Synthesis and Partial Biological Evaluation of a Small Library of Differentially Linked β -C-Disaccharides

SUPPORTING INFORMATION

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General: Unless otherwise noted, reagents were commercially available and were used without purification. Tetrahydrofuran (THF) was freshly distilled from sodium-benzophenone ketyl. Dichloromethane and TMEDA were distilled from calcium hydride while benzene and toluene were distilled from sodium. All reactions were conducted in oven or flame-dried glassware under an atmosphere of argon. Organic solutions were dried over magnesium sulfate. TLC analyses were carried out using (Merck 60F-254) thin layer chromatography plates and visualized under UV light or by charring with phosphomolybdic solution. Silica gel for flash chromatography was Merck type 60 (230-400 mesh). The spectral data and representative experimental procedures for the majority of the compounds in this paper have been published previously.¹

(22b)

Osmium tetroxide (10.7 mg, 0.042 mmol) was added to a slurry of **21a** and **21b** (2.06 g, 4.23 mmol), sodium periodate (2.06 g, 8.88 mmol) in THF- H_2O (1:4, 80 mL) and the resulting mixture was stirred at room temperature for 6 hours at which point TLC (silica, 70% Et_2O -hexanes) showed no starting material remaining. The reaction was quenched by the addition of sodium thiosulfate (0.5 M, 20 mL) and partitioned between EtOAc (40 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (3 x 50 mL). The combined organic extracts were washed with brine (1 x 25 mL), dried and filtered. The solution was concentrated and flash chromatography of the residue over silica gel using 15% Et_2O -hexanes gave the intermediate aldehyde **22a**² (1.35 g, 79%) as a pure (R_f = 0.48, TLC silica, 70% Et_2O -hexanes; ^1H NMR, 500 MHz) oil.¹ The minor isomer (**22b**) (203 mg, 79%) was also obtained as a pure (R_f = 0.57, TLC silica, 70% Et_2O -hexanes; ^1H NMR, 500 MHz) oil:

$[\alpha]_D = +18.5$ ($c = 0.35$ CHCl_3); FT-IR (neat) 3087, 3060, 3028, 2904, 2720, 1721, 1604, 1495, 1453, 1354, 1193, 1098, 1047, 736, 697 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 9.64 (s, 1H, CHO), 7.36-7.25 (m, 15 H, ArH), 4.81 (d, 1 H, $J = 12.2$ Hz, OCH_2Ph), 4.66 (d, 1 H, $J = 11.7$ Hz, OCH_2Ph), 4.65 (d, 1 H, $J = 12.2$ Hz, OCH_2Ph), 4.63 (d, 1 H, $J = 4.0$ Hz, $H-1$), 4.62 (d, 1 H, $J = 11.2$ Hz, OCH_2Ph), 4.45 (d, 1 H, $J = 11.2$ Hz, OCH_2Ph), 4.41 (d, 1 H, $J = 11.7$ Hz, OCH_2Ph), 4.09 (ddd, 1 H, $J = 8.1, 8.1, 2.5$ Hz, $H-5$), 4.03 (dd, 1 H, $J = 9.0, 5.0$ Hz, $H-3$), 3.45 (dd, 1 H, $J = 9.6, 3.6$ Hz, $H-2$), 3.43-3.38 (m, 5 H, 2 x $H-6$, OCH_3), 2.96-2.92 (m, 1 H, $H-4$), 2.68 (dd, 1 H, $J = 16.7, 3.0$ Hz, $H-7$), 2.53 (ddd, 1 H, $J = 17.3, 8.1, 2.6$ Hz, $H-7$); ^{13}C NMR (125 MHz, CDCl_3) δ 201.4, 138.3, 138.3, 137.6, 128.3, 128.3, 127.9, 127.7, 127.6, 127.6, 98.7, 77.2, 76.1, 73.3, 72.2, 69.9, 67.3, 55.1, 37.2, 35.0; HRMS (EI): calcd for $\text{C}_{23}\text{H}_{27}\text{O}_6$ ($\text{M} - \text{C}_7\text{H}_7$) $^+$ 399.1807, found 399.1800.

General procedure for oxidation of the carbohydrate-based aldehydes to the carbohydrate-based acids exemplified by the preparation of **methyl (4R)-2,3,6-tri-O-benzyl-4-deoxy-4-(2-ethanoic acid)- α -D-glucopyranoside (6b)**:

To a solution of the resultant aldehyde **22b** (130 mg, 0.260 mmol) in a mixture of *t*-BuOH-water (10:1, 1 mL) was added 2-methyl-2-butene (0.16 mL, 1.91 mmol), potassium phosphate monobasic (40 mg, 0.333 mmol), and sodium chlorite (80%, 40 mg, 0.354 mmol).³ The resulting mixture was stirred at room temperature for 1 hour, concentrated and diluted with water (10 mL). The resulting mixture was acidified with HCl (2M, ~3 mL) to approximately pH = 2-3 (litmus red). The mixture was extracted with EtOAc (5 x 10 mL) and the combined organic extracts were dried and filtered. The solution was concentrated and flash chromatography of the residue over silica gel (5.5 x 4 cm) using 40% EtOAc/hexanes with 0.2% AcOH gave **6b** (130 mg, 97%) as a pure ($R_f = 0.30$, TLC silica, EtOAc; ^1H NMR, 500 MHz) oil: $[\alpha]_D = +38.7$ ($c = 0.33$ CHCl_3); FT-IR (neat) 3028(b), 2908, 1730, 1703, 1495, 1453, 1357, 1282, 1096, 1045, 736, 696 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.36-7.22 (m, 15 H, ArH), 4.81 (d, 1 H, $J = 12.1$ Hz, OCH_2Ph), 4.70 (d, 1 H, $J = 11.6$ Hz, OCH_2Ph), 4.65 (d, 1 H, $J = 12.2$ Hz, OCH_2Ph), 4.63 (d, 1 H, $J = 4.1$ Hz, $H-1$), 4.62 (d, 1 H, $J = 11.6$ Hz, OCH_2Ph), 4.49 (d, 1 H, $J = 11.7$ Hz, OCH_2Ph), 4.42 (d, 1 H, $J = 11.7$ Hz, OCH_2Ph), 4.09 (ddd, 1 H, $J = 6.1, 6.1, 2.0$ Hz, $H-5$), 4.01 (dd, 1 H, $J = 10.1, 5.5$ Hz, $H-3$), 3.52-3.47 (m, 2 H, 2 x $H-6$), 3.45 (dd, 1 H, $J = 10.1, 4.0$ Hz, $H-2$), 3.37 (s, 3 H, OCH_3), 2.88-2.84 (m, 1 H, $H-4$), 2.68 (dd, 1 H, $J = 17.7, 4.1$ Hz, $H-7$), 2.44 (dd, 1 H, $J = 16.7, 8.6$ Hz, $H-7$); ^{13}C NMR (125 MHz, CDCl_3) δ 178.3, 138.3, 138.3, 137.8, 128.4, 128.3, 128.3, 127.9, 127.7, 127.6, 127.5, 127.5, 127.4, 98.6, 75.8, 73.4, 73.3, 71.8, 70.0, 67.7, 55.1, 37.2, 27.2; HRMS (FAB): calcd for $\text{C}_{23}\text{H}_{27}\text{O}_7$ ($\text{M} - \text{C}_7\text{H}_7$) $^+$ 415.1756, found 415.1755.

General procedure for DCC mediated esterification exemplified by the preparation **methyl (4'R)-2',3',6'-tri-O-benzyl-4'-deoxy-4'-C-((3,4,6-tri-O-benzyl-1,2-dideoxy-D-arabino-hex-1-enyl)-(2'-ethanoate))- α -D-glucopyranoside (7b)**:

4-DMAP (30 mg, 0.246 mmol) and DCC (48 mg, 0.2233 mmol) were added in one portion to a solution of **6b** (117 mg, 0.231 mmol) and alcohol **5a** (74 mg, 0.177 mmol), in dry CH_2Cl_2 (3 mL). The resulting solution was then stirred for 18 h at ambient temperature at which point TLC (R_f = 0.21, silica, 3 x 20% Et_2O -hexanes) showed the reaction was complete. The reaction mixture was diluted with ether (20 mL) and filtered by gravity through cotton to remove majority of the formed dicyclohexylurea. The resulting organic solution was washed with NH_4Cl (1 x 20 mL), dried and filtered. The solution was concentrated and careful flash chromatography of the residue over silica gel (3 x 21 cm) using 20% Et_2O /hexanes gave **7b** (130 mg, 82%) as a pure (R_f = 0.33, TLC silica, 3 x 30% Et_2O -hexanes; ^1H NMR, 500 MHz) oil: $[\alpha]_D^{25} = +27.3$ (c = 0.84, CHCl_3); FT-IR (neat) 3061, 3029, 2906, 2865, 1731, 1495, 1452, 1365, 1253, 1173, 1094, 1045, 1027, 734, 696 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.36-7.21 (m, 30 H, ArH), 5.82 (ddd, 1 H, J = 17.7, 10.1, 7.6 Hz, H -2), 5.30 (d, 1 H, J = 9.6, 1.6 Hz, H -1), 5.25-5.22 (m, 2 H, H -1, H -5), 4.79 (d, 1 H, J = 12.1 Hz, OCH_2Ph), 4.66 (d, 1 H, J = 11.2 Hz, OCH_2Ph), 4.64 (d, 1 H, J = 10.1 Hz, OCH_2Ph), 4.63 (d, 1 H, J = 4.7 Hz, H -1'), 4.62 (d, 1 H, J = 12.2 Hz, OCH_2Ph), 4.60 (d, 1 H, J = 11.1 Hz, OCH_2Ph), 4.58 (d, 1 H, J = 11.2 Hz, OCH_2Ph), 4.54 (d, 1 H, J = 11.7 Hz, OCH_2Ph), 4.42 (s, 2 H, 2 x OCH_2Ph), 4.41 (d, 1 H, J = 13.1 Hz, OCH_2Ph), 4.35 (d, 1 H, J = 12.2 Hz, OCH_2Ph), 4.29 (d, 1 H, J = 11.6 Hz, OCH_2Ph), 4.07 (ddd, 1 H, J = 6.6, 4.6, 2.0 Hz, H -5'), 3.99 (dd, 1 H, J = 10.1, 5.1 Hz, H -3'), 3.88 (dd, 1 H, J = 8.1, 6.1 Hz, H -3), 3.77-3.70 (m, 3 H, H -4, 2 x H -6), 3.47-3.42 (m, 2 H, 2 x H -6'), 3.41-3.36 (m, 4 H, H -2', OCH_3), 3.84 (ddd, 1 H, J = 7.6, 7.6, 2.5 Hz, H -4'), 3.56 (dd, 1 H, J = 16.7, 2.5 Hz, H -7'), 2.04 (dd, 1 H, J = 16.7, 8.1 Hz, H -7'); ^{13}C NMR (125 MHz, C_6D_6) δ 172.7, 138.4, 138.4, 138.3, 138.1, 138.0, 134.9, 128.3, 128.2, 128.2, 128.2, 127.9, 127.8, 127.8, 127.6, 127.6, 127.5, 127.4, 127.4, 119.4, 98.5, 81.6, 81.1, 76.1, 75.0, 73.3, 73.1, 73.1, 72.9, 71.6, 70.5, 70.4, 70.5, 68.2, 68.2, 55.0, 37.0, 27.3; HRMS (FAB): calcd for $\text{C}_{57}\text{H}_{62}\text{O}_{10}\text{Na}$ ($M + \text{Na}$) $^+$ 929.4235, found 929.4182.

General procedure for the methylenation⁴ exemplified by the preparation of methyl (4'*R*)-2',3',6'-tri-*O*-benzyl-4'-deoxy-4'-C-((3,4,6-tri-*O*-benzyl-1,2-dideoxy-D-arabino-hex-1-enyl)-2'-propene)- α -D-glucopyranoside (**8b**):

A solution of titanium tetrachloride (1.02 mL, 2 M in CH_2Cl_2 , 2.04 mmol) was added to cool (0 $^\circ\text{C}$) THF (4 mL). The resulting mixture was stirred for 30 minutes at which point TMEDA (0.59 mL, 3.91 mmol) was added in one portion. The resulting yellow-brown suspension was allowed to warm to ambient temperature and stirred for 30 minutes. At this point, zinc dust (290 mg, 4.44 mmol) and lead (II) chloride (3 mg, 0.001 mmol) were added in portion and stirring at ambient temperature was continued for 10 min. A solution of ester **7b** (109 mg, 0.120 mmol) and dibromomethane (0.09 mL, 1.25 mmol) in THF (1 mL) was then added *via* cannula to the reaction

flask in one portion. The mixture was stirred at 60 °C for 1 hour, cooled to 0 °C and then quenched by the addition of saturated potassium carbonate (1.0 mL). The resulting mixture was stirred for 30 minutes (while warming to ambient temperature) diluted with ether (20 mL) and stirred vigorously for 15 minutes. The resulting mixture was filtered through neutral alumina using a 3% triethylamine-ether as the eluent. The greenish-blue precipitate that resulted was crushed (mortar and pestle) and thoroughly extracted by vigorous stirring over diethyl ether (15-20 mL) for 30 minutes. The combined ethereal extracts were concentrated *in vacuo* and gravity chromatography of the residue over silica using 20% Et₂O-hexanes-1% triethylamine gave **8b** (56 mg, 52%) as a pure (*R*_f = 0.35, TLC silica, 40% Et₂O-hexanes; ¹H NMR, 500 MHz) oil: [α]_D = + 38.6 (*c* = 0.49, CH₂Cl₂); FT-IR (neat) 3062, 3028, 2916, 1650, 1495, 1452, 1354, 1268, 1192, 1093, 1045, 1027, 733, 695 cm⁻¹; ¹H NMR (500 MHz, C₆D₆) δ 7.40-7.00 (m, 30 H, ArH), 5.84 (ddd, 1 H, *J* = 17.7, 10.6, 7.6 Hz, *H*-2), 5.20 (d, 1 H, *J* = 17.2 Hz, *H*-1), 5.06 (d, 1 H, *J* = 10.6 Hz, *H*-1), 4.75 (d, 1 H, *J* = 12.1 Hz, OCH₂Ph), 4.74 (d, 1 H, *J* = 4.0 Hz, *H*-1'), 4.71 (d, 1 H, *J* = 11.2 Hz, OCH₂Ph), 4.69 (d, 1 H, *J* = 11.1 Hz, OCH₂Ph), 4.65 (d, 1 H, *J* = 11.6 Hz, OCH₂Ph), 4.61 (ddd, 1 H, *J* = 8.6, 8.6, 4.5 Hz, *H*-5), 4.53 (d, 1 H, *J* = 12.1 Hz, OCH₂Ph), 4.50 (d, 1 H, *J* = 12.2 Hz, OCH₂Ph), 4.44 (d, 1 H, *J* = 12.1 Hz, OCH₂Ph), 4.40 (d, 1 H, *J* = 13.2 Hz, OCH₂Ph), 4.37 (d, 1 H, *J* = 11.7 Hz, OCH₂Ph), 4.26 (d, 1 H, *J* = 11.6 Hz, OCH₂Ph), 4.24-4.22 (m, 2 H, *H*-5', OCH₂Ph), 4.19 (d, 1 H, *J* = 12.2 Hz, OCH₂Ph), 4.11 (dd, 1 H, *J* = 9.7, 5.1 Hz, *H*-3'), 4.07-4.00 (m, 4 H, *H*-3, *H*-4, 2 x *H*-9'), 3.91 (dd, 1 H, *J* = 10.1, 3.5 Hz, *H*-6), 3.80 (dd, 1 H, *J* = 10.2, 8.1 Hz, *H*-6'), 3.73-3.67 (m, 2 H, *H*-6, *H*-6'), 3.52 (dd, 1 H, *J* = 10.1, 4.0 Hz, *H*-2'), 3.27 (s, 3 H, OCH₃), 2.80 (d, 1 H, *J* = 14.7 Hz, *H*-7'), 2.60-2.57 (m, 1 H, *H*-4'), 2.36 (dd, 1 H, *J* = 14.6, 6.5 Hz, *H*-7'); ¹³C NMR (125 MHz, C₆D₆) δ 161.5, 139.6, 139.5, 139.4, 139.1, 138.8, 138.7, 135.8, 128.4, 128.4, 128.3, 128.3, 128.3, 128.1, 128.0, 127.8, 127.7, 127.7, 127.6, 127.5, 127.5, 127.4, 127.3, 118.7, 98.9, 83.2, 81.6, 81.3, 78.2, 76.9, 75.8, 75.0, 73.2, 73.1, 72.9, 71.5, 71.0, 70.9, 70.0, 68.5, 54.8, 38.5, 28.5; HRMS (FAB): calcd for C₅₈H₆₄O₉Na (*M* + Na)⁺ 927.4442, found 927.4421.

General procedure for the one-pot protocol using molybdenum-based metathesis catalyst **23** exemplified by the preparation of **methyl 2,3,6-tri-*O*-benzyl-4-deoxy-4-*C*-(2,6-anhydro-3,4,5,7-tetra-*O*-benzyl-1-deoxy-*D*-glycero-*D*-gulo-heptit-1-yl)- α -*D*-galactopyranoside (**10b**):**

Ruthenium-based metathesis catalyst **26** (12 mg, 0.014 mmol, 40 mol%), was added in three portions over 2 hours to a dry and degassed toluene (3.6 mL) solution of **8b** (32 mg, 0.036 mmol) and the resulting mixture heated to 60 °C for 3 h. The flask was removed from the glove box, placed under argon, and cooled in an ice bath. BH₃•THF (0.4 mL, 1M in THF, 0.004 mmol) was added to the cooled solution and the resulting mixture was allowed to warm up to room temperature, with the ice-bath place, and stirred overnight. The solution was cooled back down to 0 °C and NaOH (10 mL, 1 M, 10 mmol) and hydrogen peroxide (10 mL, 30% in water) were added in one portion. The solution was allowed to warm to room temperature over 2 hours. The solution was extracted with ether (3 x 5 mL) and the combined ethereal extracts were washed with brine (1 x 10 mL), dried over magnesium sulfate and

filtered. The solution was concentrated and flash chromatography of the residue over silica using 20% EtOAc-hexanes gave **10b** (18 mg, 53%) as a pure (R_f = 0.68, TLC silica, 40% EtOAc-hexanes; ^1H NMR, 500 MHz) colorless oil: $[\alpha]_D^{25} = +23.0$ (c = 0.41, CHCl_3); FT-IR (neat) 3443, 3060, 3028, 2919, 2857, 1495, 1452, 1357, 1206, 1098, 1048, 734, 696 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.36-7.16 (m, 30 H, ArH), 4.82 (d, 1 H, J = 11.7 Hz, OCH_2Ph), 4.79 (d, 1 H, J = 10.6 Hz, OCH_2Ph), 4.78 (d, 1 H, J = 11.6 Hz, OCH_2Ph), 4.77 (d, 1 H, J = 11.7 Hz, OCH_2Ph), 4.75 (d, 1 H, J = 11.6 Hz, OCH_2Ph), 4.68 (d, 1 H, J = 11.7 Hz, OCH_2Ph), 4.64 (d, 1 H, J = 12.7 Hz, OCH_2Ph), 4.62 (d, 1 H, J = 4.5 Hz, $H-1'$), 4.55 (d, 1 H, J = 12.1 Hz, OCH_2Ph), 4.53 (d, 2 H, J = 10.6 Hz, 2 x OCH_2Ph), 4.47 (d, 1 H, J = 12.1 Hz, OCH_2Ph), 4.46 (d, 1 H, J = 11.6 Hz, OCH_2Ph), 4.08 (ddd, 1 H, J = 16.6, 16.6, 2.6 Hz, $H-5'$), 3.98 (dd, 1 H, J = 10.1, 5.0 Hz, $H-3'$), 3.65-3.62 (m, 3 H, $H-2'$, 2 x $H-6$), 3.60-3.53 (m, 3 H, 2 x $H-6'$, $H-4$), 3.79-3.34 (m, 4 H, $H-3$, OCH_3), 3.28-3.25 (m, 3 H, $H-5$, $H-1$, $H-2$), 2.47-2.46 (m, 1 H, $H-4'$), 2.13-2.10 (m, 1 H, $H-7'$), 1.54-1.51 (m, 1 H, $H-7'$); ^{13}C NMR (125 MHz, C_6D_6) δ 138.7, 138.6, 138.4, 138.2, 138.1, 138.1, 128.5, 128.3, 128.3, 128.0, 127.9, 127.8, 127.7, 127.7, 127.6, 127.5, 127.5, 127.3, 98.4, 86.6, 79.3, 78.8, 78.1, 76.8, 76.2, 75.1, 74.7, 73.4, 73.2, 73.2, 72.9, 70.9, 69.5, 69.1, 55.0, 38.0, 26.8; HRMS (FAB): calcd for $\text{C}_{56}\text{H}_{62}\text{O}_{10}\text{Na}$ ($M + \text{Na}$) $^+$ 917.4235, found 917.4254.

(19c)

Phenyl chlorothionoformate⁵ (2.00 mL, 14.5 mmol) was added dropwise to a suspension of **18c**⁶ (2.61 g, 6.76 mmol) and NHS⁷ (780 mg, 6.77 mmol) in dry toluene (60 ml) at ambient temperature. Pyridine (2.73 mL, 33.8 mmol) was then added and the resulting suspension was stirred for one hour at room temperature. The reaction mixture was washed with HCl (1 M, 1 x 10 ml), saturated sodium bicarbonate (1 x 10 ml) and the organic extracts were dried and concentrated. Flash chromatography of the residue over silica gel using 3% Et₂O/toluene gave **19c** (2.15 g, 85%) as a pure (R_f = 0.63, TLC silica, 5% Et₂O/benzene; ^1H NMR, 500 MHz) yellow solid: m.p. 124-125 °C; $[\alpha]_D^{25} = +94.2$ (c = 0.59, CHCl_3); FT-IR (neat) 3066, 2936, 2866, 1724, 1600, 1590, 1490, 1451, 1414, 1375, 1334, 1268, 1192, 1155, 1093, 1070, 1043, 990, 933, 862, 753, 710, 698 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 8.17 (dd, 2 H, J = 1.5, 8.6 Hz, ArH), 7.66-7.20 (m, 11 H, ArH), 6.91-6.89 (m, 2 H, ArH), 6.08 (dd, 1 H, J = 9.7, 9.6 Hz, $H-3$), 5.64 (s, 1 H, PhCH), 5.31 (dd, 1 H, J = 10.1, 4.1 Hz, $H-2$), 5.27 (d, 1 H, J = 3.6 Hz, $H-1$), 4.42 (dd, 1 H, J = 10.1, 9.5 Hz, $H-6$), 4.11 (ddd, 1 H, J = 9.6, 9.6, 4.6 Hz, $H-5$), 3.99 (dd, 1 H, J = 9.7, 9.6 Hz, $H-4$), 3.90 (dd, 1 H, J = 10.6, 10.1 Hz, $H-6$), 3.46 (s, 3 H, OCH_3); ^{13}C NMR (125 MHz, CDCl_3) δ 194.9, 165.8, 153.3, 136.8, 133.6, 130.1, 129.3, 129.0, 128.9, 128.9, 128.5, 128.2, 128.2, 126.5, 126.1, 121.7, 101.5, 97.7, 79.0, 78.8, 72.5, 68.8, 62.3, 55.5; HRMS (FAB): calcd for $\text{C}_{28}\text{H}_{25}\text{O}_8$ ($M - \text{H}$) $^+$ 512.1270, found 512.1264.

General procedure for radical allylation exemplified by the preparation of **methyl (3S)-2-O-benzoyl-4,6-di-O-benzylidene-3-allyl-3-deoxy- α -D-glucopyranoside (20c)**:

A solution of **19c** (4.98 g, 9.50 mmol), allyltributyltin (7.40 mL, 23.9 mmol), AIBN (313 mg, 1.91 mmol) and toluene (15 mL) was heated to reflux for 4 hours at which point TLC showed complete consumption of the starting material. The solution was concentrated and flash chromatography of the residue over silica gel (5.5 x 8 cm) using 5% EtOAc-toluene gave **20c** (3.48 g, 62%) as a pure ($R_f = 0.38$, TLC silica, 10% EtOAc-hexanes; ^1H NMR, 500 MHz) solid: m.p. = 138-139 °C; $[\alpha]_D = +68.8$ ($c = 0.98$, CHCl_3); FT-IR (neat) 3066, 2931, 2863, 1717, 1600, 1450, 1375, 1333, 1314, 1274, 1176, 1107, 1096, 1070, 1048, 1028, 996, 911, 755, 711, 698 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 8.11 (dd, 2 H, $J = 1.5, 8.1$ Hz, ArH), 7.61-7.38 (m, 8 H, ArH), 5.90-5.82 (m, 1 H, H-8), 5.56 (s, 1 H, PhCH), 5.06-5.00 (m, 4 H, H-1, H-2, 2 x H-9), 4.33 (dd, 1 H, $J = 10.2, 5.1$ Hz, H-6), 3.92 (ddd, 1 H, $J = 10.2, 10.2, 4.6$ Hz, H-5), 3.77 (dd, 1 H, $J = 10.6, 10.1$ Hz, H-6), 3.50 (dd, 1 H, $J = 10.6, 9.1$ Hz, H-4), 3.42 (s, 3 H, OCH_3), 2.69-2.63 (m, 1 H, H-3), 2.54-2.48 (m, 1 H, H-7), 2.44-2.39 (m, 1 H, H-7); ^{13}C NMR (125 MHz, CDCl_3) δ 165.9, 137.4, 133.7, 133.3, 129.8, 129.5, 128.9, 128.4, 128.3, 128.2, 126.0, 118.1, 101.5, 96.9, 78.1, 71.4, 69.2, 63.4, 55.2, 38.5, 29.9; HRMS (FAB): calcd for $\text{C}_{24}\text{H}_{26}\text{O}_6$ (M) $^+$ 410.1729, found 410.1732.

General procedure for deacylation and benzylation exemplified by the preparation of **methyl (3R)-2,3,6-tri-O-benzyl-4,6-3-allyl-3-deoxy- α -D-glucopyranoside (21c)**:

NaH (60% dispersion in mineral oil, 80 mg, 2 mmol) was added to a solution of **20c** (2.48 g, 5.82 mmol), in methanol (15 mL) and the resulting mixture was stirred for 2 hours at room temperature. The solution was concentrated and dried under vacuum. NaH (60% dispersion in mineral oil, 460 mg, 11.5 mmol) and benzyl bromide (1.38 mL, 11.6 mmol) were added to a DMF (60 mL) solution of the crude deacetylated product and the resulting slurry was stirred at 23 °C for 12 hours. The solution was quenched by the addition of MeOH (3 mL) and partitioned with diethyl ether (60 mL). The ethereal extract was washed with water (1 x 30 mL), dried and filtered. The solution was concentrated and flash chromatography of the residue over silica gel (5.5 x 7 cm) using 8% EtOAc/hexanes gave **21c** (2.25 g, 94%) as a pure ($R_f = 0.26$, TLC silica, 10% EtOAc-hexanes; ^1H NMR, 500 MHz) solid: m.p. = 91-92 °C; $[\alpha]_D = +21.8$ ($c = 0.71$, CHCl_3); FT-IR (neat) 3064, 3033, 2976, 2909, 2866, 1638, 1497, 1451, 1373, 1329, 1295, 1211, 1190, 1088, 1070, 1055, 1028, 991, 915, 746, 696 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.50-7.31 (m, 10 H, ArH), 5.83-5.75 (m, 1 H, H-8), 5.47 (s, 1 H, PhCH), 5.11-5.08 (m, 2 H, 2 x H-9), 4.66 (d, 1 H, $J = 3.6$ Hz, H-1), 4.62 (s, 2 H, 2 x OCH_2Ph), 4.26 (dd, 1 H, $J = 10.1, 5.1$ Hz, H-6), 3.81 (ddd, 1 H, $J = 10.1, 10.1, 5.1$ Hz, H-5), 3.66 (dd, 1 H, $J = 10.6, 10.1$ Hz, H-6), 3.41 (s, 3 H, OCH_3), 3.38 (dd, 1 H, $J = 10.7, 7.6$ Hz, H-2), 3.34 (dd, 1 H, $J = 10.6, 9.1$ Hz, H-4), 2.55-2.46 (m, 2 H, 2 x H-7), 2.41-2.35 (m, 1 H, H-3); ^{13}C NMR (125 MHz, CDCl_3) δ 137.9, 137.5, 134.3, 128.9, 128.4, 128.2, 128.1, 127.9, 126.0, 117.8, 101.3, 97.4, 78.1, 76.3, 72.2, 69.3, 63.3, 55.1, 39.6, 29.3; HRMS (FAB): calcd for $\text{C}_{24}\text{H}_{28}\text{O}_5$ (M) $^+$ 396.1936, found 396.1935..

(22c)

Ozone was bubbled through a $-78\text{ }^{\circ}\text{C}$ solution of **21c** (2.12 g, 5.14 mmol) in CH_2Cl_2 (75 mL) until the blue color persisted. The solution was then purged with O_2 to remove excess ozone and zinc dust (3.36 g, 51.4 mmol) and glacial acetic acid (1.18 mL, 20.6 mmol) were then added in one portion. The resulting mixture was allowed to warm to room temperature with the cold bath in place and then stirred for an additional 5 hours at room temperature. The suspension was filtered and the filtrate concentrated *in vacuo*. Flash chromatography of the residue over silica gel (5.5 x 6 cm) using 30% Et_2O /hexanes gave **22c** (1.82 g, 85%) as a pure ($R_f = 0.24$, TLC silica, 20% EtOAc -hexanes; ^1H NMR, 500 MHz) solid: m.p. = $114\text{--}115\text{ }^{\circ}\text{C}$; $[\alpha]_D = +41.0$ ($c = 0.92$, CHCl_3); FT-IR (neat) 2907, 2861, 1720, 1453, 1371, 1088, 1061 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 9.65 (dd, 1 H, $J = 3.0, 2.0$ Hz, CHO), 7.43–7.31 (m, 10 H, ArH), 5.47 (s, 1 H, PhCH), 4.60 (d, 1 H, $J = 3.0$, H-1), 4.56 (d, 1 H, $J = 12.2$ Hz, OCH_2Ph), 4.52 (d, 1 H, $J = 12.1$ Hz, OCH_2Ph), 4.25 (dd, 1 H, $J = 10.1, 4.6$ Hz, H-6), 3.82 (ddd, 1 H, $J = 10.2, 10.2, 5.1$ Hz, H-5), 3.66 (dd, 1 H, $J = 10.6, 10.1$ Hz, H-6), 3.41 (s, 3 H, OCH_3), 3.36 (dd, 1 H, $J = 10.7, 3.6$ Hz, H-2), 3.31 (dd, 1 H, $J = 10.1, 9.1$ Hz, H-4), 2.85 (m, 1 H, H-3), 2.65 (ddd, 1 H, $J = 16.2, 5.6, 2.0$ Hz, H-7), 2.46 (ddd, 1 H, $J = 16.2, 7.6, 3.6$ Hz, H-7); ^{13}C NMR (125 MHz, CDCl_3) δ 201.7, 137.1, 137.0, 129.0, 128.5, 128.4, 128.2, 125.9, 101.5, 97.1, 79.6, 78.0, 72.5, 69.0, 63.5, 55.2, 43.1, 37.0; HRMS (FAB): calcd for $\text{C}_{23}\text{H}_{25}\text{O}_6$ ($M - \text{H}$) $^+$ 399.1651, found 399.1654.

(6c)

The general procedure for oxidation to the acid was followed using: Aldehyde **22c** (1.82 g, 4.64 mmol), *t*-BuOH-water (10:1, 20 mL), 2-methyl-2-butene (2.58 mL, 30.7 mmol), potassium phosphate monobasic (670 mg, 5.58 mmol) and sodium chlorite (80%, 670 mg, 5.93 mmol). After the usual work-up, flash chromatography of the residue over silica gel (5.5 x 4 cm) using 30% EtOAc /hexanes–0.2% AcOH gave **6c** (1.72 g, 91%) as a pure ($R_f = 0.28$, TLC silica, EtOAc ; ^1H NMR, 500 MHz) solid: m.p. = $159\text{--}160\text{ }^{\circ}\text{C}$; $[\alpha]_D = +25.6$ ($c = 1.51$, CHCl_3); FT-IR (neat) 2930, 2864, 1705, 1453, 1372, 1086, 1057 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.45–7.25 (m, 10 H, ArH), 5.47 (s, 1 H, PhCH), 4.63 (d, 1 H, $J = 3.1$ Hz, H-1), 4.59 (s, 2 H, 2 x OCH_2Ph), 4.24 (dd, 1 H, $J = 10.1, 4.6$ Hz, H-6), 3.80 (ddd, 1 H, $J = 10.1, 10.1, 5.0$ Hz, H-5), 3.66 (dd, 1 H, $J = 10.7, 10.1$ Hz, H-6), 3.52 (dd, 1 H, $J = 11.1, 3.6$ Hz, H-2), 3.44 (dd, 1 H, $J = 10.6, 9.6$ Hz, H-4), 3.40 (s, 3 H, OCH_3), 2.74–2.56 (m, 3 H, H-3, 2 x H-7); ^{13}C NMR (125 MHz, CDCl_3) δ 177.8, 137.4, 137.2, 128.9, 128.4, 128.2, 128.1, 128.0, 126.0, 101.4, 97.2, 79.0, 77.4, 72.5, 69.1, 63.6, 55.1, 37.9, 31.7; HRMS (FAB): calcd for $\text{C}_{23}\text{H}_{25}\text{O}_7$ ($M - \text{H}$) $^+$ 413.1600, found 413.1599.

(19d)

Methanol (0.270 mL, 6.66 mmol) and NIS (1.32 g, 5.87 mmol) were added to a solution of tri-*O*-acetylglucal (**18d**) (1.00 g, 3.68 mmol) in dry acetonitrile (15 mL).⁸ The resulting mixture was stirred at room temperature for 12 hours, diluted with EtOAc (50 mL) and washed with 10% Na₂S₂O₃ (1 x 10 ml) and water (1 x 15 ml). The organic layer was dried and evaporated. The crude residue was purified by flash chromatography over silica gel (5.5 x 4 cm) using 20% EtOAc/hexanes to give known compound **19d** (1.31 g, 85%) as a pure (*R*_f = 0.36, TLC silica, 3 x 40% Et₂O-hexanes) oil.

(20d and 20e)

The general procedure for the radical allylation was followed using **19d** (4.68 g, 10.9 mmol), allyltributyltin (8.45 mL, 27.3 mmol), AIBN (270 mg, 1.64 mmol) and toluene (22 ml). The reaction was heated to reflux for 1.5 hours at which point TLC showed complete consumption of the starting material. The solution was concentrated and flash chromatography of the residue over silica gel using 10% EtOAc/hexanes gave **20d** and **20e** (2.40 g, 64%) as a mixture of isomers (α : β :1:1.5, ¹H NMR, 500 MHz) (*R*_f = 0.38, TLC silica, 3 x 20% EtOAc-hexanes). The isomers were not separated, but carried on as a mixture to the next step.

(21d and 21e)

The general procedure for deacylation/benzylation was followed using: **20d** and **20e** (2.40 g, 6.98 mmol), NaH (60% dispersion in mineral oil, 160 mg, 4.0 mmol) and methanol (20 mL), NaH (60% dispersion in mineral oil, 1.95 mg, 48.8 mmol), benzyl bromide (3.15 mL, 26.5 mmol) and DMF (60 ml). After the usual work-up, flash chromatography of the residue over silica gel (5.5 x 7 cm) using 10% Et₂O/hexanes gave **21d** and **21e** (3.14 g, 92%) as a mixture (α : β :1:1.5, ¹H NMR, 500 MHz), (*R*_f = 0.31, TLC silica, 20% Et₂O-hexanes) oil. Once again the isomers were not separated, but carried on as a mixture to the next step.

(22e)

Ozone was bubbled through a $-78\text{ }^{\circ}\text{C}$ solution of **21d** and **21e** (3.14 g, 6.43 mmol) in CH_2Cl_2 (75 mL) until the blue color persisted. The solution was then purged with O_2 to remove excess ozone and zinc dust (4.20 g, 64.2 mmol) and glacial acetic (1.50 mL, 26.2 mmol) were then added in one portion. The resulting mixture was allowed to warm to room temperature, with the cold bath in place, and then stirred for an additional 13 hours. The suspension was filtered and the filtrate concentrated *in vacuo*. Flash chromatography of the residue over silica gel using 5% Et_2O /benzene gave **22e** (1.67 g, 88%) as a pure ($R_f = 0.52$, TLC silica, 3 x 5% Et_2O -benzene; ^1H NMR, 500 MHz) oil: $[\alpha]_D = +48.3$ ($c = 1.14$, CHCl_3); FT-IR (neat) 3062, 3029, 2915, 2856, 2724, 1721, 1605, 1496, 1453, 1364, 1251, 1208, 1133, 1098, 1069, 1027, 968, 736, 697 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 9.79 (s, 1 H, CHO), 7.37-7.14 (m, 15 H, ArH), 4.83 (d, 1 H, $J = 11.1$ Hz, OCH_2Ph), 4.66 (d, 1 H, $J = 12.1$ Hz, OCH_2Ph), 4.63 (d, 1H, $J = 1.0$ Hz, $H-1$), 4.59 (d, 1 H, $J = 11.2$ Hz, OCH_2Ph), 4.55 (d, 1 H, $J = 11.6$ Hz, OCH_2Ph), 4.51 (d, 1 H, $J = 12.2$ Hz, OCH_2Ph), 4.45 (d, 1 H, $J = 10.6$ Hz, OCH_2Ph), 4.09 (dd, $J = 9.1, 5.0$ Hz, $H-3$), 3.78-3.71 (m, 2 H, $H-6, H-5$), 3.68-3.63 (m, 2 H, $H-6, H-4$), 3.34 (s, 3H, OCH_3), 3.00-2.96 (m, 1 H, $H-2$), 2.94-2.90 (m, 1 H, $H-7$), 2.55 (dd, 1 H, $J = 18.3, 9.2$ Hz, $H-7$); ^{13}C NMR (125 MHz, CDCl_3) δ 200.8, 138.2, 138.0, 128.3, 128.3, 128.2, 127.7, 127.7, 127.6, 127.6, 127.5, 127.5, 100.9, 78.5, 74.8, 74.3, 73.3, 71.6, 70.7, 68.8, 54.7, 40.2, 36.6; HRMS (FAB): calcd for $\text{C}_{23}\text{H}_{27}\text{O}_6$ ($M - \text{C}_7\text{H}_7$) $^+$ 399.1807, found 399.1809

(22d)

and **22d** (1.12 g, 88%) as a pure ($R_f = 0.44$, TLC silica, 3 x 5% Et_2O -benzene; ^1H NMR, 500 MHz) oil: $[\alpha]_D = +109.4$ ($c = 0.94$, CHCl_3); FT-IR (neat) 3085, 3063, 3031, 2895, 2860, 2724, 1721, 1496, 1453, 1360, 1267, 1127, 1066, 1047, 1027, 914, 736, 697 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 9.66-9.65 (m, 1 H, CHO), 7.38-7.16 (m, 15 H, ArH), 4.89 (d, 1 H, $J = 10.6$ Hz, OCH_2Ph), 4.80 (d, 1 H, $J = 11.1$ Hz, OCH_2Ph), 4.77 (d, 1 H, $J = 3.0$ Hz, $H-1$), 4.68 (d, 1 H, $J = 12.2$ Hz, OCH_2Ph), 4.58 (d, 1 H, $J = 11.2$ Hz, OCH_2Ph), 4.56 (d, 1 H, $J = 10.7$ Hz, OCH_2Ph), 4.55 (d, 1 H, $J = 12.1$ Hz, OCH_2Ph), 3.82-3.66 (m, 5 H, 2 x $H-6, H-5, H-4, H-3$), 3.31 (s, 3 H, OCH_3), 2.59 (m, 1 H, $H-7$), 2.48-2.43 (m, 2 H, $H-2, H-7$); ^{13}C NMR (125 MHz, CDCl_3) δ 200.8, 138.0, 138.0, 137.9, 128.4, 128.3, 128.3, 127.8, 127.8, 127.7, 127.6, 127.6, 99.8, 80.1, 79.6, 74.9, 74.6, 73.4, 70.8, 68.5, 54.8, 42.2, 41.2; HRMS (FAB): calcd for $\text{C}_{23}\text{H}_{27}\text{O}_6$ ($M - \text{C}_7\text{H}_7$) $^+$ 399.1807, found 399.1810.

(6d)

The general procedure for oxidation to the acid was followed using: Aldehyde **22d** (356 mg, 0.726 mmol), *t*-BuOH-water (10:1, 3 mL), 2-methyl-2-butene (0.41 mL, 4.89 mmol), potassium phosphate monobasic (113 mg, 0.942 mmol) and sodium chlorite (80%, 106 mg, 0.938 mmol). After the usual work-up, flash chromatography of the residue over silica gel (5.5 x 4 cm) using 30% EtOAc/hexanes with 0.2% AcOH gave acid **6d** (350 mg, 89%) as a pure oil: $[\alpha]_D = +81.4$ ($c = 0.87$ CHCl₃); FT-IR (neat) 3273, 3089, 3027, 2925, 1706, 1495, 1452, 1361, 1304, 1208, 1124, 1088, 1046, 1026, 920, 734, 696 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.39-7.17 (m, 15 H, ArH), 4.95 (d, 1 H, $J = 11.2$ Hz, OCH₂Ph), 4.84 (d, 1 H, $J = 3.0$ Hz, H-1), 4.82 (d, 1 H, $J = 10.6$ Hz, OCH₂Ph), 4.70 (d, 1 H, $J = 11.7$ Hz, OCH₂Ph), 4.65 (d, 1 H, $J = 11.2$ Hz, OCH₂Ph), 4.57 (d, 1 H, $J = 9.1$ Hz, OCH₂Ph), 4.56 (d, 1 H, $J = 12.1$ Hz, OCH₂Ph), 3.83-3.78 (m, 2 H, H-6, H-5), 3.75-3.67 (m, 3 H, H-6, H-4, H-3), 3.35 (s, 3 H, OCH₃), 2.63 (dd, 1 H, $J = 15.7, 4.1$ Hz, H-7), 2.45-2.36 (m, 2 H, H-2, H-7); ¹³C NMR (125 MHz, CDCl₃) δ 178.4, 138.1, 138.0, 137.9, 128.3, 128.2, 127.8, 127.6, 127.6, 99.6, 80.2, 79.6, 75.1, 74.6, 73.4, 70.8, 68.5, 54.9, 42.5, 32.2; HRMS (FAB): calcd for C₂₂H₂₃O₆ (M - C₇H₈ - OCH₃)⁺ 383.1494, found 383.1498.

(6e)

The general procedure for oxidation to the acid was followed using: Aldehyde **22e** (2.17 g, 4.42 mmol), *t*-BuOH-water (10:1, 20 mL), 2-methyl-2-butene (2.58 mL, 30.7 mmol), potassium phosphate monobasic (690 mg, 5.75 mmol) and sodium chlorite (80%, 650 mg, 5.75 mmol). After the usual work-up, flash chromatography of the residue over silica gel (5.5 x 6 cm) using 30% EtOAc/hexanes with 0.2% AcOH gave **6e** (2.14 g, 95%) as a pure oil: $[\alpha]_D = +39.4$ ($c = 1.66$, CHCl₃); FT-IR (neat) 3209, 3059, 3031, 2931, 1731, 1706, 1495, 1452, 1364, 1273, 1209, 1096, 1061, 1027, 971, 734, 696 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.40-7.18 (m, 15 H, ArH), 4.87 (d, 1 H, $J = 10.6$ Hz, OCH₂Ph), 4.78 (s, 1 H, H-1), 4.68 (d, 1 H, $J = 11.7$ Hz, OCH₂Ph), 4.69 (d, 1 H, $J = 11.2$ Hz, OCH₂Ph), 4.60 (d, 1 H, $J = 11.6$ Hz, OCH₂Ph), 4.55 (d, 1 H, $J = 12.2$ Hz, OCH₂Ph), 4.49 (d, 1 H, $J = 10.6$ Hz, OCH₂Ph), 4.14 (dd, 1 H, $J = 9.6, 5.1$ Hz, H-3), 3.80-3.76 (m, 2 H, H-6, H-5), 3.72-3.64 (m, 2 H, H-6, H-4), 3.38 (s, 3 H, OCH₃), 2.90-2.85 (m, 2 H, H-2, H-7), 2.50 (dd, 1 H, $J = 17.7, 10.6$ Hz, H-7); ¹³C NMR (125 MHz, CDCl₃) δ 178.7, 138.2, 138.2, 138.0, 128.3, 128.2, 128.2, 128.2, 127.8, 127.7, 127.5, 127.5, 127.4, 127.4, 100.8, 78.4, 74.8, 74.2, 73.3, 71.4, 70.8, 68.8, 54.7, 38.7, 30.2; HRMS (FAB): calcd for C₂₃H₂₇O₇ (M - C₇H₇)⁺ 415.1756, found 415.1753.

(22f)

A solution of lithium periodate / lithium phosphate buffer⁹ (40 mL, pH = 7.0) and an aqueous solution of OsO₄ (1.95 mL, 0.078 mmol, 1%w/v) were sequentially added to a solution of olefin **21f**¹⁰ (1.49 g, 1.64 mmol) in EtOAc (40 mL). The reaction mixture was stirred for 24 hours at ambient temperature and was then quenched with saturated Na₂S₂O₃ solution (20 mL) and the resulting mixture was stirred for 15 min. The layers were separated and the aqueous phase was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with water (1 × 30 mL), dried and evaporated. Flash chromatography of the residue over silica gel using 10%-20% EtOAc-hexanes gave aldehyde **22f** (0.83 g, 56%) as a pure (*R*_f = 0.56, TLC, silica 30% EtOAc-hexanes) colorless oil: ¹H NMR (500 MHz, CDCl₃) δ 9.72 (dd, 1 H, *J* = 2.5, 2.5 Hz, CHO), 7.36-7.15 (m, 20 H, ArH), 4.94 (d, 1 H, *J* = 11.0 Hz, OCH₂Ph), 4.90 (d, 1 H, *J* = 11.5 Hz, OCH₂Ph), 4.89 (d, 1 H, *J* = 10.5 Hz, OCH₂Ph), 4.82 (d, 1 H, *J* = 11.0 Hz, OCH₂Ph), 4.62-4.55 (m, 3 H, OCH₂Ph), 4.51 (d, 1 H, *J* = 12.0 Hz, OCH₂Ph), 3.83 (ddd, 1 H, *J* = 9.6, 8.3, 4.2 Hz, *H*-1), 3.73 (dd, 1 H, *J* = 8.6, 9.1 Hz, *H*-3), 3.69 (apparent d, 2 H, *J* = 3.5 Hz, 2 × *H*-6), 3.67 (dd, 1 H, *J* = 9.6, 9.6 Hz, *H*-4), 3.48 (ddd, 1 H, *J* = 9.5, 3.0, 3.0 Hz, *H*-5), 3.35 (dd, 1 H, *J* = 9.1, 9.1 Hz, *H*-2), 2.71 (ddd, 1 H, *J* = 16.1, 4.3, 2.1 Hz, *H*-7), 2.57 (ddd, 1 H, *J* = 16, 8.0, 2.5 Hz, *H*-7); ¹³C NMR (125 MHz, CDCl₃) δ 200.5, 138.6, 138.2, 137.9, 128.8, 128.7, 128.7, 128.6, 128.4, 128.3, 128.1, 128.1, 127.9, 127.9, 127.9, 87.3, 81.4, 79.4, 78.6, 75.8, 75.3, 75.3, 74.7, 73.7, 69.0, 46.3.

(6f)

The general procedure for oxidation to the acid was followed using: Aldehyde **22f** (826 mg, 1.46 mmol), *t*-BuOH-water (10:1, 22 mL), 2-methyl-2-butene (1.55 mL, 14.6 mmol), potassium phosphate monobasic (397 mg, 2.92 mmol) and sodium chlorite (328 mg, 80%, 2.92 mmol). Flash chromatography of the residue over silica gel using 10-30% EtOAc-hexanes/1% AcOH gave acid **6f** (798 mg, 94%) as a pure (*R*_f = 0.16, TLC, 20% EtOAc-hexanes/1% AcOH) white solid: m.p. = 102.5-103.8 °C; [*α*]_D = + 5.6 (*c* = 0.75, CHCl₃); FT-IR (neat) 3062, 3030, 2909, 2866, 1712, 1492, 1447, 1361, 1209, 1094, 1208, 735, 697 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.36-7.15 (m, 20 H, ArH), 4.94 (d, 1 H, *J* = 11.0 Hz, OCH₂Ph), 4.92 (d, 1 H, *J* = 11.0 Hz, OCH₂Ph), 4.89 (d, 1 H, *J* = 10.5 Hz, OCH₂Ph), 4.82 (d, 1 H, *J* = 11.0 Hz, OCH₂Ph), 4.65 (d, 1 H, *J* = 11.0 Hz, OCH₂Ph), 4.61 (d, 1 H, *J* = 12.5 Hz, OCH₂Ph), 4.57 (d, 1 H, *J* = 10.5 Hz, OCH₂Ph), 4.51 (d, 1 H, *J* = 12.0 Hz, OCH₂Ph), 3.78-3.64 (m, 5 H, *H*-1, *H*-3, *H*-4, 2 × *H*-6), 3.48 (ddd, 1 H, *J* = 9.5, 3.5, 2.3 Hz, *H*-5), 3.37 (dd, 1 H, *J* = 9.5, 9.0 Hz, *H*-2), 2.77 (dd, 1 H, *J* = 10.5, 4.5 Hz, *H*-7), 2.50 (dd, 1 H, *J* = 10.5, 8.5 Hz, *H*-7); ¹³C NMR (125 MHz, CDCl₃) δ 175.7, 138.6, 138.3, 138.2, 138.0, 128.7, 128.7, 128.7, 128.6, 128.2, 128.2, 128.1, 128.1, 128.0, 127.9, 127.9, 87.3, 81.2, 79.3, 78.5, 75.8, 75.8, 75.4, 75.3, 73.6, 68.8, 37.4; HRMS (FAB): calcd for C₃₆H₃₈O₇ (*M* + Na)⁺ 605.2509, found 605.2491.

(7f):

The general procedure for esterification was followed using acid **6f** (1.02 g, 1.75 mmol), alcohol **5a** (488 mg, 1.17 mmol), DCC (361 mg, 1.75 mmol), 4-DMAP (122 mg, 1.0 mmol) and CH_2Cl_2 (2 ml). After the usual work-up, flash chromatography of the obtained residue over silica gel using 10-20% Et_2O -hexanes gave ester **7f** (752 mg, 77%) as a pure (R_f = 0.38, TLC, silica 40% Et_2O -hexanes) colorless oil: $[\alpha]_D^{25} = +0.69$ (c = 0.75, CHCl_3); FT-IR (neat) 3088, 3064, 3030, 2866, 1737, 1496, 1454, 1360, 1215, 1070, 1027, 732, 695, 666, 598, 523 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.40-7.10 (m, 35 H, ArH), 5.86 (ddd, 1 H, J = 19.0, 10.5, 8.5 Hz, H -2), 5.38-5.22 (m, 3 H, 2 $\times$ H -1, H -5), 4.91 (d, 1 H, J = 11.0 Hz, OCH_2Ph), 4.90 (d, 1 H, J = 9.0 Hz, OCH_2Ph), 4.87 (d, 1 H, J = 10.5 Hz, OCH_2Ph), 4.78 (d, 1 H, J = 10.5 Hz, OCH_2Ph), 4.69 (d, 1 H, J = 11.0 Hz, OCH_2Ph), 4.66-4.62 (m, 2 H, 2 $\times$ OCH_2Ph), 4.55 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 4.53 (d, 1 H, J = 9.5 Hz, OCH_2Ph), 4.47 (d, 1 H, J = 11.0 Hz, OCH_2Ph), 4.44 (d, 1 H, J = 12.0 Hz, OCH_2Ph), 4.40 (d, 1 H, J = 12.0 Hz, OCH_2Ph), 4.35 (d, 1 H, J = 12.0 Hz, OCH_2Ph), 4.33 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 3.92 (dd, 1 H, J = 8.0, 5.5 Hz, H -3), 3.82 (dd, 1 H, J = 5.0, 5.0 Hz, H -4), 3.80-3.74 (m, 3 H, H -1', 2 $\times$ H -6), 3.72-3.65 (m, 2 H, H -3', H -4'), 3.60 (dd, 1 H, J = 11.0, 4.0 Hz, H -6'), 3.54 (dd, 1 H, J = 11.0, 1.5 Hz, H -6'), 3.42-3.31 (m, 2 H, H -5', H -2'), 2.75 (dd, 1 H, J = 5.5, 3.0 Hz, H -7'), 2.44 (dd, 1 H, J = 5.5, 4.0 Hz, H -7'); ^{13}C NMR (125 MHz, CDCl_3) δ 170.5, 138.8, 138.7, 138.5, 138.5, 138.4, 138.3, 138.2, 135.5, 128.7, 128.7, 128.6, 128.6, 128.5, 128.5, 128.3, 128.2, 128.1, 128.1, 128.0, 128.0, 127.8, 127.8, 127.7, 119.5, 87.3, 81.5, 81.4, 81.3, 79.2, 78.6, 76.2, 75.7, 75.4, 75.3, 75.1, 73.6, 73.2, 73.2, 70.9, 68.9, 68.4, 37.9; HRMS (FAB): calcd for $\text{C}_{63}\text{H}_{66}\text{O}_{10}$ ($M + \text{Na}$) $^+$ 1005.4548, found 1005.4502.

(8f):

The general procedure for methylenation was followed using: Titanium tetrachloride (0.86 mL, 2 M in CH_2Cl_2 , 1.72 mmol), THF (4 mL), TMEDA (0.50 mL, 3.31 mmol), zinc dust (240 mg, 3.67 mmol), lead (II) chloride (3 mg, 0.01 mmol), ester **7f** (98.6 mg, 0.100 mmol) and dibromomethane (0.07 mL, 3.67 mmol). After the usual work-up, gravity chromatography of the residue over silica using 20% Et_2O -hexanes-1% triethylamine gave **8f** (51 mg, 52%) as a pure (R_f = 0.50, TLC silica, 40% Et_2O -hexanes; ^1H NMR, 500 MHz) oil: $[\alpha]_D^{25} = +7.19$ (c = 0.44, CH_2Cl_2); FT-IR (neat) 3029, 2858, 1654, 1495, 1452, 1360, 1209, 1093, 1027, 733, 696 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.37-7.00 (m, 35 H, ArH), 5.87 (ddd, 1 H, J = 17.8, 10.7, 7.6 Hz, H -2), 5.20 (dd, 1 H, J = 17.2, 1.0 Hz, H -1), 5.04 (dd, 1 H, J = 10.7, 2.1 Hz, H -1), 4.86 (d, 1 H, J = 11.6 Hz, OCH_2Ph), 4.85 (d, 1 H, J = 11.1 Hz, OCH_2Ph), 4.83 (d, 1 H, J = 10.2 Hz, OCH_2Ph), 4.81 (d, 1 H, J = 11.6 Hz, OCH_2Ph), 4.79 (d, 1 H, J = 13.2 Hz, OCH_2Ph), 4.76 (d, 1 H, J = 11.1 Hz, OCH_2Ph), 4.70 (dd, 1 H, J = 8.1, 8.1 Hz, H -5), 4.60 (d, 1 H, J = 11.1 Hz, OCH_2Ph), 4.55 (d, 1 H, J = 11.6 Hz, OCH_2Ph), 4.53 (d, 1 H, J = 11.1 Hz, OCH_2Ph), 4.45 (d, 1 H, J = 12.6 Hz, OCH_2Ph), 4.40 (d, 1 H, J = 12.2 Hz, OCH_2Ph), 4.32 (d, 1 H, J = 11.6 Hz, OCH_2Ph), 4.30 (d, 1 H, J = 11.6 Hz, OCH_2Ph), 4.28 (d, 1 H, J =

11.6 Hz, OCH_2Ph), 4.25 (d, 1 H, $J = 1.5$ Hz, $H-9'$), 4.22 (d, 1 H, $J = 2.1$ Hz, $H-9'$), 4.13-4.10 (m, 2 H, $H-3$, $H-4$), 3.98 (dd, 1 H, $J = 10.6$, 3.5 Hz, $H-6$), 3.82-3.78 (m, 2 H, $H-6$, $H-1'$), 3.74 (dd, 1 H, $J = 9.1$, 9.1 Hz, $H-4'$), 3.68-3.64 (m, 2 H, $H-6'$, $H-3'$), 3.60 (dd, 1 H, $J = 11.2$, 4.1 Hz, $H-6'$), 3.37 (dd, 1 H, $J = 9.6$, 9.2 Hz, $H-5'$), 3.30 (dd, 1 H, $J = 9.6$, 9.2 Hz, $H-2'$), 2.78 (dd, 1 H, $J = 14.7$, 2.5 Hz, $H-7'$), 2.29 (dd, 1 H, $J = 14.1$, 9.1 Hz, $H-7'$); ^{13}C NMR (125 MHz, C_6D_6) δ 158.2, 139.5, 139.4, 139.2, 139.1, 139.0, 138.9, 136.0, 128.4, 128.4, 128.3, 128.1, 128.0, 127.9, 127.8, 127.7, 127.7, 127.5, 127.5, 127.4, 127.4, 118.4, 87.6, 84.8, 82.3, 81.2, 81.2, 79.6, 78.9, 76.9, 75.7, 75.3, 75.2, 74.9, 74.6, 73.3, 73.3, 70.9, 69.2, 68.3, 38.5; HRMS (FAB): calcd for $\text{C}_{64}\text{H}_{68}\text{O}_9\text{Na}$ ($\text{M} + \text{Na}$) $^+$ 1003.4755, found 1003.4711.

(10f):

The general procedure for the one-pot protocol was followed using the ruthenium-based metathesis catalyst **26** (10 mg, 0.012 mmol, 40 mol%), toluene (2 mL), enol ether **8f** (26 mg, 0.027 mmol), $\text{BH}_3 \cdot \text{THF}$ (0.3 mL, 1M in THF, 0.3 mmol), NaOH (10 mL, 1 M) and hydrogen peroxide (10 mL, 30% in water). After the usual work-up, flash chromatography of the residue over silica using 20% EtOAc-hexanes gave **10f** (12.9 mg, 50%) as a pure ($R_f = 0.77$, TLC silica, 40% EtOAc-hexanes; ^1H NMR, 500 MHz) colorless oil: $[\alpha]_D^{25} = +13.3$ ($c = 0.52$, CHCl_3); FT-IR (neat) 3462, 3085, 3061, 3028, 2863, 1604, 1495, 1452, 1359, 1210, 1091, 734, 696 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.34-7.02 (m, 35 H, ArH), 4.96 (d, 1 H, $J = 11.6$ Hz, OCH_2Ph), 4.88 (d, 1 H, $J = 12.2$ Hz, OCH_2Ph), 4.86 (d, 1 H, $J = 12.2$ Hz, OCH_2Ph), 4.83 (d, 1 H, $J = 9.2$ Hz, OCH_2Ph), 4.82 (s, 2 H, 2 x OCH_2Ph), 4.79 (d, 1 H, $J = 11.7$ Hz, OCH_2Ph), 4.58 (d, 1 H, $J = 11.1$ Hz, OCH_2Ph), 4.55 (d, 1 H, $J = 11.6$ Hz, OCH_2Ph), 4.51 (d, 1 H, $J = 11.7$ Hz, OCH_2Ph), 4.41 (d, 1 H, $J = 12.1$ Hz, OCH_2Ph), 4.40 (d, 1 H, $J = 12.2$ Hz, OCH_2Ph), 4.35 (d, 1 H, $J = 12.2$ Hz, OCH_2Ph), 4.34 (d, 1 H, $J = 12.2$ Hz, OCH_2Ph), 3.74-3.50 (m, 11 H, $H-2'$, $H-4'$, $H-2$, 2 x $H-6$, 2 x $H-6'$, $H-4$, $H-1'$, $H-1$, $H-3$), 3.46-3.41 (m, 2 H, $H-3'$, $H-5$), 3.24 (dd, 1 H, $J = 9.1$, 9.1 Hz, $H-5'$), 3.29 (dd, 1 H, $J = 13.2$, 6.6 Hz, $H-7'$), 2.06-2.00 (m, 1 H, $H-7'$); ^{13}C NMR (125 MHz, C_6D_6) δ 139.8, 139.3, 139.3, 139.0, 138.7, 128.4, 128.4, 128.4, 128.3, 128.1, 128.0, 127.8, 127.7, 127.7, 127.6, 127.5, 127.5, 127.4, 87.5, 87.3, 82.5, 79.4, 79.0, 78.8, 78.5, 77.3, 76.3, 75.8, 75.3, 75.1, 75.0, 74.7, 74.6, 73.2, 69.5, 69.3, 36.0; HRMS (FAB): calcd for $\text{C}_{62}\text{H}_{66}\text{O}_{10}\text{Na}$ ($\text{M} + \text{Na}$) $^+$ 993.4548, found 993.4573.

(19h)

A mixture of alcohol **18h**¹¹ (4.10 g, 12.8 mmol), phenyl chlorothionoformate (8.45 mL, 80.0 mmol), pyridine (10 mL), DMAP (1.59 g, 13.0 mmol) and NHS⁷ (1.50 g, 13.0 mmol) in toluene (65 mL) was heated to 70 °C for 1 hour under inert atmosphere. The obtained yellow solution was cooled to room temperature and a large amount of dark-yellow solid appeared. The solid was dissolved by the addition of CH_2Cl_2 (100 mL) and the resulting organic

solution was washed with 1N H₂SO₄ (2 × 30 mL), saturated NaHCO₃ (2 × 30 mL), water (2 × 30 mL), dried and evaporated. Flash chromatography of the residue over silica gel using 2-10% Et₂O-benzene gave **19h** (4.70 g, 94%) as a pure (*R*_f = 0.15, TLC, silica 5% Et₂O-benzene) yellow solid: m.p. = 161.7-163.2 °C; [α]_D = +114.2 (*c* = 1.0, CHCl₃); FT-IR (neat) 3049, 2958, 2841, 1748, 1590, 1489, 1451, 1369, 1228, 1168, 1135, 1064, 1042, 961, 953, 940, 899, 865, 763, 734, 692 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.44-7.05 (m, 5 H, ArH), 5.82 (dd, 1 H, *J* = 10.5, 3.5 Hz, *H*-3), 5.73 (dd, 1 H, *J* = 3.3, 1.3 Hz, *H*-4), 5.30 (dd, 1 H, *J* = 10.5, 3.5 Hz, *H*-2), 5.07 (d, 1 H, *J* = 3.5 Hz, *H*-1), 4.24 (ddd, 1 H, *J* = 7.0, 7.0, 1.0 Hz, *H*-5), 4.12-4.16 (m, 2 H, 2 × *H*-6), 3.43 (s, 3 H, OCH₃), 2.16 (s, 3 H, CH₃CO₂), 2.14 (s, 3 H, CH₃CO₂), 2.06 (s, 3 H, CH₃CO₂); ¹³C NMR (125 MHz, CDCl₃) δ 194.2, 170.7, 170.5, 170.2, 153.6, 129.8, 126.9, 122.0, 97.4, 76.9, 68.5, 67.3, 66.5, 62.1, 55.8, 21.1, 20.9, 20.9; HRMS (FAB): calcd for C₂₀H₂₄O₁₀S (M + Na)⁺ 479.0982, found 479.1004.

(20h)

The general procedure for the radical allylation was followed using **19h** (4.51 g, 11.5 mmol), allytributyltin (8.90 mL, 28.7 mmol), AIBN (378 mg, 2.30 mmol) and benzene (23 mL). The reaction was heated to reflux for 1.5 hours at which point TLC showed complete consumption of the starting material. The solution was concentrated and flash chromatography of the residue over silica gel using 15-45% Et₂O/hexanes gave **20h** and the corresponding minor isomer (2.45 g, 64%) as a mixture of isomers (α : β /1.7:1, ¹H NMR, 500 MHz) (*R*_f = 0.19, TLC silica, 40% Et₂O-hexanes). The isomers were not separated, but carried on as a mixture to the next step.

(21h)

The general procedure for deacylation/benzoylation was followed using a 1:1.7 mixture of **20h** and the minor axial isomer (2.45 g, 7.12 mmol), NaOMe (1.92 g, 35.5 mmol), methanol (140 mL), NaH (60% dispersion in mineral oil, 2.80 g, 70.0 mmol), benzyl bromide (8.40 mL, 70.0 mmol) and DMF (70 mL). After the usual work-up, gravity chromatography of the residue over silica gel using 0-4% Et₂O-benzene gave **21h** (1.26 g, 98%) (*R*_f = 0.23, TLC, silica 3% Et₂O-benzene) as a pure oil: [α]_D = +50.1 (*c* = 1.17, CHCl₃); FT-IR (neat) 3063, 3030, 2912, 2866, 1639, 1606, 1586, 1496, 1454, 1350, 1330, 1208, 1192, 1094, 1048, 1028, 986, 952, 913, 883, 737, 696 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.40-7.22 (m, 15 H, ArH), 5.85-5.73 (m, 1 H, *H*-8), 5.10-5.00 (m, 2 H, 2 × *H*-9), 4.72 (d, 1 H, *J* = 3.5 Hz, *H*-1), 4.62 (d, 1 H, *J* = 11.5 Hz, OCH₂Ph), 4.60-4.51 (m, 4 H, 4 × OCH₂Ph), 4.48 (d, 1 H, *J* = 11.5 Hz, OCH₂Ph), 3.98 (dd, 1 H, *J* = 7.0, 6.0 Hz, *H*-5), 3.76 (s, 1 H, *H*-4), 3.66 (dd, 1 H, *J* = 10.5, 3.5 Hz, *H*-2), 3.60 (dd, 1 H, *J* = 9.5, 7.5 Hz, *H*-6), 3.53 (dd, 1 H, *J* = 9.3, 6.3 Hz, *H*-6), 3.41 (s, 3 H, OCH₃), 2.68-2.64 (m, 1 H,

H-7), 2.23-2.10 (m, 2 H, *H*-3, *H*-7); ^{13}C NMR (125 MHz, CDCl_3) δ 138.9, 138.6, 138.1, 137.6, 128.7, 128.6, 128.5, 128.3, 128.1, 128.0, 128.0, 127.8, 127.8, 117.0, 97.4, 76.1, 75.1, 74.9, 73.8, 72.7, 70.3, 69.4, 55.5, 41.0, 31.3; HRMS (FAB): calcd for $\text{C}_{31}\text{H}_{36}\text{O}_5$ ($\text{M} + \text{Na}$) $^+$ 511.2455, found 511.2430 and the axial isomer (1.84 g, 84%) as a pure (R_f = 0.19, TLC, silica 3% Et_2O -benzene) oil:

(22h)

Ozone was bubbled through a $-78\text{ }^\circ\text{C}$ solution of **21h** (1.27 g, 2.59 mmol) in CH_2Cl_2 (20 mL) until the blue color persisted. The solution was then purged with O_2 to remove excess ozone and then zinc dust (1.70 g, 26.0 mmol) and AcOH (1.26 mL, 22.0 mmol) were then sequentially added in one portion. The resulting mixture was allowed to warm to room temperature with the cold bath in place and then stirred for an additional 5 hours. The suspension was filtered and the solid residue was washed with CH_2Cl_2 ($2 \times 20\text{ mL}$). The combined organic fractions were washed with saturated NaHCO_3 ($2 \times 20\text{ mL}$), water ($1 \times 30\text{ mL}$), dried and filtered and evaporated. Flash chromatography of the residue over silica gel using 10-20% EtOAc-hexanes gave aldehyde **22h** (873 mg, 69%) as a pure (R_f = 0.20, TLC, silica 20% EtOAc-hexanes, ^1H NMR, 500 MHz) colorless oil that was directly oxidized to the acid as shown below.

(6h)

The general procedure for oxidation to the acid was followed using: Aldehyde **22h** (726 mg, 1.48 mmol), *t*-BuOH-water (10:1, 10 mL), 2-methyl-2-butene (1.06 mL, 10.0 mmol), potassium phosphate monobasic (265 mg, 1.95 mmol) and sodium chlorite (228 mg, 80%, 2.02 mmol). After the usual work-up, flash chromatography of the residue over silica gel using 30-80% EtOAc-hexanes-1% AcOH gave acid **6h** (634mg, 87%) as a pure (R_f = 0.39, TLC, silica 30% EtOAc-hexanes-1% AcOH) colorless oil: $[\alpha]_D^{25} = +78.8$ ($c = 1.1$, CHCl_3); FT-IR (neat) 3088, 3063, 3031, 2902, 1704, 1602, 1585, 1496, 1453, 1404, 1313, 1267, 1205, 1098, 1048, 910, 729, 694 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 11.60-10.10 (br s, 1 H, COOH), 7.40-7.24 (m, 15 H, ArH), 4.72 (d, 1 H, $J = 3.5\text{ Hz}$, *H*-1), 4.62-4.54 (m, 4 H, $4 \times \text{OCH}_2\text{Ph}$), 4.52 (d, 1 H, $J = 12.0\text{ Hz}$, OCH_2Ph), 4.51 (d, 1 H, $J = 11.0\text{ Hz}$, OCH_2Ph), 4.07 (dd, 1 H, $J = 7.0, 7.0\text{ Hz}$, *H*-5), 3.90 (d, 1 H, $J = 1.5\text{ Hz}$, *H*-4), 3.67-3.61 (m, 2 H, *H*-2, *H*-6), 3.57 (dd, 1 H, $J = 6.3, 9.3\text{ Hz}$, *H*-6), 3.41 (s, 3 H, OCH_3), 2.76 (dd, 1 H, $J = 16.3, 4.3\text{ Hz}$, *H*-7), 2.69-2.61 (m, 1 H, *H*-3), 2.37 (dd, 1 H, $J = 16.3, 9.3\text{ Hz}$, *H*-7); ^{13}C NMR (125 MHz, CDCl_3) δ 179.3 138.2, 138.2, 138.0, 128.7, 128.7, 128.5, 128.4, 128.4, 128.2, 128.1, 128.1, 97.1, 75.8, 75.4, 73.8, 72.6, 69.7, 69.2, 55.5, 37.4, 32.7; HRMS (FAB): calcd for $\text{C}_{30}\text{H}_{34}\text{O}_7$ ($\text{M} + \text{Na}$) $^+$ 529.2197, found 529.2197.

(7h):

The general procedure for esterification was followed using acid **6h** (634 mg, 1.25 mmol), alcohol **5a** (780 mg, 1.87 mmol), DCC (772 mg, 3.74 mmol), 4-DMAP (153 mg, 1.25 mmol) and CH_2Cl_2 (10 ml). After the usual work-up, flash chromatography of the obtained residue over silica gel using 10-20% Et_2O -hexanes gave ester **7h** (752mg, 77%) as a pure (R_f = 0.10, TLC, silica 40% Et_2O -hexanes) colorless liquid: $[\alpha]_D^{25} = +43.1$ (c = 1.05, CHCl_3); FT-IR (neat) 3064, 3030, 2865, 1732, 1605, 1496, 1454, 1352, 1253, 1196, 1097, 1052, 1028, 736, 697 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.40-7.10 (m, 30 H, ArH), 5.86 (ddd, 1 H, J = 17.5, 10.3, 8.0 Hz, H -2), 5.36-5.24 (m, 3 H, $2 \times H$ -1, H -5), 4.70 (d, 1 H, J = 3.0 Hz, H -1'), 4.68 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 4.61 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 4.58 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 4.55 (d, 1 H, J = 13.0 Hz, OCH_2Ph), 4.53 (d, 1 H, J = 12.0 Hz, OCH_2Ph), 4.51 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 4.48 (d, 1 H, J = 11.0 Hz, OCH_2Ph), 4.41 (d, 1 H, J = 12.0 Hz, OCH_2Ph), 4.38 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 4.32 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 4.32 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 4.31 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 3.97 (dd, 1 H, J = 7.0, 6.0 Hz, H -5'), 3.88 (dd, 1 H, J = 5.0, 8.0 Hz, H -3), 3.82 (br, 1 H, H -4'), 3.77-3.71 (m, 3 H, H -4, $2 \times H$ -6); 3.58 (dd, 1 H, J = 11.3, 3.3 Hz, H -2') 3.50-3.40 (m, 2 H, $2 \times H$ -6'), 3.38 (s, 3 H, OCH_3), 2.71 (dd, 1 H, J = 16.0, 3.5 Hz, H -7'), 2.66 (dddd, 1 H, J = 11.0, 11.0, 2.5, 2.5 Hz, H -3') 2.44 (dd, 1 H, J = 16.3, 10.8 Hz, H -7'); ^{13}C NMR (125 MHz, CDCl_3) δ 172.3, 138.5, 138.5, 138.4, 138.3, 138.3, 138.2, 135.4, 128.6, 128.6, 128.5, 128.5, 128.3, 128.3, 128.2, 128.2, 128.1, 127.9, 127.9, 127.9, 127.8, 127.8, 127.7, 119.6, 97.1, 81.3, 81.1, 75.7, 75.3, 75.3, 75.2, 73.6, 73.2, 72.7, 72.6, 70.7, 69.9, 69.5, 68.6, 55.4, 37.7, 32.2; HRMS (FAB): calcd for $\text{C}_{57}\text{H}_{62}\text{O}_{10}$ ($M + \text{Na}$) $^+$ 929.4235, found 929.4264.

(8h):

The general procedure for methylenation was followed using: Titanium tetrachloride (0.71 mL, 2 M in CH_2Cl_2 , 1.42 mmol), THF (5 mL), TMEDA (0.41 mL, 2.72 mmol), zinc dust (200 mg, 3.06 mmol), lead (II) chloride (2 mg, 0.007 mmol), ester **7h** (75.7 mg, 0.083 mmol) and dibromomethane (0.06 mL, 0.84 mmol). After the usual work-up, gravity chromatography of the residue over silica using 20% Et_2O -hexanes-1% triethylamine gave **8h** (37.8 mg, 50%) as a pure (R_f = 0.40, TLC silica, 40% Et_2O -hexanes; ^1H NMR, 500 MHz) oil: $[\alpha]_D^{25} = +45.8$ (c = 0.45 CH_2Cl_2); FT-IR (neat) 3029, 2919, 2858, 1651, 1495, 1452, 1349, 1275, 1094, 1050, 732, 695 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.40-7.00 (m, 30 H, ArH), 5.87 (ddd, 1 H, J = 17.7, 10.1, 7.6 Hz, H -2), 5.22 (d, 1 H, J = 17.2 Hz, H -1), 5.05 (dd, 1 H, J = 9.6, 1.0 Hz, H -1), 4.93 (d, 1 H, J = 11.1 Hz, OCH_2Ph), 4.77 (d, 1 H, J = 3.0 Hz, H -1'), 4.76 (s, 2 H, $2 \times \text{OCH}_2\text{Ph}$), 4.69 (ddd, 1 H, J = 4.5, 4.5, 4.5 Hz, H -5), 4.66 (d, 1 H, J = 11.1 Hz, OCH_2Ph), 4.55 (d, 1 H, J = 11.6 Hz, OCH_2Ph), 4.32 (d, 1 H, J = 11.7 Hz, OCH_2Ph), 4.30 (d, 1 H, J = 11.6 Hz, OCH_2Ph), 4.24 (s, 2

H, 2 x OCH_2Ph), 4.20-4.15 (m, 5 H, $H-4'$, $H-5'$, 3 x OCH_2Ph), 4.12-4.10 (m, 3 H, $H-3$, 2 x $H-9'$), 4.05 (dd, 1 H, $J = 5.1$, 5.1 Hz, $H-4$), 3.88 (dd, 1 H, $J = 10.7$, 3.1 Hz, $H-6$), 3.82 (dd, 1 H, $J = 11.1$, 3.0 Hz, $H-2'$), 3.74-3.70 (m, 2 H, $H-6$, $H-6'$), 3.60 (dd, 1 H, $J = 9.1$, 6.1 Hz, $H-6'$), 3.17 (s, 3 H, OCH_3), 3.08 (dd, 1 H, $J = 14.2$, 2.5 Hz, $H-7'$), 3.95-3.89 (m, 1 H, $H-3'$), 2.50 (dd, 1 H, $J = 13.7$, 11.7 Hz, $H-7'$); ^{13}C NMR (125 MHz, C_6D_6) δ 160.6, 139.7, 139.4, 139.3, 139.0, 138.9, 138.6, 136.0, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 128.0, 127.9, 127.8, 127.7, 127.6, 127.6, 127.5, 127.4, 127.4, 127.3, 118.6, 94.5, 84.1, 81.4, 81.4, 76.1, 75.6, 75.5, 75.3, 75.1, 73.2, 73.2, 71.6, 70.9, 70.5, 69.5, 68.2, 54.8, 39.8; HRMS (FAB): calcd for $\text{C}_{58}\text{H}_{64}\text{O}_9\text{Na}$ ($M + \text{Na}$) $^+$ 927.4442, found 927.4421.

(10h):

The general procedure for the one-pot protocol was followed using the ruthenium-based metathesis catalyst **26** (8 mg, 0.009 mmol, 40 mol%), toluene (2 ml), enol ether **8h** (16.4 mg, 0.021 mmol), $\text{BH}_3 \cdot \text{THF}$ (0.2 mL, 1M in THF, 0.2 mmol), NaOH (10 mL, 1 M, 10 mmol) and hydrogen peroxide (10 ml, 30% in water). After the usual work-up, flash chromatography of the residue over silica using 25% EtOAc-hexanes gave **10h** (7.9 mg, 50%) as a pure ($R_f = 0.54$, TLC silica, 40% EtOAc-hexanes; ^1H NMR, 500 MHz) colorless oil: $[\alpha]_D = +53.9$ ($c = 0.28$, CHCl_3); FT-IR (neat) 3424, 3029, 2919, 2858, 1635, 1495, 1452, 1355, 1098, 1050, 735, 696 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.36-7.16 (m, 30 H, ArH), 4.91 (d, 1 H, $J = 11.7$ Hz, OCH_2Ph), 4.78 (d, 1 H, $J = 10.6$ Hz, OCH_2Ph), 4.76 (d, 1 H, $J = 11.7$ Hz, OCH_2Ph), 4.71 (d, 1 H, $J = 9.6$ Hz, OCH_2Ph), 4.70 (d, 1 H, $J = 3.6$ Hz, $H-1'$), 4.56 (d, 1 H, $J = 8.2$ Hz, OCH_2Ph), 4.54 (d, 1 H, $J = 11.1$ Hz, OCH_2Ph), 4.49 (d, 1 H, $J = 12.2$ Hz, OCH_2Ph), 4.48 (d, 1 H, $J = 11.1$ Hz, OCH_2Ph), 4.47 (d, 1 H, $J = 11.6$ Hz, OCH_2Ph), 4.45 (d, 1 H, $J = 11.7$ Hz, OCH_2Ph), 4.43 (d, 1 H, $J = 11.6$ Hz, OCH_2Ph), 4.40 (d, 1 H, $J = 12.2$ Hz, OCH_2Ph), 4.00 (dd, 1 H, $J = 7.0$, 7.0 Hz, $H-5'$), 3.96 (d, 1 H, $J = 2.1$ Hz, $H-4'$), 3.69-3.63 (m, 3 H, 2 x $H-6$, $H-2'$), 3.61-3.58 (m, 2 H, $H-4$, $H-6'$), 3.53 (dd, 1 H, $J = 9.2$, 6.1 Hz, $H-6'$), 3.41 (dd, 1 H, $J = 9.1$, 9.1 Hz, $H-3$), 3.40-3.34 (m, 5 H, $H-5$, $H-1$, OCH_3), 3.21 (dd, 1 H, $J = 9.2$, 9.1 Hz, $H-2$), 2.32-2.28 (m, 1 H, $H-3'$), 2.20 (ddd, 1 H, $J = 14.6$, 3.0, 3.0 Hz, $H-7'$), 1.58-1.52 (m, 1 H, $H-7'$); ^{13}C NMR (125 MHz, CDCl_3) δ 138.8, 138.7, 138.1, 138.1, 138.0, 138.0, 128.5, 128.4, 128.3, 128.2, 128.2, 128.1, 127.9, 127.8, 127.7, 127.7, 127.6, 127.5, 127.3, 97.1, 86.7, 80.1, 78.4, 78.2, 77.6, 75.3, 75.1, 75.0, 74.7, 73.4, 73.3, 72.5, 69.7, 69.3, 69.1, 55.1, 38.4, 30.7; HRMS (FAB): calcd for $\text{C}_{56}\text{H}_{62}\text{O}_{10}\text{Na}$ ($M + \text{Na}$) $^+$ 917.4235, found 917.4228.

(6j)

To the solution of the corresponding known ethyl ester¹² (2.74 g, 8.29 mmol) in THF and water (100 mL, 1:1) was added LiOH (6.96 g, 165 mmol) at room temperature. The suspension was stirred for 40 hours, cooled in an ice bath and acidified with 2 M HCl until pH 2 (litmus red). The solution was extracted with EtOAc (3 x 50 mL), dried over MgSO₄ and concentrated. Flash chromatography of the residue over silica gel (5.5 x 7 cm) using EtOAc gave **6j** (2.09 g, 83%) as a pure (*R_f* = 0.55, TLC silica, EtOAc; ¹H NMR, 500 MHz) oil: [α]_D = +54.9 (*c* = 1.08, CHCl₃); FT-IR (neat) 2987, 2936, 2883, 1711, 1214, 1064, 1015 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) 5.78 (d, 1 H, *J* = 4.0 Hz, *H*-1), 4.81 (dd, 1 H, *J* = 4.6, 4.0 Hz, *H*-2), 4.11 (dd, 1 H, *J* = 8.6 Hz, 6.1 Hz, *H*-6), 3.99-3.92 (m, 2 H, *H*-5, *H*-6), 3.67 (dd, 1 H, *J* = 10.1, 8.1 Hz, *H*-4), 2.91 (dd, 1 H, *J* = 17.8, 4.1 Hz, *H*-7), 2.73 (dd, 1 H, *J* = 17.8, 10.7 Hz, *H*-7), 2.34-2.28 (m, 1 H, *H*-3), 1.50 (s, 3 H, CH₃), 1.41 (s, 3 H, CH₃), 1.32 (s, 3 H, CH₃), 1.31 (s, 3 H, CH₃); ¹³C NMR (125 MHz, CDCl₃) δ 178.2, 128.3, 111.9, 105.0, 81.2, 80.7, 77.8, 67.9, 44.3, 29.8, 26.6, 26.5, 26.3, 25.1; HRMS (FAB): calcd for C₁₃H₁₉O₇ (*M* - CH₃)⁺ 287.1130, found 287.1133.

(7k)

The general procedure for esterification was followed using known acid **6k**¹³ (420 mg, 1.23 mmol), alcohol **5a** (513 mg, 1.23 mmol), DCC (304 mg, 1.47 mmol), 4-DMAP (20 mg, 0.097 mmol) and CH₂Cl₂ (5 ml). After the usual work-up, flash chromatography of the residue **twice** over silica gel (5 x 16 cm) using 30% Et₂O/hexanes gave ester **7k** (633 mg, 69%) as a fairly pure (*R_f* = 0.44, TLC silica, 30% Et₂O-hexanes; ¹H NMR, 500 MHz) oil: [α]_D = +2.9 (*c* = 2.2, CH₂Cl₂); FT-IR (neat) 3063, 3030, 2969, 2950, 2923, 2903, 2892, 2856, 1747, 1453, 1360, 1270, 1206, 1097, 735, 697 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.30-7.15 (m, 25 H, ArH), 5.81 (ddd, 1 H, *J* = 17.5, 10, 8.0 Hz, *H*-1), 5.30-5.20 (m, 3 H, 2 x *H*-2, *H*-5), 4.71 (d, 1 H, *J* = 11.5 Hz, OCH₂Ph), 4.65 (d, 1 H, *J* = 11.0 Hz, OCH₂Ph), 4.64 (d, 1 H, *J* = 11.0 Hz, OCH₂Ph), 4.58 (d, 1 H, *J* = 11.5 Hz, OCH₂Ph), 4.56-4.53 (m, 2 H, 2 x OCH₂Ph), 4.51 (d, 1 H, *J* = 11.5 Hz, OCH₂Ph), 4.31 (d, 1 H, *J* = 12 Hz, OCH₂Ph), 4.30 (d, 1 H, *J* = 11.5 Hz, OCH₂Ph), 4.27 (d, 1 H, *J* = 11.5 Hz, OCH₂Ph), 4.11 (ddd, 1 H, *J* = 11.5, 4.5, 4.5 Hz, *H*-1'), 3.90 (dd, 1 H, *J* = 7.5, 5.5 Hz, *H*-3), 3.85 (d, 1 H, *J* = 7.5 Hz, *H*-5'), 3.80-3.75 (m, 2 H, *H*-3', *H*-4), 3.73-3.65 (m, 2 H, 2 x *H*-6), 3.61 (ddd, 1 H, *J* = 9.0, 7.5, 4.5 Hz, *H*-4'), 3.45 (ddd, 1 H, *J* = 12, 9.5, 3.0 Hz, *H*-1'), 2.11-2.03 (m, 1 H, *H*-2'), 1.76-1.62 (m, 1 H, *H*-2'); ¹³C NMR (125 MHz, CDCl₃) δ 169.2, 138.4, 138.3, 138.1, 135.1, 128.4, 128.2, 128.2, 128.2, 128.0, 127.9, 127.7, 127.6, 127.5, 127.5, 127.4, 127.4, 119.4, 81.2, 80.9, 77.7, 77.5, 77.0, 75.0, 73.9, 72.9, 71.2, 70.6, 68.0, 63.8, 29.2; HRMS (FAB): calcd for C₄₇H₅₀O₈ (*M* + Na)⁺ 765.3403, found 765.3520. An analytically pure sample was obtained by preparative TLC using 12% EtOAc-C₆H₆.

(8k)

The general procedure for methylenation was followed using: Titanium tetrachloride (0.88 mL, 2 M in CH_2Cl_2 , 1.76 mmol), THF (5 mL), TMEDA (0.51 mL, 3.39 mmol), zinc dust (250 mg, 3.82 mmol), lead (II) chloride (4 mg, 0.014 mmol), ester **7k** (76.7 mg, 0.103 mmol) and dibromomethane (0.07 mL, 0.97 mmol). After the usual work-up, gravity chromatography of the residue over silica using 20% Et_2O -hexanes-1% triethylamine gave **8k** (52 mg, 67%) as a pure (R_f = 0.32, TLC silica, 40% Et_2O -hexanes; ^1H NMR, 500 MHz) oil: $[\alpha]_D^{25}$ = - 8.23 (c = 0.385, CH_2Cl_2); FT-IR (neat) 3068, 3028, 2858, 1635, 1495, 1452, 1359, 1288, 1088, 1027, 935, 734, 696 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.38-7.01 (m, 25 H, ArH), 5.86 (ddd, 1 H, J = 17.1, 10.1, 7.1 Hz, H -2), 5.20 (d, 1 H, J = 17.2 Hz, H -1), 5.03 (dd, 1 H, J = 10.6 Hz, H -1), 4.93 (d, 1 H, J = 11.1 Hz, OCH_2Ph), 4.82 (d, 1 H, J = 11.1 Hz, OCH_2Ph), 4.78 (apparent doublet, 2 H, J = 3.6 Hz, 2 x H -7'), 4.73 (ddd, 1 H, J = 3.5, 3.5, 3.5 Hz, H -5), 4.49 (d, 1 H, J = 12.1 Hz, OCH_2Ph), 4.47 (d, 2 H, J = 12.1 Hz, 2 x OCH_2Ph), 4.44 (d, 1 H, J = 13.2 Hz, OCH_2Ph), 4.42 (d, 1 H, J = 11.6 Hz, OCH_2Ph), 4.29 (s, 2 H, 2 x OCH_2Ph), 4.28 (d, 1 H, J = 13.1 Hz, OCH_2Ph), 4.16 (dd, 1 H, J = 6.5, 6.1 Hz, H -3), 4.07 (dd, 1 H, J = 5.0, 4.1 Hz, H -4), 4.01 (dd, 1 H, J = 10.7, 4.1 Hz, H -6), 3.83-3.77 (m, 2 H, H -6, H -4'), 3.65-3.63 (m, 2 H, H -5', H -1'), 3.37 (dd, 1 H, J = 16.7, 9.1 Hz, H -3'), 2.95-2.90 (m, 1 H, H -1'), 1.57-1.55 (m, 2 H, 2 x H -2'); ^{13}C NMR (125 MHz, C_6D_6) δ 159.0, 139.7, 139.4, 139.1, 139.0, 135.9, 128.4, 128.3, 128.2, 128.1, 128.1, 128.0, 127.9, 127.7, 127.6, 127.4, 118.6, 87.7, 82.3, 82.1, 81.2, 80.8, 80.7, 77.0, 74.9, 74.6, 73.3, 71.2, 70.8, 68.8, 65.4, 31.7; HRMS (FAB): calcd for $\text{C}_{48}\text{H}_{52}\text{O}_7\text{Na}$ ($M + \text{Na}$) $^+$ 763.3605, found 763.3648.

(9k)

The ruthenium-based metathesis catalyst **26** (14 mg, 0.016 mmol, 40 mol%) was added in three portions over 4 hours to a 60 °C toluene (4 ml) solution of enol ether **8k** (30 mg, 0.04 mmol). After the usual work-up, flash chromatography of the residue over silica using 50% Et_2O -hexanes gave glycal **9k** (22 mg, 77%) as a pure (R_f = 0.25, TLC silica, 40% Et_2O -hexanes; ^1H NMR, 500 MHz) colorless oil: $[\alpha]_D^{25}$ = - 10.3 (c = 1.09 CH_2Cl_2); FT-IR (neat) 3085, 3060, 3028, 2920, 2857, 1678, 1495, 1452, 1358, 1293, 1248, 1195, 1088, 1041, 1026, 734, 696 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.49-6.98 (m, 25 H, ArH), 5.11 (d, 1 H, J = 2.0 Hz, H -2), 5.02 (d, 1 H, J = 10.7 Hz, OCH_2Ph), 4.95 (d, 1 H, J = 10.6 Hz, OCH_2Ph), 4.80 (d, 1 H, J = 11.7 Hz, OCH_2Ph), 4.57 (d, 1 H, J = 11.6 Hz, OCH_2Ph), 4.53 (s, 2 H, 2 x OCH_2Ph), 4.46 (d, 1 H, J = 11.6 Hz, OCH_2Ph), 4.35 (d, 1 H, J = 11.7 Hz, OCH_2Ph), 4.27 (d, 1 H, J = 11.6 Hz, OCH_2Ph), 4.29 (dd, 1 H, J = 6.6, 2.5 Hz, H -3), 4.18 (d, 1 H, J = 12.1 Hz, OCH_2Ph), 4.11 (dd, 1 H, J = 9.6, 6.6 Hz, H -4), 4.02 (ddd, 1 H, J = 9.1, 2.5, 2.5 Hz, H -5), 3.93 (dd, 1 H, J = 9.1, 9.1 Hz, H -4'), 3.71 (dd, 1 H, J = 10.7, 3.6 Hz, H -6), 3.65-3.62 (m, 2 H, H -6, H -1'), 3.56 (d, 1 H, J = 9.7 Hz, H -5'), 3.40-3.35 (m, 1 H, H -3'), 2.94-2.89 (m, 1 H, H -1'), 1.63-1.52 (m, 2 H, 2 x H -2'); ^{13}C NMR (125 MHz, C_6D_6) δ 152.9,

139.6, 139.6, 139.2, 139.2, 138.7, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.7, 127.7, 127.5, 127.5, 127.4, 127.4, 127.4, 127.3, 100.9, 81.1, 80.4, 80.3, 77.6, 77.5, 75.2, 74.5, 73.8, 73.1, 71.4, 70.2, 68.5, 65.5, 31.9; HRMS (FAB): calcd for $C_{46}H_{48}O_7Na$ ($M + Na$)⁺ 735.3292, found 735.3274.

General procedure for the three-step protocol exemplified by the preparation of (**10a**):

The general procedure for methylenation was followed using: Titanium tetrachloride (0.94 mL, 2 M in CH_2Cl_2 , 1.87 mmol), THF (3.0 mL), TMEDA (0.55 mL, 3.6 mmol), zinc dust (267 mg, 4.08 mmol), lead (II) chloride (3 mg, 0.011 mmol), ester **7a** (100 mg, 0.11 mmol), dibromomethane (0.07 mL, 1.02 mmol), after the usual work-up the crude acyclic enol ether was then subjected to the one-pot protocol using catalyst **26** (19 mg, 0.022 mmol, 20 mol%), toluene (11 ml), $BH_3 \cdot THF$ (1.1 mL, 1 M in THF, 1.1 mmol), NaOH (15 mL, 1 M, 15 mmol) and hydrogen peroxide (15 ml, 30% in water, 132 mmol). After the usual work-up, flash chromatography of the residue over silica using 20% EtOAc-hexanes gave **10a** (55 mg, 56% over 3 steps).

(**25a**)

The general procedure for debenzoylation/peracetylation was followed using: **10a** (74 mg, 82.9 μ mol), Pd/C (5 mg), EtOAc/MeOH (10 ml), pyridine (2 ml), acetic anhydride (1 ml) and 4-DMAP (5 mg, 41 μ mol). After the usual work-up, flash chromatography of the residue over silica gel (3.0 x 5.5 cm) using 35% EtOAc/hexanes gave **25a** (45 mg, 84% over 2 steps) as a pure (R_f = 0.26, TLC silica, 40% EtOAc-hexanes; 1H NMR, 500 MHz) oil.

(**10c**):

The general procedure for the three step protocol was followed using: Titanium tetrachloride (0.6 mL, 2 M in CH_2Cl_2 , 1.21 mmol), THF (2.0 mL), TMEDA (0.35 mL, 2.33 mmol), zinc dust (172 mg, 2.63 mmol), lead (II) chloride (2 mg, 7.1 μ mol), ester **7c** (58 mg, 0.07 mmol), dibromomethane (46 μ L, 0.66 mmol), catalyst **26** (27 mg, 32.0 μ mol, 45 mol%), toluene (7 ml), $BH_3 \cdot THF$ (0.71 mL, 1M in THF, 0.71 mmol), NaOH (10 mL, 1 M, 10 mmol) and hydrogen peroxide (10 ml, 30% in water, 88 mmol). After the usual work-up, flash chromatography of the residue over silica using 25% EtOAc-hexanes gave **10c** (34 mg, 59% over 3 steps).

(25c):

The general procedure for debenzoylation/peracetylation was followed using: **10c** (48 mg, 59.7 μ mol), Pd/C (9 mg), EtOAc/MeOH (14 ml), pyridine (1.5 ml), acetic anhydride (1.5 ml) and 4-DMAP (7 mg, 57 μ mol). After the usual work-up, flash chromatography of the residue over silica gel (2.5 x 6.0 cm) using 30% EtOAc/hexanes gave **25c** (35 mg, 90% over 2 steps) as a pure (R_f = 0.31, TLC silica, 40% EtOAc-hexanes; ^1H NMR, 500 MHz) oil: $[\alpha]_D = +29.6$ (c = 1.0, CH_2Cl_2); FT-IR (neat) 2938, 1735, 1433, 1368, 1234, 901, 732 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 5.10 (dd, 1 H, J = 9.5, 9.5 Hz, H -3), 4.99 (dd, 1 H, J = 9.5, 9.5 Hz, H -4), 4.88-4.84 (m, 1 H, H -4'), 4.85 (d, 1 H, J = 2.0 Hz, H -1'), 4.84-4.81 (m, 1 H, H -2'), 4.75 (dd, 1 H, J = 9.5, 9.5 Hz, H -2), 4.25 (dd, 1 H, J = 12, 5.0 Hz, H -6), 4.19 (dd, 1 H, J = 12, 5.0 Hz, H -6'), 4.07-4.03 (m, 1 H, H -6'), 4.02 (ddd, 1 H, J = 12, 12, 2.0 Hz, H -6), 3.86 (ddd, 1 H, J = 9.5, 5.0, 2.0 Hz, H -5'), 3.63 (ddd, 1 H, J = 9.5, 5.0, 2.0 Hz, H -5), 3.52 (ddd, 1 H, J = 10, 10, 2.0 Hz, H -1), 3.39 (s, 3 H, OCH_3), 2.48-2.40 (m, 1 H, H -3'), 2.10 (s, 3 H, CH_3CO_2), 2.09 (s, 3 H, CH_3CO_2), 2.06 (s, 3 H, CH_3CO_2), 2.05 (s, 3 H, CH_3CO_2), 1.99 (s, 6 H, 2 x CH_3CO_2), 1.96 (s, 3 H, CH_3CO_2), 1.65-1.58 (m, 1 H, H -7'), 1.49-1.40 (m, 1 H, H -7'); ^{13}C NMR (125 MHz, CDCl_3) δ 170.7, 170.5, 170.3, 170.0, 169.7, 169.5, 169.4, 95.9, 75.8, 75.3, 74.2, 72.2, 72.2, 68.2, 68.1, 67.8, 62.4, 62.0, 55.1, 36.4, 29.2, 20.8, 20.7, 20.6, 20.5, 20.5; HRMS (FAB): calcd for $\text{C}_{28}\text{H}_{40}\text{O}_{17}\text{Na}^+$ ($M + \text{Na}$) $^+$ 671.2157, found 671.2117.

(10d):

The general procedure for the three step protocol was followed using: Titanium tetrachloride (0.45 mL, 2 M in CH_2Cl_2 , 0.9 mmol), THF (1.4 mL), TMEDA (0.26 mL, 1.74 mmol), zinc dust (128 mg, 1.96 mmol), lead (II) chloride (2 mg, 7.2 μ mol), ester **7d** (48 mg, 0.053 mmol), dibromomethane (35 μ L, 0.49 mmol), catalyst **26** (9 mg, 10.6 μ mol, 20 mol%), toluene (5.3 ml), $\text{BH}_3 \cdot \text{THF}$ (0.53 mL, 1M in THF, 0.53 mmol), NaOH (10 mL, 1 M, 10 mmol) and hydrogen peroxide (10 ml, 30% in water, 88 mmol). After the usual work-up, flash chromatography of the residue over silica using 25% EtOAc-hexanes gave **10d** (25 mg, 53% over 3 steps).

(25d):

The general procedure for debenzoylation/peracetylation was followed using: **10d** (22 mg, 24.5 μ mol), Pd/C (7 mg), EtOAc/MeOH (12 ml), pyridine (2.0 ml), acetic anhydride (1.0 ml) and 4-DMAP (4 mg, 33 μ mol). After the usual work-up, flash chromatography of the residue over silica gel (1.5 x 4.5 cm) using 30% EtOAc/hexanes gave **25d**

(11 mg, 71% over 2 steps) as a pure ($R_f = 0.23$, TLC silica, 40% EtOAc-hexanes; ^1H NMR, 500 MHz) white solid: m.p. = 126 °C; $[\alpha]_D = +28.2$ ($c = 1.0$, CH_2Cl_2); FT-IR (neat) 2923, 2852, 1701, 1509, 1453, 1208, 1088, 749 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 5.24 (dd, 1 H, $J = 11, 9.0$ Hz, $H-3'$), 5.10 (dd, 1 H, $J = 9.5, 9.5$ Hz, $H-3$), 5.01 (dd, 1 H, $J = 9.5, 9.5$ Hz, $H-4$), 4.95 (dd, 1 H, $J = 9.5, 9.5$ Hz, $H-4'$), 4.79 (d, 1 H, $J = 2.5$ Hz, $H-1'$), 4.77 (dd, 1 H, $J = 10.5, 10.5$ Hz, $H-2$), 4.30 (dd, 1 H, $J = 12.5, 4.0$ Hz, $H-6'$), 4.22 (dd, 1 H, $J = 12, 5.5$ Hz, $H-6$), 4.09 (dd, 1 H, $J = 12, 2.0$ Hz, $H-6$), 4.05 (dd, 1 H, $J = 12.5, 2.0$ Hz, $H-6'$), 3.94 (ddd, 1 H, $J = 9.5, 4.0, 2.5$ Hz, $H-5'$), 3.59 (ddd, 1 H, $J = 9.5, 5.5, 2.0$ Hz, $H-5$), 3.39 (ddd, 1 H, $J = 10.5, 10.5, 2.0$ Hz, $H-1$), 3.33 (s, 3 H, OCH_3), 2.09 (s, 3 H, CH_3CO_2), 2.08 (s, 3 H, CH_3CO_2), 2.02 (s, 3 H, CH_3CO_2), 2.01 (s, 3 H, CH_3CO_2), 2.00 (s, 3 H, CH_3CO_2), 1.99 (s, 3 H, CH_3CO_2), 1.98 (s, 3 H, CH_3CO_2), 1.59 (m, 2 H, 2 x $H-7'$), 1.46 (m, 1 H, $H-2'$); ^{13}C NMR (125 MHz, CDCl_3) δ 170.7, 170.6, 170.4, 170.2, 170.0, 169.5, 169.4, 100.7, 78.0, 75.7, 74.1, 72.9, 71.9, 69.5, 68.4, 67.3, 62.2, 55.1, 42.2, 29.5, 20.7, 20.6, 20.6, 20.6, 20.5; HRMS (FAB): calcd for $\text{C}_{28}\text{H}_{40}\text{O}_{17}\text{Na}^+$ ($M + \text{Na}$) $^+$ 671.2157, found 671.2125.

(10f):

The general procedure for the three step protocol was followed using: Titanium tetrachloride (0.34 mL, 2 M in CH_2Cl_2 , 0.68 mmol), THF (1.1 mL), TMEDA (0.2 mL, 1.31 mmol), zinc dust (97 mg, 1.48 mmol), lead (II) chloride (1 mg, 3.6 μmol), ester **7f** (39 mg, 0.04 mmol), dibromomethane (26 μL , 0.37 mmol), catalyst **26** (7 mg, 8.2 μmol , 20 mol%), toluene (4.0 ml), $\text{BH}_3 \cdot \text{THF}$ (0.4 mL, 1M in THF, 0.4 mmol), NaOH (10 mL, 1 M, 10 mmol) and hydrogen peroxide (10 ml, 30% in water, 88 mmol). After the usual work-up, flash chromatography of the residue over silica using 25% EtOAc-hexanes gave **10f** (23 mg, 59% over 3 steps).

(25f)

The general procedure for debenzylation/peracetylation was followed using: **10f** (14 mg, 14.4 μmol), Pd/C (107 mg), EtOAc/MeOH (14 ml), pyridine (2.0 ml), acetic anhydride (1.0 ml) and 4-DMAP (4 mg, 33 μmol). After the usual work-up, flash chromatography of the residue over silica gel (1.5 x 4.5 cm) using 30% EtOAc/hexanes gave **25f** (9 mg, 94% over 2 steps) as a pure ($R_f = 0.28$, TLC silica, 40% EtOAc-hexanes; ^1H NMR, 500 MHz) oil: $[\alpha]_D = 0.0$ ($c = 1.0$, CH_2Cl_2); FT-IR (neat) 2923, 2852, 1748, 1433, 1367, 1221, 1032 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 5.16 (dd, 1 H, $J = 9.5, 9.5$ Hz, $H-3$), 5.03 (dd, 1 H, $J = 9.5, 9.5$ Hz, $H-4$), 4.84 (dd, 1 H, $J = 9.5, 9.5$ Hz, $H-2$), 4.22 (dd, 1 H, $J = 12.5, 5.5$ Hz, $H-6$), 4.08 (dd, 1 H, $J = 12, 2.0$ Hz, $H-6$), 3.69 (ddd, 1 H, $J = 13, 8.0, 2.0$ Hz, $H-1$), 3.59 (ddd, 1 H, $J = 9.5, 5.5, 2.5$ Hz, $H-5$), 2.09 (s, 3 H, CO_2CH_3), 2.04 (s, 3 H, CO_2CH_3), 2.02 (s, 3 H, CO_2CH_3), 1.98 (s, 3 H, CO_2CH_3), 1.59 (dd, 1 H, $J = 11, 9.5$ Hz, $H-7$); ^{13}C NMR (125 MHz, CDCl_3) δ 170.5, 170.3, 169.7, 169.4, 75.9, 74.2, 73.1, 71.8, 68.7, 62.4, 33.1, 20.8, 20.7, 20.7; HRMS (FAB): calcd for $\text{C}_{29}\text{H}_{40}\text{O}_{18}\text{Na}^+$ ($M + \text{Na}$) $^+$ 699.2048, found 699.2074. Note: Due to the symmetrical nature of the compound, ^1H

NMR data has been reported as a dimeric structure. As expected, the compound does not exhibit any optical rotation.

(101):

The general procedure for the three step protocol was followed using: Titanium tetrachloride (0.49 mL, 2 M in CH_2Cl_2 , 0.97 mmol), THF (1.5 mL), TMEDA (0.28 mL, 1.88 mmol), zinc dust (138 mg, 2.12 mmol), lead (II) chloride (2 mg, 0.007 mmol) **71** (52 mg, 0.057 mmol), dibromomethane (0.04 mL, 0.53 mmol) catalyst **26** (10 mg, 0.011 mmol, 20 mol%), toluene (7 mL), $\text{BH}_3 \cdot \text{THF}$ (0.4 mL, 1 M in THF, 0.4 mmol) NaOH (10 mL, 1 M) and hydrogen peroxide (10 mL, 30% in water). After the usual work-up, flash chromatography of the residue over silica using 20% EtOAc-hexanes gave **101** (28 mg, 55% over 3 steps).

(251):

The general procedure for debenylation/peracetylation was followed using: **101** (30 mg, 33.5 μmol), Pd/C (20 mg), EtOAc/MeOH (15 mL), pyridine (2 mL), acetic anhydride (1 mL) and 4-DMAP (5 mg, 41 μmol). After the usual work-up, flash chromatography of the residue over silica using 40% EtOAc-hexanes gave known **251**¹⁴ (17 mg, 93% over 2 steps).

Stereochemical Analysis of the Allylation Step

Entry 8, C-3 Galacto Case

The signal for *H*-2 is split into a doublet of doublets with a large (10.5 Hz) and small (3.5 Hz) coupling constant. This indicates that *H*-2 is being split by adjacent axial and equatorial hydrogens thereby setting the stereochemistry of allyl group as equatorial at C-3.

This assignment is further supported by the data for the major isomer in which *H*-2 is split into a doublet of doublets, but this time with equivalent coupling constants of 3.5 Hz. Indicating an axial-equatorial relationship between *H*-2/*H*-3 and *H*-2/*H*-1.

Inhibitory Enzymatic Assays

Enzymes were obtained from Fluka and Sigma. The following glycosidases were assayed: β -galactosidase (EC 3.2.1.23) from *Saccharomyces fragilis*, β -galactosidase (EC 3.2.1.23) from *Escherichia coli*, β -galactosidase (EC 3.2.1.23) from *Bacillus circulans*, β -galactosidase (EC 3.2.1.23) from bovine liver, and β -glucosidase from almonds.

All buffers and solution were prepared using MilliQ-deionized H_2O . Enzymes were diluted with 0.1M HEPES (4-(2-hydroxyethyl)piperazine-1-sulfonic acid) buffer pH 6.8. Substrates and inhibitors were used as 1 mM stock solutions in buffer.

Reactions were initiated by the addition of substrate to a solution containing enzyme and inhibitor in 0.1M HEPES buffer: 100- μ L assays were followed in individual wells of flat-bottom 96-well half-area polystyrene ELISA plates (Costar) using a UV Bio-Rad Model 550 Microplate Reader from Molecular Devices. The release of *p*-nitrophenol was followed at 405 nm over 1 h at 25 °C. The concentration of each enzyme in the assays was adjusted such as to give ca. 0.5 to 2.0 OD increase over 1 h as given by the instrument. The initial rate of reaction of the first 10 min was linear and was used to calculate the rate. Rates were expressed in relative units as $\text{milliOD}\cdot\text{min}^{-1}$. Our assays were calibrated against 1-deoxynojirimycin with the error range for the standard being within 5% of the reported values.

Some preliminary results of the biological testing are shown below in the Table. The peracetylated derivatives **25** were treated with NaOMe in MeOH and the product polyols tested against various glycosidase enzymes. The data shows that the 1,6-linked-C-disaccharide **24i** was not an inhibitor of the various glycosidase enzymes. The best result was obtained with compound **24f**. It gave a K_i of 126 μ M against β -glucosidase, which has no anomeric methoxy group. The results for **24a**, **24c** and **24d** displayed complex kinetics and it is possible that anomeric hydrolysis is occurring in these cases to give mixtures of compounds making the data difficult to interpret.

K_i Values (μm) for Inhibition of Various Glycosidases by Deacetylated β-C-Disaccharides 24

Enzyme	Origin	I, C-6	a, C-4	c, C-3	d, C-2	f, C-1
β-Galactosidase	<i>Saccharomyces fragilis</i>	795 ± 68	495 ± 20	588 ± 63	N.I. ^a	607 ± 68
β-Galactosidase	<i>Escherichia coli</i>	N.I. ^a	613 ± 48	678 ± 47	772 ± 105	874 ± 62
β-Galactosidase	<i>Bacillus circulans</i>	N.I. ^a	554 ± 45	N.I. ^a	980 ± 95	850 ± 74
β-Galactosidase	Bovine Liver	833 ± 130	511 ± 37	701 ± 63	845 ± 120	682 ± 65
β-Glucosidase	Almonds	N.I. ^a	— ^b	— ^b	— ^b	126 ± 7

^aN.I. Stands for no inhibition. ^bEnzyme/Substrate gave complex kinetics.

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