 mg, 0.007 mmol, 0.025 equiv) were added to a solution of 2-methylthiobenzoic acid *S-p*-tolyl ester (0.073 g, 0.300 mmol, 1.0 equiv) and (2-methyl-1-propenyl)tri-*n*-butylstannane (0.114 g, 0.330 mmol, 1.1 equiv) in THF (3.6 mL). The reaction mixture was stirred at 50 °C for 25 h and then evaporated. The residue was diluted with hexanes/CH₂Cl₂ (10/1, 10 mL) and the suspension was filtered through a plug of Celite™. The organic layer was evaporated and purified by SiO₂ column chromatography with a gradient of 10/1–3/1 hexanes/CH₂Cl₂ to give 3-methyl-1-(2-methylphenyl)-2-buten-1-one (42 mg,

¹¹ Wagner, T. *J. Am. Chem. Soc.*, **1950**, 72, 3477-3499.

81%) as a colorless oil. ^1H NMR (400 MHz, CDCl_3) 7.51–7.48 (m, 1H), 7.35–7.30 (m, 1H), 7.25–7.20 (m, 2H), 6.45–6.43 (m, 1H), 2.47 (s, 3H), 2.17 (s, 3H), 1.98 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) 195.9, 156.1, 140.6, 137.0, 131.4, 130.3, 128.1, 125.5, 124.7, 27.9, 20.9, 20.4; IR (neat, cm^{-1}) 2926, 1660, 1613, 1444, 1243; HRMS (EI) Calcd for $\text{C}_{12}\text{H}_{14}\text{O}$: 174.1045. Found 174.1047 [M^+].

Table Entry 16. 2-Thienyl-2-Tolyl Ketone. $\text{CuOP}(\text{O})\text{Ph}_2$ (0.185 g, 0.659 mmol, 2.2 equiv), tri-2-furylphosphine (14 mg, 0.060 mmol, 0.20 equiv), and Pd_2dba_3 (7 mg, 0.007 mmol, 0.025 equiv) were added to a solution of 2-methylthiobenzoic acid *S-p*-tolyl ester (0.073 g, 0.300 mmol, 1.0 equiv) and 2-(tri-*n*-butylstannyl)thiophene (0.123 g, 0.330 mmol, 1.1 equiv) in THF (3.6 mL). The reaction mixture was stirred at 50 °C for 7 h and then evaporated. To the residue was added Et_2O (10 mL) and 10% aq NH_4OH (10 mL). After stirring for 10 min, the mixture was filtered through a plug of Celite™. The organic layer was washed with brine (5 mL), dried over MgSO_4 , and evaporated. Purification by SiO_2 column chromatography with 3/1 hexanes/ CH_2Cl_2 gave 2-thienyl *o*-tolyl ketone (59 mg, 97%) as a colorless oil.¹² ^1H NMR (400 MHz, CDCl_3) 7.73 (dd, J = 5.0, 1.0 Hz, 1H), 7.45 (d, J = 7.6 Hz, 1H), 7.43 (dd, J = 3.6, 1.2 Hz, 1H), 7.39 (td, J = 7.6, 1.2 Hz, 1H), 7.30–7.24 (m, 2H), 7.12 (dd, J = 5.2, 3.6 Hz, 1H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) 190.4, 144.8, 138.4, 136.4, 135.4, 134.8, 131.0, 130.3, 128.1, 128.0, 125.1, 19.6; IR (neat, cm^{-1}) 1640, 1413, 1297, 1278, 849, 735; Anal. Calcd for $\text{C}_{12}\text{H}_{10}\text{OS}$: C, 71.26; H, 4.98; S, 15.85. Found: C, 71.06; H, 5.17; S, 15.56.

Table Entry 17. 1-Pentadecen-4-one. $\text{CuOP}(\text{O})\text{Ph}_2$ (0.185 g, 0.659 mmol, 2.2 equiv), tri-2-furylphosphine (14 mg, 0.060 mmol, 0.20 equiv), and Pd_2dba_3 (7 mg, 0.007 mmol, 0.025 equiv) were added to a solution of dodecanethioic acid *S-p*-tolyl ester (0.092 g, 0.300 mmol, 1.0 equiv) and allyltri-*n*-butylstannane (0.109 g, 0.329 mmol, 1.1 equiv) in THF (3.6 mL). The reaction mixture was stirred at 50 °C for 1 h and then evaporated. The residue was diluted with hexanes/ CH_2Cl_2 (8/1, 10 mL) and the suspension was filtered through a plug of Celite™. The organic layer was evaporated and the residue purified by SiO_2 column chromatography with a gradient of 8/1–3/1 hexanes/ CH_2Cl_2 (involved 0.1% Et_3N) to give 1-pentadecen-4-one (55 mg, 81%) as a white solid.¹³ ^1H NMR (400 MHz, CDCl_3) 5.92 (ddt, J = 17.2, 10.0, 7.2 Hz, 1H), 5.18–5.10 (m, 2H), 3.16 (d, J = 7.2 Hz, 2H), 2.42 (t, J = 7.2 Hz, 2H), 1.60–1.50 (m, 2H), 1.35–1.15 (m, 16H), 0.87 (t, J = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) 209.1, 130.7, 118.9, 47.7, 42.4, 31.9, 29.6, 29.4 (x2), 29.3, 29.2, 23.7, 22.7, 14.1; IR (neat, cm^{-1}) 2926, 1718, 1640, 992; HRMS (EI) Calcd for $\text{C}_{15}\text{H}_{28}\text{O}$: 224.2140. Found 224.2141 [M^+].

¹² T. Keumi, K. Yoshimura, M. Shimada, H. Kitajima, *Bull. Chem. Soc. Jpn.* **1988**, 61, 455–459.

¹³ L. S. Hegedus, P. M. Kendall, S. M. Lo, J. R. Sheats, *J. Am. Chem. Soc.* **1975**, 97, 5448–5452.