Total Synthesis of (+)- α -Onocerin in Four Steps Via Four-Component Coupling and Tetracyclization Steps

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Supplementary Materials

General Methods. All reactions were performed under an atmosphere of dry nitrogen in flame-dried glassware equipped with tightly fitted rubber septa. All syringes and needles were oven-dried and cooled in a desiccator before use. DME was freshly distilled from sodium and benzophenone. Cesium fluoride was dried at 300 °C under high vacuum for 12 h prior to use. Flash chromatography was performed using Baker silica gel (40 μ m particle size). NMR spectra were obtained on a Varian Inova 400 or a Varian 500 spectrometer. Proton NMR spectra were reported as δ values in parts per million (ppm) using the residual solvent signal as an internal standard: CDCl_3 (7.26 ppm), C_6D_6 (7.15 ppm) or CD_3OD (3.30 ppm). Carbon NMR spectra were recorded in ppm relative to solvent signal: CDCl_3 (77.0 ppm), C_6D_6 (128.0 ppm) or CD_3OD (49.0 ppm). IR spectra were obtained using a Nicolet 5ZDX FT-IR spectrometer. Mass spectra were obtained by Harvard University mass spectrometer.

(2Z,2'Z)-Bis-Enolsilane 4. A solution of acylsilane **2** (50.3 mg, 0.16 mmol) in ether (0.5 mL) was added slowly to vinyl lithium^a (0.31 mL of a 0.58 M solution in pentane-ether, 0.18 mmol) at $-78\text{ }^{\circ}\text{C}$ along the side of flask. After stirring for 1 h, a solution of iodine (20.6 mg, 0.08 mmol) in THF (0.5 mL) was added slowly, also along the side of flask. The resulting mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 2 h, then treated with saturated aqueous NaHCO_3 (0.3 mL), and allowed to warm up to rt. Most of solvent was then removed in vacuo, and the residue was extracted with hexane. The organic solution was washed with brine, dried (Na_2SO_4), and concentrated. Chromatography (94:6:1 hexane:EtOAc:Et₃N) provided 40 mg (73%) of the title compound as a light yellow oil: $[\alpha]_{\text{D}}^{23} -2.2$ (c 1.8, CHCl_3); $R_f = 0.28$ (6% EtOAc/hexane); IR (film) 2956, 2931, 2862, 1670, 1459 cm^{-1} ; ^1H NMR (C_6D_6 , 400 MHz) δ 5.27 (t, $J = 6.9$ Hz, 1 H x 2), 4.72-4.66 (m, 1 H x 2), 2.52 (t, $J = 6.0$ Hz, 1 H x 2), 2.42-2.20 (m, 4 H x 2), 2.20-1.95 (m, 4 H x 2), 1.70-1.40 (m, 2 H x 2), 1.56 (s, 3 H x 2), 1.15 (s, 3 H x 2), 1.10 (s, 3 H x 2), 1.03 (s, 9 H x 2), 0.17 (s, 6 H x 2); ^{13}C NMR (C_6D_6 , 100 MHz) δ 150.39, 134.79, 124.65, 108.49, 63.47, 57.31, 37.22, 36.86, 27.96, 26.37, 26.04, 24.98, 18.90, 18.49, 16.08, -3.76; HRMS (FAB) calcd for $\text{C}_{40}\text{H}_{74}\text{NaO}_4\text{Si}_2$ [$\text{M}+\text{Na}^+$] 697.5023, found 697.5032.

(2Z,2'Z)-Bis-Enolsilane 4. A solution of acylsilane **2** (38 mg, 0.12 mmol) in ether (0.4 mL) was added slowly to vinyl lithium (0.23 mL of a 0.58 M solution in pentane-ether, 0.13 mmol) at $-78\text{ }^{\circ}\text{C}$ along the side of flask. After stirring for 1 h, the reaction mixture was transferred via cannula to a pre-cooled ($-78\text{ }^{\circ}\text{C}$) solution of

^a For preparation, see: (a) Seyferth, D.; Weiner, M. A. *J. Am. Chem. Soc.* **1961**, 83, 3583; (b) Neumann, H.; Seebach, D. *Tetrahedron Lett.* **1976**, 17, 4839. For titration, see: Watson, S. C.; Eastham, J. F. *J. Organometal. Chem.* **1967**, 9, 165.

copper(II) pivalate^b (65 mg, 0.24 mmol) in THF (0.4 mL). The flask was rinsed with THF (0.2 mL), which was also cannulated to the solution of copper(II) pivalate in THF. The resulting mixture was stirred for 2 h at $-78\text{ }^{\circ}\text{C}$, and then was allowed to warm up to $-20\text{ }^{\circ}\text{C}$ during a four-hour period. The reaction mixture was treated with conc. aq. NH_3 (0.2 mL). Most of solvent was then removed in vacuo. The residue was extracted with hexane, which was dried (Na_2SO_4) and concentrated. Chromatography (94:6:1 hexane:EtOAc:Et₃N) gave 25 mg (61%) of the title compound as a light yellow oil. See above for ^1H and ^{13}C spectra data.

(2Z,2'Z)-Bis-Vinyltriflate 5. To a flame-dried flask equipped with a magnetic stirrer and a rubber septum was added a solution of *bis*-enolsilane **4** (30 mg, 0.045 mmol) in DME (0.15 mL), followed by addition of *N*-phenyltrifluoromethanesulfonimide (95 mg, 0.26 mmol) and vacuum dried (300 °C) cesium fluoride (54 mg, 0.35 mmol) under a stream of nitrogen. The septum was replaced with a three-way stopcock which was fixed with teflon tape and parafilm. The reaction was monitored by TLC every hour by cooling the reaction mixture down to -78 °C and taking a sample using capillary tube. TLC indicated that the reaction was complete in 4 h. The pressure inside flask was released carefully and the mixture was partitioned between ether and a pH 7 buffer solution. The aqueous phase was separated and extracted again with ether (3X). The combined organic solution was concentrated and further dried by azeotroping with benzene. Chromatography (gradient, 12% to 15% EtOAc/hexane) provided 23 mg (72%) of the

^b Copper(II) pivalate was prepared from excess CuCO₃ and pivalic acid in CH₃OH at reflux, filtration and removal of CH₃OH. It was dried at 100 °C under high vacuum for 24 h prior to use.

title compound as a colorless oil: $[\alpha]_D^{23} -2.2$ (c 1.0, CHCl_3); $R_f = 0.36$ (20% EtOAc/hexane); IR (film) 2967, 2927, 1675, 1412, 1206 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 5.26-5.16 (m, 1 H x 2), 5.12 (t, $J = 6.5$ Hz, 1 H x 2), 2.68 (t, $J = 6.4$ Hz, 1 H x 2), 2.38-2.32 (m, 2 H x 2), 2.30-2.04 (m, 6 H x 2), 1.65-1.58 (m, 2 H x 2), 1.63 (s, 3 H x 2), 1.30 (s, 3 H x 2), 1.26 (s, 3 H x 2); ^{13}C NMR (CDCl_3 , 100 MHz) δ 149.47, 136.38, 122.15, 119.66, 64.05, 58.32, 36.27, 33.52, 27.37, 24.97, 24.84, 18.71, 15.94; HRMS (ES) calcd for $\text{C}_{30}\text{H}_{45}\text{F}_6\text{O}_8\text{S}_2$ $[\text{M}+\text{H}^+]$ 711.2460, found 711.2468.

(2Z,2'Z)-Bis-Allylsilane 6. A solution of ZnBr_2 (65 mg, 0.29 mmol) in THF (0.6 mL) was added dropwise to a solution of $\text{TMSCH}_2\text{MgCl}$ (0.4 mL of a 0.73 M solution in THF, 0.29 mmol) at 23 $^\circ\text{C}$.^c After it was stirred for 12 h, a solution of *bis*-vinyltriflate **5** (29 mg, 0.04 mmol) in THF (0.5 mL) was added, followed by tetrakis(triphenylphosphine)palladium(0) (2.5 mg, 0.002 mmol). The suspension was stirred at 23 $^\circ\text{C}$ for 18 h, and then was partitioned between saturated aqueous NH_4Cl (1 mL, pH was adjusted to 9 by addition of conc. aq. NH_3) and hexane. The organic phase was separated, and the aqueous phase was again extracted with ether. The combined extracts were washed with brine, dried (Na_2SO_4) and concentrated. The residue was chromatographed (94:6:1 hexane:EtOAc:Et₃N) to give 22 mg (92%) of the title compound as colorless oil: $[\alpha]_D^{23} -1.3$ (c 0.58, CHCl_3); $R_f = 0.34$ (10% EtOAc/hexane); IR (film) 2958, 2849, 1638, 1444, 1381, 1244 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 5.17 (t, $J = 6.8$ Hz, 1 H x 2), 5.05-4.98 (m, 1 H x 2), 2.70 (t, $J = 6.3$ Hz, 1 H x 2), 2.20-1.88 (m, 8 H x 2), 1.72-1.54 (m, 2 H x 2), 1.62 (s, 3 H x 2), 1.52 (s, 2 H x 2), 1.30 (s, 3 H x 2), 1.26 (s, 3 H x 2), 0.02 (s, 9 H x 2); ^{13}C NMR (CDCl_3 , 100 MHz) δ 136.65, 133.93,

125.03, 121.60, 64.21, 58.32, 39.11, 36.29, 28.91, 27.44, 26.93, 24.90, 21.38, 18.75, 16.01, -0.62; HRMS (CI) calcd for $C_{36}H_{70}NO_2Si_2$ $[M+NH_4^+]$ 604.4945, found 604.4953. °See Hayashi, T.; Kabeta, K.; Hamachi, I.; Kumada, M. *Tetrahedron Lett.* **1983**, *24*, 2865.

(+)-Onocerin (1). A pre-cooled ($-78^\circ C$) solution of $MeAlCl_2$ (0.24 mL of a 1.0 M solution in CH_2Cl_2 , 0.24 mmol) in CH_2Cl_2 (12 mL) was added via cannula to a solution of *bis*-allylsilane **6** (55 mg, 0.094 mmol) in CH_2Cl_2 (24 mL) at $-94^\circ C$ along the side of flask. After stirring at $-94^\circ C$ for 15 min, the reaction mixture was quenched by successive addition of Et_3N (0.13 mL) and a 4:1 MeOH- H_2O solution (0.13 mL), also along the side of the flask. The resulting mixture was then poured into aqueous NH_4Cl . The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 . The combined organic solution was washed with brine, dried (Na_2SO_4) and concentrated. The residue was further dried by azeotroping with benzene. It was then dissolved in THF (2 mL), and treated with TBAF (0.24 mL of a 1.0 M solution in THF, 0.24 mmol). After stirring at $23^\circ C$ for 1 h, the reaction was treated with aqueous NH_4Cl . Most of the solvent was then removed in vacuo. The residue was extracted with EtOAc. The organic phase was dried (Na_2SO_4) and concentrated. Chromatography (gradient, 20% to 40% EtOAc/hexane) gave 26 mg (63%) of (+)-onocerin (**1**) as a colorless solid, along with 4 mg (9%) of **7**.

Data for (+)-onocerin (**1**): mp $207-208^\circ C$, lit.^d mp $210^\circ C$; $[\alpha]_D^{23} +8.0$ (c 0.1, $CHCl_3$), lit. $[\alpha]_D^{20} +9$ (c 0.1, $CHCl_3$); $R_f = 0.41$ (50% EtOAc/hexane); IR (solution, $CHCl_3$) 3343,

2962, 2942, 2971, 1648, 1460, 1379, 1040 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 4.83 (s, 1 H x 2), 4.56 (s, 1 H x 2), 3.25 (dd, $J = 11.7, 4.4$ Hz, 1 H x 2), 2.41 (ddd, $J = 12.7, 4.4, 2.4$ Hz, 1 H x 2), 1.97 (dt, $J = 12.9, 4.9$ Hz, 1 H x 2), 1.77-1.55 (m, 4 H x 2), 1.54-1.46 (m, 2 H x 2), 1.38 (dq, $J = 12.8, 4.4$ Hz, 1 H x 2), 1.28-1.24 (m, 1 H x 2), 1.22-1.14 (m, 1 H x 2), 1.13-1.02 (m, 2 H x 2), 0.99 (s, 3 H x 2), 0.76 (s, 3 H x 2), 0.64 (s, 3 H x 2); ^{13}C NMR (CDCl_3 , 100 MHz) δ 148.41, 106.71, 78.89, 57.56, 54.65, 39.26, 39.11, 38.25, 36.98, 28.28, 27.94, 24.02, 22.57, 15.36, 14.50; HRMS (EI) calcd for $\text{C}_{30}\text{H}_{50}\text{O}_2$ [M^+] 442.3811, found 442.3815. Recrystallization from CH_2Cl_2 - CHCl_3 gave long needles. X-Ray crystallography analysis confirmed its structure.

Data for **7**: $[\alpha]_D^{23} +17.3$ (c 0.4, CHCl_3); $R_f = 0.26$ (30% EtOAc/hexane); IR (solution, CHCl_3) 3381, 2937, 2868, 1645, 1458, 1382 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 4.82 (s, 1 H), 4.69 (s, 1 H), 4.54 (s, 1 H), 4.47 (s, 1 H), 3.28-3.16 (m, 2 H), 2.44-2.36 (m, 1 H), 2.20-1.90 (m, 3 H), 1.76-1.46 (m, 12 H), 1.44-0.94 (m, 10 H), 0.98 (s, 6 H), 0.89 (s, 3 H), 0.76 (s, 6 H), 0.65 (s, 3 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 148.96, 148.60, 109.41, 106.43, 79.27, 78.92, 58.71, 57.14, 56.92, 54.65, 44.92, 44.87, 39.53, 39.08, 38.84, 38.82, 38.21, 37.77, 36.89, 34.21, 34.17, 31.04, 28.31, 27.91, 27.72, 25.26, 23.92, 23.65, 23.22, 23.15, 22.53, 22.45, 22.38, 15.53, 15.38, 14.43; HRMS (EI) calcd for $\text{C}_{30}\text{H}_{50}\text{O}_2$ [M^+] 442.3811, found 442.3812.

(2E,2'E)-Bis-Enolsilane 9. *t*-BuLi (2.43 mL of a 1.11 M solution in pentane, 2.69 mmol) was added to a solution of sulfone **8** (0.364 g, 1.08 mmol) in THF (2.1 mL) at -78 °C. The mixture was allowed to warm up to -20 °C in an one hour period and stirred at -20 °C for 30 min. The reaction mixture was re-cooled to -78 °C. A solution of acylsilane **2** (0.668 g, 2.15 mmol) in THF (2 mL) was then added and the mixture was

^d Pauli, G.F. *Planta Medica*, **2000**, 66, 299-302.

allowed to warm up to 23 °C overnight. The reaction mixture was treated with aqueous NaHCO₃. Most of solvent was then removed in vacuo and the residue was extracted with hexane. The organic phase was washed with water, brine and dried over Na₂SO₄. Column chromatography (gradient, 8% to 10% EtOAc/hexane) gave 0.56 g (77%) of compound **9** as a colorless oil: $[\alpha]_D^{23}$ -1.4 (*c* 1.5, CHCl₃); *R*_f = 0.28 (10% EtOAc/hexane); IR (film) 2958, 2929, 2858, 1671, 1641 cm⁻¹; ¹H NMR (C₆D₆, 400 MHz) δ 5.32 (t, *J* = 6.6 Hz, 1 H x 2), 4.86-4.76 (m, 1 H x 2), 2.57 (t, *J* = 6.1 Hz, 1 H x 2), 2.42-2.20 (m, 4 H x 2), 2.20-2.00 (m, 4 H x 2), 1.68-1.46 (m, 2 H x 2), 1.61 (s, 3 H x 2), 1.15 (s, 3 H x 2), 1.11 (s, 3 H x 2), 1.02 (s, 9 H x 2), 0.21 (s, 6 H x 2); ¹³C NMR (C₆D₆, 100 MHz) δ 151.91, 134.91, 124.65, 106.87, 63.46, 57.32, 36.85, 32.03, 28.78, 28.00, 25.94, 24.97, 18.90, 18.29, 16.10, -4.24; HRMS (CI) calcd for C₄₀H₇₈NO₄Si₂ [M+NH₄⁺] 692.5469, found 692.5494.

(2E,2'E)-Bis-Vinyltriflate 10. To a flame-dried flask equipped with a magnetic stirrer and a rubber septum was added a solution of *bis*-enolsilane **9** (0.176 g, 0.26 mmol) in DME (0.9 mL), followed by addition of *N*-phenyltrifluoromethanesulfonimide (0.466 g, 1.30 mmol) and vacuum dried (300 °C) cesium fluoride (0.317 g, 2.09 mmol) under a stream of nitrogen. The septum was replaced with a plastic cap which was fixed with teflon tape and parafilm. The reaction mixture was vigorously stirred at 23 °C for 5 h. The pressure inside flask was released carefully and the mixture was partitioned between ether and a pH 7 buffer solution. The aqueous phase was separated and extracted again with ether (3X). The combined organic solution was washed with brine, dried (Na₂SO₄) and concentrated. Chromatography (gradient, 15% to 18% EtOAc/hexane) provided 0.156 g (84%) of the title compound as a colorless oil: $[\alpha]_D^{23}$ -4.0 (*c* 0.75, CHCl₃); *R*_f = 0.29 (20% EtOAc/hexane); IR (film) 2966, 2858, 1688, 1414, 1215, 1144 cm⁻¹; ¹H NMR

(CDCl₃, 400 MHz) δ 5.54-5.42 (m, 1 H x 2), 5.13, (t, J = 6.6 Hz, 1 H x 2), 2.69 (t, J = 6.2 Hz, 1 H x 2), 2.42-2.34 (m, 2 H x 2), 2.28-2.04 (m, 6 H x 2), 1.63 (s, 3 H x 2), 1.66-1.56 (m, 2 H x 2), 1.30 (s, 3 H x 2), 1.26 (s, 3 H x 2); ¹³C NMR (CDCl₃, 100 MHz) δ 150.77, 136.70, 121.97, 120.09, 64.00, 58.33, 36.28, 29.27, 27.35, 26.28, 24.84, 24.75, 18.71, 15.95; HRMS (EI) calcd for C₃₀H₄₅F₆O₈S₂ [M+H⁺] 711.2460, found 711.2451.

(2*E*,2'*E*)-Bis-Allylsilane 11. A solution of ZnBr₂ (0.20 g, 0.89 mmol) in THF (1 mL) was added dropwise to a solution of TMSCH₂MgCl (1.0 mL of a 0.85 M solution in THF, 0.85 mmol) at 23 °C. After it was stirred for 12 h, a solution of *bis*-vinyltriflate **10** (85 mg, 0.12 mmol) in THF (0.5 mL) was added, followed by addition of tetrakis-(triphenylphosphine)palladium(0) (7 mg, 0.006 mmol). The suspension was stirred at 23 °C for 5 h, and was then partitioned between saturated aqueous NH₄Cl (2 mL, pH was adjusted to 9 by addition of conc. aq. NH₃) and hexane. The organic phase was separated, and the aqueous phase was again extracted with ether. The combined extracts were washed with brine, dried (Na₂SO₄) and concentrated. The residue was chromatographed (100:7:1 hexane:EtOAc:Et₃N) to give 63 mg (90%) of the title compound as a colorless oil: $[\alpha]_D^{23}$ -1.7 (c 1.8, CHCl₃); R_f = 0.34 (10% EtOAc/hexane); IR (film) 2955, 2859, 1653, 1455 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 5.18 (t, J = 6.8 Hz, 1 H x 2), 5.00-4.90 (m, 1 H x 2), 2.70 (t, J = 6.3 Hz, 1 H x 2), 2.20-1.90 (m, 8 H x 2), 1.74-1.56 (m, 2 H x 2), 1.62 (s, 3 H x 2), 1.45 (s, 2 H x 2), 1.30 (s, 3 H x 2), 1.26 (s, 3 H x 2), -0.01 (s, 9 H x 2); ¹³C NMR (CDCl₃, 100 MHz) δ 136.53, 134.16, 124.87, 123.03, 64.18, 58.32, 36.27, 32.36, 28.89, 27.40, 26.98, 26.78, 24.89, 18.73, 15.96, -1.19; HRMS (CI) calcd for C₃₆H₇₀NO₂Si₂ [M+NH₄⁺] 604.4945, found 604.4943.

Cyclization of 11 to 7 and (+)-Onocerin (1). A pre-cooled (-78°C) solution of MeAlCl_2 (0.21 mL of a 1.0 M solution in CH_2Cl_2 , 0.21 mmol) in CH_2Cl_2 (10.5 mL) was added via cannula to a solution of *bis*-allylsilane **11** (49 mg, 0.084 mmol) in CH_2Cl_2 (21 mL) at -94°C along the side of flask. After stirring at -94°C for 15 min, the reaction mixture was quenched by successive addition of Et_3N (0.12 mL) and a 4:1 $\text{MeOH-H}_2\text{O}$ solution (0.12 mL), also along the side of the flask. The resulting mixture was then poured into aqueous NH_4Cl (20 mL). The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 . The combined organic solution was washed with brine, dried (Na_2SO_4) and concentrated. The residue was then dissolved in THF (2 mL), followed by addition of TBAF (0.20 mL of a 1.0 M solution in THF, 0.2 mmol). After stirring at 23°C for 1 h, the reaction mixture was treated with aqueous NH_4Cl . Most of solvent was then removed in vacuo. The residue was extracted with EtOAc . The organic phase was dried (Na_2SO_4) and concentrated. Chromatography (gradient, 20% to 40% EtOAc/hexane) gave 16.2 mg (44%) of **7** as a white powder, and 7.0 mg (19%) of (+)-onocerin (**1**) as a colorless solid. See above for spectra data.

Vinyltriflate 13. Enolsilane **12**^e (72 mg, 0.25 mmol) was treated with *N*-phenyltrifluoromethanesulfonimide (0.219 g, 0.61 mmol) and vacuum dried (300 °C) cesium fluoride (0.132 g, 0.87 mmol) in DME (1.0 mL) as described above (**9**→**10**) for 6 h. After releasing the pressure inside the flask, the mixture was partitioned between pentane and pH 7 buffer solution. The aqueous phase was separated and extracted with pentane (3X). The combined organic solution was concentrated *in vacuo*. Chromatography (SiO₂ was treated with 5 wt.% Et₃N before use, hexane) provided 70 mg (92%) of compound **13** as a colorless oil: *R*_f = 0.78 (10% EtOAc/hexane); ¹H NMR (CDCl₃, 500 MHz) δ 5.53 (s, 1 H), 2.35-2.24 (m, 2 H), 1.86-1.75 (m, 2 H), 1.54-1.48 (m, 1 H), 1.41-1.17 (m, 7 H), 1.04 (s, 3 H), 0.95-0.89 (m, 3 H); ¹³C NMR (CDCl₃, 125 MHz) δ 148.6, 127.6, 118.8, 42.2, 36.1, 33.7, 27.9, 27.0, 36.3, 23.6, 19.8, 14.3; EI-MS 300 [M⁺], 285, 243, 179, 113, 82.

Vinyltriflate 15. Enolsilane **14**^f (0.138 g, 0.51 mmol), *N*-phenyltrifluoromethanesulfonimide (0.365 g, 1.02 mmol), and vacuum dried (300 °C) cesium fluoride (0.233 g, 1.53 mmol) were introduced into flame-dried flask equipped with a magnetic stirrer and a rubber septum under a stream of nitrogen. DME (1.5 mL) was added and the septum was replaced by a plastic cap which was fixed with teflon tape and parafilm. The reaction mixture was vigorously stirred at 23 °C for 4 h. The pressure

^e For preparation, see: Matsuzawa, S.; Horiguchi, Y.; Nakamura, E.; Kuwajima, I. *Tetrahedron* **1989**, 45, 349.

^f For preparation, see: Krepski, L.R.; Hassner, A. *J. Org. Chem.* **1978**, 43, 3173.

inside flask was released carefully and the mixture was partitioned between hexane and sat. aq. NaHCO₃ solution. The aqueous phase was separated and extracted with hexane (3X). The combined organic solution was dried (Na₂SO₄) and concentrated *in vacuo*. Chromatography (SiO₂ was treated with 5 wt.% Et₃N before use, hexane) afforded 0.131 g (89%) of compound **15** as a colorless oil: ¹H NMR data are in agreement with those reported in the literature.^g

Enolsilane 16. To diisopropylamine (1.55 mL, 11.1 mmol) in THF (35 mL) at 0° (ice bath) was added dropwise a solution of n-BuLi in hexane (4.6 mL, 12.0 mmol). The reaction mixture was stirred at 0° for 10 min and was then cooled to -78° (dry ice/acetone bath). A solution of 2-cyclohexen-1-one (0.95 mL, 9.81 mmol) was added dropwise and after stirring for 1 h at -78°, TBS-OTf (2.5 mL, 10.9 mmol) was added dropwise to the mixture. After stirring for 1 h at -78°, the mixture was allowed to warm to room temperature (the dry ice/acetone bath was removed). The THF was evaporated *in vacuo* and pentane (100 mL) was added to the residue. A precipitation was removed by filtration. Evaporation of the pentane followed by distillation afforded 0.870 g (42%) of compound **16** as a colorless liquid: ¹H NMR data are in agreement with those reported in the literature.^h

Vinyltriflate 17. Enolsilane **16** (99 mg, 0.47 mmol) was treated with *N*-phenyltrifluoromethanesulfonimide (0.418 g, 1.17 mmol) and vacuum dried (300 °C) cesium fluoride (0.248 g, 1.63 mmol) in DME (1.9 mL) as described above (**9**→**10**) for 6

^g Scott, J. W.; Crisp, G. T.; Stille, J. K.; Lagerwall, D. R.; Paquette, L.A. *Org. Synthesis* **1990**, 68, 115.

^h Ihara, M.; Ishida, Y.; Fukumoto, K.; Kametani, T. *Chem. Pharm. Bull.* **1985**, 33, 4102.

h. After releasing the pressure inside the flask, the mixture was partitioned between pentane and pH 7 buffer solution. The aqueous phase was separated and extracted with pentane (3X). The combined organic solution was concentrated *in vacuo*. DMF (96 mg, 1.32 mmol) was added to the crude product and the yield was calculated by the relative integrals of DMF and compound **17** in the ^1H NMR spectrum (78%): ^1H NMR (CDCl_3 , 400 MHz) δ 5.96-5.92 (m, 1 H), 5.76-5.73 (m, 1 H), 5.62-5.59 (m, 1 H), 2.35-2.82 (m, 2 H), 2.20-2.14 (m, 2 H); EI-MS 225, 92.

1,4-Bis(*tert*-butyldimethylsiloxy)benzene **18.** According to a procedure described in the literatureⁱ, hydroquinone (1.67 g, 15.2 mmol) was treated with TBDMS chloride (11.4 g, 75.3 mmol) and imidazole (10.2 g, 150 mmol) in DMF (5.8 ml) for 48 h to yield 4.28 g of compound **18** as a colorless solid (83%): ^1H NMR data are in agreement with those reported in the literature.^j

Enolsilane **19.** Ammonia (5 mL) was condensed into a flask fitted with a dry ice condenser to a solution of *tert*-butanol (1.1 mL, 11.5 mmol) in THF (2.4 mL). Lithium wire (3.1 cm, 21 mmol) was added while cooling the flask using a dry ice/acetone bath. After stirring for 15 min at -78°C , a solution of compound **18** (343 mg, 1.01 mmol) in THF (1 mL) was added dropwise. The reaction mixture was stirred at reflux (-33°C) for

ⁱ Corey, E.J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.

^j Willis, J.P.; Gogins, K.A.Z.; Miller, L.L. *J. Org. Chem.* **1981**, *46*, 3215.

30 min and was then cooled to $-78\text{ }^{\circ}\text{C}$. Additional lithium wire (3.1 cm, 21 mmol) was added and the mixture was stirred for another 30 min at reflux. The excess lithium was quenched with solid NH_4Cl and 2-propanol (3 mL). The reaction mixture was poured carefully into a stirred mixture of hexane (150 mL) and saturated aqueous NH_4Cl solution. The aqueous layer was separated and extracted with hexane (150 mL). The combined organic layers were dried (MgSO_4) and evaporated *in vacuo*. Purification by silica gel chromatography (hexane) afforded 0.248 g of compound **19** (72%) as a colorless solid: $R_f = 0.24$ (hexane); ^1H NMR (CDCl_3 , 400 MHz) δ 4.77-4.75 (m, 2 H), 2.71 (m, 4 H), 0.91 (s, 9 H), 0.13 (s, 6 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 148.4, 100.7, 30.9, 25.9, -4.2; EI-MS 400 [M^+], 281, 167, 73.

Vinylsilane 20. Enolsilane **19** (57 mg, 0.27 mmol) was treated with *N*-phenyltrifluoromethanesulfonimide (0.245 g, 0.69 mmol) and vacuum dried ($300\text{ }^{\circ}\text{C}$) cesium fluoride (0.146 g, 0.96 mmol) in DME (1.0 mL) as described above (**9**→**10**) for 8 h. After releasing the pressure inside the flask, the mixture was partitioned between pentane and pH 7 buffer solution. The aqueous phase was separated and extracted with ether (3X). The combined organic solution was dried (Na_2SO_4) and concentrated *in vacuo*. Chromatography (SiO_2 was treated with 5 wt.% Et_3N before use, 5% EtOAc /hexane) afforded 25 mg (81%) of compound **20** as a yellowish solid: $R_f = 0.42$ (10% EtOAc /hexane); ^1H NMR (CDCl_3 , 400 MHz) δ 5.79-5.77 (m, 2 H), 3.23-3.22 (m, 4 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 145.0, 118.6, 114.4, 28.6; EI-MS 376 [M^+], 243, 162, 93, 69.

Vinylsilane 22. Enolsilane **21**^k (70 mg, 0.28 mmol) was treated with *N*-phenyltrifluoromethanesulfonimide (0.263 g, 0.74 mmol) and vacuum dried (300 °C) cesium fluoride (0.153 g, 1.01 mmol) in DME (1.1 mL) as described above (**9**→**10**) for 3 h. After releasing the pressure inside the flask, the mixture was partitioned between pentane and pH 7 buffer solution. The aqueous phase was separated and extracted with pentane (3X). The combined organic solution was dried (Na₂SO₄) and concentrated *in vacuo*. DMF (24 mg, 0.33 mmol) was added to the crude product and the yield was calculated by the relative integrals of DMF and compound **22** in the ¹H NMR spectrum (78%): ¹H NMR data are in agreement with those reported in the literature.¹

Enolsilane 23. To a solution of methyl phenyl sulfone (0.159 g, 1.02 mmol) at -78° (bath temperature) was added dropwise a solution of *n*-BuLi in hexane (0.4 mL, 1.02 mmol). After stirring for 10 min at -78°, a solution of acylsilane **2** (0.300 g, 0.97 mmol) in THF (1.2 mL) was added dropwise. The mixture was stirred at -78° for 30 min and was then quenched by the addition of aq. sat. NaHCO₃ solution. The aqueous phase was separated and extracted with ether (3X). The combined organic solution was dried (Na₂SO₄) and concentrated *in vacuo*. Chromatography (Et₃N:EtOAc:hexane 95:5:0.5) provided 0.23 g (74%) of compound **23** as a colorless liquid: IR (film) 2956, 2926, 2855, 1637 cm⁻¹; ¹H NMR (C₆D₆, 500 MHz) δ 5.24 (t, *J* = 6.8, 1 H), 4.17 (s, 1 H); 4.14 (s, 1 H),

^k For preparation, see Orban, J.; Turner, J.V.; Twitchin, B. *Tetrahedron Lett.* **1984**, 25, 5099.

¹ Luan, L.; Song, J.-S.; Bullock, R.M. *J. Org. Chem.* **1995**, 60, 7170.

2.55 (t, $J = 6.3$, 1 H), 2.28 (q, $J = 7.3$, 2 H), 2.16-2.08 (m, 3 H), 2.06-1.98 (m, 1 H), 1.64-1.46 (m, 2 H), 1.54 (s, 3 H), 1.14 (s, 3 H), 1.09 (s, 3 H), 0.97 (s, 9 H), 0.15 (s, 6 H); ^{13}C NMR (C_6D_6 , 100 MHz) δ 159.4, 134.8, 127.9, 124.5, 90.2, 63.4, 57.3, 37.1, 36.8, 27.9, 25.8, 25.0, 18.9, 18.2, 16.0, -4.6; HRMS (ES) calcd for $\text{C}_{19}\text{H}_{36}\text{O}_2\text{Si}$ $[\text{M}+\text{H}^+]$ 325.2563, found 325.2559.

Vinyltriflate 24. Enolsilane **23** (0.223 g, 0.69 mmol) was treated with *N*-phenyltrifluoromethanesulfonimide (0.492 g, 1.38 mmol) and vacuum dried (300 °C) cesium fluoride (0.418 g, 2.75 mmol) in DME (2.3 mL) as described above (**9**→**10**) for 6 h. After releasing the pressure inside the flask, saturated aqueous NaHCO_3 solution was added, the aqueous phase was separated and extracted with hexane (3X). The organic solutions were combined, washed with H_2O and brine, dried (Na_2SO_4), and evaporated *in vacuo*. Compound **24** was used without further purification.

Allylsilane 25. A solution of ZnBr_2 (326 mg, 1.45 mmol) in THF (1.0 mL) was added dropwise to a solution of $\text{TMSCH}_2\text{MgCl}$ (1.90 mL of a 0.73 M solution in THF, 1.38 mmol) at 23 °C. After stirring for 12 h, a solution of the crude vinyltriflate **24** in THF (2.0 mL) was added, followed by tetrakis(triphenylphosphine)palladium(0) (24 mg, 0.02 mmol). The suspension was stirred at 23 °C for 9 h and was then washed with saturated aqueous NaHCO_3 and NH_4Cl solution. The aqueous phases were extracted with hexane and the combined organic solutions were washed with H_2O and brine, dried (Na_2SO_4) and evaporated *in vacuo*. The residue was chromatographed (0.5:5:95 $\text{Et}_3\text{N}:\text{EtOAc}:\text{hexane}$) to give 0.141 g (73% over two steps) of compound **25** as a colorless oil: IR (film) 2962, 2919, 1635, 1453, 1379, 1249 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 5.17 (dt, $J = 7.0$, 1.1, 1 H), 4.58 (d, $J = 1.4$, 1 H), 4.51 (s, 1 H), 2.70 (t, $J = 6.2$, 1 H),

2.20-2.02 (m, 4 H), 2.00-1.93 (m, 2 H), 1.72-1.54 (m, 2 H), 1.62 (s, 3 H), 1.52 (s, 2 H), 1.29 (s, 3 H), 1.25 (s, 3 H), 0.01 (s, 9 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 147.4, 134.2, 124.8, 106.9, 64.2, 58.3, 38.1, 36.3, 27.4, 26.9, 26.4, 24.9, 18.7, 16.0, -1.3; ES-MS 280 $[\text{M}^+]$, 219, 153, 73.