Microwave Assisted One Pot Hydrostannylation/Stille Couplings

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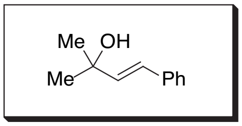
SUPPORTING INFORMATION

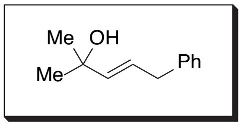
Materials and Methods

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. Chemical shifts are reported relative to the residue peaks of solvent chloroform (δ 7.24 for ^{1}H and δ 77.0 for ^{13}C). 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. The microwave oven used was a Kenmore (model 721.69182) variable power 700 W microwave oven. **Extreme caution** should be taken when heating a sealed tube in a microwave. Do not fill the reaction vessel beyond half volume. High pressures and temperatures are generated which have led to **explosions**. In the event of such explosions, glass shards from the reaction vessel can penetrate the walls of the oven. Thus, all reactions must be run in a fume hood with appropriate blast shielding in place. Pressure tubes were purchased from Ace Glass (Ace catalog No. 8648-23) and fitted with teflon® plugs (Ace catalog No. 5846-48) and teflon® encapsulated O-rings (Ace catalog No. 7855-818). These O-rings were discarded after approximately 250 minutes of microwave irradiation. (Using non-teflon® coated O-rings often resulted in catastrophic failure of the seal.) When cleaning the pressure tube, we recommend soaking and not scrubbing the tube as scratches from metal brushes can weaken the vessel and facilitate its rupture.

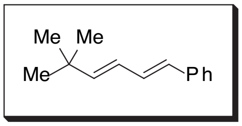
General procedure for the palladium catalyzed one-pot hydrostannylation/Stille coupling.



Preparation of E-2-methyl-4-phenyl-but-3-en-2-ol (Table 1, entry 1). To a thick walled pyrex tube containing 5 mL THF were added $Pd(PPh_3)_4$ (12 mg, 0.01 mmol), 2-methyl-3-butyn-2-ol (0.10 mL, 1 mmol), Bu_3SnCl (0.33 mL, 1.2 mmol), PMHS (90 mg, 1.5 mmol), KF (0.1743 g, 3.0 mmol), 1 mL H_2O, and catalytic TBAF (1 drop of a 1M THF solution). The reaction was closed, placed in a 250 mL beaker set in the center of a domestic microwave (glass turntable removed) and heated for 3 minutes at 140 W (20% power setting on a 700 W microwave oven). After being allowed to air cool for 10 min, $Pd(PPh_3)_4$ (12 mg, 0.01 mmol) and bromobenzene (0.16 mL, 1.5 mmol) were added and the sealed tube was irradiated at 140 W for 5 minutes. Upon cooling, the reaction was checked by TLC before a third portion of $Pd(PPh_3)_4$ (12 mg, 0.01 mmol) was added and the sealed tube was again irradiated at 140 W for another 5 minutes. After cooling, TLC showed the reaction to be complete. A saturated aqueous solution of KF (2 mL) was added and the mixture stirred for 30 min. The phases were separated and the organics were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated. The resulting residue was purified by flash chromatography (silica gel; 90/10 pentane/EtOAc with 1% TEA) to afford 153 mg (94%) of E-2-methyl-4-phenyl-but-3-en-2-ol which gave spectroscopic data consistent with those reported earlier (Marko, I. E.; Leung, C. W. J. Am. Chem. Soc. **1994**, 116, 371-372).

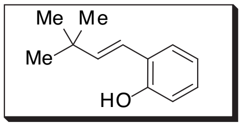


Preparation of E-2-methyl-5-phenyl-pent-3-en-2-ol (Table 1, entry 2). Applying the conditions above to 2-methyl-3-butyn-2-ol (0.10 mL, 1.0 mmol) and benzyl bromide (0.18 mL, 1.5 mmol) gave a residue which was purified by flash chromatography on silica (90/10 pentane/EtOAc; 1% TEA) to afford 180 mg (90%) of E-2-methyl-5-phenyl-pent-3-en-2-ol as a thick yellow oil. Spectroscopic data were consistent with those reported earlier (Reich, H. J.; Shah, S. K.; Chow, F. J. Am. Chem. Soc. **1979**, 101, 6648-6656.)

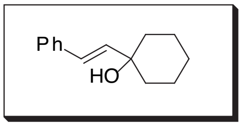


Preparation of E,E-(5,5-dimethyl-hexa-1,3-dienyl)-benzene (Table 1, entry 3). Applying the conditions above to 3,3-dimethyl-butyne (0.12 mL, 1 mmol) and E-bromostyrene (0.19 mL, 1.5 mmol) gave a residue which was purified by flash chromatography on silica (pentane) to afford 169 mg

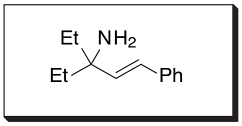
(91%) of E,E-(5,5-dimethyl-hexa-1,3-dienyl)-benzene as an oil. Spectroscopic data were consistent with those reported earlier (Maleczka, R. E., Jr.; Terstiege, I. J. Org. Chem. **1998**, 63, 9622-9623.)



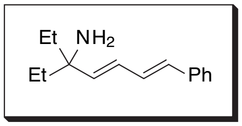
Preparation of E-2-(3,3-dimethyl-but-1-enyl)-phenol (Table 1, entry 4). Applying the conditions above to 3,3-dimethyl-butyne (0.12 mL, 1 mmol) and 2-bromophenol (0.39 mL, 1.5 mmol) gave a residue that was purified by flash chromatography on silica (pentane) to afford 120 mg (86%) of E-2-(3,3-dimethyl-but-1-enyl)-phenol as an oil. Spectroscopic data were consistent with those reported earlier (Russell, G. A.; Kim, B. H.; Kulkarni, S. V. J. Org. Chem. **1989**, 54, 3768-70.)



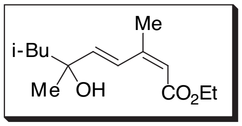
Preparation of E-1-styryl-cyclohexanol (Table 1, entry 5). Applying the conditions above to 1-ethynyl-1-cyclohexanol (0.124 g, 1 mmol) and bromobenzene (0.16 mL, 1.5 mmol) gave a residue which was purified by flash chromatography on silica (90/10 pentane/EtOAc) to afford 115 mg (57%) of E-1-styryl-cyclohexanol as an oil. Spectroscopic data were consistent with those reported earlier (Chiacchio, U; Liguori, A.; Romeo, G.; Sindona, G.; Uccella, N. Heterocycles **1993**, 36, 799-817.)



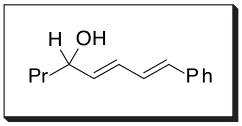
Preparation of E-1,1-diethyl-3-phenyl-allylamine (Table 1, entry 6). Applying the conditions above to 1,1-diethylpropargylamine (0.11 g, 1 mmol) and bromobenzene (0.16 mL, 1.5 mmol) gave a residue which was purified by flash chromatography on silica (50/50 pentane/EtOAc) to afford 170 mg (90%) of E-1,1-diethyl-3-phenyl-allylamine as an oil. IR (neat) 3368, 3301,1597, 1578, 972, 746 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.17-7.42 (5 H, m), 6.47 (1 H, d, J = 16.2 Hz), 6.16 (1 H, d, J = 16.2 Hz), 1.56 (4 H, qd, J = 2.5, 7.4 Hz), 1.33 (2 H, s), 0.91 (3 H, d, J = 7.4 Hz), 0.88 (3 H, d, J = 7.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.7, 137.4, 128.5, 127.3, 127.0, 126.1, 56.3, 34.1, 8.0; LRMS (EI) m/z 189.3 (M^{+}), 160.2 (100), 143.3, 128.2.



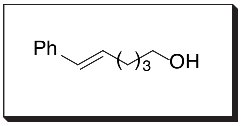
Preparation of (2E,4E)-1,1-diethyl-5-phenyl-penta-2,4-dienylamine (Table 1, entry 7). Applying the conditions above to 1,1-diethylpropargylamine (0.11 g, 1 mmol) and bromostyrene (0.19 mL, 1.5 mmol), but only irradiating in the presence of the electrophile for 5 minute, gave a residue which was purified by flash chromatography on silica (50/50 pentane/EtOAc) to afford 175 mg (81%) of (2E,4E)-1,1-diethyl-5-phenyl-penta-2,4-dienylamine as an oil. Spectroscopic data were consistent with those reported earlier (Maleczka, R. E., Jr.; Terstiege, I. J. Org. Chem. **1998**, 63, 9622-9623).



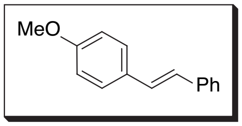
Preparation of (2Z,4E)-6-hydroxy-3,6,8-trimethyl-nona-2,4-dienoic acid ethyl ester (Table 1, entry 8). Applying the conditions above to 3,5-dimethyl-but-1-yn-3-ol (0.15 mL, 1 mmol) and Z-ethyl-3-iodo-2-butenoate (0.36 g, 1.5 mmol; prepared according to Chalcat, J. C. C. R. Acad. Sc. Paris (Serie C) **1971**, 763-765), but only irradiating in the presence of the electrophile for 5 minute, gave a residue which was purified by flash chromatography on silica (90/10 pentane/EtOAc) to afford 169 mg (81%) of (2Z,4E)-6-hydroxy-3,6,8-trimethyl-nona-2,4-dienoic acid ethyl ester as an oil. IR (neat) 3472, 1697, 1638, 1603, 1234, 1157, 735 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (1 H, d, J = 16.2 Hz), 6.15 (1 H, d, J = 16.2 Hz), 5.65 (1 H, s), 4.13 (2 H, q, J = 7.1 Hz), 1.97 (3 H, d, J = 1.2 Hz), 1.88 (1 H, br s), 1.72 (1 H, st, J = 6.6 Hz), 1.50 (2 H, dd, J = 5.8 Hz J = 2.2 Hz), 1.32 (3 H, s), 1.24 (3 H, t, J = 7.1 Hz), 0.91 (3 H, d, J = 6.8 Hz), 0.88 (3 H, d, J = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.2, 150.4, 144.6, 124.0, 117.3, 73.7, 59.7, 51.1, 28.6, 24.5, 24.4, 24.3, 21.0, 14.2; LRMS (EI) m/z 223.4 (M^{+} – OH), 197.3, 183.2, 139.2, 137.2, 109.1 (100), 95.1.



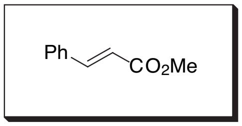
Preparation of (E,E)-8-phenyl-octa-5,7-dien-4-ol (Table 1, entry 9). Applying the conditions above to 1-hexyn-3-ol (0.12 mL, 1 mmol) and bromostyrene (0.19 mL, 1.5 mmol) gave a residue which was purified by flash chromatography on silica (90/10 pentane/EtOAc) to afford 112 mg (55%) of 8-phenyl-octa-5E,7E-dien-4-ol as an oil. IR (neat) 3352 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.98 (t, J = 7.2 Hz, 3H), 1.34-1.72 (m, 4 H), 1.81 (br s, 1 H), 4.24 (q, J = 6.5 Hz, 1 H), 5.85 (dd, J = 6.9, 15.6 Hz, 1 H), 6.41 (dd, J = 10.4, 15.3 Hz, 1 H), 6.57 (d, J = 15.7 Hz, 1 H), 6.80 (dd, J = 10.4, 15.6 Hz, 1 H), 7.21-7.49 (m, 5 H) ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.1, 136.8, 132.5, 130.5, 128.6, 128.3, 127.5, 126.3, 72.5, 39.5, 18.5, 13.9; HRMS (EI) m/z 202.1349 [(M^{+}). calcd. for $C_8H_{14}O$ 202.1358].



Preparation of 6-phenyl-hex-5-en-1-ol (Table 1, entry 10). Applying the conditions above to 5-hexyn-1-ol (0.11 mL, 1 mmol) and bromobenzene (0.16 mL, 1.5 mmol) gave a residue that was purified by flash chromatography on silica (90/10 pentane/EtOAc) to afford 90 mg (57%) of a 14:1.6:1 mixture of E-6-phenyl-hex-5-en-1-ol, Z-6-phenyl-hex-5-en-1-ol, and 5-phenyl-hex-5-en-1-ol. Spectroscopic data were consistent with those reported earlier. For E-6-phenyl-hex-5-en-1-ol and Z-6-phenyl-hex-5-en-1-ol see Shrestha, K. S.; Honda, K.; Asami, M.; Inoue, S. Bull Chem. Soc. Jpn. **1999**, 72, 73-83. For 5-phenyl-hex-5-en-1-ol see Pearson, W. H.; Szura, D. P.; Postich, M. J. J. Am. Chem. Soc. **1992**, 114, 1329-1345.

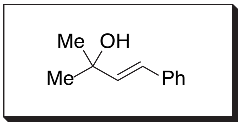


Preparation of (4-methoxyphenyl)-2-phenylethylene (Table 1, entry 11). Applying the conditions above to phenylactelylene (0.1 mL, 1 mmol) and p-bromoanisole (0.19 mL, 1.5 mmol) gave a residue which was purified by flash chromatography on silica (pentane) to afford 180 mg (86%) of E-(4-methoxyphenyl)-2-phenylethylene as a white solid. Spectroscopic data were consistent with those reported earlier (Majima, T.; Tojo, S.; Ishida, A.; Takamuku, S. J. Org. Chem. **1996**, 61, 7793-7800).

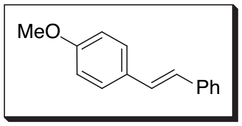


Preparation of E-3-phenyl-acrylic acid methyl ester (Table 1, entry 12). Applying the conditions above to methylpropiolate (0.08 mL, 1 mmol) and bromobenzene (0.16 mL, 1.5 mmol) gave a residue which was purified by flash chromatography on silica (99/1 pentane/EtOAc) to afford 130 mg (80%) of E-3-phenyl-acrylic acid methyl ester as an oil. The product was identical to an authentic sample (Aldrich).

General procedure for the one-pot free radical hydrostannylation/ palladium catalyzed Stille coupling (Method A).

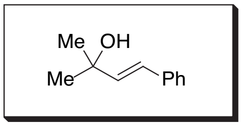


Preparation of E-2-methyl-4-phenyl-but-3-en-2-ol (Table 2, entry 1). To a thick walled pyrex tube containing 5 mL THF were added AIBN (2 mg), 2-methyl-3-butyn-2-ol (0.10 mL, 1 mmol), Bu_3SnCl (0.33 mL, 1.2 mmol), PMHS (90 mg, 1.5 mmol), KF (0.1743 g, 3.0 mmol), 1 mL H_2O, and catalytic TBAF (1 drop of a 1M THF solution). The reaction was closed, placed in a 250 mL beaker set in the center of a domestic microwave (glass turntable removed) and heated for 3 minutes at 140 W (20% power setting on a 700 W microwave oven). After being allowed to air cool for 10 min, $Pd(PPh_3)_4$ (12 mg, 0.01 mmol) and bromobenzene (0.16 mL, 1.5 mmol) were added and the sealed tube was irradiated at 140 W for 5 minutes. Upon cooling, the reaction was checked by TLC before a third portion of $Pd(PPh_3)_4$ (12 mg, 0.01 mmol) was added and the sealed tube was again irradiated at 140 W for another 5 minutes. After cooling, TLC showed the reaction to be complete. The reaction was poured into 10% ammonium hydroxide (25 mL), ether was added (25 mL) and the mixture stirred for 30 min. The phases were separated and the organics were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated. The resulting residue was purified by flash chromatography (silica gel; 90/10 pentane/EtOAc with 1% TEA) to afford 140 mg (86%) of a 20:1:1 mixture of E-2-methyl-4-phenyl-but-3-en-2-ol, Z-2-methyl-4-phenyl-but-3-en-2-ol, and 2-methyl-3-phenyl-but-3-en-2-ol which gave spectroscopic data consistent with those reported earlier. For E-2-methyl-4-phenyl-but-3-en-2-ol Z-2-methyl-4-phenyl-but-3-en-2-ol see Marko, I. E.; Leung, C. W. J. Am. Chem. Soc. **1994**, 116, 371-372. For 2-methyl-3-phenyl-but-3-en-2-ol see Yu, W.-Y.; Bensimon, C.; Alper, H. Chem. Eur. J. **1997**, 3, 417-423.

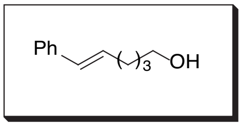


Preparation of (4-methoxyphenyl)-2-phenylethylene (Table 2, entry 2). Applying the conditions above to phenylactelylene (0.1 mL, 1 mmol) and p-bromoanisole (0.19 mL, 1.5 mmol) gave a residue which was purified by flash chromatography on silica (pentane) to afford 178 mg (85%) of E-(4-methoxyphenyl)-2-phenylethylene as a white solid. Spectroscopic data were consistent with those reported earlier (Majima, T.; Tojo, S.; Ishida, A.; Takamuku, S. J. Org. Chem. **1996**, 61, 7793-7800.)

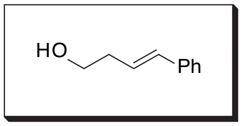
General procedure for the one-pot free radical hydrostannylation/ palladium catalyzed Stille coupling (Method B).



Preparation of E-2-methyl-4-phenyl-but-3-en-2-ol (Table 2, entry 5). To a thick walled pyrex tube containing 5 mL THF were added AIBN (2 mg), 2-methyl-3-butyn-2-ol (0.10 mL, 1 mmol), Bu_3SnH (0.32 mL, 1.2 mmol), 1 mL H_2O, and catalytic TBAF (1 drop of a 1M THF solution). The reaction was closed, placed in a 250 mL beaker set in the center of a domestic microwave (glass turntable removed) and heated for 3 minutes at 140 W (20% power setting on a 700 W microwave oven). After being allowed to air cool for 10 min, $Pd(PPh_3)_4$ (12 mg, 0.01 mmol) and bromobenzene (0.16 mL, 1.5 mmol) were added and the sealed tube was irradiated at 140 W for 5 minutes. Upon cooling, the reaction was checked by TLC before a third portion of $Pd(PPh_3)_4$ (12 mg, 0.01 mmol) was added and the sealed tube was again irradiated at 140 W for another 5 minutes. After cooling, TLC showed the reaction to be complete. The reaction was poured into 10% ammonium hydroxide (25 mL), ether was added (25 mL and the mixture stirred for 30 min. The phases were separated and the organics were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated. The resulting residue was purified by flash chromatography (silica gel; 90/10 pentane/EtOAc with 1% TEA) to afford 128 mg (79%) of a 23:1 (E/Z) mixture of 3-methyl-1-phenyl-but-1-en-3-ol. See above for spectroscopic data.



Preparation of E-6-phenyl-hex-5-en-1-ol (Table 2, entry 3). Applying the conditions above to 5-hexyn-1-ol (0.11 mL, 1 mmol) and bromobenzene (0.16 mL, 1.5 mmol) gave a residue that was purified by flash chromatography on silica (90/10 pentane/EtOAc) to afford 84 mg (48%) of a 31:7:1 mixture of E-6-phenyl-hex-5-en-1-ol, Z-6-phenyl-hex-5-en-1-ol, and 5-phenyl-hex-5-en-1-ol. See above for spectroscopic data.



Preparation of E-4-phenyl-but-3-en-1-ol (Table 2, entry 4). Applying the conditions above to 3-butyn-1-ol (0.07 mL, 1 mmol) and bromobenzene (0.16 mL, 1.5 mmol) gave a residue that was purified by flash chromatography on silica (90/10 pentane/EtOAc) to afford 65 mg (46%) of 27:4:1 E/Z mixture of E-1-phenyl-but-1-en-4-ol, Z-1-phenyl-but-1-en-4-ol, and 2-phenyl-but-1-en-4-ol. Spectroscopic data obtained were consistent with those reported earlier. For E-4-phenyl-but-3-en-1-ol and Z-4-phenyl-but-3-en-1-ol see Charette, A. B.; Juteau, H.; Lebel, H.; Molinaro, C. J. Am. Chem. Soc. **1998**, 120, 11943-11952. For 3-phenyl-but-3-en-1-ol see Maercker, A.; Weber, K. Liebigs Ann. Chem. **1972**, 756, 20-32.