Total Synthesis of Ecteinascidin 743

Atsushi Endo, Arata Yanagisawa, Masanao Abe, Shigemitsu Tohma, Toshiyuki Kan, and Tohru Fukuyama*

Supporting Information

Experimental Section

General

All non-aqueous reactions were carried out in oven-dried glass tubes under a slight positive pressure of argon unless otherwise noted. CH_2Cl_2 and toluene were distilled from calcium hydride. Dehydrated THF, Et_2O , CH_3CN , DMF, MeOH, and EtOH were purchased from Kanto Chemical Co., Inc. and stored over molecular sieves 3A or 4A. Pyridine, Et_3N and *i*- Pr_2NEt were dried over KOH. All other reagents were commercially available and used without further purification. Preparative flash chromatography was performed using Silica Gel 60 (spherical, 40-100 μm) purchased from Kanto Chemical Co., Inc. ^1H and ^{13}C NMR spectra were obtained on JEOL LA-400 MHz. IR spectra were recorded on a JASCO FT/IR-410 Fourier Transform Infrared Spectrophotometer. Mass spectra (MS) were obtained on a JEOL JMS-GCmate. Optical rotations were measured on a JASCO DIP-1000.

MOM Ether

To a solution of NaH (60% w/w in mineral oil, 40 g, 1.0 mol, 1.0 equiv) in a mixture of THF (500 ml) and DMF (200 ml) at 0 °C was slowly added sesamol (138 g, 1.0 mol) in THF (300 ml), and the mixture was stirred at room temperature for 30 min. The reaction mixture was cooled to 0 °C, and to the solution was added chloromethyl methyl ether (84.5 g, 1.05 mol, 1.05 equiv) dropwise. The resulting slurry was allowed to warm to room temperature and stirred for additional 1h. To the reaction mixture were added *n*-hexane and H_2O , and the organic layer was separated. The aqueous phase was further extracted with hexane (200 ml x 2), and the combined organic phase was concentrated under reduced pressure. The residue was dissolved in *n*-hexane and washed with saturated aqueous NaCl. The organic phase was dried over Na_2SO_4 , and concentrated under reduced pressure, and the crude product was purified by distillation (103 °C/0.35 mmHg) to afford the MOM ether (177 g, 0.97 mol, 97%) as a colorless oil. IR (neat film) 1244, 1215, 1176, 1153, 1099, 1069, 1040, 1004, 940, 922, 842, 813 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.71 (d, J = 8.4 Hz, 1H) 6.63 (s, 1H), 6.49 (d, J = 8.4 Hz, 1H), 5.90 (s, 2H), 5.08 (s, 2H), 3.46 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 152.5, 148.1, 142.5, 108.4, 108.0, 101.2, 99.7, 95.4, 55.8; HRMS (FAB $^+$) m/z : Calcd. for $\text{C}_9\text{H}_{10}\text{O}_4$ (M^+) 182.0579, found 182.0563.

Phenol 5

To a solution of the MOM ether (5.44 g, 29.9 mmol) in THF (100 ml) at 0 °C was added *n*-BuLi (3.02 M solution in *n*-hexane, 11.0 ml, 33.2 mmol, 1.1 equiv), and the mixture was allowed to warm to room temperature. After cooling to 0 °C, to the solution were sequentially added trimethylboronate (4.10 ml, 36.1 mmol, 1.2 equiv), AcOH (3.4 ml, 59 mmol, 2.0 equiv), and 7% aqueous H₂O₂ (26 ml, 60 mmol, 2.0 equiv). The resulting mixture was allowed to warm to room temperature and stirred for additional 4.5 h. To the reaction mixture were added saturated aqueous (NH₄)₂SO₄ (100 ml) and saturated aqueous Na₂SO₃ (50 ml), and the organic phase was separated. The aqueous phase was further extracted with CHCl₃, and the combined organic phase was concentrated under reduced pressure. The residue was diluted with CHCl₃ and washed with saturated aqueous NaHCO₃, and the organic phase was dried over anhydrous MgSO₄ and concentrated under reduced pressure. The crude product was purified by flash column chromatography (70% EtOAc in *n*-hexane) to afford **5** (5.42g, 27.3 mmol, 92%) as a yellow oil. IR (neat film) 3439, 1652, 1493, 1292, 1245, 1157, 1044, 932, 791cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 6.55 (d, *J* = 8.4 Hz, 1H), 6.45 (br, 1H), 6.32 (d, *J* = 8.4 Hz, 1H), 5.94 (s, 2H), 5.09 (s, 2H), 3.50 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 144.3, 141.3, 134.4, 132.0, 109.2, 101.6, 99.1, 97.3, 60.4, 56.3; HRMS (FAB⁺) *m/z*: Calcd. for C₉H₁₀O₅ (M⁺) 198.0528, found 198.0558.

Aminolactone **7**

To a mixture of **5** (19.8 g, 100 mmol) and **6** (20.3 g, 100 mmol) in CH_2Cl_2 (200 ml) at $-10\text{ }^\circ\text{C}$ was slowly added TFA (38 ml, 0.49 mol, 5 equiv) over 1.5 h. After addition was completed, the reaction mixture was stirred at this temperature for additional 40 min. To the reaction mixture was carefully added a mixture of Na_2CO_3 (40 g, 0.38 mol, 3.8 equiv) and H_2O (200 ml), and the resulting mixture was extracted with CH_2Cl_2 . The organic layer was separated, and the aqueous phase was further extracted with CH_2Cl_2 (100 ml). The combined organic phase was washed with saturated aqueous NaCl, dried over Na_2SO_4 , and concentrated under reduced pressure. The crude product was purified by flash column chromatography (30% EtOAc in *n*-hexane) to afford **7** (35.6g, 89 mmol, 89%) as a yellow amorphous. $[\alpha]_{\text{D}}^{27} -75\text{ }^\circ$ ($c = 1.7$, CHCl_3); IR (neat film) 3327, 1724, 1506, 1457, 1299, 1151, 1118, 1082, 1049, 1101, 934 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.29-7.37 (m, 5H), 6.51 (s, 1H), 5.93 (s, 1H), 5.91 (s, 1H), 5.09 (d, $J = 8.0$ Hz, 1H), 5.05 (d, $J = 8.0$ Hz, 1H), 5.03 (s, 1H), 4.15 (s, 1H), 3.51 (s, 3H), 2.03 (br, 1H), 1.37 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 169.0, 141.8, 141.4, 138.2, 134.8, 132.4, 128.4, 128.3, 128.3, 111.6, 110.0, 101.9, 86.7, 61.0, 57.1, 56.4, 26.6, 22.0; HRMS (FAB⁺) m/z : Calcd. for $\text{C}_{21}\text{H}_{23}\text{NO}_7$ (M^+) 401.1475, found 401.1467.

Triflate

To a mixture of **7** (242 mg, 0.603 mmol) and pyridine (0.15 ml, 1.9 mmol, 3.1 equiv) in CH_2Cl_2 (3.0 ml) at $0\text{ }^\circ\text{C}$ was added Tf_2O (0.13 ml, 0.77 mmol, 1.3 equiv), and the resulting mixture was stirred for 5 minutes, poured into saturated aqueous NaHCO_3 , and extracted with EtOAc. The organic phase was sequentially washed with 1M aqueous HCl, saturated aqueous NaHCO_3 , and saturated aqueous NaCl. The solution was dried over anhydrous MgSO_4 , and concentrated under reduced pressure, and the residue was purified by flash column chromatography (50% EtOAc in *n*-hexane) to afford the triflate (290 mg, 0.544 mmol, 90%) as a white foam. $[\alpha]_{\text{D}}^{26} -32\text{ }^\circ$ ($c = 2.6$, CHCl_3); IR (neat film) 3333, 1733, 1496, 1462, 1427, 1299, 1216, 1138, 1056, 999, 979, 936, 832 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.32-7.40 (m, 5H), 6.71 (s, 1H), 6.06 (s, 1H), 6.03 (s, 1H), 5.19 (d, $J = 5.8$ Hz, 1H), 5.14 (d, $J = 5.8$ Hz, 1H), 5.09 (s, 1H), 4.23 (s, 1H), 3.49 (s, 3H), 2.01 (br, 1H), 1.40 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 167.8, 144.9, 141.2, 140.2, 137.8, 128.3, 128.2, 128.1, 123.1, 120.2, 116.7, 108.0,

103.1, 95.9, 86.7, 61.3, 56.9, 56.3, 26.4, 21.8; HRMS (FAB⁺) *m/z*: Calcd. for C₂₂H₂₂F₃NO₉S (M⁺) 533.0967, found 553.0993.

Amino Alcohol

To a solution of the triflate (4.70 g, 8.8 mmol) in MeOH (50 ml) at 0 °C was added NaBH₄ (1.33 g, 35 mmol, 4.0 equiv), and the mixture was stirred for 30 min. The reaction mixture was diluted with EtOAc (300 ml) and sequentially washed with 1M aqueous HCl (100 ml) and saturated aqueous NaHCO₃. The organic phase was dried over MgSO₄ and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (60% EtOAc in *n*-hexane) to afford the amino alcohol (4.04 g, 7.5 mmol, 85%) as a colorless foam. $[\alpha]_D^{27} -102^\circ$ (*c* = 1.7, CHCl₃). IR (neat film) 3398, 1497, 1456, 1426, 1218, 1136, 1054, 937, 833 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.25-7.33 (m, 5H), 6.63 (s, 1H), 5.94 (s, 1H), 5.93 (s, 1H), 5.11 (d, *J* = 6.8 Hz, 1H), 5.07 (d, *J* = 6.8 Hz, 1H), 3.65 (br, 1h), 3.52-3.64 (br, 2H), 3.50 (s, 3H), 3.39 (s, 1H), 2.71 (br, 1H), 1.11 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 144.8, 141.6, 139.9, 139.2, 128.7, 128.1, 127.5, 122.4, 120.9, 120.1, 116.9, 107.1, 102.9, 95.6, 72.7, 68.9, 64.9, 56.9, 56.3, 27.9, 23.8; HRMS (FAB⁺) *m/z*: Calcd. for C₂₂H₂₆F₃NO₉S (M⁺) 537.1280, found 537.1222.

Silyl Ether 8

To a mixture of the amino alcohol (1.00 g, 1.86 mmol) and imidazole (0.63 g, 9.3 mmol, 5.0 equiv) in DMF was added TBDPSCl (1.22 ml, 4.7 mmol, 2.5 equiv), and the solution was stirred at room temperature and partitioned between Et₂O and H₂O. The ethereal layer was washed with saturated aqueous NaCl, dried over anhydrous Na₂SO₄, and concentrated under reduced pressure. The residue was purified by flash column chromatography (10% EtOAc in *n*-hexane) to afford **8** (1.31 g, 1.69 mmol, 91%) as a pale yellow oil. $[\alpha]_D^{27} -75^\circ$ (*c* = 1.7, CHCl₃). IR (neat film) 3445, 1469, 1428, 1363, 1263, 1109, 1062, 991, 944, 826 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.61 (d, *J* = 8.0 Hz, 2H), 7.56 (d, *J* = 8.0 Hz, 2H), 7.23-7.42 (m, 11H), 6.62 (s, 1H), 5.83 (s, 2H), 5.10 (d, *J* = 6.8 Hz, 1H), 5.08 (d, *J* = 6.8 Hz, 1H), 3.77 (dd, *J* = 6.0, 6.8 Hz, 1H), 3.67 (m, 2H), 3.47 (s, 3H), 3.37 (s, 1H), 3.34 (br, 1H), 1.09 (s, 6H), 1.08 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 144.7, 141.8, 139.8, 139.5, 135.6, 132.9, 129.7, 128.5,

128.1, 127.7, 127.6, 127.4, 122.5, 121.0, 120.1, 116.9, 107.7, 102.7, 95.8, 72.2, 68.6, 66.4, 56.8, 56.3, 27.4, 26.8, 24.2, 19.2; HRMS (FAB⁺) *m/z*: Calcd. for C₃₈H₄₅F₃NO₉SSi (M+H)⁺ 776.2536, found 776.2596.

Amino Alcohol

To a degassed solution of **8** (16.7 g, 21.5 mmol) in THF (105 ml) at 0 °C was added MeZnCl (2.0 M solution in THF, 37.5 ml, 75.1 mmol, 3.5 equiv), and the mixture was allowed to warm to room temperature. To the mixture was added PdCl₂(dppf) (314 mg, 0.43 mmol, 2.0 mol%), and the resulting mixture was heated to reflux. After stirring for 1h, to the mixture was added PdCl₂(dppf) (472 mg, 0.65 mmol, 3.0 mol%), and the mixture was heated at reflux for additional 3.5 h. The reaction mixture was diluted with EtOAc and washed sequentially with 1N aqueous HCl, saturated aqueous NaHCO₃, and saturated aqueous NaCl. The organic layer was dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (10% EtOAc in *n*-hexane) to afford the amino alcohol (13.4 g, 20.9 mmol, 97%) as a white amorphous. [α]_D²⁶ –99 ° (c = 0.81, CHCl₃). IR (neat film) 3457, 2931, 1494, 1457, 1427, 1362, 1216, 1139, 1110, 1056, 1006, 936, 828 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.63 (d, *J* = 6.8 Hz, 2H), 7.56 (d, *J* = 6.8 Hz, 2H), 7.22-7.47 (m, 11H), 6.30 (s, 1H), 5.77 (s, 2H), 5.03 (d, *J* = 5.6 Hz, 1H), 5.01 (d, *J* = 5.6 Hz, 1H), 3.83 (dd, *J* = 10.8, 10.8, 1H), 3.61-3.66 (m, 2H), 3.44 (s, 3H), 3.38 (s, 1H), 2.08 (s, 3H), 1.09 (s, 9H), 1.06 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 150.8, 146.6, 140.0, 139.7, 135.6, 135.6, 133.2, 133.1, 130.9, 130.4, 130.0, 129.7, 129.6, 128.5, 128.4, 128.0, 127.7, 127.6, 127.2, 117.7, 109.6, 107.0, 100.8, 95.6, 72.1, 68.5, 66.6, 57.7, 56.0, 27.3, 26.8, 24.0, 19.2. 8.8; HRMS (FAB⁺) *m/z*: Calcd. for C₃₈H₄₇NO₆Si (M⁺) 641.3173, found 641.3156.

Amine 9

To a solution of the amino alcohol (640 mg, 1.0 mmol) in CH₃CN (12 ml) at 0 °C was added Pb(OAc)₄ (0.56 g, 1.26 mmol, 1.3 equiv). To the reaction mixture was added saturated aqueous NaHCO₃, and extracted with EtOAc. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na₂SO₄, and concentrated under reduced pressure to afford the crude product, which was used in the next step without further purification. To a

mixture of hydroxylamine hydrochloride (347 mg, 5.0 mmol, 5.0 equiv) and sodium acetate (410 mg, 5.0 mmol, 5.0 equiv) in EtOH (10 ml) at room temperature was added the crude product, and the resulting slurry was stirred for 1.5 h. The reaction mixture was diluted with EtOAc, filtered through a pad of Celite, and concentrated under reduced pressure. The residue was dissolved in EtOAc, and sequentially washed with 1N aqueous HCl, saturated aqueous NaHCO₃, and saturated aqueous NaCl. The organic layer was dried over anhydrous Na₂SO₄, and concentrated under reduced pressure. The resulting crude product was purified by flash column chromatography (EtOAc) to afford **9** (436mg, 0.88 mmol, 89% in 2 steps, >98% ee (ee was determined by ¹H NMR analysis of the corresponding (*R*)-MTPA amide)) as a yellow oil. [α]_D²³ -2.0 ° (c = 1.3, CHCl₃). IR (neat film) 1440, 1115, 1062, 991, 938, 826 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.61-7.65 (m, 4H), 7.35-7.45 (m, 6H), 6.57 (s, 1H), 5.81 (s, 2H), 5.09 (s, 2H), 4.16 (dd, *J* = 6.8, 4.8 Hz, 1H), 3.87 (dd, *J* = 10.0, 4.8 Hz, 1H), 3.76 (dd, *J* = 10.0, 6.8 Hz, 1H), 3.48 (s, 3H), 2.14 (s, 3H), 1.08 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 150.8, 146.1, 139.1, 135.5, 135.5, 133.4, 133.3, 129.5, 129.5, 127.5, 120.7, 109.1, 105.8, 100.7, 95.7, 68.1, 55.9, 53.4, 26.7, 19.1, 8.8; HRMS (FAB⁺) *m/z*: Calcd. for C₂₈H₃₆NO₅Si (M+H)⁺ 494.2363, found 494.2387.

Tosylate

To a mixture of 3-methylcatechol (185 mg, 1.49 mmol) and TEA (0.315 ml, 2.26 mmol, 1.5 equiv) in CH₂Cl₂ (3.0 ml) at 0 °C was added *p*-toluenesulfonyl chloride (292 mg, 1.53 mmol, 1.03 equiv) portionwise. The reaction mixture was diluted with CH₂Cl₂, and sequentially washed with 10% aqueous citric acid and saturated aqueous NaCl. The organic layer was dried over anhydrous MgSO₄ and concentrated under reduced pressure. The crude product was purified by flash column chromatography (20% EtOAc in *n*-hexane) to afford the tosylate (345 mg, 1.24 mmol, 83%) as a white solid. IR (neat film) 3488, 1597, 1473, 1373, 1249, 1199, 1173, 1092, 1007, 941, 785 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.76 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 6.99 (d, *J* = 7.6 Hz, 1H), 6.64 (dd, *J* = 8.0, 7.6 Hz, 1H), 6.58 (d, *J* = 8.0 Hz, 1H), 6.01 (s, 1H), 2.46 (s, 3H), 2.24 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 146.6, 146.1, 137.0, 131.3, 129.9, 129.5, 128.6, 127.8, 120.3, 119.8, 21.7, 15.9; HRMS (FAB⁺) *m/z*: Calcd. for C₁₄H₁₄O₄S (M⁺) 278.0613, found 278.0639.

Bromide

To a mixture of the tosylate (193 mg, 0.693 mmol) and acetic acid (0.20 ml, 3.5 mmol, 5.0 equiv) in CH_2Cl_2 (2.5 ml) at room temperature was added bromine (36.0 μl , 0.70 mmol, 1.0 equiv). After stirring for 30 min, the reaction mixture was poured into saturated aqueous Na_2SO_3 and extracted with CH_2Cl_2 , and the organic layer was sequentially washed with saturated aqueous NaHCO_3 and saturated aqueous NaCl , dried over anhydrous MgSO_4 , and concentrated under reduced pressure. The crude product was purified by flash column chromatography (20% EtOAc in *n*-hexane) to afford the bromide (240 mg, 0.672 mmol, 97%) as a white solid. IR (neat film) 3503, 1569, 1482, 1373, 1204, 1175, 1090, 1013, 961, 870, 815 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.78 (d, J = 8.5 Hz, 2H), 7.38 (d, J = 8.5 Hz, 2H), 7.14 (d, J = 2 Hz, 1H), 6.75 (d, J = 2 Hz, 1H), 5.97 (s, 1H), 2.49 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 146.5, 146.0, 137.0, 132.3, 130.9, 130.1, 129.6, 128.6, 123.3, 110.8, 21.8, 15.8; HRMS (FAB $^+$) m/z : Calcd. for $\text{C}_{14}\text{H}_{14}\text{BrO}_4\text{S}$ ($\text{M}+\text{H}$) $^+$ 356.9796, found 356.9792.

Methyl Ether

To a mixture of the bromide (143 mg, 0.401 mmol) and K_2CO_3 (275 mg, 1.99 mmol, 5.0 equiv) in acetone (2.0 ml) was added iodomethane (75.0 μl , 1.20 mmol, 3.0 equiv), and the resulting slurry was heated at reflux for 1 h. After cooling, the mixture was diluted with Et_2O , filtered through a pad of Celite, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (20% Et_2O in *n*-hexane) to afford the methyl ether (142 mg, 0.385 mmol, 96%) as a colorless oil. IR (neat film) 1596, 1479, 1404, 1377, 1273, 1221, 1189, 1178, 1093, 1020, 969, 860, 814 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.79 (d, J = 8.3 Hz, 2H), 7.34 (d, J = 8.3 Hz, 2H), 7.20 (d, J = 2 Hz, 1H), 7.09 (d, J = 2 Hz, 1H), 3.69 (s, 3H), 2.47 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 150.1, 145.5, 142.7, 134.9, 132.7, 132.2, 129.7, 128.2, 124.3, 115.1, 60.6, 21.7, 15.8; HRMS (FAB $^+$) m/z : Calcd. for $\text{C}_{15}\text{H}_{15}\text{BrO}_4\text{S}$ (M^+) 369.9874, found 369.9835.

Phenol

To a solution of the methyl ether (98.9 mg, 0.267 mmol) in EtOH (1.5 ml) was added 2 M aqueous NaOH (0.20 ml, 0.40 mmol, 1.5 equiv), and the mixture was heated at reflux for 30 min. After cooling, the reaction mixture was poured into 10% aqueous citric acid and extracted with Et_2O . The ethereal layer was washed with saturated aqueous NaCl, dried over

anhydrous MgSO_4 , and concentrated under reduced pressure. The residue was purified by flash column chromatography (20% Et_2O in *n*-hexane) to afford the phenol (56.0 mg, 0.258 mmol, 97%) as a colorless oil: IR (neat film) 3336, 1717, 1457, 1367, 1249, 1160, 1065, 1003 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.96 (d, $J = 2$ Hz, 1H), 6.85 (d, $J = 2$ Hz, 1H), 5.67 (s, 1H), 3.77 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 149.6, 144.6, 132.5, 125.2, 116.8, 116.5, 60.7, 15.6; HRMS (FAB $^+$) m/z : Calcd. for $\text{C}_8\text{H}_9\text{BrO}_2$ (M^+) 215.9786, found 215.9809.

MOM Ether 10

To a mixture of the phenol (116 mg, 0.532 mmol) and *i*-Pr₂NEt (0.186 ml, 1.07 mmol, 2.0 equiv) in CH₂Cl₂ (1.5 ml) at 0 °C was added chloromethylmethyl ether (60 μ l, 0.80 mmol, 1.5 equiv), and the reaction mixture was allowed to warm to room temperature, poured into 10% aqueous citric acid, and extracted with Et₂O. The ethereal layer was washed with saturated aqueous NaCl, dried over anhydrous MgSO₄, and concentrated under reduced pressure. The residue was purified by flash column chromatography (20% EtOAc in *n*-hexane) to afford **10** (136 mg, 0.521 mmol, 97%) as a colorless oil. IR (neat film) 1592, 1480, 1423, 1394, 1269, 1221, 1155, 1095, 1048, 1007 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.12 (s, 1H), 6.95 (s, 1H), 5.16 (s, 2H), 3.77 (s, 3H), 3.49 (s, 3H), 2.21 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 150.7, 147.2, 133.8, 126.8, 117.4, 115.8, 95.1, 60.1, 56.2, 15.7; HRMS (FAB⁺) *m/z*: Calcd. for C₁₀H₁₃BrO₃ (M⁺) 260.0048, found 260.0079.

Benzaldehyde

To a solution of **10** (114 g, 437 mmol) in THF (900 ml) at -78 °C was added *n*-BuLi (2.46 M solution in *n*-hexane, 270 ml, 664 mmol, 1.5 equiv), and to the resultant mixture was slowly added DMF (170 ml, 2.20 mol, 5.0 equiv), maintaining the internal temperature below -60 °C. The reaction mixture was allowed to warm to room temperature, quenched with H₂O, and concentrated under reduced pressure. The resulting residue was diluted with Et₂O, and sequentially washed with saturated aqueous NaHCO₃ and saturated aqueous NaCl. The ethereal layer was dried over anhydrous MgSO₄ and concentrated under reduced pressure. The crude product was purified by flash column chromatography (30% Et₂O in *n*-hexane) to afford the benzaldehyde (73.0 g, 347 mmol, 79%) as a colorless oil. IR (neat film) 1699, 1585, 1488, 1451, 1382, 1299, 1235, 1155, 1133, 1099, 1051, 1003, 928, 863 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.83 (s, 1H), 7.49 (s, 1H), 7.36 (s, 1H), 5.25 (s, 2H), 3.90 (s, 3H), 3.51 (s, 3H), 2.31 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 191.2, 153.5, 150.5, 132.8, 132.1, 126.9, 114.2, 95.0, 60.3, 56.3, 16.0; HRMS (FAB⁺) *m/z*: Calcd. for C₁₁H₁₄O₄ (M⁺) 210.0892, found 210.0870.

Iodobenzaldehyde

To a mixture of the benzaldehyde (331 mg, 1.57 mmol) and trimethyl orthoformate (1.0 ml, 9.14 mmol, 5.8 equiv) in MeOH (5.0 ml) was added CSA (20.2 mg, 0.09 mmol, 5.5 mol%), and the resulting mixture was stirred at room temperature for 1 h. To the reaction mixture was added K_2CO_3 (103 mg, 0.75 mmol, 0.47 equiv) and concentrated to a small volume. The residue was dissolved in Et_2O and passed through a pad of basic alumina, and the ethereal solution was concentrated to afford the dimethylacetal (381mg, 1.49 mmol, 94%) as a colorless oil, which was used for the next reaction without further purification. To a solution of the dimethyl acetal (381 mg, 1.49 mmol) in Et_2O (4.0 ml) at 0 °C was added *n*-BuLi (2.46 M solution in *n*-hexane, 0.95 ml, 2.34 mmol, 1.57 equiv), and the resulting mixture was allowed to warm to room temperature. After cooling to 0 °C, to the reaction mixture was added a solution of I_2 (648 mg, 2.55 mmol, 1.7 equiv) in Et_2O (3.0 ml), and the reaction was quenched with H_2O , and partitioned between $EtOAc$ and saturated aqueous Na_2SO_3 . The organic layer was washed with saturated aqueous $NaCl$, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The resulting crude yellow syrup was dissolved in THF (5.0 ml), and to the solution at room temperature was added concentrated HCl solution (2.0 ml). After stirring for 15 min, the reaction mixture was neutralized with saturated aqueous $NaHCO_3$ and extracted with $EtOAc$. The organic phase was washed with saturated aqueous $NaCl$, dried over anhydrous $MgSO_4$, and concentrated. The resulting crude product was dissolved in CH_2Cl_2 and filtered through a pad of silica gel, and the filtrate was concentrated, and triturated with *n*-hexane to afford the iodobenzaldehyde (314 mg, 1.07 mmol, 72% in 2 steps) as a yellow solid. IR (neat film) 3389, 1670, 1583, 1464, 1412, 1299, 1247, 1127, 997 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 10.0 (s, 1H), 7.37 (s, 1H), 6.43 (bs, 1H), 3.89 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.9, 149.9, 149.2, 131.3, 130.9, 125.3, 125.3, 60.8, 15.8; HRMS (FAB $^+$) m/z : Calcd. for $C_9H_9IO_3$ (M^+) 291.9596, found 291.9583.

Benzyl Ether 11

To a mixture of the iodobenzaldehyde (325 mg, 1.11 mmol) and K_2CO_3 (465 mg, 3.37 mmol, 3.07 equiv) in CH_3CN (3.0 ml) was added benzyl bromide (140 μ l, 1.18 mmol, 1.05 equiv), and the resulting mixture was heated at reflux for 40 min. The reaction mixture was diluted with CH_2Cl_2 , filtered through a pad of Celite, and concentrated under reduced pressure. The residue was purified by flash column chromatography (50% CH_2Cl_2 in *n*-hexane) to afford **11** (415 mg, 1.09 mmol, 98%) as a yellow solid. IR (neat film) 1684, 1576, 1464, 1303, 1153, 1068, 1005 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 10.0 (s, 1H), 7.60 (d, 8.0 Hz, 2H), 7.59 (s, 1H), 7.30-7.45 (m, 3H), 5.01 (s, 2H), 3.93 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.3, 157.1, 151.3, 136.3, 133.3, 131.3, 128.7, 128.5, 128.4, 128.2, 98.2, 74.9, 60.6, 15.7; HRMS (FAB $^+$) m/z : Calcd. for $C_{16}H_{15}IO_3$ (M^+) 382.0066, found 382.0083.

Dehydroamino Ester 13

To a mixture of **11** (8.30 g, 21.7 mmol) and phosphonate **12** (7.76 g, 26.1 mmol, 1.2 equiv) in CH_2Cl_2 (100 ml) at 10 °C was added *N,N,N',N'*-tetramethylguanidine (4.10 ml, 32.7 mmol, 1.5 equiv), and the mixture was allowed to warm to room temperature and stirred for 24 h. The reaction mixture was sequentially washed with 10% aqueous citric acid and saturated aqueous NaHCO_3 , and the organic layer was dried over anhydrous MgSO_4 , and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (30% EtOAc in *n*-hexane) to afford **13** (11.2 g, 20.2 mmol, 93%) as a yellow solid. Recrystallization of the crude product from EtOAc/*n*-hexane also afforded a pure sample of **13**. IR (neat film) 3336, 1717, 1457, 1367, 1249, 1160, 1065, 1003 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.60 (d, J = 6.8 Hz, 2H), 7.36–7.60 (m, 3H), 7.24 (s, 1H), 7.20 (s, 1H), 5.00 (s, 2H), 3.88 (s, 3H), 3.86 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 165.6, 152.4, 151.6, 151.5, 136.8, 134.2, 132.5, 131.7, 128.7, 128.4, 128.2, 126.8, 125.4, 96.9, 80.9, 74.6, 60.5, 52.7, 28.0, 15.8; HRMS (FA B^+) m/z : Calcd. for $\text{C}_{24}\text{H}_{28}\text{INO}_6$ (M^+) 553.0961, found 553.0982.

Amino Ester 14

A degassed mixture of **13** (5.04 g, 9.10 mmol) and $\text{Rh}[(\text{COD})-(S,S)\text{-Et-DuPHOS}]^+\text{TfO}^-$ (99.0 mg, 0.14 mmol, 1.5 mol%) in EtOAc (30 ml) was placed in a high pressure Parr reactor and sealed under hydrogen (500 psi). After stirring at 50 °C for 22 h, the solution was concentrated under reduced pressure, and the residue was purified by flash column chromatography (50% EtOAc in *n*-hexane) to afford **14** (5.01 g, 9.02 mmol, 99%, 94% ee) as a pale yellow foam. Enantiomeric excess was determined by chiral HPLC (Chiralcel OD column, 97:3 *n*-hexane/2-propanol). $[\alpha]_D^{27} +7.4^\circ$ (c = 1.1, CHCl_3); IR (neat film) 3374, 1746, 1711, 1510, 1457, 1363, 1162, 1068, 1003 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.60 (d, J = 8.8 Hz, 2H), 7.32–7.45 (m, 3H), 6.85 (s, 1H), 5.06 (d, J = 8.8 Hz, 1H), 4.99 (s, 1H), 4.62 (ddd, J = 9.2, 8.8, 5.6 Hz, 1H), 3.82 (s, 3H), 3.72 (s, 3H), 3.28 (dd, J = 14.4, 5.6 Hz, 1H), 3.09 (dd, J = 14.4, 9.2 Hz, 1H), 2.23 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 172.4, 154.9, 151.7, 150.4, 136.9, 135.4, 132.3, 128.6, 128.4, 128.1, 127.8, 97.0, 79.8, 74.5, 60.4, 53.8, 52.3, 42.7, 28.2, 15.6; HRMS (FAB $^+$) m/z : Calcd. for $\text{C}_{24}\text{H}_{31}\text{INO}_6$ ($\text{M}+\text{H}^+$) 556.1196, found

556.1222.

Carboxylic Acid **15**

To a solution of **14** (5.01 g, 9.02 mmol) in a mixture of MeOH (40 ml), H₂O (10 ml), and THF (10 ml) at 0 °C was added lithium hydroxide (750 mg, 17.9 mmol, 2.0 equiv), and the mixture was allowed to warm to room temperature. The reaction mixture was diluted with benzene and concentrated under reduced pressure. To the residue was added 10% aqueous citric acid, and the resulting suspension was extracted with EtOAc. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous MgSO₄, and concentrated under reduced pressure to afford **15** (4.90 g, 9.05 mmol, quant) as a white foam. $[\alpha]_D^{27} -14^\circ$ (c = 5.0, CHCl₃). IR (neat film) 3309, 2560, 1716, 1497, 1471, 1404, 1368, 1307, 1243, 1163, 1063, 1008, 907, 845, 804 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.61 (br, 2H), 7.36-7.44 (br, 3H), 6.90 (s, 1H), 5.00 (br, 2H), 4.63 (br, 1H), 3.83 (s, 3H), 3.43 (br, 1H), 2.94-3.20 (br, 1H), 2.25 (s, 3H), 1.10-1.40 (br, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 176.2, 175.4, 156.7, 155.2, 151.4, 150.4, 150.3, 136.9, 135.8, 135.3, 132.3, 132.2, 128.7, 128.6, 128.4, 128.4, 128.1, 127.9, 97.1, 96.7, 81.1, 80.1, 77.2, 74.5, 60.4, 60.3, 54.1, 53.8, 53.7, 44.6, 42.3, 42.2, 42.2, 28.2, 27.9, 15.6; HRMS (FAB⁺) m/z: Calcd. for C₂₃H₂₉INO₆ (M+H)⁺ 542.1039, found 542.1083.

Amide **18** (epimeric mixture)

To a mixture of amine **9** (9.63 g, 19.5 mmol), carboxylic acid **15** (10.57 g, 19.5 mmol, 1.0 equiv), and *p*-methoxy isocyanide (PMP-NC) (**16**) (3.90 g, 29.3 mmol, 1.5 equiv) in MeOH (200 ml) at room temperature was added acetaldehyde (**17**) (22 ml, 0.39 mol, 20 equiv), and the resulting solution was heated at reflux for 1 h. The reaction mixture was concentrated under reduced pressure, and the resulting orange syrup was purified by flash column chromatography (40% EtOAc in *n*-hexane) to afford **18** (21.02 g, 17.6 mmol, 90%) as a yellow solid. IR (neat film) 3315, 1699, 1687, 1511, 1463, 1428, 1367, 1245, 1159, 1112, 1062, 826 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.60-9.20 (m, 1H), 7.25-7.75 (m, 17H), 6.50-7.20 (m, 4H), 4.80-5.85 (m, 9H), 3.90-4.80 (m, 3H), 3.60-3.85 (m, 6H), 3.40-3.50 (m, 3H),

2.90-3.50 (m, 2H), 1.85-2.25 (m, 6H), 0.75-1.50 (m, 21H); ^{13}C NMR (100 MHz, CDCl_3) δ 173.4, 172.0, 171.3, 170.1, 168.7, 167.9, 156.2, 156.1, 155.9, 155.6, 155.3, 154.3, 151.5, 151.4, 151.3, 151.0, 150.9, 150.8, 150.5, 150.1, 150.0, 146.9, 146.5, 139.8, 139.7, 136.8, 136.7, 136.6, 136.5, 135.6, 135.5, 135.4, 135.3, 135.2, 132.6, 132.5, 132.4, 132.2, 132.1, 132.0, 131.6, 131.1, 131.0, 129.9, 129.7, 129.6, 129.3, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.7, 127.5, 127.4, 127.3, 123.0, 121.7, 121.5, 120.5, 113.7, 113.5, 113.4, 113.3, 113.1, 110.9, 106.2, 106.0, 100.9, 100.8, 100.6, 97.5, 96.7, 96.6, 96.2, 95.8, 95.5, 95.3, 80.6, 80.5, 80.3, 79.3, 79.0, 74.4, 74.3, 71.5, 70.4, 62.6, 62.5, 60.2, 60.1, 59.7, 57.2, 56.2, 56.1, 55.9, 55.1, 54.5, 54.4, 51.5, 51.3, 42.9, 41.8, 41.1, 41.1, 28.1, 28.0, 27.9, 27.8, 27.1, 27.0, 26.9, 26.4, 19.1, 19.0, 18.9, 17.8, 17.1, 15.4, 15.3, 15.2, 15.1, 14.9, 14.8, 8.8, 8.7, 8.5; LRMS (FAB $^+$) m/z: 1193.4 (M^+).

Alcohol (epimeric mixture)

To a solution of **18** (21.02 g, 17.6 mmol) in THF (200 ml) at room temperature was added TBAF (1M solution in THF, 20 ml, 020 mmol, 1.1 equiv), and the mixture was stirred for 30 min. The reaction mixture was diluted with a mixture of EtOAc and *n*-hexane and concentrated under reduced pressure. The residue was purified by flash column chromatography (EtOAc) to afford the alcohol (14.90 g, 15.6 mmol, 89%) as a yellow solid. IR (neat film) 3309, 1699, 1694, 1652, 1511, 1435, 1367, 1304, 1245, 1170, 1112, 1060, 1008 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.84 & 7.91 (br, 1H), 7.31-7.63 (m, 5H), 6.81-7.10 (m, 3H), 6.46-6.74 (m, 2H), 5.81-5.97 (m, 2H), 5.59-5.73 (m, 1H), 5.30-5.46 (m, 1H), 4.78-5.30 (m, 6H), 4.33-4.52 (m, 1H), 3.90-4.13 (m, 2H), 3.70-3.88 (m, 3H), 3.79 (s, 3H), 2.78-3.67 (m, 3H), 3.47 & 3.41 (s, 3H), 2.05-2.37 (m, 6H), 1.09-1.47 (m, 12H); ^{13}C NMR (100 MHz, CDCl_3) δ 172.5, 170.5, 156.3, 156.2, 156.1, 154.6, 15.5, 151.4, 151.2, 151.1, 151.0, 150.6, 150.5, 151.2, 146.8, 140.2, 137.1, 137.0, 136.9, 135.9, 132.3, 131.8, 131.0, 130.6, 129.2, 128.7, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 122.2, 122.1, 122.0, 121.9, 121.8, 121.7, 121.6, 121.3, 116.7, 114.2, 114.1, 114.0, 113.9, 113.8, 113.7, 113.6, 113.4, 111.2, 105.9, 105.7, 101.2, 100.9, 97.2, 95.7, 95.5, 95.2, 79.9, 79.7, 79.4, 78.9, 77.6, 74.6, 74.5, 74.4, 68.5, 60.5, 60.4, 60.3, 58.1, 56.4, 56.3, 56.2, 56.0, 55.3, 54.0, 53.7, 50.4, 43.2, 42.3, 28.3, 28.1, 28.0, 21.0, 20.2, 15.6, 15.5, 15.4, 14.9, 14.0, 13.9, 9.0, 8.9, 8.7; LRMS (FAB $^+$) m/z : 955.4 (M^+).

Acetate (epimeric mixture)

The alcohol (14.90 g, 15.6 mmol) was dissolved in a mixture of acetic anhydride (30 ml) and pyridine (60 ml), and to the solution at room temperature was added DMAP (97 mg, 0.79 mmol, 0.05 equiv). The reaction mixture was stirred at 50 °C for 30 min, and concentrated under reduced pressure. The residue was diluted with toluene and concentrated under reduced pressure. The crude product was purified by flash column chromatography (60% EtOAc in *n*-hexane) to afford the acetate (14.54 g, 14.6 mmol, 93%) as a yellow solid. IR (neat film) 3318, 1743, 1700, 1511, 1436, 1368, 1304, 1245, 1170, 1112, 1060, 830 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.90-9.30 (m, 1H), 7.55 (d, $J = 6.8$ Hz, 2H), 7.20-7.50 (m, 5H), 6.30-7.20 (m, 2H), 6.80 (d, $J = 6.8$ Hz, 2H), 5.84-5.88 (br, 2H), 5.60-5.80 (m, 2H), 5.20-5.45 (m, 2H), 5.00-5.20 (m, 2H), 4.93-4.97 (m, 2H), 4.70-4.90 (m, 1H), 4.40-4.70 (m, 1H), 3.65-3.80 (m, 6H), 3.35-3.50 (m, 3H), 2.90-3.35 (m, 1H), 1.80-2.25 (m, 9H), 1.10-1.55 (m, 12H); ^{13}C NMR (100 MHz, CDCl_3) δ 173.6, 173.2, 172.7, 172.0, 170.1, 170.0, 169.7, 169.5, 169.5, 169.4, 168.2, 168.2, 156.4, 156.1, 155.8, 155.2, 154.3, 151.5, 151.3, 151.2, 151.2, 151.1, 150.6, 150.3, 147.1, 146.8, 146.6, 140.0, 139.8, 139.3, 136.8, 136.7, 136.7, 136.7, 136.5, 135.0, 134.9, 134.6, 132.5, 132.0, 131.1, 131.0, 130.1, 128.8, 128.5, 128.4, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 121.8, 121.8, 121.8, 121.6, 121.4, 121.2, 120.6, 113.9, 113.9, 113.8, 113.5, 113.1, 112.6, 112.1, 111.7, 111.3, 105.9, 105.7, 105.3, 101.1, 101.0, 100.7, 96.8, 96.5, 95.9, 95.4, 95.4, 95.1, 79.6, 79.1, 74.4, 70.6, 62.0, 60.3, 60.2, 57.3, 56.5, 56.2, 56.0, 55.8, 55.2, 50.6, 50.1, 43.5, 28.1, 28.0, 27.9, 27.8, 20.9, 20.7, 17.6, 15.3, 14.8, 8.8; LRMS (FAB^+) m/z : 997.3 (M^+).

Diketopiperazine **19** (epimeric mixture)

To a mixture of the acetate (14.5 g, 14.5 mmol) and anisole (79 ml, 0.73 mol, 50 equiv) in CH₂Cl₂ (290 ml) at 0 °C was added TFA (58 ml, 0.75 mol, 52 equiv), and the mixture was allowed to warm to room temperature and stirred for 9 h. The resulting red solution was poured into water and extracted with EtOAc. The organic phase was separated, and sequentially washed with saturated aqueous NaHCO₃ and saturated aqueous NaCl. The solution was dried over anhydrous MgSO₄, concentrated under reduced pressure to a volume of about 300 ml, and heated at reflux for 1 h. The reaction mixture was concentrated under reduced pressure, and the resultant residue was purified by flash column chromatography (70% EtOAc in *n*-hexane) to afford **19** (19.7 g, 27.0 mmol, 87% in 2 steps) as a pale brown amorphous. **19a** (minor isomer) IR (neat film) 3345, 1752, 1683, 1652, 1456, 1306, 1232, 1093, 1037, 1007 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.56 (d, *J* = 8.2, 2H), 7.38-7.41 (m, 3H), 6.85 (s, 1H), 6.23 (s, 1H), 6.20 (br, 1H), 5.89 (s, 1H), 5.86 (s, 1H), 5.70 (dd, *J* = 8.4, 7.2 Hz, 1H), 4.95 (s, 2H), 4.69 (dd, *J* = 11.0, 7.2 Hz, 1H), 4.57 (dd, *J* = 11.0, 8.4 Hz, 1H), 4.29 (dd, *J* = 9.3, 3.9 Hz, 1H), 3.88 (q, *J* = 7.1 Hz, 1H), 3.80 (s, 3H), 3.46 (dd, *J* = 13.7, 3.9 Hz, 1H), 3.21 (dd, *J* = 13.7, 9.3 Hz, 1H), 2.21 (s, 3H), 2.09 (s, 3H), 2.05 (s, 3H), 1.45 (d, *J* = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 170.7, 168.7, 166.5, 151.8, 15.0, 151.0, 147.0, 139.0, 136.7, 134.5, 133.2, 128.6, 128.4, 128.2, 128.1, 111.8, 109.1, 106.3, 100.9, 97.3, 74.6, 62.7, 60.4, 57.0, 55.0, 44.9, 21.2, 20.8, 15.5, 8.7; LRMS (FAB⁺) *m/z*: 731.3 (M+H)⁺. **19b** (major isomer) IR (neat film) 3374, 1751, 1683, 1651, 1430, 1314, 1265, 1233, 1094, 1040, 1006 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.58 (d, *J* = 8.3 Hz, 2H), 7.36-7.43 (m, 3H), 6.86 (s, 1H), 6.40 (s, 1H), 5.93 (s, 1H), 5.92 (s, 1H), 5.62 (dd, *J* = 8.9, 5.8 Hz, 1H), 5.50 (s, 1H), 5.15 (br, 1H), 5.03 (d, *J* = 6.8 Hz, 1H), 5.01 (d, *J* = 6.8 Hz, 1H), 4.76 (dd, *J* = 11.7, 8.9 Hz, 1H), 4.60 (dd, *J* = 11.7, 5.8 Hz, 1H), 4.34 (dd, *J* = 10.7, 3.9 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 1H), 3.84 (s, 3H), 3.81 (dd, *J* = 14.2, 3.9 Hz, 1H), 2.84 (dd, *J* = 14.2, 10.7 Hz, 1H), 2.25 (s, 3H), 2.13 (s, 3H), 2.07 (s, 3H), 1.15 (d, *J* = 7.1 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 170.7, 170.3, 166.9, 152.2, 151.0, 150.8, 146.8, 138.9, 136.6, 134.1, 133.4, 128.6, 128.4, 128.3, 128.2, 112.5, 108.9, 106.5, 101.0, 96.2, 74.6, 62.0, 60.4, 54.9, 53.3, 52.5, 41.5, 20.8, 18.0, 15.6, 8.7; LRMS (FAB⁺) *m/z*: 731.4 (M+H)⁺.

Mesylate (epimeric mixture)

To a mixture of **154** (19.3 g, 26.4 mmol) and TEA (11.8 ml, 84.6 mmol, 3.2 equiv) in CH_2Cl_2 (100 ml) at 0 °C was slowly added methanesulfonyl chloride (2.60 ml, 33.8 mmol, 1.3 equiv). After stirring at 0 °C for 1h, the reaction mixture was diluted with EtOAc (400 ml), and sequentially washed with 6% aqueous NaCl (230 ml), saturated aqueous NaHCO_3 , and saturated aqueous NaCl. The organic phase was dried over anhydrous MgSO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (70% EtOAc in *n*-hexane) to afford the mesylate (19.4 g, 24.0 mmol, 91%) as a pale yellow amorphous. minor isomer: IR (neat film) 1743, 1685, 1424, 1367, 1307, 1230, 1172, 1126, 1065, 1006, 970 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.57 (d, J = 8.0 Hz, 2H), 7.32-7.41 (m, 3H), 6.87 (s, 1H), 6.83 (s, 1H), 6.02 (d, J = 2.0 Hz, 1H), 5.99 (s, 2H), 5.49 (dd, J = 8.0, 8.0 Hz, 1H), 4.99 (d, J = 10.8 Hz, 1H), 4.96 (d, J = 10.8 Hz, 1H), 4.67 (dd, J = 12.0, 8.0 Hz, 1H), 4.62 (dd, J = 12.0, 8.0 Hz, 1H), 4.34 (ddd, J = 8.8, 4.0, 2.0 Hz, 1H), 3.81 (s, 3H), 3.80 (q, J = 6.8 Hz, 1H), 3.49 (dd, J = 14.0, 4.0 Hz, 1H), 3.18 (s, 3H), 3.17 (dd, J = 14.0, 8.8 Hz, 1H), 2.21 (s, 3H), 2.20 (s, 3H), 2.05 (s, 3H), 1.38 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.5, 168.1, 165.6, 151.9, 151.0, 147.1, 144.0, 142.4, 136.6, 134.4, 133.1, 128.6, 128.4, 128.3, 128.2, 115.1, 113.3, 102.1, 97.1, 74.6, 62.0, 60.4, 56.7, 55.2, 54.3, 45.0, 37.9, 21.1, 20.7, 15.5, 9.8; HRMS (FAB $^+$) m/z : Calcd. for $\text{C}_{32}\text{H}_{34}\text{IN}_2\text{O}_9\text{S}$ (M–AcO) $^+$ 749.1029, found 749.1046. major isomer: IR (neat film) 1743, 1688, 1424, 1367, 1312, 1229, 1173, 1132, 1065, 1006, 970 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.54 (d, J = 6.8 Hz, 2H), 7.29-7.39 (m, 3H), 6.91 (s, 1H), 6.84 (s, 1H), 6.00 (s, 2H), 5.64 (s, 1H), 5.42 (dd, J = 8.0, 6.0 Hz, 1H), 4.99 (d, J = 7.2 Hz, 1H), 4.96 (d, J = 7.2 Hz, 1H), 4.75 (dd, J = 11.6, 8.0 Hz, 1H), 4.66 (dd, J = 11.6, 6.0 Hz, 1H), 4.35 (dd, J = 10.8, 4.0 Hz, 1H), 4.11 (q, J = 8.0 Hz, 1H), 3.80 (s, 3H), 3.68 (dd, J = 13.8, 4.0 Hz, 1H), 3.19 (s, 3H), 2.83 (dd, J = 13.8, 10.8 Hz, 1H), 2.21 (s, 3H), 2.20 (s, 3H), 2.04 (s, 3H), 1.21 (d, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.3, 169.5, 166.2, 151.9, 150.8, 146.8, 144.0, 142.3, 136.5, 134.1, 133.1, 128.4, 128.2, 128.0, 115.1, 115.1, 113.9, 102.0, 96.1, 74.4, 61.5, 60.2, 56.2, 53.2, 52.3, 41.2, 37.7, 20.6, 17.8, 15.5, 14.0, 9.8; HRMS (FAB $^+$) m/z : Calcd. for $\text{C}_{32}\text{H}_{34}\text{IN}_2\text{O}_9\text{S}$ (M–AcO) $^+$ 749.1029, found 749.0997.

Imide (epimeric mixture)

To a mixture of the mesylate (3.00 g, 3.71 mmol) and $(\text{Boc})_2\text{O}$ (1.36 g, 6.22 mmol, 1.7 equiv) in CH_3CN (15 ml) was added DMAP (45 mg, 0.37 mmol, 0.1 equiv), and the solution was stirred at room temperature for 6.5 h. The reaction mixture was diluted with EtOAc, and sequentially washed with 0.5 M aqueous HCl, saturated aqueous NaHCO_3 , and saturated aqueous NaCl. The organic layer was dried over anhydrous MgSO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (50% EtOAc in

n-hexane) to afford the imide (3.27 g, 3.60 mmol, 97%) as a pale yellow amorphous. minor isomer: IR (neat film) 1775, 1733, 1670, 1455, 1429, 1368, 1308, 1285, 1244, 1172, 1148, 1066, 1007, 970, 937 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.58 (d, J = 6.8 Hz, 2H), 7.33-7.41 (m, 3H), 6.87 (s, 1H), 6.82 (s, 1H), 5.97 (s, 1H), 5.96 (s, 1H), 5.56 (dd, J = 8.0, 8.0 Hz, 1H), 5.14 (dd, J = 8.0, 4.8 Hz, 1H), 4.95 (d, J = 10.0 Hz, 1H), 4.91 (d, J = 10.0 Hz, 1H), 4.63 (dd, J = 10.8, 8.0 Hz, 1H), 4.56 (dd, J = 10.8, 8.0 Hz, 1H), 3.98 (q, J = 8.0, 1H), 3.78 (s, 3H), 3.53 (dd, J = 14.8, 4.8 Hz, 1H), 3.23 (dd, J = 14.8, 8.0 Hz, 1H), 3.16 (s, 3H), 2.20 (s, 3H), 2.19 (s, 3H), 2.03 (s, 3H), 1.45 (d, J = 8.0 Hz, 3H), 1.34 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.5, 167.8, 166.0, 151.8, 150.9, 149.5, 147.3, 144.1, 142.5, 136.8, 134.9, 132.9, 128.7, 128.4, 128.4, 128.2, 115.3, 115.1, 113.1, 102.1, 97.5, 84.4, 74.6, 62.0, 60.4, 59.5, 56.5, 56.5, 53.5, 44.6, 38.0, 27.8, 20.8, 20.8, 15.5, 9.9; LRMS (FAB $^+$) m/z : 909.1 (M+H) $^+$. major isomer: IR (film) 1777, 1737, 1672, 1468, 1455, 1424, 1368, 1308, 1285, 1245, 1172, 1150, 1064, 1008, 970, 934 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.58 (d, J = 6.8 Hz, 2H), 7.32-7.41 (m, 3H), 7.04 (s, 1H), 6.73 (s, 1H), 6.02 (s, 1H), 5.99 (s, 1H), 5.08 (dd, J = 10.0, 4.0 Hz, 1H), 4.91 (s, 2H), 4.80-4.90 (m, 3H), 4.30 (q, J = 6.8 Hz, 1H), 3.77 (s, 3H), 3.28 (dd, J = 13.6, 4.8 Hz, 1H), 3.19 (s, 3H), 3.01 (dd, J = 8.8, 4.8 Hz, 1H), 2.19 (s, 3H), 2.13 (s, 3H), 2.02 (s, 3H), 1.69 (d, J = 6.8 Hz, 3H), 1.29 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.4, 167.7, 167.5, 151.5, 150.6, 149.4, 146.6, 143.5, 142.3, 136.7, 134.1, 132.5, 128.5, 128.3, 128.1, 128.1, 115.1, 115.1, 114.8, 101.8, 97.3, 83.8, 74.4, 62.4, 60.3, 58.7, 56.8, 52.7, 42.5, 37.7, 27.5, 20.7, 16.7, 15.3, 9.8; LRMS (FAB $^+$) m/z : 909.2 (M+H) $^+$.

Enamide 20

To a solution of the imide (4.11 g, 4.52 mmol) in a mixture of EtOH (100 ml) and CH_2Cl_2 (10 ml) at $0\text{ }^\circ\text{C}$ was added H_2SO_4 (3.0 M solution in EtOH, 3.0 ml, 9.0 mmol, 2.0 equiv), and to the mixture was added NaBH_4 (867 mg, 22.9 mmol, 5.1 equiv) portionwise. Excess reagent was quenched with acetone (10 ml), and the mixture was neutralized with saturated aqueous NaHCO_3 (50 ml), diluted with EtOAc, and filtered through a pad of Celite. The filtrate was concentrated under reduced pressure, and the residue was partitioned between EtOAc and saturated aqueous NaHCO_3 . The organic layer was dried over MgSO_4 and concentrated under reduced pressure to give the crude aminal (4.19 g), which was used in the next step without further purification. To a solution of the aminal in toluene (40 ml) were added CSA (1.07 g, 4.61 mmol, 1.0 equiv) and quinoline (0.82 ml, 7.0 mmol, 1.5 equiv), and the resulting mixture was heated at reflux for 3 h. The reaction mixture was diluted with EtOAc, and sequentially washed with 1M aqueous HCl, saturated aqueous NaHCO_3 , and saturated aqueous NaCl. The

organic layer was dried over MgSO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (50% EtOAc in *n*-hexane) to afford **20** (3.54 g, 3.97 mmol, 88% in 2 steps) as a yellow foam. $[\alpha]_D^{27} +2.9^\circ$ ($c = 3.0$, CHCl_3). IR (neat film) 1742, 1692, 1463, 1418, 1362, 1336, 1240, 1172, 1065, 1005, 962, 890, 805 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.60 (d, $J = 6.8$ Hz, 2H), 7.36-7.44 (m, 3H), 6.87 (br, 1H), 6.69 (s, 1H), 6.21 (s, 1H), 6.01 (s, 1H), 5.96 (s, 1H), 4.97 (s, 2H), 4.93 (br, 1H), 4.85 (br, 2H), 3.80 (s, 3H), 3.19 (s, 3H), 2.91 (br, 2H), 2.22 (s, 3H), 2.20 (s, 3H), 2.05 (s, 3H), 1.32 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.3, 151.5, 151.3, 151.1, 150.9, 150.1, 150.1, 150.1, 146.7, 143.1, 143.0, 142.2, 142.1, 136.7, 136.6, 135.8, 134.7, 134.7, 132.0, 131.5, 129.2, 129.1, 128.4, 128.4, 128.2, 127.9, 127.9, 127.9, 127.7, 127.5, 126.2, 121.3, 120.8, 115.4, 115.2, 114.0, 113.9, 101.7, 97.0, 96.5, 80.8, 80.7, 77.3, 77.2, 77.0, 76.7, 74.2, 62.4, 62.3, 60.1, 60.0, 57.2, 55.7, 39.1, 38.8, 37.4, 37.4, 27.8, 27.5, 20.4, 16.3, 15.2, 9.6; HRMS (FAB $^+$) m/z : Calcd. for $\text{C}_{39}\text{H}_{45}\text{N}_2\text{O}_{12}\text{S}$ (M^+) 892.1738, found 892.1750.

Tricycle 21

To a degassed mixture of **20** (6.27 g, 7.02 mmol), tris(*o*-tolyl)phosphine (428 mg, 1.41 mmol, 0.2 equiv), and TEA (4.0 ml, 29 mmol, 4.1 equiv) in CH_3CN (50 ml) under argon was added tris(dibenzylideneacetone)dipalladium(0) ($\text{Pd}_2(\text{dba})_3$) (325 mg, 0.36 mmol, 5 mol%), and the solution was heated at reflux for 2 h. The reaction mixture was diluted with EtOAc and concentrated under reduced pressure. The residue was dissolved in EtOAc and sequentially washed with 10% aqueous citric acid, saturated aqueous NaHCO_3 , and saturated aqueous NaCl . The organic phase was dried over anhydrous MgSO_4 and concentrated under reduced pressure. The crude product was purified by flash column chromatography (50% EtOAc in *n*-hexane) to afford **21** (4.44 g, 5.81 mmol, 83%) as a yellow solid. $[\alpha]_D^{27} +38^\circ$ ($c = 1.9$, CHCl_3); IR (neat film) 1743, 1699, 1636, 1424, 1367, 1309, 1233, 1173, 1113, 1065, 861, 808 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.26-7.70 (m, 5H), 6.60-6.75 (br, 1H), 6.30-6.50 (br, 1H), 5.65-6.20 (br, 3H), 4.20-5.30 (br, 8H), 3.80 (s, 3H), 3.09 (s, 3H), 2.90-3.30 (br, 2H), 2.24 (s, 3H), 2.15 (s, 3H), 1.68 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.4, 149.7, 148.8, 147.0, 142.9, 142.6, 137.6, 132.3, 128.5, 127.8, 125.7, 115.2, 115.2, 114.0, 113.2, 113.1, 113.0, 113.0, 112.9, 101.8, 96.3, 95.4, 81.1, 74.1, 73.7, 60.3, 60.2, 59.9, 54.0, 54.0, 52.6, 50.5, 50.5, 37.5, 31.9, 28.3, 20.1, 15.7, 9.9; HRMS (FAB $^+$) m/z : Calcd. for $\text{C}_{39}\text{H}_{45}\text{N}_2\text{O}_{12}\text{S}$ ($\text{M}+\text{H}^+$) 765.2693, found 765.2653.

Acetate

To a solution of **21** (120 mg, 0.157 mmol) in MeOH (1.5 ml) was added 2 M aqueous NaOH (0.5 ml, 1 mmol, 6 equiv), and the resulting mixture was heated at reflux for 2.5 h. The reaction mixture was diluted with a mixture of Et₂O and H₂O, acidified with 1 M aqueous HCl, and extracted with EtOAc. The organic phase was sequentially washed with saturated aqueous NaHCO₃ and saturated aqueous NaCl, dried over anhydrous Na₂SO₄, and concentrated under reduced pressure. To a solution of the crude product in CH₂Cl₂ (1 ml) at room temperature were added pyridine (0.26 ml, 3.2 mmol, 20 equiv), acetic anhydride (0.15 ml, 1.6 mmol, 10 equiv), and DMAP (1 mg, 0.008 mmol). The reaction mixture was concentrated under reduced pressure, and the residue was purified by flash column chromatography (30% EtOAc in *n*-hexane) to afford the acetate (106 mg, 0.145 mmol, 93% in 2 steps) as a white solid. $[\alpha]_D^{26} +47^\circ$ (*c* = 1.3, CHCl₃); IR (neat film) 1766, 1746, 1699, 1634, 1484, 1427, 1368, 1307, 1208, 1183, 1109, 1081, 937, 913, 862; ¹H NMR (400 MHz, CDCl₃) δ 7.26-7.42 (m, 5H), 6.64 (br, 1H), 6.13 (br, 1H), 5.70-5.95 (br, 3H), 4.15-5.30 (br, 8H), 3.73 (s, 3H), 2.90-3.20 (br, 2H), 2.19 (s, 3H), 2.17 (s, 3H), 1.89 (s, 3H), 1.51 (s, 3H), 1.39 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 170.4, 169.2, 169.1, 149.8, 149.7, 149.7, 148.8, 146.8, 146.8, 146.7, 144.3, 141.8, 140.4, 137.6, 137.6, 137.6, 132.1, 132.1, 128.6, 128.5, 128.0, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.7, 127.6, 127.6, 127.5, 127.5, 127.5, 127.5, 125.7, 125.7, 125.7, 125.7, 115.3, 115.2, 115.2, 115.2, 115.2, 112.6, 112.2, 112.2, 112.2, 112.2, 101.6, 101.5, 81.0, 81.0, 81.0, 74.1, 74.1, 74.1, 73.6, 60.2, 59.6, 54.0, 52.8, 52.7, 52.7, 52.5, 52.5, 50.8, 50.8, 50.7, 50.7, 50.7, 32.0, 28.3, 20.6, 20.6, 20.0, 15.7, 9.3; HRMS (FAB⁺) *m/z*: Calcd. for C₄₀H₄₅N₂O₁₁ (M+H)⁺ 729.3024, found 729.3038.

Enamide

To a solution of the acetate (2.56 g, 3.51 mmol) in CH₂Cl₂ (12 ml) was added TFA (3.0 ml, 39

mmol, 11 equiv), and the resulting mixture was stirred at room temperature for 4 h. The reaction mixture was carefully poured into cold saturated aqueous NaHCO_3 , and extracted with CH_2Cl_2 . The organic layer was concentrated under reduced pressure, and the resulting brown oil was dissolved in a mixture of CH_2Cl_2 (12 ml) and saturated aqueous NaHCO_3 (20 ml). To the two-phase mixture at 0 °C was added 2,2,2-trichloroethyl chloroformate (0.47 ml, 3.5 mmol, 1.0 equiv), and the reaction mixture was vigorously stirred for 10 min. The organic phase was separated, dried over anhydrous MgSO_4 and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (40% EtOAc in *n*-hexane) to afford the enamide (2.08 g, 2.59 mmol, 74% in 2 steps) as a white foam. $[\alpha]_D^{26} +40^\circ$ ($c = 1.1$, CHCl_3); IR (neat film) 1763, 1724, 1684, 1636, 1486, 1429, 1368, 1353, 1298, 1222, 1209, 1184, 1124, 1078, 1031, 913, 863; ^1H NMR (400 MHz, CDCl_3) δ 7.31-7.50 (m, 5H), 6.72 & 6.74 (s, 1H), 6.22 & 6.20 (s, 1H), 6.00 & 5.96 (s, 1H), 5.87 & 5.77 (s, 2H), 4.50-5.25 (m, 9H), 4.37 & 4.29 (s, 1H), 3.79 (s, 3H), 3.10-3.30 (m, 2H), 2.25 (s, 3H), 2.24 (s, 3H), 1.95 (s, 3H), 1.55 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.3, 169.2, 149.8, 144.3, 141.8, 137.4, 132.5, 128.5, 128.5, 127.9, 127.8, 127.6, 125.7, 124.8, 115.0, 112.5, 112.2, 101.5, 95.1, 75.0, 74.0, 73.8, 60.2, 53.9, 53.3, 52.5, 32.2, 31.8, 20.6, 19.9, 15.7, 9.2; HRMS (FAB $^+$) m/z : Calcd. for $\text{C}_{38}\text{H}_{37}\text{Cl}_3\text{N}_2\text{O}_{11}$ (M^+) 802.1463, found 802.1413.

Methoxyalcohol 22

To a solution of the enamide (681 mg, 0.847 mmol) in MeOH (15.0 ml) at 0 °C was added freshly prepared dimethyldioxirane (0.1 M solution in acetone, 15 ml, 1.5 mmol, 2 equiv), and the resulting mixture was stirred at this temperature for 2 h. To the reaction mixture was added anhydrous Na_2SO_4 (10 g), and the resulting slurry was stirred for 10 minutes. To the reaction mixture was added CSA (7.2 mg, 0.03 mmol, 4 mol%) and allowed to warm to room temperature, and the mixture was neutralized with pyridine (25 μl , 0.31 mmol, 0.4 equiv), filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (50% EtOAc in *n*-hexane) to afford **22** (652 mg, 0.765 mmol, 90%) as a yellow foam. $[\alpha]_D^{23} +66^\circ$ ($c = 1.3$, CHCl_3); IR (neat film) 3445, 1722, 1668, 1418, 1369, 1339, 1300, 1228, 1183, 1124, 1097 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.30-7.60 (m, 5H), 6.60-6.80 (br, 2H), 5.78-5.95 (br, 3H), 5.28 (br, 1H), 5.16 (br, 1H), 5.06 (br, 1H), 4.75-4.95 (m, 4H), 4.60-4.75 (m, 2H), 3.82 & 3.76 (s, 3H), 3.65-3.90 (m, 1H), 3.61 & 3.50 (s, 3H), 3.45 (dd, $J = 12.0, 6.0$ Hz, 1H), 3.27 & 3.25 (dd, $J = 16.0, 8.0$ Hz, 1H), 3.13 & 3.12 (d, $J = 16.0$ Hz, 1H), 2.25 (s, 3H), 2.21 (s, 3H), 2.01 (s, 3H), 1.91 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.2, 170.8, 170.3, 170.2, 168.7, 151.7, 151.6, 149.5, 149.4, 148.6, 148.1, 145.9, 145.9,

144.2, 141.8, 141.7, 136.4, 136.2, 133.1, 132.9, 129.3, 129.1, 129.0, 128.6, 128.5, 128.4, 128.2, 128.0, 127.6, 126.6, 126.5, 123.6, 123.3, 116.7, 114.3, 114.2, 112.8, 112.7, 101.3, 101.3, 95.0, 94.8, 93.3, 92.9, 77.2, 76.2, 75.3, 75.2, 74.9, 63.5, 62.8, 62.1, 60.3, 53.2, 52.7, 51.6, 51.2, 51.2, 51.0, 50.8, 50.3, 30.5, 29.9, 20.8, 20.4, 15.7, 9.2; HRMS (FAB⁺) m/z: Calcd. for C₃₈H₃₈Cl₃N₂O₁₂ (M–MeO)⁺ 819.1490, found 819.1467.

Alcohol **23**

To a solution of sodium cyanoborohydride (330 mg, 5.25 mmol, 10 equiv) in TFA (9.0 ml) at 0 °C was added **22** (440 mg, 0.516 mmol) in THF (1.5 ml), and the resulting mixture was stirred at this temperature for 30 min. The reaction mixture was diluted with CHCl₃ and carefully poured into vigorously stirred saturated aqueous NaHCO₃. The organic layer was separated, washed with saturated aqueous NaCl, and concentrated under reduced pressure. The residue was purified by flash column chromatography (50% EtOAc in *n*-hexane) to afford **23** (400 mg, 0.535 mmol, 94%) as a white foam. $[\alpha]_D^{22} +33^\circ$ (*c* = 1.2, CHCl₃); IR (neat film) 3510, 1764, 1722, 1664, 1484, 1428, 1369, 1342, 1304, 1227, 1185, 1126, 1062, 938, 911 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.54 (d, *J* = 6.8 Hz, 2H), 7.38-7.48 (m, 3H), 6.83 & 6.80 (s, 1H), 6.36 & 6.33 (s, 1H), 5.78-5.87 (m, 3H), 5.40 (br, 1H), 5.26-5.30 (m, 1H), 5.11-5.16 (m, 1H), 4.70-4.93 (m, 3H), 4.52 (br, 1H), 4.44 (m, 1H), 3.91 & 3.87 (s, 3H), 3.55-3.65 (br, 2H), 3.00-3.30 (m, 3H), 2.29 & 2.28 (s, 3H), 2.22 (s, 3H), 1.95 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 170.4, 170.3, 170.2, 169.8, 169.1, 152.0, 151.6, 149.4, 149.0, 148.5, 146.5, 146.4, 144.3, 144.2, 142.0, 142.0, 135.2, 135.2, 133.4, 133.2, 129.4, 129.2, 129.2, 129.1, 129.0, 129.0, 128.9, 127.3, 127.2, 122.3, 121.8, 113.7, 113.5, 113.1, 113.0, 101.7, 101.6, 95.2, 95.1, 77.2, 76.4, 75.2, 75.1, 62.7, 62.6, 60.5, 60.5, 59.5, 53.9, 53.2, 47.5, 46.9, 31.9, 31.6, 20.7, 20.6, 20.6, 15.7, 9.3; HRMS (FAB⁺) m/z: Calcd. for C₃₈H₄₀Cl₃N₂O₁₂ (M+H)⁺ 821.1647, found 821.1671.

Silyl Ether

To a mixture of **23** (101 mg, 0.123 mmol) and imidazole (21.3 mg 0.313 mmol, 2.5 equiv) in

DMF (0.10 ml) was added TBSCl (28.0 mg, 0.186 mmol, 1.5 equiv), and the mixture was stirred at room temperature for 2h. The reaction mixture was directly purified by flash column chromatography (40% EtOAc in *n*-hexane) to afford the silyl ether (106 mg, 0.127 mmol, 92%) as a colorless oil. $[\alpha]_D^{23}$ -8.0° ($c = 1.3$, CHCl_3); IR (neat film) 1766, 1723, 1669, 1424, 1368, 1340, 1299, 1255, 1208, 1184, 1126, 1097, 1036, 1006, 935, 908, 838 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.32-7.60 (m, 5H), 6.78 & 6.78 (s, 1H), 5.99 & 5.98 (s, 1H), 5.68-5.78 (m, 2H), 5.60-5.68 (m, 2H), 5.13-5.28 (br, 1H), 4.96-5.07 (br, 1H), 4.64-4.90 (m, 5H), 4.49 (dd, $J = 15.6, 12.0$ Hz, 1H), 4.17 (ddd, $J = 15.6, 8.8, 4.0$ Hz, 1H), 3.87 & 3.84 (s, 3H), 3.21 (dd, $J = 12.0, 8.8$ Hz, 1H), 3.17 (br, 2H), 2.29 & 2.28 (s, 3H), 2.18 (s, 3H), 2.02 & 2.00 (s, 3H), 1.91 (s, 3H), 0.69 & 0.68 (s, 9H), -0.26 & -0.29 (s, 3H), -0.33 & -0.36 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.4, 168.9, 168.8, 168.5, 153.4, 152.2, 151.5, 150.0, 148.6, 148.1, 146.1, 145.0, 143.7, 143.2, 141.1, 141.1, 139.4, 136.7, 134.4, 132.7, 132.5, 129.3, 129.1, 128.9, 128.7, 128.7, 128.6, 128.5, 128.4, 126.1, 123.2, 122.7, 116.8, 113.0, 113.0, 111.4, 101.0, 101.0, 95.3, 95.1, 75.5, 75.2, 75.1, 67.3, 66.5, 62.7, 62.7, 62.6, 60.3, 60.3, 55.0, 54.9, 53.5, 52.8, 48.1, 47.5, 31.9, 31.7, 25.5, 20.9, 20.9, 20.6, 17.8, 17.8, 15.9, 9.1, -5.9 , -6.0 , -6.1 , -6.3 ; HRMS (FAB $^+$) m/z : Calcd. for $\text{C}_{14}\text{H}_{54}\text{Cl}_3\text{N}_2\text{O}_{12}\text{Si}$ (M+H) $^+$ 935.2511, found 935.2400.

Phenol

The alcohol (524 mg, 0.560 mmol) was dissolved in guanidine/guanidinium nitrate solution (8.0 ml)²⁹. The mixture was stirred at 40 °C for 2.5 h. The reaction mixture was diluted with EtOAc, and sequentially washed with 1M HCl, saturate aqueous NaHCO_3 , and saturated aqueous NaCl. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (50% EtOAc in *n*-hexane) to afford the phenol (405 mg, 0.475 mmol, 85%) as a yellow foam. $[\alpha]_D^{23}$ -34° ($c = 1.5$, CHCl_3); IR (neat film) 3309, 1723, 1640, 1423, 1345, 1304, 1257, 1133, 1127, 1095, 838 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.35-7.54 (m, 5H), 6.87 & 6.83 (s, 1H), 6.30 (br, 1H), 5.35-5.73 (m, 5H), 5.17-5.28 (m, 1H), 5.06-5.16 (m, 1H), 4.98 & 4.90 (d, $J = 12.0$ Hz, 1H), 4.60-4.86 (m, 3H), 4.27-4.40 (m, 3H), 4.08 (br, 1H), 3.80 & 3.74 (s, 3H), 3.15-3.35 (m, 3H), 2.28 (s, 3H), 1.94 & 1.91 (s, 3H), 0.69 & 0.68 (s, 9H), -0.27 & -0.30 (s, 3H), -0.32 & -0.35 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 151.9, 151.3, 150.1, 149.4, 148.7, 146.0, 136.6, 136.4, 133.2, 132.8, 129.2, 129.1, 128.7, 128.7, 128.6, 128.5, 128.4, 128.4, 126.5, 126.3, 123.2, 116.1, 106.3, 106.2, 105.0, 100.2, 95.0, 75.5, 75.3, 75.1, 68.3, 67.3, 63.1, 62.9, 62.0, 60.2, 58.7, 58.7, 53.6, 53.0, 48.8, 47.9, 32.2, 25.5, 17.8, 17.8, 15.6, 15.6, 8.4, 8.4, -5.9 , -6.0 , -6.1 , -6.2 ; HRMS (FAB $^+$) m/z : Calcd. for $\text{C}_{40}\text{H}_{50}\text{Cl}_3\text{N}_2\text{O}_{10}\text{Si}$ (M+H) $^+$ 851.2300, found 851.2337.

Benzyl Ether

To a mixture of the phenol (404 mg, 0.474 mmol) and K_2CO_3 (196 mg, 1.42 mmol, 3.0 equiv) in CH_3CN (6.0 ml) was added benzyl bromide (73.0 μl , 0.615 mmol, 1.3 equiv), and the resulting mixture was heated at reflux for 1 h. After cooling, the reaction mixture was diluted with CHCl_3 and filtered through a pad of Celite. The filtrate was concentrated under reduced pressure, and the residue was purified by flash column chromatography (50% EtOAc in *n*-hexane) to afford the benzyl ether (409 mg, 0.434 mmol, 91%) as a yellow foam. $[\alpha]_{\text{D}}^{23} -37^\circ$ ($c = 2.1$, CHCl_3); IR (neat film) 3749, 1717, 1419, 1340, 1253, 1111, 838 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.30-7.60 (m, 10H), 6.77 & 6.73 (s, 1H), 5.83 (s, 1H), 5.77 (br, 2H), 5.69 (s, 1H), 5.51 (br, 1H), 5.22 & 5.21 (d, $J = 10.0$ Hz, 1H), 5.14 (br, 1H), 5.00 & 4.88 (d, $J = 11.6$ Hz, 1H), 4.74 (d, $J = 11.6$ Hz, 1H), 4.68 (d, $J = 10.0$ Hz, 1H), 4.59 (d, $J = 10.8$ Hz, 1H), 4.50 & 4.46 (d, $J = 11.6$ Hz, 1H), 4.37 & 4.25 (br, 1H), 4.30 & 4.29 (d, $J = 10.8$ Hz, 1H), 4.05 & 3.95 (br, 2H), 3.80 & 3.75 (s, 3H), 3.13-3.37 (m, 3H), 1.99 & 1.96 (s, 9H), -0.27 & -0.32 (s, 3H), -0.33 & -0.36 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.2, 152.1, 152.1, 150.0, 148.8, 146.2, 137.2, 137.1, 136.5, 133.1, 129.2, 128.7, 128.7, 128.6, 128.6, 128.5, 128.5, 128.0, 127.9, 127.8, 126.4, 126.3, 123.3, 115.8, 108.1, 102.6, 100.6, 75.5, 75.3, 75.2, 70.8, 67.5, 66.7, 63.5, 62.3, 60.3, 60.3, 59.8, 53.4, 52.7, 47.9, 47.2, 32.0, 31.5, 25.5, 22.6, 17.8, 15.5, 14.1, 8.7, -5.9 , -6.0 , -6.3 ; LRMS (FAB $^+$) m/z : 940.5 (M^+).

Oxazolidinone 24

To a solution of the benzyl ether (224 mg, 0.238 mmol) in THF (2.0 ml) at 0 °C was slowly added Red-Al (1.3 M solution in toluene, 0.25 ml, 0.325 mmol, 1.4 equiv). The reaction mixture was quenched with 1M aqueous HCl, and extracted with EtOAc. The organic layer was sequentially washed with saturated aqueous NaHCO₃ and saturated aqueous NaCl, dried over anhydrous MgSO₄, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (30% EtOAc in *n*-hexane) to afford **24** (181 mg, 0.195 mmol, 82%) as a white foam. $[\alpha]_D^{22} -37^\circ$ (*c* = 1.2, CHCl₃); IR (neat film) 1717, 1435, 1263, 1118, 1024, 840 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.58 (d, *J* = 8.0 Hz, 1H), 7.50 (d, *J* = 6.8 Hz, 1H), 7.26-7.49 (m, 8H), 6.77 & 6.73 (s, 1H), 6.41 & 6.40 (s, 1H) 5.86 (s, 1H), 5.77 (s, 1H), 5.57 & 5.51 (s, 1H), 5.41 (br, 1H), 5.21 (dd, *J* = 10.4, 10.4 Hz, 1H), 4.93 (dd, *J* = 7.2, 6.0 Hz, 1H), 4.69-5.02 (m, 5H), 4.20-4.35 (m, 3H), 3.87 & 3.83 (s, 3H), 3.74 (m, 1H), 3.14-3.35 (m, 3H), 2.73 (dd, *J* = 17.6, 6.0 Hz, 1H), 2.21 (s, 3H), 2.09 (s, 3H), 0.71 & 0.69 (s, 9H), -0.21 & -0.26 (s, 3H), -0.27 & -0.31 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 153.1, 153.5, 151.8, 149.5, 149.4, 148.1, 147.6, 146.5, 138.2, 137.4, 137.3, 131.4, 131.2, 130.2, 129.9, 128.6, 128.5, 128.4, 128.3, 128.0, 127.9, 127.7, 127.7, 127.2, 127.2, 125.5, 125.0, 124.4, 120.7, 120.6, 107.9, 101.9, 101.7, 100.7, 100.6, 95.4, 92.1, 92.1, 75.5, 75.2, 75.0, 74.8, 70.3, 68.9, 68.3, 68.1, 66.7, 66.6, 60.5, 60.3, 60.2, 60.1, 60.0, 59.9, 48.5, 48.1, 47.5, 46.7, 30.7, 30.5, 25.6, 17.8, 15.7, 15.7, 8.7, -5.9, -5.9, -6.0, -6.0; LRMS (FAB⁺) *m/z*: 925.3 (M+H)⁺.

Aminonitrile

To a mixture of **24** (295 mg, 0.318 mmol) and trimethylsilyl cyanide (127 μl , 0.952 mmol, 3.0 equiv) in CH_2Cl_2 (5.0 ml) at $0\text{ }^\circ\text{C}$ was added $\text{BF}_3 \cdot \text{OEt}_2$ (1.0 M solution in CH_2Cl_2 , 480 μl , 0.48 mmol, 1.5 equiv). The reaction mixture was poured into cold saturated aqueous NaHCO_3 and extracted with CH_2Cl_2 . The organic layer was dried over MgSO_4 and concentrated under reduced pressure, and the resulting crude product was purified by flash column chromatography (50% EtOAc in *n*-hexane) to afford the aminonitrile (221 mg, 0.23 mmol, 73%) as a white solid. $[\alpha]_{\text{D}}^{23} +47\text{ }^\circ$ ($c = 1.6$, CHCl_3); IR (neat film) 3457, 1718, 1498, 1429, 1309, 1259, 1120, 1065, 902 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.26-7.60 (m, 10H), 6.46 & 6.50 (s, 1H), 5.92 & 5.91 (s, 1H), 5.63 (s, 1H), 5.30-5.47 (m, 2H), 4.85-5.30 (m, 3H), 4.65-4.80 (m, 2H), 4.35-4.53 (m, 2H), 4.20-4.35 (m, 2H), 3.88 & 3.82 (s, 3H), 3.80-4.00 (m, 2H), 3.35-3.50 (m, 2H), 3.15 & 3.20 (d, $J = 8.0$ Hz, 1H), 2.75 & 2.80 (dd, $J = 17.0, 6.0$ Hz, 1H), 2.20 & 2.19 (s, 3H), 2.17 (s, 3H), 1.60 & 1.50 (d, $J = 17.0$ Hz, 1H), 0.77 & 0.75 (s, 9H), -0.04 & -0.10 (s, 3H), -0.09 & -0.15 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 152.7, 152.3, 151.2, 151.0, 149.0, 148.9, 147.6, 147.0, 146.6, 139.5, 139.5, 137.5, 137.3, 137.1, 131.5, 131.1, 130.9, 130.6, 128.9, 128.7, 128.6, 128.5, 128.2, 128.1, 128.1, 127.9, 127.8, 127.1, 125.4, 125.1, 125.0, 124.8, 117.8, 117.7, 115.8, 109.6, 109.5, 103.5, 100.5, 95.2, 75.8, 75.3, 75.1, 75.0, 70.5, 70.3, 63.7, 63.6, 62.5, 61.9, 60.3, 60.2, 56.3, 56.1, 51.1, 50.9, 50.4, 49.6, 49.3, 49.1, 29.9, 29.7, 25.7, 18.2, 18.2, 15.6, 8.9, -5.6 , -5.7 , -6.0 , -6.2 ; HRMS (FAB^+) m/z : Calcd. for $\text{C}_{47}\text{H}_{56}\text{Cl}_3\text{N}_2\text{O}_9\text{Si}$ ($\text{M}-\text{CN}$) $^+$ 925.2820, found 925.2774.

Acetate

To a solution of the aminonitrile (221 mg, 0.232 mmol) in a mixture of acetic anhydride (1.0 ml) and pyridine (2.0 ml) was added DMAP (5.6 mg, 0.05 mmol, 0.2 equiv), and the mixture was stirred at room temperature. The reaction mixture was concentrated under reduced pressure, and the resulting residue was purified by flash column chromatography (30% EtOAc in *n*-hexane) to afford the acetate (213 mg, 0.214 mmol, 92%) as a white solid. $[\alpha]_{\text{D}}^{23} +50^\circ$ ($c = 1.8$, CHCl_3); IR (neat film) 1720, 1430, 1251, 1122, 840 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.26-7.65 (m, 10H), 6.52, 6.49 (s, 1H), 6.10 (br, 1H), 5.67 (s, 1H), 5.50 & 5.35 (s, 1H), 5.37 (s, 1H), 4.55-5.30 (m, 8H), 5.50-5.55 (m, 3H), 3.89 & 3.83 (s, 3H), 3.65-3.80 (br, 1H), 3.40-3.55 (br, 2H), 2.85 & 2.80 (dd, $J = 17.6, 8.0$ Hz, 1H), 2.20-2.30 (br, 6H), 1.90-2.00 (br, 3H), 1.53 & 1.65 (d, $J = 17.0$ Hz, 1H), 0.77 (br, 9H), -0.04 & -0.11 (s, 3H), -0.08 & -0.14 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.2, 170.1, 152.6, 152.2, 151.0, 150.8, 149.0, 148.9, 147.6, 147.0, 146.7, 139.7, 139.7, 137.6, 137.4, 137.2, 131.2, 130.9, 130.6, 128.6, 128.6, 128.5, 128.4, 128.4, 128.1, 128.0, 127.8, 127.7, 127.1, 125.4, 124.9, 124.9, 124.8, 117.9, 1117.9, 117.8, 115.6, 115.6, 109.4, 109.3, 103.6, 103.5, 100.5, 95.2, 95.1, 75.6, 75.2, 75.1, 74.8, 70.4, 70.2, 63.3, 63.1, 61.9, 61.2, 60.2, 59.3, 54.2, 54.0, 51.8, 51.6, 50.2, 49.3, 49.1, 48.7, 29.8, 29.7, 25.7, 20.8, 20.8, 18.1, 18.1, 15.5, 8.9, -5.7 , -5.8 , -6.0 , -6.1 ; LRMS (FAB $^+$) m/z : 993.5 (M^+).

Alcohol

To a solution of the acetate (200 mg, 0.20 mmol) in CH_3CN (2.0 ml) was added HF (48 wt. % solution in H_2O , 1.0 ml, 28 mmol), and the mixture was stirred at room temperature for 3 h. The reaction mixture was poured into saturated aqueous NaHCO_3 and extracted with EtOAc. The organic layer was washed with saturated aqueous NaCl, dried with MgSO_4 , and concentrated under reduced pressure. The residue was purified by flash column chromatography (40% EtOAc in *n*-hexane) to afford the alcohol (180 mg, 0.20 mmol, quant) as a white foam. $[\alpha]_{\text{D}}^{24} +67^\circ$ ($c = 2.3$, CHCl_3); IR (neat film) 3504, 1717, 1453, 1436, 1373, 1312, 1258, 1236, 1122, 1058 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.26-7.70 (m, 10H), 6.60 & 6.56 (s, 1H), 5.85 (s, 1H), 5.70 (s, 1H), 5.69 & 5.59 (s, 1H), 5.48 & 5.46 (s, 1H), 5.23 & 5.25 (d, $J = 10$ Hz, 1H), 4.80-5.02 (m, 4H), 4.50-4.75 (m, 3H), 4.35 (m, 1H), 4.10 (m, 1H), 3.98 (m, 1H), 3.93 & 3.85 (s, 3H), 3.75 (m, 1H), 3.58 & 3.52 (d, $J = 2.0$ Hz, 1H), 3.48 (m, 1H), 3.30 (m, 1H), 2.95 & 2.88 (dd, $J = 17.2, 8.0$ Hz, 1H), 2.19 (s, 3H), 2.16 (s, 3H), 2.07 (s, 3H), 1.80 & 1.69 (d, $J = 17.2$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.4, 170.3, 152.8, 152.3, 151.5, 151.3, 148.5, 148.4, 148.1, 147.4, 146.6, 139.2, 139.2, 137.2, 137.1, 135.8, 135.6, 131.5, 131.4, 131.2, 131.1, 128.9, 128.8, 127.9, 127.8, 127.0, 125.6, 124.6, 124.1, 117.4, 117.4, 114.5, 110.0, 109.9, 103.4, 100.7, 95.2, 95.1, 75.3, 75.1, 70.4, 70.3, 61.3, 61.3, 61.2, 60.6, 60.6, 60.5, 59.9, 53.4, 53.1, 51.8, 51.6, 50.1, 49.0, 48.8, 48.3, 30.1, 29.9, 20.8, 15.6, 8.9; HRMS (FAB $^+$) m/z : Calcd. for $\text{C}_{43}\text{H}_{44}\text{Cl}_3\text{N}_2\text{O}_{10}$ (M-CN) $^+$ 853.2061, found 853.2082.

Aldehyde 25

To a solution of the alcohol (180 mg, 0.204 mmol) in CH_2Cl_2 (2.5 ml) at room temperature was added Dess-Martin periodinane (103 mg, 0.243 mmol, 1.2 equiv), and the resulting slurry was stirred at room temperature for 40 min. Excess reagent was quenched with 2-propanol (2 drops), and the mixture was diluted with Et_2O , filtered through a pad of Celite, and concentrated under reduced pressure. The residue was dissolved in EtOAc , and sequentially washed with saturated aqueous NaHCO_3 and saturated aqueous NaCl . The organic layer was dried over anhydrous MgSO_4 and concentrated under reduced pressure, and the resultant residue was purified by flash column chromatography (40% EtOAc in *n*-hexane) to afford **25** (165 mg, 0.188 mmol, 92%) as a white foam. $[\alpha]_{\text{D}}^{24} +23^\circ$ ($c = 0.90$, CHCl_3); IR (neat film) 1732, 1607, 1584, 1488, 1428, 1382, 1315, 1238, 1122, 1035, 939, 906, 826 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 9.17 & 9.12 (d, $J = 2.8$ Hz), 7.23-7.45 (m, 10H), 6.61 & 6.59 (s, 1H), 5.93 (br, 1H), 5.80 (br, 1H), 5.75 & 5.72 (br, 1H), 5.62 (br, 1H), 5.21 & 5.18 (d, $J = 10.8$ Hz, 1H), 4.65-5.00 (m, 8H), 4.27-4.52 (m, 3H), 3.78 & 3.71 (s, 3H), 3.68 (br, 1H), 3.13 & 3.08 (dd, $J = 17.6, 8.0$ Hz, 1H), 2.12 (br, 1H), 2.04-2.11 (br, 6H), 2.01 & 2.01 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 196.9, 196.4, 170.2, 152.4, 152.1, 146.7, 139.8, 137.1, 137.1, 132.0, 130.5, 128.6, 128.5, 128.4, 128.0, 128.0, 127.9, 127.9, 127.8, 127.2, 127.2, 127.0, 125.0, 124.9, 123.9, 113.5, 113.4, 110.4, 103.9, 100.9, 95.0, 75.3, 75.3, 74.4, 70.5, 70.4, 68.9, 68.4, 62.3, 60.5, 60.4, 56.8, 51.8, 51.7, 50.1, 49.1, 47.2, 30.0, 20.9, 15.8, 9.0; HRMS (FAB $^+$) m/z : Calcd. for $\text{C}_{44}\text{H}_{42}\text{Cl}_3\text{N}_3\text{O}_{10}$ (M^+) 877.1936, found 877.1921.

Pentacycle 26

A mixture of **25** (51.2 mg, 0.058 mmol) and 10% palladium on carbon (AD-type (wet, 50 % water), purchased from Kawaken Fine Chemicals Co., 51.1 mg, 0.024 mmol, 0.41 equiv) in THF (1.2 ml) was stirred under 1 atm of hydrogen at room temperature for 18 h. The reaction mixture was filtered through a pad of Cellite, and concentrated under reduced pressure. The resulting crude product was purified by flash column chromatography (50% EtOAc in *n*-hexane) to afford **26** (34.2 mg, 0.049 mmol, 84%) as a yellow film. $[\alpha]_D^{24} +23^\circ$ ($c = 1.4$, CHCl_3); IR (neat film) 3749, 1722, 1623, 1587, 1501, 1435, 1380, 1317, 1265, 1232, 1127, 1105, 1056, 1032, 1012, 965 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.55 (s, 1H), 5.92 (s, 1H), 5.85 & 5.80 (s, 1H), 5.83 (s, 1H), 4.91 & 4.87 (d, $J = 8.0$ Hz, 1H), 4.87 & 4.85 (d, $J = 11.6$ Hz, 1H), 4.69 & 4.67 (d, $J = 11.6$ Hz, 1H), 4.48 (d, $J = 10.4$ Hz, 1H), 4.46 (m, 1H), 4.19 (br, 1H), 4.07 (br, 1H), 3.77 & 3.76 (s, 3H), 3.66 (dd, $J = 10.8, 8.0$ Hz, 1H), 3.34 & 3.31 (dd, $J = 10.4, 2.8$ Hz, 1H), 3.25 (dd, $J = 17.6, 8.0$ Hz, 1H), 2.85 & 2.80 (d, $J = 17.6$ Hz, 1H), 2.25 & 2.24 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.3, 153.1, 152.5, 149.3, 149.2, 145.9, 145.9, 144.0, 143.7, 142.5, 142.3, 135.4, 135.3, 131.6, 131.3, 130.1, 130.1, 123.2, 122.9, 117.0, 116.9, 115.9, 115.8, 110.0, 109.9, 108.0, 101.0, 95.3, 95.0, 75.3, 75.1, 68.9, 68.8, 64.1, 61.6, 61.5, 61.1, 61.0, 58.9, 58.8, 56.3, 49.6, 48.9, 47.1, 46.4, 30.5, 29.6, 20.2, 15.7, 15.7, 8.6; HRMS (FAB $^+$) m/z : Calcd. for $\text{C}_{30}\text{H}_{30}\text{Cl}_3\text{N}_3\text{O}_{10}$ (M^+) 697.0997, found 697.0983.

Allyl Ether

To a mixture of **26** (34.2 mg, 0.049 mmol) and *i*-Pr₂NEt (0.20 ml, 1.2 mmol, 24 equiv) in CH₂Cl₂ (1.2 ml) was added allyl bromide (40 μl, 0.47 mmol, 10 equiv), and the resulting mixture was heated at reflux for 3 h. The reaction mixture was diluted with CH₂Cl₂, and sequentially washed with 1M aqueous HCl, saturated aqueous NaHCO₃, and saturated aqueous NaCl. The organic layer was dried over anhydrous MgSO₄ and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (50% EtOAc in *n*-hexane) to afford the allyl ether (32.3 mg, 0.044 mmol, 89%) as a colorless film. $[\alpha]_D^{23} +33^\circ$ (*c* = 1.2, CHCl₃); IR (neat film) 3290, 1724, 1435, 1378, 1338, 1313, 1297, 1264, 1227, 1125, 1102, 1057, 1032, 1013, 967, 940, 914, 827 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.65 & 9.62 (s, 1H), 6.78 & 6.76 (s, 1H), 6.22 (m, 1H), 6.12 & 6.10 (d, *J* = 17.6 Hz, 1H), 5.92 (s, 1H), 5.84 & 5.83 (s, 1H), 5.78 & 5.68 (s, 1H), 5.37-5.60 (m, 2H), 4.75-5.00 (m, 3H), 4.69 & 4.69 (d, *J* = 11.6 Hz, 1H), 4.40-4.56 (m, 2H), 4.30-4.40 (m, 1H), 4.10-4.19 (m, 1H), 4.02-4.10 (m, 1H), 3.83 & 3.82 (s, 3H), 3.65 (m, 1H), 3.17-3.32 (m, 2H), 2.85 (d, *J* = 17.6 Hz, 1H), 2.24 & 2.23 (s, 3H), 2.09 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 170.3, 170.2, 152.9, 152.2, 149.4, 149.4, 148.5, 147.4, 146.9, 146.0, 145.9, 135.4, 135.4, 132.6, 132.5, 132.0, 131.4, 131.0, 127.0, 123.9, 123.1, 121.8, 121.3, 115.8, 110.0, 109.9, 109.9, 108.1, 101.1, 95.1, 76.3, 75.8, 75.6, 75.3, 69.0, 68.9, 64.2, 61.9, 61.5, 60.7, 60.6, 58.9, 56.5, 56.4, 49.8, 48.5, 47.3, 47.0, 30.4, 30.3, 20.3, 15.7, 14.3, 8.6; HRMS (FAB⁺) *m/z*: Calcd. for C₃₃H₃₄Cl₃N₃O₁₀ (M⁺) 737.1310, found 737.1328.

Alcohol

To a solution of the allyl ether (32.3 mg, 0.044 mmol) in MeOH (0.6 ml) was added K_2CO_3 (70.8 mg, 0.51 mmol, 12 equiv), and the resulting slurry was stirred at room temperature for 30 min. The reaction mixture was diluted with EtOAc, and sequentially washed with 10% aqueous citric acid, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl. The organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The resulting crude product was purified by flash column chromatography (50% EtOAc in *n*-hexane) to afford the alcohol (30.3 mg, 0.044 mmol, 99%) as a colorless film. $[\alpha]_D^{26} +44^\circ$ ($c = 1.1$, $CHCl_3$); IR (neat film) 3298, 1720, 1486, 1434, 1378, 1336, 1315, 1267, 1229, 1125, 1058, 1032, 965, 827 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 9.59 & 9.57 (s, 1H), 6.81 & 6.78 (s, 1H), 6.20 (m, 1H), 5.65-5.95 (m, 4H), 5.40-5.60 (m, 2H), 4.60-5.00 (m, 4H), 4.50 (m, 2H), 4.20-4.40 (m, 2H), 4.00 (m, 1H), 3.84 & 3.82 (s, 3H), 3.60 (m, 1H), 3.20-3.35 (m, 3H), 2.86 (d, $J = 17.6$ Hz, 1H), 2.24 & 2.23 (s, 3H), 2.06 & 2.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.8, 152.2, 149.4, 149.3, 148.7, 148.7, 147.4, 147.0, 145.8, 135.4, 135.3, 133.0, 132.7, 132.0, 130.5, 130.1, 126.5, 126.5, 123.8, 123.0, 121.7, 121.3, 115.7, 115.7, 110.2, 109.5, 109.4, 107.9, 100.9, 100.9, 95.1, 15.0, 77.2, 76.1, 75.6, 75.5, 75.2, 68.9, 68.7, 68.5, 65.5, 65.5, 62.0, 61.4, 60.6, 60.6, 59.3, 59.3, 58.3, 58.2, 49.8, 48.6, 47.4, 47.0, 30.7, 30.7, 30.6, 15.8; HRMS (FAB $^+$) m/z : Calcd. for $C_{30}H_{32}Cl_3N_2O_9$ (M-CN) $^+$ 669.1173, found 669.1201.

Ester 28

To a mixture of the alcohol (51.0 mg, 0.073 mmol) and acid **27** (42.7 mg, 0.173 mmol, 2.4 equiv) in CH_2Cl_2 (1.6 ml) at room temperature was added WSCD·HCl (37.2 mg, 0.194 mmol, 2.7 equiv) followed by DMAP (1.0 mg, 0.008 mmol, 0.1 equiv). After 10 min., the reaction mixture was diluted with CH_2Cl_2 , and sequentially washed with 1M aqueous HCl, saturated aqueous NaHCO_3 , and saturated aqueous NaCl. The organic phase was concentrated under reduced pressure, and the residue was purified by flash column chromatography (50% EtOAc in *n*-hexane) to afford **28** (64.0 mg, 0.070 mmol, 94%) as a pale yellow film. $[\alpha]_{\text{D}}^{21} +24^\circ$ ($c = 0.5$, CHCl_3); IR (neat film) 3351, 1725, 1520, 1436, 1262, 1214, 1129, 1102, 1057 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 9.62 & 9.63 (s, 1H), 6.78 & 6.75 (s, 1H), 5.75-6.30 (m, 5 H), 5.00-5.75 (m, 6 H), 4.63-5.03 (m, 3H), 4.45-4.63 (m, 5H), 4.05-4.45 (m, 3H), 3.80-3.90 (br, 2H), 3.75 (s, 3H), 2.80-3.50 (m, 4H), 2.05-2.45 (m, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 194.0, 169.8, 154.7, 152.0, 151.3, 148.7, 148.3, 131.7, 131.6, 131.5, 131.2, 131.2, 130.0, 125.8, 120.7, 117.2, 117.1, 108.1, 100.1, 74.4, 68.0, 65.1, 60.8, 59.9, 58.4, 55.3, 52.7, 52.0, 49.0, 46.1, 30.3, 29.7, 15.0, 15.0, 13.2, 7.7; HRMS (FAB⁺) m/z : Calcd. for $\text{C}_{40}\text{H}_{43}\text{Cl}_3\text{N}_4\text{O}_{13}\text{S}$ (M^+) 924.1613, found 924.1609.

Thiol

To a solution of **28** (29.5 mg, 0.032 mmol) in CH₃CN (0.80 ml) was added hydrazine solution (the upper phase of a 1:3 (v/v) mixture of hydrazine hydrate and CH₃CN, 35 μ l), and the resulting mixture was stirred at room temperature for 80 min. The reaction mixture was diluted with CHCl₃ and sequentially washed with 1M aqueous HCl, saturated aqueous NaHCO₃, and saturated aqueous NaCl. The organic phase was dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to afford the thiol (27.8 mg, 0.031 mmol, 98%) as a colorless film. $[\alpha]_D^{24} +23^\circ$ (c = 1.1, CHCl₃); IR (neat film) 3297, 1718, 1507, 1436, 1375, 1338, 1298, 1263, 1125, 1102, 1059, 1032, 1013, 968, 939, 827 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.50-9.65 (m, 1H), 7.26-7.40 (m, 5H), 6.72-6.83 (m, 1H), 6.23 (m, 1H), 6.12 & 6.09 (d, *J* = 4.0 Hz, 1H), 5.95 (s, 1H), 5.88 (m, 1H), 5.81 (s, 1H), 5.79 & 5.69 (s, 1H), 5.20-5.60 (m, 4H), 4.77-5.02 (m, 3H), 4.63-4.72 (m, 1H), 4.27-4.64 (m, 4H), 4.08-4.27 (m, 3H), 3.95-4.68 (m, 1H), 3.87 (s, 3H), 3.89 (s, 3H), 3.15-3.35 (m, 2H), 2.70-3.05 (m, 1H), 2.88 (d, *J* = 17.6 Hz, 1H), 2.50-2.70 (m, 2H), 2.24 & 2.25 (s, 3H), 2.08 (s, 3H), 0.85-1.45 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 169.8, 169.5, 155.3, 152.8, 152.2, 149.6, 149.5, 148.6, 148.5, 147.5, 147.0, 145.9, 135.4, 135.3, 132.7, 132.5, 132.4, 132.4, 132.3, 132.0, 132.0, 131.0, 130.6, 126.7, 126.6, 123.9, 123.2, 121.7, 121.6, 121.1, 118.4, 118.2, 118.1, 115.6, 115.6, 110.0, 109.9, 109.2, 108.4, 108.2, 101.0, 95.2, 95.1, 76.2, 75.6, 75.6, 75.3, 68.9, 68.7, 68.6, 66.2, 66.1, 66.0, 65.1, 61.9, 61.4, 60.8, 60.7, 59.1, 58.8, 56.7, 55.2, 55.1, 54.8, 52.8, 49.7, 48.4, 47.1, 46.9, 46.8, 31.6, 30.5, 30.3, 30.1, 27.2, 26.8, 26.5, 22.6, 15.9, 15.8, 15.8, 14.2, 14.1, 8.6; HRMS (FAB⁺) *m/z*: Calcd. for C₃₈H₄₁Cl₃N₄O₁₂S (M⁺) 882.1507, found 882.1577.

Sulfide 29

To a solution of the thiol (24.6 mg, 0.028 mmol) in 2,2,2-trifluoroethanol (3.0 ml) at room temperature was added TFA (10% solution in 2,2,2-trifluoroethanol, 0.15ml, 0.19 mmol, 7 equiv), and the mixture was stirred at room temperature for 3 h. The reaction mixture was diluted with a large excess of benzene (50 ml), and concentrated under reduced pressure. The resulting yellow syrup was dissolved in a mixture of acetic anhydride (0.1 ml) and pyridine (0.2ml). To the mixture at room temperature was added DMAP (1.5 mg, 0.012 mmol, 0.4 equiv), and the reaction was stirred for 30 min and concentrated under reduced pressure. The residue was purified by PTLC (30% EtOAc in *n*-hexane) to afford the sulfide **29** (18.0 mg, 0.020 mmol, 71% in 2 steps) as a colorless film. $[\alpha]_D^{23} -22^\circ$ ($c = 1.1$, CHCl₃); IR (neat film) 3402, 1759, 1721, 1510, 1431, 1372, 1332, 1309, 1265, 1236, 1193, 1125, 1101, 1087, 1060, 1029, 1007, 983, 916, 826 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 6.79 & 6.78 (s, 1H), 6.18 (m, 1H), 6.10 (s, 1H), 6.01 & 5.99 (s, 1H), 5.94 (m, 1H), 5.45-5.68 (m, 2H), 5.22-5.35 (m, 3H), 4.97-5.15 (m, 3H), 4.65-4.90 (m, 3H), 4.42-4.63 (m, 5H), 4.33 (br, 1H), 4.15-4.27 (m, 4H), 3.81 & 3.78 (s, 3H), 3.43 (s, 1H), 3.12-3.29 (m, 2H), 2.30-2.38 (m, 2H), 2.29 & 2.28 (s, 3H), 2.26 & 2.25 (s, 3H), 2.03 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 170.4, 168.6, 168.5, 155.3, 152.6, 152.2, 149.5, 148.9, 148.8, 148.7, 146.0, 146.0, 141.0, 140.3, 140.3, 134.6, 134.5, 132.9, 132.7, 132.7, 132.6, 130.1, 129.6, 127.1, 126.5, 125.1, 125.0, 119.5, 119.4, 118.1, 116.2, 116.2, 116.2, 116.0, 115.9, 113.9, 112.7, 112.6, 102.1, 102.1, 95.2, 95.0, 75.3, 75.3, 73.4, 72.7, 65.9, 61.3, 61.3, 60.4, 60.4, 60.4, 59.4, 59.4, 58.4, 58.2, 58.0, 57.7, 53.8, 49.0, 48.1, 47.9, 47.7, 41.2, 41.1, 32.9, 32.9, 28.1, 27.7, 20.5, 20.4, 15.8, 15.8, 9.6; HRMS (FAB⁺) *m/z*: Calcd. for C₄₀H₄₁Cl₃N₄O₁₂S (M⁺) 906.1507, found 906.1494.

Amine

To a mixture of **29** (17.3 mg, 0.0190 mmol) and zinc powder (96.1 mg, 1.47 mmol, 78 equiv) in Et₂O (0.40 ml) at room temperature was added AcOH (0.20 ml), and the resulting slurry was stirred at room temperature for 2.5 hours. The reaction mixture was filtered through a pad of Celite, and the filtrate was concentrated under reduced pressure. The residue was dissolved in EtOAc, and sequentially washed with saturated aqueous NaHCO₃ and saturated aqueous NaCl. The organic phase was concentrated under reduced pressure, and the crude product was purified by PTLC (50% EtOAc in *n*-hexane) to afford the amine (12.8 mg, 0.0175 mmol, 92%) as a colorless film. $[\alpha]_D^{22} -12^\circ$ (*c* = 1.3, CHCl₃); IR (neat film) 3393, 1758, 1724, 1509, 1448, 1432, 1372, 1332, 1241, 1229, 1195, 1101, 1086, 1065, 915 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 6.80 (s, 1H), 6.09 (s, 1H), 6.08 (m, 1H), 6.00 (s, 1H), 5.95 (m, 1H), 5.44 (d, *J* = 17.6 Hz, 1H), 5.32 (d, *J* = 17.6 Hz, 1H), 5.26 (d, *J* = 12.4 Hz, 2H), 5.03 (d, *J* = 12.0 Hz, 1H), 4.70-4.80 (m, 2H), 4.26-4.55 (m, 5H), 4.25 (s, 1H), 4.10-4.19 (m, 2H), 3.83 (d, *J* = 8.8 Hz, 1H), 3.79 (s, 3H), 3.44 (d, *J* = 4.0 Hz, 1H), 3.10 (d, *J* = 17.6 Hz, 1H), 2.98 (dd, *J* = 17.6, 8.8 Hz, 1H), 2.28 (s, 3H), 2.27 (s, 3H), 2.05-2.40 (m, 2H), 2.04 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 170.4, 168.6, 155.4, 148.6, 148.5, 145.8, 140.9, 140.3, 134.3, 132.8, 131.9, 130.4, 130.4, 125.2, 120.1, 118.0, 117.9, 116.7, 113.5, 113.2, 102.0, 73.0, 65.8, 61.4, 60.4, 60.4, 59.3, 58.8, 58.4, 53.8, 48.6, 47.9, 41.7, 32.6, 27.9, 20.4, 15.7, 9.6; HRMS (FAB⁺) *m/z*: Calcd. for C₃₆H₄₀N₃O₁₀S (M-CN)⁺ 706.2434, found 706.2411.

Methylamine

To a mixture of the amine (5.6 mg, 0.0076 mmol), formalin solution (30 μ l), and sodium cyanoborohydride (12 mg, 0.19 mmol, 24 equiv) in MeOH (0.4 ml) was slowly added AcOH (0.10 ml), and the resulting mixture was stirred at room temperature for 1 h. The reaction mixture was concentrated under reduced pressure, and the residue was diluted with EtOAc and sequentially washed with saturated aqueous NaHCO₃ and saturated aqueous NaCl. The organic layer was concentrated under reduced pressure, and the residue was purified by PTLC (50% EtOAc in hexane) to afford the methylamine (5.5 mg, 0.0074 mmol, 96%) as a colorless film. $[\alpha]_D^{23} -26^\circ$ (*c* = 0.9, CHCl₃); IR (neat film) 3401, 1759, 1724, 1507, 1446, 1372, 1331, 1235, 1194, 1145, 1106, 1088, 1067, 998, 915 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 6.78 (s, 1H), 6.08 (s, 1H), 6.08 (m, 1H), 5.99 (s, 1H), 5.96 (m, 1H), 5.45 (d, *J* = 17.6 Hz, 1H), 5.31 (d, *J* = 17.6 Hz, 1H), 5.25 (d, *J* = 10.8 Hz, 2H), 5.02 (d, *J* = 12.0 Hz, 1H), 4.80 (m, 2H), 4.40-4.55 (m, 3H), 4.27-4.40 (m, 2H), 4.24 (s, 1H), 4.19 (m, 1H), 4.16 (m, 2H), 3.79 (s, 3H), 3.35-3.45 (m, 2H), 2.85-2.97 (m, 2H), 2.29 (s, 3H), 2.27 (s, 3H), 2.20-2.40 (m, 1H), 2.20

Ketolactone

To a solution of the aminophenol (3.7 mg, 0.0059 mmol) in a mixture of DMF (0.15 ml) and CH_2Cl_2 (0.15 ml) was added 4-formyl-1-methylpyridinium benzenesulfonate (16.5 mg, 0.057 mmol, 10 equiv), and the solution was stirred at room temperature for 15 min. To the mixture was added DBU (8.0 μl , 0.053 mmol, 9 equiv), and the resulting dark purple suspension was stirred at room temperature. After 25 min, to the mixture were added CH_2Cl_2 (0.30 ml) and saturated aqueous citric acid (10 drops). The resulting orange solution was stirred at room temperature for 40 min before it was partitioned between saturated aqueous NaHCO_3 and Et_2O . The ethereal layer was concentrated under reduced pressure, and the crude product was purified by PTLC (70% EtOAc in *n*-hexane) to afford the ketolactone (2.0 mg, 0.0032 mmol, 54%) as a white film. $[\alpha]_D^{22} +153^\circ$ ($c = 0.2$, CHCl_3); IR (neat film) 3447, 1763, 1728, 1622, 1589, 1500, 1456, 1373, 1270, 1236, 1194, 1160, 1145, 1108, 1087, 1063 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.49 (s, 1H), 6.11 (s, 1H), 6.03 (s, 1H), 5.69 (s, 1H), 5.09 (d, $J = 11.6$ Hz, 1H), 4.66 (br, 1H), 4.39 (s, 1H), 4.24 (d, $J = 4.8$ Hz, 1H), 4.22 (d, $J = 11.6$ Hz, 1H), 4.16 (d, $J = 2.8$ Hz, 1H), 3.76 (s, 3H), 3.54 (d, $J = 4.8$ Hz, 1H), 3.43 (dd, $J = 9.6, 2.8$ Hz, 1H), 2.90 (dd, $J = 18.4, 9.6$ Hz, 1H), 2.84 (d, $J = 13.6$ Hz, 1H), 2.70 (d, $J = 18.4$ Hz, 1H), 2.57 (d, $J = 13.6$ Hz, 1H), 2.33 (s, 3H), 2.24 (s, 3H), 2.14 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 186.7, 168.5, 160.5, 147.1, 146.4, 142.9, 141.6, 140.7, 130.4, 129.8, 121.7, 121.7, 120.0, 117.9, 117.1, 113.5, 113.3, 102.2, 61.7, 61.4, 60.3, 59.8, 58.9, 54.6, 43.2, 41.6, 36.8, 24.1, 20.4, 15.8, 9.7; HRMS (FAB $^+$) m/z : Calcd. for $\text{C}_{31}\text{H}_{32}\text{N}_3\text{O}_9\text{S}$ ($\text{M}+\text{H}$) $^+$ 622.1859, found 622.1812.

Ecteinascidin 770 (2)

Ecteinascidin 770 (2)

To a mixture of the ketolactone (2.0 mg, 0.0026 mmol) and amine **30** (12.4 mg, 0.062 mmol, 19 equiv) in EtOH (0.25 ml) at room temperature was added sodium acetate (7.4 mg, 0.090 mmol, 28 equiv), and the slurry was stirred at room temperature for 5.5 h. The reaction mixture was purified by PTLC (5% MeOH in CH₂Cl₂) to afford Et 770 (**2**) (2.4 mg, 0.0031 mmol, 96%) as a white film. $[\alpha]_D^{23} -57^\circ$ ($c = 0.2$, CHCl₃); IR (neat film) 3437, 2931, 1743, 1591, 1507, 1456, 1369, 1236, 1193, 1107, 1087, 1053, 1028 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 6.60 (s, 1H), 6.48 (s, 1H), 6.45 (s, 1H), 6.05 (s, 1H), 5.98 (s, 1H), 5.73 (s, 1H), 5.38 (br, 1H), 5.02 (d, $J = 11.6$ Hz, 1H), 4.57 (br, 1H), 4.33 (s, 1H), 4.28 (d, $J = 5.2$ Hz, 1H), 4.19 (d, $J = 2.8$ Hz, 1H), 4.12 (dd, $J = 11.6, 2.8$ Hz, 1H), 3.79 (s, 3H), 3.63 (s, 3H), 3.51 (d, $J = 4.8$ Hz, 1H), 3.42 (m, 1H), 3.10 (ddd, $J = 11.6, 10.8, 4.0$ Hz, 1H), 2.94 (m, 2H), 2.78 (m, 1H), 2.62 (m, 1H), 2.47 (m, 1H), 2.35 (m, 1H), 2.32 (s, 3H), 2.27 (s, 3H), 2.20 (s, 3H), 2.09 (m, 1H), 2.04 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 172.6, 168.1, 147.8, 145.3, 144.5, 144.3, 143.0, 141.3, 140.1, 130.8, 129.3, 129.1, 125.8, 121.2, 120.7, 118.2, 118.1, 114.1, 114.1, 113.4, 109.8, 101.9, 64.6, 61.1, 60.4, 60.0, 59.7, 59.5, 55.2, 54.7, 54.6, 42.2, 41.8, 41.6, 39.6, 28.8, 24.2, 20.5, 15.8, 9.7; HRMS (FAB+) m/z : Calcd. for C₄₀H₄₃N₄O₁₀S (MH)⁺ 744.2704, found 744.2698.

Ecteinascidin 743 (1)

To a solution of Et 770 (**2**) (2.4 mg, 0.0031 mmol, 1.0 equiv) in a mixture of CH_3CN (0.3 ml) and water (0.2 ml) was added silver nitrate (10.2 mg, 0.060 mmol, 19 equiv), and the suspension was stirred at room temperature for 17 h. The reaction mixture was partitioned between EtOAc (2 ml x 3) and saturated aqueous NaHCO_3 (2 ml), and the combined organic layer (6 ml) was washed again with saturated aqueous NaHCO_3 . The aqueous layer was further extracted with EtOAc (1.5 ml) and the combined organic layer (7.5 ml) was washed with saturated aqueous Na_2SO_4 . The organic layer was concentrated under reduced pressure to afford Et 743 (**1**) (2.2 mg, 0.0029 mmol, 93%) as a pale yellow film. $[\alpha]_D^{22} -58^\circ$ ($c = 0.2$, CH_2Cl_2); IR (neat film) 3347, 2930, 1763, 1741, 1590, 1509, 1458, 1431, 1369, 1237, 1195, 1122, 1109, 1088, 1053, 1029, 1003, 958, 916 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.61 (s, 1H), 6.47 (s, 1H), 6.45 (s, 1H), 6.02 (s, 1H), 5.94 (s, 1H), 5.69 (br, 1H), 5.39 (br, 1H), 5.13 (d, $J = 11.2$ Hz, 1H), 4.81 (s, 1H), 4.48 (d, $J = 3.3$ Hz, 1H), 4.48 (br, 1H), 4.16 (d, $J = 5.1$ Hz, 1H), 4.05 (dd, $J = 11.2, 2.2$ Hz, 1H), 3.79 (s, 3H), 3.62 (s, 3H), 3.57 (d, $J = 4.9$ Hz, 1H), 3.22 (br, 1H), 3.12 (ddd, $J = 10.0, 10.0, 4.0$ Hz, 1H), 2.82-2.97 (m, 2H), 2.81 (m, 1H), 2.60 (ddd, $J = 15.9, 10.0, 4.0$ Hz, 1H), 2.48 (ddd, $J = 15.9, 4.0, 3.4$ Hz, 1H), 2.37 (br, 1H), 2.32 (s, 3H), 2.27 (s, 3H), 2.20 (s, 3H), 2.19 (br, 1H), 2.03 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 172.6, 168.3, 147.7, 145.1, 144.4, 144.2, 142.9, 141.3, 140.5, 131.5, 129.2, 129.1, 126.1, 121.8, 120.9, 117.9, 115.9, 114.0, 112.5, 109.8, 101.7, 82.1, 64.7, 61, 3, 60.4, 57.8, 57.7, 56.0, 55.1, 54.9, 42.2, 42.1, 41.4, 39.7, 28.9, 24.1, 20.5, 15.8, 9.7; HRMS (FAB $^+$) m/z : Calcd. for $\text{C}_{39}\text{H}_{42}\text{N}_3\text{O}_{10}\text{S}$ ($\text{M}-\text{OH}$) $^+$ 744.2591, found 744.2629.