Stereoselective Organozinc Addition Reactions to 1,2–Dihydropyrans for the Assembly of Complex Pyran Structures

Supplementary Material
(10 pages)

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General. All reagents were commercially obtained unless otherwise noted. Reactions were performed using oven-dried glassware under an atmosphere of dry nitrogen. Air- and moisture-sensitive liquids and solutions were transferred via syringe or stainless steel cannula. Organic solutions were concentrated under reduced pressure (~15 mm Hg) by rotary evaporation. Dichloromethane was freshly distilled from CaH_2 immediately prior to use. Tetrahydrofuran (THF) and diethyl ether were freshly distilled from sodium benzophenone ketyl immediately prior to use. Toluene was distilled from sodium metal. *N,N*–Dimethylacetamide (DMA) was distilled from $CaSO_4$ and stored in a Schlenk flask over activated 4Å molecular sieves under an atmosphere of N_2. Alkyl iodides were prepared from the corresponding bromides by treatment with NaI in acetone, and passed through a short plug of basic alumina immediately prior to use. Dihydropyranyl substrates were prepared following established procedures.[1] Zinc chloride ($ZnCl_2$) was fused under vacuum (~1 mm Hg), ground to a fine powder, and stored in an inert atmosphere N_2 glove box. Zn(Cu) couple was prepared with zinc powder (Fisher, 99.2%) by the method of Simmons and Smith.[2] The couple was heated under vacuum at 40 °C for 12 h and stored in a N_2 glovebox (note: it is necessary that the couple be stored in a glove box or prepared immediately prior to use). $MgBr_2 \cdot (Et_2O)_2$ was flame dried under vacuum (~1 mm Hg) and stored in a N_2 glove box. Chromatographic purification of products was accomplished using forced-flow chromatography on EM Science Geduran silica gel 60 (35–75 μm). Thin-layer chromatography (TLC) was performed on EM Science silica gel 60 F_{254} plates (250 μm). Visualization of the developed chromatogram was accomplished by fluorescence quenching and by staining with ethanolic anisaldehyde, aqueous potassium permanganate, or aqueous ceric ammonium molybdate (CAM) solution.

NMR spectra were acquired on a Varian Inova spectrometer operating at 500 and 125 MHz for ^1H and ^{13}C, respectively, and are referenced internally according to residual protio solvent signals. Data for ^1H are recorded as follows: chemical shift (δ, ppm), multiplicity (s, singlet; br s, broad singlet; d, doublet; t, triplet; q, quartet; sext, sextet; sept, septet; m, multiplet), integration, coupling constant (Hz). Data for ^{13}C are reported in terms of chemical shift (δ, ppm). ^1H NMR nOe difference spectra were measured on degassed samples using a Varian Inova 500 spectrometer and quantitated by integrating the difference spectrum. IR spectra were recorded on a Perkin-Elmer Paragon 500 FTIR spectrometer using NaCl salt plates and are reported in frequency of absorption. High-resolution mass spectra were obtained from the Mass Spectrometry Facility, University of California at Riverside.

Experimental procedures and characterization data for arylzinc addition reactions (see Table 1):

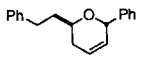
Procedure A

To a stirred solution of aryl halide (0.82 mmol, 2.0 equiv) in 0.8 mL of Et_2O at –78 °C was added dropwise a 1.7 M solution of *t*–BuLi (960 μL, 1.63 mmol, 4.0 equiv) in pentane. A solution of $ZnCl_2$ (116 mg, 0.85 mmol, 2.1 equiv) in 1.2 mL of Et_2O was next added via cannula. Transfer of the $ZnCl_2$ was made quantitative with an additional 0.2 mL of Et_2O. Following the addition of $ZnCl_2$ the reaction flask was removed from the cold bath and the contents stirred for 20 min. To the resulting white slurry was then added via cannula a solution of dihydropyranyl acetate (0.41 mmol) in 1.0 mL of Et_2O. An additional 0.2 mL of Et_2O was used to quantitate the transfer. The white suspension was stirred at 23 °C until TLC indicated the complete consumption of the starting dihydropyran (3–8 h). The reaction was quenched by the addition of 5 mL of saturated aqueous NH_4Cl and poured into a separatory funnel with 15 mL of CH_2Cl_2. The organic phase was collected and the aqueous layer was extracted with 2 x 10 mL of CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure to an oily residue. Purification by chromatography on silica gel (conditions given below) afforded the desired product.

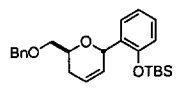
Procedure B

A 1.7 M solution of *t*–BuLi in pentane was added dropwise to a stirred solution of aryl halide (0.82 mmol, 2.0 equiv) in 0.8 mL of Et_2O at –78 °C. A solution of $ZnCl_2$ (116 mg, 0.85 mmol, 2.1 equiv) in 1.2 mL of Et_2O was next added via cannula. Transfer of the $ZnCl_2$ was made quantitative with 0.2 mL of Et_2O. Following the addition of $ZnCl_2$ the

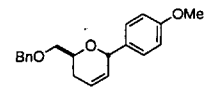
reaction flask was removed from the cold bath and the contents stirred for 20 min. To the resulting white suspension was added via cannula a solution of $MgBr_2$ (105 mg, 0.57 mmol, 1.4 equiv) in 1.0 mL of Et_2O. An additional 0.2 mL of Et_2O was used to complete the transfer. Dihydropyranyl acetate (0.41 mmol) as a solution in 1.0 ml of Et_2O was then added dropwise via cannula to the reaction mixture. Quantitative transfer of this material was ensured with 0.2 mL of Et_2O. The resulting suspension was stirred at 23 °C until TLC indicated the complete consumption of the starting dihydropyran (12–24 h). The reaction was quenched by the addition of 5 mL of saturated aqueous NH_4Cl and poured into a separatory funnel with 15 mL of CH_2Cl_2. The organic phase was collected and the aqueous layer was extracted with 2 x 10 mL of CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure to an oily residue. Purification by chromatography on silica gel (conditions given below) afforded the desired product.



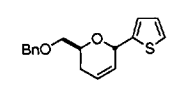
Prepared according to procedure **A** and purified by chromatography on silica gel (32:1 hexanes/EtOAc); colorless oil (88%): TLC R_f = 0.73 (6:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.45-7.35 (m, 5H), 7.19-7.12 (m, 3H), 6.94-6.91 (m, 2H), 6.10-6.02 (m, 2H), 5.34 (br s, 1H), 3.58-3.53 (m, 1H), 2.78-2.73 (m, 1H), 2.53 (dt, 1H, *J* = 13.4, 8.3 Hz), 2.15-2.08 (m, 1H), 2.05-2.00 (m, 1H), 1.94-1.87 (m, 1H), 1.74-1.67 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 142.1, 141.1, 128.5, 128.4, 128.24, 128.17, 127.6, 127.4, 126.0, 125.5, 74.1, 66.2, 37.4, 31.5, 31.1 ppm; IR (thin film) ν 3028, 2923, 1494, 1453, 1259, 1194, 1177, 1068, 1030, 751, 698 cm^{-1}; HRMS (EI) calcd for $C_{19}H_{20}O$ 264.1514 found 264.1511 (M^+).



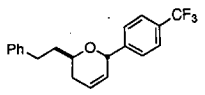
Prepared according to procedure **A** and purified by chromatography on silica gel (32:1 hexanes/EtOAc); colorless oil (82%): TLC R_f = 0.65 (6:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.42 (dd, 1H, *J* = 7.6, 1.5 Hz), 7.36-7.28 (m, 5H), 7.20 (dt, 1H, *J* = 7.8, 1.7 Hz), 6.96 (dt, 1H, *J* = 7.5, 0.7 Hz), 6.87 (dd, 1H, *J* = 8.1, 0.7 Hz), 6.08-6.04 (m, 1H), 5.97-5.94 (m, 1H), 5.70 (br s, 1H), 4.57 (q, 2H, *J* = 12.2 Hz), 4.00 (sext, 1H, *J* = 4.6 Hz), 3.60 (dd, 1H, *J* = 10.3, 5.6 Hz), 3.53 (dd, 1H, *J* = 10.1, 4.9 Hz), 2.27-2.20 (m, 1H), 2.16-2.11 (m, 1H), 1.06 (s, 9H), 0.28 (s, 3H), 0.26 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 153.6, 138.4, 130.9, 128.9, 128.6, 128.3, 128.0, 127.7, 127.4, 124.7, 120.4, 118.8, 73.4, 72.8, 69.1, 67.4, 27.4, 25.8, 18.3, -4.0, -4.4 ppm; IR (thin film) ν 3033, 2895, 2955, 2929, 2858, 1598, 1484, 1452, 1277, 1252, 1102, 1074, 920, 839, 782 cm^{-1}; HRMS (EI) calcd for $C_{25}H_{34}O_3Si$ 410.2277 found 411.2367 (MH^+).



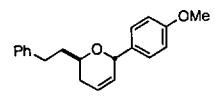
Prepared according to procedure **A** and purified by chromatography on silica gel (32:1 hexanes/EtOAc); colorless oil (81%): TLC R_f = 0.44 (6:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.39-7.27 (m, 7H), 6.92-6.89 (m, 2H), 6.09-6.05 (m, 1H), 6.03-5.99 (m, 1H), 5.30 (br s, 1H), 4.56 (d, 1H, *J* = 11.6 Hz), 3.86-3.82 (m, 4H), 3.57 (dd, 1H, *J* = 10.3, 5.6 Hz), 3.50 (dd, 1H, *J* = 10.3, 4.4 Hz), 2.28-2.21 (m, 1H), 2.07-2.02 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 159.1, 138.3, 133.0, 129.4, 128.2, 127.62, 127.58, 127.4, 125.3, 113.5, 73.6, 73.1, 72.6, 66.4, 55.2, 27.3 ppm; IR (thin film) ν 3032, 2896, 1610, 1510, 1453, 1245, 1174, 1070, 834, 737 cm^{-1}; HRMS (EI) calcd for $C_{20}H_{22}O_3$ 310.1569 found 310.1580 (M^+).



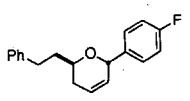
Prepared according to procedure **A** and purified by chromatography on silica gel (24:1 hexanes/EtOAc); colorless oil (74%): TLC R_f = 0.61 (6:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.35-7.25 (m, 6H), 7.01-6.98 (m, 2H), 6.13-6.01 (m, 2H), 5.50 (br s, 1H), 4.56 (d, 1H, *J* = 12.1 Hz), 4.53 (d, 1H, *J* = 12.0 Hz), 3.95-3.91 (m, 1H), 3.55 (dd, 1H, *J* = 10.3, 5.5 Hz), 3.50 (dd, 1H, *J* = 10.5, 4.4 Hz), 2.29-2.22 (m, 1H), 2.04-1.98 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 144.7, 138.3, 128.3, 127.6, 127.5, 127.0, 126.6, 126.4, 125.8, 125.7, 73.2, 72.6, 70.1, 66.8, 27.2 ppm; IR (thin film) ν 3033, 2865, 1719, 1666, 1453, 1415, 1362, 1276, 1260, 1095, 1075, 737 cm^{-1}; HRMS (EI) calcd for $C_{17}H_{18}O_2S$ 286.1028 found 287.1117 (MH^+).



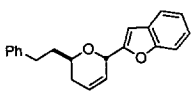
Prepared according to procedure **A** and purified by chromatography on silica gel (28:1 hexanes/EtOAc); white solid (78%): TLC R_f = 0.53 (6:1 hexanes/EtOAc), 0.67 (100:1 toluene/Et_2O); ^1H NMR ($CDCl_3$, 500 MHz) δ 7.65 (d, 2 H, J = 8.1 Hz), 7.55 (d, 2H, J = 8.6 Hz), 7.17-7.11 (m, 3H), 6.92-6.90 (m, 2H), 6.12-6.08 (m, 1H), 6.03-5.99 (m, 1H), 5.34 (br s, 1H), 3.50-3.44 (m, 1H), 2.78-2.72 (m, 1H), 2.56-2.50 (m, 1H), 2.15-2.08 (m, 1H), 2.05-2.00 (m, 1H), 1.94-1.87 (m, 1H), 1.76-1.69 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 145.1, 141.7, 129.8 (q, J_{C-F} = 32.0 Hz), 128.5, 128.4, 128.2, 126.8, 126.5, 125.6, 125.19, 125.16, 73.4, 66.5, 37.2, 31.4, 30.9 ppm; IR (thin film) ν 3036, 3030, 2927, 2890, 1618, 1605, 1496, 1454, 1418, 1325, 1164, 1018, 890 cm^{-1}; HRMS (EI) calcd for $C_{20}H_{19}F_3O$ 332.1388 found 332.1396 (M^+).



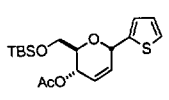
Prepared according to procedure **A** and purified by chromatography on silica gel (24:1 hexanes/EtOAc); colorless oil (88%): TLC R_f = 0.66 (6:1 hexanes/EtOAc); ^1H NMR ($CDCl_3$, 500 MHz) δ 7.40-7.37 (m, 2H), 7.20-7.14 (m, 3H), 6.97-6.92 (m, 4H), 6.09-6.05 (m, 1H), 6.02-5.99 (m, 1H), 5.31 (br s, 1H), 3.89 (s, 3H), 3.56-3.51 (m, 1H), 2.77-2.72 (m, 1H), 2.56-2.50 (m, 1H), 2.14-2.08 (m, 1H), 2.05-1.99 (m, 1H), 1.93-1.86 (m, 1H), 1.73-1.66 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 159.2, 142.1, 133.2, 129.8, 128.5, 128.1, 127.6, 125.9, 125.5, 113.5, 73.8, 65.7, 55.3, 37.4, 31.5, 31.1 ppm; IR (thin film) ν 3000, 3028, 2930, 2835, 1609, 1509, 1245, 1174, 1070, 1036,834, 820, 700 cm^{-1}; HRMS (EI) calcd for $C_{20}H_{22}O_2$ 294.1620 found 294.1623 (M^+).



Prepared according to procedure **A** and purified by chromatography on silica gel (19:1 hexanes/EtOAc); colorless oil (85%): TLC R_f = 0.70 (6:1 hexanes/EtOAc); ^1H NMR ($CDCl_3$, 500 MHz) δ 7.44-7.41 (m, 2H), 7.21-7.08 (m, 5H), 6.96-6.93 (m, 2H), 6.11-6.07 (m, 1H), 6.02-5.98 (m, 1H), 5.31 (br s, 1H), 3.53-3.48 (m, 1H), 2.78-2.73 (m, 1H), 2.56-2.50 (m, 1H), 2.15-2.09 (m, 1H), 2.06-2.01 (m, 1H), 1.94-1.87 (m, 1H), 1.75-1.68 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 162.4 (d, J_{C-F} = 246.7 Hz), 141.9, 136.9 (d, J_{C-F} = 3.2 Hz), 130.1 (d, J_{C-F} = 7.5 Hz), 128.4, 128.2, 127.1, 126.3, 125.6, 115.0 (d, J_{C-F} = 21.3 Hz), 73.4, 66.0, 37.3, 31.4, 31.0 ppm; IR (thin film) ν 3029, 2925, 2888, 1602, 1506, 1223, 1156, 1073, 838, 700 cm^{-1}; HRMS (EI) calcd for $C_{19}H_{19}FO$ 282.1420 found 282.1429 (M^+).

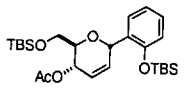


Prepared according to procedure **A** and purified by chromatography on silica gel (32:1 hexanes/EtOAc); white solid (66% of a 6:1 mixture of α/β anomers): TLC R_f = 0.70 (6:1 hexanes/EtOAc); ^1H NMR ($CDCl_3$, 500 MHz) δ 7.61-7.58 (m, 2H), 7.39-7.34 (m, 1H), 7.31-7.28 (m, 1H), 7.05-7.02 (m, 1H), 6.91 (d, 4H, J = 4.4 Hz), 6.61 (s, 1H), 6.14-6.10 (m, 1H), 6.03-5.99 (m, 1H), 5.48 (br d, 1H, J = 2.2 Hz), 3.69-3.64 (m, 1H), 2.79-2.74 (m, 1H), 2.76-2.64 (m, 1H), 2.20-2.13 (m, 1H), 2.03-1.90 (m, 2H), 1.79-1.72 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.1, 155.2, 141.7, 128.5, 128.1, 128.0, 127.4, 125.4, 124.6, 124.4, 122.7, 121.1, 111.5, 106.2, 68.9, 66.5, 37.3, 31.2, 31.0 ppm; IR (thin film) ν 3030, 2923, 1453, 1256, 1166, 1074, 971 cm^{-1}; HRMS (EI) calcd for $C_{21}H_{20}O_2$ 304.1463 found 304.1473 (M^+).

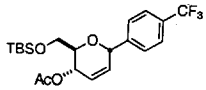


Prepared according to procedure **B** (note: the reaction mixture was stirred for 10 h at 23 °C. The reaction vessel was then equipped with a reflux condenser and the contents stirred at 35 °C for 8 h) and purified by chromatography on silica gel (19:1 hexanes/EtOAc); colorless oil (69% of a 7:1 mixture of α/β anomers); purification by chromatography on silica gel using 100:1 toluene/Et_2O as eluent provided a sample of the pure α anomer: TLC R_f = 0.50 (6:1 hexanes/EtOAc); ^1H NMR (α anomer, $CDCl_3$, 500 MHz) δ 7.31 (dd, 1H, J = 5.1, 0.7 Hz), 7.03 (br d, 1H, J = 3.4 Hz), 6.98 (dd, 1H, J = 5.0, 3.5 Hz), 6.16 (ddd, 1H, J = 10.3, 3.2, 1.7 Hz), 5.96 (dt, 1H, J = 10.3, 2.2 Hz), 5.50 (br d, 1H, J = 2.2 Hz), 5.32-5.30 (m, 1H), 3.76-3.71 (m, 3H), 2.07 (s, 3H), 0.86 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.4, 142.5, 130.4, 126.7, 126.6, 126.2, 126.1, 71.4, 69.7, 65.3, 62.9, 25.9, 21.1, 18.3, -5.4, -5.5 ppm; IR (thin film) ν 2954, 2929, 2857, 1740,

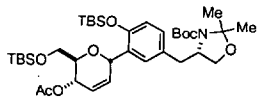
1370, 1233, 1121, 1094, 1036, 837, 778 cm^{-1}; HRMS (EI) calcd for $C_{18}H_{28}O_4SiS$ 368.1478 found 369.1544 (MH^+).



Prepared according to procedure **B** and purified by chromatography on silica gel (32:1 hexanes/EtOAc); colorless oil (75%): TLC R_f = 0.65 (6:1 hexanes/EtOAc); ^1H NMR ($CDCl_3$, 500 MHz) δ 7.45 (dd, 1H, J = 7.8, 1.7 Hz), 7.17 (dt, 1H, J = 7.6, 1.7 Hz), 6.95 (dt, 1H, J = 7.5, 1.1 Hz), 6.82 (dd, 1H, J = 8.1, 1.2 Hz), 6.08 (ddd, 1H, J = 11.0, 3.6, 1.2 Hz), 5.95 (ddd, 1H, J = 10.4, 3.2, 2.2 Hz), 5.64 (dd, 1H, J = 4.6, 2.2 Hz), 5.30-5.27 (m, 1H), 3.89 (q, 1H, J = 5.3 Hz), 3.77 (dd, 2H, J = 5.0, 1.1 Hz), 2.10 (s, 3H), 1.02 (s, 9H), 0.88 (s, 9H), 0.26 (s, 3H), 0.25 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.5, 153.3, 132.4, 129.6, 128.8, 128.4, 123.7, 120.9, 118.7, 73.1, 68.1, 65.3, 62.7, 25.84, 25.78, 21.2, 18.3, 18.2, -4.0, -4.4, -5.4, -5.5 ppm; IR (thin film) ν 2956, 2930, 2886, 2858, 1741, 1599, 1582, 1487, 1279, 1253, 1232, 1094, 920, 839, 780 cm^{-1}; HRMS (EI) calcd for $C_{26}H_{44}O_5Si_2$ 492.2727 found 493.2805 (MH^+).



Prepared according to procedure **B** and purified by chromatography on silica gel (22:1 hexanes/EtOAc); colorless oil (77%): TLC R_f = 0.34 (6:1 hexanes/EtOAc); ^1H NMR ($CDCl_3$, 500 MHz) δ 7.59 (d, 2H, J = 8.3 Hz), 7.53 (d, 2H, J = 8.5 Hz), 6.15 (ddd, 1H, J = 10.4, 3.1, 1.5 Hz), 5.98 (ddd, 1H, J = 11.9, 2.9, 2.2 Hz), 5.32 (br s, 1H), 5.25-5.23 (m, 1H), 3.75-3.66 (m, 3H), 2.05 (s, 3H), 0.85 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.5, 143.6, 130.9, 130.0 (q, J_{C-F} = 32.0 Hz), 127.8, 125.6, 125.4, 125.3, 72.72, 72.69, 65.2, 62.9, 25.8, 21.1, 18.3, -5.4, -5.5 ppm; IR (thin film) ν 2955, 2931, 2859, 1743, 1372, 1327, 1235, 1166, 1128, 1068, 1018, 837, 776 cm^{-1}; HRMS (EI) calcd for $C_{21}H_{29}F_3O_3Si$ 430.1787 found 431.1864 (MH^+).



Prepared according to procedure **B** (note: the reaction vessel was equipped with a reflux condenser following the addition of dihydropyran and the mixture stirred at 35 °C for 24 h) and purified by chromatography on silica gel (16:1 hexanes/EtOAc); white foam (75%): TLC R_f = 0.57 (6:1 hexanes/EtOAc); ^1H NMR (C_6D_6, 500 MHz, VT 70 °C) δ 7.50 (s, 1H), 6.97 (br d, 1H, J = 6.4 Hz), 6.77 (d, 1H, J = 8.1 Hz), 5.94 (ddd, 1H, J = 10.3, 3.2, 2.2 Hz), 5.89 (ddd, 1H, J = 10.3, 2.5, 1.3 Hz), 5.79 (dd, 1H, J = 4.4, 2.2 Hz), 5.53-5.52 (m, 1H), 4.04 (q, 1H, J = 5.4 Hz), 3.99 (br s, 1H), 3.84-3.78 (m, 2H), 3.71 (dd, 1H, J = 9.0, 1.7 Hz), 3.56 (dd, 1H, J = 8.8, 6.0 Hz), 3.15 (br s, 1H), 2.69 (dd, 1H, J = 13.1, 10.0 Hz), 1.78 (s, 3H), 1.62 (br s, 3H) 1.47 (br s, 12H), 1.01 (s, 9H), 0.91 (s, 9H), 0.20 (s, 3H), 0.16 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H) ppm; ^{13}C NMR (C_6D_6, 125 MHz, VT 70 °C) δ 169.7, 152.7, 152.0, 132.4, 131.6, 130.5, 130.3, 130.1, 127.5, 125.1, 119.2, 79.3, 78.3, 73.4, 68.5, 66.4, 65.7, 63.4, 59.7, 28.7, 26.1, 26.0, 20.7, 18.5, -4.0, -4.2, -5.2, -5.3 ppm; (thin film) ν 2955, 2929, 2858, 1739, 1699, 1495, 1386, 1365, 1255, 1235, 1094, 839, 780 cm^{-1}; HRMS (FAB^+) calcd for $C_{37}H_{63}NO_8Si_2$ 709.4092 found 728.4023 (MNa^+).

Experimental procedures and characterization data for alkylzinc addition reactions (see Table 2):

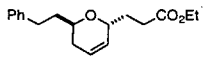
Procedure C

In a N_2 glove box, a 10 mL flask was charged with Zn(Cu) couple (151 mg, 2.3 mmol, 3.3 equiv) and capped with a reflux condenser and rubber septum. The apparatus was removed from the glove box and to it was added via cannula a solution of the alkyl iodide (1.46 mmol, 2.0 equiv) and DMA (270 μL, 2.91 mmol, 4.0 equiv) in 1.0 mL of toluene. After 5 min of stirring, the suspension was heated at 63–65 °C until the starting iodide was consumed, as determined by TLC (2–4 h). The solution was then cooled to 25 °C and transferred via cannula to a flask containing $ZnCl_2$ (150 mg, 1.10 mmol, 0.75 equiv). After stirring for 10 min, a solution of dihydropyranyl acetate (0.75 mmol) in 0.3 mL of toluene was added dropwise via cannula. Transfer of this material was made quantitative with 0.2 mL of toluene. The resulting suspension was stirred vigorously for 12 h. The reaction was quenched by the addition of 5 mL of 1 M aqueous HCl and the biphasic mixture was stirred for 5 min. The organic phase was collected and the

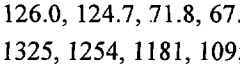
aqueous layer was extracted with 3 x 10 mL of CH_2Cl_2. The combined organic extracts were washed successively with 1 x 10 mL portions of saturated aqueous NH_4Cl, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to an oily residue. Purification by chromatography on silica gel (conditions given below) afforded the desired product.

Procedure D

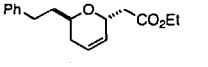
In a N_2 glove box, a 10 mL flask was charged with Zn(Cu) couple (528 mg, 8.1 mmol, 8.0 equiv) and capped with a reflux condenser and rubber septum. The apparatus was removed from the glove box and to it was added via cannula a solution of ethyl iodoacetate (480 μL, 4.1 mmol, 4.0 equiv) in 1.0 mL of CH_2Cl_2. Gas evolution was evident within 5 min following the addition; stirring was continued until TLC indicated the complete consumption of the starting iodide (45 min). The suspension was diluted with 1.0 mL of CH_2Cl_2 and added via cannula to a flask containing $ZnCl_2$ (277 mg, 2.00 mmol, 0.5 equiv). Transfer of this material was made quantitative with 1.0 mL of CH_2Cl_2. After stirring for 10 min, a solution of dihydropyranyl acetate (1.00 mmol) in 0.3 mL toluene was added dropwise via cannula. Quantitative transfer of the dihydropyran was ensured with an additional 0.2 mL of toluene. The resulting suspension was stirred for 12 h. The reaction was quenched by the addition of 5 mL of 1 M aqueous HCl and the biphasic mixture was stirred vigorously for 5 min. The organic phase was collected and the aqueous layer was extracted with 3 x 10 mL of CH_2Cl_2. The combined organic extracts were washed successively with 1 x 10 mL portions of saturated aqueous NH_4Cl, saturated aqueous NaHCO3, and saturated aqueous NaCl. The organic layer was dried over Na2SO4 and concentrated under reduced pressure to an oily residue. Purification by chromatography on silica gel (conditions given below) afforded the desired product.



Prepared according to procedure C and purified by chromatography on silica gel (13:1 hexanes/EtOAc); colorless oil (72%): TLC R_f = 0.37 (7:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.33-7.28 (m, 2H), 7.25-7.19 (m, 3H), 5.86-5.82 (m, 1H), 5.73-5.70 (m, 1H), 4.22 (br d, 1H, *J* = 10.0 Hz), 4.18 (q, 2H, *J* = 7.0 Hz), 3.69 (sept, 1H, *J* = 4.0 Hz), 2.91-2.85 (m, 1H), 2.71-2.65 (m, 1H), 2.59-2.46 (m, 2H), 2.07-1.75 (m, 6H), 1.29 (t, 3H, *J* = 7.5 Hz) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 173.9, 142.4, 129.4, 128.7, 128.6, 126.0, 124.7, 71.8, 67.2, 60.6, 37.3, 32.3, 31.1, 30.9, 29.2, 14.5 ppm; IR (thin film) ν 2929, 1733, 1496, 1454, 1374, 1325, 1254, 1181, 1095, 1080, 1030, 750 cm^{-1}; HRMS (EI) calcd for $C_{18}H_{24}O_3$ 288.1725 found 288.1729 (M^+).

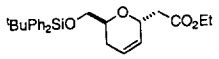


Prepared according to procedure **C** and purified by chromatography on silica gel (13:1 hexanes/EtOAc); colorless oil (72%): TLC R_f = 0.29 (10:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.75-7.70 (m, 4H), 7.47-7.39 (m, 6H), 5.87-5.83 (m, 1H), 5.73-5.69 (m, 1H), 4.19 (br d, 1H, *J* = 10.0 Hz), 4.16-4.10 (m, 2H), 3.85-3.80 (m, 1H), 3.77 (dd, 1H, *J* = 10.5, 6.5 Hz), 3.62 (dd, 1H, *J* = 10.3, 5.0 Hz), 2.60-2.54 (m, 1H), 2.50-2.44 (m, 1H), 2.06-1.91 (m, 3H), 1.85-1.78 (m, 1H), 1.82 (t, 3H, *J* = 7.0 Hz), 1.09 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 174.0, 135.9, 133.9, 133.8, 129.91, 129.89, 129.6, 127.9, 124.4, 71.9, 68.6, 66.9, 60.5, 30.9, 29.0, 27.4, 27.1, 19.5, 14.5 ppm; IR (thin film) ν 3033, 2930, 2858, 1737, 1473, 1428, 1373, 1254, 1183, 1108, 1038, 824, 800, 741cm^{-1}; HRMS (FAB$^+$) calcd for $C_{27}H_{36}O_4Si$ 452.2383 found 475.2298 (MNa^+).



Prepared according to procedure **D** and purified by chromatography on silica gel (14:1 hexanes/EtOAc); clear oil (60%): TLC R_f = 0.37 (7:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.32-7.29 (m, 2H), 7.26-7.19 (m, 3H), 5.91-5.87 (m, 1H), 5.76-5.72 (m, 1H), 4.79-4.75 (m, 1H), 4.23 (q, 2H, *J* = 7.0 Hz), 3.70 (sept, 1H, *J* = 4.0 Hz), 2.88-2.83 (m, 1H), 2.73-2.64 (m, 2H), 2.49 (dd, 1H, *J* = 15.0, 5.0 Hz), 2.06-1.88 (m, 3H), 1.81-1.74 (m, 1H), 1.33 (t, 3H, *J* = 7.5 Hz) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.4, 142.6, 128.7, 128.6, 128.4, 126.0, 125.6, 69.9, 67.5, 60.9, 39.8, 37.4, 32.1, 30.8, 14.6 ppm; IR (thin film) ν 2981, 2929, 1736, 1604, 1496, 1455, 1392, 1369, 1272, 1196, 1157, 1094, 1030 cm^{-1}; HRMS (EI) calcd for $C_{17}H_{22}O_3$ 274.1569

found 274.1568 (M^+).

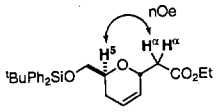


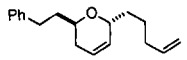
Prepared according to procedure **D** and purified by chromatography on silica gel (15:1 hexanes/EtOAc); colorless oil (60%): TLC R_f = 0.30 (10:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.73-7.69 (m, 4H), 7.47-7.39 (m, 6H), 5.93-5.89 (m, 1H), 5.76-5.72 (m, 1H), 4.73-4.71 (m, 1H), 4.19-4.12 (m, 2H), 3.85-3.82 (m, 1H), 3.79 (dd, 1H, J = 10.0, 5.0 Hz), 3.64 (dd, 1H, J = 10.0, 5.5 Hz), 2.69 (dd, 1H, J = 15.0, 5.5 Hz), 2.50 (dd, 1H, J = 15.0, 5.5 Hz), 2.13-1.99 (m, 2H), 1.25 (t, 3H, J = 7.5 Hz), 1.09 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.2, 135.9, 133.9, 133.8, 129.9, 128.5, 127.9, 125.2, 69.8, 69.0, 66.8, 60.8, 39.7, 27.3, 27.1, 19.5, 14.5 ppm; IR (thin film) ν 2931, 2858, 1737, 1428, 1372, 1271, 1198, 1158, 1112, 1038, 824, 741, 703 cm^{-1}; HRMS (FAB$^+$) calcd for $C_{26}H_{34}O_2Si$ 438.2226 found 461.2121 (MNa^+).

^{1}H NMR nOe ($CDCl_3$, 500 MHz)

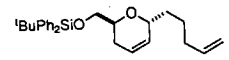
C5 → Cα: 1.4%

Cα → **C5**: 1.6%

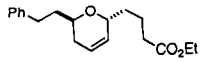




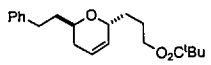
Prepared according to procedure **C** and purified by chromatography on silica gel (30:1 hexanes/EtOAc); colorless oil (63%): TLC R_f = 0.47 (10:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.35-7.32 (m, 2H), 7.28-7.22 (m, 3H), 5.93-5.81 (m, 2H), 5.77-5.73 (m, 1H), 5.12-5.07 (m, 1H), 5.04-5.01 (m, 1H), 4.23-4.21 (m, 1H), 3.71 (sept, 1H, J = 4.0 Hz), 2.94-2.89 (m, 1H), 2.75-2.69 (m, 1H), 2.21-2.13 (m, 2H), 2.07-1.91 (m, 3H), 1.84-1.76 (m, 1H), 1.74-1.66 (m, 2H), 1.59-1.48 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 142.6, 139.0, 130.2, 128.7, 128.6, 126.0, 124.0, 114.9, 72.7, 67.1, 37.4, 34.0, 33.7, 32.3, 31.1, 25.6 ppm; IR (thin film) ν 3029, 2930, 1640, 1604, 1496, 1455, 1392, 1195, 1079, 1031, 994, 910, 748 cm^{-1}; HRMS (EI) calcd for $C_{18}H_{24}O$ 256.1827 found 256.1833 (M^+).



Prepared according to procedure **C** and purified by chromatography on silica gel (40:1 hexanes/EtOAc); colorless oil (63%): TLC R_f = 0.50 (10:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.76-7.72 (m, 4H), 7.48-7.40 (m, 6H), 5.88-5.80 (m, 2H), 5.74-5.71 (m, 1H), 5.07-5.02 (m, 1H), 5.00-4.97 (m, 1H), 4.19-4.17 (m, 1H), 3.88-3.79 (m, 2H), 3.64 (dd, 1H, J = 10.0, 5.0 Hz), 2.15-1.94 (m, 4H), 1.72-1.64 (m, 2H), 1.56-1.45 (m, 2H), 1.11 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 139.1, 135.9, 134.0, 133.9, 130.3, 129.9, 127.9, 123.7, 114.8, 72.7, 68.6, 67.0, 33.9, 33.6, 27.5, 27.1, 25.4, 19.5 ppm; IR (thin film) ν 3072, 2930, 2858, 1641, 1472, 1428, 1361, 1194, 1113, 998, 910, 824, 799, 740 cm^{-1}; HRMS (FAB$^+$) calcd for $C_{27}H_{36}O_2Si$ 420.2485 found 443.2381 (MNa^+).



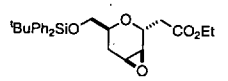
Prepared according to procedure **C** and purified by chromatography on silica gel (15:1 hexanes/EtOAc); colorless oil (67%): TLC R_f = 0.35 (7:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.32-7.29 (m, 2H), 7.25-7.19 (m, 3H), 5.83-5.79 (m, 1H), 5.73-5.69 (m, 1H), 4.21-4.19 (m, 1H), 4.17 (q, 2H, J = 7.0 Hz), 3.69 (sept, 1H, J = 4.0 Hz), 2.91-2.86 (m, 1H), 2.72-2.66 (m, 1H), 2.39 (t, 2H, J = 7.0 Hz), 2.06-1.87 (m, 4H), 1.82-1.64 (m, 3H), 1.54-1.47 (m, 1H), 1.29 (t, 3H, J = 7.5 Hz) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 173.8, 142.5, 129.8, 128.7, 128.6, 126.0, 124.3, 72.4, 67.1, 60.5, 37.4, 34.4, 33.6, 32.3, 31.0, 21.9, 14.5 ppm; IR (thin film) ν 2932, 1734, 1668, 1604, 1496, 1455, 1374, 1241, 1186, 1155, 1098, 1079, 1031, 750 cm^{-1}; HRMS (EI) calcd for $C_{19}H_{26}O_3$ 302.1882 found 302.1892 (M^+).



Prepared according to procedure **C** (note: for optimal results 3 equiv of 3-iodopropanol pivaloate ester and 4 equiv of Zn(Cu) are employed) and purified by chromatography on silica gel (14:1 hexanes/EtOAc); colorless oil (69%): TLC R_f = 0.43 (7:1 heaxnes/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.33-7.29 (m, 2H), 7.25-7.20 (m, 3H), 5.85-5.81 (m, 1H), 5.73-5.71 (m, 1H), 4.22-4.21 (m, 1H), 4.18-4.10

(m, 2H), 3.69 (sept, 1H, J = 4.0 Hz), 2.92-2.86 (m, 1H), 2.72-2.66 (m, 1H), 2.07-1.89 (m, 4H), 1.83-1.67 (m, 3H), 1.58-1.51 (m, 1H), 1.24 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 178.8, 142.4, 129.8, 128.7, 128.6, 126.0, 124.4, 72.3, 67.2, 64.5, 39.0, 37.3, 32.3, 31.0, 30.6, 27.5, 25.7 ppm; IR (thin film) ν 2933, 1728, 1495, 1480, 1465, 1397, 1365, 1285, 1158, 1071, 1034 cm^{-1}; HRMS (EI) calcd for $C_{21}H_{30}O_3$ 330.2195 found 330.2195 (M^+).

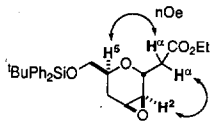
Epoxidation (see eq 2)



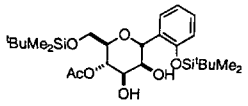
meta-Chloroperbenzoic acid (80 mg, 0.46 mmol, 3.0 equiv) was added to a solution of ethyl ester **4** (67 mg, 0.15 mmol) in 4.0 mL of CCl_4. The mixture was stirred for 12 h and quenched by the addition of 5 mL of 0.1 M aqueous $Na_2S_2O_3$. The organic phase was collected and the aqueous layer was extracted with 3 x 10 mL of CH_2Cl_2. The combined organic extracts were washed successively with 2 x 10 mL of saturated aqueous $NaHCO_3$ and 2 x 10 mL of saturated aqueous NaCl. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to an oily residue. Purification by chromatography on silica gel (5:1 hexanes/EtOAc) gave epoxide **5** as a colorless oil (48 mg, 70%): TLC R_f = 0.32 (4:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.69-7.67 (m, 4H), 7.46-7.39 (m, 6H), 4.70-4.67 (m, 1H), 4.19-4.12 (m, 2H), 3.73-3.68 (m, 1H), 3.64 (dd, 1H, J = 10.5, 5.5 Hz), 3.55 (dd, 1H, J = 10.5, 5.0 Hz), 3.47 (dt, 1H, J = 4.0, 2.0 Hz), 3.37 (t, 1H, J = 4.0 Hz), 2.75 (d, 2H, J = 7.0 Hz), 2.06 (dt, 1H, J = 15.0, 2.0 Hz), 1.80-1.75 (m, 1H), 1.25 (t, 3H, J = 7.5 Hz), 1.07 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.2, 135.9, 133.7, 129.9, 127.9, 68.0, 66.8, 60.9, 53.3, 52.1, 35.8, 27.5, 27.0, 19.5, 14.4 ppm; IR (thin film) ν 2931, 2858, 1736, 1473, 1428, 1374, 1279, 1184, 1113, 1035, 824, 741, 703 cm^{-1}; HRMS (FAB$^+$) calcd for $C_{26}H_{34}O_5Si$ 454.2176 found 477.2075 (MNa^+).

^{1}H NMR nOe ($CDCl_3$, 500 MHz)

C5 → Cα: 1.6%
Cα → **C5**: 1.8%
Cα → **C2**: 1.5%

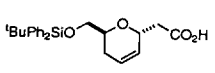


OsO_4-Catalyzed Dihydroxylation (see eq 3)



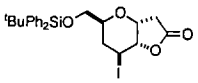
An aqueous solution of OsO_4 (2.5 wt% in H_2O, 200 μL, 20 μmol, 0.1 equiv) was added to a solution of **6** (93 mg, 0.19 mmol), NMO (25 mg, 0.21 mmol, 1.1 equiv) and DABCO (3.4 mg, 30 μmol, 0.2 equiv) in 1.8 mL of acetone. Stirring of this mixture for 5 h was followed by the addition of a second portion of both NMO (25 mg, 0.21 mmol, 1.1 equiv) and aqueous OsO_4 solution (100 μL, 10 μmol, 0.05 equiv). After 2 h the reaction was quenched by the addition of 10 mL of 0.1 M aqueous $Na_2S_2O_3$. The biphasic mixture was stirred vigorously for 20 min then transferred to a separatory funnel with 15 mL of CH_2Cl_2. The organic phase was collected and the aqueous layer was extracted with 2 x 10 mL of CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by chromatography on silica gel (5:1 hexanes/EtOAc) gave diol **7** as a white solid (82 mg, 82%): TLC R_f = 0.17 (6:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.57 (dd, 1H, J = 7.8, 1.7 Hz), 7.23-7.19 (m, 1H), 7.05 (dt, 1H, J = 7.5, 1.0 Hz), 6.85 (dd, 1H, J = 8.2, 1.0 Hz), 5.28 (dd, 1H, J = 4.0, 2.2 Hz), 5.21 (d, 1H, J = 8.8 Hz), 4.16 (dd, 1H, J = 10.2, 6.5 Hz), 4.07 (q, 1H, J = 3.5 Hz), 4.00 (dt, 1H, J = 6.2, 2.0 Hz), 3.96-3.91 (m, 2H), 2.90 (d, 1H, J = 3.7 Hz), 2.65 (d, 1H, J = 5.1 Hz), 2.15 (s, 3H), 1.05 (s, 9H), 0.92 (s, 9H), 0.32 (s, 3H), 0.28 (s, 3H), 0.10 (s, 3H), 0.08 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.2, 153.1, 129.6, 128.8, 127.8, 121.9, 118.5, 76.6, 71.5, 70.7, 69.1, 66.7, 61.9, 25.9, 25.8, 21.2, 18.3, 18.2, -3.9, -4.4, -5.37, -5.42 ppm; IR (thin film) ν 3446 (br), 2955, 2930, 2858, 1744, 1492, 1372, 1254, 1103, 1037, 919, 838, 780 cm^{-1}; HRMS (EI) calcd for $C_{26}H_{46}O_7Si_2$ 526.2782 found 527.2879 (MH^+).

Iodolactonization (see eq 4)



To a stirred solution of ethyl ester **4** (186 mg, 0.42 mmol) in 2.0 mL of MeOH was added $Ba(OH)_2$•$8H_2O$ (171 mg, 0.54 mmol, 1.2 equiv). After 12 h the volatiles were removed

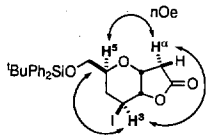
under reduced pressure and the resulting oily residue was partitioned between 3 mL of 1 M aqueous HCl and 3 mL of CH_2Cl_2. The organic phase was collected and the aqueous layer was extracted with 3 x 10 mL of CH_2Cl_2. The combined organic extracts were washed with 1 x 10 mL of saturated aqueous NaCl, dried over Na_2SO_4, and concentrated under reduced pressure. Purification by chromatography on silica gel (30:10:0.3 hexanes/EtOAc/AcOH) afforded carboxylic acid **8** as a colorless oil (139 mg, 80%): TLC R_f = 0.22 (30:10:0.3 hexanes/EtOAc/AcOH); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.75-7.71 (m, 4H), 7.48-7.40 (m, 6H), 5.94-5.89 (m, 1H), 5.75-5.71 (m, 1H), 4.73-4.71 (m, 1H), 3.90-3.85 (m, 1H), 3.81 (dd, 1H, *J* = 10.5, 6.5 Hz), 3.66 (dd, 1H, *J* = 10.5, 5.0 Hz), 2.74 (dd, 1H, *J* = 15.5, 9.0 Hz), 2.55 (dd, 1H, *J* = 15.5, 5.0 Hz), 2.10-1.98 (m, 2H), 1.11 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 176.4, 135.9, 133.8, 133.7, 130.0, 128.0, 127.9, 125.5, 69.4, 69.3, 66.6, 39.2, 27.1, 27.0, 19.5 ppm; IR (thin film) ν 3071, 2931, 2858, 1712, 1473, 1428, 1294, 1207, 1135, 1112, 824, 740 cm^{-1}; HRMS (FAB$^+$) calcd for $C_{24}H_{30}O_4Si$ 410.1913 found 433.1796 (MNa^+).



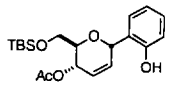
To a solution of carboxylic acid **8** (67 mg, 0.16 mmol) in 1.0 mL of THF was added 100 μL of 2 M aqueous NaOH (0.20 mmol, 1.2 equiv). The flask was wrapped in aluminum foil and I_2 (133 mg, 0.52 mmol, 3.2 equiv) was added. After stirring this mixture for 16 h, 3 mL portions of EtOAc, saturated aqueous NaCl, and 0.1 M aqueous $Na_2S_2O_3$ were added successively. The organic phase was collected and the aqueous layer was extracted with 3 x 10 mL of EtOAc. The combined organic extracts were washed with 1 x 10 mL of saturated aqueous NaCl, dried over Na_2SO_4, and concentrated under reduced pressure. Purification by chromatography on silica gel (7:1 hexanes/EtOAc) afforded lactone **9** as a colorless oil (57 mg, 65%): TLC R_f = 0.48 (3:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.69-7.67 (m, 4H), 7.50-7.41 (m, 6H), 4.83 (dd, 1H, *J* = 7.8, 5.5 Hz), 4.65-4.62 (m, 1H), 4.13-4.08 (m, 1H), 3.93 (sext, 1H, *J* = 5.5 Hz), 3.77 (dd, 1H, *J* = 11.2, 4.5 Hz), 3.72 (dd, 1H, *J* = 11.3, 4.5 Hz), 2.68 (dd, 1H, *J* = 18.0, 6.5 Hz), 2.63 (dd, 1H, *J* = 18.0, 4.0 Hz), 2.38 (ddd, 1H, *J* = 13.8, 5.5, 4.5 Hz), 2.31-2.24 (m, 1H), 1.10 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 173.8, 135.9, 135.8, 133.3, 133.2, 130.24, 130.20, 128.1, 86.6, 74.3, 70.0, 65.6, 34.7, 34.5, 27.1, 19.5, 18.4 ppm; IR (thin film) ν 2931, 2858, 1792, 1652, 1472, 1428, 1159, 1113, 1040, 824, 740 cm^{-1}; HRMS (FAB$^+$) calcd for $C_{24}H_{29}IO_4Si$ 536.0880 found 559.0764 (MNa^+).

^{1}H NMR nOe (C_6D_6, 500 MHz)

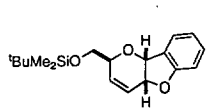
C5 → **C3**: 0.8%
C5 → **Cα**: 1.3%
Cα → **C5**: 1.6%
Cα → **C3**: 0.8%
C3 → **C5**: 1.1%
C3 → **Cα**: 0.6%



Pd(PPh$_3$)$_4$-Catalyzed π-Allyl Cyclization (see eq 5)



Potassium fluoride (12 mg, 0.20 mmol, 1.1 equiv) was added to a solution of **6** (89 mg, 0.18 mmol) in 1.8 mL of methanol. The reaction mixture was stirred for 1 h then poured into a separatory funnel containing 10 mL of saturated aqueous NH_4Cl and 10 mL of CH_2Cl_2. The organic layer was collected and the aqueous layer was extracted with 10 ml of CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by chromatography on silica gel (9:1 hexanes/EtOAc) gave phenol **10** as a colorless oil (53 mg, 78%): TLC R_f = 0.27 (6:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.52 (s, 1H), 7.26 (dt, 1H, *J* = 7.7, 1.5 Hz), 7.08 (d, 1H, *J* = 6.6 Hz), 6.94 (d, 1H, *J* = 8.3 Hz), 6.89 (t, 1H, *J* = 7.4 Hz), 6.29 (ddd, 1H, *J* = 10.3, 2.0, 1.0 Hz), 6.08-6.05 (m, 1H), 5.49 (d, 1H, *J* = 2.0), 5.25-5.21 (m, 1H), 3.81-3.75 (m, 3H), 2.10 (m, 3H), 0.91 (s, 9H), 0.09 (s, 3H), 0.07 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.4, 156.1, 131.0, 130.0, 128.3, 124.8, 124.2, 119.8, 117.3, 73.6, 72.3, 65.0, 62.1, 25.8, 21.0, 18.3, -5.5, -5.6 ppm; IR (thin film) ν 3400 (br), 2959, 2930, 2857, 1742, 1486, 1371, 1233, 1087, 838, 755 cm^{-1}.



A solution of **10** (34 mg, 90 μmol) in 0.8 mL of THF was transferred via cannula to a flask containing $Pd(PPh_3)_4$ (10 mg, 9 μmol, 0.1 equiv). To the resulting yellow solution was then added $^iPr_2NEt$ (35 μL, 0.20 mmol, 2.2 equiv). After stirring this mixture for 7 h a second portion of $Pd(PPh_3)_4$ (10 mg, 9 μmol, 0.1 equiv) was added as a solution in 0.8 mL of THF. The reaction was stirred for an additional 10 h following which time the contents were diluted with 10 mL of CH_2Cl_2 and poured into a separatory funnel containing 10 mL of saturated aqueous NH_4Cl. The organic phase was collected and the aqueous layer was extracted with 2 x 10 ml of CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure to an oily residue. Purification by chromatography on silica gel (12:1 hexanes/EtOAc) gave benzofuran **11** as a colorless oil (23 mg, 80%): TLC R_f = 0.59 (6:1 hexanes/EtOAc); ^1H NMR ($CDCl_3$, 500MHz) δ 7.44 (dd, 1H, *J* = 7.3, 0.7 Hz), 7.27 (t, 1H, *J* = 7.1 Hz), 6.97 (dt, 1H, *J* = 7.5, 0.8 Hz), 6.88 (d, 1H, *J* = 8.1 Hz), 6.21-6.16 (m, 2H), 5.61 (d, 1H, *J* = 6.1 Hz), 4.81-4.79 (m, 1H), 4.23 (t, 1H, *J* = 4.9 Hz), 3.86-3.81 (m, 2H), 0.94 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 160.1, 132.9, 130.4, 126.2, 125.9, 122.3, 120.9, 110.8, 74.9, 73.4, 71.2, 64.8, 25.8, 18.2, -5.35, -5.40 ppm; IR (thin film) ν 2927, 2856, 1464, 1253, 1104, 938, 837, 777, 750 cm^{-1}; HRMS (EI) calcd for $C_{18}H_{26}O_3Si$ 318.1651 found 319.1717 (MH^+).

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(1) (a) Rainier, J. D.; Allwein, S. P.; Cox, J. M. *J. Org. Chem.* **2001**, *66*, 1380-1386; (b) Paterson, I.; Smith, J. D.; Ward, R. A. *Tetrahedron* **1995**, *51*, 9413-9436; (c) Danishefsky, S. J.; DeNinno, S.; Lartey, P. *J. Am. Chem. Soc.* **1987**, *109*, 2082-2089.

(2) Smith, R. D.; Simmons, H. E. *Organic Syntheses*; Baumgarten, H. E., Ed.; Wiley: New York, 1973; Vol. V, pp 855-858.