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Stille Couplings Catalytic in Tin: A Sn-F Approach

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SUPPORTING INFORMATION

Materials and Methods

Reactions were carried out in oven- or flame-dried glassware under nitrogen atmosphere, unless otherwise noted. All commercial reagents were used without purification. All solvents were reagent grade. THF was freshly distilled from sodium/benzophenone under nitrogen. Except as otherwise indicated, all reactions were magnetically stirred and monitored by thin layer chromatography with Whatman 0.25-mm precoated silica gel plates or capillary GC with a Perkin-Elmer 8500 gas chromatograph fitted with a fused silica column. Flash chromatography was performed with silica gel 60 Å (particle size 230-400 Mesh ASTM) supplied by Silicycle. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated. Infrared spectra were recorded on a Nicolet IR/42 spectrometer. Proton and carbon NMR spectra were recorded on a Varian Gemini-300 spectrometer or a Varian VXR-500 spectrometer. Chemical shifts are reported relative to the residue peaks of solvent chloroform (δ 7.24 for ¹H and δ 77.0 for ¹³C). High-resolution mass spectra were obtained at either the Michigan State University Mass Spectrometry Service Center with a JEOL-AX505 mass spectrometer (resolution 7000) or at the Mass Spectrometry Laboratory of the University of South Carolina, Department of Chemistry & Biochemistry with a Micromass VG-70S mass spectrometer. Pd₂dba₃ (Aldrich), tri-2-furylphosphine (Strem) and isopropylacetylene (GFS) were all used as received.

Representative procedure for the tandem one pot hydrostannation/Stille coupling with 6 mol% Me₃SnCl. Preparation of 2-methyl-6-phenyl-hexa-3,5-dien-2-ol (Table 1, entry 1). Tri-2-furylphosphine (9.3 mg, 0.04 mmol) was added to a solution of Pd₂dba₃ (9.2 mg, 0.01 mmol) in Et₂O (5 mL). After stirring at room temperature for 15 min, (E)-β-bromostyrene (274.5 mg, 1.5 mmol), Me₃SnCl (0.06 mL, 0.06 mmol; 1M solution in THF), aq. KF (0.1743 g, 3 mmol; 1 mL
H₂O), TBAF (1 drop of a 1M solution in THF) and PdCl₂(PPh₃)₂ (7.0 mg, 0.01 mmol) were all added to the solution. The solution was heated to reflux and then a solution of 2-methyl-but-3-yn-2-ol (0.10 mL, 1 mmol) and PMHS (0.09 mL, 1.5 mmol) in Et₂O (4mL) was added via a syringe pump over 11 hrs. The phases were separated and the organics washed with brine, dried over MgSO₄, filtered and concentrated. The resulting residue was purified by column chromatography (silica gel, hexane/EtOAc 90:10) to afford (165 mg, 88%) of 2-methyl-6-phenyl-hexa-3,5-dien-2-ol¹ as an oil.

Preparation of 13-(1-hydroxy-cyclohexyl)-trideca-10,12-dienoic acid methyl ester (Table 1, entry 2). Applying the above conditions to 1-ethynyl-cyclohexanol (124.2 mg, 1.0 mmol) and (E)-11-iodo-undec-10-enoic acid methyl ester (see below for preparation) (486.3 mg, 1.5 mmol) afforded after column chromatography (silica gel; hexane/EtOAc 90:10) 13-(1-hydroxy-cyclohexyl)-trideca-10,12-dienoic acid methyl ester (235 mg, 73%) as an oil. IR 3356, 1774 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 1.21-1.38 (m, 11 H), 1.42-1.68 (m, 12 H), 2.03 (q, J = 7.51 Hz, 2 H), 2.26 (t, J = 7.29 Hz, 2 H), 3.70 (s, 3 H), 5.65 (m, 2 H), 5.99 (dd, J = 10.38, 15.02 Hz, 1 H); 6.19 (dd, J = 10.38, 15.46 Hz, 1 H); ¹³C (75 MHz, CDCl₃) δ 22.14, 24.88, 25.50, 29.07, 29.13, 29.15, 29.19, 29.22, 32.50, 34.05, 37.94, 51.41, 71.30, 127.59, 129.84, 134.82, 138.58, 174.26; HRMS (EI) m/z 322.2511[(M⁺), calcd. for C₂₀H₃₄O₃ 322.2508].

Preparation of 2,4-dimethyl-8-phenyl-octa-5,7-dien-4-ol (Table 1, entry 3). Applying the above conditions to 3,5-dimethyl-hex-1-yn-3-ol (0.15 mL, 1.0 mmol) and (E)-β-bromostyrene (274.5 mg, 1.5 mmol), afforded after column chromatography (silica gel; hexane/EtOAc 90:10) 2,4-dimethyl-8-phenyl-octa-5,7-dien-4-ol¹ (205 mg, 89%) as an oil.

Preparation of 4-(4-methoxy-phenyl)-2-methyl-but-3-en-2-ol (Table 1, entry 4). Applying the above conditions to 2-methyl-but-3-yn-2-ol (0.10 mL, 1.0 mmol) and p-iodoanisole (351.1 mg, 1.5 mmol), afforded after column chromatography (silica gel; hexane/EtOAc 90:10) 4-(4-methoxy-phenyl)-2-methyl-but-3-en-2-ol² (198 mg, 78%) as an oil.

Preparation of 1,1-diethyl-5-phenyl-penta-2,4-dienylamine (Table 1, entry 5). Applying the above conditions to 1,1-diethyl-prop-2-ynylamine (0.10 mL, 1.0 mmol) and (E)-β-bromostyrene (274.5 mg, 1.5 mmol), afforded after column chromatography (silica gel; hexane/EtOAc 60:40) 1,1-diethyl-5-phenyl-penta-2,4-dienylamine¹ (163 mg, 82%) as an oil.
Preparation of 1-(4-phenyl-buta-1,3-dienyl)-cyclohexanol (Table 1, entry 6). Applying the above conditions to 1-ethynyl-cyclohexanol (124.2 mg, 1.0 mmol) and (E)-β-bromostyrene (274.5 mg, 1.5 mmol) afforded after column chromatography (silica gel; hexane/EtOAc 90:10) 1-(4-phenyl-buta-1,3-dienyl)-cyclohexanol (205 mg, 90%) as an oil.

Preparation of 8-phenyl-octa-5,7-dien-4-ol (Table 1, entry 7). Applying the above conditions to hex-1-yn-3-ol (0.12 mL, 1.0 mmol) and (E)-β-bromostyrene (274.5 mg, 1.5 mmol) afforded after column chromatography (silica gel; hexane/EtOAc 90:10) 8-phenyl-octa-5,7-dien-4-ol (117 mg, 60%) as an oil.

Preparation of 1,5-diphenyl-penta-2,4-dien-1-ol (Table 1, entry 8). Applying the above conditions to 1-phenyl-prop-2-yn-1-ol (0.13 mL, 1.0 mmol) and (E)-β-bromostyrene (274.5 mg, 1.5 mmol) afforded after column chromatography (silica gel; hexane/EtOAc 90:10) 1,5-diphenyl-penta-2,4-dien-1-ol (137 mg, 68%) as an oil.

Preparation of 2-methyl-5-phenyl-pent-3-en-2-ol (Table 1, entry 9). Applying the above conditions to 2-methyl-but-3-yn-2-ol (0.10 mL, 1.0 mmol) and benzyl bromide (0.18 mL, 1.5 mmol) afforded after column chromatography (silica gel; hexane/EtOAc 90:10) 2-methyl-5-phenyl-pent-3-en-2-ol (149 mg, 85%) as an oil.

Preparation of 8-phenyl-octa-5,7-dien-1-ol (Table 1, entry 10). Applying the above conditions to 6-bromo-hex-5-yn-1-ol (0.13 mL, 1.0 mmol) and (E)-β-bromostyrene (274.5 mg, 1.5 mmol) afforded after column chromatography (silica gel; hexane/EtOAc 80:20) 8-phenyl-octa-5,7-dien-1-ol (123 mg, 61%) as an oil.

Preparation of 4,4-dimethyl-hex-5-yn-1-ol (4) (Scheme 3). Isopropylacetylene (7.51 mL, 73.4 mmol) was added to 50 mL of dry Et₂O in a flame dried 500 mL round bottom flask under N₂ and the solution was cooled to 0 °C. n-BuLi (92 mL of 1.6 M solution in hexanes, 147 mmol) was then added dropwise via an addition funnel. When the addition was complete the solution had a clear yellow appearance. Upon addition of TMEDA (11.65 mL, 77.1 mmol) in one portion, the solution turned to a thick white slurry within minutes. This solution was then placed in a 60 °C oil bath and gently refluxed for 15 hours to produce a deep red solution (the dianion). The dianion solution was then allowed to cool to room temperature and then cooled to −78 °C. OXG (4.75 mL, 73.4 mmol) was then added followed by addition of BF₃•OEt₂ (9.31 mL, 73.4 mmol) via a syringe pump over 6 hours. The solution was then warmed to room temperature, diluted with 1 M HCl, and stirred for 30
minutes. The mixture was then diluted with Et₂O and the phases separated. The aqueous phase was extracted with Et₂O (3x) and the combined organics were washed with brine, dried over MgSO₄, filtered and concentrated. The resulting residue was purified by column chromatography (silica gel; hexane/EtOAc 90:10 → 80:20) to afford 4,4-dimethyl-hex-5-yn-1-ol (2.58 g, 35%) as a pale yellow oil. ¹H NMR (300 MHz, CDCl₃) δ 1.24 (s, 6 H), 1.43-1.53 (m, 2 H), 1.69-1.83 (m, 3 H), 2.11 (s, 1 H), 3.70 (t, J = 6.46 Hz, 2 H); ¹³C (75 MHz, CDCl₃) δ 28.67, 29.10, 30.75, 39.27, 63.16, 67.94, 91.62.

**Preparation of (3-bromo-prop-2-ynyloxy)-t-butyl-diphenyl-silane (6)** (Scheme 4). To a solution of propargyl alcohol (1.40 g, 25 mmol) and imidazole (3.74 g, 55 mmol) in DMF (25 mL) was added TBDPSCl (7.15 mL, 27.5 mmol) dropwise at room temperature and stirred for 5 h. The reaction was then partitioned between sat. aq. NH₄Cl (100 mL) and hexane (100 mL) and the aqueous phase extracted with hexane (2x). The combined organics were washed with brine, dried over MgSO₄, filtered, and concentrated. The resulting residue was purified by column chromatography (silica gel; hexane/EtOAc 95:5) to afford t-butyl-diphenyl-prop-2-ynyloxy-silane (7.36 g, 100%). The silylated propargyl alcohol was then dissolved in 75 mL of dry acetone. N-Bromosuccimide (4.90 g, 27.5 mmol) and AgNO₃ (375 mg, 2.2 mmol) were added and the reaction was allowed to stir for 8 hours. The reaction was then diluted with ether and washed with H₂O. The aqueous phase was extracted with ether. The combined organics were washed with brine, dried over MgSO₄, filtered, and concentrated. The resulting residue was then purified by column chromatography (silica, hexane/EtOAc 95/5) to afford (3-bromo-prop-2-ynyloxy)-t-butyl-diphenyl-silane (6) (7.93 g, 85%) as a light yellow oil. IR (neat) 3071, 2221 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 1.11 (s, 9 H), 4.38 (s, 2 H), 7.40-7.50 (m, 6 H), 7.70-7.80 (m, 4 H); ¹³C (75 MHz, CDCl₃) δ 19.1, 26.7, 44.7, 53.5, 78.3, 127.7, 129.8, 132.8, 135.6; HRMS (EI) m/z 314.9851 [M–t-Bu]+ calcd for C₁₉H₂₁BrOSi 314.9841.

**Preparation of t-butyl-diphenyl-(3-tributylstannanyl-allyloxy)-silane (7)** (Scheme 3). To 100 mL of THF was added (3-bromo-prop-2-ynyloxy)-t-butyl-diphenyl-silane (6) (7.55 g, 20.2 mmol), Bu₃SnCl (6.60 ml, 24.3 mmol), KF (3.55 g, 61 mmol), H₂O (6 mL), PMHS (1.82 mL, 30.3 mmol), TBAF (1 drop of a 1M solution in THF) and PdCl₂(PPh₃)₂. The reaction was stirred at room temperature until complete by TLC (2 hours). Once complete, the reaction was diluted with ether. The phases were separated and the aqueous phase extracted with ether. The combined organics were washed with brine, dried over MgSO₄, filtered, and concentrated. The resulting residue was purified by column chromatography (silica gel, hexane, 1% NEt₃) to afford (E)-t-butyl-diphenyl-(3-
tributylstannanyl-allyloxy)-silane \(^4\) (7) (8.27 g, 70%) as a clear oil. IR (neat) 2956, 1112 cm\(^{-1}\); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 0.94 (m, 15 H), 1.12 (s, 9 H), 1.37 (m, 6 H), 1.56 (m, 6 H), 4.30 (dd, \(J = 1.8, 4.2\) Hz, 2 H), 6.02-6.43 (m, 2 H), 7.38-7.48 (m, 6 H), 7.71-7.77 (m, 4 H); \(^{13}\)C (125 MHz, CDCl\(_3\)) \(\delta\) 9.44, 13.73, 19.30, 26.89, 27.23, 29.09, 67.15, 126.85, 127.54, 129.54, 133.95, 135.56, 146.71; HRMS (EI) \(m/z\) 529.1950 [(M–Bu)+, calcd. for C\(_{31}\)H\(_{50}\)OSiSn 529.1953].

Preparation of (3-bromo-allyloxy)-t-butyl-diphenyl-silane (8) (Scheme 3). N-Bromosuccinimide (3.07 g, 17.23 mmol) was added to a cold solution of (E)-t-butyl-diphenyl-(3-tributylstannanyl-allyloxy)-silane (7) (9.61 g, 16.41 mmol) in dry CH\(_2\)Cl\(_2\) (100 mL). Upon completion (TLC, 1 hr), the reaction was quenched by the addition of sat. aq. Na\(_2\)S\(_2\)O\(_3\) (25 mL). CH\(_2\)Cl\(_2\) was added and the aqueous phase extracted with CH\(_2\)Cl\(_2\) (3X). The combined organics were washed with brine, dried over Na\(_2\)SO\(_4\), filtered and concentrated. The resulting residue was purified by column chromatography (silica gel, hexanes) to afford (E)-(3-bromo-allyloxy)-t-butyl-diphenyl-silane (8) (6.01 g, 97%) as a clear liquid. IR 2959, 2857, 1112 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 1.10 (s, 9 H), 4.17 (m, 2 H), 6.30 (m, 1 H), 6.38 (m, 1 H), 7.44 (m, 6 H), 7.70 (m, 4 H); \(^{13}\)C (75 MHz, CDCl\(_3\)) \(\delta\) 19.20, 26.80, 64.03, 105.93, 127.76, 129.82, 133.13, 135.45, 136.29; HRMS (EI) \(m/z\) 316.9998 [(M–t-Bu)+, calcd. for C\(_{19}\)H\(_{23}\)BrOSi 316.9997].

Preparation of 9-(t-butyl-diphenyl-silanyloxy)-4,4-dimethyl-nona-5,7-dien-1-ol (1). Applying the above one pot conditions to 4,4-dimethyl-hex-5-yn-1-ol (126.2 mg, 1 mmol) (4) and (E)-(3-bromo-allyloxy)-t-butyl-diphenyl-silane (8) (563.1 mg, 1.5 mmol) afforded after column chromatography (silica gel; hexane/EtOAc 80:20) 9-(t-butyl-diphenyl-silanyloxy)-4,4-dimethyl-nona-5,7-dien-1-ol \(^5\) (1) (336 mg, 80%) as an oil. IR (neat) 3352, 3071 cm\(^{-1}\); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 1.04 (s, 6 H), 1.08 (s, 9 H), 1.37 (m, 3 H), 1.51 (m, 2 H), 3.61 (t, \(J = 6.4\) Hz, 2 H), 4.25 (dd, \(J = 1.1, 5.1\) Hz, 2 H), 5.61 (d, \(J = 15.5\) Hz, 1 H), 5.70 (dt, \(J = 5.1, 15.2\) Hz, 1 H), 5.98 (dd, \(J = 10.4, 15.5\) Hz, 1 H), 6.24 (dd, \(J = 10.4, 15.2, 1\) H), 7.36-7.45 (m, 6 H), 7.68-7.72 (m, 4 H); \(^{13}\)C (125 MHz, CDCl\(_3\)) \(\delta\) 19.17, 26.80, 27.13, 28.04, 35.71, 38.95, 63.47, 64.22, 125.99, 127.57, 129.52, 129.91, 130.47, 133.65, 135.48, 143.73; HRMS (EI) \(m/z\) 365.1923 [(M–t-Bu)+, calcd. for C\(_{27}\)H\(_{38}\)O\(_2\)Si 365.1937].

Preparation of (E)-11-iodo-undec-10-enoic acid methyl ester. \(^8\) Methyl 10-undecenoate (10.0 g, 50.42 mmol) was dissolved in a 2:1 CH\(_2\)Cl\(_2\)/MeOH solution (200 mL) with 1 mL of NEt\(_3\) added. The solution was purged with N\(_2\) for 15 minutes and then cooled to \(-78\) °C. O\(_3\) was then bubbled through the solution until a blue color persisted (~1.5 h). At this time N\(_2\) was bubbled through the solution until the blue color disappeared.
Dimethyl sulfide (15 mL, 202 mmol) was added dropwise and the solution was allowed to warm to room temperature overnight (~8 h). The solvent was then concentrated and the resulting residue was purified by column chromatography (silica gel; hexanes/EtOAc 80:20) to afford 10-oxo-decanoic acid methyl ester\(^6\) (8.96 g, 90%) as a clear liquid.

Under an Ar atmosphere, TMSCl (15.3 mL, 120 mmol) was added to a suspension of CrCl\(_3\) (0.6334 g, 4 mmol), Zn (7.84 g, 120 mmol), and NaI (3.0 g, 20 mmol) in dioxane (100 mL) at 25 °C. After the reaction was stirred for 40 min, a solution of 10-oxo-decanoic acid methyl ester (4.01 g, 20 mmol) and CHI\(_3\) (15.75 g, 40 mmol) in dioxane (50 mL) was added at 25 °C via a syringe pump over 24 hours. After the addition the mixture became very thick. The reaction was quenched by the addition of water. The reaction was then extracted with hexanes (5X). The combined organics were washed with brine, dried over MgSO\(_4\), filtered and concentrated. The resulting residue was purified by column chromatography (silica gel; hexanes/EtOAc 95:5 to afford (E)-11-iodo-undec-10-enoic acid methyl ester\(^7\) (12.14 g, 63%) as a peach colored liquid. \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 1.14-1.40 (m, 10 H), 1.45-1.62 (m, 2 H), 1.98 (q, \(J = 6.94\) Hz, 2 H), 2.24 (t, \(J = 7.42\) Hz, 2 H), 3.60 (s, 3 H), 5.92 (dt, \(J = 1.40, 14.34\) Hz, 1 H), 6.44 (dt, \(J = 7.14, 14.34\) Hz, 1 H); \(^13\)C (75 MHz, CDCl\(_3\)) \(\delta\) 24.85, 28.25, 28.80, 29.00, 29.04, 29.09, 34.21, 35.92, 51.27, 74.43, 146.58, 174.36.

References


(8) This procedure is a modification of the procedure reported by Takai: Takai, K.; Ichiguchi, T.; Hikasa, S. Synlett 1999, 1268-1270.
Spectra