Carbon-Bridged Trehalose. Synthesis of Bis[C-(β-D-galactopyranosyl)]methanol

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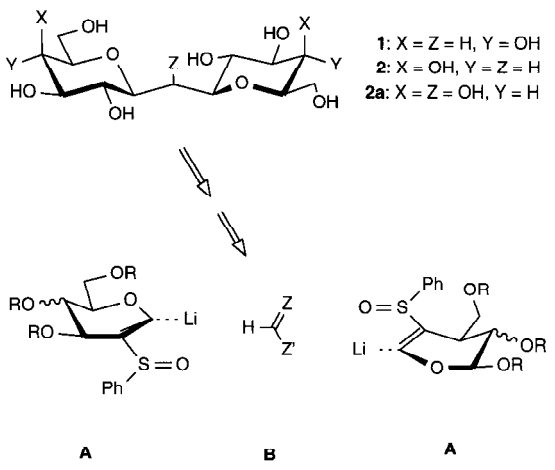
Abstract: Reaction of 1-*C*-lithiated 2-phenylsulfinyl-D-galactals (*R*)- and (*S*)-**3A** as nucleophiles with dimethylformamide as electrophile furnished after workup 1-formyl derivatives (*R*)- and (*S*)-**4**. Their reaction with (*R*)- and (*S*)-**3A** then afforded *C*-trehalose intermediates (*R,R*)- and (*S,S*)-**5**, respectively. Ensuing treatment with sodium cyanoborohydride and then with Raney nickel led to removal of the phenylsulfinyl groups furnishing galactal intermediate **7**, which on reaction with BH_3•SMe_2 and then H_2O_2/NaOH followed by hydrogenolytic debenzylation resulted in target molecule **2a**. Extension of this convenient method to *C*-trehalose synthesis is shown for the corresponding glucose derivative.

Key words: *C*-glycosides, *C*-disaccharides, trehaloses, vinyllithium species, glycals

C-Disaccharides have become very popular target molecules because they are potential reversible inhibitors of glycosidases and disaccharidases which are, for example, present in the digestive tract.[1–3] Some glycosidase inhibitors were also found to possess antiretroviral activity.[4] Therefore, quite a few methods for the synthesis of carbon-bridged *C*-disaccharides have been developed.[5] Unique disaccharides are trehaloses in which two carbohydrate residues are linked via their anomeric hydroxy groups. Some trehaloses also exhibit important biological functions, such as ,for example, α,α-trehalose (i.e., α-D-glucopyranosyl-α-D-glucopyranoside).[6] Trehaloses provide also core structures for the generation of interesting structural motifs, as recently shown.[7] Also approaches to the synthesis of corresponding *C*-trehalose have been already reported (for example, **1** in Scheme 1).[8–10] The syntheses started from a *C*-glucopyranosyl derivative which was used for the attachment of the second sugar chain; then, via ring closure and protective group manipulations the target molecules were obtained.[8, 9]

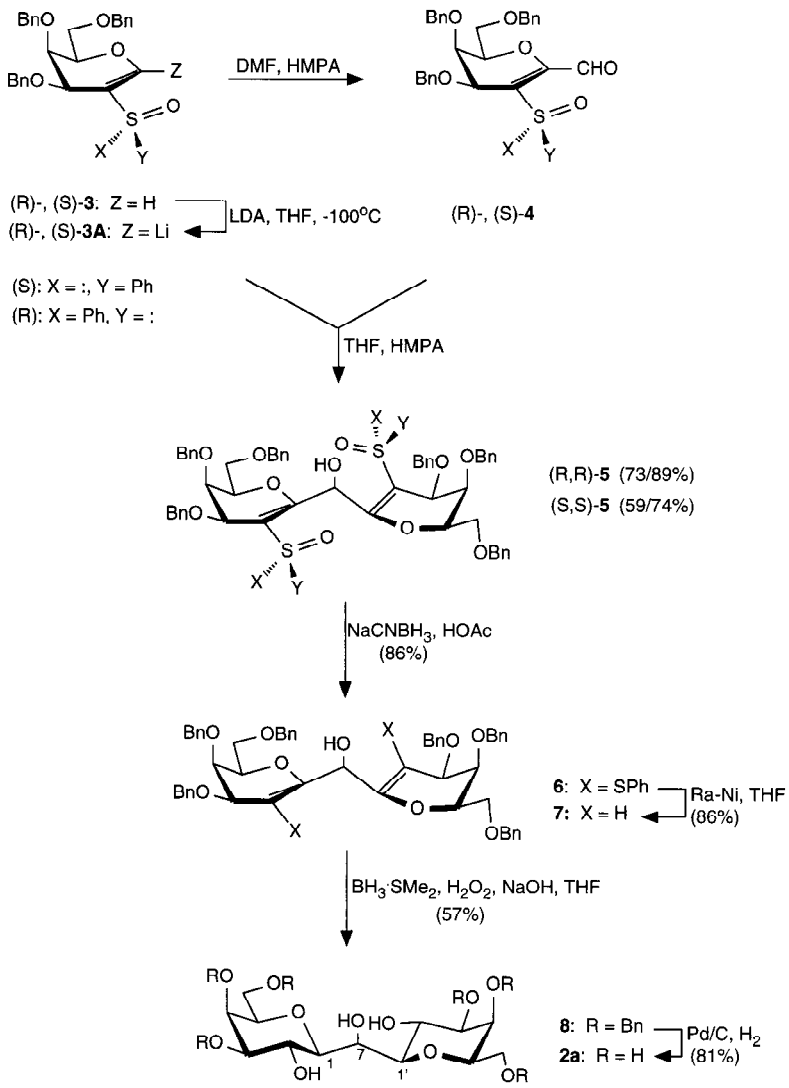
Obviously, a more direct approach with a C_1-electrophile and two glycopyranosyl nucleophiles should readily lead to this type of *C*-disaccharides. For two identical sugar residues even the same nucleophile can be employed as indicated in the retrosynthesis in Scheme 1. We would like to demonstrate application of this method to galactose and glucose; the method is based on ready access of heteroatom-stabilized vinyllithium species[11] and, consequently, to generation of 1-*C*-lithiated glycals **A** as C_6-nucleophiles[12] and their reaction with C_1-electrophile **B**. In order to demonstrate the efficiency of this method, the galactose derived *C*-trehalose intermediate is finally transformed into the title compound **2a**, having, in comparison with the parent compound **2**, an additional hydroxy group in the bridge for further modifications.



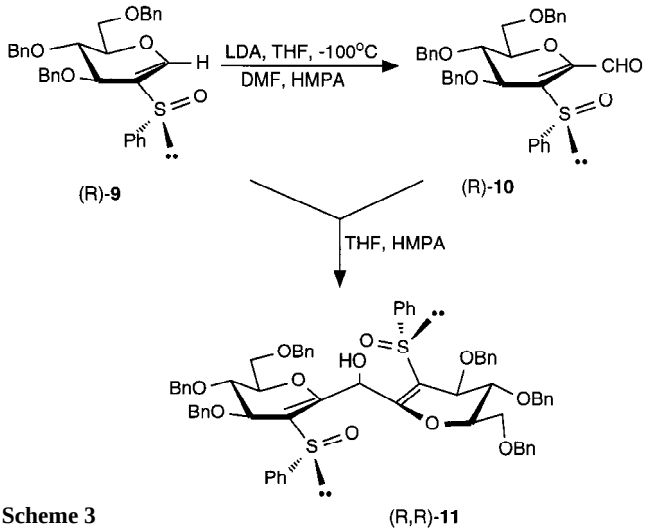
Scheme 1

Tri-*O*-benzyl-D-galactal was readily converted into known 2-phenylsulfinyl derivatives (*R*)- and (*S*)-**3** (Scheme 2).[13] Their treatment with LDA in THF at –100 °C afforded the corresponding 1-*C*-lithiated species (*R*)- and (*S*)-**3A**, which gave with equivalent amounts of DMF as C_1-electrophile of type **B** in the presence of hexamethylphosphorous triamide (HMPA) 1-formyl derivatives (*R*)-**4** and (*S*)-**4**, respectively, in high yields.[14] Immediate formation of the bis-reaction products (*R,R*)-**5** and (*S,S*)-**5** was not observed, even when excess (*R*)- or (*S*)-**3A** was generated. This finding is presumably due to generation of the aldehyde **4** only after hydrolysis of the addition product between **3A** and DMF during workup; thus, the method employed should enable also combination of two different sugar residues. Then, reaction of (*R*)-**3A** or (*S*)-**3A** with (*R*)-**4** and (*S*)-**4** gave the desired *C*-trehalose intermediates (*R,R*)-**5** and (*S,S*)-**5**, respectively, in 73% and 59% yields; based on consumed **3**, yields were 89% and 74%, respectively. Removal of the phenylsulfinyl group in (*R,R*)-**5** and (*S,S*)-**5** was best performed in two steps: reduction of the sulfoxide moiety with sodium cyanoborohydride ($NaCNBH_3$) in acetic acid gave phenyl sulfide **6** in high yields, which upon Raney nickel (WII)[15] treatment led to the desired bis-galactal derivative **7**. The galactose structure was readily introduced into **7** by regio- and diastereoselective hydrogen and hydroxy group addition to the enol ether moieties with borane–dimethyl sulfide complex and then H_2O_2/NaOH treatment,[16] thus furnishing hydroxymethylene-bridged *C*-trehalose **8**. Hydrogenolytic removal of the benzyl groups in the presence of Pd/C as catalyst afforded target molecule **2a**. The structural assignment was based on the ^{1}H NMR data (2-H: δ = 3.70, $J_{1,2} = J_{2,3}$ = 9.4 Hz; 2'-H: δ = 3.72, $J_{1',2'} = J_{2',3'}$ = 9.4 Hz) which are in accordance with β-galactopyranosyl residues in $^4C_1$-conformation.

Similarly, from known glucal derivative (*R*)-**9**[17] (Scheme 3) the corresponding C-1 lithiated species (*R*)-**9A** was generated; reaction with DMF under the same conditions



Scheme 2



Scheme 3

afforded only aldehyde (*R*)-**10**. Upon further reaction with (*R*)-**9A** the desired *C*-trehalose intermediate (*R*,*R*)-**11** was obtained in good yield, thus exhibiting the general applicability of this method for *C*-trehalose synthesis.

Solvents were purified in the usual way; petroleum ether bp 35–65 °C. Column chromatography: flash chromatography: silica gel (Baker, T. J.; particle size 40 μm). TLC: DC plastikfolien Kieselgel $60F_{254}$ (Merck; layer thickness 0.2 mm). Mps were uncorrected. Optical rotations: Perkin–Elmer 241 MC polarimeter; 1-dm cell. NMR Bruker AC 250, Avanca-DRX 600; internal standard TMS or deuterated solvent. FAB-MS: Finnigan MAT 312 (modified), 70 ev, 70 °C.

Bis{1,5-anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-2-[(*R*)-phenylsulfinyl]-D-*lyxo*-hex-1-enit-1-yl}methanol [(*R*,*R*)-5]:

To a well-stirred solution of freshly prepared LDA (1.1 equiv) in anhyd THF (200 mL) was added at –100 °C a solution of 1,5-anhydro-3,4,6-tri-*O*-benzyl-2-[(*R*)-phenylsulfinyl]-D-*lyxo*-hex-1-enitol [(*R*)-**3**][13] (5.41 g, 10 mmol) in anhyd THF. After stirring for 1 h, HMPA (1.5 mL, 8 mmol) was added and after another 30 min was added dropwise a solution of 2,6-anhydro-4,5,7-tri-*O*-benzyl-3-deoxy-3-[(*R*)-phenylsulfinyl]-aldehydo-D-*lyxo*-hept-2-enose [(*R*)-**4**][14] (6.25 g, 11 mmol) in THF (50 mL). The mixture was stirred for 2 h at this temperature and quenched with sat. NH_4Cl and extracted with Et_2O (3 × 100 mL). The combined organic extract was washed with sat. brine and then dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc 1:1) to give colorless crystals; yield 8.08 g (73%) [89% based on consumed (*R*)-**3**)]; mp 56.7 °C; TLC (petroleum ether/EtOAc 4:6) R_f 0.19; $[\alpha]_{20}$ +46.9 (*c* = 1, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.65–3.67 (m, 2 H, 3'-*H*, 6-*H*), 3.79 (dd, 1 H, $H_{5,6a}$ = 8.4, $J_{6a,6b}$ = 11.6 Hz, 6-*H*), 3.84 (d, 1 H, *J* = 10.4 Hz, C*H*Ph), 3.86–3.90 (m, 2 H, 6'-*H*), 3.96–3.98 (m, 2 H, C*H*Ph, 3-*H*), 4.34 (d, 1 H, *J* = 12.1 Hz, C*H*Ph), 4.37 (d, 1 H, *J* = 12.1 Hz, C*H*Ph), 4.38–4.41 (m, 2 H, C*H*Ph), 4.44 (d, 1 H, *J* = 12.1 Hz, C*H*Ph), 4.47 (d, 1 H, *J* = 12.1 Hz, C*H*Ph), 4.51 (d, 1 H, *J* = 12 Hz, C*H*Ph), 4.54 (d, 1 H, *J* = 11.9 Hz, C*H*Ph), 4.55–4.58 (m, 3 H, C*H*Ph, 4-*H*, 5'-*H*), 4.67–4.69 (m, 2 H, 5-*H*, C*H*Ph), 4.75 (dd, 1 H, $J_{3,4}$ = 3.5, $J_{4,5}$ = 1 Hz, 4'-*H*), 6.27 (s, 1 H, 7-*H*), 6.52–6.54 (m, 2 H, Ar*H*), 6.68, 6.69 (m, 2 H, Ar*H*), 7.09–7.3 (m, 32 H, Ar*H*), 7.61–7.65 (m, 4 H, Ar*H*).
^{13}C NMR (150 MHz, $CDCl_3$): δ = 63.68 (4-*C*), 65.38 (5'-*C*), 66.89 (6-*C*), 66.94 (6'-*C*), 68.04 (3'-*C*), 72.07, 72.54, 72.95, 73.27, 73.27, 73.43, 73.63, 73.86 (CH_2), 74.55 (*C*-3), 76.92 (5'-*C*), 77.71 (5-*C*), 113.74, 115.48 (2-*C*, 2'-*C*), 124.30, 125.86, 126.72, 126.79, 126.99, 127.25, 127.47, 127.52, 127.67, 127.86, 127.92, 128.34, 128.44, 128.53, 129.39, 129.77, 137.37, 137.58, 137.95, 142.55, 143.23 (Ar*C*), 156.96, 157.79 (1-*C*, 1'-*C*).
MS (FAB, NaI): *m/z* = 1131 (M + Na).
Anal. calcd for $C_{67}H_{64}O_{11}S_2$ (1109.37): C, 72.54; H, 5.82. Found: C, 71.79; H, 5.95.

Bis{1,5-anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-2-[(*S*)-phenylsulfinyl]-D-*lyxo*-hex-1-enit-1-yl}methanol [(*S*,*S*)-5]:
Compound (*S*,*S*)-**5** was prepared in a similar manner to that described for compound (*R*,*R*)-**5** by starting from 1,5-anhydro-3,4,6-tri-*O*-ben-zyl-2-[(*R*)-phenylsulfinyl]-D-*lyxo*-hex-1-enitol [(*S*)-**3**][13] (5.41 g, 10 mmol). A solution of 2,6-anhydro-4,5,7-tri-*O*-benzyl-3-deoxy-3-[(*S*)-phenylsulfinyl]-aldehydo-D-*lyxo*-hept-2-enose [(*S*)-**4**][14] (6.25 g, 11 mmol) in THF (50 mL) was added dropwise. The mixture was stirred for 2 h at this temperature and in a similar work up and purification by flash chromatography (petroleum ether/EtOAc 7:3), colorless crystals were obtained; yield: 6.53 g (59%) [74% based on (*S*)-**3** consumed]; mp 68.8°C; TLC (petroleum ether/EtOAc 6:4) R_f 0.14; $[\alpha]_D$ –31.8 (*c* = 1, $CHCl_3$).
^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.31 (dd, 1 H, $J_{4,5}$ = 3.2, $J_{3,4}$ = 5.9 Hz, 4-*H*), 3.49 (dd, 1 H, $J_{3',4'}$ = 3.5, $J_{4',5'}$ = 1.7 Hz, 4'-H), 3.76 (d, 1 H, *J* = 2.9 Hz, 3-*H*), 3.84 (dd, 1 H, $J_{5',6'a}$ = 7.9, $J_{6'a,6'b}$ = 11.4 Hz, 6'-*H*), 3.91 (m, 2 H, C*H*Ph, 6-*H*), 3.93 (m, 2 H, C*H*Ph, 6'-*H*), 3.99 (d, 1 H, *J* = 11.8 Hz, C*H*Ph), 4.02 (dd, 1 H, $J_{5,6a}$ = 8.5, $J_{6a,6b}$ = 11.7 Hz, 6-*H*), 4.12 (brs, 1 H, 3'-*H*), 4.21 (d, 2 H, *J* = 11.7 Hz, C*H*Ph), 4.31 (d, 2 H, *J* = 11.7 Hz, C*H*Ph), 4.38–4.43 (m, 3 H, C*H*Ph), 4.52–4.56 (m, 2 H, C*H*Ph, 5'-*H*), 4.58 (dd, 1 H, $J_{5,6a}$ = $J_{5,6b}$ = 7 Hz, 5-*H*), 4.72 (d, 2 H, *J* = 11.2 Hz, C*H*Ph), 6.51 (s, 1 H, 7-*H*), 7.05–7.13 (m, 2 H, Ar*H*), 7.16–7.38 (m, 31 H, Ar*H*), 7.43–7.46 (m, 3 H, Ar*H*), 7.57–7.61 (m, 2 H, Ar*H*), 7.72–7.76 (m, 2 H, Ar*H*).
^{13}C NMR (150 MHz, $CDCl_3$): δ = 66.21 (7-*C*), 67.63 (3-*C*), 68.3 (3'-*C*), 68.74 (6-*C*), 69.15 (6'-*C*), 71.18, 72.00, 72.72, 72.95, 73.00, 73.27 (CH_2), 72.44 (4'-*C*), 74.00 (4-*C*), 77.05 (5'-*C*), 77.45 (5-*C*), 116.14, 116.27 (2-*C*, 2'-*C*), 124.72, 124.88, 127.27, 127.41, 127.51, 127.76, 127.80, 127.89, 127.95, 127.98, 128.15, 128.17, 128.21, 128.28, 128.39, 128.85, 129.06, 130.19, 137.04, 137.19, 137.85, 138.14, 142.21, 143.48 (Ar*C*), 157.80, 157.42 (1-*C*, 1'-*C*).
MS (FAB, NaI): *m/z* = 1131 (M + Na).
Anal. calcd for $C_{67}H_{64}O_{11}S_2$ (1109.37): C, 72.54; H, 5.82. Found: C, 72.22; H, 5.76.

Bis[1,5-anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-2-(phenylthio)-D-*lyxo*-hex-1-enit-1-yl]methanol (6):
To a solution of (*R*,*R*)-**5** or (*S*,*S*)-**5** (5.51 g, 5 mmol) in HOAc (30 mL) $NaCNBH_3$ (2.5 g, 38 mmol) was added portionwise at r.t. When the addition was complete the mixture was stirred at this temperature for 10 h and then heated to 50°C for 4 h and monitored by TLC. The mixture was poured onto crushed ice (200 g) and brought to r.t. and extracted with Et_2O (4 × 50 mL). The combined extracts were washed with brine (2 × 30 mL) and dried ($MgSO_4$) and concentrated in vacuo. The crude residue was purified by flash chromatography (petroleum ether/EtOAc 8:2) to give a viscous liquid; yield: 4.68 g (86%); TLC (petroleum ether/EtOAc 7:3) R_f 0.42; $[\alpha]_D$ –17.7 (*c* = 1, $CHCl_3$).
^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.75–3.76 (m, 2 H, 4'-*H*, 3'-*H*), 3.83 (dd, 2 H, $J_{6'a,6'b}$ = 10.9, $J_{5',6'}$ = 4.5 Hz, 6'-*H*), 3.91 (m, 2 H, 6-*H*), 4.03 (dd, 1 H, $J_{3,4}$ = $J_{4,5}$ = 3.5 Hz, 4-*H*), 4.09 (d, 1 H, *J* = 3.6 Hz, 3-*H*), 4.38 (d, 1 H, *J* = 12 Hz, C*H*Ph), 4.41 (m, 1 H, 5'-*H*), 4.42 (d, 2 H, *J* = 11.9 Hz, C*H*Ph), 4.47 (s, 1 H, C*H*Ph), 4.49–4.50 (m, 3 H, C*H*Ph), 4.53 (d, 1 H, $J_{5,6a}$ = 5.3 Hz, 5-*H*), 4.55 (d, 2 H, *J* = 11.7 Hz, C*H*Ph), 4.65 (s, 2 H, C*H*Ph), 4.74 (d, 1 H, *J* = 11.7 Hz, C*H*Ph), 6.26 (s, 1 H, 7-*H*), 7.08–7.31 (m, 40 H, Ph).
^{13}C NMR (150 MHz, $CDCl_3$): δ = 67.56 (6'-*C*), 68.1 (6-*C*), 68.19, 72.51, 72.70, 73.44 (CH_3), 73.05 (4-*C*), 73.3 (4'-*C*), 74.00, 74.14, 74.42 (3-*C*, 3'-*C*), 76.2 (5'-*C*), 76.2 (5-C), 77.71, 101.44, 102.29 (2-*C*, 2'-*C*), 124.97, 126.95, 127.26, 127.29, 127.51, 127.63, 127.65, 127.73, 127.87, 127.98, 128.22, 128.31, 128.44, 128.50, 137.62, 138.02, 138.12, 138.15, 138.27, 138.56, 157.63, 158.36 (1-*C*, 1'-*C*).
MS (FAB, NaI): *m/z* = 1099 (M + Na).
Anal. calcd for $C_{67}H_{64}O_9S_2$ (1077.37): C, 74.69; H, 5.99. Found: C, 74.77; H, 5.93.

Bis(1,5-anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-D-*lyxo*-hex-1-enit-1-yl)methanol (7):
A solution of **6** (4.4 g, 4.08 mmol) in anhyd THF (50 mL) was stirred with W-2 Raney Nickel (25 g) and monitored by TLC (45 min). When the reaction was complete the solid was filtered out and washed with EtOAc and the combined filtrate was evaporated to dryness. The residue was chromatographed by flash chromatography (petroleum ether/EtOAc 3:1) to give **7** as a colorless oil; yield: 2.87 g (86%); TLC (petroleum ether/EtOAc 7:3) R_f 0.15; $[\alpha]_D$ –20.3 (*c* = 1, $CHCl_3$).
^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.72–2.78 (brs, 1 H, -O*H*), 3.61 (dd, 1 H, $J_{3',4'}$ = $J_{4',5'}$ = 2.9 Hz, 4'-*H*), 3.72–3.74 (m, 1 H, 3'-*H*), 3.83 (dd, 2 H, $J_{6'a,6'b}$ = 12, $J_{5',6'}$ = 5.5 Hz, 6'-*H*), 3.89–3.95 (m, 2 H, 6-*H*), 4.08–4.13 (m, 2 H, 4-*H*, 3-*H*), 4.18–4.26 (m, 2 H, 7-*H*, C*H*Ph), 4.42–4.46 (m, 4 H, CHPh, 5'-*H*), 4.48 (d, 2 H, *J* = 11.8 Hz, C*H*Ph), 4.62–4.64 (m, 5 H, 5-*H*, C*H*Ph), 4.80 (d, 1 H, *J* = 11.9 Hz, C*H*Ph), 4.91 (d, 1 H, *J* = 11.6 Hz, C*H*Ph), 5.16 (d, 2 H, *J* = 3.2 Hz, 2-*H*, 2'-*H*), 7.19–7.32 (m, 30 H, Ph).
MS (MALDI, NaI): *m/z* = 882 (M + Na).
Anal. calcd for $C_{55}H_{56}O_9$ (861.044): C, 76.72; H, 6.56. Found: C, 76.35; H, 6.43.

Bis(3,4,6-tri-*O*-benzyl-α-D-galactopyranosyl)methanol (8):
A solution of **7** (2.0 g, 2.3 mmol) in THF (15 mL) was added to a cooled (4°C) solution of BH_3•SMe_2 in anhyd THF (9.2 mL, 18.4 mmol) and stirred at this temperature for 3 d. Then 10% aq NaOH (18 mL) was added followed by 35% H_2O_2 (5.2 mL). After stirring for 30 min, the mixture was poured into water (50 mL) and extracted with Et_2O (5 × 50 mL). The combined organic layers were neutralized with 20% aq sodium bisulfite (18 mL) and then sat. NH_4Cl, followed by brine. The organic extract was dried ($MgSO_4$) and concentrated. Purification by flash chromatography of the residue afforded **8**; yield: 1.18g (57%); TLC (petroleum ether/EtOAc 1:1) R_f 0.33; $[\alpha]_D$ –1.3 (*c* = 1, $CHCl_3$).
^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.32 (d, 1 H, $J_{7,1}$ = 7.8, $J_{1,2}$ = 9 Hz, 1-*H*), 3.40 (dd, 1 H, $J_{2',3'}$ = 10, $J_{3',4'}$ = 2.9 Hz, 3'-*H*), 3.46 (dd, 1 H, $J_{2,3}$ = 9.4, $J_{3,4}$ = 2.9 Hz, 3-*H*), 3.48 (dd, 1 H, $J_{1',2'}$ = 10, $J_{7,1'}$ = 2.5 Hz, 1'-*H*), 3.44–3.52 (m, 2 H, 6-*H*), 3.52 (d, 1 H, $J_{4,5}$ <1 Hz, 5-*H*), 3.52–3.56 (m, 2 H, 6'-*H*), 3.60 (d, 1 H, $J_{4',5'}$ <1 Hz, 5'-*H*), 3.70 (brs, 2 H, C*H*Ph), 3.85 (d, 1 H, $J_{3,4}$ = 2.9 Hz, 4-*H*), 3.93 (d, 1 H, $J_{3',4'}$ = 2.9 Hz, 4'-*H*), 4.07 (dd, 1 H, $J_{7,1}$ = 7.8, $J_{1,2}$ = 9 Hz, 7-*H*), 4.15 (dd, 1 H, $J_{1',2'}$ = $J_{2',3'}$ = 9.4 Hz, 2'-H), 4.23 (dd, 1 H, $J_{2,3}$ = $J_{3,4}$ = 9.4 Hz, 2-*H*), 4.40–4.95 (m, 4 H, C*H*Ph), 4.54–4.58 (m, 3 H, C*H*Ph), 4.71–4.74 (m, 2 H, C*H*Ph), 4.80 (d, 1 H, *J* = 12 Hz, C*H*Ph), 4.85 (d, 1 H, *J* = 11.6 Hz, C*H*Ph), 4.90 (d, 1 H, *J* = 11.6 Hz, C*H*Ph), 7.25–7.36 (m, 30 H, Ar*H*).
^{13}C NMR (150 MHz, $CDCl_3$): δ = 66.3 (2'-*C*), 68.7 (6'-*C*), 69.2 (6-*C*), 71.1 (2-*C*), 72.8 (4'-*C*), 72.9 (7-*C*), 73.7 (4-*C*), 76.9 (5'-*C*), 77.0 (5-*C*), 77.1 (1-*C*), 78.1 (1'-*C*), 83.3 (3-*C*), 84.1 (3'-*C*).
MS (FAB, NaI): *m/z* = 919 (M + Na).

Anal. calcd for $C_{55}H_{60}O_{11}$ (897.074): C, 73.64; H, 6.74. Found: C, 73.29; H, 6.92.

Bis[C-(β-D-galactopyranosyl)]methanol (2a):
Compound **8** (179 mg, 0.20 mmol) was dissolved in EtOAc/MeOH (1:1) (20 mL) and to this 10% Pd/C (20 mg) was added. The suspension was stirred for 20 h under hydrogen at normal pressure. Then the catalyst was filtered and washed repeatedly with MeOH and the combined filtrate was evaporated to dryness. Flash chromatography (CH_2Cl_2/MeOH, 7:3) of the residue afforded **2a**; yield: 58 mg (81%).
TLC (CH_2Cl_2/MeOH 7:3) R_f 0.33; $[\alpha]_D$ –1.6 (c = 0.42, dioxane).
^{1}H NMR (600 MHz, MeOH-d_4): δ = 3.32 (dd, 1 H, $J_{7,1'}$ = 6.8, $J_{1',2'}$ = 9.4 Hz, 1'-*H*), 3.38 (dd, 1 H, $J_{2',3'}$ = 9.4, $J_{3',4'}$ = 3.2 Hz, 3'-*H*), 3.40 (dd, 1 H, $J_{7,1}$ = 2.5, $J_{1,2}$ = 9.4 Hz, 1-*H*), 3.40–3.42 (m, 1 H, 5'-*H*), 3.42 (dd, 1 H, $J_{2,3}$ = 9.4, $J_{3,4}$ = 3.2 Hz, 3-*H*), 3.46 (1 H, $J_{5,6a}$ = 5, $J_{5,6b}$ = 7.6 Hz, 5-*H*), 3.55 (dd, 1 H, $J_{5,6a}$ = 5, $J_{6a,6b}$ = 11.4 Hz, 6-*H*), 3.58 (dd, 1 H, $J_{5,6a}$ = 5, $J_{6a,6b}$ = 11.4 Hz, 6-*H*), 3.62 (dd, 1 H, $J_{5',6'b}$ = 7.0, $J_{6'a,6'b}$ = 11.4 Hz, 6'-*H*), 3.64 (dd, 1 H, $J_{5',6'b}$ = 7.3, $J_{6'a,6'b}$ = 11.4 Hz, 6'-*H*), 3.70 (dd, 1 H, $J_{1,2}$ = $J_{2,3}$ = 9.4 Hz, 2-*H*), 3.72 (dd, 1 H, $J_{1',2'}$ = $J_{2',3'}$ = 9.4 Hz, 2'-*H*), 3.75 (m, 1 H, 4-*H*), 3.76 (m, 1 H, 4'-H), 4.05 (dd, 1 H, $J_{7,1'}$ = 6.8, $J_{7,1}$ = 2.5 Hz, 7-*H*).
^{13}C NMR (150 MHz, MeOH-d_4): δ = 62.84, 62.94 (6-*C*, 6'-*C*), 67.97, 71.76 (2-*C*, 2-*C*), 70.66, 71.12 (4-*C*, 4'-*C*), 72.85 (7-*C*), 76.27, 76.75 (3-*C*, 3'-*C*), 79.0, 79.5 (1-*C*, 1'-*C*), 80.1, 80.4 (5-*C*, 5'-*C*).
MS (FAB, NaI): *m/z* = 379 (M + Na).
Anal. calcd for $C_{13}H_{24}O_{11}$ (356.324): C, 43.82; H, 6.79. Found: C, 43.49; H, 6.43.

2,6-Anhydro-4,5,7-tri-*O*-benzyl-3-deoxy-3-[(*R*)-phenylsulfinyl]-aldehydo-D-arabino-hept-2-enose [(*R*)-10]:
(*R*)-**10** was prepared by following a similar procedure to that in the case of **4**.[14] The analytical data for this compound are as follows. Flash chromatography of the crude residue yielded 89% of (*R*)-**10**; TLC (petroleum ether/EtOAc 7:3) R_f 0.26; $[\alpha]_D$ +56.8 (c = 1, $CHCl_3$).
^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.47 (dd, 1 H, $J_{5,7a}$ = $J_{7a,7b}$ = 5.4 Hz, 7a-*H*), 3.61 (dd, 1 H, $J_{5,7b}$ = 3.3, $J_{7a,7b}$ = 7.4 Hz, 7b-*H*), 3.85 (dd, 1 H, $J_{4,5}$ = 2.5, $J_{5,6}$ <1 Hz, 5-*H*), 4.23–4.60 (m, 6 H, C*H*Ph), 4.69–4.70 (m, 1 H, 6-*H*), 4.77 (dd, 1 H, $J_{4,5}$ = 2.5, $J_{4,6}$ <1 Hz, 4-*H*), 6.73, 6.77 (m, 2 H, Ar*H*), 7.12–7.35 (m, 16 H, Ar*H*), 7.53–7.57 (m, 2 H, Ar*H*), 9.94 (s, 1 H, C*H*O).
^{13}C NMR (62.7 MHz, $CDCl_3$): δ = 62.7, 63.91, 66.78, 70.96, 71.47, 72.03, 72.87, 76.49, 77.39, 124.70, 126.70, 127.30, 127.43, 127.47, 127.60, 127.86, 127.93, 128.24, 128.73, 129.94, 136.83, 137.02, 137.49, 143.70, 149.65 (*C*=*C*, Ar*C*), 185.08 (*C*HO).
MS (FAB, NaI): *m/z* = 591 (M + Na).

Bis{1,5-anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-2-[(*R*)-phenylsulfinyl]-D-*arabino*-hex-1-enit-1-yl}methanol [(*R*,*R*)-11]:
To a well-stirred solution of freshly prepared LDA (1.1 equiv) in anhyd THF (50 mL), a solution of 1,5-anhydro-3,4,6-tri-*O*-benzyl-2-[(*R*)-phenylsulfinyl]-D-*arabino*-hex-1-enitol [(*R*)-**9**] (150 mg, 0.27 mmol) in anhyd THF was added at –100 °C. After stirring for 1 h, HMPA (0.15 mL, 0.21 mmol) was added and after another 30 min a solution of 2,6-anhydro-4,5,7-tri-*O*-benzyl-3-deoxy-3-[(*R*)-phenylsulfinyl]-aldehydo-D-*arabino*-hept-2-enose [(*R*)-**10**] (171 mg, 0.3 mmol) in THF (10 mL) was added dropwise. The mixture was stirred for 2 h at this temperature and quenched with a sat. NH_4Cl solution and extracted with Et_2O (3 × 25 mL). The combined organic extract was washed with sat. brine and dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc 7:3) to give a viscous oil; yield: 106 mg (35%) [72% based on (*R*)-**9** consumed]; TLC (petroleum ether/EtOAc 6:4) R_f 0.12; $[\alpha]_D$ –14.5 (c = 1, $CHCl_3$).
^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.42 (dd, 1 H, $J_{4,5}$ = 5, $J_{3,4}$ = 9.6 Hz, 4-*H*), 3.53–3.55 (m, 2 H), 3.58–3.77 (m, 7 H, C*H*, C*H*Ph), 3.81–3.91 (m, 2 H, C*H*Ph, 6-*H*), 4.03 (dd, 2 H, $J_{5,6a}$ = 3.6, $J_{6a,6b}$ = 12 Hz, 6-*H*), 4.34 (d, 1 H, J = 11.7 Hz, C*H*Ph), 4.36–4.46 (m, 5 H, C*H*Ph), 4.58 (d, 1 H, J = 11.4 Hz, C*H*Ph), 4.62 (d, 1 H, J = 11.6 Hz, C*H*Ph), 6.60 (s, 1 H, 7-*H*), 6.72–6.74 (m, 2 H, Ar*H*), 6.79–6.82 (m, 2 H, Ar*H*), 6.97–7.01 (m, 2 H, Ar*H*), 7.12–7.29 (m, 30 H, Ar*H*), 7.58–7.76 (m, 4 H, Ar*H*).
MS (FAB, NaI): *m/z* = 1131 (M + Na).
Anal. calcd for $C_{67}H_{64}O_{11}S_2$ (1109.37): C, 72.54; H, 5.82. Found: C, 72.13; H, 5.88.

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