A new strategy for synthesis of the disaccharide moiety of the highly potent anticancer natural product OSW-1

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Phenyl-2,3,4-tri-*O*-acetyl-1-thio- β -D-xylopyranoside (3):

A solution of **2** (3.0 g, 9.43 mmol) in dry dichloromethane (50 mL) was cooled to 0 °C. Thiophenol (1.12 mL, 11.3 mmol) was added followed by the addition of SnCl₄ (0.77 mL, 6.60 mmol). The reaction solution was stirred at room temperature for 4 h until the starting material disappeared on TLC. Saturated aqueous NaHCO₃ was added. The organic layer was separated and the water layer was extracted with CH₂Cl₂ three times. The combined organic layers were washed with brine and dried over anhydrous Na₂SO₄. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (EtOAc/hexane, 1:4) to afford **3** (2.1 g, 60%) as a pale yellow syrup; $[\alpha]_D^{25}$ -38.3, (*c* = 0.96, CHCl₃); IR (neat) $\nu_{\max}$ 1767, 1756, 1748 (C=O stretching), 1583 (C=C stretching), 1372 (C-H bending of CH₃COO-), 1248 (C-O-C asymmetric stretching), 1070 (C-O-C symmetric stretching) cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.38-7.42 (m, 2H, Ar(H)), 7.22-7.26 (m, 3H, Ar(H)), 5.11 (t, *J* = 8.2 Hz, 1H, H-3), 4.87 (t, *J* = 8.2 Hz, 1H, H-2), 4.85 (td, *J* = 8.6, 4.9 Hz, 1H, H-4), 4.74 (d, *J* = 8.2 Hz, 1H, H-1), 4.20 (dd, *J* = 11.8, 4.9 Hz, 1H, H-5), 3.35 (dd, *J* = 11.8, 8.6 Hz, 1H, H-5), 2.01 (s, 3H, OCOCH₃), 1.97 (s, 3H, OCOCH₃), 1.96 (s, 3H, OCOCH₃); ¹³C NMR (100 MHz, CDCl₃): δ 169.7, 169.6, 169.2 (OCOCH₃), 132.6×2 (CH-Ar), 132.1 (C-Ar), 128.9×2 (CH-Ar), 128.1 (CH-Ar), 86.1 (C-1), 70.9 (C-3), 69.7 (C-2), 68.3 (C-4), 65.1 (C-5), 20.65, 20.59, 20.57 (OCOCH₃).

Phenyl 1-thio- β -D-xylopyranoside (4):

Compound **3** (3.56 g, 9.66 mmol) was dissolved in methanol (44 mL) followed by the addition of sodium methoxide (31 mg, 0.48 mmol). The reaction mixture was stirred at room temperature for 12 h. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (100%EtOAc) to give **4** (1.90 g, 81%) as a white

solid; mp. 142-144 °C (lit.^[14]. 143-145 °C); $[\alpha]_D^{25}$ -65.3, ($c = 1.02$, CHCl_3); IR (neat, cm^{-1}) ν_{max} 3391 (O-H stretching), 1047 (C-O stretching of 2° alcohol); ^1H NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$): δ 7.48 – 7.52 (m, 2H, Ar(H)), 7.25 – 7.34 (m, 3H, Ar(H)), 4.70 (d, $J = 8.0$ Hz, 1H), 4.41 (brm, 2H, O-H), 4.25 (brm, 1H, O-H), 3.98 (dd, $J = 4.7, 11.3$ Hz, 1H, H-5), 3.50 – 3.55 (m, 1H, H-4), 3.46 (t, $J = 8.0$ Hz, 1H, H-3), 3.31 (t, $J = 8.0$ Hz, 1H, H-2), 3.30 (dd, $J = 9.1, 11.3$ Hz, 1H, H-5); ^{13}C NMR (100 MHz, $(\text{CD}_3)_2\text{CO}$): δ 135.6 (C-Ar), 132.1×2 (CH-Ar), 129.6×2 (CH-Ar), 127.8 (CH-Ar), 89.3 (C-1), 78.3 (C-3), 73.5 (C-2), 70.6 (C-4), 69.4 (C-5).

Phenyl 3,4-*O*-(2',3'-dimethoxybutane-2'3'-diyl)-1-thio- β -D-xylopyranoside (5):

$\text{BF}_3 \cdot \text{OEt}_2$ (1.9 mL, 14.8 mmol) was added to a solution of **4** (1.80 g, 7.42 mmol), butane-2,3-dione (0.7 mL, 8.17 mmol) and trimethyl orthoformate (2.7 mL, 24.5 mmol), in methanol (225 mL). The mixture was stirred at room temperature for 12 h and then neutralized by addition of triethylamine. The reaction mixture was concentrated under reduced pressure and purified by flash column chromatography (EtOAc/hexane, 1:4) to yield **5** (1.98 g, 75%) as a white solid; m.p. 177-179 °C (hexane-EtOAc); $[\alpha]_D^{25}$ +114.4 ($c = 0.24$, CH_2Cl_2); IR (neat, cm^{-1}) ν_{max} 3479 (O-H stretching), 1584 (C=C stretching), 1131 (C-O); ^1H NMR (400 MHz, CDCl_3): δ 7.46 – 7.49 (m, 2H, Ar(H)), 7.23 – 7.27 (m, 3H, Ar(H)), 4.42 (d, $J = 9.3$ Hz, 1H, H-1), 3.92 (dd, $J = 4.6, 10.8$ Hz, 1H, H-5), 3.67 (ddd, $J = 9.8, 9.8, 4.6$ Hz, 1H, H-4), 3.62 (dd, $J = 10.1, 10.1$ Hz, 1H, H-3), 3.43 (ddd, $J = 9.0, 9.0, 1.9$ Hz, 1H, H-2), 3.39 (dd, $J = 10.5, 10.5$ Hz, 1H, H-5), 3.25 (s, 3H, OCH_3), 3.19 (s, 3H, OCH_3), 2.46 (brs, 1H, OH), 1.28 (s, 3H, CCH_3), 1.23 (s, 3H, CCH_3); ^{13}C NMR (100 MHz, CDCl_3) δ 133.4×2 (CH-Ar), 131.2 (C-Ar), 129.0×2 (CH-Ar), 128.4 (CH-Ar), 99.9 ($\underline{\text{CCH}}_3$), 99.5 ($\underline{\text{CCH}}_3$), 89.3 (C-1), 74.0 (C-3), 69.2 (C-2), 68.0 (C-5), 65.5 (C-4), 48.0

(OCH₃), 47.9 (OCH₃), 17.7 (CCH₃), 17.5 (CCH₃); HRMS (ESI) m/z : C₁₇H₂₄O₆Na [M+Na]⁺
Calcd 379.1191; found: 379.1191.

Phenyl-2-*O*-(4-methoxybenzoyl)-3,4-*O*-(2',3'-dimethoxybutane-2'3'-diyl)-1-thio- β -D-xylopyranoside (6):

To a solution of 2-methoxybenzoic acid (38.0 mg, 0.25 mmol) and *N,N*-dimethylaminopyridine (DMAP) (5.0 mg, 0.042 mmol) in CH₂Cl₂ (2.45 mL) was added a solution of **5** (60 mg, 0.17 mmol) in CH₂Cl₂ (3.6 mL) at room temperature. After the reaction was stirred for 5 min. the solution of *N,N*-dicyclohexylcarbodiimide (DCC) (52 mg, 0.25 mmol) in CH₂Cl₂ (1.5 mL) was introduced. The reaction was stirred at room temperature for 12 h and then filtered and rinsed successively with CH₂Cl₂. The combined CH₂Cl₂ were extracted with saturated aq. NH₄Cl. The combined organic layers were dried (Na₂SO₄) and filtered. The solvent was removed under reduced pressure. The residue was purified by flash column chromatography (EtOAc/hexane, 1:9) to give **6** (77.0 mg, 93%) as a pale yellow syrup; $[\alpha]_D^{25} +145.2$ ($c = 1.52$, CHCl₃); IR (neat, cm⁻¹) $\nu_{\max}$ 1724 (C=O stretching), 1605 (C=C stretching), 1258 (C-O stretching); ¹H NMR (400 MHz, CDCl₃): δ 7.95 (d, $J = 9.0$ Hz, 2H, Ar(H)), 7.38 (m, 2H, Ar(H)), 7.20 (m, 3H, Ar(H)), 6.86 (d, $J = 9.0$ Hz, 2H, Ar(H)), 5.12 (dd, $J = 9.6, 9.6$ Hz, 1H, H-2), 4.68 (d, $J = 9.6$ Hz, 1H, H-1), 3.96 (dd, $J = 4.6, 10.8$ Hz, 1H, H-5), 3.84 (dd, $J = 9.7, 9.7$ Hz, 1H, H-3), 3.82 (ddd, $J = 8.1, 8.1, 4.2$ Hz, 1H, H-4), 3.42 (dd, $J = 10.5, 10.5$ Hz, 1H, H-5), 3.79 (s, 3H, ArOCH₃), 3.18 (s, 3H, OCH₃), 3.10 (s, 3H, OCH₃), 1.20 (s, 3H, CCH₃), 1.15 (s, 3H, CCH₃); ¹³C NMR (100 MHz, CDCl₃): δ 164.6 (C=O), 163.5 (C-Ar), 132.7 $\times$ 2 (CH-Ar), 132.6 (C-Ar), 131.8 (CH-Ar), 128.8 $\times$ 2 (CH-Ar), 127.9 $\times$ 2 (CH-Ar), 122.2 (C-Ar), 113.7 $\times$ 2 (CH-Ar), 99.9 (CCH₃), 99.5 (CCH₃), 87.6 (C-1), 72.4 (C-3), 69.6 (C-2), 67.8 (C-5), 65.8 (C-4), 55.4 (ArOCH₃), 47.9

(OCH₃), 47.6 (OCH₃), 17.6 (CCH₃), 17.5 (CCH₃); HRMS (ESI) m/z : C₂₅H₃₀O₈SNa [M+Na]⁺
Calcd 513.1559, found: 513.1557.

2-*O*-(4-Methoxybenzoyl-3,4-*O*-(2',3'-dimethoxybutane-2',3'-diyl)- α/β -D-xylopyranose (7):

To a solution of **6** (39.0 mg, 0.080 mmol) in CH₂Cl₂ (1.8 mL) and water (0.2 mL) was added NBS (16.0 mg, 0.087 mmol) in one portion. After the reaction was stirred at 25 °C for 1 h, saturated aq. Na₂SO₃ was added. The organic layer was separated and washed with brine, dried (Na₂SO₄) and filtered. The solvent was removed under reduced pressure. The residue was purified by flash column chromatography (EtOAc/hexane, 3:7) to give **7** (25.0 mg, 79%) as a colorless oil; $[\alpha]_D^{25}$ +194.9 (c = 0.49, CHCl₃); IR (neat, cm⁻¹) $\nu_{\max}$ 3447 (O-H stretching), 1718 (C=O), 1606, 1512, 1259 (C-O-C asymmetric stretching), 1169, 1135, 1112, 1078, 1034 (C-O-C symmetric stretching); ¹H NMR (400 MHz, CDCl₃): δ 7.95 (d, J = 9.0 Hz, 2H, Ar(H β)), 7.92 (d, J = 9.0 Hz, 2H, Ar(H α)), 6.85 (d, J = 9.1 Hz, 2H, Ar(H β)), 6.84 (d, J = 9.0 Hz, 2H, Ar(H α)), 6.33 (d, J = 3.4 Hz, 1H, H-1 β), 5.50 (d, J = 3.7 Hz, 1H, H-1 α), 4.90 (dd, J = 3.7, 10.6 Hz, 1H, H-2 β), 4.22 (dd, J = 10.0, 10.0 Hz, 1H, H-2 α), 3.78-3.99 (m, 6H, H-3 α,β , H-4 α,β , H-5 α,β), 3.79 (s, 3H, ArOCH₃), 3.77 (s, 3H, ArOCH₃), 3.66 (dd, J = 2.5, 5.3 Hz, 1H, H-5 β), 3.55 (dd, J = 4.6, 9.9 Hz, 1H, H-5 α), 3.28 (s, 3H, OCH₃ β), 3.27 (s, 3H, OCH₃ α), 3.22 (s, 3H, OCH₃ β), 3.20 (s, 3H, OCH₃ α), 1.28 (s, 3H, CCH₃ β), 1.26 (s, 3H, CCH₃ β), 1.23 (s, 3H, CCH₃ α), 1.20 (s, 3H, CCH₃ α); ¹³C NMR (100 MHz, CDCl₃): δ 166.8, 165.6 (C=O), 164.9, 163.8 (C-Ar), 132.0 $\times$ 2 (CH-Ar), 131.8 $\times$ 2 (CH-Ar), 121.7, 122.2 (C-Ar), 113.8 $\times$ 2 (CH-Ar), 113.6 $\times$ 2 (CH-Ar), 100.0, 99.7 (CCH₃), 99.9, 99.6 (CCH₃), 92.3 (C-1 β), 90.9 (C-1 α), 71.4 (C-2 β), 70.7, 69.1, 66.4, 65.7 (C-3 β,α , C-4 β,α), 67.1 (C-2 α), 62.1 (C-5 β), 59.4 (C-5 α), 55.4 $\times$ 2 (ArOCH₃), 48.1, 48.0 (OCH₃),

47.9, 47.8 (OCH₃), 17.7, 17.4 (CCH₃), 17.5×2 (CCH₃); MS (ESI), *m/z* (relative intensity): 421.2 ([M+Na]⁺, 100 %).

2-*O*-(4-Methoxybenzoyl)-3,4-*O*-(2',3'-dimethoxybutane-2',3'-diyl)- α/β -D-xylopyranosyl trichloro acetimidate (8):

Compound **7** (20.0 mg, 0.05 mmol) was dissolved in dry CH₂Cl₂ (2.0 mL). Trichloroacetonitrile (0.025 mL, 0.25 mmol) and DBU (1 drop) were added. The reaction was stirred at 25 °C for 12 h. The solvent was removed and the product was isolated by silica gel short column chromatography (EtOAc/hexane/Et₃N, 15:4:1) to afford **8** (26.0 mg, 96%) as a pale yellow oil. IR (neat, cm⁻¹) $\nu_{\max}$ 3342, 1720, 1606, 1257, 1169, 1138, 1085, 1030; ¹H NMR (400 MHz, CDCl₃) δ 8.49 (brs, 1H, NH α), 8.45 (brs, 1H, NH β), 7.99 (d, *J* = 9.0 Hz, 2H, Ar(H β)), 7.94 (d, *J* = 9.0 Hz, 2H, Ar(H α)), 6.91 (d, *J* = 9.0 Hz, 2H, Ar(H β)), 6.88 (d, *J* = 9.0 Hz, 2H, Ar(H α)), 6.76 (d, *J* = 3.8 Hz, 1H, H-1 β), 6.61 (d, *J* = 3.7 Hz, 1H, H-1 α), 5.26 (dd, *J* = 3.7, 10.6 Hz, 1H, H-2 α), 5.18 (dd, *J* = 3.8, 10.6 Hz, 1H, H-2 β), 4.36 (dd, *J* = 8.3, 9.6 Hz, 1H, H-3 β), 4.33 (dd, *J* = 9.6, 10.4 Hz, 1H, H-3 α), 4.01 (dd, *J* = 5.1, 10.9 Hz, 1H, H-4 β), 3.98 (dd, *J* = 4.7, 10.8 Hz, 1H, H-4 α), 3.92 (dd, *J* = 10.5, 10.5 Hz, 1H, H-5 α,β), 3.86 (s, 3H, ArOCH₃ β), 3.84 (s, 3H, ArOCH₃ α), 3.82 (dd, *J* = 4.9, 10.3 Hz, 1H, H-5 α,β), 3.37 (s, 3H, OCH₃ β), 3.32 (s, 3H, OCH₃ α), 3.30 (s, 3H, OCH₃ β), 3.30 (s, 3H, OCH₃ α), 1.34 (s, 3H, CCH₃ β), 1.33 (s, 3H, CCH₃ β), 1.32 (s, 3H, CCH₃ α), 1.28 (s, 3H, CCH₃ α); ¹³C NMR (100 MHz, CDCl₃) δ 165.2 (C=O), 163.6, 160.8 (C-Ar), 131.8×2 (CH-Ar), 131.7×2 (CH-Ar), 121.7 (C-Ar), 113.8×2 (CH-Ar β), 113.6×2 (CH-Ar α), 100.0, 99.7 (CCH₃), 94.1 (C-1), 88.9 (CCl₃), 69.8 (C-4), 67.5 (C-2), 65.8 (C-3), 62.2

(C-5), 55.4 (ArOCH₃), 48.1 (OCH₃), 47.6 (OCH₃), 17.7 (CCH₃), 17.5 (CCH₃); MS (ESI), *m/z* (relative intensity): 564.0 ([M+Na]⁺, 100 %).

Bromo 2,3,4-*O*-triacetyl- α/β -L-arabinopyranoside (10):

Tetraacetyl L-arabinose **9** (5.46 g, 17.2 mmol) was dissolved in acetic acid (95.7 mL) then phosphorus tribromide (1M in CH₂Cl₂, 164.9 mL, 164.9 mmol) was added dropwise. After stirring at room temperature for 4 h, the mixture was diluted with CH₂Cl₂, poured into ice-water, and extracted with CH₂Cl₂. The organic extracts were separated, dried (Na₂SO₄) and concentrated *in vacuo* to give **10** (4.63 g, 80%) as a white solid. The crude product was immediately used in the next step without purification.

4-Methoxybenzyl 2,3,4-*O*-triacetyl- β -L-arabinopyranoside (11):

The bromide (**10**) (4.63 g, 13.7 mmol) was then mixed with toluene (58.2 mL) and 4Å MS (10.2 g) for 40 min. before addition of 4-methoxybenzyl alcohol (8.61 mL, 68.4 mmol), I₂ (5.19 g, 20.5 mmol), and Ag₂CO₃ (7.54 g, 27.2 mmol). After stirring at room temperature for 24 h, the reaction mixture was filtered through celite and the pad was washed with toluene. The organic layer was then washed with 20% aq. Na₂S₂O₃ (115 mL), water (115 mL) and saturated aqueous NaCl (115 mL), respectively. The organic extract was separated, dried (Na₂SO₄) and concentrated *in vacuo*. The residue was purified by flash column chromatography (EtOAc/hexane, 3:7) to afford **11** (3.73 g, 70%) as a colorless syrup; [α]_D²⁵ -20.2, (*c* = 0.31, CHCl₃); IR (neat, cm⁻¹) $\nu_{\max}$ 1747, 1612, 1514, 1370, 1249, 1224, 1103, 1056, 1023; ¹H NMR (400 MHz, CDCl₃) δ 7.20 (d, *J* = 8.7 Hz, 2H, Ar(H)), 6.85 (d, *J* = 8.7 Hz, 2H, Ar(H)), 5.22 - 5.24 (m, 1H, H-4), 5.20 (dd, *J* = 9.4, 6.9 Hz, 1H, H-2), 4.98 (dd, *J* = 9.2, 3.6 Hz, 1H, H-3), 4.79 (d, *J*

= 11.9 Hz, 1H, OCH₂ArOCH₃), 4.51 (d, J = 11.9 Hz, 1H, OCH₂ArOCH₃), 4.44 (d, J = 6.8 Hz, 1H, H-1), 4.03 (dd, J = 13.0, 3.5 Hz, 1H, H-5), 3.78 (s, 3H, OCH₃), 3.59 (dd, J = 12.9, 1.9 Hz, 1H, H-5), 2.11 (s, 3H, OCOCH₃), 2.00 (s, 3H, OCOCH₃), 1.98 (s, 3H, OCOCH₃); ¹³C NMR (100 MHz, CDCl₃) δ 170.2 (OCOCH₃), 170.0 (OCOCH₃), 169.3 (OCOCH₃), 159.3 (C-Ar), 129.2 $\times$ 2 (CH-Ar), 128.8 (C-Ar), 113.7 $\times$ 2 (CH-Ar), 99.1 (C-1), 70.0 (C-3), 70.0 (OCH₂ArOCH₃), 69.1 (C-2), 67.5 (C-4), 62.9 (C-5), 55.1 (OCH₃), 20.6 (OCOCH₃), 20.5 (OCOCH₃), 20.4 (OCOCH₃); MS (ESI), m/z (relative intensity): 419 ([M+Na]⁺, 100%).

4-Methoxybenzyl- β -L-arabinopyranoside (12):

Compound **11** (3.73 g, 9.42 mmol) in a mixture of MeOH/Et₃N/H₂O (8:1:1, 45 mL) was stirred at room temperature for 16 h. The reaction mixture was then evaporated under reduced pressure and the crude residue was purified by flash column chromatography (EtOAc then EtOAc/MeOH, 9:1) to give **12** (2.54 g, 100%) as a white solid; m.p. 107-109 °C; [α]_D²⁵ -26.1, (c = 1.0, CH₃OH); IR (neat, cm⁻¹) $\nu_{\max}$ 3269, 1611, 1514, 1257, 1088, 1075, 1004; ¹H NMR (400 MHz, CD₃OD) δ 7.30 (d, J = 8.5 Hz, 2H, Ar(H)), 6.86 (d, J = 8.6 Hz, 2H, Ar(H)), 4.76 (d, J = 11.4 Hz, 1H, OCH₂ArOCH₃), 4.52 (d, J = 11.3 Hz, 1H, OCH₂ArOCH₃), 4.26 (d, J = 6.8 Hz, 1H, H-1), 3.88 (dd, J = 12.5, 3.1 Hz, 1H, H-5), 3.79 – 3.81 (m, 1H, H-4), 3.76 (s, 3H, OCH₃), 3.59 (dd, J = 8.7, 6.9 Hz, 1H, H-2), 3.51 (dd, J = 12.6, 1.6 Hz, 1H, H-5), 3.50 (dd, J = 8.6, 3.6 Hz, 1H, H-3); ¹³C NMR (100 MHz, CD₃OD) δ 159.7 (C-Ar), 129.8 (C-Ar), 129.7 $\times$ 2 (CH-Ar), 113.6 $\times$ 2 (CH-Ar), 102.3 (C-1), 73.0 (C-3), 71.2 (C-2), 70.1 (OCH₂ArOCH₃), 68.4 (C-4), 65.6 (C-5), 54.6 (OCH₃); MS (ESI), m/z (relative intensity): 293 ([M+Na]⁺, 100%).

4-Methoxybenzyl *exo/endo*-3,4-*O*-benzylidene- β -L-arabinopyranosides (13):

To a solution of **12** (4.28 g, 15.8 mmol) in dry DMF (35.3 mL) were added α,α -dimethoxytoluene (3.53 mL, 25.4 mmol) and *p*-toluenesulfonic acid monohydrate (30 mg, 0.16 mmol). The reaction mixture was stirred at room temperature for 24 h. Triethylamine was added and the mixture was concentrated to give the syrup which was dissolved in EtOAc was extracted with saturated aq. NaHCO₃, water, dried (Na₂SO₄) and concentrated *in vacuo*. The residue was purified by flash column chromatography (EtOAc/hexane, 3:7) to afford **13_{exo}** (647 mg, 11%) and **13_{endo}** (4.14 g, 73%) as a white solid.

Compound **13_{exo}**: m.p. 118-119 °C; $[\alpha]_D^{25}$ -12.4, (c = 0.2, CH₂Cl₂); IR (neat, cm⁻¹) $\nu_{\max}$ 3452, 1515, 1251, 1102, 1075; ¹H NMR (400 MHz, CDCl₃) δ 7.44 – 7.47 (m, 2H, Ar(H)), 7.34-7.40 (m, 3H, Ar(H)), 7.30 (d, *J* = 8.4 Hz, 2H, Ar(H)), 6.90 (d, *J* = 8.8 Hz, 2H, Ar(H)), 6.19 (s, 1H, CHAr), 4.87 (d, *J* = 11.2 Hz, 1H, OCH₂ArOCH₃), 4.55 (d, *J* = 11.2 Hz, 1H, OCH₂ArOCH₃), 4.36 (dd, *J* = 7.4, 5.7 Hz, 1H, H-3), 4.31 (dd, *J* = 13.4, 2.4 Hz, 1H, H-5), 4.29 (d, *J* = 7.7 Hz, 1H, H-1), 4.18 - 4.21 (m, 1H, H-4), 3.82 (dd, *J* = 9.1, 7.5 Hz, 1H, H-2), 3.81 (s, 3H, OCH₃), 3.74 (dd, *J* = 13.4, 2.9 Hz, 1H, H-5); ¹³C NMR (100 MHz, CDCl₃) δ 159.5 (C-Ar), 138.5 (C-Ar), 129.9×2 (CH-Ar), 129.1 (CH-Ar), 128.9 (C-Ar), 128.3×2 (CH-Ar), 126.1×2 (CH-Ar), 113.9×2 (CH-Ar), 103.3 (CHAr), 100.6 (C-1), 79.2 (C-3), 73.0 (C-4), 71.0 (C-2), 70.3 (OCH₂ArOCH₃), 63.2 (C-5), 55.2 (OCH₃); HRMS (ESI) *m/z*: C₂₀H₂₂O₆Na [M+Na]⁺ Calcd 381.1309; found: 381.1322.

Compound **13_{endo}**: m.p. 119-121 °C; $[\alpha]_D^{25}$ +6.33, (c = 0.12, CHCl₃); IR (neat, cm⁻¹) $\nu_{\max}$ 3452, 1513, 1249, 1118, 1093; ¹H NMR (400 MHz, CDCl₃) δ 7.50 – 7.52 (m, 2H, Ar(H)), 7.35-7.38 (m, 3H, Ar(H)), 7.29 (d, *J* = 8.4 Hz, 2H, Ar(H)), 6.89 (d, *J* = 8.7 Hz, 2H, Ar(H)), 5.94 (s, 1H, CHAr), 4.83 (d, *J* = 11.2 Hz, 1H, OCH₂ArOCH₃), 4.53 (d, *J* = 11.2 Hz, 1H, OCH₂ArOCH₃), 4.36 (d, *J* = 7.4 Hz, 1H, H-1), 4.31 (dd, *J* = 14.0, 3.3 Hz, 1H, H-5), 4.30 (dd, *J* = 6.3, 4.7 Hz, 1H, H-4), 4.20 (dd, *J* = 7.2, 6.3 Hz, 1H, H-3), 3.87 (dd, *J* = 14.0, 4.7 Hz, 1H, H-5),

3.80 (s, 3H, OCH₃), 3.76 (dd, $J = 7.3, 7.3$ Hz, 1H, H-2); ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 159.3 (C-Ar), 136.9 (C-Ar), 129.8 $\times$ 2 (CH-Ar), 129.3 (CH-Ar), 129.0 (C-Ar), 128.3 $\times$ 2 (CH-Ar), 126.6 $\times$ 2 (CH-Ar), 113.8 $\times$ 2 (CH-Ar), 104.5 (CHAr), 100.5 (C-1), 77.8 (C-3), 74.8 (C-4), 73.4 (C-2), 70.0 (OCH₂ArOCH₃), 62.5 (C-5), 55.1 (OCH₃); HRMS (ESI) m/z : C₂₀H₂₂O₆Na [M+Na]⁺ Calcd 381.1309; found: 381.1312.

4-Methoxybenzyl 2-*O*-acetyl-*exo*-3,4-*O*-benzylidene- β -L-arabinopyranoside (**14_{exo}**):

Compound **13_{exo}** (647 mg, 1.81 mmol) was dissolved in CH₂Cl₂ (9.44 mL). Triethylamine (0.37 mL, 2.71 mmol), acetic anhydride (0.20 mL, 2.17 mmol), and DMAP (5 mg, 0.04 mmol) were added. The reaction mixture was stirred at room temperature for 1 h. then was quenched with saturated aq. NaHCO₃. The organic layer was separated and the water layer was extracted with CH₂Cl₂ three times. The combined organic layer was washed with brine and dried (Na₂SO₄). The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (EtOAc/hexane, 3:7) to give **14_{exo}** (624 mg, 86%) as a colorless syrup then became a white solid; m.p. 99-101 °C; $[\alpha]_D^{25}$ -33.0 ($c = 0.40$, CH₂Cl₂); IR (neat, cm⁻¹) $\nu_{\max}$ 1746, 1612, 1514, 1247, 1229, 1099, 1061; ¹H NMR (400 MHz, CDCl₃) δ 7.43 – 7.45 (m, 2H, Ar(H)), 7.35-7.38 (m, 3H, Ar(H)), 7.26 (d, $J = 8.4$ Hz, 2H, Ar(H)), 6.89 (d, $J = 8.8$ Hz, 2H, Ar(H)), 6.22 (s, 1H, CHAr), 5.25 (dd, $J = 6.2, 6.2$ Hz, 1H, H-2), 4.80 (d, $J = 12.0$ Hz, 1H, OCH₂ArOCH₃), 4.55 (d, $J = 12.0$ Hz, 1H, OCH₂ArOCH₃), 4.49 (d, $J = 6.2$ Hz, 1H, H-1), 4.36 – 4.38 (m, 2H, H-3, H-4), 4.19 (dd, $J = 13.0, 3.8$ Hz, 1H, H-5), 3.81 (s, 3H, OCH₃), 3.78 (dd, $J = 13.0, 4.2$ Hz, 1H, H-5), 2.08 (s, 3H, OCOCH₃); ¹³C NMR (100 MHz, CDCl₃) δ 169.6 (OCCOCH₃), 159.3 (C-Ar), 138.1 (C-Ar), 129.4 $\times$ 2 (CH-Ar), 129.2 (CH-Ar), 129.1 (C-Ar), 128.4 $\times$ 2 (CH-Ar), 126.2 $\times$ 2 (CH-Ar), 113.8 $\times$ 2 (CH-Ar), 103.4 (CHAr), 97.6 (C-1), 76.7 (C-3),

72.3 (C-4), 70.1 (C-2), 69.3 (OCH₂ArOCH₃), 61.6 (C-5), 55.2 (OCH₃), 20.9 (OCOCH₃); HRMS (ESI) *m/z*: C₂₂H₂₄O₇Na [M+Na]⁺ Calcd 423.1414; found: 423.1419.

4-Methoxybenzyl 2-*O*-acetyl-*endo*-3,4-*O*-benzylidene- β -L-arabinopyranoside (**14endo**):

Compound **13endo** (4.14 g, 11.6 mmol) was dissolved in CH₂Cl₂ (60.5 mL). Triethylamine (2.4 mL, 17.4 mmol), acetic anhydride (1.3 mL, 13.9 mmol), and DMAP (34.0 mg, 0.28 mmol) were added. The reaction mixture was stirred at room temperature for 1 h then was quenched with saturated aq. NaHCO₃. The organic layer was separated and the water layer was extracted with CH₂Cl₂ three times. The combined organic layer was washed with brine and dried (Na₂SO₄). The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (EtOAc/hexane, 3:7) to give **14endo** (4.05 g, 88%) as a colorless syrup; [α]_D²⁵ 21.8, (c = 0.60, CH₂Cl₂); IR (neat, cm⁻¹) $\nu_{\max}$ 1744, 1612, 1514, 1244, 1232, 1119, 1091, 1066; ¹H NMR (400 MHz, CDCl₃) δ 7.51-7.55 (m, 2H, Ar(H)), 7.34-7.39 (m, 3H, Ar(H)), 7.25 (d, *J* = 8.9 Hz, 2H, Ar(H)), 6.88 (d, *J* = 8.7 Hz, 2H, Ar(H)), 5.89 (s, 1H, CHAr), 5.24 (dd, *J* = 5.7, 5.7 Hz, 1H, H-2), 4.75 (d, *J* = 11.8 Hz, 1H, OCH₂ArOCH₃), 4.57 (d, *J* = 5.5 Hz, 1H, H-1), 4.52 (d, *J* = 11.8 Hz, 1H, OCH₂ArOCH₃), 4.38 (dd, *J* = 5.5, 11.6 Hz, 1H, H-4), 4.27 (dd, *J* = 6.2, 6.2 Hz, 1H, H-3), 4.12 (dd, *J* = 12.7, 5.7 Hz, 1H, H-5), 3.84 (dd, *J* = 12.6, 5.0 Hz, 1H, H-5), 3.81 (s, 3H, OCH₃), 2.09 (s, 3H, OCOCH₃); ¹³C NMR (100 MHz, CDCl₃) δ 169.4 (OCOCH₃), 159.3 (C-Ar), 136.4 (C-Ar), 129.5 (CH-Ar), 129.4 $\times$ 2 (CH-Ar), 129.1 (C-Ar), 128.4 $\times$ 2 (CH-Ar), 126.9 $\times$ 2 (CH-Ar), 113.7 $\times$ 2 (CH-Ar), 104.9 (CHAr), 97.5 (C-1), 75.8 (C-3), 72.8 (C-4), 72.2 (C-2), 69.3 (OCH₂ArOCH₃), 61.3 (C-5), 55.2 (OCH₃), 20.9 (OCOCH₃); HRMS (ESI) *m/z*: C₂₂H₂₄O₇Na [M+Na]⁺ Calcd 423.1414; found: 423.1422.

4-Methoxybenzyl 2-*O*-acetyl-4-*O*-benzyl- β -L-arabinopyranoside (**15**)

Reductive ring opening of **14_{exo}**

To a solution of **14_{exo}** (173 mg, 0.43 mmol) in CH₂Cl₂ (1.73 mL) was added Et₃SiH (0.09 mL, 0.58 mmol). The mixture was cooled to -78 °C and slowly added a solution of TiCl₄ (0.05 mL, 0.49 mmol) in CH₂Cl₂ (0.54 mL). The reaction mixture was stirred at -78 °C for 5 h. and then poured into ice and extracted with EtOAc. The organic layers were washed with saturated aq. NaHCO₃ and brine, dried (Na₂SO₄) and concentrated *in vacuo*. The residue was purified by flash column chromatography (EtOAc/hexane, 2:3) to afford **15** (75.0 mg, 43%) as a white solid and **16** (20.0 mg, 11%) as a white solid.

Reductive ring opening of **14_{endo}**

To a solution of **14_{endo}** (3.02 g, 7.55 mmol) in CH₂Cl₂ (30.2 mL) was added Et₃SiH (1.65 mL, 10.2 mmol). The reaction mixture was cooled to -78 °C and slowly added a solution of TiCl₄ (0.93 mL, 8.46 mmol) in CH₂Cl₂ (9.3 mL). The reaction mixture was stirred at -78 °C for 5 h. and then poured into ice and extracted with EtOAc. The organic layer was washed with saturated aq. NaHCO₃ and brine, dried (Na₂SO₄) and concentrated *in vacuo*. The residue was purified by flash column chromatography (EtOAc/hexane, 2:3) to afford **15** as a white solid (2.21 g, 73%) and **16** (428 mg, 14%) as a white solid.

Compound **15**: m.p. 57-58 °C; [α]_D²⁵ -29.4 (c = 0.60, CH₂Cl₂); IR (neat, cm⁻¹) ν_{max} 3481, 1738, 1612, 1514, 1244, 1088, 1057; ¹H NMR (400 MHz, CDCl₃) δ 7.22 – 7.30 (m, 5H, Ar(H)), 7.18 (d, *J* = 8.4 Hz, 2H, Ar(H)), 6.81 (d, *J* = 8.7 Hz, 2H, Ar(H)), 4.97 (dd, *J* = 4.8, 6.5 Hz, 1H, H-2), 4.69 (d, *J* = 11.8 Hz, 1H, OCH₂ArOCH₃), 4.62 (d, *J* = 11.8 Hz, 1H, OCH₂Ar), 4.53 (d, *J* = 11.8 Hz, 1H, OCH₂Ar), 4.45 (d, *J* = 4.8 Hz, 1H, H-1), 4.45 (d, *J* = 11.3 Hz, 1H, OCH₂ArOCH₃),

3.98 (dd, $J = 6.2, 12.3$ Hz, 1H, H-5), 3.75 – 3.78 (m, 1H, H-4), 3.74 (s, 3H, OCH₃), 3.67 (dd, $J = 3.2, 6.5$ Hz, 1H, H-3), 3.41 (dd, $J = 3.1, 12.3$ Hz, 1H, H-5), 1.99 (s, 3H, OCOCH₃); ¹³C NMR (100 MHz, CDCl₃) δ 170.0 (OCOCH₃), 159.4 (C-Ar), 137.5 (C-Ar), 129.5 $\times$ 2 (CH-Ar), 128.8 (C-Ar), 128.5 $\times$ 2 (CH-Ar), 127.9 (CH-Ar), 127.8 $\times$ 2 (CH-Ar), 113.8 $\times$ 2 (CH-Ar), 97.8 (C-1), 73.4 (C-3), 71.8 (C-2), 71.2 (OCH₂Ar), 69.6 (OCH₂ArOCH₃), 69.4 (C-4), 59.6 (C-5), 55.2 (OCH₃), 20.9 (OCOCH₃); HRMS (ESI) m/z : C₂₂H₂₆O₇Na [M+Na]⁺ Calcd 425.1571; found: 425.1572.

Compound **16**: m.p. 89-91 °C; [α]_D²⁵ -47.4 ($c = 0.08$, CHCl₃); IR (neat, cm⁻¹) $\nu_{\max}$ 3478, 1739, 1612, 1514, 1243, 1084, 1052; ¹H NMR (400 MHz, CDCl₃) δ 7.24 – 7.34 (m, 5H, Ar(H)), 7.22 (d, $J = 8.5$ Hz, 2H, Ar(H)), 6.84 (d, $J = 8.5$ Hz, 2H, Ar(H)), 5.21 (dd, $J = 5.9, 4.5$ Hz, 1H, H-2), 4.74 (d, $J = 11.5$ Hz, 1H, OCH₂ArOCH₃), 4.68 (d, $J = 11.5$ Hz, 1H, OCH₂Ar), 4.56 (d, $J = 11.5$ Hz, 1H, OCH₂Ar), 4.50 (d, $J = 4.5$ Hz, 1H, H-1), 4.46 (d, $J = 11.5$ Hz, 1H, OCH₂ArOCH₃), 3.98 (dd, $J = 11.2, 6.3$ Hz, 1H, H-5), 3.93 (m, 1H, H-4), 3.79 (s, 3H, OCH₃), 3.59 (dd, $J = 5.9, 3.3$ Hz, 1H, H-3), 3.46 (dd, $J = 11.0, 9.0$ Hz, 1H, H-5), 2.03 (s, 3H, OCOCH₃); ¹³C NMR (100 MHz, CDCl₃) δ 169.7 (OCOCH₃), 159.2 (C-Ar), 137.4 (C-Ar), 129.4 $\times$ 2 (CH-Ar), 129.4 (C-Ar), 128.4 $\times$ 2 (CH-Ar), 128.0 (CH-Ar), 127.9 $\times$ 2 (CH-Ar), 113.7 $\times$ 2 (CH-Ar), 97.8 (C-1), 76.5 (C-3), 71.7 (OCH₂Ar), 69.4 (C-2), 69.2 (OCH₂ArOCH₃), 65.0 (C-4), 62.6 (C-5), 55.2 (OCH₃), 20.9 (OCOCH₃); HRMS (ESI) m/z : C₂₂H₂₆O₇Na [M+Na]⁺ Calcd 425.1571; found: 425.1570.

4-Methoxybenzyl 2-*O*-acetyl-4-*O*-benzyl-3-*O*-[2-*O*-(4-methoxybenzoyl)-3,4-*O*-(2',3'-dimethoxybutan -2',3'-diyl)- β -D-xylopyranosyl]- β -L-arabinopyranoside (17**)**

A solution of **15** (163 mg, 0.40 mmol), **8** (514 mg, 0.95 mmol), and activated 4 Å MS (1.65 g) in dry dichloromethane (24.8 mL) was stirred for 1 h at room temperature. The mixture was cooled to -78 °C for 30 min followed by the dropwise addition of a 0.1M solution of TMSOTf in dry CH₂Cl₂ (0.07 mL, 0.007 mmol). Stirring was continued and the reaction mixture

was allowed to warm to -20 °C for 2 h. Then the reaction mixture was quenched with triethylamine, filtered through celite, and the solvents were evaporated. Purification by flash column chromatography (EtOAc/hexane, 3:7) gave **17** (152 mg, 49%) as a white solid.

Compound **17**: m.p. 84-86 °C; $[\alpha]_D^{25} +45.0$, ($c = 0.23$, CHCl_3); IR (neat, cm^{-1}) ν_{max} 1745, 1726, 1606, 1513, 1456, 1371, 1256, 1168, 1138, 1111, 1098, 1048; ^1H NMR (400 MHz, CDCl_3) δ 7.98 (d, $J = 9.0$ Hz, 2H, Ar(H)), 7.38 – 7.40 (m, 2H, Ar(H)), 7.30 – 7.34 (m, 2H, Ar(H)), 7.23 – 7.28 (m, 1H, Ar(H)), 7.02 (d, $J = 8.6$ Hz, 2H, Ar(H)), 6.90 (d, $J = 9.0$ Hz, 2H, Ar(H)), 6.76 (d, $J = 8.7$ Hz, 2H, Ar(H)), 5.22 (dd, $J = 7.3, 9.6$ Hz, 1H, H-2'), 5.14 (dd, $J = 6.0, 7.5$ Hz, 1H, H-2), 4.82 (d, $J = 12.3$ Hz, 1H, $\text{OCH}_2\text{ArOCH}_3$), 4.67 (d, $J = 12.2$ Hz, 1H, $\text{OCH}_2\text{ArOCH}_3$), 4.67 (d, $J = 7.3$ Hz, 1H, H-1'), 4.50 (d, $J = 12.2$ Hz, 1H, OCH_2Ar), 4.37 (d, $J = 12.2$ Hz, 1H, OCH_2Ar), 4.25 (d, $J = 6.0$ Hz, 1H, H-1), 3.85 – 3.96 (m, 4H, H-3', H-4', H-5, H-5'), 3.83 (s, 3H, ArOCH_3), 3.75 – 3.81 (m, 2H, H-3, H-4), 3.76 (s, 3H, ArOCH_3), 3.40 – 3.46 (m, 1H, H-5'), 3.35 (dd, $J = 1.8, 12.1$ Hz, 1H, H-5), 3.27 (s, 3H, OCH_3), 3.18 (s, 3H, OCH_3), 1.67 (s, 3H, OCOCH_3), 1.28 (s, 3H, CCH_3), 1.22 (s, 3H, CCH_3); ^{13}C NMR (100 MHz, CDCl_3) δ 169.0 (OCOCH_3), 164.3 (OCOArOCH_3), 163.3 (C-Ar), 159.0 (C-Ar), 138.5 (C-Ar), 131.7×2 (CH-Ar), 129.3×2 (CH-Ar), 129.3 (C-Ar), 128.1×2 (CH-Ar), 128.0×2 (CH-Ar), 127.4 (CH-Ar), 122.6 (C-Ar), 113.6×2 (CH-Ar), 113.5×2 (CH-Ar), 102.9 (C-1'), 99.7, 99.5 (CCH_3), 98.4 (C-1), 77.6 (C-4), 73.6 (C-3), 71.9 ($\text{OCH}_2\text{ArOCH}_3$), 70.1 (C-2'), 70.7 (C-3'), 70.5 (C-2), 68.5 (OCH_2Ar), 65.7 (C-4'), 63.9 (C-5), 62.7 (C-5'), 55.4 (OCOArOCH_3), 55.2 (ArOCH_3), 47.9, 47.6 (OCH_3), 20.5 (OCOCH_3), 17.6, 17.5 (CCH_3); HRMS (ESI) m/z : $\text{C}_{41}\text{H}_{50}\text{O}_{15}\text{Na}$ $[\text{M}+\text{Na}]^+$ Calcd 805.3042; found: 805.3066.

¹H NMR (400 MHz, CDCl₃): Compound 3

¹³C NMR (100 MHz, CDCl₃): Compound 3

¹H NMR (400 MHz, CDCl₃): Compound **4**

¹³C NMR (100 MHz, CDCl₃): Compound **4**

^1H NMR (400 MHz, CDCl_3): Compound 5

^{13}C NMR (100 MHz, CDCl_3): Compound 5

^1H NMR (400 MHz, CDCl_3): Compound 6

^{13}C NMR (100 MHz, CDCl_3): Compound 6

^1H NMR (400 MHz, CDCl_3): Compound 7

^{13}C NMR (100 MHz, CDCl_3): Compound 7

^1H NMR (400 MHz, CDCl_3): Compound 8

^{13}C NMR (100 MHz, CDCl_3): Compound 8

¹H NMR (400 MHz, CDCl₃): Compound **11**

¹³C NMR (100 MHz, CDCl₃): Compound **11**

^1H NMR (400 MHz, CDCl_3): Compound **12**

^{13}C NMR (100 MHz, CDCl_3): Compound **12**

^1H NMR (400 MHz, CDCl_3): Compound **13 $_{exo}$**

SpinWorks 2.3: 5.56-213JR-1-1-full in CDCl_3

^{13}C NMR (100 MHz, CDCl_3): Compound **13 $_{exo}$**

^1H NMR (400 MHz, CDCl_3): Compound **13*endo***

^{13}C NMR (100 MHz, CDCl_3): Compound **13*endo***

^1H NMR (400 MHz, CDCl_3): Compound **14_{exo}**

^{13}C NMR (100 MHz, CDCl_3): Compound **14_{exo}**

^1H NMR (400 MHz, CDCl_3): Compound **14endo**

^{13}C NMR (100 MHz, CDCl_3): Compound **14endo**

^1H NMR (400 MHz, CDCl_3): Compound 15

^{13}C NMR (100 MHz, CDCl_3): Compound 15

¹H NMR (400 MHz, CDCl₃): Compound **16**

¹³C NMR (100 MHz, CDCl₃): Compound **16**

¹H NMR (400 MHz, CDCl₃): Compound 17

SpinWorks 2.3: 5,91-233JR-3-3a in CDCl₃

¹³C NMR (100 MHz, CDCl₃): Compound 17

¹H NMR (400 MHz, CDCl₃): Compound 18

¹³C NMR (100 MHz, CDCl₃): Compound 18