Supporting Information for

Enantioselective Total Synthesis of FR900482

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General Methods. All reactions sensitive to oxygen and moisture were carried out in oven-dried glassware under a slightly positive pressure of argon unless otherwise noted. Melting points (mp) were uncorrected. ^1H -NMR and ^{13}C -NMR spectra were recorded at 400 MHz and 100 MHz, respectively. The chemical shifts for ^1H NMR are reported in parts per million (ppm) downfield from tetramethylsilane as the internal standard and coupling constants are in Hertz (Hz). The following abbreviations are used for spin multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad. The chemical shifts for ^{13}C NMR were reported in ppm relative to the central line of a triplet at 77.0 ppm for CDCl_3 . IR spectra are reported in wavenumbers (cm^{-1}). Analytical thin layer chromatography (TLC) was performed on pre-coated analytical plates, 0.25 mm thick, silica gel 60 F_{245} . Preparative TLC was performed on 6.7 x 20 cm pre-coated analytical plates, 0.50 mm thick, silica gel 60 F_{245} . Dichloromethane, dimethyl sulfoxide, benzene, toluene were distilled from calcium hydride and stored over molecular sieves 4Å. Dehydrated tetrahydrofuran, *N,N*-dimethylformamide, methanol, ethanol, diethyl ether, and acetonitrile were purchased from Kanto chemical and stored over molecular sieves 3Å or 4Å under argon. Pyridine, triethylamine and diisopropylethylamine were distilled from calcium hydride and stored over potassium hydroxide pellets. All other reagents were purchased as reagent grade and used without further purification.

Methyl 3-benzyloxy-4-((2*R*)-2-[(4*R*,5*R*)-5-(*tert*-butyldimethylsilyloxymethyl)-2,2-dimethyl-[1,3]dioxolan-4-yl]-2-hydroxy}ethyl-5-nitrobenzoate (21**).** To a stirred solution of ketone **20** (9.84 g, 17.1 mmol) in Et_2O (100 mL), cooled to $-19\text{ }^\circ\text{C}$, was added $\text{Zn}(\text{BH}_4)_2$ (0.13 M solution in Et_2O , 150 mL, 19.5 mmol) dropwise over 1 h. The reaction mixture was stirred for 1.5 h, quenched by addition of 0.5N HCl (150 mL), and extracted with Et_2O . The combined organic extracts were washed with saturated aqueous NaHCO_3 and brine, dried over MgSO_4 , and concentrated under reduced pressure to afford crude **21** (10.2 g) as a 95:5 mixture of diastereomers, which was used without further purification. A small portion of the crude product was purified by preparative TLC (hexane/ EtOAc , 7:3) to give pure **21** as a colorless oil: ^1H NMR (400 MHz, CDCl_3) δ 8.11 (d, $J = 1.5$ Hz, 1H), 7.82 (d, $J = 1.5$ Hz, 1H), 7.46-7.36 (m, 5H), 5.19 (s, 2H), 4.05-4.01 (m, 1H), 3.96 (s, 3H), 3.95-3.90 (m, 2H), 3.73 (dd, $J = 4.1, 10.7$ Hz, 1H), 3.66 (dd, $J = 5.8, 10.7$ Hz, 1H), 3.39 (dd, $J = 10.2, 13.4$ Hz, 1H), 3.14 (dd, $J = 3.6, 13.4$ Hz, 1H), 2.49 (d, $J = 9.8$ Hz, 1H), 1.38 (s, 3H), 1.33 (s, 3H), 0.85 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 165.0, 157.7, 151.5, 135.4, 129.9, 128.8, 128.5, 127.8, 127.4, 117.9, 115.6, 109.3, 81.2, 77.1, 71.4, 70.0, 63.5, 52.7, 30.7, 27.1, 27.0, 25.9,

18.3, -5.48, -5.56; IR (neat) 3560, 1730, 1538, 1291 cm^{-1} ; $[\alpha]_{\text{D}}^{23} +25.6$ (c 0.76, CHCl_3); HRMS (ESI) m/z calcd for $\text{C}_{29}\text{H}_{42}\text{NO}_9\text{Si}$ ($[\text{M}+\text{H}]^+$) 576.2629, found 576.2634.

Methyl 4-((2R)-2-acetoxy-2-[(4S,5R)-5-(tert-butyl dimethylsilyloxymethyl)-2,2-dimethyl-[1,3]dioxolan-4-yl])ethyl-3-benzyloxy-5-nitrobenzoate (22). To a solution of alcohol **21** (10.2 g) in pyridine (20 mL) containing DMAP (0.20 g, 1.64 mmol) was added Ac_2O (3.2 mL, 33.9 mmol) and the mixture was stirred for 3 h at room temperature. After removal of the solvent under reduced pressure, the residue was taken up in EtOAc and the solution was washed with 1N HCl (ice-cooled) and brine, dried over MgSO_4 , and concentrated. The resulting residue was purified by flash column chromatography (hexane/EtOAc, 50:1 then 9:1) on silica gel to afford **22** (9.8 g, 92% from **20**) as a colorless oil: ^1H NMR (400 MHz, CDCl_3) δ 8.01 (d, $J = 1.4$ Hz, 1H), 7.78 (d, $J = 1.5$ Hz, 1H), 7.49-7.36 (m, 5H), 5.30 (ddd, $J = 3.2, 4.9, 10.3$ Hz, 1H), 5.20 (s, 2H), 4.02 (dd, $J = 4.9, 7.1$ Hz, 1H), 3.95 (s, 3H), 3.80 (td, $J = 4.6, 7.1$ Hz, 1H), 3.64 (d, $J = 4.6$ Hz, 2H), 3.43 (dd, $J = 10.3, 13.9$ Hz, 1H), 3.31 (dd, $J = 3.2, 13.9$ Hz, 1H), 1.88 (s, 3H), 1.37 (s, 3H), 1.35 (s, 3H), 0.85 (s, 9H), 0.03 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.2, 165.0, 157.7, 151.8, 135.4, 130.3, 128.8, 128.5, 127.5, 126.1, 117.4, 115.3, 109.7, 79.1, 77.6, 71.6, 71.4, 63.5, 52.8, 27.3, 27.2, 26.8, 25.9, 20.7, 18.3, -5.39, -5.49; IR (neat) 1733, 1540, 1292, 1277 cm^{-1} ; $[\alpha]_{\text{D}}^{23} +49.9$ (c 0.56, CHCl_3); HRMS (ESI) m/z calcd for $\text{C}_{31}\text{H}_{44}\text{NO}_{10}\text{Si}$ ($[\text{M}+\text{H}]^+$) 618.2735, found 618.2753.

Methyl 4-((2R)-2-acetoxy-2-[(4S,5R)-5-(tert-butyl dimethylsilyloxymethyl)-2,2-dimethyl-[1,3]dioxolan-4-yl])ethyl-3-amino-5-benzyloxybenzoate (23). A mixture of acetate **22** (3.30 g, 5.34 mmol) and 5% Pt/C (0.5 g) in MeOH (175 mL) was stirred for 52 h at room temperature under a hydrogen atmosphere (ca. 1 atm). The mixture was filtered through a pad of Celite, and the filtrate was concentrated. The resulting residue was purified by flash column chromatography (hexane/EtOAc, 9:1) on silica gel to afford **23** (2.05 g, 65%) as a yellow oil: ^1H NMR (400 MHz, CDCl_3) δ 7.51 (d, $J = 7.3$ Hz, 2H), 7.30-7.40 (m, 3H), 7.03 (s, 2H), 5.12 (d, $J = 12.2$ Hz, 1H), 5.09 (d, $J = 12.2$ Hz, 1H), 5.08-5.04 (m, 1H), 4.40 (br-s, 2H), 3.93 (dd, $J = 2.0, 8.0$ Hz, 1H), 3.89 (s, 3H), 3.80 (ddd, $J = 3.9, 5.1, 8.0$ Hz, 1H), 3.63 (dd, $J = 3.9, 11.0$ Hz, 1H), 3.57 (dd, $J = 5.1, 11.0$ Hz, 1H), 3.32 (dd, $J = 9.5, 13.4$ Hz, 1H), 2.90 (dd, $J = 5.1, 13.4$ Hz, 1H), 2.10 (s, 3H), 1.43 (s, 3H), 1.26 (s, 3H), 0.74 (s, 9H), -0.09 (s, 3H), -0.13 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.8, 167.2, 157.8, 147.0, 137.0, 129.8, 128.4, 127.7, 127.2, 114.1, 110.4, 109.2, 102.4, 77.7, 76.8, 70.6, 70.1, 62.8, 52.0, 29.7, 26.9, 26.8, 25.7, 21.1, 18.1,

–5.66, –5.84; IR (neat) 3379, 1722, 1583, 1239 cm^{-1} ; $[\alpha]_{\text{D}}^{23}$ –4.1 (*c* 0.27, CHCl_3); HRMS (ESI) m/z calcd for $\text{C}_{31}\text{H}_{46}\text{NO}_8\text{Si}$ ($[\text{M}+\text{H}]^+$) 588.2993, found 588.3016.

Methyl 4-((2*R*)-2-acetoxy-2-[(4*S*,5*R*)-5-(*tert*-butyldimethylsilyloxymethyl)-2,2-dimethyl-[1,3]dioxolan-4-yl]}ethyl-3-benzyloxy-5-(2-nitrobenzenesulfonylamino)benzoate (24**).** To a stirred solution of aniline **23** (2.05 g, 3.49 mmol) in pyridine (10 mL) was added 2-nitrobenzenesulfonyl chloride (3.30 g, 14.9 mmol) portionwise over 30 min at room temperature. After completion of the addition, the reaction mixture was stirred for an additional 30 min. The mixture was diluted with EtOAc and sequentially washed with brine, 1N HCl, and brine. The organic layer was dried over MgSO_4 , concentrated under reduced pressure, and purified by flash column chromatography (hexane/EtOAc, 4:1) on silica gel to afford **24** (1.96 g, 73%) as a yellow oil: ^1H NMR (400 MHz, CDCl_3) δ 8.93 (brs, 1H), 7.96 (d, J = 1.2 Hz, 1H), 7.80 (dd, J = 1.2, 7.8 Hz, 1H), 7.77 (dd, J = 1.2, 7.8 Hz, 1H), 7.67 (dt, J = 1.2, 7.8 Hz, 1H), 7.55 (dt, J = 1.2, 7.8 Hz, 1H), 7.50 (d, J = 1.2 Hz, 1H), 7.44 (d, J = 6.8 Hz, 2H), 7.39-7.28 (m, 3H), 5.19 (dt, J = 2.2, 7.8 Hz, 1H), 5.14 (d, J = 11.5 Hz, 1H), 5.07 (d, J = 11.5 Hz, 1H), 3.94 (s, 3H), 3.81 (td, J = 4.3, 8.0 Hz, 1H), 3.70 (dd, J = 2.2, 8.0 Hz, 1H), 3.60 (d, J = 4.3 Hz, 2H), 2.93 (d, J = 7.8 Hz, 2H), 2.07 (s, 3H), 1.54 (s, 3H), 1.45 (s, 3H), 0.71 (s, 9H), –0.09 (s, 3H), –0.12 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 169.9, 166.2, 157.1, 147.8, 136.3, 135.9, 133.7, 133.2, 132.3, 130.9, 130.3, 128.5, 128.0, 127.6, 127.2, 124.8, 120.0, 110.2, 110.0, 77.2, 76.5, 70.5, 69.5, 62.3, 52.4, 27.1, 26.9, 26.4, 25.6, 20.9, 18.0, –5.63, –5.79; IR (neat) 1726, 1583, 1546, 1233 cm^{-1} ; $[\alpha]_{\text{D}}^{23}$ –10.9 (*c* 1.63, CHCl_3); HRMS (ESI) m/z calcd for $\text{C}_{37}\text{H}_{52}\text{N}_3\text{O}_{12}\text{SSi}$ ($[\text{M}+\text{NH}_4]^+$) 790.3041, found 790.3164.

Benzazocine (26**).** To a stirred solution of sulfonamide **24** (1.90 g, 2.46 mmol) in THF (5 mL) was added TBAF (1 M solution in THF, 11 mL, 11 mmol). The reaction mixture was stirred for 41 h at room temperature, diluted with EtOAc, and sequentially washed with 10% aqueous citric acid and brine. The organic layer was dried over MgSO_4 and concentrated under reduced pressure to give crude primary alcohol **25** (1.50 g) as a pale yellow oil. To a stirred solution of the crude alcohol **25** and Ph_3P (1.13 g, 4.32 mmol) in benzene (100 mL) was added DEAD (40% solution in toluene, 1.6 mL, 3.52 mmol) dropwise over 15 min at room temperature. After 45 min, the reaction mixture was concentrated under reduced pressure, and purified by flash column chromatography (hexane/EtOAc, 3:2) on silica gel to afford **26** (1.15 g, 71% from **24**) as a white crystalline solid: mp 181-182 $^{\circ}\text{C}$; ^1H NMR (400

MHz, CDCl₃) δ 7.77-7.70 (m, 2H), 7.67 (d, J = 1.5 Hz, 1H), 7.62-7.49 (m, 2H), 7.43-7.33 (m, 5H), 7.11 (d, J = 1.5 Hz, 1H), 5.13 (s, 2H), 5.08 (ddd, J = 2.9, 3.6, 8.8 Hz, 1H), 4.83 (dd, J = 3.9, 14.6 Hz, 1H), 4.22 (ddd, J = 3.9, 8.6, 10.5 Hz, 1H), 3.82 (s, 3H), 3.66 (dd, J = 2.9, 15.1 Hz, 1H), 3.51 (dd, J = 8.6, 8.8 Hz, 1H), 3.31 (dd, J = 3.6, 15.1 Hz, 1H), 3.14 (dd, J = 10.5, 14.6 Hz, 1H), 1.51 (s, 3H), 1.38 (s, 3H), 1.27 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 170.3, 165.4, 158.3, 147.8, 139.3, 135.6, 134.1, 133.0, 132.5, 132.2, 131.4, 130.6, 128.7, 128.6, 128.4, 127.4, 127.2, 124.2, 123.2, 114.1, 109.5, 81.1, 76.3, 74.7, 71.2, 55.0, 52.4, 26.7, 26.6, 20.8; IR (KBr) 1726, 1546, 1249 cm⁻¹; [α]_D²³ -55.5 (c 0.54, CHCl₃); HRMS (ESI) m/z calcd for C₃₁H₃₆N₃O₁₁S ([M+NH₄]⁺) 658.2071, found 658.2088; Anal. calcd for C₃₁H₃₂N₂O₁₁S: C, 58.12; H, 5.03; N, 4.37; found: C, 57.81; H, 4.97; N, 4.56.

***p*-Methoxyphenyl ether (28).** To a solution of benzazocine **26** (28.6 g, 44.6 mmol) in CH₂Cl₂ (150 mL) was added DIBAL (1 M solution in toluene, 270 mL) dropwise over 1 h at -78 °C. After the reaction mixture was stirred for 15 min, the reaction was quenched by addition of MeOH (190 mL), and allowed to warm to room temperature. The mixture was stirred for an additional 1 h, poured into 1 N HCl (500 mL), and extracted with CHCl₃. The organic layer was washed with brine, saturated aqueous NaHCO₃ and brine, dried over MgSO₄, and concentrated to afford crude benzyl alcohol **27** (31.5 g) as a yellow oil. To a stirred solution of the crude benzyl alcohol **27** in benzene (250 mL), containing Ph₃P (14.0 g, 53.5 mmol) and *p*-methoxyphenol (6.64 g, 53.5 mmol), was added DEAD (40% solution in toluene, 24.3 mL, 53.5 mmol) dropwise over 10 min at room temperature. After the reaction mixture had been stirred for 10 min, the solution was concentrated. The crude product was triturated with CHCl₃ and filtered to remove Ph₃P(O). After removal of the solvent, the residue was purified by flash column chromatography (benzene/EtOAc, 9:1) on silica gel to afford **28** (21.2 g, 68% from **26**) as a colorless oil. This material was obtained as a mixture of two conformational isomers: ¹H NMR (400 MHz, CDCl₃) δ 7.67-7.61 (m, 3H), 7.46-7.36 (m, 6H), 7.09 (s, (2/3)1H), 7.05 (s, (1/3)1H), 6.83-6.71 (m, 4H), 6.51 (s, (1/3)1H), 6.49 (s, (2/3)1H), 5.17-5.06 (m, 2H), 4.86-4.73 (m, 2H+(2/3)1H), 4.18 (t, J = 8.3 Hz, (1/3)1H), 4.01-4.13 (m, 1H), 3.775 (s, (2/3)3H), 3.773 (s, (1/3)3H), 3.73 (dd, J = 4.6, 11.7 Hz, (2/3)1H), 3.54-3.48 (m, (1/3)1H), 3.41-3.26 (m, 3H), 3.07 (dd, J = 10.5, 14.4 Hz, (2/3)1H), 3.02 (dd, J = 11.5, 13.0 Hz, (1/3)1H), 2.93 (d, J = 3.7 Hz, (2/3)1H), 2.56 (brs, (1/3)1H), 1.46 (s, (1/3)3H), 1.41 (s, (2/3)3H), 1.31 (s, (1/3)3H), 1.29 (s, (2/3)3H); IR (neat) 3546, 1545, 1508, 1372, 1228, 1074 cm⁻¹; [α]_D²² -26.1 (c 0.65, CHCl₃); HRMS (ESI) m/z calcd for C₃₅H₄₀N₃O₁₀S ([M+NH₄]⁺) 694.2434, found 694.2449.

Ketone (29). To a stirred solution of oxalyl chloride (3.6 mL, 41.7 mmol) in CH₂Cl₂ (150 mL) was added a solution of DMSO (3.9 mL, 55.6 mmol) in CH₂Cl₂ (10 mL) at -78 °C. After 10 min, a solution of alcohol **28** (21.0 g, 31.0 mmol) in CH₂Cl₂ (200 mL) was added dropwise to the mixture. After the reaction mixture had been stirred for additional 30 min, Et₃N (11.6 mL, 83.4 mmol) was added. The reaction mixture was allowed to warm to room temperature, poured into 10% aqueous citric acid, and extracted with CH₂Cl₂. The organic layer was washed with saturated aqueous NaHCO₃ and brine, dried over MgSO₄, and concentrated under reduced pressure. The crude product was purified by recrystallization from hexane/EtOAc to afford ketone **29** (15.1 g, 72%) as colorless crystals: mp 154-156 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.70-7.30 (m, 5H), 7.05 (s, 1H), 6.83-6.70 (m, 4H), 6.56 (s, 1H), 5.10 (d, *J* = 13.2 Hz, 1H), 5.07 (d, *J* = 12.0 Hz, 1H), 4.93 (dd, *J* = 4.1, 14.6 Hz, 1H), 4.82 (d, *J* = 12.4 Hz, 1H), 4.77 (d, *J* = 12.7 Hz, 1H), 4.39-4.31 (m, 1H), 4.27 (d, *J* = 8.8 Hz, 1H), 4.16 (d, *J* = 13.9 Hz, 1H), 4.12 (d, *J* = 12.0 Hz, 1H), 3.78 (s, 3H), 3.23 (dd, *J* = 10.2, 14.6 Hz, 1H), 1.45 (s, 3H), 1.36 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 201.7, 157.6, 154.3, 152.3, 147.8, 139.5, 139.3, 135.7, 134.1, 132.5, 131.3, 128.7, 128.2, 127.2, 124.4, 124.1, 120.3, 115.7, 114.7, 111.9, 110.9, 83.3, 76.8, 70.6, 69.7, 55.7, 55.4, 37.7, 26.5, 25.7; IR (KBr) 1728, 1544, 1508, 1372, 1228, 1168, 1054 cm⁻¹; [α]_D²² -10.9 (*c* 0.88, CHCl₃); MS (ESI) *m/z* 675 ([M+H]⁺); Anal. calcd for C₃₅H₃₄N₂O₁₀S: C, 62.30; H, 5.08; N, 4.15; found: C, 62.19; H, 5.14; N, 4.10.

α, β-Unsaturated ketone (30). A 500-mL autoclave was charged with ketone **29** (15.1 g, 22.4 mmol), Me₂NH·HCl (2.19 g, 26.9 mmol), 37% formalin (8.5 mL, 0.11 mol), Et₃N (0.94 mL, 6.72 mmol), 2-PrOH (150 mL) and water (15 mL). The autoclave was capped and heated at 90 °C for 4.5 h. The reaction mixture was diluted with CHCl₃, and sequentially washed with 10% aqueous citric acid, saturated aqueous NaHCO₃ and brine. The organic layer was dried over MgSO₄ and concentrated under reduced pressure to afford α, β-unsaturated ketone **30** (18.8 g), which was used for the next reaction without further purification. A small portion of the crude product was purified by preparative silica gel TLC (hexane/EtOAc, 7:3) to give pure **30** as a colorless oil: ¹H NMR (400 MHz, CDCl₃) δ 7.62-7.67 (m, 2H), 7.56 (dd, *J* = 1.2, 7.8 Hz, 1H), 7.44 (dd, *J* = 1.4, 8.0 Hz, 1H), 7.27-7.37 (m, 5H), 7.14 (s, 1H), 6.86-6.76 (m, 5H), 6.72 (d, *J* = 1.5 Hz, 1H), 5.60 (d, *J* = 1.7 Hz, 1H), 5.12 (d, *J* = 12.0 Hz, 1H), 5.04 (d, *J* = 12.0 Hz, 1H), 4.92 (d, *J* = 12.7 Hz, 1H), 4.87 (d, *J* = 12.7 Hz, 1H), 4.82 (dd, *J* = 4.9, 14.4 Hz, 1H), 4.44 (d, *J* = 8.8 Hz, 1H), 4.25 (ddd, *J* = 4.9, 8.8, 10.5 Hz, 1H), 3.78 (s, 3H), 3.20 (dd, *J* =

10.7, 14.4 Hz, 1H), 1.52 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 193.4, 157.1, 154.4, 152.4, 148.2, 140.7, 139.1, 136.3, 135.9, 134.1, 133.7, 132.1, 132.0, 131.2, 128.7, 128.1, 126.9, 123.9, 120.3, 115.9, 114.8, 112.8, 111.5, 82.1, 78.3, 70.7, 69.8, 55.8, 54.5, 26.9, 26.0; IR (neat) 1707, 1546, 1507, 1373, 1228 cm^{-1} ; $[\alpha]_{\text{D}}^{22}$ -11.7 (c 0.55, CHCl_3); HRMS (ESI) m/z calcd for $\text{C}_{36}\text{H}_{35}\text{N}_2\text{O}_{10}\text{S}$ ($[\text{M}+\text{H}]^+$) 687.2012, found 687.1998.

Sulfide (31). To a stirred solution of α,β -unsaturated ketone **30** (18.7 g) in THF/MeOH (50 mL/50 mL) was added Et_3N (1.2 mL, 8.96 mmol) followed by PhSH (3.4 mL, 33.6 mmol) at room temperature. After the reaction mixture had been stirred for 3 h, the solution was cooled to 0 $^\circ\text{C}$, to which was added NaBH_4 (0.85 g, 22.4 mmol) and the stirring was continued for 15 min. The reaction mixture was diluted with CHCl_3 , and washed with 10% aqueous citric acid, saturated aqueous NaHCO_3 and brine. The organic layer was dried over MgSO_4 , concentrated under reduced pressure, and purified by flash column chromatography (benzene/EtOAc, 50:1 then 20:1) on silica gel to afford **31** (15.0 g, 84% from **29**) as a yellow oil: ^1H NMR (400 MHz, CDCl_3) δ 7.64-7.61 (m, 3H), 7.46-7.35 (m, 7H), 7.18-7.06 (m, 5H), 6.85-6.75 (m, 5H), 5.13 (d, J = 10.8 Hz, 1H), 5.01 (d, J = 10.8 Hz, 1H), 4.91 (d, J = 12.5 Hz, 1H), 4.87 (d, J = 12.5 Hz, 1H), 4.59 (br-s, 1H), 4.16 (dd, J = 2.4, 8.1 Hz, 1H), 4.02 (t, J = 11.0 Hz, 1H), 3.78 (s, 3H), 3.78-3.56 (m, 4H), 3.32 (dd, J = 4.2, 11.9 Hz, 1H), 2.31 (d, J = 1.2 Hz, 1H), 1.43 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 159.9, 154.2, 152.5, 148.1, 138.9, 138.1, 136.9, 135.9, 134.0, 132.3, 131.7, 131.3, 128.8, 128.33, 128.30, 128.3, 128.0, 127.5, 125.4, 124.2, 120.2, 115.8, 114.7, 112.6, 108.8, 84.2, 71.5, 70.0, 69.8, 69.7, 55.7, 54.0, 40.5, 36.7, 26.7; IR (neat) 3555, 1546, 1507, 1373, 1227 cm^{-1} ; $[\alpha]_{\text{D}}^{22}$ -7.5 (c 1.69, CHCl_3); HRMS (ESI) m/z calcd for $\text{C}_{42}\text{H}_{43}\text{N}_2\text{O}_{10}\text{S}_2$ ($[\text{M}+\text{H}]^+$) 799.2359, found 799.2422.

Acetate (32). To a stirred solution of sulfide **31** (14.9 g, 18.7 mmol) and DMAP (0.27 g, 2.24 mmol) in pyridine (30 mL) was added Ac_2O (10.5 mL, 0.11 mol) at 0 $^\circ\text{C}$. The reaction mixture was stirred for 2.5 h at room temperature, diluted with EtOAc, and washed with 1N HCl, brine, saturated aqueous NaHCO_3 , and brine. The organic layer was dried over MgSO_4 , concentrated under reduced pressure, and purified by flash column chromatography (hexane/ CH_2Cl_2 , 1:2) on silica gel to afford **32** (12.5 g, 80%) as a yellow oil: ^1H NMR (400 MHz, C_6D_6) δ 7.50-7.47 (m, 1H), 7.32-7.29 (m, 2H), 7.17-6.73 (m, 15H), 6.57-6.53 (m, 2H), 6.17 (d, J = 2.4 Hz, 1H), 4.63 (d, J = 10.9 Hz, 1H), 4.59 (d, J = 10.9 Hz, 1H), 4.57 (d, J = 12.2 Hz, 1H), 4.53 (d, J = 12.2 Hz, 1H), 4.43 (dd, J = 10.8, 11.2 Hz, 1H),

4.38 (dd, $J = 2.4, 8.0$ Hz, 1H), 4.11 (dd, $J = 7.1, 8.8$ Hz, 1H), 4.01 (dd, $J = 4.6, 11.2$ Hz, 1H), 3.89 (ddd, $J = 4.6, 8.0, 10.8$ Hz, 1H), 3.77 (dd, $J = 6.8, 12.0$ Hz, 1H), 3.62 (dd, $J = 9.3, 12.0$ Hz, 1H), 3.36 (s, 3H), 1.60 (s, 3H), 1.32 (s, 3H), 1.16 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 170.0, 160.7, 155.1, 153.3, 149.0, 139.7, 139.5, 137.7, 136.1, 133.9, 132.8, 132.4, 131.2, 129.7, 129.4, 129.2, 128.8, 128.4, 126.1, 124.3, 120.7, 116.3, 115.3, 112.8, 109.7, 83.5, 72.0, 71.9, 71.4, 70.1, 55.5, 55.2, 40.7, 37.5, 27.1, 27.0, 21.0; IR (neat) 1743, 1546, 1508, 1372, 1229 cm^{-1} ; $[\alpha]_{\text{D}}^{22} -12.6$ (c 0.92, CHCl_3); HRMS (ESI) m/z calcd for $\text{C}_{44}\text{H}_{48}\text{N}_3\text{O}_{11}\text{S}_2$ ($[\text{M}+\text{NH}_4]^+$) 858.2730, found 858.2731.

Primary alcohol (34). To a stirred solution of sulfide **32** (6.0 g, 7.13 mmol) in CH_2Cl_2 (30 mL) was added a solution of *m*-CPBA (1.70 g, 6.90 mmol) in CH_2Cl_2 (50 mL) dropwise over 1 h at -13 °C. After the reaction mixture was stirring for 15 min, the solution was poured into saturated aqueous NaHCO_3 , and extracted with CH_2Cl_2 . The organic layer was dried over Na_2SO_4 , and concentrated to afford a crude sulfoxide **33** (7.14 g) as a yellow oil. To a stirred solution of the resulting sulfoxide **33** in toluene (30 mL) was added Et_3N (4.0 mL, 28.5 mmol) followed by TFAA (2.0 mL, 14.3 mmol) at 0 °C. After the reaction mixture had been stirred for 30 min, the solution was poured into a suspension of NaBH_4 (2.7 g, 71 mmol) in MeOH (150 mL) dropwise over 10 min at -78 °C. Then the reaction mixture was allowed to warm to room temperature, stirred for 1 h, poured into 10% aqueous citric acid, and extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4 , concentrated, and purified by flash column chromatography (hexane/EtOAc, 7:3 then EtOAc) on silica gel to afford **34** (3.90 g, 73% from **32**) as a colorless oil: ^1H NMR (400 MHz, C_6D_6) δ 7.42 (dd, $J = 1.4, 7.8$ Hz, 1H), 7.21-6.62 (m, 12H), 6.23 (d, $J = 1.7$ Hz, 1H), 5.97 (d, $J = 2.4$ Hz, 1H), 4.63 (s, 2H), 4.58 (d, $J = 12.2$ Hz, 1H), 4.54 (d, $J = 12.2$ Hz, 1H), 4.46 (dd, $J = 11.0, 11.7$ Hz, 1H), 4.41 (dd, $J = 2.7, 8.3$ Hz, 1H), 4.22 (dd, $J = 9.0, 10.2$ Hz, 1H), 4.03 (dd, $J = 4.6, 11.7$ Hz, 1H), 3.92-3.86 (m, 2H), 3.77 (dd, $J = 5.8, 8.4$ Hz, 1H), 3.38 (s, 3H), 1.61 (s, 3H), 1.34 (s, 3H), 1.17 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 170.0, 160.1, 154.9, 153.0, 148.4, 139.24, 139.16, 136.2, 133.7, 132.2, 131.0, 128.9, 128.6, 127.9, 127.6, 124.1, 121.0, 116.1, 115.0, 112.7, 109.3, 83.4, 71.7, 71.5, 69.8, 69.2, 63.2, 55.3, 54.8, 44.3, 26.9, 26.8, 20.7; IR (neat) 3515, 1742, 1546, 1508, 1372, 1231 cm^{-1} ; $[\alpha]_{\text{D}}^{22} +13.5$ (c 0.51, CHCl_3); HRMS (ESI) m/z calcd for $\text{C}_{38}\text{H}_{44}\text{N}_3\text{O}_{12}\text{S}$ ($[\text{M}+\text{NH}_4]^+$) 766.2646, found 766.2739.

Diol (35). To a stirred solution of primary alcohol **34** (7.9 g, 10.5 mmol) in CH_2Cl_2 (40 mL) was added DIBAL (1 M solution in toluene, 32 mL, 32 mmol) dropwise over 10 min, at -78 °C. After the

reaction mixture was stirred for 1 h at $-78\text{ }^{\circ}\text{C}$, the reaction was quenched by the addition of MeOH (22.4 mL), allowed to warm to room temperature, and stirring was continued for an additional 1 h. Then, the reaction mixture was poured into 1 N HCl (40 mL), and extracted with CHCl_3 . The organic layer was washed with brine, saturated aqueous NaHCO_3 and brine, dried over MgSO_4 , and concentrated under reduced pressure to afford **35** (8.4 g), which was used for the next reaction without further purification. A small portion of the crude product was purified by preparative silica gel TLC (hexane/EtOAc, 7:3) to give pure **35** as a colorless oil: ^1H NMR (400 MHz, CDCl_3) δ 7.66-7.59 (m, 3H), 7.50-7.30 (m, 6H), 7.10 (s, 1H), 6.85-6.73 (m, 4H), 6.61 (d, $J = 1.2$ Hz, 1H), 5.10 (d, $J = 10.8$ Hz, 1H), 5.04 (d, $J = 11.0$ Hz, 1H), 4.86 (d, $J = 12.5$ Hz, 1H), 4.81 (d, $J = 12.4$ Hz, 1H), 4.45 (br-s, 1H), 4.18 (dd, $J = 2.4, 8.3$ Hz, 1H), 4.13-4.03 (m, 2H), 3.95-3.91 (m, 1H), 3.80 (dd, $J = 4.6, 12.0$ Hz, 1H), 3.77 (s, 3H), 3.67-3.57 (m, 2H), 2.34 (br-s, 1H), 1.89 (br, 1H), 1.43 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 159.7, 154.3, 152.6, 148.1, 138.8, 138.4, 135.8, 134.1, 132.4, 131.9, 131.4, 128.9, 128.5, 128.1, 127.8, 124.1, 120.2, 115.9, 114.8, 112.9, 109.0, 84.5, 71.7, 70.0, 69.8, 68.8, 63.9, 55.8, 54.3, 43.9, 26.8; IR (neat) 3521, 1546, 1508, 1374, 1228 cm^{-1} ; $[\alpha]_{\text{D}}^{22} +23.9$ (c 1.07, CHCl_3); HRMS (ESI) m/z calcd for $\text{C}_{36}\text{H}_{42}\text{N}_3\text{O}_{11}\text{S}$ ($[\text{M}+\text{NH}_4]^+$) 724.2540, found 724.2555.

TBS ether (36). To a stirred solution of diol **35** (8.3 g) in CH_2Cl_2 (40 mL) were sequentially added Et_3N (4.4 mL, 3.2 g, 31.6 mmol), DMAP (120 mg, 1.0 mmol) and TBSCl (2.70 g, 17.9 mol) at room temperature. After the reaction mixture had been stirred for 1 h, 10% aqueous citric acid was added to the solution, and the mixture was extracted with CHCl_3 . The organic layer was washed with saturated aqueous NaHCO_3 and brine, dried over MgSO_4 , and concentrated under reduced pressure to afford **36** (9.0 g), which was used for the next reaction without further purification. A small portion of the crude product was purified by preparative silica gel TLC (hexane/EtOAc, 7:3) to give pure **36** as a colorless oil: ^1H NMR (400 MHz, CDCl_3) δ 7.66-7.57 (m, 3H), 7.47-7.32 (m, 6H), 7.09 (d, $J = 1.0$ Hz, 1H), 6.99-6.80 (m, 4H), 6.75 (d, $J = 1.2$ Hz, 1H), 5.06 (d, $J = 10.5$ Hz, 1H), 4.96 (d, $J = 10.5$ Hz, 1H), 4.91 (d, $J = 12.2$ Hz, 1H), 4.87 (d, $J = 12.2$ Hz, 1H), 4.47 (d, $J = 2.2$ Hz, 1H), 4.31 (t, $J = 10.0$ Hz, 1H), 4.17 (dd, $J = 2.4, 8.3$ Hz, 1H), 4.07 (t, $J = 11.0$ Hz, 1H), 3.78 (s, 3H), 3.76 (dd, $J = 4.4, 11.0$ Hz, 1H), 3.66-3.59 (m, 1H), 3.43 (dd, $J = 3.2, 10.0$ Hz, 1H), 3.35 (dd, $J = 3.2, 10.0$ Hz, 1H), 2.24 (br-s, 1H), 1.45 (s, 3H), 1.34 (s, 3H), 0.77 (s, 9H), -0.12 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 159.7, 154.3, 152.6, 148.1, 138.7, 138.1, 135.9, 133.9, 132.2, 132.0, 131.2, 128.7, 128.4, 128.2, 127.9, 124.2, 120.6, 115.9, 114.7, 112.4, 108.8, 84.6, 71.5, 69.9, 69.8, 68.3, 63.6, 55.8, 54.0, 44.5, 26.8, 26.0, 18.2, $-5.36, -5.44$; IR

(neat) 3500, 1547, 1508, 1373, 1228 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{42}\text{H}_{56}\text{N}_3\text{O}_{11}\text{SSi}$ ($[\text{M}+\text{NH}_4]^+$) 838.3405, found 838.3348.

Secondary amine (37). To a stirred solution of TBS ether **36** (8.9 g) in MeCN (40 mL) were sequentially added PhSH (2.0 mL, 20 mmol) and Cs_2CO_3 (7.0 g, 20 mmol) at room temperature. After the reaction mixture had been stirred for 1 h, the solution was partitioned between EtOAc and 10% aqueous citric acid. The organic layer was washed with brine, dried over MgSO_4 , and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (CH_2Cl_2 /hexane, 35:65 to 75:25, then EtOAc/hexane, 3:1) on silica gel to afford **37** (4.90 g, 73% from **34**) as a colorless oil: ^1H NMR (400 MHz, CDCl_3) δ 7.47-7.33 (m, 5H), 6.92-6.83 (m, 6H), 5.10 (d, $J = 10.7$ Hz, 1H), 4.96 (s, 2H), 4.92 (d, $J = 10.7$ Hz, 1H), 4.55 (br-s, 1H), 4.38 (t, $J = 10.0$ Hz, 1H), 4.06 (dd, $J = 2.4, 8.3$ Hz, 1H), 3.78 (s, 3H), 3.84-3.76 (m, 1H), 3.71 (dd, $J = 3.2, 9.8$ Hz, 1H), 3.63 (dd, $J = 2.9, 9.8$ Hz, 1H), 3.45 (dd, $J = 4.9, 10.3$ Hz, 1H), 3.06 (t, $J = 10.3$ Hz, 1H), 3.04 (br, 1H), 2.50 (brs, 1H), 1.41 (s, 3H), 1.36 (s, 3H), 0.80 (s, 9H), -0.090 (s, 3H), -0.095 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 158.8, 154.1, 152.8, 147.8, 138.0, 136.2, 128.7, 128.3, 128.1, 123.9, 118.1, 115.8, 114.7, 108.4, 108.4, 85.3, 71.1, 70.5, 70.3, 68.8, 64.8, 55.7, 53.8, 44.7, 27.1, 26.7, 25.8, 18.3, -5.38, -5.48; IR (neat) 3499, 3325, 1508, 1228, 1070 cm^{-1} ; $[\alpha]_{\text{D}}^{22} -69.0$ (c 0.59, CHCl_3); HRMS (ESI) m/z calcd for $\text{C}_{36}\text{H}_{50}\text{NO}_7\text{Si}$ ($[\text{M}+\text{H}]^+$) 636.3357, found 636.3340.

Acetate (39). To a stirred solution of secondary amine **37** (4.76 g, 7.49 mmol) in CH_2Cl_2 (50 mL) was added a solution of *m*-CPBA (2.06 g, 8.37 mmol) in CH_2Cl_2 (60 mL) dropwise over 20 min at room temperature. After 10 min, the reaction mixture was poured into saturated aqueous NaHCO_3 and extracted with CH_2Cl_2 . The organic layer was washed with brine, dried over Na_2SO_4 , and concentrated under reduced pressure to afford the crude hydroxylamine **38** (4.24 g) as a colorless oil. The crude hydroxylamine **38** was then dissolved in Ac_2O (20 mL) and stirred for 12 h at room temperature. The reaction mixture was concentrated under reduced pressure, and the residue was partitioned between EtOAc and 10% aqueous citric acid. The organic layer was washed with brine, dried over Na_2SO_4 , and concentrated to afford **39** (5.88 g), which was used for the next reaction without further purification. A small portion of the crude product was purified by preparative TLC (hexane/EtOAc, 7:3) to give pure **39** as a colorless oil: ^1H NMR (400 MHz, CDCl_3) δ 7.46-7.34 (m, 5H), 7.18 (s, 1H), 6.97 (s, 1H), 6.91 (d, $J = 6.8$ Hz, 2H), 6.85 (d, $J = 6.8$ Hz, 2H), 5.11 (d, $J = 10.7$ Hz, 1H), 4.98 (s, 2H), 4.94 (d, $J = 10.7$

Hz, 1H), 4.61 (d, $J = 2.7$ Hz, 1H), 4.41 (t, $J = 10.2$ Hz, 1H), 4.23 (dd, $J = 2.7, 7.8$ Hz, 1H), 4.05 (dd, $J = 3.7, 10.2$ Hz, 1H), 3.78 (s, 3H), 3.73 (dd, $J = 3.7, 10.2$ Hz, 1H), 3.54-3.39 (m, 3H), 2.04 (s, 3H), 1.41 (s, 3H), 1.34 (s, 3H), 0.81 (s, 9H), -0.06 (s, 3H), -0.07 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 168.1, 158.6, 154.2, 152.7, 149.9, 138.4, 136.1, 128.7, 128.3, 128.1, 122.3, 115.9, 114.7, 112.8, 110.2, 108.5, 84.8, 71.2, 70.4, 69.12, 69.08, 64.1, 62.6, 55.7, 44.0, 26.8, 26.7, 26.0, 19.5, 18.3, -5.37 , -5.46 ; IR (neat) 3515, 1767, 1508, 1210, 1078 cm^{-1} ; $[\alpha]_{\text{D}}^{22} -5.4$ (c 0.48, CHCl_3).

Ketone (40). To a stirred solution of oxalyl chloride (1.3 mL, 15.3 mmol) in CH_2Cl_2 (40 mL) was added a solution of DMSO (2.1 mL, 30.0 mmol) in CH_2Cl_2 (5 mL) at -78 °C. After 10 min, a solution of acetate **39** (5.88 g) in CH_2Cl_2 (10 mL) was added dropwise to the mixture. After the reaction mixture had been stirred for additional 30 min, Et_3N (5.3 mL, 38.3 mmol) was added to the solution. The reaction mixture was allowed to warm to room temperature, poured into 10% aqueous citric acid, and extracted with CH_2Cl_2 . The organic layer was washed with saturated aqueous NaHCO_3 and brine, dried over MgSO_4 , concentrated under reduced pressure, and purified by flash column chromatography (Et_2O /hexane, 1:1) on silica gel to afford **40** (3.70 g, 70% from **37**) as a colorless oil: ^1H NMR (400 MHz, C_6D_6) δ 7.46 (d, $J = 7.3$ Hz, 2H), 7.31-7.13 (m, 4H), 6.90-6.77 (m, 4H), 6.76 (s, 1H), 5.82 (dd, $J = 2.9, 9.5$ Hz, 1H), 5.46 (dd, $J = 9.5, 9.8$ Hz, 1H), 5.07 (d, $J = 8.5$ Hz, 1H), 4.70 (s, 2H), 4.61 (d, $J = 11.0$ Hz, 1H), 4.52 (d, $J = 11.2$ Hz, 1H), 4.11 (dd, $J = 3.2, 9.8$ Hz, 1H), 3.71 (dd, $J = 5.2, 8.6$ Hz, 1H), 3.58 (dd, $J = 8.6, 10.0$ Hz, 1H), 3.46-3.40 (m, 1H), 3.37 (s, 3H), 1.55 (s, 3H), 1.32 (s, 3H), 1.26 (s, 3H), 0.98 (s, 9H), 0.131 (s, 3H), 0.125 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 200.1, 167.2, 158.2, 154.9, 153.1, 149.7, 139.8, 136.5, 128.8, 128.2, 127.5, 120.0, 116.2, 115.1, 113.2, 111.2, 111.0, 88.1, 75.1, 70.8, 70.3, 62.8, 61.4, 55.2, 51.9, 26.8, 26.2, 26.0, 18.6, 14.2, -5.18 ; IR (neat) 1769, 1733, 1508, 1228 cm^{-1} ; $[\alpha]_{\text{D}}^{22} -91.8$ (c 0.410, CHCl_3); MS (ESI) m/z 692 ($[\text{M}+\text{H}]^+$).

Hydroxylamine hemiacetal (41). To a stirred solution of ketone **40** (44 mg, 63 μmol) in $\text{MeOH}/\text{CH}_2\text{Cl}_2$ (0.3 mL/0.3 mL) was added hydrazine hydrate (35 μL , 0.72 mmol) at room temperature. After the reaction mixture had been stirred for 1 h, the solution was concentrated under reduced pressure. The crude product was purified by preparative TLC (hexane/ EtOAc , 7:3) to afford hydroxylamine hemiacetal **41a** and **41b** (32 mg, 78%) as a mixture of diastereomers (**41a**:**41b** = 79:21). The major isomer **41a**: ^1H NMR (400 MHz, CDCl_3) δ 7.42-7.31 (m, 5H), 6.90-6.82 (m, 5H), 6.60 (s, 1H), 5.17 (d, $J = 12.0$ Hz, 1H), 5.13 (d, $J = 12.0$ Hz, 1H), 4.93 (s, 2H), 4.15 (dd, $J = 3.6, 9.3$ Hz, 1H), 4.00 (t, $J =$

9.5 Hz, 1H), 3.78 (s, 3H), 3.69 (d, $J = 9.8$ Hz, 1H), 3.63 (dd, $J = 3.6, 9.5$ Hz, 1H), 3.59-3.44 (m, 3H), 2.04 (s, 1H), 1.48 (s, 3H), 1.33 (s, 3H), 0.85 (s, 9H), -0.035 (s, 3H), -0.040 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 155.7, 154.2, 152.6, 147.4, 138.3, 136.3, 128.7, 128.3, 127.4, 115.9, 114.9, 114.7, 111.3, 109.4, 107.1, 101.6, 83.6, 70.3, 68.1, 63.7, 59.8, 55.7, 35.8, 26.6, 26.4, 25.7, 18.1, -5.53 , -5.90 ; IR (neat) 3327, 1508, 1230, 1092 cm^{-1} ; $[\alpha]_{\text{D}}^{22} -23.1$ (c 0.35, CHCl_3); HRMS (ESI) m/z calcd for $\text{C}_{36}\text{H}_{48}\text{NO}_8\text{Si}$ ($[\text{M}+\text{H}]^+$) 650.3149, found 650.3196.

Tetraol (42). To a stirred solution of hemiacetal **41** (15 mg, 23 μmol) in MeOH (0.3 mL) was added Amberlyst 15E (15 mg), and the resulting suspension was heated at 40 $^{\circ}\text{C}$ for 1 h. The reaction mixture was filtered through a pad of Celite, and the residue was washed with a 1:1 mixture of MeOH and CHCl_3 . The filtrate was concentrated under reduced pressure, and purified by preparative TLC ($\text{CHCl}_3/\text{MeOH}$, 10:1) to give tetraol **42** (11 mg, 90%) as a colorless oil: ^1H NMR (400 MHz, $\text{CDCl}_3+\text{CD}_3\text{OD}$) δ 7.45-7.34 (m, 5H), 6.89-6.81 (m, 4H), 6.79 (s, 1H), 6.59 (s, 1H), 5.09 (s, 2H), 4.92 (s, 2H), 4.04-4.01 (m, 1H), 3.91-3.86 (m, 1H), 3.77 (s, 3H), 3.68-3.65 (m, 1H), 3.61 (d, $J = 8.8$ Hz, 1H), 3.45-3.37 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 156.2, 154.2, 152.7, 146.8, 138.1, 136.5, 128.8, 128.2, 127.5, 116.0, 114.8, 114.1, 111.3, 106.8, 100.3, 80.1, 77.3, 70.5, 70.3, 65.0, 62.6, 61.0, 55.8, 35.3; IR (neat) 3365, 1508, 1229, 1029 cm^{-1} ; $[\alpha]_{\text{D}}^{22} -2.9$ (c 0.84, CHCl_3); HRMS (ESI) m/z calcd for $\text{C}_{27}\text{H}_{50}\text{NO}_8$ ($[\text{M}+\text{H}]^+$) 496.1971, found 496.1980.

Acetonide (43). To a stirred solution of tetraol **42** (0.46 g, 0.93 mmol) in acetone/ $\text{Me}_2\text{C}(\text{OMe})_2$ (3 mL/3 mL) was added PPTS (0.10 g, 0.40 mmol) at room temperature. After the reaction mixture had been stirred for 40 min, the solution was concentrated under reduced pressure, and the residue was partitioned between CHCl_3 and saturated aqueous NaHCO_3 . The organic layer was washed with 10% aqueous citric acid and brine, dried over MgSO_4 , concentrated, and purified by flash column chromatography (CHCl_3 then $\text{CHCl}_3/\text{MeOH} = 20:1$) on silica gel to afford **43** (0.39 g, 78%) as a colorless oil: ^1H NMR (400 MHz, C_6D_6) δ 7.18-7.03 (m, 5H), 6.84 (d, $J = 9.2$ Hz, 2H), 6.75 (d, $J = 9.0$ Hz, 2H), 6.65 (s, 1H), 6.53 (s, 1H), 4.66 (s, 2H), 4.62 (s, 2H), 4.56 (dd, $J = 11.7, 17.1$ Hz, 1H), 3.96-3.89 (m, 2H), 3.67 (d, $J = 8.8$ Hz, 1H), 3.60-3.48 (m, 2H), 3.38 (dd, $J = 4.4, 12.7$ Hz, 1H), 3.35 (s, 3H), 1.60 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 157.0, 154.7, 153.2, 147.6, 138.4, 136.8, 128.8, 128.2, 127.5, 116.1, 115.1, 115.0, 112.0, 107.0, 99.6, 99.5, 80.6, 70.4, 70.2, 65.1, 61.1, 59.6, 55.3,

30.2, 28.8, 24.5; IR (neat) 3435, 1585, 1506, 1208, 1031 cm^{-1} ; $[\alpha]_{\text{D}}^{23}$ -8.8 (c 0.55, CHCl_3); HRMS (ESI) m/z calcd for $\text{C}_{30}\text{H}_{34}\text{NO}_8$ ($[\text{M}+\text{H}]^+$) 536.2284, found 536.2313.

TES ether (44). To a solution of acetone **43** (0.34 g, 0.63 mmol) and Et_3N (0.21 mL, 1.5 mmol) in CH_2Cl_2 (3 mL) was added TESCl (0.15 mL, 0.89 mmol) followed by DMAP (12 mg, 0.10 mmol) at 0 $^\circ\text{C}$. After the reaction mixture had been stirred for 3 h, the solution was poured into saturated aqueous NaHCO_3 , and extracted with CH_2Cl_2 . The organic layer was washed with 10% aqueous citric acid and brine, dried over MgSO_4 , and concentrated under reduced pressure to afford **44** (0.43 g), which was used for the next reaction without further purification. A small portion of the crude product was purified by preparative silica gel TLC (hexane/EtOAc, 7:3) to give pure **44** as a colorless oil: ^1H NMR (400 MHz, CDCl_3) δ 7.41-7.33 (m, 5H), 6.85-6.79 (m, 4H), 6.76 (s, 1H), 6.59 (s, 1H), 5.11 (s, 2H), 4.93 (s, 2H), 4.36 (dd, J = 5.6, 10.8 Hz, 1H), 3.82 (t, J = 10.8 Hz, 1H), 3.76 (s, 3H), 3.68 (dd, J = 5.6, 10.8 Hz, 1H), 3.59 (d, J = 8.4 Hz, 1H), 3.54-3.50 (m, 1H), 3.42-3.30 (m, 2H), 2.31 (br-s, 1H), 1.57 (s, 3H), 1.44 (s, 3H), 0.82 (t, J = 7.6 Hz, 9H), 0.49-0.42 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 156.6, 154.1, 152.7, 146.7, 138.1, 136.4, 128.7, 128.0, 127.3, 115.8, 114.7, 114.5, 110.9, 106.6, 99.4, 99.3, 79.7, 70.2, 70.1, 65.7, 62.0, 59.2, 55.7, 30.0, 28.3, 24.2, 6.58, 4.82; IR (neat) 3491, 1507, 1230, 1207, 1106 cm^{-1} ; $[\alpha]_{\text{D}}^{22}$ $+9.8$ (c 0.54, CHCl_3).

Mesylate (45). To a stirred solution of TES ether **44** (0.43 g) in CH_2Cl_2 (3 mL) was added Et_3N (0.53 mL, 3.8 mmol) followed by MsCl (0.16 mL, 2.0 mmol). After the reaction mixture had been stirred for 3 h at room temperature, the solution was partitioned between CH_2Cl_2 and saturated aqueous NaHCO_3 . The organic layer was washed with 10% aqueous citric acid and brine, dried over MgSO_4 , and concentrated under reduced pressure to afford crude mesylate **45** (0.45 g), which was used for the next reaction without further purification. A small portion of the crude product was purified by preparative silica gel TLC (hexane/EtOAc, 7:3) to give pure **45** as a colorless oil: ^1H NMR (400 MHz, CDCl_3) δ 7.41-7.35 (m, 5H), 6.85-6.79 (m, 4H), 6.78 (s, 1H), 6.59 (s, 1H), 5.13 (s, 2H), 4.93 (s, 2H), 4.57 (d, J = 9.3 Hz, 1H), 4.34 (dd, J = 6.3, 11.5 Hz, 1H), 3.83 (dd, J = 10.7, 11.5 Hz, 1H), 3.76 (s, 3H), 3.69-3.65 (m, 1H), 3.54 (dd, J = 6.3, 10.7 Hz, 1H), 3.44-3.41 (m, 2H), 3.16 (s, 3H), 1.58 (s, 3H), 1.46 (s, 3H), 0.82 (t, J = 7.8 Hz, 9H), 0.49-0.42 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 156.5, 154.1, 152.6, 145.9, 138.8, 136.2, 128.8, 128.2, 127.5, 115.7, 114.7, 113.5, 110.6, 106.9, 100.4, 98.1, 87.5,

70.4, 70.1, 64.8, 62.1, 59.4, 55.7, 39.6, 29.8, 29.3, 24.4, 6.56, 4.80; IR (neat) 1508, 1366, 1181 cm^{-1} ; $[\alpha]_{\text{D}}^{22} + 8.2$ (*c* 0.46, CHCl_3).

Secondary alcohol (46). To a stirred solution of mesylate **45** (0.45 g) in THF (3 mL) was added TBAF (1 M solution in THF, 1.2 mL, 1.2 mol) at room temperature. After the reaction mixture had been stirred for 1 h, the solution was partitioned between EtOAc and 10% aqueous citric acid. The organic layer was washed with brine, dried over MgSO_4 , concentrated under reduced pressure, and purified by flash column chromatography (hexane/EtOAc, 70:30 then 65:35) on silica gel to give **46** (0.31 g, 80% from **43**) as a colorless oil: ^1H NMR (400 MHz, CDCl_3) δ 7.42-7.35 (m, 5H), 6.87-6.81 (m, 4H), 6.80 (s, 1H), 6.59 (s, 1H), 5.10 (s, 2H), 4.92 (s, 2H), 4.47 (d, $J = 9.0$ Hz, 1H), 4.34 (dd, $J = 6.1$, 11.7 Hz, 1H), 3.81 (t, $J = 11.5$ Hz, 1H), 3.77 (s, 3H), 3.78-3.70 (m, 1H), 3.61-3.51 (m, 2H), 3.45 (dd, $J = 10.7$, 13.9 Hz, 1H), 3.21 (s, 3H), 2.84 (brs, 1H), 1.59 (s, 3H), 1.44 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 156.6, 154.2, 152.5, 145.7, 138.7, 136.1, 128.8, 128.3, 127.6, 116.0, 114.7, 113.1, 111.2, 107.1, 100.3, 97.4, 88.0, 70.5, 70.2, 64.0, 61.1, 59.2, 55.7, 38.5, 29.9, 24.2; IR (neat) 3509, 1586, 1507, 1346, 1208, 1178 cm^{-1} ; $[\alpha]_{\text{D}}^{22} - 11.2$ (*c* 0.80, CHCl_3); HRMS (ESI) m/z calcd for $\text{C}_{31}\text{H}_{36}\text{NO}_{10}\text{S}$ ($[\text{M}+\text{H}]^+$) 614.2060, found 614.2116.

Epoxide (7). To a stirred solution of secondary alcohol **46** (50 mg, 81 μmol) in DMF (0.3 mL) was added NaH (60% in oil, 5 mg, 0.12 mmol) at room temperature. The reaction mixture was heated at 120 $^\circ\text{C}$ for 10 min, cooled to room temperature, poured into saturated aqueous NH_4Cl , and extracted with EtOAc. The organic layer was washed with brine, dried over MgSO_4 , concentrated under reduced pressure, and purified by preparative TLC (hexane/EtOAc, 6:4) to afford epoxide **7** (38 mg, 90%) as a colorless oil: ^1H NMR (400 MHz, CDCl_3) δ 7.42-7.35 (m, 5H), 6.89-6.77 (m, 4H), 6.74 (s, 1H), 6.54 (s, 1H), 5.12 (d, $J = 11.4$ Hz, 1H), 5.05 (d, $J = 11.4$ Hz, 1H), 4.93 (s, 2H), 4.32 (dd, $J = 5.8$, 11.5 Hz, 1H), 3.96 (d, $J = 15.6$ Hz, 1H), 3.91 (t, $J = 11.2$ Hz, 1H), 3.77 (s, 3H), 3.50 (dd, $J = 5.1$, 15.1 Hz, 1H), 3.35 (dd, $J = 5.8$, 11.0 Hz, 1H), 3.22 (t, $J = 5.1$ Hz, 1H), 3.06 (d, $J = 3.7$ Hz, 1H), 1.59 (s, 3H), 1.50 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 157.2, 154.1, 152.6, 147.1, 138.3, 136.2, 128.8, 128.3, 127.5, 115.8, 114.7, 113.0, 111.2, 105.6, 99.9, 93.1, 70.3, 59.3, 55.7, 54.8, 51.5, 49.8, 32.6, 30.1, 24.3; IR (neat) 1585, 1507, 1228, 1120 cm^{-1} ; $[\alpha]_{\text{D}}^{23} - 24.2$ (*c* 0.39, CHCl_3); HRMS (EI) m/z calcd for $\text{C}_{30}\text{H}_{31}\text{NO}_7$ ($[\text{M}]^+$), found 517.2145.

[(4*R*,5*R*)-5-(*tert*-Butyldimethylsilyloxymethyl)-2,2-dimethyl-[1,3]dioxolan-4-yl]methanol (14)

[(4*R*,5*R*)-5-(*tert*-Butyldimethylsilyloxymethyl)-2,2-dimethyl-[1,3]dioxolan-4-yl]ethyne (16)

Methyl 3-benzyloxy-4-[(4*R*,5*R*)-5-(*tert*-butyldimethylsilyloxymethyl)-2,2-dimethyl-[1,3]dioxolan-4-yl]ethynyl-5-nitrobenzoate (18)

Methyl 3-benzyloxy-4-{2-[(4*S*,5*R*)-5-(*tert*-butyldimethylsilyloxymethyl)-2,2-dimethyl-[1,3]dioxolan-4-yl]-2-oxo}ethyl-5-nitrobenzoate (20)

Methyl 3-benzyloxy-4-((2*R*)-2-[(4*R*,5*R*)-5-(*tert*-butyldimethylsilyloxymethyl)-2,2-dimethyl-[1,3]dioxolan-4-yl]-2-hydroxy)ethyl-5-nitrobenzoate (21)

Methyl 4-{(2*R*)-2-acetoxy-2-[(4*S*,5*R*)-5-(*tert*-butyldimethylsilyloxymethyl)-2,2-dimethyl-[1,3]dioxolan-4-yl]}ethyl-3-benzyloxy-5-nitrobenzoate (22)

Methyl

4-{(2*R*)-2-acetoxy-2-[(4*S*,5*R*)-5-(*tert*-butyldimethylsilyloxymethyl)-2,2-dimethyl-[1,3]dioxolan-4-yl]}ethyl-3-amino-5-benzyloxybenzoate (23)

Methyl

4-{(2*R*)-2-acetoxy-2-[(4*S*,5*R*)-5-(*tert*-butyldimethylsilyloxymethyl)-2,2-dimethyl-[1,3]dioxolan-4-yl]}ethyl-3-benzyloxy-5-(2-nitrobenzenesulfonylamino)benzoate (24)

Benzazocine (26)

***p*-Methoxyphenyl ether (28)**

Ketone (29)

α , β -unsaturated ketone (30)

Sulfide (31)

Acetate (32)

Primary alcohol (34)

Diol (35)

TBS ether (36)

Secondary amine (37)

Acetate (39)

Ketone (40)

Hydroxylamine hemiacetal (41)

Tetraol (42)

Acetonide (43)

TES ether (44)

Mesylate (45)

Secondary alcohol (46)

Epoxide (7)

Methyl 3-benzyloxy-4-{{(2*S*)-2-[(4*R*,5*S*)-5-(*tert*-butyldimethylsilyloxymethyl)-2,2-dimethyl-[1,3]dioxolan-4-yl]-2-triisopropylsilyloxy}ethyl-5-nitrobenzoate (49)

Methyl 3-benzyloxy-5-nitro-4-[(2*S*,3*R*,4*S*)-3,4,5-trihydroxy-2-triisopropylsilyloxypropyl] benzoate
(50)

Methyl

3-benzyloxy-4-[(2*S*,3*R*,4*S*)-5-(*tert*-butyldimethylsilyloxy)-3,4-dihydroxy-2-triisopropylsilyloxy]pentyl-5-nitrobenzoate (51)

Methyl 3-benzyloxy-4-[(2*S*,3*R*,4*S*)-5-(*tert*-butyldimethylsilyloxy)-3-hydroxy-4-(toluene-4-sulfonyl)oxy-2-triisopropylsilyloxy]pentyl-5-nitrobenzoate (52)

Methyl 3-benzyloxy-4-((2*S*)-2-[(2*R*,3*R*)-3-(*tert*-butyldimethylsilyloxymethyl)oxiran-2-yl]-2-triisopropylsilyloxy}ethyl-5-nitrobenzoate (53)

Methyl 3-benzyloxy-4-((2S)-2-[(2R,3R)-3-hydroxymethyl-oxiran-2-yl]-2-triisopropylsilyloxy)ethyl-5-nitrobenzoate (54)

Methyl 3-benzyloxy-4-{(2*S*)-2-[(2*R*,3*R*)-3-formyloxiran-2-yl]-2-triisopropylsilyloxy}ethyl-5-nitrobenzoate (**55**)

N-Hydroxybenzazocine (56)

Secondary alcohol (58)

Ketone (59)

7-Hydroxymethyl benzazocinone (60)

7-Hydroxymethyl benzazocinone (60')

Hemiacetal (61a, 61b)

Acetonide (62a)

Acetonide (62b)

Benzyl alcohol (63)

p-methoxyphenyl ether (7)

Hydroxyazide (64)

Mesyloxyazide (65)

Carbonate (66)

Benzyl alcohol (67)

Dimethyl acetal (68)

Aziridine (69)

Phenol (70)

Benzaldehyde (71)

FR900482 (1)