Supporting Information for

Intramolecular 1,3-Dipolar Cycloaddition Strategy for Enantioselective Synthesis of FR-900482 Analogs

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General:

All reactions sensitive to oxygen and moisture were carried out in oven-dried glassware under a slight positive pressure of argon unless otherwise noted. Melting points (mp), determined on a Yanako MP-500V melting point apparatus, are uncorrected. ^{1}H-NMR (400 Hz), and ^{13}C-NMR (100 Hz) spectra were determined on a JEOL JNMLA400 instrument. Chemical shifts for ^{1}H-NMR were 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. Chemical shifts for ^{13}C-NMR were reported in ppm relative to the central line of a triplet at 77.0 ppm for deuteriochloroform. Infrared (IR) spectra were recorded on a JASCO FT/IR-410 Fourier Transform Infrared Spectrophotometer and are reported in wavenumbers (cm^{-1}). Mass spectra (MS) were obtained on a JEOL JMS-GCmate at 70 eV, using direct probe insertion at temperatures of 70 to 350 °C. High resolution mass spectra were obtained under similar conditions. Optical rotations were measured on a JASCO DIP-1000 Digital Polarimeter at room temperature, using the sodium D line. Analytical thin layer chromatography (TLC) were performed on Merck precoated analytical plates, 0.25 mm thick, silica gel 60 F_{245}. Preparations TLC separations were performed on 6.7 x 20 cm Merck precoated analytical plates, 0.50 mm thick, silica gel 60 F_{245}. Compounds were eluted from the absorbent with 10% methanol in dichloromethane. Flash column chromatography were performed on Merck Kieselgel 60 (230-400 mesh) or KANTO CHEMICAL Silica Gel (spherical 40-100 μm). Reagents and solvents were commercial grades and were used as supplied. Dichloromethane, dimethyl sulfoxide, benzene, toluene were distilled from calcium hydride and stored over molecular sieves 4Å. THF, *N*,*N*-dimethylformamide, methanol, ethanol, diethyl ether, and acetonitrile were purchased anhydrous and stored over molecular sieves 4Å under argon. Methanol was purchased anhydrous and stored over molecular sieves 3Å. Triethylamine was distilled from calcium hydride and stored over potassium hydroxide pellets.

2-(*N*-nitrobenzenesulfonyl)aminostyrene (4). To a stirred solution of 2-nitrotoluene (25 g, 0.18 mol) in DMSO (455 mL) were added HCHO (37% aqueous solution, 44 mL , 0.54 mol) and KOH (85%, aqueous solution, 45 mL, 0.45 mol) dropwise over 10 minutes at 0 °C, and then the reaction mixture was stirred for additional 5 hours. The reaction mixture was poured into sat. NH_4Cl. The combined mixture was extracted with chloroform. The extracts were washed with brine, dried over $MgSO_4$, filtered, and evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (5-50% EtOAc in Hexane) to give 2-(2-nitrophenyl)ethanol (14 g, 46%) as a red oil.

To a stirred solution of 2-(2-nitrophenyl)ethanol (14 g, 84 mmol) in dichloromethane (85 mL) were added triethylamine (19 mL, 0.14 mol) and then mesyl chloride (7.1 mL, 92 mmol) at 0 °C. After stirring for 10 minutes, the reaction mixture was poured into sat. NH_4Cl, diluted with ethyl acetate, and washed with 1 N HCl and brine. The aqueous layer was extracted dichloromethane, and the combined

extracts were washed with sat. $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to afford the corresponding mesylate (20 g).

To a stirred solution of the above mesylate (20 g) in dichloromethane (80 mL) was added DBU (24 mL, 0.16 mol) at 0 °C. After stirring for 1 hour at room temperature, the reaction mixture was poured into sat. NH_4Cl, diluted with ethyl acetate, and washed with 1 N HCl and brine. The aqueous layer was extracted dichloromethane, and the combined extracts were washed with sat. $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (7% EtOAc in Hexane) to give 2-nitrostyrene (10 g, 80%, 2 steps) as a yellow oil.

To a stirred solution of 2-nitrostyrene (2.0 g, 13 mmol) in acetic acid (27 mL) was added zinc powder (4.3 g, 66 mmol) portionwise over 30 minutes. After stirring for 10 minutes, the reaction mixture was filtered through a pad of celite and the residue was washed with diethyl ether. The filtrate and the washings were combined and poured into sat. $NaHCO_3$. The combined mixture was extracted with diethyl ether. The extracts were washed with brine, dried over $MgSO_4$, filtered, and evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (7% EtOAc in Hexane) to give the corresponding aniline (1.0 g) as a red oil.

To the solution of the resultant aniline (1.0 g) and 4-nitrobenzenesulfonyl chloride (2.0 g, 9.9 mmol) in dichloromethane (30 mL) was added pyridine (1.6 mL, 19 mmol). After stirring overnight, the reaction mixture was poured into 1 N HCl. The combined mixture was extracted with dichloromethane. The extracts were combined, washed with sat. $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (15% EtOAc in Hexane) to give 2-(*N*-nitrobenzenesulfonyl)aminostyrene (**4**) (2.1 g, 79%, in 2 steps).
IR (film) 3263, 3111, 1526, 1348, 1162; ^{1}H-NMR ($CDCl_3$) δ 5.24 (dd, *J* = 1.0, 11.0 Hz, 1H), 5.51 (dd, *J* = 1.0, 17.3 Hz, 1H), 6.49 (dd, *J* = 11.0, 17.3 Hz, 1H), 6.73 (s, 1H), 7.25 (m, 2H), 7.32 (m, 1H), 7.40 (m, 1H), 7.89 (d, *J* = 9.0 Hz, 2H), 8.27 (d, *J* = 9.0 Hz, 2H); ^{13}C-NMR ($CDCl_3$) δ 118.7, 124.2, 125.9, 127.1, 127.6, 128.5, 128.9, 130.8, 131.8, 133.3, 144.9, 150.2; HR-MS (EI) calcd for $C_{14}H_{12}N_2O_4S$ 304.0518, found 304.0517.

Primary Alcohol 6. To a stirred solution of alcohol **5** (0.45 g, 1.6 mmol), triphenylphosphine (0.56 g, 2.1 mmol), and sulfonamide **4** (0.50 mg, 1.6 mmol) in benzene (7 mL) was added DEAD (40% toluene solution, 0.93 mL, 2.1 mmol) dropwise over 5 minutes at room temperature. After stirring for an hour at 50 °C, the reaction mixture was evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (10% EtOAc in Hexane) to give the protected secondary amine (0.85 g, 92%).

To a stirred solution of the above protected secondary amine (0.84 g, 1.5 mmol) in THF (5 mL) was added TBAF (1.0 M THF solution, 1.5 mL, 1.5 mmol) at room temperature. After complete consumption of the starting material, the reaction mixture was poured into sat. NH_4Cl. The combined mixture was extracted with ethyl acetate. The extracts were washed with brine, dried over $MgSO_4$, filtered, and, evaporated *in vacuo.* The crude product was purified by flash column chromatography on silica gel (50% EtOAc in Hexane) to give the primary alcohol (0.63 g, 94%) as a white powder.
IR (film) 3471, 2987, 1531, 1350, 1168, 739; ^{1}H-NMR ($CDCl_3$) δ 1.27 (s, 3H), 1.34 (s, 3H), 1.91 (br, s, 1H,), 3.59-4.00 (m, 6H), 5.33 (d, *J* = 11.2 Hz, 1H), 5.75 (d, *J* = 17.3 Hz, 1H), 6.75 (d, *J* = 7.7 Hz, 1H), 6.90 (dd, *J* = 11.2, 17.3 Hz, 1H), 7.22 (m, 1H), 7.36 (t, *J* = 7.7 Hz, 1H), 7.66 (d, *J* = 7.7 Hz, 1H), 7.91 (d, *J* = 8.8 Hz, 2H), 8.31 (d, *J* = 8.8 Hz, 2H); $[\alpha]_D^{23}$ -7.45 ° (*c* = 0.132, $CHCl_3$).

Isoxazoline 8 To a stirred solution of oxalyl chloride (0.15 mL, 1.7 mmol) in dichloromethane (4 mL) at –78 °C under argon was added DMSO (0.15 mL, 2.1 mmol). After stirring for 10 minutes, a

solution of alcohol **6** (0.63 g, 1.4 mmol) in dichloromethane (4.5 mL) was added dropwise to the mixture. After stirring for additional 10 minutes, triethylamine was added, and the temperature was raised to room temperature. The reaction mixture was diluted with ethyl acetate, and washed with 1 N HCl and brine. The aqueous layer was extracted ethyl acetate, and the combined extracts were washed with sat. $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to afford aldehyde.

To a stirred solution of the above aldehyde in ethanol (7 mL) were added sodium acetate (0.30 g, 4.3 mmol) and hydroxylamine hydrochloride (0.15 g, 2.2 mmol) under argon. After complete consumption of the starting material, the reaction mixture was poured into NH_4Cl. The combined mixture was extracted with ethyl acetate. The extracts were washed with brine, dried over Na_2SO_4, filtered, and evaporated to dryness *in vacuo* to give oxime **7**.

The above residue was dissolved in dichloromethane (30 mL) and cooled to 0 °C. To the solution was added sodium hypochlorite solution (ca. 5% available chlorine, 2.1 mL) dropwise over 10 minutes. After stirring overnight, the mixture was partitioned between dichloromethane and brine. The aqueous layer was extracted with dichloromethane. The extracts were combined, dried over $MgSO_4$, filtered, and evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (40% EtOAc in Hexane) to give isoxazoline **8** (360 mg, 58% in 3 steps) as yellow solid.

IR (film) 2988, 1532, 1350, 1165, 1084, 738; ^{1}H-NMR ($CDCl_3$) δ 1.34 (s, 3H), 1.51 (s, 3H), 3.00 (dd, *J* = 9.8, 14.1 Hz, 1H), 4.00 (dd, *J* = 1.2, 9.8 Hz, 1H), 4.47 (dt, *J* = 4.0, 9.8 Hz, 1H), 4.63 (dd, *J* = 4.0, 14.1 Hz, 1H), 4.82 (t, *J* = 9.7 Hz, 1H), 4.87 (t, *J* = 9.7 Hz, 1H), 5.37 (t, *J* = 9.7 Hz, 1H), 6.63 (d, *J* = 8.3 Hz, 1H), 7.29 (m, 1H), 7.50 (m, 2H), 8.00 (d, *J* = 8.8 Hz, 2H), 8.42 (d, *J* = 8.8 Hz, 2H); ^{13}C-NMR ($CDCl_3$) δ 26.4, 26.6, 49.0, 55.2, 71.7, 76.5, 78.2, 111.1, 124.6, 126.6, 128.5, 129.7, 131.0, 136.4, 138.7, 145.1, 150.5, 155.7; HR-MS (EI) calcd for $C_{21}H_{21}N_3O_7S$ 459.1100, found 459.1100; $[\alpha]_D^{23}$ -46.5 ° (*c* = 0.233, $CHCl_3$).

6-Azido-2-methoxy-4-methylbenzaldehyde (9). To a stirred solution of the 6-azido-4-methyl-salicylaldehyde (26.0 g, 118 mmol) and K_2CO_3 (24.4 g, 177 mmol) in DMF (170 mL) was added iodomethane (8.10 mL, 130 mmol) at room temperature under argon. After stirring for an hour, the mixture was partitioned between ether and water. The aqueous layer was thoroughly extracted with ether. The extracts were combined, washed with brine, dried over $MgSO_4$, filtered, and evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (25% EtOAc in Hexane) to give ethyl 6-azido-2-methoxy-4-methylbenzoate (26.0 g, 94%) as yellow crystals.

A solution of the above ethyl ester (22.5 g, 95.6 mmol) in dichloromethane (190 mL) was cooled to –78 °C. To the stirred solution was added DIBAL (1.0 M toluene solution, 210 mL, 210 mmol) dropwise over 30 minutes. After completion of the addition, the reaction mixture was stirred at –78 °C for additional 30 minutes, and the reaction was quenched by addition of methanol (150 mL), and 3 N HCl was carefully added to the mixture. The aqueous layer was thoroughly extracted with dichloromethane. The extracts were combined, washed with sat. $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (30% EtOAc in Hexane) to give alcohol (17.1 g, 92%) as pale yellow crystals.

The alcohol (17.0 g, 88.0 mmol) was dissolved in dichloromethane (180 mL). To the solution was added pyridinium chlorochromate (57.0 g, 268 mmol) portionwise over 30 minutes. After stirring for additional 30 minutes at room temperature, the reaction mixture was added $MgSO_4$ and then the reaction was quenched with ether and hexane. The mixture was passed through a pad of silica gel and washed with ether to give aldehyde **9** (15.3 g, 91%) as yellow crystals.

^{1}H-NMR ($CDCl_3$) δ 2.40 (s, 3H), 3.90 (s, 3H), 6.55 (s, 1H), 6.64 (s, 1H), 10.4 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ 22.6, 56.3, 108.8, 112.5, 114.4, 142.7, 147.4, 162.8, 188.3.

6-Azido-2-methoxy-4-methylstyrene (10). To a stirred solution of benzaldehyde **9** (10 g, 54 mmol) in 1,4-dioxane (110 mL) were added K_2CO_3 (15 g, 0.11 mmol) and methyl triphenyl phosphonium bromide (29 g, 81 mmol) at room temperature, and then the reaction mixture was heated at 60 °C. The reaction mixture was poured into sat. NH_4Cl. The combined mixture was extracted with ether. The extracts were washed with brine, dried over $MgSO_4$, filtered, and evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (5% EtOAc in Hexane) to give styrene **10** (4.2 g, 41%) as a pale yellow oil.
^{1}H-NMR ($CDCl_3$) δ 2.35 (s, 3H), 3.84 (s, 3H), 5.44 (dd, *J* = 2.4, 12.2 Hz, 1H), 5.99 (dd, *J* = 2.4, 18.2 Hz, 1H), 6.50 (s, 1H), 6.61 (s, 1H), 6.78 (dd, *J* = 12.4, 18.2 Hz, 1H).

6-(*N*-nitrobenzenesulfonyl)amino-2-methoxy-4-methylstyrene (11). To a stirred solution of styrene **10** (4.2 g, 22 mmol) in acetic acid (4 mL)-dichloromethane (12 mL) was added zinc powder (4.3 g, 66 mmol) portionwise over 20 minutes. After stirring for 20 minutes, the reaction mixture was filtered through a pad of celite and the residue was washed with dichloromethane. The filtrate and the washings were combined and poured into sat. $NaHCO_3$. The combined mixture was extracted with diethyl ether. The extracts were washed with brine, dried over $MgSO_4$, filtered, and evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (5% EtOAc in Hexane) to give the corresponding aniline (3.5 g) as a yellow oil.

To the solution of the resultant aniline (3.5 g) and 4-nitrobenzenesulfonyl chloride (5.1 g, 23 mmol) in dichloromethane (70 mL) was added pyridine (3.6 mL, 44 mmol). After stirring overnight, the reaction mixture was poured into 1 N HCl. The combined mixture was extracted with dichloromethane. The extracts were combined, washed with $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (15% EtOAc in Hexane) to give sulfonamide **11** (6.6g, 86%, in 2 steps).
IR (film) 3298, 3104, 2939, 1609, 1531, 1349, 1169, 1089, 852, 736; ^{1}H-NMR ($CDCl_3$) δ 2.34 (s, 3H), 3.75 (s, 3H), 5.22 (d, *J* = 18.1 Hz, 1H), 5.48 (d, *J* = 11.7 Hz, 1H), 6.30 (dd, *J* = 11.7 Hz, *J* = 18.1 Hz, 1H), 6.50 (s, 1H), 7.05 (br, s, 1H), 7.09 (s, 1H), 7.92 (d, *J* = 8.8 Hz, 2H), 8.28 (d, *J* = 8.8 Hz, 2H); ^{13}C-NMR ($CDCl_3$) δ 21.9, 55.6, 108.9, 114.1, 116.7, 120.9, 128.4, 129.2, 133.1, 139.4, 144.8, 150.2, 157.4; LR-MS (EI) 348 (M^+), 226, 162, 147, 118, 91.

Primary alcohol 12. To a stirred solution of primary alcohol **5** (1.95 g, 7.03 mmol), triphenylphosphine (2.40 g, 9.14 mmol), and sulfonamide **11** (2.45 g, 7.03 mmol) in benzene (35 mL) was added DEAD (40% toluene solution, 4.0 mL, 9.14 mmol) dropwise over 10 minutes at room temperature. After stirring for 30 minutes at 50 °C, the reaction mixture was evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (15% EtOAc in Hexane) to give the TBS ether (4.26 g, 99%) as a white powder.

To a stirred solution of the above TBS ether (4.26 g, 7.02 mmol) in THF (25 mL) was added TBAF (1.0 M THF solution, 7.02 mL, 7.02 mmol) at room temperature. After consumption of the starting material, the reaction mixture was poured into sat. NH_4Cl. The combined mixture was extracted with ethyl acetate. The extracts were washed with brine, dried over $MgSO_4$, filtered, and, evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (50% EtOAc in Hexane) to give the alcohol **12** (3.38 g, 97%) as a white powder.
^{1}H-NMR ($CDCl_3$) for the major comformational isomer δ 1.27 (s, 3H), 1.37 (s, 3H), 2.22 (s, 2H), 3.58 (m, 1H), 3.74 (m, 2H), 3.85 (m, 1H), 4.01 (s, 1H), 5.43 (d, *J* = 11.6 Hz, 1H), 6.39 (d, *J* = 17.6 Hz, 1H), 6.59 (dd, *J* = 11.6 Hz, *J* = 17.6 Hz, 1H), 6.75 (s, 1H), 7.96 (d, *J* = 8.8 Hz, 2H), 8.30 (d, *J* = 8.8 Hz, 2H) ; $[\alpha]_D^{26}$ -1.01 ° (*c* = 0.162, $CHCl_3$).

Isoxazoline 15. To a stirred solution of oxalyl chloride (0.90 mL, 10.3 mmol) in dichloromethane (20 mL) at –78 °C under argon was added dimethyl sulfoxide (0.97 mL, 13.7 mmol). After stirring for 10 minutes, a solution of alcohol **12** (3.38 g, 6.86 mmol) in dichloromethane (20 mL) was added dropwise. After stirring for additional 30 minutes, triethylamine (3.82 mL, 27.4 mmol) was added, and the temperature was raised to room temperature. The reaction mixture was diluted with ethyl acetate, and washed with 1 N HCl and brine. The aqueous layer was extracted with ethyl acetate, and the combined extracts were washed with sat. $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to afford aldehyde.

To a stirred solution of the above aldehyde in ethanol (34 mL) was added sodium acetate (1.12 g, 13.7 mmol) and hydroxylamine hydrochloride (476 mg, 6.86 mmol) at room temperature under argon. After consumption of the starting material, the reaction mixture was poured into sat. NH_4Cl. The combined mixture was extracted with ethyl acetate. The extracts were washed with brine, dried over Na_2SO_4, filtered, and evaporated to dryness *in vacuo*.

The above residue was dissolved in dichloromethane (140 mL) and cooled to 0 °C. To the mixture was added aqueous sodium hypochlorite (ca. 5% available chlorine, 9.0 mL) dropwise over 10 minutes. The mixture was stirred overnight and allowed to warm to room temperature. The mixture was partitioned between dichloromethane and brine. The aqueous layer was extracted with dichloromethane. The extracts were combined, dried over $MgSO_4$, filtered, and evaporated *in vacuo*. The crude product was purified by trituration with diethyl ether to give isoxazoline **15** (761 mg, 22%) as a mixture of diastereomers. The diastereomers could be separated by flash column chromatography on silica gel (25% EtOAc in Hexane) to give the less polar diastereomer **15A** (399mg) and the other diastereomer **15B** (362 mg).

^{1}H-NMR ($CDCl_3$) the less polar diastereomer **15A** δ 1.47 (s, 3H), 1.56 (s, 3H), 2.04 (s, 3H), 3.20 (dd, *J* = 10.8, 14.6 Hz, 1H), 3.25 (dd, *J* = 7.6, 14.6 Hz, 1H), 3.90 (s, 3H), 4.10 (d, *J* = 14.6 Hz, 1H), 4.29 (d, *J* = 8.8 Hz, 1H), 4.79 (t, *J* = 8.8 Hz, 1H), 5.39 (s, 1H), 6.27 (d, *J* = 7.6 Hz, 1H), 6.76 (s, 1H), 7.73 (d, *J* = 8.8 Hz, 2H), 8.33 (d, *J* = 8.8 Hz, 2H) ; $[\alpha]_D^{27}$ 1.6 ° (*c* = 0.211, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) the other diastereomer **15B** δ 1.46 (s, 3H), 1.54 (s, 3H), 2.09 (s, 3H), 3.27 (dd, *J* = 6.8, 14.8 Hz, 1H), 3.50 (dd, *J* = 8.8, 14.8 Hz, 1H), 3.66 (m, 1H), 3.93 (s, 1H), 4.06 (d, *J* = 14.8 Hz, 1H), 4.23 (dd, *J* = 10.8, 11.6 Hz, 1H), 4.84 (d, *J* = 8.8 Hz, 1H), 5.54 (s, 1H), 6.78 (s, 1H), 7.78 (d, *J* = 8.8 Hz, 2H), 8.36 (d, *J* = 8.8 Hz, 2H).

Ethyl 6-Azido-2-methoxy-4-methylcinnamate (16). To a stirred solution of benzaldehyde **9** (11 g, 58 mmol) in ethanol (120 mL) was added carboethoxymethylene triphenylposporane (22 g, 64 mmol) at room temperature. After stirring for 20 minutes at room temperature, the reaction mixture was poured into sat. NH_4Cl. The combined mixture was extracted with ether. The extracts were washed with brine, dried over $MgSO_4$, filtered, and evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (30% EtOAc in Hexane) to give cinnamate **16** (14.6 g, 96%) as a pale yellow solid.

mp 78.1-78.5 °C; IR (film) 2925, 2113, 1699, 1604, 1559, 1260, 1162, 1071; ^{1}H-NMR ($CDCl_3$) δ 1.34 (t, *J* = 7.0 Hz, 3H), 2.37 (s, 3H), 3.88 (s, 3H), 4.26 (q, *J* = 7.0 Hz, 2H), 6.51 (s, 1H), 6.63 (s, 1H), 6.84 (d, *J* = 16.6 Hz, 1H), 7.93 (t, *J* = 16.6 Hz, 1H); ^{13}C-NMR ($CDCl_3$) δ 14.4, 21.9, 55.7, 60.2, 108.1, 111.5, 112.5, 121.3, 135.0, 140.4, 141.9, 160.0, 168.1; LR-MS (EI) 261 (M^+), 233 (M^+–N_2), 219, 205, 188, 172, 160, 146, 130, 114, 103, 89.

Ethyl 6-(*N*-nitrobenzenesulfonyl)amino-2-methoxy-4-methylcinnamate (17). To a stirred solution of cinnamate **16** (11.5 g, 44.0 mmol) in acetic acid (25 mL)-dichloromethane (88 mL) was added zinc powder (8.60 g, 132 mmol) in portions over 30 minutes. After stirring for 30 minutes, the reaction mixture was filtered through a pad of celite and the residue was washed with dichloromethane. The

filtrate and the washings were combined and poured into sat. $NaHCO_3$. The combined mixture was extracted with dichloromethane. The extracts were washed with brine, dried over $MgSO_4$, filtered, and evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (10% EtOAc in Hexane) to give the corresponding aniline (9.60 g, 93%) as yellow crystals.

To a stirred solution of the above aniline (9.60 g, 40.8 mmol) and 4-nitrobenzenesulfonyl chloride (11.7 g, 53.0 mmol) in dichloromethane (80 mL) was added pyridine (13.0 mL, 163 mmol). After stirring overnight, the reaction mixture was poured into 1 N HCl. The combined mixture was extracted with dichloromethane. The extracts were combined, washed with sat. $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude product was purified by trituration with diethyl ether to give sulfonamide **17** (15.0 g, 87%) as a pale a yellow powder.
mp 173.4 – 175.6 °C; IR (film) 3254, 3106, 2980, 1707, 1685, 1610, 1564, 1532, 1349, 1314, 1170, 853, 737; ^{1}H-NMR ($CDCl_3$) δ 1.30 (t, *J* = 7.2 Hz, 3H), 2.38 (s, 3H), 3.83 (s, 3H), 4.19 (q, *J* = 7.2 Hz, 2H), 6.35 (d, *J* = 16.0 Hz, 1H), 6.66 (s, 1H), 6.85 (br, s, 1H), 7.02 (s, 1H), 7.12 (d, *J* = 16.0 Hz, 1H), 7.18 (d, *J* = 16.0 Hz, 1H), 7.90 (d, *J* = 8.8 Hz, 2H), 8.25 (d, *J* = 8.8 Hz, 2H); ^{13}C-NMR ($CDCl_3$) δ 14.2, 22.0, 55.7, 60.8, 111.1, 116.1, 120.7, 122.4, 124.2, 128.6, 134.8, 135.0, 142.1, 144.7, 150.1, 159.2, 167.7; LR-MS (EI) 420 (M^+), 419 (M^+–1), 374, 310, 309, 295, 283, 263, 252.

Primary alcohol 18. To a stirred solution of alcohol **5** (6.70 g, 24.2 mmol), triphenylphosphine (7.50 g, 28.0 mmol), and sulfonamide **17** (9.20 g, 28.6 mmol) in benzene (45 mL) was added DEAD (40% toluene solution, 12.4 mL, 28.6 mmol) dropwise over 10 minutes at room temperature. After stirring for 30 minutes at 50 °C, the reaction mixture was evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (10% EtOAc in Hexane) to give TBS ether (13.9 g, 93%) as a white powder.

To a stirred solution of TBS ether (13.9 g, 20.5 mmol) in THF (40 mL) was added TBAF (1.0 M THF solution, 22.5 mL, 22.5 mmol) at room temperature. After stirring 45 minutes, the reaction mixture was poured into sat. NH_4Cl. The combined mixture was extracted with ethyl acetate. The extracts were washed with brine, dried over $MgSO_4$, filtered, and evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (50% EtOAc in Hexane) to give primary alcohol **18** (11.0 g, 95%) as a white powder.
IR (film) 3485, 2937, 1708, 1607, 1562, 1562, 1532, 1464, 1351, 1311, 1279, 1208, 1168, 1055, 995, 885; ^{1}H-NMR ($CDCl_3$) δ 1.37 (s, 3H), 1.57 (s, 3H), 2.29 (s, 1.5H), 2.36 (s, 1.5H), 3.79 (m, 4H), 3.89 (s, 1.5H), 3.91 (s, 1.5H), 3.96 (m, 1H), 4.00 (m, 1H), 4.13 (m, 1H), 4.21 (m, 1H), 6.48 (s, 1H), 6.65 (d, *J* = 16.4 Hz, 0.5H), 6.75 (d, *J* = 15.6 Hz, 0.5H), 7.26 (d, *J* = 15.6 Hz, 0.5H), 7.44 (d, *J* = 16.4 Hz, 0.5H), 7.86 (d, *J* = 8.8 Hz, 1H), 7.89 (d, *J* = 8.8 Hz, 1H), 8.27 (d, *J* = 8.8 Hz, 1H), 8.28 (d, *J* = 8.8 Hz, 1H); LR-MS (EI) 563 (M^+), 548 (M^+–CH_3), 532, 518, 502, 474, 461, 428, 377, 357, 347; $[\alpha]_D^{27}$ -2.00 ° (*c* = 0.202, $CHCl_3$).

Isoxazoline 20. To a stirred solution of oxalyl chloride (3.00 mL, 35.1 mmol) in dichloromethane (20 mL) at –78 °C under argon was added dimethyl sulfoxide (3.20 mL, 45.8 mmol). After stirring for 10 minutes, a solution of alcohol **18** (11.0 g, 19.5 mmol) in dichloromethane (20 mL) was added dropwise to the mixture. After stirring for additional 30 minutes, triethylamine was added, and the temperature was raised to room temperature. The reaction mixture was diluted with ethyl acetate, and washed with 1 N HCl and brine. The aqueous layer was extracted ethyl acetate, and the combined extracts were washed with $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to afford aldehyde.

To a stirred solution of the above aldehyde in ethanol (40 mL) were added sodium acetate (3.20 g, 39.0 mmol) and hydroxylamine hydrochloride (2.00 g, 29.2 mmol) under argon. After consumption of the starting material, the reaction mixture was poured into sat. NH_4Cl. The combined

mixture was extracted with ethyl acetate. The extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and evaporated to dryness *in vacuo*.

The above residue was dissolved in dichloromethane (410 mL) and cooled to 0 °C. To the solution was added aqueous sodium hypochlorite (ca. 5% available chlorine, 20.2 mL) dropwise over 10 minutes. After stirring for 4 hours, the mixture was partitioned between dichloromethane and brine. The aqueous layer was extracted with dichloromethane. The extracts were combined, dried over $MgSO_4$, filtered, and evaporated *in vacuo*. The crude product was purified by trituration with diethyl ether to give isoxazoline **20** (6.43 g, 57%) as a white solid.

IR (film) 2986, 1746, 1608, 1577, 1532, 1464, 1351, 1312, 1229, 1167, 1139, 1087, 1061, 855, 788, 734; ^{1}H-NMR ($CDCl_3$) δ 1.32 (s, 3H), 1.48 (s, 3H), 2.25 (s, 3H), 2.93 (dd, *J* = 10.4, 14.1 Hz, 1H), 3.84 (s, 3H), 3.99 (d, *J* = 8.8 Hz, 1H), 4.31 (m, 3H), 4.58 (dd, *J* = 3.4, 14.1 Hz, 1H), 5.54 (d, *J* = 5.8 Hz, 1H), 5.97 (d, *J* = 5.8 Hz, 1H), 6.18 (s, 1H), 6.78 (s, 1H), 8.09 (d, *J* = 8.8 Hz, 2H), 8.42 (d, *J* = 8.8 Hz, 2H); ^{13}C-NMR($CDCl_3$) δ 14.1, 21.5, 26.5, 51.5, 55.4, 55.9, 62.1, 76.1, 77.2, 77.8, 79.2, 111.1, 114.0, 120.7, 124.5, 129.0, 139.9, 141.2, 145.2, 150.4, 153.4, 158.9; LR-MS (EI) 575 (M^+), 559, 517, 501, 483, 473, 443, 425, 389, 343, 331, 315, 303, 287; $[\alpha]_D^{20}$ 341 ° (*c* = 0.155, $CHCl_3$).

Aniline 21. To a stirred solution of sulfonamide **20** (6.43 g, 11.1 mmol) and cesium carbonate (10.8 g, 33.3 mmol) in acetonitrile (22 mL) was added thiophenol (1.70 mL, 16.7 mmol). After stirring for 30 minutes at 50 °C, the reaction mixture was partitioned between ethyl acetate and sat. $NaHCO_3$. The aqueous layer was thoroughly extracted with ethyl acetate. The extracts were combined, washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (30% EtOAc in Hexane) to give aniline **21** (3.23 g, 74%) as colorless crystals.

IR (film) 3342, 3059, 2985, 1738, 1732, 1608, 1583, 1505, 1463, 1403, 1372, 1349, 1232, 1084, 1022, 947, 872, 736; ^{1}H-NMR ($CDCl_3$) δ 1.32 (t, *J* = 7.2 Hz, 3H), 1.44 (s, 3H), 1.57 (s, 3H), 2.31 (s, 3H), 2.5-5.0 (br, 6H), 5.26 (br, 2H), 6.51 (s, 1H), 6.55 (s, 1H); LR-MS (EI): 391 (M^++1), 389 (M^+–1), 375 (M^+–CH_3), 372 (M^+–H_2O), 358, 332, 316, 300, 286, 273; HR-MS (EI) calcd for $C_{20}H_{26}N_2O_6$ 390.1791, found 390.1789; $[\alpha]_D^{27}$ -219 ° (*c* = 0.204, $CHCl_3$).

β,γ-Dihydroxyketone 22. To a stirred solution of aniline **21** (3.20 g, 8.20 mmol) in ethanol (20 mL)-THF (20 mL) was added sodium borohydride (465 mg, 12.3 mmol). After stirring for 4 hours at room temperature, the reaction mixture was poured into sat. NH_4Cl. The combined mixture was extracted with ethyl acetate. The extracts were washed with brine, dried over Na_2SO_4, filtered, and evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (60% EtOAc in Hexane) to give primary alcohol (2.80 g, 99%) as a pale yellow powder.

To a stirred solution of the primary alcohol (2.80 g, 8.20 mmol) in dichloromethane (40 mL) was added triethylamine (4.50 mL, 32.8 mmol), and trifluoroacetic anhydride (2.30 mL, 16.4 mmol) at 0 °C. After consumption of the starting material, the reaction mixture was poured into sat. $NaHCO_3$. The combined mixture was extracted with ethyl acetate. The extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (60% EtOAc in Hexane) to give trifluoroacetamide (3.13 g, 86%) as a white powder.

A solution of the trifluoroacetamide (228 mg, 0.51 mmol) in ethanol (10 mL)-aqueous boric acid (5% aqueous solution, 2.0 mL) was hydrogenated over freshly prepared W-2 Raney Ni under hydrogen. After consumption of the starting material, the reaction mixture was filtered through a pad of celite, and the residue was washed with chloroform. The filtrate and the washings were combined, and poured into sat. NH_4Cl. The combined mixture was extracted with chloroform. The extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and evaporated *in vacuo*. The crude

product was purified by flash column chromatography on silica gel (60% EtOAc in Hexane) to give β,γ-dihydroxyketone **22** (144 mg, 62%) as a white powder.
^{1}H-NMR ($CDCl_3$) δ 1.43 (s, 1H), 1.52 (s, 3H), 2.37 (s, 3H), 3.41 (dd, *J* = 5.6, 12.8 Hz, 1H), 3.80 (m, 1H), 3.88 (s, 3H), 3.95 (d, *J* = 9.6 Hz, 1H), 4.03 (t, *J* = 9.6 Hz, 1H), 4.39 (s, 1H), 4.43 (d, *J* = 9.6 Hz, 1H), 4.61 (s, 1H), 4.70 (s, 1H), 6.65 (s, 1H), 6.83 (s, 1H); LR-MS (EI) 447(M^+), 429, 416, 387, 371, 358, 329, 302, 273, 258, 248.

Diol 23. To a stirred solution of β,γ-dihydroxyketone **22** (1.5 g, 3.3 mmol) in acetic acid (3.3 mL)-THF (33 mL) was added sodium triacetoxyborohydride (3.5 g, 17 mmol) at 0 °C. After stirring for 30 minutes, the reaction mixture was poured into sat. $NaHCO_3$. The combined mixture was extracted with chloroform. The extracts were washed with brine, dried over Na_2SO_4, filtered, and evaporated *in vacuo* to afford the corresponding triol.

To the solution of the above triol in methanol (10 mL) was added 3 N NaOH (1.0 mL). After stirring for 5 minutes at room temperature, the reaction mixture was partitioned between chloroform and brine. The aqueous layer was extracted with chloroform. The extracts were dried over Na_2SO_4, filtered, and evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (80% EtOAc in Hexane) to give triol (1.0 g, 85%) as a white powder.

To a stirred solution of triol (1.00 g, 2.82 mmol) in acetonitrile-water (3:2, 14 mL) was added sodium periodate (1.20 g, 5.61 mmol) in water (4.0 mL) at 0 °C. After stirring for 10 minutes, the reaction mixture was filtered and the residue was washed with chloroform. The filtrate and the washings were combined, and the mixture was washed with brine. The organic layer was dried over Na_2SO_4, filtered, and evaporated *in vacuo*.

To a solution of the above residue in methanol (10 mL) was added sodium borohydride (317 mg, 8.38 mmol). After stirring for 10 minutes at room temperature, the reaction mixture was poured into sat. NH_4Cl. The combined mixture was extracted with chloroform. The extracts were washed with brine, dried over Na_2SO_4, filtered, and evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (80% EtOAc in Hexane) to give diol **23** (683 mg, 75%) as a white powder.
IR (film) 3336, 2937, 1610, 1581, 1462, 1371, 1230, 1122, 1073, 830; ^{1}H-NMR ($CDCl_3$) δ 1.27 (s, 3H), 1.43 (s, 3H), 2.64 (dd, *J* = 9.6, 12.8 Hz, 1H), 3.47 (dd, *J* = 4.0, 7.6 Hz, 1H), 3.69 (dd, *J* = 4.0,12.8 Hz, 1H), 3.75 (s, 3H), 4.03 (m, 3H), 4.55 (dd, *J* = 6.8, 10.8 Hz, 1H), 6.48 (s, 2H); ^{13}C-NMR ($CDCl_3$) δ 21.4, 26.8, 27.1, 43.1, 55.3, 55.5, 66.7, 70.2, 74.4, 82.2, 108.4, 108.9, 118.8, 119.9, 138.8, 149.3, 158.6; MS (EI) 323 (M^+), 175, 162; HR-MS (EI) calcd for $C_{17}H_{25}NO_5$ 323.1733, found 323.1747; $[\alpha]_D^{28}$ -37.9 ° (*c* = 0.130, $CHCl_3$).

Ketone 24. To a solution of diol **23** (620 mg, 1.91 mmol) in dichloromethane (10 mL) were added TBSCl (347 mg, 2.20 mmol), triethylamine (0.83 mL, 6.0 mmol), and DMAP (73.0 mg, 0.597 mmol). After stirring for 2 hours at room temperature, the reaction mixture was partitioned between ethyl acetate and 1 N HCl and brine. The aqueous layer was extracted with ethyl acetate. The extracts were washed with brine, dried over $MgSO_4$, filtered, and evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (10% EtOAc in Hexane) to give TBS ether (581 mg, 70%) as a white powder.

To a stirred solution of the TBS ether (580 mg, 1.32 mmol) in dichloromethane (4.0 mL) was added a solution of *m*-chloroperbenzoic acid (495 mg, 1.72 mmol) in dichloromethane (2.8 mL) at 0 °C. After stirring for 5 minutes, the reaction was quenched by addition of aqueous sodium sulfite. The combined mixture was poured into sat. $NaHCO_3$ and extracted with chloroform. The extracts were washed with brine. The organic layer was dried over Na_2SO_4, filtered, and evaporated *in vacuo* to afford the corresponding hydroxylamine.

The residue was dissolved in acetic anhydride (2.0 mL). After stirring for an hour, the solution was evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (5~10% EtOAc in Hexane) to give hydroxylamine *O*-acetate (423 mg, 65%).

To a stirred solution of alcohol (423 mg, 0.853 mmol) in dichloromethane (4.0 mL) was added Dess-Martin periodinane (1.03 g, 1.70 mmol) at room temperature. After stirring for 5 minutes, the reaction mixture was evaporated to a small volume *in vacuo*. The crude product was purified by flash column chromatography on silica gel (10% EtOAc in Hexane) to give β-silyloxyketone **24** (410 mg, 97 %) as a yellow oil.

^{1}H-NMR ($CDCl_3$) for the major conformational isomer δ 0.07 (s, 6H), 0.86 (s, 9H), 1.34 (s, 3H), 1.47 (s, 3H), 2.36 (s, 3H), 3.36 (dd, *J* = 8.0, 12.2 Hz, 1H), 3.57 (s, 1H) 3.74 (dd, *J* = 5.6, 10.0 Hz, 1H), 3.81 (s, 3H) 4.05 (m, 3H), 4.58 (dd, *J* = 6.8, 10.0 Hz, 1H) 4.86 (m, 1H), 5.42 (dd, *J* = 4.2, 12.2 Hz, 1H), 6.64 (s, 1H), 6.98 (s, 1H); LR-MS (EI) 493 (M^+), 478, 433, 376, 318, 302, 290, 276, 264, 244, 232, 216, 202, 188, 174, 162, 117; $[\alpha]_D^{25}$ -23.7 ° (*c* = 0.173, $CHCl_3$).

Diol 26. To a stirred solution of ketone **24** (0.41 mg, 0.83 mmol) in dichloromethane-methanol (1:1, 8.0 mL) was added hydradine monohydrate (0.40 mL, 8.3 mmol) at room temperature. After stirring 10 minutes, the reaction mixture was evaporated to a small volume *in vacuo*. The crude product was purified by flash column chromatography on silica gel (10~20% EtOAc in Hexane) to give hemiketal **25** (0.29 mg, 78 %) as a white powder.

To a stirred solution of hemiketal **25** (0.29 mg, 0.64 mmol) and acetic acid (51 μL, 0.89 mmol) in THF (6.4 mL) was added TBAF (1 M THF solution, 0.77 mL, 0.77 mmol) at 0 °C. After stirring for 2 hours, the reaction mixture was poured into sat. NH_4Cl. The combined mixture was extracted with ethyl acetate. The extracts were washed with brine, dried over Na_2SO_4, filtered, and evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (50% EtOAc in Hexane) to give hemiketal bearing primary alcohol (0.21 mg, 98 %) as a yellow powder.

To a stirred solution of diol (100 mg, 0.296 mmol) in methanol (3.0 mL) was added Amberlyst 15E® (100 mg). After consumption of the starting material, the reaction mixture was filtered and evaporated to dryness *in vacuo*

To a stirred solution of the above residue in DMF were added PPTS (15.0 mg, 0.0592 mmol), 2,2-dimethoxypropane (180 μL, 1.48 mmol), and 2-methoxypropene (56 μL, 0.592 mmol) at 0 °C. After consumption of the starting material, the reaction mixture was partitioned between ethyl acetate and water. The organic layer was combined, dried over $MgSO_4$, filtered, and evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (50% EtOAc in Hexane) to give diol **26** (77.2 mg, 77%) as a yellow powder.

^{1}H-NMR ($CDCl_3$) δ 1.46 (s, 3H), 1.56 (s, 3H), 2.30 (s, 3H), 3.44 (m, 2H), 3.55 (dd, *J* = 5.6, 10.8 Hz, 1H), 3.77 (t, *J* = 10.8 Hz, 1H), 3.63 (m, 2H), 3.79 (s, 3H), 4.27 (dd, *J* = 5.6, 11.6 Hz, 1H), 6.36 (s, 1H), 6.42 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ 21.6, 24.1, 27.9, 30.1, 55.3, 59.3, 60.7, 64.5, 80.2, 99.2, 99.5, 107.7, 111.6, 112.8, 138.6, 146.1, 157.1; MS (EI) 338 (M^++1), 280, 271, 252, 236, 219, 203, 190, 175, 163, 150, HR-MS (EI) calcd for $C_{17}H_{23}NO_6$ 337.1525, found 337.1523; $[\alpha]_D^{23}$ -28 ° (*c* = 0.020, $CHCl_3$).

Mesylate 27. To a solution of diol **26** (76.0 mg, 0.225 mmol) in dichloromethane (2.2 mL) was added triethylsilyl chloride (41 μL, 0.247 mmol), triethylamine (94 μL, 0.675 mmol), and DMAP (13.0 mg, 0.110 mmol). After stirring for an hour at room temperature, the reaction mixture was partitioned between ethyl acetate, and 1 N HCl and brine. The aqueous layer was extracted with ethyl acetate. The extracts were washed with brine, dried over $MgSO_4$, filtered, and evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (30% EtOAc in Hexane) to give TES ether (76.7 mg, 75%) as a white powder.

To a stirred solution of TES ether (76.0 mg, 0.168 mmol) in dichloromethane (1.0 mL) were

added triethylamine (70 μL, 0.504 mmol) and mesyl chloride (20 μL, 0.252 mmol). After stirring for 20 minutes at room temperature, the reaction mixture was partitioned between ethyl acetate, and 1 N HCl and brine. The aqueous layer was extracted with ethyl acetate. The extracts were washed with brine, dried over $MgSO_4$, filtered, and evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (30% EtOAc in Hexane) to give mesylate **27** (82.3 mg, 92%) as a white powder.
^{1}H-NMR ($CDCl_3$) δ 0.47 (q, *J* = 7.8 Hz, 6H), 0.82 (t, *J* = 7.8 Hz, 9H), 1.47 (s, 3H), 1.58 (s, 3H), 2.30 (s, 3H), 3.41 (d, *J* = 7.6 Hz, 1H), 3.46 (dd, *J* = 5.6 Hz, *J* = 10.4 Hz, 1H), 3.67 (dd, *J* = 7.6, 17.6 Hz, 1H), 3.78 (t, *J* = 11.2 Hz, 1H), 3.82 (s, 3H), 4.24 (dd, *J* = 5.6, 12.0 Hz, 1H), 4.55 (d, *J* = 8.8 Hz, 1H), 6.34 (s, 1H), 6.44 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ 4.77, 6.47, 21.6, 24.4, 28.9, 29.9, 55.3, 59.4, 62.1, 64.8, 87.5, 98.2, 100.3, 107.7, 110.7, 112.1, 139.0, 145.2, 157.0; LR-MS (EI) 529 (M^+), 528 (M^+–1), 483, 470, 441, 392, 376, 364, 318, 308, 278, 261, 252, 235, 219, 203, 191, 174, 162, 149, 131.

Epoxide 28. To a stirred solution of mesylate **27** (80 mg, 0.15 mmol) in THF (1.5 mL) was added TBAF (1 M THF solution, 0.18 mL, 0.18 mmol) at 0 °C. After stirring for 5 minutes, the reaction mixture was poured into sat. NH_4Cl. The combined mixture was extracted with ethyl acetate. The extracts were washed with brine, dried over Na_2SO_4, filtered, and evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (70% EtOAc in Hexane) to give alcohol (59 mg, 95 %) as colorless crystals.

To a stirred solution of sodium hydride (21 mg, 0.53 mmol) in DMF-THF (1:3, 1.0 mL) was added a dichloromethane solution of the alsohol (22 mg, 0.053 mmol) and then the reaction mixture was heated at 60 °C. After stirring for 5 minutes, the reaction mixture was partitioned between ethyl acetate and water. The organic layer was combined, dried over Na_2SO_4, filtered, and evaporated *in vacuo*. The crude product was purified on a preparative silica gel TLC to give epoxide **28** (14 mg, 80%) as a white powder.
^{1}H-NMR ($CDCl_3$) δ 1.52 (s, 3H), 1.59 (s, 3H), 2.30 (s, 3H), 3.07 (d, *J* = 4.8 Hz, 1H), 3.22 (t, *J* = 4.8 Hz, 1H), 3.28 (dd, *J* = 6.0. 10.8 Hz, 1H), 3.48 (dd, *J* = 4.8, 15.6 Hz, 1H), 3.81 (s, 3H), 3.84 (t, *J* = 11.6 Hz, 1H), 3.92 (d, *J* = 15.6 Hz, 1H), 4.23 (dd, *J* = 6.0, 11.6 Hz, 1H), 6.28 (s, 1H), 6.40 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ 21.7, 24.4, 30.2, 32.5, 50.0, 51.7, 54.9, 55.4, 59.4, 93.2, 100.0, 106.6, 110.4, 112.4, 138.8, 146.6, 157.7; MS (EI) 319 (M^+), 304 (M^+-CH_3), 262, 244, 216, 202, 188; $[\alpha]_D^{20}$ 107 ° (*c* = 0.17, MeOH).

Azide mesylate 29. A solution of epoxide **28** (12.0 mg, 0.37 mmol) and lithium azide (36.8 mg, 0.75 mmol) in DMF (0.3 mL) was heated at 100 °C. After consumption of the starting material, the reaction mixture was partitioned between ethyl acetate and water. The aqueous layer was extracted with ethyl acetate. The extracts were combined, dried over $MgSO_4$, filtered, and evaporated *in vacuo*. The crude product was purified on a preparative silica gel TLC to give azido alcohol (11.1 mg, 82 %) as a white powder.

To a stirred solution of alcohol (10 mg, 0.028 mmol) in dichloromethane (0.3 mL) were added triethylamine (23 μL, 0.17 mmol) and mesyl chloride (8.7 μL, 0.11 mmol). After stirring for 15 minutes at room temperature, the mixture was partitioned between ethyl acetate, and 1 N HCl and brine. The aqueous layer was extracted with ethyl acetate. The extracts were washed with brine, dried over $MgSO_4$, filtered, and evaporated *in vacuo*. The crude product was purified on a preparative silica gel TLC to give azido mesylate **29** (9.8 mg, 79%) as colorless crystals.
IR (film) 2995, 2941, 2112, 1616, 1586, 1360; ^{1}H-NMR ($CDCl_3$) δ 1.49 (s, 3H), 1.58 (s, 3H), 2.30 (s, 3H), 3.15 (s, 3H) 3.26 (m, 2H), 3.83 (d, *J* = 11.7 Hz, 1H), 4.09 (dd, *J* = 3.4 Hz, *J* = 5.1 Hz, 1H), 4.15 (dd, *J* = 4.9 Hz, *J* = 14.2 Hz, 1H), 4.30 (dd, *J* = 6.1 Hz, *J* = 11.7 Hz, 1H), 4.45 (d, *J* = 5.1 Hz, 1H), 6.35 (s, 1H), 6.44 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ 21.6, 24.3, 29.9, 33.1, 38.7, 78.7, 93.7, 100.6, 107.8, 111.0,

112.2, 139.0, 146.9, 157.4; MS (EI) 440 (M^+), 382, 287, 279, 248, 167, 149, 129; $[\alpha]_D^{25}$ -3.3 ° (*c* = 0.027, $CHCl_3$).

Aziridine 30. To a stirred solution of azido mesylate **29** (9.2 mg, 0.21 mmol) in dichloromethane (1.0 mL) was added trifluoroacetic acid (10 μL). After consumption of the starting material, the reaction mixture was purified on a preparative silica gel TLC to give diol (7.6 mg, 91%) as colorless crystals.

To a stirred solution of a triphosgene (6.1 mg, 0.12 mmol) in dichloromethane (0.15 mL) was added pyridine (10 μL) at 0 °C. After stirring for 5 minutes, a dichloromethane solution of the diol (7.3 mg, 0.018 mmol) was added. After consumption of the starting material, the reaction mixture was diluted with ethyl acetate, partitioned between ethyl acetate and water. The organic layer was combined, dried over Na_2SO_4, filtered, and evaporated *in vacuo*. The crude product was purified on a preparative silica gel TLC to give carbonate (5.8 mg, 75%) as a white powder.

To a stirred solution of carbonate (5.8 mg, 0.013 mmol) in THF-water (10:1, 0.8 mL) was added Hunig's base (4.7 μL, 0.027 mmol), followed by addition of triphenylphosphine (14 mg, 0.54 mmol). After consumption of the starting material, the reaction mixture was purified on a preparative silica gel TLC to give aziridine **30** (2.8 mg, 70 %) as a white powder.
IR (film) 3303, 2927, 1774, 1614, 1588, 1467, 1389, 1345, 1291, 1232, 1159, 1129, 1094, 1081; ^{1}H-NMR ($CDCl_3$) δ 2.30 (s, 3H), 2.44 (t, *J* = 2.4, 8.8 Hz, 1H), 3.04 (dt, *J* = 6.1, 10.7 Hz, 1H), 3.58 (dd, *J* = 5.1, 11.5 Hz, 1H), 3.61 (d, *J* = 14.4 Hz, 1H), 3.95 (t, *J* = 15.2 Hz, 1H), 4.23 (dd, *J* = 11.5 Hz, 1H), 4.66 (dd, *J* = 5.1, 10.7 Hz, 1H), 6.26 (s, 1H), 6.38 (s, 1H); LR-MS (EI) 304 (M^+), 277 (M^++1–N_2), 269, 254, 252, 235, 219, 203, 201, 187, 185, 177, 167, 162, 149, 122, 111, 97; HR-MS (EI) calcd for $C_{15}H_{16}N_2O_5$ 304.1059, Found 304.1052; $[\alpha]_D^{24}$ -25 ° (*c* = 0.012, $CHCl_3$).

FR-900482 analog 31. To a solution of the carbonate **30** (2.4 mg, 0.0079 mmol) in dichloromethane was babbled ammonia gas for 2 minutes. The reaction mixture was then evaporated *in vacuo*. The crude product was purified on a preparative silica gel TLC to give FR-900482 analog **31** (1.9 mg, 75%) as a white powder.
IR (film) 3600-3000, 1699, 1615, 1586, 1463, 1412, 1343, 1119, 1082, 1041; ^{1}H-NMR ($CDCl_3$) δ 2.31 (s, 3H), 2.81 (1H), 3.17 (1H), 3.52 (1H), 3.56 (1H), 3.65 (1H), 3.85 (3H, s), 4.56 (1H), 5.01 (d, *J* = 12.8 Hz, 1H), 6.26 (s, 1H), 6.40 (s, 1H); LR-MS (EI): 306 (M^+-NH), 304 (M^+-OH), 277 (M^+-$CONH_2$); $[\alpha]_D^{20}$ -39 ° (*c* = 0.16, MeOH).

FR-900482 analog 32. To a stirred solution of epoxide **28** (5.5 mg, 0.017 mmol) in dichloromethane (0.75 mL) was added trifluoroacetic acid (15 μL, 0.19 mmol). The reaction mixture was purified on a preparative silica gel TLC to give diol (2.3 mg, 46%) as colorless crystals.

To a stirred solution of triphosgene (2.3 mg, 0.079 mmol) in dichloromethane (0.2 mL) was added pyridine (4.0 μl, 0.047 mmol) at 0 °C. After stirring for 5 minutes, a dichloromethane solution of the above alcohol (2.0 mg, 0.079 mmol) was added to the mixture. After consumption of the starting material, the reaction mixture was poured into 1 N HCl. The combined mixture was extracted with dichloromethane. The extracts were combined, dried over Na_2SO_4, filtered, and evaporated *in vacuo*. The crude product was purified on a preparative silica gel TLC to give carbonate (1.5 mg, 62%) as a white powder.

To a solution of the carbonate (1.5 mg, 0.049 mmol) in dichloromethane was babbled ammonia gas for 2 minutes. The reaction mixture was then evaporated *in vacuo*. The crude product was purified on a preparative silica gel TLC to give FR-900482 analog **32** (1.3 mg, 79 %) as a white powder.
IR (film) 3600-3050, 1716, 1616, 1585, 1457, 1418, 1347, 1266, 1125, 1044; ^{1}H-NMR ($CDCl_3$) δ 2.32 (s, 3H), 3.10 (d, *J* = 3.6 Hz, 1H), 3.25 (t, *J* = 4.0 Hz, 1H), 3.31 (dd, *J* = 2.2, 5.4 Hz, 1H), 3.50 (dd, *J* =

5.1, 15.4 Hz, 1H), 3.87 (s, 3H), 3.90 (d, *J* = 15.4 Hz, 1H), 4.49 (dd, *J* = 5.4, 12.0 Hz, 1H), 4.62 (dd, *J* = 2.2, 12.0 Hz, 1H), 6.29 (s, 1H), 6.44 (s, 1H); MS (EI) 322 (M^+), 279, 261, 252, 235, 219, 203, 188, 167, 149, 129, 119, 105; $[\alpha]_D^{20}$ 59 ° (*c* = 0.067, MeOH).