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First Synthesis of a Branched *β*-*C*-Tetrasaccharide Using a Triple Ring Closing Metathesis Cyclization

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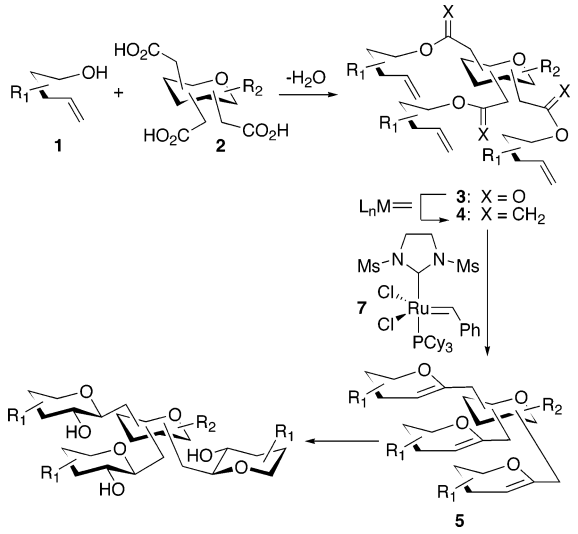
Abstract: The first synthesis of a branched *β*-*C*-tetrasaccharide has been carried out through the use of an esterification−ring closing metathesis (RCM) strategy. The precursor triacid **2a** was readily prepared via standard chemical methods from a known starting material, and dehydrative coupling with an excess of olefin alcohol **1a** gave triester **3a** in excellent yield. Methylenation of the triester **3a** and subsequent triple RCM reaction was followed by an in situ hydroboration−oxidation to furnish the branched *β*-*C*-tetrasaccharide **6a** in good overall yield.

The preparation of stable carbohydrate mimetics[3] is of paramount importance given the vast array of biological functions in which carbohydrates partake.[4−8] The replacement of the interglycosidic oxygen atom of a naturally occurring *O*-glycoside results in the formation of a stable *C*-glycoside derivative that should not be prone to enzymatic or chemical hydrolysis. The field of *C*-glycoside synthesis is a mature field that has seen the use of a wide array of interesting chemistry[9−12] for the attachment of a variety of carbon-based groups to the anomeric center of carbohydrates.

We have shown that *β*-*C*-glycosides,[13−15] *β*-*C*-disaccharides,[16,17] and more recently *β*-*C*-trisaccharides[18] can be generated using an esterfication−RCM strategy. In this Note, we demonstrate that use of a *triple* RCM reaction[19] allows for efficient access to a *β*-*C*-tetrasaccharide. Most of the published syntheses of *C*-saccharides[20] have focused on the preparation of *C*-disaccharides and *C*-trisaccharides. Two research groups have synthesized linear *β*-*C*-tetrasaccharides. Dondoni[21] relied upon an iterative Wittig-based approach, and Sinaÿ[22] employed the addition of a C-6 acetylide anion addition to anomeric lactone followed by stereoselective reduction. The synthesis of a branched *C*-tetrasaccharide has yet to appear.

SCHEME 1. Triple-RCM Approach to *β*-*C*-Tetrasaccharides



Our generic approach to *β*-*C*-tetrasaccharide synthesis is shown in Scheme 1. The approach begins with dehydrative coupling of 3 equiv of a generic olefin alcohol **1** with a suitable carbohydrate-based triacid, such as **2**, to provide triester **3** (Scheme 1). Methylenation (**3** → **4**) is followed by RCM[23] with the second generation Grubbs catalyst **7**,[24] to furnish the tris-*C*-glycal **5**. Hydroboration of the formed double bonds should afford the *β*-*C*-tetrasaccharide **6**.

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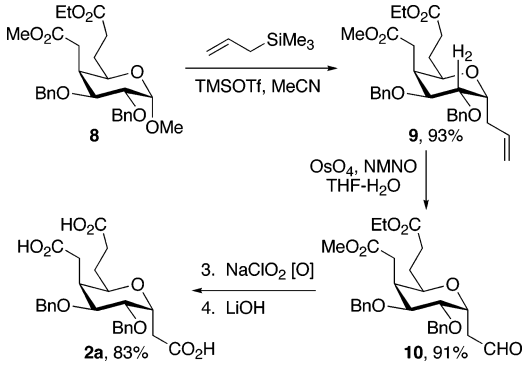
SCHEME 2. Synthesis of Triacid 2a



Diester **8**[18] was allylated along literature guidelines[25] to furnish **9** in 93% yield. Oxidative cleavage[26] of the terminal olefin of **9** gave aldehyde **10** in 91% yield. Further oxidation[27] of **10** to the corresponding carboxylic acid, followed by saponification of the two alkyl esters, delivered triacid **2a** in 83% overall yield, Scheme 2. The stereochemistry of the allylation step was established as α by verification of the H-2 splitting pattern.

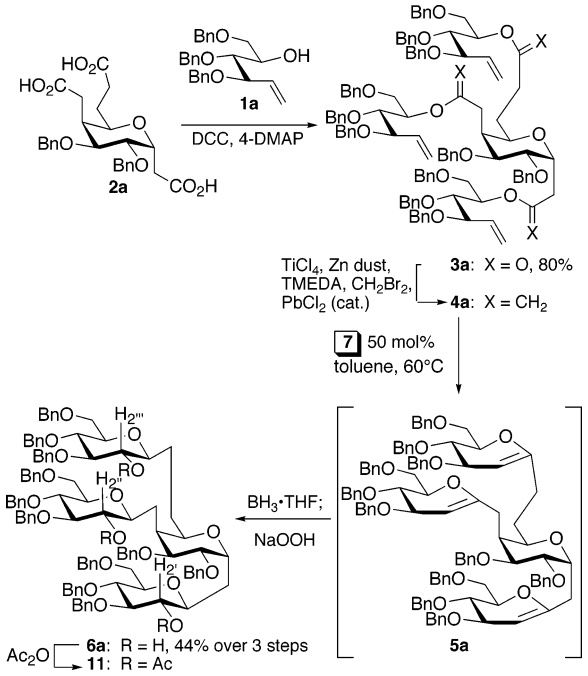
With sufficient quantities of triacid **2a** in hand, the esterification−RCM sequence was explored. DCC-mediated coupling of triacid **2a** with 3 equiv of alcohol **1a**[28] proceeded smoothly to provide ester **3a** in 80% yield. Takai methylenation[29] of triester **3a** to the corresponding triacyclic enol ether **4a** was followed by a triple RCM reaction in the presence of 50 mol % of catalyst **7**,[24] added portion-wise in hot toluene, to provide the intermediate tris-glycal **5a**. Hydroboration[30,31] of the crude tris-glycal **5a** with an excess of BH_3·THF (followed by H_2O_2, NaOH, THF−H_2O) afforded the target *β-C*-tetrasaccharide **6a** in 44% yield over three steps, Scheme 3. The intermediate tris-glycal **5a** was stable for brief periods of time, but not long enough to be fully characterized. The stereochemistry of hydroboration was verified by acetylation (**6a** → **11**, Ac_2O, pyridine, 4-DMAP) of **6a** and examination of the H_2 coupling constants in the proton NMR spectrum.[32]

These results show that triple RCM sequences can now be applied for the synthesis of carbohydrate mimics of greater complexity and biological relevance.

Experimental Section

Allyl Diester (9). The procedure of Hosomi[25] was followed with slight modifications. TMSOTf (20 μL, 0.001 mmol) was added dropwise over 1 min to a cool (0 °C) solution of ester **8**[18] (125 mg, 0.25 mmol) and allyltrimethylsilane (79 μL, 0.5 mmol) in dry acetonitrile (2 mL). The ice−water bath was left in place, and the resulting solution was stirred for 12 h. The solution was

SCHEME 3



quenched with saturated sodium bicarbonate (5 mL) and extracted with diethyl ether (3 × 20 mL). The combined ethereal extracts were washed with saturated ammonium chloride (1 × 20 mL), dried, filtered, and concentrated. Flash chromatography of the residue over silica using 15% → 20% EtOAc−hexanes gave **9** (118 mg, 93%) as a pure (R_f = 0.37, TLC silica, 20% EtOAc−hexanes; ^{1}H NMR, 500 MHz) clear oil: $[\alpha]_D$ = +39.3 (c = 1.0, $CHCl_3$); FT-IR (neat) 3066, 3030, 2978, 2947, 1732, 1453, 1436, 1370, 1259, 1208, 1170, 1084, 1028, 913, 737, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.26 (m, 10 H, Ar*H*), 5.76 (dddd, 1 H, J = 16.5, 10, 6.5, 6.5 Hz, *H*-10), 5.06 (dd, 1 H, J = 17.5, 1.5 Hz, *H*-11$_{trans}$), 5.04 (dd, J = 10, 1.0 Hz, *H*-11$_{cis}$), 4.67 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 4.53 (d, 1 H, J = 12.5 Hz, OCH_2Ph), 4.51 (d, 1 H, J = 12 Hz, OCH_2Ph), 4.47 (d, 1 H, J = 12 Hz, OCH_2Ph), 4.11 (q, 2 H, J = 7.0 Hz, OCH_2CH$_3$), 3.90 (ddd, 1 H, J = 8.5, 4.5, 4.5 Hz, *H*-1), 3.78−3.72 (m, 2 H, *H*-3, *H*-5), 3.61 (s, 3 H, OCH_3), 3.43 (dd, 1 H, J = 5.5, 3.5 Hz, *H*-2), 2.83 (dddd, 1 H, J = 6.5, 6.5, 4.0, 4.0 Hz, Hz, *H*-4), 2.50 (dd, 1 H, J = 16.5, 7.5 Hz, *H*-8), 2.47−2.38 (m, 2 H, *H*-7, *H*-9), 2.38−2.27 (m, 3 H, *H*-7, *H*-8, *H*-9), 2.18−2.08 (bm, hump, 1 H, *H*-6), 1.63 (dddd, 1 H, J = 15, 7.5, 7.5, 2.5 Hz, *H*-6), 1.25 (t, 3 H, J = 7.0 Hz, OCH$_2$CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 173.1, 138.2, 135.1, 128.3, 127.9, 127.7, 127.6, 116.8, 75.7, 73.9, 72.7, 72.0, 60.1, 51.6, 36.1, 33.3, 30.9, 30.2, 24.3, 14.2; HRMS (ES) calcd for $C_{30}H_{38}O_7Na$ $(M)^+$ 533.2510, found 533.2513.

Diester Aldehyde (10). Osmium tetroxide (~10 mg) was added to a slurry of **9** (700 mg, 1.37 mmol) and sodium metaperiodate (645 mg, 3.01 mmol) in THF−H_2O (4:1, 12 mL), and the resulting mixture was stirred at room temperature for 3 h at which point TLC (silica, 20% Et_2O−hexanes) showed no starting material remaining. The reaction was quenched by the addition of saturated sodium thiosulfate (5 mL) and partitioned between EtOAc (10 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic extracts were washed with brine (1 × 10 mL), dried, and filtered. The solution was concentrated, and flash chromatography of the residue over silica gel using 10% → 20% EtOAc−hexanes gave aldehyde **10** (639 mg, 91%) as a pure (R_f = 0.19, TLC silica, 10% EtOAc−hexanes; ^{1}H NMR, 500 MHz) oil: $[\alpha]_D$ = +10.0 (c = 1, $CHCl_3$); FT-IR (neat) 3061, 3029, 2980, 2905, 1727, 1454, 1372, 1257, 1171, 1088, 739, 699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.69 (dd, 1 H, J = 2.5, 1.5 Hz, C*H*O), 7.36−7.26 (m, 10 H, Ar*H*), 4.64 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 4.52 (d, 1 H, J = 12 Hz, OCH_2Ph), 4.46 (d, 1 H, J = 12.5 Hz,

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OCH_2Ph), 4.45 (d, 1 H, J = 12 Hz, OCH_2Ph), 4.47−4.43 (buried m, 1 H, *H*-1), 4.10 (q, 2 H, J = 7.0 Hz, OCH_2CH$_3$), 3.78−3.72 (m, 2 H, *H*-3, *H*-5), 3.61 (s, 3 H, OCH_3), 3.43 (dd, 1 H, J = 5.5, 3.5 Hz, *H*-2), 2.82 (dddd, 1 H, J = 7.0, 7.0, 4.5, 4.5 Hz, *H*-4), 2.69 (ddd, 1 H, J = 16.5, 7.5, 2.5 Hz, *H*-9), 2.55 (dd, 1 H, J = 16.5, 5.0 Hz, *H*-9), 2.48 (dd, 1 H, J = 16.5, 8.0 Hz, *H*-8), 2.41−2.23 (m, 3 H, 2 × *H*-7, *H*-8), 2.18 (dddd, 1 H, J = 14, 14, 6.5, 6.5 Hz, *H*-6), 1.63 (dddd, 1 H, J = 14.5, 7.0, 7.0, 2.5 Hz, *H*-6), 1.23 (t, 3 H, J = 7.0 Hz, OCH$_2$CH_3); ^{13}C NMR (125 MHz, CDCl$_3$) δ 200.6, 173.4, 172.9, 137.8, 137.6, 128.4, 128.3, 128.1, 127.9, 127.7, 127.6, 75.2, 73.4, 72.9, 72.8, 72.1, 65.0, 60.2, 51.6, 43.8, 35.6, 30.9, 30.3, 24.0, 14.1; HRMS (ES) calcd for $C_{29}H_{36}O_8Na$ (M)$^+$ 535.2302, found 535.2305.

Triacid (2a). 2-Methyl-2-butene (660 μL, 7.84 mmol), potassium phosphate monobasic (207 mg, 1.52 mmol), and sodium chlorite (tech., 80%, 169 mg, 1.52 mmol) were added to a *t*-BuOH−water (4:1, 20 mL) solution of aldehyde **10** (600 mg, 1.17 mmol). The resulting mixture was stirred at room temperature for 6 h, concentrated, and diluted with water (10 mL). The resulting mixture was acidified with HCl (∼5 mL, 2 M) to approximately pH = 2−3 (litmus red). The mixture was extracted with EtOAc (5 × 20 mL), and the combined organic extracts were dried, filtered, and concentrated. The residue was passed through a short plug of silica gel using 40% EtOAc−hexanes−1/2% AcOH as the eluent to give the monoacid (585 mg, 95%) as a fairly pure (R_f = 0.23, TLC silica, 40% EtOAc−hexanes−1/2% AcOH; ^{1}H NMR, 500 MHz) waxy solid: $[\alpha]_D$ = +16.9 (c = 1, CHCl$_3$); FT-IR (neat) 3030 (br), 1728, 1715, 1454, 1437, 1372, 1261, 1173, 1075, 1027, 738, 699 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 11.14 (br s, 1 H, CO$_2$*H*), 7.36−7.23 (m, 9 H, Ar*H*), 7.18−7.13 (m, 1 H, Ar*H*), 4.67 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 4.54 (d, 1 H, J = 12.5 Hz, OCH_2Ph), 4.51 (d, 1 H, J = 12 Hz, OCH_2Ph), 4.48 (d, 1 H, J = 13 Hz, OCH_2Ph), 4.24 (dddd, 1 H, J = 4.5, 4.5, 4.5, 4.5 Hz, *H*-1), 4.10 (q, 2 H, J = 7.5 Hz, OCH_2-CH$_3$), 3.78 (ddd, 1 H, J = 11.5, 3.0, 3.0 Hz, *H*-5), 3.75 (dd, 1 H, J = 5.5, 3.5, *H*-3), 3.61 (s, 3 H, OCH_3), 3.43 (dd, 1 H, J = 6.0, 3.5 Hz, *H*-2), 2.82 (dddd, 1 H, J = 6.5, 6.5, 4.0, 4.0 Hz, Hz, *H*-4), 2.71 (dd, 1 H, J = 16, 9.0 Hz, *H*-9), 2.60 (dd, 1 H, J = 16, 5.0 Hz, *H*-9), 2.50 (dd, 1 H, J = 16.5, 7.0 Hz, *H*-8), 2.38−2.28 (m, 3 H, 2 × *H*-7, *H*-8), 2.22−2.10 (bm, 1 H, *H*-6), 1.63 (dddd, 1 H, J = 15.5, 8.0, 8.0, 3.0 Hz, *H*-6), 1.22 (t, 3 H, J = 7.5 Hz, OCH$_2$CH_3); ^{13}C NMR (125 MHz, CDCl$_3$) δ 176.7, 173.5, 172.9, 137.8, 137.6, 128.2, 128.2, 127.8, 127.6, 127.6, 127.5, 75.1, 73.3, 72.6, 71.9, 69.8, 65.5, 60.1, 51.5, 35.7, 34.5, 30.4, 29.9, 24.1, 14.0; HRMS (ES) calcd for $C_{29}H_{36}O_9Na$ (M)$^+$ 551.2251, found 551.2239.

LiOH (795 mg, 18.9 mmol, 20 equiv) was added to a 0 °C solution of the diester-acid (500 mg, 0.95 mmol) in THF (6 mL). Water (6 mL) was added, and the resulting suspension was vigorously stirred at 0 °C for 1 h, allowed to warm to ambient temperature, and then stirred overnight (12 h). The mixture was cooled to 0 °C and acidified by the addition of HCl (∼5 mL, 2 M) until litmus red was obtained. The resulting solution was extracted with EtOAc (5 × 20 mL), dried, and concentrated. Flash chromatography over silica gel using 5% → 10% MeOH−CH_2Cl_2−1/2% AcOH gave **2a** (400 mg, 83% over 2 steps) as a fairly pure (R_f = 0.25, TLC silica, 70% EtOAc−hexanes; ^{1}H NMR, 500 MHz) white solid: mp = 139−140 °C; $[\alpha]_D$ = +51.3 (c = 1, CHCl$_3$); FT-IR (neat) 3031 (br), 1698, 1453, 1413, 1360, 1281, 1176, 1073, 698 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.33−7.24 (m, 10 H, Ar*H*), 4.62 (d, 1 H, J = 12 Hz, OCH_2Ph), 4.50−4.44 (m, 3 H, 3 × OCH_2Ph), 4.24 (dddd, 1 H, J = 8.5, 3.5, 3.5, 3.5 Hz, *H*-1), 3.78 (ddd, 1H, J = 11.5, 3.0, 3.0 Hz, *H*-5), 3.71 (dd, 1 H, J = 6.0, 4.0, *H*-3), 3.43 (dd, 1 H, J = 5.5, 3.5 Hz, *H*-2), 2.77 (dddd, 1 H, J = 7.0, 7.0, 4.5, 4.5 Hz, *H*-4), 2.64 (dd, 1 H, J = 16, 9.0 Hz, *H*-9), 2.49−2.38 (m, 3 H, *H*-7, *H*-8, *H*-9), 2.37−2.26 (m, 2 H, *H*-7, *H*-8), 2.18−2.05 (bm, 1 H, *H*-6), 1.68−1.58 (m, 1 H, *H*-6); ^{13}C NMR (125 MHz, CDCl$_3$) δ 176.7, 175.5, 174.3, 137.9, 137.7, 128.3, 128.0, 127.8, 127.6, 127.6, 75.5, 73.7, 72.8, 72.5, 72.0, 35.8, 34.6, 30.4, 30.1, 24.1; HRMS (ES) calcd for $C_{26}H_{30}O_9$-Na (M)$^+$ 509.1728, found 509.1772.

Triester (3a). 4-DMAP (75 mg, 0.62 mmol) and DCC (395 mg, 1.91 mmol) were added in one portion to a solution of triacid **2a** (300 mg, 0.62 mmol) and alcohol **1a**[28] (774 mg, 1.85 mmol) in dry CH_2Cl_2 (5 mL). The resulting solution was then stirred for 5 h at ambient temperature, at which point TLC (silica, 30% EtOAc−hexanes) showed the reaction was complete. The reaction mixture was diluted with ether (20 mL) and filtered by gravity through cotton to remove most of the formed dicyclohexylurea. The resulting organic solution was washed with saturated NH_4Cl (1 × 20 mL), dried, and concentrated. Flash chromatography over silica gel using 30% EtOAc−hexanes gave ester **3a** (833 mg, 80%) as a pure (R_f = 0.32, TLC silica, 30% EtOAc−hexanes; ^{1}H NMR, 500 MHz) oil: $[\alpha]_D$ = −1.60 (c = 1, CHCl$_3$); FT-IR (neat) 3062, 3029, 2868, 1733, 1496, 1453, 1352, 1256, 1203, 1170, 1090, 1027, 932, 735, 696 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.33−7.22 (m, 55 H, Ar*H*), 5.91−5.80 (m, 3 H, *H*-1′, *H*-1″, *H*-1‴), 5.33−5.21 (m, 9 H, 2 × *H*-1′, 2 × *H*-1″, 2 × *H*-1‴, *H*-5′, *H*-5″, *H*-5‴), 4.66 (d, 1 H, J = 11 Hz, OCH_2Ph), 4.64 (d, 1 H, J = 12.5 Hz, OCH_2Ph), 4.64 (d, 1 H, J = 12 Hz, OCH_2-Ph), 4.63 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 4.59 (d, 1 H, J = 12.5 Hz, OCH_2Ph), 4.58 (d, 1 H, J = 11 Hz, OCH_2Ph), 4.57 (d, 1 H, J = 11 Hz, OCH_2Ph), 4.56 (d, 1 H, J = 11 Hz, OCH_2Ph), 4.55 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 4.54 (d, 1 H, J = 12 Hz, OCH_2Ph), 4.52 (d, 1 H, J = 12 Hz, OCH_2Ph), 4.45 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 4.43 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 4.43 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 4.41 (d, 1 H, J = 13 Hz, OCH_2Ph), 4.40 (d, 1 H, J = 13 Hz, OCH_2Ph), 4.40 (d, 1 H, J = 13 Hz, OCH_2Ph), 4.40 (d, 1 H, J = 13 Hz, OCH_2Ph), 4.41−4.39 (m, 1 H, *H*-1), 4.37 (d, 1 H, J = 12.5 Hz, OCH_2Ph), 4.34 (d, 1 H, J = 12 Hz, OCH_2Ph), 4.30 (d, 1 H, J = 12 Hz, OCH_2Ph), 4.29 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 4.26 (d, 1 H, J = 12 Hz, OCH_2Ph), 3.91−3.84 (m, 3 H, *H*-3′, *H*-3″, *H*-3‴), 3.78−3.67 (m, 11 H, *H*-3, *H*-5, *H*-4′, *H*-4″, *H*-4‴, 2 × *H*-6′, 2 × *H*-6″, 2 × *H*-6‴), 3.36 (dd, 1 H, J = 5.5, 3.5 Hz, *H*-2), 2.75 (dddd, 1 H, J = 9.0, 9.0, 5.0, 5.0 Hz, *H*-4), 2.56 (dd, 1 H, J = 17, 8.5 Hz, *H*-9), 2.40 (dd, 1 H, J = 17, 8.0 Hz, *H*-8), 2.35−2.27 (m, 2 H, *H*-9, CH_2), 2.25−2.17 (m, 2 H, *H*-8, CH_2), 1.59−1.50 (m, 2 H, 2 × CH_2); ^{13}C NMR (125 MHz, CDCl$_3$) δ 172.8, 171.6, 170.4, 138.4, 138.3, 138.2, 138.2, 138.2, 138.1, 138.1, 138.0, 138.0, 135.2, 135.1, 135.0, 128.3, 128.3, 128.3, 128.2, 128.2, 128.1, 128.0, 128.0, 127.9, 127.8, 127.7, 127.7, 127.6, 127.6, 127.5, 127.4, 119.4, 119.3, 119.2, 81.1, 80.9, 80.8, 80.7, 80.7, 75.0, 74.9, 74.9, 73.0, 72.5, 72.5, 72.4, 72.4, 72.2, 70.4, 70.3, 70.3, 68.1, 68.1, 68.0, 65.9, 35.2, 23.7; HRMS (ES) calcd for $C_{107}H_{114}O_{18}Na$ (M)$^+$ 1710.7931, found 1710.7903.

***β*-*C*-Tetrasaccharide (6a).** A solution of titanium tetrachloride (1.0 mL, 2 M in CH_2Cl_2, 2.0 mmol) was added to cool (0 °C) THF (3 mL). The resulting mixture was stirred for 30 min, at which point TMEDA (0.58 mL, 3.87 mmol) was added in one portion. The resulting yellow-brown suspension was allowed to warm to ambient temperature and stirred for 30 min. At this point, zinc dust (285 mg, 4.37 mmol) and lead(II) chloride (3 mg, 10.7 μmol) were added in portion, and stirring at ambient temperature was continued for 10 min. A solution of ester **3a** (100 mg, 0.059 mmol) and dibromomethane (0.77 μL, 10.9 μmol) in THF (1 mL plus 1 mL rinse) was then added via cannula to the reaction flask in one portion. The mixture was stirred at 60 °C for 1 h, cooled to 0 °C, and then quenched by the addition of saturated potassium carbonate (1 mL). The resulting mixture was stirred for 30 min (while warming to ambient temperature), diluted with ether (20 mL), and stirred vigorously for 15 min. The resulting mixture was filtered through neutral alumina using 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 min. The combined ethereal extracts were then concentrated in vacuo to give the acyclic enol ether **4a**.

Ruthenium-based metathesis catalyst **7** (25 mg, 0.30 mmol, 50 mol %) was added in five equivalent portions over 2.5 h (10 mol % every 30 min) to a dry and degassed toluene (6 mL) solution of crude **4a** from the above experiment. The resulting mixture (0.01 M in substrate) was heated to 60 °C for 3 h, at which point TLC (silica, 30% Et$_2$O−hexanes) showed the reaction was complete. The resulting solution was concentrated, diluted with THF (3 mL), and cooled to 0 °C. BH_3·THF (0.59 mL, 1 M in THF, 0.59 mmol) was added to the cooled solution, and the resulting mixture was allowed to warm to room temperature and stirred overnight. The solution was cooled back down to 0 °C, and NaOH (20 mL, 1 M, 20 mmol) and hydrogen

peroxide (20 mL, 30% in water) were added in one portion. The solution was allowed to warm to room temperature over 2 h. The solution was then extracted with EtOAc (3 × 10 mL), and the combined organic extracts were washed with saturated sodium thiosulfate (1 × 20 mL) and brine (1 × 10 mL), dried, and filtered. The solution was concentrated, and flash chromatography of the residue over silica using 40% → 50% EtOAc−hexanes gave **6a** (43 mg, 44% over 3 steps) as a pure (R_f = 0.41, TLC silica, 45% EtOAc−hexanes; ^{1}H NMR, 500 MHz) waxy solid: mp = 47−48 °C; $[\alpha]_D$ = +6.2 (c = 1.0, $CHCl_3$); FT-IR (neat) 3454 (br), 3030, 2921, 2853, 1496, 1454, 1256, 1098, 737, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40−7.13 (m, 43 H, Ar*H*), 7.11−7.07 (m, 2 H, Ar*H*), 4.95 (d, 1 H, J = 11 Hz, OCH_2Ph), 4.93 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 4.82 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 4.79 (d, 1 H, J = 11 Hz, OCH_2Ph), 4.78 (d, 1 H, J = 10.5 Hz, OCH_2Ph), 4.77 (d, 1 H, J = 10.5 Hz, OCH_2Ph), 4.75 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 4.73 (d, 1 H, J = 12 Hz, OCH_2Ph), 4.71 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 4.60 (d, 1 H, J = 12 Hz, OCH_2Ph), 4.57 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 4.57 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 4.56 (d, 1 H, J = 12 Hz, OCH_2Ph), 4.55 (d, 1 H, J = 10 Hz, OCH_2Ph), 4.55 (d, 1 H, J = 10.5 Hz, OCH_2Ph), 4.52 (d, 1 H, J = 12.5 Hz, OCH_2Ph), 4.50 (d, 1 H, J = 10.5 Hz, OCH_2Ph), 4.49 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 4.46 (d, 1 H, J = 11.5 Hz, OCH_2Ph), 4.45 (d, 1 H, J = 12 Hz, OCH_2Ph), 4.44 (d, 1 H, J = 12 Hz, OCH_2Ph), 4.28 (d, 1 H, J = 12.5 Hz, OCH_2Ph), 4.24 (m, 1 H, *H*-1′), 2.23 (ddd, 1 H, J = 4.0, 2.0, 0 Hz, *H*-5), 3.80−3.55 (m, 10 H, 10 × OC*H*), 3.47−3.44 (m, 2 H, 2 × OC*H*), 3.43−3.38 (m, 2 H, 2 × OC*H*), 3.38−3.30 (m, 4 H, 4 × OC*H*), 3.25−3.17 (m 2 H, 1 × OC*H* and also contains dd at 3.19, J = 9.5, 9.5 Hz, 1 H, *H*-2″), 3.07 (dd, 1 H, J = 9.0, 9.0 Hz, *H*-2‴), 2.97 (ddd, 1 H, J = 9.5, 9.5, 1.5 Hz, *H*-1‴), 2.87 (ddd, 1 H, J = 9.0, 9.0, 2.0 Hz, *H*-1″), 2.63 (dddd, 1 H, J = 9.5, 6.5, 3.5, 3.5 Hz, *H*-4), 2.30−2.23 (m, 1 H, *H*-9), 2.18−2.08 (m, 2 H, 2 × *H*-6 **or** *H*-6, *H*-7), 2.00−1.94 (m, 1 H, *H*-8), 1.91−1.85 (m, 1 H, *H*-9), 1.80−1.69 (m, 1 H, *H*-7 **or** *H*-6), 1.35−1.20 (m, 2 H, *H*-8, *H*-6); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.1, 138.8, 138.4, 138.4, 138.3, 138.2, 138.1, 138.1, 128.6, 128.6, 128.4, 128.3, 128.3, 128.2, 128.2, 128.0, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.7, 127.6, 127.6, 127.5, 127.3, 86.7, 86.3, 80.7, 79.2, 79.0, 78.9, 78.3, 78.2, 78.0, 75.6, 75.1, 74.9, 74.8, 74.1, 73.5, 73.4, 73.2, 72.8, 72.0, 69.5, 69.3, 68.9, 63.0, 61.4, 30.3, 30.0, 29.7, 29.2; HRMS (ES) calcd for $C_{104}H_{114}O_{18}Na$ $(M)^+$ 1674.7931, found 1674.7916.

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Supporting Information Available: Stereochemical assignment information for **6a** and ^{1}H and GCOSY NMR spectra of **2a**, **3a**, **6a**, and **9**−**11**. This material is available free of charge via the Internet at http://pubs.acs.org.

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