Cascade Rearrangements of Polyunsaturated Sugars: A Novel Approach to the Synthesis of Oligosaccharide Mimetics

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The readily available tri-unsaturated trisaccharide **4** undergoes a stereoselective cascade of reductive rearrangements with TIBAL (triisobutylaluminium) to afford, after oxidative workup, the (1→4) ether-linked trisaccharide mimetics **3** and **10**.

Introduction

The conversion of carbohydrates into carbocycles[1] provides a powerful method for the synthesis of highly functionalized cyclohexane derivatives. In contrast to the classical Ferrier-II carbocyclization reaction,[2] the triisobutylaluminium[3] (TIBAL) and titanium(IV)-promoted[4] rearrangement of 6-deoxyhex-5-enopyranosides into cyclohexanes proceeds with retention of both the aglycon moiety and the anomeric stereochemistry. Application of these novel reactions has led to the synthesis of carba-L-idopyranosides and a 5′a-carbadisaccharide from unsaturated sugars;[5] these transformations would not otherwise be attainable using the classical Ferrier-II reaction. Similarly, we have recently reported[6] the extension of this rearrangement methodology to the direct synthesis of the ether-linked disaccharide mimetic **1** by a tandem reductive rearrangement of the bis(hex-5-enopyranoside) **2** with TIBAL. Carba-oligosaccharides[7] in which two or more carba-sugar or carbocyclic rings are connected through stable ether linkages are of interest as nonhydrolyzable analogues of their parent oligosaccharides. Such analogues of cellulose and starch might also have potential applications as new materials. We therefore aimed to extend the TIBAL-mediated methodology to the synthesis of higher oligosaccharide mimetics. This paper reports the stereoselective synthesis of the (1→4) ether-linked trisaccharide mimetic **3** from the readily prepared tri-unsubstituted **4** as a preliminary evaluation of the cascade rearrangement of polyunsaturated systems (Figure 1).

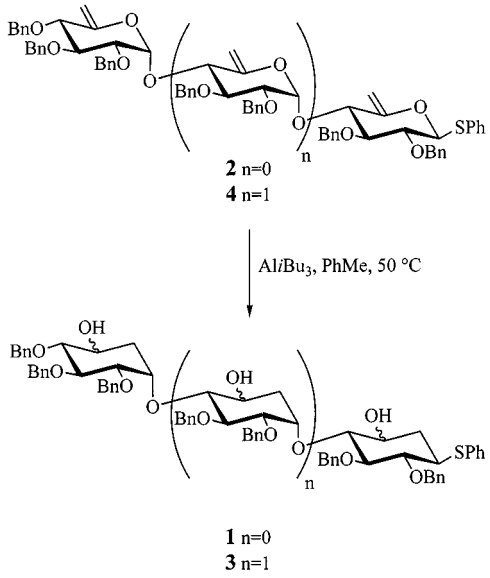

Figure 1. TIBAL-promoted cascade rearrangement of polyunsaturated systems

Results and Discussion

Construction of the tri-unsaturated β-thiophenyl maltotrioside **4** was readily achieved from D-maltotriose (**5**) as summarized in Scheme 1. Silylation of phenyl 1-thio-β-D-maltotrioside (**6**)[8] with *tert*-butyldimethylsilyl chloride in DMF containing triethylamine and a catalytic quantity of 4-dimethylaminopyridine gave the 6,6′,6′′-tri-protected thiomaltotrioside **7** (64%). Perbenzylation of **7** with benzyl bromide and sodium hydride in DMF was followed by desilylation with tetrabutylammonium fluoride in THF to afford the triol **8** (58% from **7**). Iodination of triol **8** under Garegg′s conditions[9] gave the corresponding triiodide **9** (46%) which was rather unstable and was therefore immediately subjected to elimination with sodium hydride in DMF to afford the desired tri-unsaturated β-thiophenyl maltoside **4** (57%). The structure of **4** was supported by its ^{13}C NMR spectrum which showed clear signals for the three exocyclic double bonds [δ = 154.3, 153.6, 151.8, 3 × s, C-5, C-5′, C-5′′ and δ = 100.1 (t, C-6′), 98.0 (t, C-6′′), 97.1 (t, C-6)].

Reaction of the tri-unsaturated β-thiophenyl maltotrioside **4** with excess TIBAL at 50 °C in toluene indeed resulted in a smooth cascade rearrangement, with transposition of three endocyclic oxygen atoms of the pyranose rings with the corresponding exocyclic carbon atoms, to afford the ether-linked trisaccharide mimetic **3** as an inseparable mixture of diastereomers (Scheme 2).[10] Oxidation of the crude mixture of **3** with acetic anhydride in DMSO signific-

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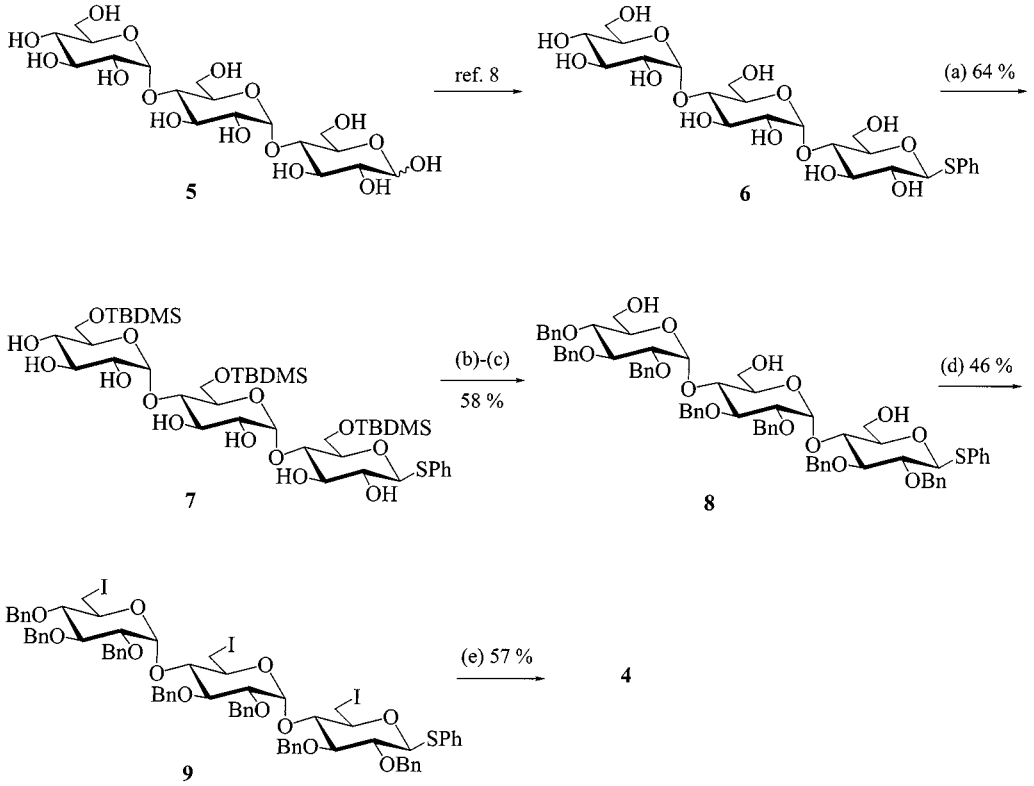
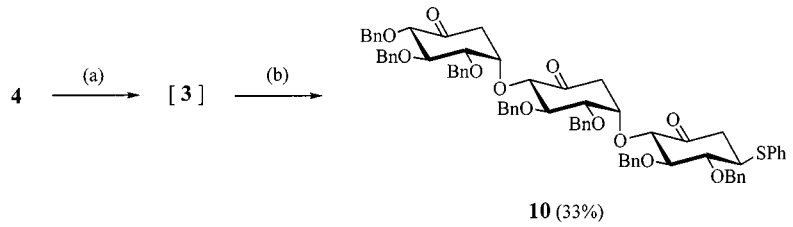


Scheme 1. Reagents and Conditions: (a) TBDMSCl, DMF, Et_3N, cat. DMAP, 0 °C → room temp., 2.5 h; (b) NaH, BnBr, DMF, 0 °C → room temp., 2 h; (c) TBAF·$3H_2O$, THF, room temp., 3 h; (d) Ph_3P, I_2, Im, PhMe, 70 °C, 1 h; (e) NaH, DMF, room temp., 8 h



Scheme 2. Reagents and Conditions: (a) TIBAL, PhMe, 50 °C, 6 h; (b) DMSO, Ac_2O, room temp., 24 h

antly simplified the workup, and the tri-ketone **10** was isolated as a single diastereomer in 33% yield from **4**. Analysis of vicinal coupling constants in the ^1H NMR spectrum of **10** confirmed that: (i) rearrangement with TIBAL occurred with complete retention of configuration at all three anomeric centres ($J_{1'-2'} = J_{1''-2''} = 2$ Hz and $J_{1-2} = 10.2$ Hz); and (ii) each cyclohexyl ring adopted approximately a $^4C_1$ conformation. It is noteworthy that assuming a quantitative yield for the oxidation step, an isolated yield of 33% for tri-ketone **10** represents a geometric average efficiency of ca. 69% per double bond rearrangement, a figure consistent with isolated yields for mono-rearrangements.[3] Oxidation of the trisaccharide mimetic **3** to the tri-ketone **10** is also advantageous given that the ketone function is ideal for homologation to a carba-sugar.[6]

Conclusion

This paper reports the first TIBAL-mediated cascade rearrangement of a tri-unsaturated trisaccharide providing direct access to a highly functionalized ether-linked cyclohexane derivative **3** (as a mixture of diastereomers) which is a stable trisaccharide mimetic.

The two-step rearrangement-oxidation strategy (Scheme 2) significantly simplifies product analysis by removal of 3 stereocentres and, furthermore, provides a potential intermediate **10** for homologation to a tricarba-trisaccharide.

This work establishes new methodology for the synthesis of novel oligosaccharide mimetics. Although individual double bond rearrangement is fairly efficient (ca. 69% per double bond) the overall isolated yield of the final cascade product is correspondingly moderate (33%, after oxidative workup). This may therefore limit application of the cascade rearrangement to oligosaccharides of only moderate chain length.

Experimental Section

General: Melting points: Büchi 510 apparatus and were uncorrected. – IR: Nicolet Impact 400D. – Optical rotations: Perkin–Elmer

241 digital polarimeter. – Mass spec: Nermag R10–10 spectrometer, C.I.(ammonia) or FAB(NBA)+ as indicated. – Elemental analyses: performed by Service d'Analyse de l'Université Pierre et Marie Curie, 75252 Paris Cedex 05, France. – NMR: Bruker AM-400 (400 MHz and 100.6 MHz, for ^1H and ^{13}C, respectively), TMS as internal standard. – TLC: silica gel 60 F_{254} (Merck) and detection by charring with conc. H_2SO_4. – Flash column chromatography: silica gel 60 (230–400 mesh, Merck).

Phenyl 6,6′,6′′-Tri-*O*-*tert*-butyldimethylsilyl-1-thio-β-D-maltotrioside (7): Triethylamine (2.25 mL, 16.10 mmol), DMAP (50 mg, 0.41 mmol) and then TBDMSCl (2.43 g, 16.10 mmol) were added to a stirred solution of phenyl 1-thio-β-D-maltotrioside (**6**)[8] (2.4 g, 4.0 mmol) in anhydrous DMF (150 mL) at 0 °C under argon. The mixture was immediately warmed to room temperature and stirred for 2.5 h until TLC (DCM/MeOH, 9:1) indicated no starting material (R_f = 0.0), and product (R_f = 0.2). Methanol (20 mL) was then added and the solvent was removed in vacuo. The residue was purified by flash chromatography (DCM/MeOH, 9:1) to afford **7** (2.33 g, 64%), as a colourless foam. – $[\alpha]_D^{22}$ = +54.6 (c = 0.9 in $CHCl_3$). – ^1H NMR ($CDCl_3$): δ = 7.60–7.29 (m, 5 H, arom. H), 6.14 (br s, 2 H, 2 × OH), 5.83 (br s, 1 H, OH), 5.63 (br s, 1 H, OH), 5.20 (br s, 1 H, OH), 5.03 (d, J = 3.0 Hz, 1 H, 1′-H or 1′′-H), 5.00 (d, J = 3.3 Hz, 1 H, 1′-H or 1′′-H), 4.51 (d, J_{1-2} = 9.7 Hz, 1 H, 1-H), 4.13–3.34 (m, 18 H), 2.42 (br s, 2 H, 2 × OH), 0.93 [s, 9 H, $(CH_3)_3C$], 0.91 [s, 9 H, $(CH_3)_3C$], 0.90 [s, 9 H, $(CH_3)_3C$], 0.12 (s, 3 H, Si–CH_3), 0.10 (s, 3 H, Si–CH_3), 0.09 (s, 6 H, 2 × Si–CH_3), 0.07 (s, 3 H, Si–CH_3), 0.06 (s, 3 H, Si–CH_3). – ^{13}C NMR ($CDCl_3$): δ = 132.4 (d, Ph), 132.39 (s, C-arom. quat.), 128.8 (d, Ph), 101.7, 101.5 (C-1′, C-1′′), 87.4 (C-1), 79.9, 79.7, 79.5, 77.3, 74.0, 73.4, 73.2, 73.1, 72.7, 72.3, 71.8, 71.0 (12 × d, *C*H), 63.7, 62.2, 61.6 (3 × t, C-6, C-6′, C-6′′), 25.9 [3 × q, 3 × ($CH_3)_3C$], 18.4, 18.34, 18.3 [3 × s, 3 × $(CH_3)_3C$], –5.09, –5.17, –5.24, –5.30, –5.35, –5.35 (6 × q, 6 × Si–CH_3). – MS (FAB): *m*/*z* (%) = 961.6 (100) [M + Na^+]. – $C_{42}H_{78}O_{15}SSi_3$ (939.4): calcd. C 53.70, H 8.37; found C 54.04, H 8.44.

Phenyl 2,2′,2′′,3,3′,3′′,4′′-Hepta-*O*-benzyl-1-thio-β-D-maltotrioside (8): Sodium hydride (1.4 g, 35.0 mmol, 60% in mineral oil) was added to a stirred solution of **7** (2.33 g, 2.48 mmol) in anhydrous DMF (30 mL) and benzyl bromide (3.1 mL, 26.4 mmol) at 0 °C. The mixture was stirred at room temperature for 2 h until TLC (EtOAc/cyclohexane, 3:7) indicated formation of product (R_f = 0.7). The mixture was then cooled to 0 °C and anhydrous methanol (15 mL) was added dropwise. The reaction mixture was then warmed to room temperature, the solvent was removed in vacuo and the resulting residue was partitioned between DCM (75 mL) and water (75 mL). The aqueous layer was extracted with DCM (3 × 75 mL) and combined extracts were dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The residue was dissolved in THF (50 mL) and stirred at room temperature. TBAF·$3H_2O$ (3.6 g, 11.4 mmol) was added and, after stirring for 3 h, the solvent was removed in vacuo. The residue was partitioned between DCM (75 mL) and water (75 mL). The aqueous layer was extracted with DCM (3 × 75 mL) and the combined extracts were dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The residue was purified by flash chromatography (eluent gradient, 30–60% EtOAc in cyclohexane) to afford **8** (1.78 g, 58%), as a colourless foam. – $[\alpha]_D^{22}$ = +47.5 (c = 1.0 in $CHCl_3$). – ^1H NMR ($CDCl_3$): δ = 7.59–7.07 (m, 40 H, arom. H), 5.67 (d, J_{1A-2A} = 3.9 Hz, 1 H, 1A-H), 5.66 (d, J_{1B-2B} = 3.9 Hz, 1 H, 1B-H), 5.02–4.85 (m, 7 H, 7 × C*H*Ph), 4.82 (d, J_{1-2} = 9.6 Hz, 1 H, 1-H), 4.80 (d, J = 11.9 Hz, 1 H, C*H*Ph), 4.67 (d, J = 10.4 Hz, 1 H, C*H*Ph), 4.64 (d, J = 11.4 Hz, 1 H, C*H*Ph), 4.61 (d, J = 12.9 Hz, 1 H, C*H*Ph), 4.50 (d, J = 11.8 Hz, 1 H, C*H*Ph), 4.49 (d, J = 11.9 Hz, 1 H, C*H*Ph), 4.45 (d, J = 11.9 Hz, 1 H, C*H*Ph), 4.12 (t, J_{3-4} = J_{4-5} = 9.0 Hz, 1 H, 4-H), 4.08–3.90 (m, 9 H, 3A-H, 3B-H, 4B-H, 5B-H, 6-Ha, 6-Hb, 6A-Ha, 6B-Ha, 6B-Hb), 3.89 (t, J_{2-3} = 9.0 Hz, 1 H, 3-H), 3.81 (ddd, J_{4A-5A} = 9.5, J_{5A-6Ab} = 6.0, J_{5A-6Aa} = 2.0 Hz, 1 H, 5A-H), 3.65 (br dd, $J_{6Aa-6Ab}$ = 10.9, 1 H, 6A-Hb), 3.60 (dd, 1 H, 2-H), 3.56 (dd, J_{2B-3B} = 9.3 Hz, 1 H, 2B-H), 3.59–3.53 (m, 1 H, 5-H), 3.50 (dd, J_{2A-3A} = 9.8 Hz, 1 H, 2A-H), 3.43 (t, J_{3A-4A} = 9.5 Hz, 1 H, 4A-H), 2.90 (br s, 1 H, OH), 2.50 (br s, 2 H, 2 × OH). – ^{13}C NMR ($CDCl_3$): δ = 138.6, 138.5, 138.4, 137.8, 137.8, 137.6, 137.4, 133.5 (8 × s, C-arom. quat.), 131.8–126.2 (40 × d, Ph), 97.0 (C-1A), 97.0 (C-1B), 87.6 (C-1), 86.4 (C-3), 81.7, 81.2 (C-2), 81.2, 79.3 (C-2A), 78.9 (C-2B), 78.7 (C-5), 78.0 (C-4A), 75.4, 75.3, 75.0, 74.3, 73.8, 73.2, 73.2 (7 × t, *C*H_2Ph), 72.7, 72.5 (C-4), 72.3 (C-5A), 71.7, 62.1, 61.6, 61.6 (C-6, C-6A, C-6B). – MS (FAB): *m*/*z* (%) = 1249.4 (100) [M + Na^+]. – $C_{73}H_{78}O_{15}S$ (1226.5): calcd. C 71.43, H 6.41; found C 71.26, H 6.48.

Phenyl 2,2′,2′′,3,3′,3′′,4′′-Hepta-*O*-benzyl-6,6′,6′′-trideoxy-6,6′,6′′-triiodo-1-thio-β-D-maltotrioside (9): Triphenylphosphane (1.24 g, 4.70 mmol), imidazole (0.74 g, 10.90 mmol) and iodine (1.37 g, 5.40 mmol) were added to a stirred solution of **8** (1.66 g, 1.35 mmol) in anhydrous toluene (50 mL) at room temperature under argon. The mixture was heated at 70 °C for 1 h until TLC (50% EtOAc in cyclohexane) indicated no starting material (R_f = 0.3), only product (R_f = 0.9). The reaction mixture was then cooled to room temperature and saturated sodium thiosulfate (40 mL) was added. After 15 min the aqueous layer was extracted with EtOAc (2 × 50 mL) and the combined extracts were dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The residue was purified by flash chromatography (eluent gradient, 5–10% EtOAc in cyclohexane) to afford **9** (945 mg, 46%), as a colourless unstable foam . – $[\alpha]_D^{22}$ = +36.7 (c = 1.0 in $CHCl_3$). – ^1H NMR ($CDCl_3$): δ = 7.75–7.15 (m, 40 H, arom. H), 5.58 (d, J_{1A-2A} = 3.8 Hz, 1 H, 1A-H), 5.51 (d, J_{1B-2B} = 3.6 Hz, 1 H, 1B-H), 4.99 (d, J = 10.8 Hz, 1 H, C*H*Ph), 4.95 (d, J = 10.8 Hz, 1 H, C*H*Ph), 4.92 (s, 2 H, *C*H_2Ph), 4.91 (d, J = 10.2 Hz, 1 H, C*H*Ph), 4.85 (d, J = 10.9 Hz, 1 H, C*H*Ph), 4.82 (s, 2 H, *C*H_2Ph), 4.79 (d, J_{1-2} = 9.8 Hz, 1 H, 1-H), 4.78 (d, J = 10.8 Hz, 1 H, C*H*Ph), 4.67 (d, J = 12.0 Hz, 1 H, C*H*Ph), 4.66 (d, J = 10.2 Hz, 1 H, C*H*Ph), 4.56 (d, J = 10.7 Hz, 1 H, C*H*Ph), 4.53 (d, J = 11.7 Hz, 1 H, C*H*Ph), 4.46 (d, J = 10.7 Hz, 1 H, C*H*Ph), 4.05 (t, J_{2A-3A} = J_{3A-4A} = 7.9 Hz, 1 H, 3A-H), 4.03 (t, J_{2B-3B} = J_{3B-4B} = 8.2 Hz, 1 H, 3B-H), 3.88 (t, J_{3-4} = J_{4-5} = 8.6 Hz, 1 H, 4-H), 3.86–3.80 (m, 3 H, 3-H, 6-Ha, 4B-H), 3.73 (dd, $J_{6Ba-6Bb}$ = 10.5, J_{5B-6Ba} = 2.3 Hz, 1 H, 6B-Ha), 3.67–3.57 (m, 5 H, 2-H, 5B-H, 6A-Ha, 6-Hb, 6B-Hb), 3.55 (dd, 1 H, 2B-H), 3.53 (dd, 1 H, 2A-H), 3.49–3.43 (m, 3 H, 4A-H, 5A-H, 6A-Hb), 3.40 (ddd, J_{4-5} = 8.6, J = 6.2, J = 2.5 Hz, 1 H, 5-H). – ^{13}C NMR ($CDCl_3$): δ = 138.4, 138.3, 138.2, 137.8, 137.7, 137.6, 137.5 (7 × s, C-arom. quat.), 129.0–126.5 (40 × d, Ph), 97.1, 96.8 (C-1A, C-1B), 87.1 (C-1), 85.5 (C-3), 81.5 (C-4A), 81.1 (C-3A), 80.5 (C-2), 80.1 (C-3B), 79.4 (C-2A), 78.9 (C-2B), 78.5 (C-4B), 78.1 (C-4), 77.3 (C-5), 75.5 (2 × t, *C*H_2Ph), 75.2, 74.4, 74.1, 73.5, 73.4 (5 × t, *C*H_2Ph), 70.3 (C-5A), 69.9 (C-5B), 9.6, 8.6 (C-6A, C-6B), 7.9 (C-6). – MS (FAB); *m*/*z* (%): 1579.0 (1) [MNa^+], 1497.1 (15), 323.2 (100). – $C_{73}H_{75}I_3O_{12}S$ (1556.2): calcd. C 56.31, H 4.85; found C 56.35, H 4.97.

Phenyl (2,3,4-Tri-*O*-benzyl-6-deoxy-α-D-xylo-hex-5-enopyranosyl)-(1→4)-(2,3-di-*O*-benzyl-6-deoxy-α-D-xylo-hex-5-enopyranosyl)-(1→4)-2,3-di-*O*-benzyl-6-deoxy-1-thio-β-D-xylo-hex-5-enopyranoside (4): Sodium hydride (381 mg, 9.5 mmol, 60% in mineral oil) was added to a stirred solution of **9** (742 mg, 0.48 mmol) in anhydrous DMF (30 mL) at room temperature. After 8 h TLC (10%

EtOAc in cyclohexane) indicated no starting material (R_f 0.35) and product (R_f 0.3), and the reaction mixture was cooled to 0 °C and methanol (10 mL) was added dropwise. The solvent was removed in vacuo and the residue was partitioned between DCM (100 mL) and water (50 mL). The organic layer was washed with brine (50 mL), dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The residue was purified by flash chromatography (10% EtOAc in cyclohexane) to afford **4** (319 mg, 57%), as a colourless oil. – $[\alpha]_D^{22}$ = –34.7 (c = 0.8 in $CHCl_3$). – ^{1}H NMR ($CDCl_3$): δ = 7.60–7.11 (m, 40 H, arom. H), 5.67 (d, $J_{1''-2''}$ = 3.4 Hz, 1 H, 1''-H), 5.48 (d, $J_{1'-2'}$ = 3.4 Hz, 1 H, 1'-H), 5.10 (d, J_{1-2} = 8.6 Hz, 1 H, 1-H), 4.99 (d, J = 12.0 Hz, 1 H, C*H*Ph), 4.94 (br s, 1 H, 6'-Ha), 4.93–4.89 (m, 2 H, CH_2Ph), 4.88 (m, 1 H, 6''-Ha), 4.86–4.79 (m, 9 H, 6-Ha, 6-Hb, 7 × C*H*Ph), 4.69 (m, 1 H, 6'-Hb), 4.67 (m, 1 H, 6''-Hb), 4.66–4.49 (m, 5 H, 4-H, 4 × C*H*Ph), 4.45 (dt, $J_{3'-4'}$ = 9.3, $J_{4'-6'a}$ = $J_{4'-6'b}$ = 1.9 Hz, 1 H, 4'-H), 4.09 (t, $J_{2'-3'}$ = $J_{3'-4'}$ = 9.3 Hz, 1 H, 3'-H), 4.07 (t, $J_{2''-3''}$ = $J_{3''-4''}$ = 9.5 Hz, 1 H, 3''-H), 3.95 (dt, $J_{4''-6''a}$ = $J_{4''-6''b}$ = 1.9 Hz, 1 H, 4''-H), 3.85 (dd, 1 H, 3-H), 3.72 (dd, J_{2-3} = 7.2 Hz, 1 H, 2-H), 3.69 (dd, 1 H, 2'-H), 3.66 (dd, 1 H, 2''-H). – ^{13}C NMR ($CDCl_3$): δ = 154.3, 153.6, 151.8 (3 × s, C-5, C-5', C-5''), 138.8, 138.5, 138.2, 137.9, 137.8, 137.5, 137.3, 133.9 (8 × s, C-arom. quat.), 132.0–126.1 (40 × d, Ph), 100.1 (C-6'), 98.3 (C-1''), 98.0 (C-6''), 97.4 (C-1'), 97.1 (C-6), 87.1 (C-1), 83.9 (C-3), 81.1 (C-3'), 80.9 (C-2), 80.7 (C-3''), 79.6 (C-4''), 79.2 (C-2'), 78.6 (C-2''), 75.4, 74.5, 74.4, 74.2 (4 × t, *C*H_2Ph), 73.8 (C-4), 73.4 (C-4'), 73.4 (t, *C*H_2Ph), 73.0 (2 × t, *C*H_2Ph). – MS (CI): m/z (%) = 1190.7 (35) [M + NH_4^+], 358.3 (100). – $C_{73}H_{72}O_{12}S$ (1173.4): calcd. C 74.72, H 6.18; found C 74.66, H 6.29.

[1D-(1,2,4/3)-2,3,4-Tri-*O*-benzyl-1,2,3,4-tetrahydroxy-cyclohexon-5-yl]-(1→4)-[1D-(1,2,4/3)-2,3-di-*O*-benzyl-1,2,3,4-tetrahydroxy-cyclohexon-5-yl]-(1→4)-[1L-(1,3/2,4)-2,3-di-*O*-benzyl-2,3,4-trihydroxy-1-thiophenyl-cyclohex-5-one] (10): TIBAL (2.0 mL, 2.0 mmol, 1.0 M in toluene) was added to a stirred solution of **4** (118 mg, 0.10 mmol) in anhydrous toluene (3 mL) at room temperature under argon. The reaction mixture was heated at 50 °C for 6 h until TLC (EtOAc/cyclohexane, 2:1) indicated no starting material (R_f = 0.9) and formation of a complex mixture of products (R_f = 0–0.4). The mixture was then cooled to 0 °C and ice-water (10 mL) was added. The mixture was stirred (15 mins) then filtered into a separating funnel, washed with EtOAc (10 mL) and the aqueous layer was extracted with EtOAc (3 × 15 mL). The combined extracts were dried ($MgSO_4$), filtered and the solvent was removed in vacuo.[10] The crude residue of cyclohexanes **3** was dissolved in anhydrous DMSO (5 mL) at room temperature under argon. Acetic anhydride (1.0 mL, 10.6 mmol) was then added and the reaction mixture was stirred for 24 h. TLC (EtOAc/cyclohexane, 1:2) indicated no starting material (R_f = 0) and formation of a major product (R_f = 0.5). The reaction mixture was diluted with EtOAc (50 mL) and then washed with water (3 × 15 mL), brine (15 mL), dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The residue was purified by flash chromatography (eluent gradient, 25–33% EtOAc in cyclohexane) to afford **10** (39 mg, 33%), as a colourless oil. – $[\alpha]_D^{21}$ = –8.6 (c = 0.7 in $CHCl_3$). – IR (film): $\tilde{\nu}$ = 1736 cm^{-1} (C=O, st), 1171–1031 (C–O, st), 741 (st), 697 (st). – ^{1}H NMR ($CDCl_3$): δ = 7.46–7.21 (m, 40 H, arom. H), 5.08 (d, J = 11.2 Hz, 1 H, C*H*Ph), 5.04 (d, J = 10.4 Hz, 1 H, C*H*Ph), 4.96 (d, J = 10.3 Hz, 1 H, C*H*Ph), 4.96–4.89 (m, 2 H, 4-H, 4A-H), 4.81 (d, J = 11.8 Hz, 1 H, C*H*Ph), 4.78 (d, J = 11.8 Hz, 1 H, C*H*Ph), 4.76 (s, 2 H, CH_2Ph), 4.59–4.56 (m, 3 H, 1B-H, 2 × C*H*Ph), 4.53 (d, J = 11.8 Hz, 1 H, C*H*Ph), 4.47 (d, J = 11.0 Hz, 1 H, C*H*Ph), 4.45 (d, J = 11.0 Hz, 1 H, C*H*Ph), 4.40 (d, J = 11.0 Hz, 1 H, C*H*Ph), 4.30–4.26 (m, 2 H, 1A-H, C*H*Ph), 4.13 (t, J_{2B-3B} = J_{3B-4B} = 9.1 Hz, 1 H, 3B-H), 4.03 (d, 1 H, 4B-H), 3.92 (t, J_{2A-3A} = J_{3A-4A} = 9.1 Hz, 1 H, 3A-H), 3.81 (dd, J_{1B-2B} = 1.9 Hz, 1 H, 2B-H), 3.74 (dd, J_{1-2} = 10.2, J_{2-3} = 8.5 Hz, 1 H, 2-H), 3.70 (dd, J_{1A-2A} = 2.1 Hz, 1 H, 2A-H), 3.57 (dd, J_{3-4} = 9.8 Hz, 1 H, 3-H), 3.24 (ddd, $J_{1-5a(ax)}$ = 13.1, $J_{1-5a(eq)}$ 4.7 Hz, 1 H, 1-H), 3.04 (dd, $J_{5Ba(a)-5Ba(b)}$ = 14.7, $J_{1B-5Ba(a)}$ = 4.2 Hz, 1 H, 5Ba-Ha), 2.81 (dd, $J_{5Aa(a)-5Aa(b)}$ = 14.1, $J_{1A-5Aa(a)}$ = 4.1 Hz, 1 H, 5Aa-Ha), 2.52 (dd, J = 14.0, J 4.7 Hz, 2 H, 5Ba-Hb, 5a-Heq), 2.24 (dd, $J_{1-5Aa(b)}$ = 2.6 Hz, 1 H, 5Aa-Hb), 2.21 (dd, $J_{5a(ax)-5a(eq)}$ = 14.0 Hz, 1 H, 5a-Hax). – ^{13}C NMR ($CDCl_3$): δ = 204.4, 203.9, 203.8 (3 × s, C-5, C-5A, C-5B), 138.7, 138.6, 138.2, 138.1, 138.1, 138.0, 137.9, 132.7 (8 × s, C-arom. quat.), 133.3–127.1 (40 × d, Ph), 86.0 (C-4B), 85.3 (C-4A), 85.3 (C-4), 84.2 (C-3), 83.2 (C-2A + C-2B), 82.7 (C-2), 81.5 (C-3B), 81.3 (C-3A), 75.9, 75.8, 75.3, 75.2, 73.7, 73.6, 73.4 (7 × t, *C*H_2Ph), 72.5 (C-1A), 72.4 (C-1B), 46.9 (C-1), 43.4 (2 × t, C-5a + C-5Ba), 43.0 (t, C-5Aa). – MS (CI): m/z (%) = 1190.4 (5) [M + NH_4^+], 342.3 (100). – $C_{73}H_{72}O_{12}S$ (1173.4): calcd. C 74.72, H 6.18; found C 74.60, H 6.26.

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[10] Purification of a small sample of the crude reaction mixture by flash chromatography (EtOAc) afforded a complex mixture of cyclohexanes **3** with the correct mass: m/z (%) = 1196.7 (100) [M + NH_4^+].

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