Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Synthesis and Biological Evaluation of Flexible and Conformationally Constrained LpxC Inhibitors

Marius Löppenberg, Hannes Müller, Carla Pulina, Alberto Oddo, Mark Teese, Joachim Jose, Ralph Holl*

Institut für Pharmazeutische und Medizinische Chemie der Universität Münster, Corrensstraße 48, D-48149 Münster, Germany

Supplementary Information

Synthetic Procedures

General

Unless otherwise mentioned, THF was dried with sodium/benzophenone and was freshly distilled before use. Thin layer chromatography (tlc): Silica gel 60 F254 plates (Merck). Flash chromatography (fc): Silica gel 60, 40 – 64 µm (Macherey-Nagel); parentheses include: diameter of the column, fraction size, eluent, R_f value. Melting point (m.p.): Melting point apparatus SMP 3 (Stuart Scientific), uncorrected. Optical rotation α [deg] was determined with a Polarimeter 341 (Perkin Elmer); path length 1 dm, wavelength 589 nm (sodium D line); the unit of the specific rotation $[\alpha]_D^{20}$ [deg · mL · dm^{-1} · g^{-1}] is omitted; the concentration of the sample c [mg · mL^{-1}] and the solvent used are given in brackets. ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz):

Mercury plus 400 spectrometer (Varian); δ in ppm related to tetramethylsilane; coupling constants are given with 0.5 Hz resolution. Where necessary, the assignment of the signals in the ^{1}H NMR and ^{13}C NMR spectra was performed using ^{1}H-^{1}H and ^{1}H-^{13}C COSEY NMR spectra as well as NOE (nuclear Overhauser effect) difference spectroscopy. IR: IR Prestige-21(Shimadzu). HRMS: MicrOTOF-QII (Bruker). HPLC methods for the determination of product purity: Method 1: Merck Hitachi Equipment; UV detector: L-7400; autosampler: L-7200; pump: L-7100; degasser: L-7614; column: LiChrospher® 60 RP-select B (5 µm); LiCroCART® 250-4 mm cartridge; flow rate: 1.00 mL/min; injection volume: 5.0 µL; detection at λ = 210 nm for 30 min; solvents: A: water with 0.05 % (V/V) trifluoroacetic acid; B: acetonitrile with 0.05 % (V/V) trifluoroacetic acid: gradient elution: (A %): 0 – 4 min: 90 % , 4 – 29 min: gradient from 90 % to 0 %, 29 – 31 min: 0 %, 31 – 31.5 min: gradient from 0 % to 90 %, 31.5 – 40 min: 90 %. Method 2: Merck Hitachi Equipment; UV detector: L-7400; pump: L-6200A; column: phenomenex Gemini® 5 µm C6-Phenyl 110 Å; LC Column 250 x 4.6 mm; flow rate: 1.00 mL/min; injection volume: 5.0 µL; detection at λ = 254 nm for 20 min; solvents: A: acetonitrile : 10 mM ammonium formate = 10 : 90 with 0.1 % formic acid; B: acetonitrile : 10 mM ammonium formate = 90 : 10 with 0.1 % formic acid; gradient elution: (A %): 0 – 5 min: 100 % , 5 – 15 min: gradient from 100 % to 0 %, 15 – 20 min: 0 %, 20 – 22 min: gradient from 0 % to 100 %, 22 – 30 min: 100 %.

(3a*S*,6*R*,6a*S*)-6-((*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl)-4-(3-iodophenyl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-ol (5b)

Under N_2 atmosphere a 1.6 M solution of *n*-butyllithium in hexanes (2.0 mL, 3.2 mmol) was added to a solution of 1,3-diiodobenzene (2.97 g, 9 mmol) in THF (40

mL). After stirring at -78 °C for 15 min, a solution of **4** (775 mg, 3 mmol) in THF (20 mL) was added dropwise and the mixture was stirred for additional 30 min at -78 °C. Then the mixture was allowed to warm to room temperature and a saturated aqueous solution of $NaHCO_3$ was added. The mixture was extracted with CH_2Cl_2 (3×), the combined organic layers were dried (Na_2SO_4), filtered and the solvent was removed in vacuo. The residue was purified by flash column chromatography (4 cm, 30 mL, *n*-hexane/ethyl acetate = 8/2, R_f = 0.23) to give **5b** as colorless oil (1.25 g, 2.70 mmol, 90%). $[\alpha]_D^{20}$ = +40.4 (1.0; CH_2Cl_2); ^{1}H NMR (DMSO-D_6): δ 1.16 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 1.30 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 3.95 (dd, *J* = 8.4/5.8 Hz, 1 H, OCHCH_2O 6-H), 4.07 (dd, *J* = 8.4/6.5 Hz, 1H, OCHCH_2O), 4.20 (dd, *J* = 6.0/3.8 Hz, 1H, 6-H), 4.39 (q, *J* = 6.1 Hz, 1H, OC*H*CH_2O), 4.46 (d, *J* = 5.8 Hz, 1H, 3a-H), 4.85 (dd, *J* = 5.8/3.8 Hz, 1H, 6a-H), 6.77 (s, 1H, O*H*), 7.15 (t, *J* = 7.8 Hz, 1H, 5'-$H_{3\text{-iodophenyl}}$), 7.44 – 7.47 (m, 1H, 6'-$H_{3\text{-iodophenyl}}$), 7.64 – 7.67 (m, 1H4'-$H_{3\text{-iodophenyl}}$), 7.75 – 7.77 (m, 1H, 2'-$H_{3\text{-iodophenyl}}$,); ^{13}C-NMR (DMSO-D_6): δ 24.0 (1C, C(CH_3)$_2$), 25.2 (1C, C(CH_3)$_2$), 25.4 (1C, C(CH_3)$_2$), 26.6 (1C, C(CH_3)$_2$), 65.8 (1C, OCHCH_2O), 73.0 (1C, O$CHCH_2$O), 78.1 (1C, C-6), 79.9 (1C, C-6a), 86.2 (1C, C-3a), 93.6 (1C, C-3'$_{3\text{-iodophenyl}}$), 104.4 (1C, C-4), 107.9 (1C, $C(CH_3)_2$), 111.5 (1C, $C(CH_3)_2$), 126.5 (1C, C-6'$_{3\text{-iodophenyl}}$), 129.6 (1C, C-5'$_{3\text{-iodophenyl}}$), 135.8 (1C, C-4'$_{3\text{-iodophenyl}}$), 136.4 (1C, C-2'$_{3\text{-iodophenyl}}$), 142.8 (1C, C-1'$_{3\text{-iodophenyl}}$); IR (neat): ν [cm^{-1}] = 3362, 2986, 2937, 1372, 1244, 1208, 1040, 844, 698; HRMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{18}H_{23}IO_6Na$, 485.0432; found, 485.0434; HPLC (method 1): t_R = 20.2 min, purity 97.5%.

(3a*S*,6*R*,6a*S*)-4-(4-Bromophenyl)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-ol (5c)

Under N_2 atmosphere a 1.6 M solution of *n*-butyllithium in hexanes (2.0 mL, 3.2 mmol) was added to a solution of 1,4-dibromobenzene (2.83 g, 12 mmol) in THF (40 mL). After stirring at -78 °C for 15 min, a solution of **4** (775 mg, 3 mmol) in THF (20 mL) was added dropwise and the mixture was stirred for additional 30 min at -78 °C. Then the mixture was allowed to warm to room temperature and a saturated aqueous solution of $NaHCO_3$ was added. The mixture was extracted with CH_2Cl_2 (3×), the combined organic layers were dried (Na_2SO_4), filtered and the solvent was removed in vacuo. The residue was purified by flash column chromatography (4 cm, 30 mL, *n*-hexane/ethyl acetate = 8/2, R_f = 0.23) to give **5c** as colorless solid (1.1 g, 2.65 mmol, 88%). m.p.: 137 °C; $[\alpha]_D^{20}$ = +64.9 (5.0; CH_2Cl_2); ^{1}H NMR (DMSO-D_6): δ 1.15 (s, 3H, C*H*$_3$), 1.24 (s, 3H, C*H*$_3$), 1.30 (s, 3H, C*H*$_3$), 1.35 (s, 3H, C*H*$_3$), 3.96 (dd, *J* = 8.2/6.1 Hz, 1 H, OCHC*H*$_2$O), 4.05 (dd, *J* = 8.2/6.5 Hz, 1H, OCHC*H*$_2$O), 4.22 (dd, *J* = 5.7/4.0 Hz, 1H, 6-H), 4.39 (q, *J* = 6.1 Hz, 1H, OC*H*CH$_2$O), 4.46 (d, *J* = 5.7 Hz, 1H, 3a-H), 4.86 (dd, *J* = 5.7/4.0 Hz, 1H, 6a-H), 6.77 (s, 1H, O*H*), 7.36 – 7.40 (d, *J* = 8.4 Hz, 2H, 2'-H$_{4\text{-bromophenyl}}$, 6'-H$_{4\text{-bromophenyl}}$), 7.50 – 7.55 (d, *J* = 8.4 Hz, 2H, 3'-H$_{4\text{-bromophenyl}}$, 5'-H$_{4\text{-bromophenyl}}$); ^{13}C NMR (DMSO-D_6): δ 24.0 (1C, C(*C*H$_3$)$_2$), 25.3 (1C, C(*C*H$_3$)$_2$), 25.4 (1C, C(*C*H$_3$)$_2$), 26.6 (1C, C(*C*H$_3$)$_2$), 65.7 (1C, OCH*C*H$_2$O), 73.1 (1C, O*C*HCH$_2$O), 78.0 (1C, C-6), 79.9 (1C, C-6a), 86.1 (1C, C-3a), 104.8 (1C, C-4), 107.8 (1C, *C*(CH$_3$)$_2$), 111.5 (1C, *C*(CH$_3$)$_2$), 121.2 (1C, C-4'$_{4\text{-bromophenyl}}$), 129.3 (2C, C-2'$_{4\text{-bromophenyl}}$, C-6'$_{4\text{-bromophenyl}}$), 130.2 (2C, C-3'$_{4\text{-bromophenyl}}$, C-5'$_{4\text{-bromophenyl}}$), 139.8 (1C, C-1'$_{4\text{-bromophenyl}}$); IR (neat): ν [cm^{-1}] = 3366, 2986, 2938, 1374, 1258, 1064, 1023, 1009, 849, 826; HRMS (*m*/*z*): [M+Na]$^+$ calcd for $C_{18}H_{23}{}^{79}BrO_6Na$, 437.0570; found, 437.0562; HPLC (method 1): t_R = 20.0 min, purity 96.4%.

(3a*S*,6*R*,6a*S*)-4-(3-Bromophenyl)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-ol (5d)

Under N_2 atmosphere a 1.6 M solution of *n*-butyllithium in hexanes (2.0 mL, 3.2 mmol) was added to a solution of 1,3-dibromobenzene (1.88 g, 8 mmol) in THF (40 mL). After stirring at -78 °C for 15 min, a solution of **4** (775 mg, 3 mmol) in THF (20 mL) was added dropwise and the mixture was stirred for additional 30 min at -78 °C. Then the mixture was allowed to warm to room temperature and a saturated aqueous solution of $NaHCO_3$ was added. The mixture was extracted with CH_2Cl_2 (3×), the combined organic layers were dried (Na_2SO_4), filtered and the solvent was removed in vacuo. The residue was purified by flash column chromatography (4 cm, 30 mL, *n*-hexane/ethyl acetate = 8/2, R_f = 0.23) to give **5d** as colorless oil (1.2 g, 2.89 mmol, 96%). $[\alpha]_D^{20}$ = +34.7 (1.2; CH_2Cl_2); ^{1}H NMR (DMSO-D_6): δ 1.16 (s, 3H, C*H*$_3$), 1.25 (s, 3H, C*H*$_3$), 1.30 (s, 3H, C*H*$_3$), 1.36 (s, 3H, C*H*$_3$), 3.96 (dd, *J* = 8.3/5.8 Hz, 1 H, OCHC*H*$_2$O), 4.07 (dd, *J* = 8.3/6.6 Hz, 1H, OCHC*H*$_2$O), 4.21 (dd, *J* = 6.0/3.8 Hz, 1H, 6-H), 4.39 (q, *J* = 6.1 Hz, 1H, OC*H*CH$_2$O), 4.48 (d, *J* = 5.8 Hz, 1H, 3a-H), 4.86 (dd, *J* = 5.8/3.8 Hz, 1H, 6a-H),6.81 (s, 1H, O*H*), 7.31 (t, *J* = 7.8 Hz, 1H, 5'-H$_{3\text{-bromophenyl}}$), 7.43 – 7.46 (m, 1H, 6'-H$_{3\text{-bromophenyl}}$), 7.48 – 7.51 (m, 1H, 4'-H$_{3\text{-bromophenyl}}$), 7.55 – 7.57 (m, 1H, 2'-H$_{3\text{-bromophenyl}}$); ^{13}C NMR (DMSO-D_6): δ 24.0 (1C, C(*C*H$_3$)$_2$), 25.2 (1C, C(*C*H$_3$)$_2$), 25.4 (1C, C(*C*H$_3$)$_2$), 26.6 (1C, C(*C*H$_3$)$_2$), 65.8 (1C, OCH*C*H$_2$O), 73.0 (1C, OC*H*CH$_2$O), 78.1 (1C, C-6), 79.9 (1C, C-6a), 86.2 (1C, C-3a), 104.5 (1C, C-4), 107.9 (1C, *C*(CH$_3$)$_2$), 111.5 (1C, *C*(CH$_3$)$_2$), 120.6 (1C, C-3'$_{3\text{-bromophenyl}}$), 126.2 (1C, C-6'$_{3\text{-bromophenyl}}$), 129.5 (1C, C-4'$_{3\text{-bromophenyl}}$), 129.9 (1C, C-5'$_{3\text{-bromophenyl}}$), 130.6 (1C, C-2'$_{3\text{-bromophenyl}}$), 143.0 (1C, C-1'$_{3\text{-bromophenyl}}$); IR (neat): ν [cm^{-1}] = 3368, 2986, 2936, 1372, 1246, 1208, 1040, 845, 698; HRMS (*m*/*z*): [M+Na]$^+$ calcd for $C_{18}H_{23}{}^{79}BrO_6Na$, 437.0570; found, 437.0566; HPLC (method 1): t_R = 19.9 min, purity 98.5%.

(3a*S*,4*R*,6*S*,6a*R*)-4-((*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl)-6-(3-iodophenyl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxole (6b)

Under N_2 atmosphere Et_3SiH (0.52 mL, 377 mg, 3.2 mmol) was added to a solution of **5b** (1.25 g, 2.7 mmol) and $BF_3{\cdot}Et_2O$ (0.34 mL, 384 mg, 2.7 mmol) in acetonitrile (30 mL) at -40 °C. The mixture was stirred at -40 °C for 1 h, then a saturated aqueous solution of K_2CO_3 (3 mL) was added and the mixture was stirred for 1 h at ambient temperature. Then water was added and the mixture was extracted with ethyl acetate (3×). The combined organic layers were dried (Na_2SO_4), filtered and the solvent was removed in vacuo. The residue was purified by flash column chromatography (4 cm, 30 mL, *n*-hexane/ethyl acetate = 8/2 → 1/2) to give **6b** (*n*-hexane/ethyl acetate = 8/2, R_f = 0.34) as colorless oil (320 mg, 0.72 mmol, 27%) and **7b** (*n*-hexane/ethyl acetate = 1/2, R_f = 0.20) as colorless solid (430 mg, 1.1 mmol, 39%).

6b: $[\alpha]_D^{20}$ = +63.8 (3.3; CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 1.29 (s, 3H, C*H*$_3$), 1.41 (s, 3H, C*H*$_3$), 1.45 (s, 3H, C*H*$_3$), 1.48 (s, 3H, C*H*$_3$), 3.67 (dd, *J* = 7.5/3.7 Hz, 1H, 4-H), 4.10 – 4.19 (m, 2H, OCHC*H*$_2$O), 4.49 – 4.56 (m, 2H, OC*H*CH$_2$O, 6-H), 4.78 (dd, *J* = 6.0/3.7 Hz, 1H, 6a-H), 4.86 (dd, *J* = 6.0/3.7 Hz, 1H, 3a-H), 7.08 (t, *J* = 7.8 Hz, 1H, 5'-H$_{3\text{-iodophenyl}}$), 7.30 – 7.33 (m, 1H, 6'-H$_{3\text{-iodophenyl}}$), 7.60 – 7.64 (m, 1H, 4'-H$_{3\text{-iodophenyl}}$), 7.69 – 7.71 (m, 1H, 2'-H$_{3\text{-iodophenyl}}$,); ^{13}C NMR ($CDCl_3$): δ 24.4 (1C, C(*C*H$_3$)$_2$), 25.4 (1C, C(*C*H$_3$)$_2$), 25.6 (1C, C(*C*H$_3$)$_2$), 27.1 (1C, C(*C*H$_3$)$_2$), 67.2 (1C, OCH*C*H$_2$O), 73.3 (1C, O*C*HCH$_2$O), 80.9 (1C, C-3a), 81.7 (1C, C-4), 82.2 (1C, C-6a), 83.0 (1C, C-6), 94.0 (1C, C-3'$_{3\text{-iodophenyl}}$), 109.3 (1C, *C*(CH$_3$)$_2$), 112.9 (1C, *C*(CH$_3$)$_2$), 126.8 (1C, C-6'$_{3\text{-iodophenyl}}$), 129.8 (1C, C-5'$_{3\text{-iodophenyl}}$), 136.6 (1C, C-4'$_{3\text{-iodophenyl}}$), 137.0 (1C, C-2'$_{3\text{-iodophenyl}}$), 137.9 (1C, C-1'$_{3\text{-iodophenyl}}$); IR (neat): ν [cm^{-1}] = 2984, 2934, 2870, 1736,

1567, 1371, 1206, 1065, 842, 746; HRMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{18}H_{23}IO_5Na$, 469.0482; found, 469.0481; HPLC (method 1): t_R = 21.6 min, purity 97.9%.

(3a*R*,4*S*,6*R*,6a*S*)-4-(4-Bromophenyl)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxole (6c)

Under N_2 atmosphere Et_3SiH (0.40 mL, 286 mg, 2.46 mmol) was added to a solution of **5c** (850 mg, 2.05 mmol) and $BF_3{\cdot}Et_2O$ (0.26 mL, 290 mg, 2.05 mmol) in acetonitrile (30 mL) at -40 °C. The mixture was stirred at -40 °C for 1 h, then a saturated aqueous solution of K_2CO_3 (3 mL) was added and the mixture was stirred for 1 h at ambient temperature. Then water was added and the mixture was extracted with ethyl acetate (3×). The combined organic layers were dried (Na_2SO_4), filtered and the solvent was removed in vacuo. The residue was purified by flash column chromatography (4 cm, 30 mL, *n*-hexane/ethyl acetate = 8/2 → 1/2) to give **6c** (*n*-hexane/ethyl acetate = 8/2, R_f = 0.22) as colorless solid (245 mg, 0.61 mmol, 30%) and **7c** (*n*-hexane/ethyl acetate = 1/2, R_f = 0.14) as colorless solid (113 mg, 0.31 mmol, 15%).

6c: m.p.: 112 °C; $[\alpha]_D^{20}$ = +83.6 (11.4; CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 1.28 (s, 3H, C*H*$_3$), 1.41 (s, 3H, C*H*$_3$), 1.43 (s, 3H, C*H*$_3$), 1.47 (s, 3H, C*H*$_3$), 3.70 (dd, *J* = 7.2/3.7 Hz, 1H, 6-H), 4.11 – 4.18 (m, 2H, OCHC*H*$_2$O), 4.51 (dt, *J* = 7.2/5.6 Hz, 1H, OC*H*CH$_2$O), 4.57 (d, *J* = 3.7 Hz, 1H, 4-H), 4.79 (dd, *J* = 6.1/3.7 Hz, 1H, 3a-H), 4.86 (dd, *J* = 6.1/3.7 Hz, 1H, 6a-H), 7.22 – 7.26 (m, 2H, 2'-H$_{4\text{-bromophenyl}}$, 6'-H$_{4\text{-bromophenyl}}$), 7.45 – 7.49 (m, 2H, 3'-H$_{4\text{-bromophenyl}}$, 5'-H$_{4\text{-bromophenyl}}$); ^{13}C NMR ($CDCl_3$): δ 24.3 (1C, C(*C*H$_3$)$_2$), 25.4 (1C, C(*C*H$_3$)$_2$), 25.7 (1C, C(*C*H$_3$)$_2$), 27.1 (1C, C(*C*H$_3$)$_2$), 67.1 (1C, OCH*C*H$_2$O), 73.4 (1C, O*C*HCH$_2$O), 80.9 (1C, C-6a), 81.7 (1C, C-6), 82.2 (1C, C-3a), 83.2 (1C, C-4), 109.2

(1C, *C*(CH_3)$_2$), 112.8 (1C, *C*(CH_3)$_2$), 122.0 (1C, C-4'$_{4\text{-bromophenyl}}$), 129.2 (2C, C-2'$_{phenyl}$, C-6'$_{phenyl}$), 131.2 (2C, C-3'$_{phenyl}$, C-5'$_{phenyl}$), 134.7 (1C, C-1'$_{4\text{-bromophenyl}}$); IR (neat): ν [cm^{-1}] = 2991, 2939, 2878, 1488, 1371, 1207, 1051, 1010, 818, 732; HRMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{18}H_{23}{}^{79}BrO_5Na$, 423.0602; found, 423.0616; HPLC (method 1): t_R = 21.7 min, purity 99.3%.

(3a*R*,4*S*,6*R*,6a*S*)-4-(3-Bromophenyl)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxole (6d)

Under N_2 atmosphere Et_3SiH (0.56 mL, 403 mg, 3.47 mmol) was added to a solution of **5d** (1.2 g, 2.89 mmol) and $BF_3{\cdot}Et_2O$ (0.36 mL, 410 mg, 2.89 mmol) in acetonitrile (30 mL) at -40 °C. The mixture was stirred at -40 °C for 1 h, then a saturated aqueous solution of K_2CO_3 (3 mL) was added and the mixture was stirred for 1 h at ambient temperature. Then water was added and the mixture was extracted with ethyl acetate (3×). The combined organic layers were dried (Na_2SO_4), filtered and the solvent was removed in vacuo. The residue was purified by flash column chromatography (4 cm, 30 mL, *n*-hexane/ethyl acetate = 8/2 → 1/1) to give **6d** (*n*-hexane/ethyl acetate = 8/2, R_f = 0.25) as colorless oil (350 mg, 0.88 mmol, 30%) and **7d** (*n*-hexane/ethyl acetate = 1/1, R_f = 0.15) as colorless oil (490 mg, 1.36 mmol, 47%).

6d: $[\alpha]_D^{20}$ = +67.4 (1.9; CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 1.28 (s, 3H, C*H*$_3$), 1.41 (s, 3H, C*H*$_3$), 1.44 (s, 3H, C*H*$_3$), 1.47 (s, 3H, C*H*$_3$), 3.68 (dd, *J* = 7.5/3.7 Hz, 1H, 6-H), 4.11 – 4.18 (m, 2H, OCHC*H*$_2$O), 4.49 – 4.54 (m, 1H, OC*H*CH_2O), 4.57 (d, *J* = 3.9 Hz, 1H, 4-H), 4.79 (dd, *J* = 6.0/3.9 Hz, 1H, 3a-H), 4.86 (dd, *J* = 6.0/3.7 Hz, 1H, 6a-H), 7.20 (t, *J* = 7.8 Hz, 1H, 5'-H$_{3\text{-bromophenyl}}$), 7.26 – 7.29 (m, 1H, 6'-H$_{3\text{-bromophenyl}}$), 7.40 – 7.43 (m,

1H, 4'-$H_{3\text{-bromophenyl}}$), 7.50 – 7.52 (m, 1H, 2'-$H_{3\text{-bromophenyl}}$); ^{13}C NMR ($CDCl_3$): δ 24.4 (1C, C(CH_3)$_2$), 25.4 (1C, C(CH_3)$_2$), 25.6 (1C, C(CH_3)$_2$), 27.1 (1C, C(CH_3)$_2$), 67.1 (1C, OCHCH_2O), 73.3 (1C, OCHCH_2O), 80.9 (1C, C-6a), 81.7 (1C, C-6), 82.3 (1C, C-3a), 83.0 (1C, C-4), 109.3 (1C, C(CH$_3$)$_2$), 112.8 (1C, C(CH$_3$)$_2$), 122.2 (1C, C-3'$_{3\text{-bromophenyl}}$), 126.1 (1C, C-6'$_{3\text{-bromophenyl}}$), 129.6 (1C, C-4'$_{3\text{-bromophenyl}}$), 130.7 (1C, C-5'$_{3\text{-bromophenyl}}$), 131.1 (1C, C-2'$_{3\text{-bromophenyl}}$), 138.0 (1C, C-1'$_{3\text{-bromophenyl}}$); IR (neat): ν [cm^{-1}] = 2986, 2934, 2871, 1571, 1476, 1371, 1205, 1066, 842, 784, 746; HRMS (*m*/*z*): [M+Na]$^+$ calcd for $C_{18}H_{23}{}^{79}BrO_5Na$, 423.0602; found, 423.0595; HPLC (method 1): t_R = 21.1 min, purity 99.4%.

(*R*)-1-((3a*S*,4*R*,6*S*,6a*R*)-6-(3-Iodophenyl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)ethane-1,2-diol (7b)

1: *p*-Toluenesulfonic acid monohydrate (13 mg, 0.07 mmol) was added to a solution of **6b** (320 mg, 0.72 mmol) in methanol (20 mL). The mixture was stirred at ambient temperature for 4 h. Then a saturated aqueous solution of $NaHCO_3$ was added and the mixture was extracted with ethyl acetate (3×). The combined organic layers were dried (Na_2SO_4), filtered and the solvent was removed in vacuo. The residue was purified by flash column chromatography (2 cm, 10 mL, *n*-hexane/ethyl acetate = 1/2, R_f = 0.20) to give **7b** as colorless solid (130 mg, 0.32 mmol, 45%).

2: Under N_2 atmosphere Et_3SiH (1.2 mL, 884 mg, 7.6 mmol) was added to a solution of **5b** (2.9 g, 6.3 mmol) and $BF_3{\cdot}Et_2O$ (0.81 mL, 894 mg, 6.3 mmol) in acetonitrile (50 mL) at -40 °C. The mixture was stirred at -40 °C for 1 h, then a saturated aqueous solution of K_2CO_3 (7 mL) was added and the mixture was stirred for 1 h at ambient temperature. Then water was added and the mixture was extracted with ethyl acetate

(3×). The combined organic layers were dried (Na_2SO_4), filtered and the solvent was removed in vacuo. The residue was dissolved in methanol (30 mL) and *p*-toluenesulfonic acid monohydrate (240 mg, 1.3 mmol) was added. The mixture was stirred at ambient temperature for 16 h. Then a saturated aqueous solution of $NaHCO_3$ was added and the mixture was extracted with ethyl acetate (3×). The combined organic layers were dried (Na_2SO_4), filtered and the solvent was removed in vacuo. The residue was purified by flash column chromatography (6 cm, 50 mL, *n*-hexane/ethyl acetate = 1/2, R_f = 0.20) to give **7b** as colorless solid (1.8 g, 4.4 mmol, 71%).

m.p.: 67 °C; $[\alpha]_D^{20}$ = +58.1 (2.9; CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 1.29 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 3.69 (dd, *J* = 8.2/4.0 Hz, 1H, 4-H), 3.78 (dd, *J* = 11.5/5.7 Hz, 1H, HOCHCH_2OH), 3.93 (dd, *J* = 11.5/3.3 Hz, 1H, HOCHCH_2OH), 4.12 – 4.19 (m, 1H, HOC*H*CH_2OH), 4.54 (d, *J* = 3.7 Hz, 1H, 6-H), 4.78 (dd, *J* = 6.0/3.7 Hz, 1H, 6a-H), 4.92 (dd, *J* = 6.0/4.0 Hz, 1H, 3a-H), 7.08 (t, *J* = 7.8 Hz, 1H, 5'-$H_{3\text{-iodophenyl}}$), 7.29 – 7.34 (m, 1H, 6'-$H_{3\text{-iodophenyl}}$), 7.60 – 7.64 (m, 1H, 4'-$H_{3\text{-iodophenyl}}$), 7.70 – 7.72 (m, 1H, 2'-$H_{3\text{-iodophenyl}}$,); ^{13}C NMR ($CDCl_3$): δ 24.6 (1C, C(CH_3)$_2$), 25.8 (1C, C(CH_3)$_2$), 64.8 (1C, HOCHCH_2OH), 70.4 (1C, HO*C*HCH_2OH), 81.0 (1C, C-4), 81.5 (1C, C-3a), 82.1 (1C, C-6a), 82.8 (1C, C-6), 94.1 (1C, C-3'$_{3\text{-iodophenyl}}$), 113.0 (1C, *C*(CH_3)$_2$), 126.8 (1C, C-6'$_{3\text{-iodophenyl}}$), 129.9 (1C, C-5'$_{3\text{-iodophenyl}}$), 136.6 (1C, C-4'$_{3\text{-iodophenyl}}$), 137.1 (1C, C-2'$_{3\text{-iodophenyl}}$), 137.8 (1C, C-1'$_{3\text{-iodophenyl}}$); IR (neat): ν [cm^{-1}] = 3397, 2984, 2935, 2866, 1566, 1373, 1205, 1083, 1018, 883, 746; HRMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{15}H_{19}IO_5Na$, 429.0169; found, 429.0177; HPLC (method 1): t_R = 17.1 min, purity 99.2%.

(*R*)-1-((3a*S*,4*R*,6*S*,6a*R*)-6-(4-Bromophenyl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)ethane-1,2-diol (7c)

1: *p*-Toluenesulfonic acid monohydrate (12 mg, 0.06 mmol) was added to a solution of **6c** (245 mg, 0.61 mmol) in methanol (20 mL). The mixture was stirred at ambient temperature for 4 h. Then a saturated aqueous solution of $NaHCO_3$ was added and the mixture was extracted with ethyl acetate (3×). The combined organic layers were dried (Na_2SO_4), filtered and the solvent was removed in vacuo. The residue was purified by flash column chromatography (2 cm, 10 mL, *n*-hexane/ethyl acetate = 1/2, R_f = 0.14) to give **7c** as colorless solid (192 mg, 0.53 mmol, 87%).

2: Under N_2 atmosphere Et_3SiH (0.51 mL, 370 mg, 3.18 mmol) was added to a solution of **5c** (1.1 g, 2.65 mmol) and $BF_3{\cdot}Et_2O$ (0.33 mL, 376 mg, 2.65 mmol) in acetonitrile (30 mL) at -40 °C. The mixture was stirred at -40 °C for 1 h, then a saturated aqueous solution of K_2CO_3 (3 mL) was added and the mixture was stirred for 1 h at ambient temperature. Then water was added and the mixture was extracted with ethyl acetate (3×). The combined organic layers were dried (Na_2SO_4), filtered and the solvent was removed in vacuo. The residue was dissolved in methanol (30 mL) and *p*-toluenesulfonic acid monohydrate (50 mg, 0.26 mmol) was added. The mixture was stirred at ambient temperature for 4 h. Then a saturated aqueous solution of $NaHCO_3$ was added and the mixture was extracted with ethyl acetate (3×). The combined organic layers were dried (Na_2SO_4), filtered and the solvent was removed in vacuo. The residue was purified by flash column chromatography (4 cm, 30 mL, *n*-hexane/ethyl acetate = 1/2, R_f = 0.14) to give **7c** as colorless solid (600 mg, 1.67 mmol, 63%).

m.p.: 140 °C; $[\alpha]_D^{20}$ = +74.1 (6.4; CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 1.29 (s, 3H, C*H*$_3$), 1.45 (s, 3H, C*H*$_3$), 3.71 (dd, *J* = 8.0/4.1 Hz, 1H, 4-H), 3.80 (dd, *J* = 11.5/5.7 Hz, 1H,

HOCHC*H*$_2$OH), 3.92 (dd, *J* = 11.5/3.5 Hz, 1H, HOCHC*H*$_2$OH), 4.16 (ddd, *J* = 8.0/5.7/3.5 Hz, 1H, HOC*H*CH$_2$OH), 4.59 (d, *J* = 3.7 Hz, 1H, 6-H), 4.80 (dd, *J* = 6.0/3.7 Hz, 1H, 6a-H), 4.93 (dd, *J* = 6.0/4.1 Hz, 1H, 3a-H), 7.23 – 7.26 (m, 2H, 2'-H$_{4\text{-bromophenyl}}$, 6'-H$_{4\text{-bromophenyl}}$), 7.46 – 7.49 (m, 2H, 3'-H$_{4\text{-bromophenyl}}$, 5'-H$_{4\text{-bromophenyl}}$); ^{13}C NMR ($CDCl_3$): δ 24.5 (1C, C(*C*H$_3$)$_2$), 25.8 (1C, C(*C*H$_3$)$_2$), 64.8 (1C, HOCH*C*H$_2$OH), 70.4 (1C, HO*C*HCH$_2$OH), 81.0 (1C, C-4), 81.5 (1C, C-3a), 82.1 (1C, C-6a), 83.1 (1C, C-6), 112.9 (1C, *C*(CH$_3$)$_2$), 122.1 (1C, C-4'$_{4\text{-bromophenyl}}$), 129.2 (2C, C-2'$_{4\text{-bromophenyl}}$, C-6'$_{4\text{-bromophenyl}}$), 131.3 (2C, C-3'$_{4\text{-bromophenyl}}$, C-5'$_{4\text{-bromophenyl}}$), 134.5(1C, C-1'$_{4\text{-bromophenyl}}$); IR (neat): ν [cm^{-1}] = 3454, 2975, 2921, 2861, 1487, 1380, 1208, 1012, 821, 747; HRMS (*m*/*z*): [M+Na]$^+$ calcd for $C_{15}H_{19}{}^{79}BrO_5Na$, 381.0308; found, 381.0315; HPLC (method 1): t_R = 16.5 min, purity 98.7%.

(*R*)-1-((3a*S*,4*R*,6*S*,6a*R*)-6-(3-Bromophenyl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)ethane-1,2-diol (7d)

p-Toluenesulfonic acid monohydrate (17 mg, 0.09 mmol) was added to a solution of **6d** (350 mg, 0.88 mmol) in methanol (20 mL). The mixture was stirred at ambient temperature for 4 h. Then a saturated aqueous solution of $NaHCO_3$ was added and the mixture was extracted with ethyl acetate (3×). The combined organic layers were dried (Na_2SO_4), filtered and the solvent was removed in vacuo. The residue was purified by flash column chromatography (2 cm, 10 mL, *n*-hexane/ethyl acetate = 1/1, R_f = 0.15) to give **7d** as colorless oil (100 mg, 0.28 mmol, 32%). $[\alpha]_D^{20}$ = +54.3 (1.6; CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 1.29 (s, 3H, C*H*$_3$), 1.45 (s, 3H, C*H*$_3$), 3.71 (dd, *J* = 8.0/3.9 Hz, 1H, 4-H), 3.80 (dd, *J* = 11.4/5.7 Hz, 1H, HOCHC*H*$_2$OH), 3.93 (dd, *J* = 11.4/3.3 Hz, 1H, HOCHC*H*$_2$OH), 4.14 – 4.20 (m, 1H, HOC*H*CH$_2$OH), 4.59 (d, *J* = 3.5 Hz, 1H, 6-H), 4.81 (dd, *J* = 5.8/3.5 Hz, 1H, 6a-H), 4.93 (dd, *J* = 5.8/3.9 Hz, 1H, 3a-H),

7.21 (t, *J* = 7.8 Hz, 1H, 5'-$H_{3\text{-bromophenyl}}$), 7.25 – 7.30 (m, 1H, 6'-$H_{3\text{-bromophenyl}}$), 7.40 – 7.44 (m, 1H, 4'-$H_{3\text{-bromophenyl}}$), 7.50 – 7.53 (m, 1H, 2'-$H_{3\text{-bromophenyl}}$); ^{13}C NMR ($CDCl_3$): δ 24.5 (1C, C(CH_3)$_2$), 25.6 (1C, C(CH_3)$_2$), 64.7 (1C, HOCHCH_2OH), 70.4 (1C, HOCHCH_2OH), 81.0 (1C, C-4), 81.4 (1C, C-3a), 82.1 (1C, C-6a), 82.9 (1C, C-6), 113.0 (1C, C(CH_3)$_2$), 122.3 (1C, C-3'$_{3\text{-bromophenyl}}$), 126.0 (1C, C-6'$_{3\text{-bromophenyl}}$), 129.6 (1C, C-4'$_{3\text{-bromophenyl}}$), 130.7 (1C, C-5'$_{3\text{-bromophenyl}}$), 131.1 (1C, C-2'$_{3\text{-bromophenyl}}$), 137.8 (1C, C-1'$_{3\text{-bromophenyl}}$); IR (neat): ν [cm^{-1}] = 3383, 2979, 2935, 2871, 1570, 1476, 1373, 1206, 1083, 1019, 885, 747; HRMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{15}H_{19}{}^{79}BrO_5Na$, 381.0308; found, 381.0301; HPLC (method 1): t_R = 16.3 min, purity 99.4%.

(3a*R*,4*S*,6*S*,6a*R*)-Methyl 6-(3-iodophenyl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxole-4-carboxylate (8b)

An oxidant solution (20 mL), which was prepared by dissolving H_5IO_6 (11.4 g, 50 mmol) and CrO_3 (23 mg, 0.23 mmol) in wet acetonitrile (114 mL, 0.75% water V/V), was added to a solution of **7b** (1.4 g, 3.4 mmol) in acetonitrile (20 mL). The mixture was stirred at ambient temperature for 3 h. The reaction was quenched by the addition of ethylene glycol. Then hydrochloric acid (1 M) was added and the mixture was extracted with ethyl acetate (3×). The combined organic layers were dried (Na_2SO_4), filtered and the solvent was removed in vacuo. The residue was dissolved in methanol (30 mL) and *p*-toluenesulfonic acid monohydrate (65 mg, 0.34 mmol) was added. The mixture was heated to reflux for 16 h. Then the solvent was removed in vacuo and the residue was purified by flash column chromatography (4 cm, 30 mL, *n*-hexane/ethyl acetate = 8/2 → 1/1) to give **8b** (*n*-hexane/ethyl acetate = 8/2, R_f = 0.14) as colorless solid (670 mg, 1.7 mmol, 49%) and **9b** (*n*-hexane/ethyl acetate = 1/1, R_f = 0.32) as colorless solid (390 mg, 1.1 mmol, 32%).

8b: m.p.: 132 °C; $[\alpha]_D^{20}$ = +33.0 (1.7; CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 1.27 (s, 3H, C*H*$_3$), 1.43 (s, 3H, C*H*$_3$), 3.85 (s, 3H, OC*H*$_3$), 4.38 (d, *J* = 4.5 Hz, 1H, 4-H), 4.60 (d, *J* = 3.6 Hz, 1H, 6-H), 4.80 (dd, *J* = 5.8/3.6 Hz, 1H, 6a-H), 5.08 (dd, *J* = 5.8/4.5 Hz, 1H, 3a-H), 7.10 (t, *J* = 7.8 Hz, 1H, 5'-H$_{3\text{-iodophenyl}}$), 7.43 – 7.47 (m, 1H, 6'-H$_{3\text{-iodophenyl}}$), 7.62 – 7.67 (m, 1H, 4'-H$_{3\text{-iodophenyl}}$), 7.78 – 7.81 (m, 1H, 2'-H$_{3\text{-iodophenyl}}$,); ^{13}C NMR ($CDCl_3$): δ 25.1 (1C, C(*C*H$_3$)$_2$), 25.8 (1C, C(*C*H$_3$)$_2$), 52.4 (1C, O*C*H$_3$), 80.8 (1C, C-4), 81.6 (1C, C-6a), 82.0 (1C, C-3a), 82.7 (1C, C-6), 94.0 (1C, C-3'$_{3\text{-iodophenyl}}$), 113.7 (1C, *C*(CH$_3$)$_2$), 127.0 (1C, C-6'$_{3\text{-iodophenyl}}$), 129.9 (1C, C-5'$_{3\text{-iodophenyl}}$), 136.6 (1C, C-4'$_{3\text{-iodophenyl}}$), 137.1 (1C, C-1'$_{3\text{-iodophenyl}}$), 137.3 (1C, C-2'$_{3\text{-iodophenyl}}$), 167.6 (1C, *C*=O); IR (neat): ν [cm^{-1}] = 2986, 2953, 1757, 1566, 1440, 1380, 1214, 1104, 1040, 863, 740; HRMS (*m*/*z*): [M+Na]$^+$ calcd for $C_{15}H_{17}IO_5Na$, 427.0013; found, 427.0010; HPLC (method 1): t_R = 19.6 min, purity 96.6%.

(3a*R*,4*S*,6*S*,6a*R*)-Methyl 6-(4-bromophenyl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxole-4-carboxylate (8c)

An oxidant solution (4.4 mL), which was prepared by dissolving H_5IO_6 (11.4 g, 50 mmol) and CrO_3 (23 mg, 0.23 mmol) in wet acetonitrile (114 mL, 0.75% water V/V), was added to a solution of **7c** (275 mg, 0.77 mmol) in acetonitrile (10 mL). The mixture was stirred at ambient temperature for 3 h. The reaction was quenched by the addition of ethylene glycol. Then hydrochloric acid (1 M) was added and the mixture was extracted with ethyl acetate (3×). The combined organic layers were dried (Na_2SO_4), filtered and the solvent was removed in vacuo. The residue was dissolved in methanol (20 mL) and *p*-toluenesulfonic acid monohydrate (15 mg, 0.08 mmol) was added. The mixture was heated to reflux for 16 h. Then the solvent was removed in vacuo and the residue was purified by flash column chromatography (2

cm, 10 mL, *n*-hexane/ethyl acetate = 8/2 → 1/1) to give **8c** (*n*-hexane/ethyl acetate = 8/2, R_f = 0.12) as colorless solid (80 mg, 0.22 mmol, 29%) and **9c** (*n*-hexane/ethyl acetate = 1/1, R_f = 0.19) as colorless solid (61 mg, 0.19 mmol, 25%).

8c: m.p.: 142 °C; $[\alpha]_D^{20}$ = +43.7 (0.7; CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 1.26 (s, 3H, C*H*$_3$), 1.42 (s, 3H, C*H*$_3$), 3.85 (s, 3H, OC*H*$_3$), 4.39 (d, *J* = 4.6 Hz, 1H, 4-H), 4.64 (d, *J* = 3.6 Hz, 1H, 6-H), 4.80 (dd, *J* = 5.9/3.6 Hz, 1H, 6a-H), 5.08 (dd, *J* = 5.9/4.6 Hz, 1H, 3a-H), 7.33 – 7.37 (m, 2H, 2'-H$_{4\text{-bromophenyl}}$, 6'-H$_{4\text{-bromophenyl}}$), 7.47 – 7.51 (m, 2H, 3'-H$_{4\text{-bromophenyl}}$, 5'-H$_{4\text{-bromophenyl}}$); ^{13}C NMR ($CDCl_3$): δ 25.0 (1C, C(*C*H$_3$)$_2$), 25.8 (1C, C(*C*H$_3$)$_2$), 52.3 (1C, O*C*H$_3$), 80.8 (1C, C-4), 81.7 (1C, C-6a), 82.0 (1C, C-3a), 82.9 (1C, C-6), 113.6 (1C, *C*(CH$_3$)$_2$), 122.3 (1C, C-4'$_{4\text{-bromophenyl}}$), 129.3 (2C, C-2'$_{4\text{-bromophenyl}}$, C-6'$_{4\text{-bromophenyl}}$), 131.3 (2C, C-3'$_{4\text{-bromophenyl}}$, C-5'$_{4\text{-bromophenyl}}$), 133.9 (1C, C-1'$_{4\text{-bromophenyl}}$), 167.7 (1C, *C*=O); IR (neat): ν [cm^{-1}] = 2986, 2939, 1754, 1489, 1438, 1383, 1213, 1100, 1074, 913, 818, 744; HRMS (*m*/*z*): [M+Na]$^+$ calcd for $C_{15}H_{17}{}^{79}BrO_5Na$, 379.0152; found, 379.0146; HPLC (method 1): t_R = 19.5 min, purity 98.7%.

(3a*R*,4*S*,6*S*,6a*R*)-Methyl 6-(3-bromophenyl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxole-4-carboxylate (8d)

An oxidant solution (9.4 mL), which was prepared by dissolving H_5IO_6 (11.4 g, 50 mmol) and CrO_3 (23 mg, 0.23 mmol) in wet acetonitrile (114 mL, 0.75% water V/V), was added to a solution of **7d** (590 mg, 1.64 mmol) in acetonitrile (20 mL). The mixture was stirred at ambient temperature for 3 h. The reaction was quenched by the addition of ethylene glycol. Then hydrochloric acid (1 M) was added and the mixture was extracted with ethyl acetate (3×). The combined organic layers were

dried (Na_2SO_4), filtered and the solvent was removed in vacuo. The residue was dissolved in methanol (20 mL) and *p*-toluenesulfonic acid monohydrate (31 mg, 0.16 mmol) was added. The mixture was heated to reflux for 16 h. Then the solvent was removed in vacuo and the residue was purified by flash column chromatography (3 cm, 20 mL, *n*-hexane/ethyl acetate = 8/2 → 1/1) to give **8d** (*n*-hexane/ethyl acetate = 8/2, R_f = 0.13) as colorless solid (70 mg, 0.20 mmol, 12%) and **9d** (*n*-hexane/ethyl acetate = 1/1, R_f = 0.27) as colorless solid (90 mg, 0.28 mmol, 17%).

8d: m.p.: 135 °C; $[\alpha]_D^{20}$ = +33.4 (2.0; CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 1.27 (s, 3H, C*H*$_3$), 1.43 (s, 3H, C*H*$_3$), 3.85 (s, 3H, OC*H*$_3$), 4.38 - 4.40 (m, 1H, 4-H), 4.62 – 4.65 (m, 1H, 6-H), 4.80 – 4.83 (m, 1H, 6a-H), 5.06 – 5.11 (m, 1H, 3a-H), 7.21 – 7.27 (m, 1H, 5'-$H_{3\text{-bromophenyl}}$), 7.38 – 7.46 (m, 2H, 4'-$H_{3\text{-bromophenyl}}$, 6'-$H_{3\text{-bromophenyl}}$), 7.60 – 7.63 (m, 1H, 2'-$H_{3\text{-bromophenyl}}$); ^{13}C NMR ($CDCl_3$): δ 25.1 (1C, C(*C*H_3)$_2$), 25.8 (1C, C(*C*H_3)$_2$), 52.3 (1C, O*C*H_3), 80.8 (1C, C-4), 81.6 (1C, C-6a), 82.0 (1C, C-3a), 82.8 (1C, C-6), 113.7 (1C, *C*(CH_3)$_2$), 122.3 (1C, C-3'$_{3\text{-bromophenyl}}$), 126.3 (1C, C-6'$_{3\text{-bromophenyl}}$), 129.7 (1C, C-4'$_{3\text{-bromophenyl}}$), 130.7 (1C, C-5'$_{3\text{-bromophenyl}}$), 131.3 (1C, C-2'$_{3\text{-bromophenyl}}$), 137.1 (1C, C-1'$_{3\text{-bromophenyl}}$), 167.6 (1C, *C*=O); IR (neat): ν [cm^{-1}] = 2986, 2932, 1748, 1438, 1375, 1205, 1100, 1071, 1033, 858, 741; HRMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{15}H_{17}{}^{79}BrO_5Na$, 379.0152; found, 379.0146; HPLC (method 1): t_R = 19.5 min, purity 99.4%.

(3a*R*,4*S*,6*S*,6a*R*)-Methyl 2,2-dimethyl-6-phenyl-tetrahydrofuro[3,4-d][1,3]dioxole-4-carboxylate (8e)

An oxidant solution (20 mL), which was prepared by dissolving H_5IO_6 (11.4 g, 50 mmol) and CrO_3 (23 mg, 0.23 mmol) in wet acetonitrile (114 mL, 0.75% water V/V), was added to a solution of **7e** (970 mg, 3.46 mmol) in acetonitrile (10 mL). The

mixture was stirred at ambient temperature for 2 h. After filtration on silica gel, the solvent was removed in vacuo. The crude product was dissolved in methanol (20 mL), chlorotrimethylsilane (0.9 mL, 761 mg, 7.0 mmol) was added and the mixture was heated to reflux for 60 h. Then the solvent was removed in vacuo and the residue was purified by flash column chromatography (4 cm, 30 mL, *n*-hexane/ethyl acetate = 8/2 → 1/2) to give **8e** (*n*-hexane/ethyl acetate = 8/2, R_f = 0.15) as colorless solid (400 mg, 1.44 mmol, 42%) and **9e** (*n*-hexane/ethyl acetate = 1/2, R_f = 0.35) as colorless solid (120 mg, 0.5 mmol, 15%).

8e: m.p.: 124 °C; $[\alpha]_D^{20}$ = +40.4 (3.8; CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 1.27 (s, 3H, C*H*$_3$), 1.44 (s, 3H, C*H*$_3$), 3.85 (s, 3H, OC*H*$_3$), 4.40 (d, *J* = 4.7 Hz, 1H, 4-H), 4.67 (d, *J* = 3.5 Hz, 1H, 6-H), 4.83 (dd, *J* = 5.5/3.5 Hz, 1H, 6a-H), 5.09 (dd, *J* = 5.5/4.7 Hz, 1H, 3a-H), 7.29 – 7.41 (m, 3H, $H_{arom.}$), 7.46 – 7.50 (m, 2H, $H_{arom.}$); ^{13}C NMR ($CDCl_3$): δ 25.1 (1C, C(*C*H_3)$_2$), 25.8 (1C, C(*C*H_3)$_2$), 52.3 (1C, O*C*H_3), 80.8 (1C, C-4), 81.8 (1C, C-6a), 82.1 (1C, C-3a), 83.6 (1C, C-6), 113.5 (1C, *C*(CH$_3$)$_2$), 127.7 (2C, C-2'$_{phenyl}$, C-6'$_{phenyl}$), 128.1 (2C, C-3'$_{phenyl}$, C-5'$_{phenyl}$), 128.3 (1C, C-4'$_{phenyl}$), 134.8 (1C, C-1'$_{phenyl}$), 167.9 (1C, *C*=O); IR (neat): ν [cm^{-1}] = 2985, 1763, 1216, 1117, 1099, 733, 698; HRMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{15}H_{18}O_5Na$, 301.1046; found, 301.1042; HPLC (method 1): t_R = 17.2 min, purity 97.6%.

(2*S*,3*R*,4*S*,5*S*)-Methyl 3,4-dihydroxy-5-(3-iodophenyl)-tetrahydrofuran-2-carboxylate (9b)

p-Toluenesulfonic acid monohydrate (32 mg, 0.17 mmol) was added to a solution of **8b** (670 mg, 1.66 mmol) in methanol (30 mL). The mixture was heated to reflux for 16 h. Then the solvent was removed in vacuo and the residue was purified by flash

column chromatography (3 cm, 20 mL, *n*-hexane/ethyl acetate = 1/1, , R_f = 0.32) to give **9b** as colorless solid (190 mg, 0.52 mmol, 31%). m.p.: 113 °C; $[\alpha]_D^{20}$ = +51.5 (1.0; CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 2.87 (s br, 1H, O*H*), 3.19 (s br, 1H, O*H*), 3.86 (s, 3H, OCH_3), 4.23 – 4.28 (m, 1H, 4-H), 4.69 – 4.75 (m, 2H, 2-H, 3-H), 5.08 (d, *J* = 3.6 Hz, 1H, 5-H), 7.13 (t, *J* = 7.8 Hz, 1H, 5'-$H_{3\text{-iodophenyl}}$), 7.43 – 7.47 (m, 1H, 6'-$H_{3\text{-iodophenyl}}$), 7.64 – 7.68 (m, 1H, 4'-$H_{3\text{-iodophenyl}}$), 7.82 – 7.84 (m, 1H, 2'-$H_{3\text{-iodophenyl}}$,); ^{13}C NMR ($CDCl_3$): δ 52.8 (1C, O*C*H_3), 73.8 (1C, C-4), 74.1 (1C, C-3), 78.8 (1C, C-2), 82.8 (1C, C-5), 94.5 (1C, C-3'$_{3\text{-iodophenyl}}$), 126.3 (1C, C-6'$_{3\text{-iodophenyl}}$), 130.2 (1C, C-5'$_{3\text{-iodophenyl}}$), 136.0 (1C, C-4'$_{3\text{-iodophenyl}}$), 137.3 (1C, C-2'$_{3\text{-iodophenyl}}$), 138.4 (1C, C-1'$_{3\text{-iodophenyl}}$), 172.6 (1C, *C*=O); IR (neat): ν [cm^{-1}] = 3345, 2939, 1745, 1563, 1438, 1220, 1098, 775, 743; HRMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{12}H_{13}IO_5Na$, 386.9700; found, 386.9701; HPLC (method 1): t_R = 15.0 min, purity 99.5%.

(2*S*,3*R*,4*S*,5*S*)-Methyl 5-(4-bromophenyl)-3,4-dihydroxytetrahydrofuran-2-carboxylate (9c)

p-Toluenesulfonic acid monohydrate (4 mg, 0.02 mmol) was added to a solution of **8c** (80 mg, 0.22 mmol) in methanol (20 mL). The mixture was heated to reflux for 16 h. Then the solvent was removed in vacuo and the residue was purified by flash column chromatography (1 cm, 5 mL, *n*-hexane/ethyl acetate = 1/1, R_f = 0.19) to give **9c** as colorless solid (30 mg, 0.09 mmol, 42%). m.p.: 140 °C; $[\alpha]_D^{20}$ = +52.9 (0.4; CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 3.84 (s, 3H, OCH_3), 4.24 (t, *J* = 3.8 Hz, 1H, 4-H), 4.69 – 4.74 (m, 2H, 2-H, 3-H), 5.09 (d, *J* = 3.8 Hz, 1H, 5-H), 7.33 – 7.37 (m, 2H, 2'-$H_{4\text{-bromophenyl}}$, 6'-$H_{4\text{-bromophenyl}}$), 7.50 – 7.54 (m, 2H, 3'-$H_{4\text{-bromophenyl}}$, 5'-$H_{4\text{-bromophenyl}}$); ^{13}C NMR ($CDCl_3$): δ 52.8 (1C, O*C*H_3), 73.7 (1C, C-4), 74.1 (1C, C-3), 78.9 (1C, C-2), 83.1 (1C, C-5), 122.2 (1C, C-4'$_{4\text{-bromophenyl}}$), 128.7 (2C, C-2'$_{4\text{-bromophenyl}}$, C-6'$_{4\text{-bromophenyl}}$), 131.7 (2C, C-

3'$_{4\text{-bromophenyl}}$, C-5'$_{4\text{-bromophenyl}}$), 135.1 (1C, C-1'$_{4\text{-bromophenyl}}$), 172.7 (1C, *C*=O); IR (neat): v [cm^{-1}] = 3453, 3373, 2945, 1741, 1485, 1222, 1123, 1085, 1010, 812, 744; HRMS (*m*/*z*): [M+Na]$^+$ calcd for $C_{12}H_{13}{}^{79}BrO_5Na$, 338.9839; found, 338.9840; HPLC (method 1): t_R = 14.6 min, purity 98.1%.

(2*S*,3*R*,4*S*,5*S*)-Methyl 5-(3-bromophenyl)-3,4-dihydroxytetrahydrofuran-2-carboxylate (9d)

p-Toluenesulfonic acid monohydrate (6 mg, 0.03 mmol) was added to a solution of **8d** (60 mg, 0.17 mmol) in methanol (15 mL). The mixture was heated to reflux for 16 h. Then the solvent was removed in vacuo and the residue was purified by flash column chromatography (1 cm, 5 mL, *n*-hexane/ethyl acetate = 1/1, R_f = 0.27) to give **9d** as colorless solid (19 mg, 0.06 mmol, 35%). m.p.: 89 °C; $[\alpha]_D^{20}$ = +51.9 (3.1; CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 3.85 (s, 3H, OC*H*$_3$), 4.26 (t, *J* = 3.9 Hz, 1H, 4-H), 4.69 – 4.74 (m, 2H, 2-H, 3-H), 5.09 (d, *J* = 3.9 Hz, 1H, 5-H), 7.24 – 7.28 (m, 1H, 5'-H$_{3\text{-bromophenyl}}$), 7.38 – 7.42 (m, 1H, H$_{arom.}$), 7.44 – 7.47 (m, 1H, H$_{arom.}$), 7.63 – 7.65 (m, 1H, 2'-H$_{3\text{-bromophenyl}}$); ^{13}C NMR ($CDCl_3$): δ 52.8 (1C, O*C*H$_3$), 73.9 (1C, C-4), 74.0 (1C, C-3), 78.8 (1C, C-2), 83.0 (1C, C-5), 122.7 (1C, C-3'$_{3\text{-bromophenyl}}$), 125.6 (1C, C-6'$_{3\text{-bromophenyl}}$), 130.0 (1C, C-4'$_{3\text{-bromophenyl}}$), 130.1 (1C, C-5'$_{3\text{-bromophenyl}}$), 131.3 (1C, C-2'$_{3\text{-bromophenyl}}$), 138.5 (1C, C-1'$_{3\text{-bromophenyl}}$), 172.6 (1C, *C*=O); IR (neat): v [cm^{-1}] = 3438, 2953, 1729, 1570, 1438, 1223, 1071, 768; HRMS (*m*/*z*): [M+Na]$^+$ calcd for $C_{12}H_{13}{}^{79}BrO_5Na$, 338.9839; found, 338.9830; HPLC (method 1): t_R = 14.4 min, purity 95.2%.

(2*S*,3*R*,4*S*,5*S*)-Methyl 3,4-dihydroxy-5-phenyl-tetrahydrofuran-2-carboxylate (9e)

p-Toluenesulfonic acid monohydrate (52 mg, 0.27 mmol) was added to a solution of **8e** (420 mg, 1.51 mmol) in methanol (20 mL). The mixture was heated to reflux for 16 h. Then the solvent was removed in vacuo and the residue was purified by flash column chromatography (3 cm, 20 mL, *n*-hexane/ethyl acetate = 2/1, R_f = 0.08) to give **9e** as colorless solid (90 mg, 0.38 mmol, 25%). m.p.: 76 °C; $[\alpha]_D^{20}$ = +40.3 (2.6; CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 2.76 (d br, *J* = 9.0 Hz, 1H, O*H*), 3.17 (d br, *J* = 7.1 Hz, 1H, O*H*), 3.85 (s, 3H, OC*H*$_3$), 4.23 – 4.29 (m, 1H, 4-H), 4.70 – 4.78 (m, 2H, 2-H, 3-H), 5.15 (d, *J* = 3.9 Hz, 1H, 5-H), 7.31 – 7.36 (m, 1H, 4'-H_{phenyl}), 7.38 – 7.43 (m, 2H, 3'-H_{phenyl}, 5'-H_{phenyl}), 7.47 – 7.51 (m, 2H, 2'-H_{phenyl}, 6'-H_{phenyl}); ^{13}C NMR ($CDCl_3$): δ 52.8 (1C, O*C*H$_3$), 73.9 (1C, C-4), 74.3 (1C, C-3), 79.0 (1C, C-2), 83.7 (1C, C-5), 127.0 (2C, C-2'$_{phenyl}$, C-6'$_{phenyl}$), 128.4 (1C, C-4'$_{phenyl}$), 128.8 (2C, C-3'$_{phenyl}$, C-5'$_{phenyl}$), 135.9 (1C, C-1'$_{phenyl}$), 172.7 (1C, *C*=O); IR (neat): ν [cm^{-1}] = 3431, 2955, 1724, 1221, 1087, 1071, 715, 700; HRMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{12}H_{14}O_5Na$, 261.0733; found, 261.0725; HPLC (method 1): t_R = 8.3 min, purity 98.6%.

(2*S*,3*R*,4*S*,5*S*)-*N*,3,4-Trihydroxy-5-(4-iodophenyl)-tetrahydrofuran-2-carboxamide (10a)

Hydroxylamine hydrochloride (63 mg, 0.90 mmol) and sodium methoxide (73 mg, 1.35 mmol) were added to a solution of **9a** (109 mg, 0.30 mmol) in methanol (20 mL) and the mixture was stirred at ambient temperature for 16 h. Then the solvent was evaporated. The residue was dissolved in ethyl acetate and extracted with HCl (1 M). The aqueous phase was then extracted with ethyl acetate (3×) and the combined organic layers were dried (Na_2SO_4), filtered and evaporated. The residue was purified by flash column chromatography (1 cm, 5 mL, CH_2Cl_2/methanol = 9.5/0.5 + 0.1% TFA). The fractions containing **10a** were collected and evaporated. The residue

was dissolved in ethyl acetate and extracted with HCl (1 M). The aqueous phase was then extracted with ethyl acetate (3×) and the combined organic layers were dried (Na_2SO_4), filtered and evaporated to give **10a** as colorless solid (11 mg, 0.03 mmol, 10%). m.p.: 162 °C; TLC (CH_2Cl_2/methanol = 9/1): R_f = 0.47; $[\alpha]_D^{20}$ = +56.4 (0.8; methanol); ^{1}H NMR (D_3COD): δ 4.18 (t, *J* = 4.5 Hz, 1H, 4-H), 4.45 (d, *J* = 7.0 Hz, 1H, 2-H), 4.69 (dd, J = 7.0/4.7 Hz, 1H, 3-H), 4.99 (d, J = 4.3 Hz, 1H, 5-H), 7.21 – 7.25 (m, 2H, 2'-$H_{4\text{-iodophenyl}}$, 6'-$H_{4\text{-iodophenyl}}$), 7.66 – 7.70 (m, 2H, 3'-$H_{4\text{-iodophenyl}}$, 5'-$H_{4\text{-iodophenyl}}$); ^{13}C NMR (D_3COD): δ 74.3 (1C, C-3), 74.7 (1C, C-4), 80.2 (1C, C-2), 85.0 (1C, C-5), 93.5 (1C, C-4'$_{4\text{-iodophenyl}}$), 130.7 (2C, C-2'$_{4\text{-iodophenyl}}$, C-6'$_{4\text{-iodophenyl}}$), 138.0 (2C, C-3'$_{4\text{-iodophenyl}}$, C-5'$_{4\text{-iodophenyl}}$), 138.6 (1C, C-1'$_{4\text{-iodophenyl}}$), a signal for the *C*=O carbon was not visible in the spectrum; IR (neat): ν [cm^{-1}] = 3271, 2923, 1651, 1134, 1044, 1006, 772; HRMS (*m*/*z*): $[M+H]^+$ calcd for $C_{11}H_{13}INO_5$, 365.9833; found, 365.9827; HPLC (method 2): t_R = 13.6 min, purity 95.4%.#

(2*S*,3*R*,4*S*,5*S*)-*N*,3,4-Trihydroxy-5-(3-iodophenyl)-tetrahydrofuran-2-carboxamide (10b)

Hydroxylamine hydrochloride (63 mg, 0.90 mmol) and sodium methoxide (73 mg, 1.35 mmol) were added to a solution of **9b** (109 mg, 0.30 mmol) in methanol (20 mL) and the mixture was stirred at ambient temperature for 16 h. Then the solvent was evaporated. The residue was dissolved in ethyl acetate and extracted with HCl (1 M). The aqueous phase was then extracted with ethyl acetate (3×) and the combined organic layers were dried (Na_2SO_4), filtered and evaporated. The residue was purified by flash column chromatography (1 cm, 5 mL, CH_2Cl_2/methanol = 9.5/0.5 + 0.1% TFA). The fractions containing **10b** were collected and evaporated. The residue was dissolved in ethyl acetate and extracted with HCl (1 M). The aqueous phase was

then extracted with ethyl acetate (3×) and the combined organic layers were dried (Na_2SO_4), filtered and evaporated to give **10b** as colorless solid (32 mg, 0.09 mmol, 29%). m.p.: 143 °C; TLC (CH_2Cl_2/methanol = 9/1): R_f = 0.47; $[\alpha]_D^{20}$ = +50.8 (2.5; methanol); ^{1}H NMR (D_3COD): δ 4.18 (t, *J* = 4.2 Hz, 1H, 4-H), 4.45 (d, *J* = 7.2 Hz, 1H, 2-H), 4.70 (dd, J = 7.2/4.7 Hz, 1H, 3-H), 4.99 (d, J = 4.1 Hz, 1H, 5-H), 7.11 (t, *J* = 7.8 Hz, 1H, 5'-$H_{3\text{-iodophenyl}}$), 7.41 – 7.45 (m, 1H, 6'-$H_{3\text{-iodophenyl}}$), 7.60 – 7.64 (m, 1H, 4'-$H_{3\text{-iodophenyl}}$), 7.83 – 7.85 (m, 1H, 2'-$H_{3\text{-iodophenyl}}$,); ^{13}C NMR (D_3COD): δ 74.2 (1C, C-3), 74.8 (1C, C-4), 80.1 (1C, C-2), 84.7 (1C, C-5), 94.4 (1C, C-3'$_{3\text{-iodophenyl}}$), 127.9 (1C, C-6'$_{3\text{-iodophenyl}}$), 130.7 (1C, C-5'$_{3\text{-iodophenyl}}$), 137.5 (1C, C-2'$_{3\text{-iodophenyl}}$), 137.6 (1C, C-4'$_{3\text{-iodophenyl}}$), 141.3 (1C, C-1'$_{3\text{-iodophenyl}}$), 169.3 (1C, *C*=O); IR (neat): ν [cm^{-1}] = 3321, 2938, 1666, 1604, 1325, 1252, 1108, 1025, 839, 753; HRMS (*m*/*z*): $[M+H]^+$ calcd for $C_{11}H_{13}INO_5$, 365.9833; found, 365.9882; HPLC (method 2): t_R = 14.3 min, purity 95.4%.

(2*S*,3*R*,4*S*,5*S*)-5-(4-Bromophenyl)-*N*,3,4-trihydroxytetrahydrofuran-2-carboxamide (10c)

Hydroxylamine hydrochloride (63 mg, 0.90 mmol) and sodium methoxide (73 mg, 1.35 mmol) were added to a solution of **9c** (95 mg, 0.30 mmol) in methanol (20 mL) and the mixture was stirred at ambient temperature for 16 h. Then the solvent was evaporated. The residue was dissolved in ethyl acetate and extracted with HCl (1 M). The aqueous phase was then extracted with ethyl acetate (3×) and the combined organic layers were dried (Na_2SO_4), filtered and evaporated. The residue was purified by flash column chromatography (1 cm, 5 mL, CH_2Cl_2/methanol = 9.5/0.5 + 0.1% TFA). The fractions containing **10c** were collected and evaporated. The residue was dissolved in ethyl acetate and extracted with HCl (1 M). The aqueous phase was

then extracted with ethyl acetate (3×) and the combined organic layers were dried (Na_2SO_4), filtered and evaporated to give **10c** as colorless solid (14 mg, 0.04 mmol, 15%). m.p.: 149 °C; TLC (CH_2Cl_2/methanol = 9/1): R_f = 0.47; $[\alpha]_D^{20}$ = +44.5 (2.6; methanol); ^{1}H NMR (D_3COD): δ 4.18 (t, *J* = 4.5 Hz, 1H, 4-H), 4.46 (d, *J* = 7.0 Hz, 1H, 2-H), 4.69 (dd, J = 7.0/4.8 Hz, 1H, 3-H), 5.01 (d, J = 4.3 Hz, 1H, 5-H), 7.35 – 7.39 (m, 2H, 2'-$H_{4\text{-bromophenyl}}$, 6'-$H_{4\text{-bromophenyl}}$), 7.46 – 7.50 (m, 2H, 3'-$H_{4\text{-bromophenyl}}$, 5'-$H_{4\text{-bromophenyl}}$); ^{13}C NMR (D_3COD): δ 74.3 (1C, C-3), 74.7 (1C, C-4), 80.2 (1C, C-2), 84.9 (1C, C-5), 122.2 (1C, C-4'$_{4\text{-bromophenyl}}$), 130.6 (2C, C-2'$_{4\text{-bromophenyl}}$, C-6'$_{4\text{-bromophenyl}}$), 131.8 (2C, C-3'$_{4\text{-bromophenyl}}$, C-5'$_{4\text{-bromophenyl}}$), 138.0 (1C, C-1'$_{4\text{-bromophenyl}}$), 169.3 (1C, *C*=O); IR (neat): ν [cm^{-1}] = 3248, 2919, 2865, 1649, 1487, 1401, 1133, 1041, 773, 724; HRMS (*m*/*z*): $[M+H]^+$ calcd for $C_{11}H_{13}{}^{79}BrNO_5$, 317.9972; found, 317.9987; calcd for $C_{11}H_{13}{}^{81}BrNO_5$, 319.9951; found, 319.9977; HPLC (method 1): t_R = 12.7 min, purity 96.8%.

(2*S*,3*R*,4*S*,5*S*)-5-(3-Bromophenyl)-*N*,3,4-trihydroxytetrahydrofuran-2-carboxamide (10d)

Hydroxylamine hydrochloride (63 mg, 0.90 mmol) and sodium methoxide (73 mg, 1.35 mmol) were added to a solution of **9d** (95 mg, 0.30 mmol) in methanol (20 mL) and the mixture was stirred at ambient temperature for 16 h. Then the solvent was evaporated. The residue was dissolved in ethyl acetate and extracted with HCl (1 M). The aqueous phase was then extracted with ethyl acetate (3×) and the combined organic layers were dried (Na_2SO_4), filtered and evaporated. The residue was purified by flash column chromatography (1 cm, 5 mL, CH_2Cl_2/methanol = 9.5/0.5 + 0.1% TFA). The fractions containing **10d** were collected and evaporated. The residue was dissolved in ethyl acetate and extracted with HCl (1 M). The aqueous phase was

then extracted with ethyl acetate (3×) and the combined organic layers were dried (Na_2SO_4), filtered and evaporated to give **10d** as colorless solid (29 mg, 0.09 mmol, 30%). m.p.: 149 °C; TLC (CH_2Cl_2/methanol = 9/1): R_f = 0.40; $[\alpha]_D^{20}$ = +59.7 (2.6; methanol); ^{1}H NMR (D_3COD): δ 4.19 (t, *J* = 4.5 Hz, 1H, 4-H), 4.46 (d, *J* = 7.1 Hz, 1H, 2-H), 4.70 (dd, J = 7.1/4.8 Hz, 1H, 3-H), 5.02 (d, J = 4.2 Hz, 1H, 5-H), 7.25 (t, *J* = 7.8 Hz, 5'-$H_{3\text{-bromophenyl}}$), 7.37 – 7.43 (m, 2H, 4'-$H_{3\text{-bromophenyl}}$, 6'-$H_{3\text{-bromophenyl}}$), 7.65 – 7.67 (m, 1H, 2'-$H_{3\text{-bromophenyl}}$); ^{13}C NMR (D_3COD): δ 74.2 (1C, C-3), 74.8 (1C, C-4), 80.2 (1C, C-2), 84.8 (1C, C-5), 122.9 (1C, C-3'$_{3\text{-bromophenyl}}$), 127.3 (1C, C-6'$_{3\text{-bromophenyl}}$), 130.6 (1C, C-5'$_{3\text{-bromophenyl}}$), 131.5 (1C, C-4'$_{3\text{-bromophenyl}}$), 131.6 (1C, C-2'$_{3\text{-bromophenyl}}$), 141.4 (1C, C-1'$_{3\text{-bromophenyl}}$), 169.3 (1C, *C*=O); IR (neat): ν [cm^{-1}] = 3315, 2908, 1643, 1429, 1030, 763, 693; HRMS (*m*/*z*): $[M+H]^+$ calcd for $C_{11}H_{13}{}^{79}BrNO_5$, 317.9972; found, 317.9984; calcd for $C_{11}H_{13}{}^{81}BrNO_5$, 319.9951; found, 319.9969; HPLC (method 2): t_R = 13.5 min, purity 98.4%.

(2*S*,3*R*,4*S*,5*S*)-*N*,3,4-Trihydroxy-5-phenyl-tetrahydrofuran-2-carboxamide (10e)

Hydroxylamine hydrochloride (42 mg, 0.60 mmol) and sodium methoxide (49 mg, 0.90 mmol) were added to a solution of **9e** (71 mg, 0.30 mmol) in methanol (20 mL) and the mixture was stirred at ambient temperature for 16 h. Then the solvent was evaporated. The residue was dissolved in ethyl acetate and extracted with HCl (1 M). The aqueous phase was then extracted with ethyl acetate (3×) and the combined organic layers were dried (Na_2SO_4), filtered and evaporated. The residue was purified by flash column chromatography (1 cm, 5 mL, CH_2Cl_2/methanol = 9.5/0.5 + 0.1% TFA). The fractions containing **10e** were collected and evaporated. The residue was dissolved in ethyl acetate and extracted with HCl (1 M). The aqueous phase was then extracted with ethyl acetate (3×) and the combined organic layers were dried

(Na_2SO_4), filtered and evaporated to give **10e** as colorless solid (12 mg, 0.05 mmol, 17%). m.p.: 159 °C; TLC (CH_2Cl_2/methanol = 9/1): R_f = 0.37; $[\alpha]_D^{20}$ = +73.3 (1.1; methanol); ^{1}H NMR (D_3COD): δ 4.17 (dd, *J* = 4.7/3.9 Hz, 1H, 4-H), 4.47 (d, *J* = 7.4 Hz, 1H, 2-H), 4.72 (dd, J = 7.3/4.7 Hz, 1H, 3-H), 5.03 (d, J = 3.9 Hz, 1H, 5-H), 7.24 – 7.29 (m, 1H, 4'-H_{phenyl}), 7.31 – 7.35 (m, 2H, 3'-H_{phenyl}, 5'-H_{phenyl}), 7.43 – 7.46 (m, 2H, 2'-H_{phenyl}, 6'-H_{phenyl}); ^{13}C NMR (D_3COD): δ 74.4 (1C, C-3), 74.8 (1C, C-4), 80.1 (1C, C-2), 85.5 (1C, C-5), 128.5 (1C, C-4'$_{phenyl}$), 128.6 (2C, C-2'$_{phenyl}$, C-6'$_{phenyl}$), 128.8 (2C, C-3'$_{phenyl}$, C-5'$_{phenyl}$), 138.5 (1C, C-1'$_{phenyl}$), 169.5 (1C, *C*=O); IR (neat): ν [cm^{-1}] = 3265, 2924, 1644, 1457, 1133, 1073, 1011, 719; HRMS (*m*/*z*): $[M+H]^+$ calcd for $C_{11}H_{14}NO_5$, 240.0866; found, 240.0909; HPLC (method 1): t_R = 5.7 min, purity 98.3%.

(3a*R*,4*S*,*6S*,6a*R*)-Methyl 6-([1,1'-biphenyl]-3-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxole-4-carboxylate (11b)

Under N_2 atmosphere sodium methoxide (84 mg, 1.55 mmol) and phenylboronic acid (142 mg, 1.16 mmol) were dissolved in 1,2-dimethoxyethane (30 mL) and the mixture was stirred at room temperature for 30 min. Then (1,1'-bis(diphenylphosphino)ferrocene)dichloropalladium(II) (88 mg, 0.12 mmol) was added. After stirring the mixture for 10 min at room temperature a solution of **8b** (275 mg, 0.68 mmol) in 1,2-dimethoxyethane (20 mL) was added. Then the reaction mixture was heated to 80 °C for 16 h, cooled to room temperature and evaporated. The crude residue was purified by flash column chromatography (2 cm, 10 mL, cyclohexane/ethyl acetate = 8/2, R_f = 0.20) to give **11b** as colorless solid (130 mg, 0.37 mmol, 54%). m.p.: 122 °C; $[\alpha]_D^{20}$ = +47.9 (1.2; CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 1.28 (s, 3H, C*H*$_3$), 1.47 (s, 3H, C*H*$_3$), 3.86 (s, 3H, OC*H*$_3$), 4.42 (d, *J* = 4.6 Hz, 1H, 4-H), 4.73 (d, *J* = 3.5 Hz, 1H, 6-H), 4.87 (dd, *J* = 5.9/3.5 Hz, 1H, 6a-H), 5.11 (dd, *J* =

5.9/4.6 Hz, 1H, 3a-H), 7.32 – 7.37 (m, 1H, $H_{arom.}$), 7.40 – 7.50 (m, 4H, $H_{arom.}$), 7.53 – 7.56 (m, 1H, $H_{arom.}$), 7.58 – 7.62 (m, 2H, $H_{arom.}$), 7.68 – 7.70 (m, 1H, $H_{arom.}$); ^{13}C NMR ($CDCl_3$): δ 25.1 (1C, C(CH_3)$_2$), 25.9 (1C, C(CH_3)$_2$), 52.3 (1C, OCH_3), 80.8 (1C, C-4), 81.8 (1C, C-6a), 82.1 (1C, C-3a), 83.7 (1C, C-6), 113.6 (1C, *C*(CH_3)$_2$), 126.6 (1C, $C_{arom.}$), 126.8 (1C, $C_{arom.}$), 127.2 (1C, $C_{arom.}$), 127.3 (1C, $C_{arom.}$), 127.4 (2C, $C_{arom.}$), 128.6 (1C, $C_{arom.}$), 128.8 (2C, $C_{arom.}$), 135.3 (1C, $C_{arom.}$), 141.0 (1C, $C_{arom.}$), 141.3 (1C, $C_{arom.}$), 167.8 (1C, *C*=O); IR (neat): ν [cm^{-1}] = 2984, 1744, 1435, 1381, 1277, 1211, 1107, 1036, 856, 806, 739, 698; HRMS (*m*/*z*): $[M+H]^+$ calcd for $C_{21}H_{23}O_5$, 355.1540; found, 355.1560; HPLC (method 1): t_R = 20.5 min, purity 96.0%.

(2*S*,3*R*,4*S*,5*S*)-Methyl 5-([1,1'-biphenyl]-3-yl)-3,4-dihydroxytetrahydrofuran-2-carboxylate (12b)

p-Toluenesulfonic acid monohydrate (10 mg, 0.05 mmol) and ethylene glycol (3 drops) were added to a solution of **11b** (160 mg, 0.45 mmol) in methanol (30 mL). The mixture was heated to reflux for 16 h. Then the solvent was removed in vacuo and the residue was purified by flash column chromatography (2 cm, 10 mL, cyclohexane/ethyl acetate = 1/1, R_f = 0.25) to give **12b** as colorless solid (80 mg, 0.25 mmol, 56%). m.p.: 115 °C; $[\alpha]_D^{20}$ = +49.5 (1.7; CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 2.82 (d, *J* = 9.2 Hz, 1H, O*H*), 3.19 (d, *J* = 7.4 Hz, 1H, O*H*), 3.86 (s, 3H, OC*H*$_3$), 4.31 (dt, *J* = 8.7/3.8 Hz 1H, 4-H), 4.73 – 4.81 (m, 2H, 2-H, 3-H), 5.22 (d, *J* = 3.9 Hz, 1H, 5-H), 7.33 – 7.38 (m, 1H, $H_{arom.}$), 7.42 – 7.49 (m, 4H, H_{arom}), 7.54 – 7.58 (m, 1H, H_{arom}), 7.60 – 7.63 (m, 2H, H_{arom}), 7.70 – 7.72 (m, 1H, H_{arom}); ^{13}C NMR ($CDCl_3$): δ 52.8 (1C, OCH_3), 73.8 (1C, C-4), 74.3 (1C, C-3), 78.9 (1C, C-2), 83.7 (1C, C-5), 125.8 (1C, $C_{arom.}$), 125.9 (1C, $C_{arom.}$), 127.2 (1C, $C_{arom.}$), 127.4 (2C, $C_{arom.}$), 127.5 (1C, $C_{arom.}$), 128.9 (2C, $C_{arom.}$), 129.1 (1C, $C_{arom.}$), 136.4 (1C, $C_{arom.}$), 141.1 (1C, $C_{arom.}$), 141.6 (1C,

$C_{arom.}$), 172.6 (1C, *C*=O); IR (neat): v [cm^{-1}] = 3460, 3348, 2928, 1744, 1597, 1435, 1331, 1219, 1126, 1096, 980, 926, 745, 694; HRMS (*m*/*z*): $[M+H]^+$ calcd for $C_{18}H_{19}O_5$, 315.1227; found, 315.1250; HPLC (method 1): t_R = 17.4 min, purity 97.6%.

(2*S*,3*R*,4*S*,5*S*)-5-([1,1'-Biphenyl]-3-yl)-*N*,3,4-trihydroxytetrahydrofuran-2-carboxamide (13b)

Hydroxylamine hydrochloride (156 mg, 2.24 mmol) and sodium methoxide (121 mg, 2.24 mmol) were added to a solution of **12b** (100 mg, 0.32 mmol) in methanol (20 mL) and the mixture was stirred at ambient temperature for 48 h. Then the solvent was evaporated. The residue was dissolved in ethyl acetate and extracted with HCl (1 M). The aqueous phase was then extracted with ethyl acetate (3×) and the combined organic layers were dried (Na_2SO_4), filtered and evaporated. The residue was purified by flash column chromatography (1 cm, 5 mL, CH_2Cl_2/methanol = 9.5/0.5 + 0.1% TFA). The fractions containing **13b** were collected and evaporated. The residue was dissolved in ethyl acetate and extracted with HCl (1 M). The aqueous phase was then extracted with ethyl acetate (3×) and the combined organic layers were dried (Na_2SO_4), filtered and evaporated to give **13b** as colorless solid (15 mg, 0.05 mmol, 15%). m.p.: 157 °C; TLC (CH_2Cl_2/methanol = 9/1): R_f = 0.44; $[\alpha]_D^{20}$ = +51.5 (2.4; methanol); ^{1}H NMR (D_3COD): δ 4.23 (t, *J* = 4.4 Hz, 1H, 4-H), 4.50 (d, *J* = 7.3 Hz, 1H, 2-H), 4.75 (dd, J = 7.3/4.7 Hz, 1H, 3-H), 5.12 (d, J = 3.9 Hz, 1H, 5-H), 7.30 – 7.34 (m, 1H, $H_{arom.}$), 7.39 – 7.45 (m, 4H, $H_{arom.}$), 7.51 – 7.55 (m, 1H, $H_{arom.}$), 7.62 – 7.65 (m, 2H, $H_{arom.}$), 7.73 – 7.75 (m, 1H, $H_{arom.}$); ^{13}C NMR (D_3COD): δ 74.4 (1C, C-3), 74.9 (1C, C-4), 80.1 (1C, C-2), 85.5 (1C, C-5), 127.2 (1C, $C_{arom.}$), 127.3 (1C, $C_{arom.}$), 127.6 (1C, $C_{arom.}$), 128.1 (2C, $C_{arom.}$), 128.3 (1C, $C_{arom.}$), 129.3 (1C, $C_{arom.}$), 129.8 (2C, $C_{arom.}$), 139.2 (1C, $C_{arom.}$), 142.1 (1C, $C_{arom.}$), 142.5 (1C, $C_{arom.}$),

169.5 (1C, *C*=O); IR (neat): v [cm^{-1}] = 3306, 2901, 1643, 1454, 1423, 1258, 1142, 1030, 841, 748, 733; HRMS (*m*/*z*): $[M+H]^+$ calcd for $C_{17}H_{18}NO_5$, 316.1179; found, 316.1167; HPLC (method 2): t_R = 15.1 min, purity 98.1%.

(3a*R*,4*S*,6*S*,6a*R*)-Methyl 2,2-dimethyl-6-(3-((*E*)-styryl)phenyl)tetrahydrofuro[3,4-d][1,3]dioxole-4-carboxylate (14b)

Under N_2 atmosphere sodium methoxide (40 mg, 0.74 mmol) and *trans*-β-styreneboronic acid (82 mg, 0.56 mmol) were dissolved in 1,2-dimethoxyethane (10 mL) and the mixture was stirred at room temperature for 30 min. Then tetrakis(triphenylphosphine)palladium(0) (43 mg, 0.04 mmol) was added. After stirring the mixture for 10 min at room temperature a solution of **8b** (150 mg, 0.37 mmol) in 1,2-dimethoxyethane (5 mL) was added. Then the reaction mixture was heated to 80 °C for 16 h, cooled to room temperature and evaporated. The crude residue was purified by flash column chromatography (2 cm, 10 mL, cyclohexane/ethyl acetate = 8/2, 10 mL, R_f = 0.15) to give **14b** as colorless solid (90 mg, 0.24 mmol, 64%). m.p.: 142 °C; $[\alpha]_D^{20}$ = +55.3 (3.8; CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 1.28 (s, 3H, C*H*$_3$), 1.46 (s, 3H, C*H*$_3$), 3.87 (s, 3H, OC*H*$_3$), 4.42 (d, *J* = 4.6 Hz, 1H, 4-H), 4.70 (d, *J* = 3.5 Hz, 1H, 6-H), 4.86 (dd, *J* = 5.8/3.5 Hz, 1H, 6a-H), 5.11 (dd, *J* = 5.8/4.6 Hz, 1H, 3a-H), 7.12 – 7.13 (m, 2H, C*H*=C*H*), 7.24 – 7.28 (m, 1H, $H_{arom.}$), 7.34 – 7.39 (m, 4H, $H_{arom.}$), 7.47 – 7.50 (m, 1H, $H_{arom.}$), 7.50 – 7.54 (m, 2H, $H_{arom.}$), 7.59 – 7.61 (m, 1H, $H_{arom.}$); ^{13}C NMR ($CDCl_3$): δ 25.1 (1C, C(*C*H_3)$_2$), 25.9 (1C, C(*C*H_3)$_2$), 52.3 (1C, O*C*H_3), 80.8 (1C, C-4), 81.8 (1C, C-6a), 82.0 (1C, C-3a), 83.5 (1C, C-6), 113.6 (1C, *C*(CH$_3$)$_2$), 126.0 (1C, $C_{arom.}$), 126.3 (1C, $C_{arom.}$), 126.7 (2C, $C_{arom.}$), 127.0 (1C, $C_{arom.}$), 127.7 (1C, $C_{arom.}$), 128.5 (1C, $C_{arom.}$), 128.8 (2C, $C_{arom.}$), 128.9 (1C, *C*H=CH), 129.0 (1C, CH=*C*H), 135.2 (1C, $C_{arom.}$), 137.2 (1C, $C_{arom.}$), 137.5 (1C, $C_{arom.}$), 167.8 (1C, *C*=O); IR (neat): v [cm^{-1}]

= 2994, 2954, 1760, 1429, 1380, 1206, 1126, 1099, 1027, 967, 907, 857, 802, 754, 691; HRMS (*m*/*z*): $[M+H]^+$ calcd for $C_{23}H_{25}O_5$, 381.1697; found, 381.1722; HPLC (method 1): t_R = 21.3 min, purity 97.3%.

(2*S*,3*R*,4*S*,5*S*)-Methyl 3,4-dihydroxy-5-(3-((*E*)-styryl)phenyl)tetrahydrofuran-2-carboxylate (15b)

p-Toluenesulfonic acid monohydrate (16 mg, 0.08 mmol) and ethylene glycol (2 drops) were added to a solution of **14b** (160 mg, 0.42 mmol) in methanol (30 mL). The mixture was heated to reflux for 16 h. Then the solvent was removed in vacuo and the residue was purified by flash column chromatography (2 cm, 10 mL, cyclohexane/ethyl acetate = 1/1, R_f = 0.28) to give **15b** as colorless solid (72 mg, 0.21 mmol, 50%). m.p.: 133 °C; $[\alpha]_D^{20}$ = +55.4 (1.6; CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 2.80 (d br, *J* = 9.1 Hz, 1H, O*H*), 3.22 (d br, *J* = 6.6 Hz, 1H O*H*), 3.87 (s, 3H, OC*H*$_3$), 4.27 – 4.32 (m, 1H, 4-H), 4.72 – 4.79 (m, 2H, 2-H, 3-H), 5.17 (d, *J* = 3.9 Hz, 1H, 5-H), 7.14 (s, 2H, Ar-C*H*=C*H*-Ar), 7.24 – 7.29 (m, 1H, $H_{arom.}$), 7.34 – 7.42 (m, 4H, $H_{arom.}$), 7.47 – 7.54 (m, 3H, $H_{arom.}$), 7.63 – 7.64 (m, 1H, $H_{arom.}$); ^{13}C NMR ($CDCl_3$): δ 52.8 (1C, O*C*H$_3$), 73.8 (1C, C-4), 74.2 (1C, C-3), 78.9 (1C, C-2), 83.5 (1C, C-5), 125.1 (1C, $C_{arom.}$), 126.2 (1C, $C_{arom.}$), 126.4 (1C, $C_{arom.}$), 126.7 (2C, $C_{arom.}$), 127.8 (1C, $C_{arom.}$), 128.6 (1C, $C_{arom.}$), 128.8 (2C, $C_{arom.}$), 129.0 (1C, *C*H=CH), 129.3 (1C, CH=*C*H), 136.3 (1C, $C_{arom.}$), 137.4 (1C, $C_{arom.}$), 137.7 (1C, $C_{arom.}$), 172.5 (1C, *C*=O); IR (neat): ν [cm^{-1}] = 3472, 3321, 3024, 2936, 2889, 1744, 1601, 1489, 1435, 1331, 1219, 1123, 1096, 964, 791, 741, 694; HRMS (*m*/*z*): $[M+H]^+$ calcd for $C_{20}H_{21}O_5$, 341.1384; found, 341.1415; HPLC (method 1): t_R = 18.9 min, purity 96.9%.

(2*S*,3*R*,4*S*,5*S*)-*N*,3,4-Trihydroxy-5-(3-((*E*)-styryl)phenyl)tetrahydrofuran-2-carboxamide (16b)

Hydroxylamine hydrochloride (69 mg, 1.0 mmol) and sodium methoxide (54 mg, 1.0 mmol) were added to a solution of **15b** (49 mg, 0.14 mmol) in methanol (20 mL) and the mixture was stirred at ambient temperature for 72 h. Then the solvent was evaporated. The residue was dissolved in ethyl acetate and extracted with HCl (1 M). The aqueous phase was then extracted with ethyl acetate (3×) and the combined organic layers were dried (Na_2SO_4), filtered and evaporated. The residue was purified by flash column chromatography (1 cm, 5 mL, CH_2Cl_2/methanol = 9.5/0.5 + 0.1% TFA). The fractions containing **16b** were collected and evaporated. The residue was dissolved in ethyl acetate and extracted with HCl (1 M). The aqueous phase was then extracted with ethyl acetate (3×) and the combined organic layers were dried (Na_2SO_4), filtered and evaporated to give **16b** as colorless solid (14 mg, 0.04 mmol, 31%). m.p.: 141°C; TLC (CH_2Cl_2/methanol = 9/1): R_f = 0.38; $[\alpha]_D^{20}$ = +49.5 (2.0; methanol); ^{1}H NMR (D_3COD): δ 4.22 (t, *J* = 4.4 Hz, 1H, 4-H), 4.49 (d, *J* = 7.3 Hz, 1H, 2-H), 4.74 (dd, *J* = 7.3/4.8 Hz, 1H, 3-H), 5.07 (d, *J* = 3.9 Hz, 1H, 5-H), 7.20 (s, 2H, Ar-C*H*=C*H*-Ar), 7.21 – 7.26 (m, 1H, $H_{arom.}$), 7.32 – 7.37 (m, 4H, $H_{arom.}$), 7.45 – 7.49 (m, 1H, $H_{arom.}$), 7.54 – 7.57 (m, 2H, $H_{arom.}$), 7.67 – 7.69 (s, 1H, $H_{arom.}$); ^{13}C NMR (D_3COD): δ 74.4 (1C, C-3), 74.8 (1C, C-4), 80.1 (1C, C-2), 85.5 (1C, C-5), 126.7 (1C, $C_{arom.}$), 126.8 (1C, $C_{arom.}$), 127.5 (2C, $C_{arom.}$), 127.9 (1C, $C_{arom.}$), 128.6 (1C, $C_{arom.}$), 129.2 (1C, $C_{arom.}$), 129.69 (2C, $C_{arom.}$), 129.72 (2C, *C*H=*C*H), 138.4 (1C, $C_{arom.}$), 138.9 (1C, $C_{arom.}$), 139.0 (1C, $C_{arom.}$), 169.5 (1C, *C*=O); IR (neat): ν [cm^{-1}] = 3306, 2955, 2878, 1655, 1450, 1204, 1138, 1049, 964, 775, 691; HRMS (*m*/*z*): $[M+H]^+$ calcd for $C_{19}H_{20}NO_5$, 342.1336; found, 342.1343; HPLC (method 1): t_R = 17.6 min, purity 97.1%.

(3aR,4*S*,6*S*,6a*R*)-Methyl 2,2-dimethyl-6-(3-(phenylethynyl)phenyl)tetrahydrofuro[3,4-d][1,3]dioxole-4-carboxylate (17b)

Under N_2 atmosphere triethylamine (0.52 mL, 3.7 mmol), copper(I) iodide (20 mg, 0.11 mmol) and tetrakis(triphenylphosphine)palladium(0) (61 mg, 0.053 mmol) were added to a solution of **8b** (215 mg, 0.53 mmol) in acetonitrile (10 mL). Then a solution of phenylacetylene (0.49 mL, 4.4 mmol) in acetonitrile (5 mL) was added dropwise over a period of 2 h. After evaporation of the solvent the residue was purified by flash column chromatography (2 cm, 10 mL, cyclohexane/ethyl acetate = 8/2, R_f = 0.19) to give **17b** as colorless solid (190 mg, 0.50 mmol, 94%). m.p.: 150 °C; $[\alpha]_D^{20}$ = +43.3 (4.1; CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 1.28 (s, 3H, C*H*$_3$), 1.44 (s, 3H, C*H*$_3$), 3.86 (s, 3H, OC*H*$_3$), 4.41 (d, *J* = 4.5 Hz, 1H, 4-H), 4.67 (d, *J* = 3.5 Hz, 1H, 6-H), 4.85 (dd, *J* = 5.8/3.5 Hz, 1H, 6a-H), 5.10 (dd, *J* = 5.8/4.5 Hz, 1H, 3a-H), 7.32 – 7.38 (m, 4H, $H_{arom.}$), 7.46 – 7.50 (m, 2H, $H_{arom.}$), 7.51 – 7.55 (m, 2H, $H_{arom.}$), 7.60 – 7.62 (m, 1H, $H_{arom.}$); ^{13}C NMR ($CDCl_3$): δ 25.1 (1C, C(*C*H$_3$)$_2$), 25.8 (1C, C(*C*H$_3$)$_2$), 52.3 (1C, O*C*H$_3$), 80.8 (1C, C-4), 81.7 (1C, C-6a), 82.0 (1C, C-3a), 83.2 (1C, C-6), 89.5 (1C, *C*≡C), 89.6 (1C, *C*≡C), 113.6 (1C, *C*(CH$_3$)$_2$), 123.1 (1C, $C_{arom.}$), 123.4 (1C, $C_{arom.}$), 127.7 (1C, $C_{arom.}$), 128.2 (1C, $C_{arom.}$), 128.4 (1C, $C_{arom.}$), 128.5 (2C, $C_{arom.}$), 130.6 (1C, $C_{arom.}$), 131.5 (1C, $C_{arom.}$), 131.8 (2C, $C_{arom.}$), 135.2 (1C, $C_{arom.}$), 167.7 (1C, *C*=O); IR (neat): ν [cm^{-1}] = 2932, 1763, 1493, 1436, 1380, 1213, 1107, 743, 690; HRMS (*m*/*z*): $[M+H]^+$ calcd for $C_{23}H_{23}O_5$, 379.1540; found, 379.1551; HPLC (methid 1): t_R = 22.1 min, purity 95.8%.

(3a*R*,4*S*,6*S*,6a*R*)-Methyl 2,2-dimethyl-6-(3-phenethylphenyl)tetrahydrofuro[3,4-d][1,3]dioxole-4-carboxylate (21b)

17b (90 mg, 0.24 mmol) was dissolved in methanol (20 mL) and 10% Pd/C (9 mg) was added. The mixture was stirred under hydrogen (balloon) for 16 h at room temperature. Then the suspension was filtered through Celite® and the filtrate was concentrated in vacuo. The residue was purified by flash column chromatography (1 cm, 5 mL, cyclohexane/ethyl acetate = 8/2, R_f = 0.23) to give **21b** as colorless solid (84 mg, 0.22 mmol, 92%). m.p.: 113 °C; $[\alpha]_D^{20}$ = +37.1 (3.8; CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 1.27 (s, 3H, C*H*$_3$), 1.45 (s, 3H, C*H*$_3$), 2.89 – 2.98 (m, 4H, ArC*H*$_2$C*H*$_2$Ar), 3.86 (s, 3H, OC*H*$_3$), 4.39 (d, *J* = 4.6 Hz, 1H, 4-H), 4.64 (d, *J* = 3.6 Hz, 1H, 6-H), 4.81 (dd, *J* = 5.8/3.6 Hz, 1H, 6a-H), 5.08 (dd, *J* = 5.8/4.6 Hz, 1H, 3a-H), 7.12 – 7.15 (m, 1H, $H_{arom.}$), 7.17 – 7.22 (m, 3H, $H_{arom.}$), 7.25 – 7.33 (m, 5H, $H_{arom.}$); ^{13}C NMR ($CDCl_3$): δ 25.1 (1C, C(*C*H$_3$)$_2$), 25.9 (1C, C(*C*H$_3$)$_2$), 38.0 (1C, Ar*C*H$_2$CH$_2$Ar), 38.1 (1C, ArCH$_2$*C*H$_2$Ar), 52.3 (1C, O*C*H$_3$), 80.8 (1C, C-4), 81.9 (1C, C-6a), 82.0 (1C, C-3a), 83.7 (1C, C-6), 113.5 (1C, *C*(CH$_3$)$_2$), 125.3 (1C, $C_{arom.}$), 126.0 (1C, $C_{arom.}$), 127.8 (1C, $C_{arom.}$), 128.1 (1C, $C_{arom.}$), 128.5 (3C, $C_{arom.}$), 128.6 (2C, $C_{arom.}$), 134.7 (1C, $C_{arom.}$), 141.5 (1C, $C_{arom.}$), 142.0 (1C, $C_{arom.}$), 167.8 (1C, *C*=O); IR (neat): ν [cm^{-1}] = 2987, 2861, 1759, 1603, 1446, 1381, 1208, 1101, 858, 740, 700; HRMS (*m*/*z*): [M+H]$^+$ calcd for $C_{23}H_{27}O_5$, 383.1853; found, 383.1895; HPLC (method 1): t_R = 21.9 min, purity 95.2%.

(2*S*,3*R*,4*S*,5*S*)-Methyl 3,4-dihydroxy-5-(3-phenethylphenyl)tetrahydrofuran-2-carboxylate (22b)

p-Toluenesulfonic acid monohydrate (6 mg, 0.03 mmol) was added to a solution of **21b** (63 mg, 0.16 mmol) in methanol (20 mL). The mixture was heated to reflux for 16 h. Then the solvent was removed in vacuo and the residue was purified by flash column chromatography (1 cm, 5 mL, cyclohexane/ethyl acetate = 1/1, R_f = 0.33) to give **22b** as colorless solid (51 mg, 0.15 mmol, 90%). m.p.: 85 °C; $[\alpha]_D^{20}$ = +55.4 (3.0; CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 2.63 (d, *J* = 9.0 Hz, 1H, O*H*), 2.90 – 2.99 (m, 4H, ArC*H*$_2$C*H*$_2$Ar), 3.14 (d, *J* = 7.9 Hz, 1H, O*H*), 3.86 (s, 3H, OC*H*$_3$), 4.22 (dt, *J* = 9.0/3.9 Hz, 1H, 4-H), 4.70 – 4.76 (m, 2H, 2-H, 3-H), 5.11 (d, *J* = 3.9 Hz, 1H, 5-H), 7.14 – 7.22 (m, 4H, $H_{arom.}$), 7.25 – 7.30 (m, 3H, $H_{arom.}$), 7.31 – 7.33 (m, 2H, $H_{arom.}$); ^{13}C NMR ($CDCl_3$): δ 37.9 (1C, Ar*C*H$_2$CH$_2$Ar), 38.0 (1C, ArCH$_2$*C*H$_2$Ar), 52.7 (1C, O*C*H$_3$), 73.7 (1C, C-4), 74.2 (1C, C-3), 79.0 (1C, C-2), 83.6 (1C, C-5), 124.5 (1C, $C_{arom.}$), 126.1 (1C, $C_{arom.}$), 126.9 (1C, $C_{arom.}$), 128.4 (2C, $C_{arom.}$), 128.5 (1C, $C_{arom.}$), 128.6 (2C, $C_{arom.}$), 128.7 (1C, $C_{arom.}$), 135.7 (1C, $C_{arom.}$), 141.8 (1C, $C_{arom.}$), 142.2 (1C, $C_{arom.}$), 172.4 (1C, *C*=O); IR (neat): ν [cm^{-1}] = 3335, 3028, 2952, 2859, 1714, 1441, 1376, 1225, 1082, 769, 698; HRMS (*m*/*z*): $[M+H]^+$ calcd for $C_{20}H_{23}O_5$, 343.1540; found, 343.1548; HPLC (method 1): t_R = 18.5 min, purity 97.7%.

(2*S*,3*R*,4*S*,5*S*)-*N*,3,4-Trihydroxy-5-(3-phenethylphenyl)tetrahydrofuran-2-carboxamide (23b)

Hydroxylamine hydrochloride (132 mg, 1.9 mmol) and sodium methoxide (144 mg, 2.66 mmol) were added to a solution of **22b** (130 mg, 0.38 mmol) in methanol (20 mL) and the mixture was stirred at ambient temperature for 16 h. Then the solvent was evaporated. The residue was dissolved in ethyl acetate and extracted with HCl (1 M). The aqueous phase was then extracted with ethyl acetate (3×) and the combined organic layers were dried (Na_2SO_4), filtered and evaporated. The residue

was purified by flash column chromatography (1 cm, 5 mL, CH_2Cl_2/methanol = 9.5/0.5 + 0.1% TFA). The fractions containing **23b** were collected and evaporated. The residue was dissolved in ethyl acetate and extracted with HCl (1 M). The aqueous phase was then extracted with ethyl acetate (3×) and the combined organic layers were dried (Na_2SO_4), filtered and evaporated to give **23b** as colorless solid (64 mg, 0.19 mmol, 49%). m.p.: 136 °C; TLC (CH_2Cl_2/methanol = 9/1): R_f = 0.44; $[\alpha]_D^{20}$ = +66.4 (2.1; methanol); ^{1}H NMR (D_3COD): δ 2.91 (s, 4H, ArC*H*$_2$C*H*$_2$Ar), 4.15 (t, *J* = 4.3 Hz, 1H, 4-H), 4.46 (d, *J* = 7.3 Hz, 1H, 2-H), 4.71 (dd, J = 7.3/4.8 Hz, 1H, 3-H), 5.00 (d, J = 3.9 Hz, 1H, 5-H), 7.07 – 7.10 (m, 1H, $H_{arom.}$), 7.12 – 7.28 (m, 7H, $H_{arom.}$), 7.29 – 7.31 (m, 1H, $H_{arom.}$); ^{13}C NMR (D_3COD): δ 39.1 (1C, Ar*C*H$_2$CH$_2$Ar), 39.2 (1C, Ar*C*H$_2$CH$_2$Ar), 74.4 (1C, C-3), 74.9 (1C, C-4), 80.0 (1C, C-2), 85.6 (1C, C-5), 126.2 (1C, $C_{arom.}$), 126.8 (1C, $C_{arom.}$), 128.7 (1C, $C_{arom.}$), 128.8 (2C, $C_{arom.}$), 129.3 (2C, $C_{arom.}$), 129.5 (2C, $C_{arom.}$), 138.4 (1C, $C_{arom.}$), 142.7 (1C, $C_{arom.}$), 143.2 (1C, $C_{arom.}$), 169.5 (1C, *C*=O); IR (neat): ν [cm^{-1}] = 3318, 2909, 1643, 1493, 1454, 1138, 1103, 1030, 984, 841, 768, 698; HRMS (*m*/*z*): $[M+H]^+$ calcd for $C_{19}H_{22}NO_5$, 344.1492; found, 344.1526; HPLC (method 2): t_R = 15.4 min, purity 95.6%.

(2S,3R,4S,5S)-Methyl 5-(3-(hex-1-yn-1-yl)phenyl)-3,4-dihydroxytetrahydrofuran-2-carboxylate (24b)

Under N_2 atmosphere triethylamine (0.4 mL, 2.9 mmol), copper(I) iodide (16 mg, 0.08 mmol) and tetrakis(triphenylphosphine)palladium(0) (48 mg, 0.04 mmol) were added to a solution of **9b** (150 mg, 0.41 mmol) in acetonitrile (10 mL). Then a solution of 1-hexyne (0.4 mL, 3.4 mmol) in acetonitrile (5 mL) was added dropwise over a period of 2 h. After evaporation of the solvent the residue was purified by flash column chromatography (2 cm, 10 mL, *n*-hexane:ethyl acetate = 1/1, R_f = 0.33) to give **24b**

as colorless oil (105 mg, 0.33 mmol, 80%). $[\alpha]_D^{20}$ = +47.3 (10.0; CH_2Cl_2); ^{1}H-NMR ($CDCl_3$): δ 0.94 (t, *J* = 7.3 Hz, 3H, $CH_2CH_2CH_2CH_3$), 1.43 – 1.52 (m, 2H, $CH_2CH_2CH_2CH_3$), 1.54 – 1.62 (m, 2H, $CH_2CH_2CH_2CH_3$), 2.40 (t, *J* = 7.0 Hz, 2H, $CH_2CH_2CH_2CH_3$), 3.84 (s, 3H, OCH_3), 4.24 (t, *J* = 3.9 Hz 1H, 4-H), 4.68 – 4.74 (m, 2H, 2-H, 3-H), 5.08 (d, *J* = 3.8 Hz, 1H, 5-H), 7.29 – 7.37 (m, 2H, $H_{arom.}$), 7.39 – 7.43 (m, 1H, $H_{arom.}$), 7.46 – 7.47 (m, 1H, $H_{arom.}$); ^{13}C-NMR ($CDCl_3$): δ 13.8 (1C, $CH_2CH_2CH_2CH_3$), 19.2 (1C, $CH_2CH_2CH_2CH_3$), 22.2 (1C, $CH_2CH_2CH_2CH_3$), 30.9 (1C, $CH_2CH_2CH_2CH_3$), 52.7 (1C, OCH_3), 73.7 (1C, C-4), 74.1 (1C, C-3), 78.9 (1C, C-2), 80.5 (1C, Ar-C≡C), 83.3 (1C, C-5), 90.9 (1C, Ar-C≡C), 124.4 (1C, C-3'$_{phenyl}$), 126.1 (1C, C-6'$_{phenyl}$), 128.5 (1C, C-5'$_{phenyl}$), 130.0 (1C, C-4'$_{phenyl}$), 131.4 (1C, C-2'$_{phenyl}$), 136.0 (1C, C-1'$_{phenyl}$), 172.5 (1C, C=O); IR (neat): ν [cm^{-1}] = 3456, 2956, 2932, 2871, 1730, 1438, 1221, 1082, 773; HRMS (*m*/*z*): $[M+H]^+$ calcd for $C_{18}H_{23}O_5$, 319.1540; found, 319.1589; HPLC (method 1): t_R = 19.5 min, purity 95.0%.

(2*S*,3*R*,4*S*,5*S*)-Methyl 3,4-dihydroxy-5-(3-(2-phenylethynyl)phenyl)-tetrahydrofuran-2-carboxylate (25b)

Under N_2 atmosphere triethylamine (0.54 mL, 3.85 mmol), copper(I) iodide (21 mg, 0.11 mmol) and tetrakis(triphenylphosphine)palladium(0) (63 mg, 0.055 mmol) were added to a solution of **9b** (200 mg, 0,55 mmol) in acetonitrile (10 mL). Then a solution of phenylacetylene (0.5 mL, 4.55 mmol) in acetonitrile (5 mL) was added dropwise over a period of 2 h. After evaporation of the solvent the residue was purified by flash column chromatography (2 cm, 10 mL, *n*-hexane:ethyl acetate = 2/1, R_f = 0.11) to give **25b** as colorless oil (175 mg, 0.52 mmol, 94%). $[\alpha]_D^{20}$ = +46.3 (0.8; CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 3.87 (s, 3H, OCH_3), 4.29 (t, *J* = 3.8 Hz, 1H, 4-H), 4.71 – 4.80 (m, 2H, 2-H, 3-H), 5.14 (d, *J* = 3.8 Hz, 1H, 5-H), 7.32 – 7.43 (m, 4H, $H_{arom.}$), 7.46 – 7.56 (m,

4H, $H_{arom.}$), 7.61 – 7.64 (m, 1H, $H_{arom.}$); ^{13}C NMR ($CDCl_3$): δ 52.8 (1C, O*C*H_3), 73.8 (1C, C-4), 74.2 (1C, C-3), 78.9 (1C, C-2), 83.3 (1C, C-5), 89.3 (1C, *C*≡C), 89.8 (1C, *C*≡C), 123.3 (1C, $C_{arom.}$), 123.7 (1C, $C_{arom.}$), 126.9 (1C, $C_{arom.}$), 128.4 (1C, $C_{arom.}$), 128.5 (2C, $C_{arom.}$), 128.7 (1C, $C_{arom.}$), 130.1 (1C, $C_{arom.}$), 131.5 (1C, $C_{arom.}$), 131.8 (2C, $C_{arom.}$), 136.3 (1C, $C_{arom.}$), 172.6 (1C, *C*=O); IR (neat): ν [cm^{-1}] = 3424, 2954, 2925, 2853, 1733, 1602, 1492, 1441, 1223, 756, 690; HRMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{20}H_{18}O_5Na$, 361.1046; found, 361.1057; HPLC (method 1): t_R = 19.0 min, purity 96.2%.

(2*S*,3*R*,4*S*,5*S*)-Methyl 3,4-dihydroxy-5-(3-(2-(4-(morpholinomethyl)phenyl)ethynyl)phenyl)-tetrahydrofuran-2-carboxylate (27b)

Under N_2 atmosphere triethylamine (0.63 mL, 4.5 mmol), copper(I) iodide (25 mg, 0.13 mmol) and tetrakis(triphenylphosphine)palladium(0) (72 mg, 0.06 mmol) were added to a solution of **9b** (240 mg, 0.66 mmol) in acetonitrile (30 mL). Then a solution of 4-(4-ethynylbenzyl)morpholine (**26**) (1.0 g, 5.0 mmol) in acetonitrile (10 mL) was added dropwise over a period of 2 h. After stirring at ambient temperature for 2 h, the solvent was evaporated and the residue was purified by flash column chromatography (4 cm, 30 mL, ethyl acetate, R_f = 0.26) to give **27b** as colorless solid (240 mg, 0.55 mmol, 83%). m.p.: 167 °C; $[\alpha]_D^{20}$ = +43.5 (5.1; CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 2.46 – 2.56 (m, 4H, NC*H*$_2$CH_2O), 2.90 (s br, 1H, O*H*), 3.23 (s br, 1H, O*H*), 3.57 (s, 2H, NC*H*$_2$Ar), 3.72 – 3.80 (m, 4H, NCH_2*CH*$_2$O), 3.87 (s, 3H, OC*H*$_3$), 4.26 – 4.34 (m, 1H, 4-H), 4.71 – 4.80 (m, 2H, 2-H, 3-H), 5.14 (d, *J* = 3.8 Hz, 1H, 5-H), 7.33 – 7.42 (m, 3H, 5'-$H_{3\text{-ethynylphenyl}}$, 3''-$H_{4\text{-morpholinomethylphenyl}}$, 5''-$H_{4\text{-morpholinomethylphenyl}}$), 7.46 – 7.52 (m, 4H, 4'-$H_{3\text{-ethynylphenyl}}$, 6'-$H_{3\text{-ethynylphenyl}}$, 2''-$H_{4\text{-morpholinomethylphenyl}}$, 6''-$H_{4\text{-morpholinomethylphenyl}}$), 7.62 – 7.64 (m, 1H, 2'-$H_{3\text{-ethynylphenyl}}$); ^{13}C NMR ($CDCl_3$): δ 52.7 (1C,

OCH_3), 53.5 (2C, NCH_2CH_2O), 63.1 (1C, NCH_2Ar), 66.8 (2C, NCH_2CH_2O), 73.7 (1C, C-4), 74.0 (1C, C-2), 79.0 (1C, C-3), 83.3 (1C, C-5), 89.5 (1C, *C*≡C), 89.6 (1C, *C*≡C), 112.4 (1C, C-1''$_{4\text{-morpholinomethylphenyl}}$), 123.5 (1C, C-3'$_{3\text{-ethynylphenyl}}$), 127.0 (1C, C-6'$_{3\text{-ethynylphenyl}}$), 128.6 (1C, C-5'$_{3\text{-ethynylphenyl}}$), 129.5 (2C, C-3''$_{4\text{-morpholinomethylphenyl}}$, C-5''$_{4\text{-morpholinomethylphenyl}}$), 130.1 (1C, C-2'$_{3\text{-ethynylphenyl}}$), 131.4 (1C, C-4'$_{3\text{-ethynylphenyl}}$), 131.7 (2C, C-2''$_{4\text{-morpholinomethylphenyl}}$, C-6''$_{4\text{-morpholinomethylphenyl}}$), 136.4 (1C, C-1'$_{3\text{-ethynylphenyl}}$), 137.4 (1C, C-4''$_{4\text{-morpholinomethylphenyl}}$), 172.4 (1C, *C*=O); IR (neat): ν [cm^{-1}] = 3421, 2918, 2865, 2811, 1747, 1434, 1209, 1093, 1003, 861, 787; HRMS (*m*/*z*): $[M+H]^+$ calcd for $C_{25}H_{27}NO_6H$, 438.1911; found, 438.1906; HPLC (method 1): t_R = 14.8 min, purity 98.2%.

(2*S*,3*R*,4*S*,5*S*)-5-(3-(Hex-1-yn-1-yl)phenyl)-*N*,3,4-trihydroxytetrahydrofuran-2-carboxamide (28b)

Hydroxylamine hydrochloride (175 mg, 2.5 mmol) and sodium methoxide (190 mg, 3.5 mmol) were added to a solution of **24b** (160 mg, 0.50 mmol) in methanol (20 mL) and the mixture was stirred at ambient temperature for 48 h. Then the solvent was evaporated. The residue was dissolved in ethyl acetate and extracted with HCl (1 M). The aqueous phase was then extracted with ethyl acetate (3×) and the combined organic layers were dried (Na_2SO_4), filtered and evaporated. The residue was purified by flash column chromatography (1 cm, 5 mL, CH_2Cl_2/methanol = 9.5/0.5 + 0.1% TFA). The fractions containing **28b** were collected and evaporated. The residue was dissolved in ethyl acetate and extracted with HCl (1 M). The aqueous phase was then extracted with ethyl acetate (3×) and the combined organic layers were dried (Na_2SO_4), filtered and evaporated to give **28b** as colorless solid (56 mg, 0.18 mmol, 35%). m.p.: 120 °C; TLC (CH_2Cl_2/methanol = 9/1): R_f = 0.38; $[\alpha]_D^{20}$ = +53.4 (1.1;

methanol); ^{1}H-NMR (D_3COD): δ 0.97 (t, *J* = 7.3 Hz, 3H, $CH_2CH_2CH_2CH_3$), 1.43 – 1.62 (m, 4H, $CH_2CH_2CH_2CH_3$), 2.41 (t, *J* = 6.9 Hz, 2H, $CH_2CH_2CH_2CH_3$), 4.17 (t, *J* = 4.4 Hz, 1H, 4-H), 4.46 (d, *J* = 7.3 Hz, 1H, 2-H), 4.71 (dd, J = 7.3/4.7 Hz, 1H, 3-H), 5.00 (d, J = 4.0 Hz, 1H, 5-H), 7.25 – 7.29 (m, 2H, $H_{arom.}$), 7.35 – 7.38 (m, 1H, $H_{arom.}$), 7.45 – 7.46 (m, 1H, $H_{arom.}$); ^{13}C NMR (D_3COD): δ 14.0 (1C, $CH_2CH_2CH_2CH_3$), 19.7 (1C, $CH_2CH_2CH_2CH_3$), 23.0 (1C, $CH_2CH_2CH_2CH_3$), 32.1 (1C, $CH_2CH_2CH_2CH_3$), 74.3 (1C, C-3), 74.8 (1C, C-4), 80.1 (1C, C-2), 81.6 (1C, Ar-C≡C), 85.2 (1C, C-5), 90.7 (1C, Ar-C≡C), 125.0 (1C, C-3'$_{phenyl}$), 127.8 (1C, $C_{arom.}$), 128.8 (1C, $C_{arom.}$), 131.5 (1C, $C_{arom.}$), 131.6 (1C, $C_{arom.}$), 138.8 (1C, C-1'$_{phenyl}$), 169.4 (1C, C=O); IR (neat): ν [cm^{-1}] = 3240, 2928, 1659, 1481, 1431, 1184, 1134, 1072, 1030, 772, 691; HRMS (*m*/*z*): $[M+H]^+$ calcd for $C_{17}H_{22}NO_5$, 320.1492; found, 320.1524; HPLC (method 2): t_R = 15.7 min, purity 97.4%.

(2*S*,3*R*,4*S*,5*S*)-*N*,3,4-Trihydroxy-5-(3-(2-phenylethynyl)phenyl)-tetrahydrofuran-2-carboxamide (29b)

Hydroxylamine hydrochloride (63 mg, 0.90 mmol) and sodium methoxide (73 mg, 1.35 mmol) were added to a solution of **25b** (102 mg, 0.30 mmol) in methanol (20 mL) and the mixture was stirred at ambient temperature for 16 h. Then the solvent was evaporated. The residue was dissolved in ethyl acetate and extracted with HCl (1 M). The aqueous phase was then extracted with ethyl acetate (3×) and the combined organic layers were dried (Na_2SO_4), filtered and evaporated. The residue was purified by flash column chromatography (Ø = 1 cm, 5 mL, CH_2Cl_2/methanol = 9.5/0.5 + 0.1% TFA). The fractions containing **29b** were collected and evaporated. The residue was dissolved in ethyl acetate and extracted with HCl (1 M). The aqueous phase was then extracted with ethyl acetate (3×) and the combined organic

layers were dried (Na_2SO_4), filtered and evaporated to give **29b** as colorless solid (22 mg, 0.06 mmol, 22%). m.p.: 154°C; TLC (CH_2Cl_2/methanol = 9/1): R_f = 0.45; $[\alpha]_D^{20}$ = +47.1 (1.3; methanol); ^{1}H NMR (D_3COD): δ 4.21 (t, *J* = 4.5 Hz, 1H, 4-H), 4.48 (d, *J* = 7.2 Hz, 1H, 2-H), 4.73 (dd, *J* = 7.2/4.7 Hz, 1H, 3-H), 5.05 (d, *J* = 4.0 Hz, 1H, 5-H), 7.32 – 7.40 (m, 4H, $H_{arom.}$), 7.41 – 7.46 (m, 2H, $H_{arom.}$), 7.49 – 7.53 (m, 2H, $H_{arom.}$),7.63 – 7.65 (m, 1H, $H_{arom.}$); ^{13}C NMR (D_3COD): δ 74.3 (1C, C-3), 74.8 (1C, C-4), 80.1 (1C, C-2), 85.1 (1C, C-5), 89.9 (1C, *C*≡C), 90.3 (1C, *C*≡C), 124.1 (1C, $C_{arom.}$), 124.6 (1C, $C_{arom.}$), 128.7 (1C, $C_{arom.}$), 129.0 (1C, $C_{arom.}$), 129.4 (1C, $C_{arom.}$), 129.5 (2C, $C_{arom.}$), 131.6 (1C, $C_{arom.}$), 131.7 (1C, $C_{arom.}$), 132.5 (2C, $C_{arom.}$), 139.2 (1C, $C_{arom.}$), 169.4 (1C, *C*=O); IR (neat): ν [cm^{-1}] = 3282, 2926, 1655, 1493, 1024, 753, 688; HRMS (*m*/*z*): $[M+H]^+$ calcd for $C_{19}H_{18}NO_5$, 340.1179; found, 340.1205; HPLC (method 2): t_R = 15.7 min, purity 95.2%.

(2*S*,3*R*,4*S*,5*S*)-*N*,3,4-Trihydroxy-5-(3-(2-(4-(morpholinomethyl)phenyl)ethynyl)phenyl)-tetrahydrofuran-2-carboxamide (3b)

A 2.5 M solution of sodium methoxide in methanol (0.53 mL, 1.33 mmol) was added to a solution of **27b** (240 mg, 0.55 mmol) and hydroxylamine hydrochloride (84 mg, 1.2 mmol) in methanol (30 mL) and the mixture was stirred at ambient temperature for 16 h. Then the solvent was evaporated. After the addition of water, the mixture was extracted with ethyl acetate (3×). Then the aqueous phase was extracted with CH_2Cl_2 / methanol (8:2, 3×). The combined CH_2Cl_2 phases were dried (Na_2SO_4), filtered and evaporated to give **3b** as colorless solid (115 mg, 0.26 mmol, 48%). m.p.: 151 °C; TLC (CH_2Cl_2/methanol = 9/1): R_f = 0.35; $[\alpha]_D^{20}$ = +48.4 (1.7; methanol); ^{1}H NMR (D_3COD): δ 2.44 – 2.48 (m, 4H, NC*H*$_2$$CH_2O$), 3.54 (s, 2H, NC*H*$_2$Ar), 3.68 – 3.71 (m, 4H, NCH_2*C*H_2O), 4.21 (t, *J* = 4.4 Hz, 1H, 4-H), 4.48 (d, *J* = 7.2 Hz, 1H, 2-H), 4.73

(dd, *J* = 7.2/4.7 Hz, 1H, 3-H), 5.06 (d, *J* = 4.0 Hz, 1H, 5-H), 7.33 – 7.38 (m, 3H, $H_{arom.}$), 7.41 – 7.46 (m, 2H, $H_{arom.}$), 7.47 – 7.50 (m, 2H, $H_{arom.}$), 7.63 – 7.64 (m, 1H, $H_{arom.}$); ^{13}C NMR (D_3COD): δ 54.6 (2C, N*C*H_2CH_2O), 64.0 (1C, N*C*H_2Ar), 67.8 (2C, NCH_2*C*H_2O), 7.43 (1C, C-3), 74.8 (1C, C-4), 80.1 (1C, C-2), 85.1 (1C, C-5), 89.8 (1C, *C*≡C), 90.4 (1C, *C*≡C), 123.7 (1C, $C_{arom.}$), 124.1 (1C, $C_{arom.}$), 128.7 (1C, $C_{arom.}$), 129.0 (1C, $C_{arom.}$), 130.7 (2C, $C_{arom.}$), 131.6 (1C, $C_{arom.}$), 131.7 (1C, $C_{arom.}$), 132.5 (2C, $C_{arom.}$), 138.9 (1C, $C_{arom.}$), 139.2 (1C, $C_{arom.}$), a signal for the *C*=O carbon was not visible in the spectrum; IR (neat): ν [cm^{-1}] = 3190, 2866, 1659, 1454, 1350, 1265, 1107, 1030, 841, 775, 694; HRMS (*m*/*z*): $[M+H]^+$ calcd for $C_{24}H_{27}N_2O_6$, 439.1864; found, 439.1874; HPLC (method 2): t_R = 11.1 min, purity 98.3%.

(*S*)-Methyl 3-hydroxy-2-((*S*)-2-hydroxy-1-(4-(phenylethynyl)phenyl)ethoxy)propanoate (40)

Under nitrogen atmosphere copper(I) iodide (7 mg, 0.04 mmol), tetrakis(triphenylphosphine)palladium(0) (21 mg, 0.02 mmol) and triethylamine (0.18 mL, 1.30 mmol) were added to a solution of **39** (68 mg, 0.19 mmol) in dry acetonitrile (20 mL). Then a solution of phenylacetylene (0.17 mL, 1.54 mmol) in dry acetonitrile (5 mL) was added dropwise over a period of 3 h. Afterwards the solvent was removed in vacuo. The residue was purified twice by flash column chromatography (1 cm, 5 mL, cyclohexane/EtOAc = 1/2, R_f = 0.23) to give **40** as yellowish solid (62 mg, 0.18 mmol, 98% yield). m.p.: 71 °C; $[\alpha]_D^{20}$ = +50.8 (c = 3.0; CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 3.63 (s, 3H, COOC*H*$_3$), 3.67 – 3.77 (m, 1H, C*H*$_2$OH), 3.79 – 3.93 (m, 2H, C*H*$_2$OH), 3.95 – 4.04 (m, 1H, C*H*$_2$OH), 4.05 – 4.11 (m, 1H, H_3COOCC*H*CH_2OH), 4.24 (s br, 1H, O*H*), 4.34 (s br, 1H, O*H*), 4.65 – 4.72 (m, 1H, PhC*H*CH_2OH), 7.30 – 7.41 (m, 5H, $H_{arom.}$), 7.47-7.57 (m, 4H, $H_{arom.}$); ^{13}C NMR ($CDCl_3$): δ 52.3 (1C, COO*C*H_3), 62.4 (1C,

CH_2OH), 67.0 (1C, *C*H_2OH), 78.8 (1C, H_3COOC*C*HCH_2OH), 83.5 (1C, Ph*C*HCH_2OH), 89.0 (1C, Ph*C*≡CPh), 90.0 (1C, Ph*C*≡CPh), 123.2 (1C, $C_{arom.}$), 123.6 (1C, $C_{arom.}$), 127.2 (2C, $C_{arom.}$), 128.5 (3C, $C_{arom.}$), 131.8 (2C, $C_{arom.}$), 131.9 (2C, $C_{arom.}$), 137.7 (1C, $C_{arom.}$), 171.2 (1C, *C*OOCH_3); IR (neat): ν [cm^{-1}] = 3302, 2947, 2878, 1736, 1435, 1196, 1096, 1053, 752, 691; HRMS (*m*/*z*): $[M+H]^+$ calcd for $C_{20}H_{21}O_5$: 341.1384; found: 341.1405; HPLC (method 1): t_R = 18.6 min, purity 97.2%.

(*S*)-*N*,3-Dihydroxy-2-((*S*)-2-hydroxy-1-(4-(phenylethynyl)phenyl)ethoxy)propanamide (42)

Hydroxylamine hydrochloride (39 mg, 0.56 mmol) and a 2 M solution of sodium methanolate in methanol (0.28 mL, 0.56 mmol) were added to a solution of **40** (76 mg, 0.22 mmol) in dry methanol (20 mL) and the mixture was stirred at ambient temperature for 16 h. Then water was added and the mixture was extracted with ethyl acetate (3×). The combined organic layers were dried (Na_2SO_4), filtered and the solvent was removed in vacuo. The residue was purified by flash column chromatography (1 cm, 5 mL, CH_2Cl_2/methanol = 10/1, R_f = 0.22) to give **42** as colorless solid (40 mg, 0.12 mmol, 52% yield). m.p.: 157 °C; $[\alpha]_D^{20}$ = +47.1 (2.0; methanol); ^{1}H NMR (D_3COD): δ 3.64 – 3.95 (m, 5H, HOHNOCC*H*CH_2OH, PhCHCH_2OH), 4.69 – 4.75 (m, 1H, PhC*H*CH_2OH), 7.32 – 7.45 (m, 5H, $H_{arom.}$), 7.45 – 7.54 (m, 4H, $H_{arom.}$); ^{13}C NMR (D_3COD): δ 61.4 (1C, *C*H_2OH), 66.1 (1C, *C*H_2OH), 78.5 (1C, HOHNOC*C*HCH_2OH), 82.5 (1C, Ph*C*HCH_2OH), 88.6 (1C, Ph*C*≡CPh), 89.3 (1C, Ph*C*≡CPh), 123.3 (1C, $C_{arom.}$), 123.4 (1C, $C_{arom.}$), 127.5 (2C, $C_{arom.}$), 128.3 (1C, $C_{arom.}$), 128.4 (2C, $C_{arom.}$), 131.3 (2C, $C_{arom.}$), 131.5 (2C, $C_{arom.}$), 138.6 (1C, $C_{arom.}$), 168.1 (1C, *C*ONHOH); IR (neat): ν [cm^{-1}] = 3730, 3391, 3063, 2839, 1647, 1504,

1119, 1049, 752, 691; HRMS (*m*/*z*): $[M+H]^+$ calcd for $C_{19}H_{20}NO_5$: 342.1336; found: 342.1318; HPLC (method 2): t_R = 15.1 min, purity 99.4%.