Total Synthesis of 6-*O*-Benzoylzeylenol from Diacetone Glucose

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Abstract: A total synthesis of 6-*O*-benzoylzeylenol from diacetone glucose is described. The key steps were a crossed aldol–Cannizzaro reaction to create a quaternary carbon stereocenter, and cyclization through ring closure metathesis (RCM). Of the four stereogenic centers, two were derived from diacetone glucose, the quaternary stereocenter was created by means of the crossed aldol–Cannizzaro reaction, and the fourth stereogenic center was produced by a Sharpless asymmetric epoxidation. Finally, cyclization through RCM and deprotection by removal of a benzyl group with titanium(IV) chloride gave the target molecule.

Key words: ring closure, metathesis, aldol reactions, Cannizzaro reactions, stereoselective synthesis

Zeylenols are polyoxygenated cyclohexene natural products that have been isolated from various sources. (+)-Zeylenol (**1**; Figure 1)[1–5] was first isolated in 1987 by Tuntiwachwuttikul and co-workers from a natural source, initially described as a member of the genus *Bosenbergia*,[1a] but subsequently identified, in 1989, as a species of *Kaempferia*.[1b] (+)-Zeylenol (**1**) showed selective cytotoxicity towards HL-60 leukemia cells.[1c] The related compounds 6-*O*-benzoylzeylenol (**2**)[1b] and uvaribonol A (**3**)[1b] also were isolated from the same *Kaempferia* species.

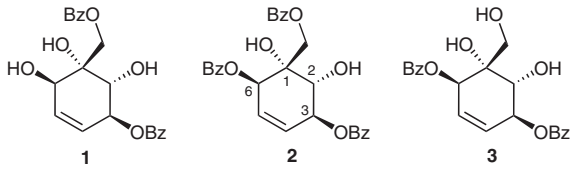
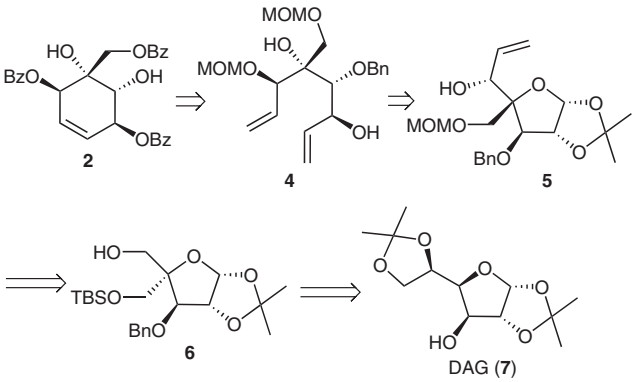


Figure 1 Structures of (+)-zeylenol (**1**) and its congeners 6-*O*-benzoylzeylenol (**2**) and uvaribonol A (**3**)

6-*O*-Benzoylzeylenol (**2**) is an attractive synthetic target by virtue of its interesting structural features, including a chiral quaternary carbon center, five hydroxy/alkoxy groups, and a double bond in a six-carbon system, besides its biological activities. Recently, Palframan et al.[6] reported a total synthesis of (+)-zeylenol (**1**) and its congeners **2** and **3** by photooxygenation of a microbial arene oxidation product.

The retrosynthetic analysis of 6-*O*-benzoylzeylenol (**2**) is shown in Scheme 1. The synthesis of **2** might be achieved by ring closure metathesis of diene **4**, followed by deprotection and benzoylation. Diene **4** might be derived from alcohol **5**, which in turn might be obtained from alcohol **6**. The known alcohol **6**[7] can be prepared from diacetone glucose [DAG (**7**); 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose].



Scheme 1 Retrosynthetic analysis for 6-*O*-benzoylzeylenol (**2**)

Accordingly, the aldehyde **7a**[7a] derived from DAG (**7**) underwent a crossed aldol–Cannizzaro reaction with 37% aqueous formaldehyde in the presence of 1 M aqueous sodium hydroxide in a 1:1 mixture of tetrahydrofuran and water at room temperature for 16 hours to give the 1,3-diol **7b**[7a] in 78% yield (Scheme 2). Selective protection of diol **7b** with *tert*-butyl(chloro)dimethylsilane and imidazole at –20 °C for one hour gave the known alcohol **6**[7b,7c] in 58% yield. Treatment of alcohol **6** with chloro(methoxy)methane (MOMCl), diisopropyl(ethyl)amine (DIPEA), and 4-(*N*,*N*-dimethylamino)pyridine (DMAP) in dichloromethane at 0 °C to room temperature for eight hours gave the protected compound **8** in 92% yield (Scheme 2). Desilylation of **8** by treatment with tetrabutylammonium fluoride in tetrahydrofuran at 0 °C to room temperature for four hours gave alcohol **9** (82%). Oxidation under Swern conditions using oxalyl dichloride, dimethyl sulfoxide, and triethylamine in dichloromethane gave aldehyde **10**. Treatment of **10** with vinylmagnesium bromide in tetrahydrofuran at 0 °C to room temperature for 20 minutes gave the diastereomeric allylic alcohols **5** and *ent*-**5** as an inseparable mixture (~1:5 ratio) in 76% yield.

An alternative synthesis of segment **5** was achieved by an asymmetric approach. Wittig olefination of aldehyde **10** with ethyl (triphenylphosphoranylidene)acetate in CH_2Cl_2 at 0 °C to room temperature for two hours gave the α,β-unsaturated ester **11** exclusively in 88% yield

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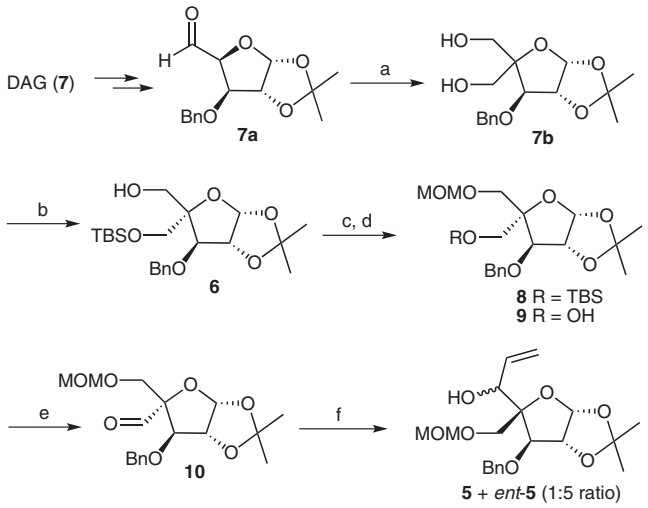
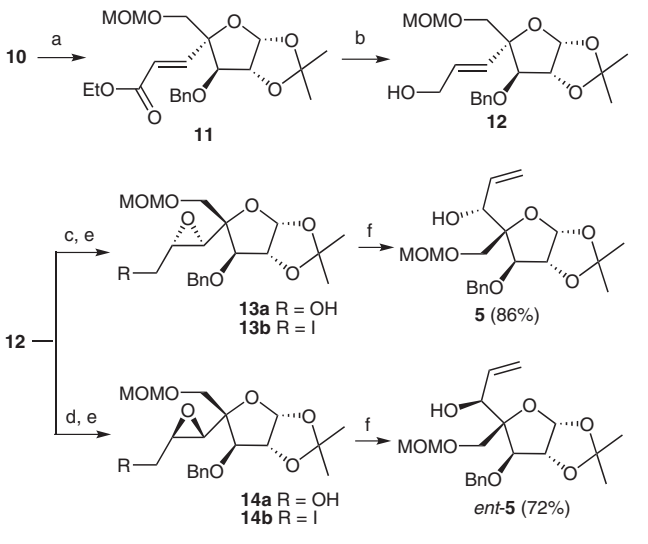


Scheme 2 Synthesis of segment **5**. *Reagents and conditions:* (a) 37% aq HCHO, THF, H_2O, 1 M aq NaOH, 0 °C to r.t, 16 h, 78%; (b) TBSCl, imidazole, CH_2Cl_2, –20 °C, 1 h, 58%; (c) MOMCl, DIPEA, DMAP, CH_2Cl_2, 0 °C to r.t., 8 h, 92%; (d) TBAF, THF, 0 °C to r.t., 4 h, 82%; (e) $(ClCO)_2$, DMSO, Et_3N, CH_2Cl_2, –78 °C, 2 h; (f) CH_2=CHMgBr, THF, 0 °C to r.t., 20 min, 76%.

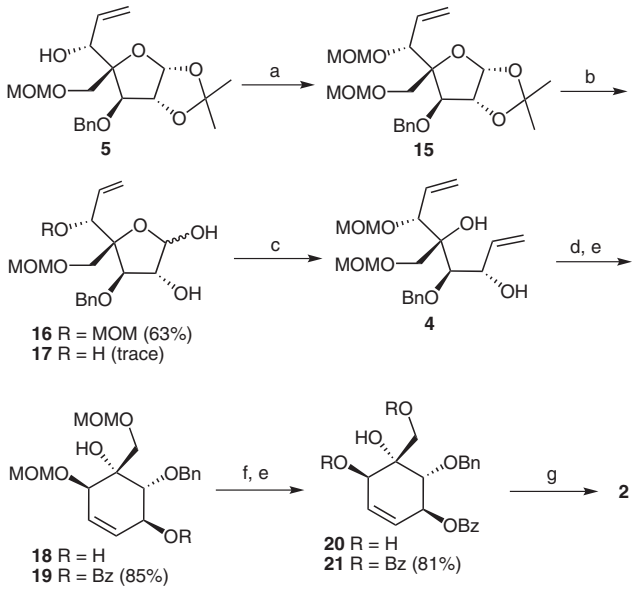
(Scheme 3). Reduction of **11** with diisobutylaluminum hydride in dichloromethane at 0 °C to room temperature for 30 minutes gave allylic alcohol **12** (70%), which was independently subjected to Sharpless asymmetric epoxidation with cumene hydroperoxide (CHP) and diisopropyl (+)-tartrate [(+)-DIPT] or (–)-DIPT in anhydrous dichloromethane at –20 °C for 14 hours (Scheme 3) to give the epoxy alcohols **13a** (86%) and **14a** (90%), respectively. Treatment of **13a** and **14a** separately with triphenylphosphine, diiodine, and imidazole at 0 °C to room temperature for 20 minutes gave the corresponding iodo compounds **13b** and **14b**, which on reaction with zinc and sodium iodide in refluxing methanol gave the allylic alcohols **5** (86%) and *ent*-**5** (72%), respectively. The product obtained from (+)-DIPT corresponded to the minor allylic alcohol **5**, whereas the product from (–)-DIPT corresponded to *ent*-**5** obtained by the Grignard reaction.

Treatment of alcohol **5** with MOMCl, DIPEA, and DMAP in dichloromethane at 0 °C to room temperature for 12 hours gave the methoxymethyl ether **15** in 78% yield (Scheme 4). Acid-mediated hydrolysis of ether **15** with 70% aqueous acetic acid at 55 °C for eight hours gave the lactol **16** (63%) along with traces of triol **17**. Wittig olefination[8] of lactol **16** with methyl(triphenyl)phosphonium bromide and butyllithium in tetrahydrofuran at 0 °C to room temperature for two hours gave the diene **4** in 65% yield. RCM[9,10] of diene **4** with the Grubbs second-generation catalyst in toluene at room temperature for two hours gave the olefin **18** in 76% yield. Treatment of olefin **18** with benzoyl chloride and pyridine in dichloromethane at 0 °C to room temperature for eight hours gave benzoate **19** (85%), which on deprotection of the methoxymethyl groups by using trifluoroacetic acid in dichloromethane at 0 °C to room temperature for two hours gave triol **20** in 70% yield (Scheme 4). Triol **20** reacted with benzoyl chloride and pyridine in dichloromethane at 0 °C to room temperature for four hours to give the tribenzoate **21** in 81% yield.

Finally, treatment of tribenzoate **21** with titanium(IV) chloride in dichloromethane at 0 °C to room temperature for two hours gave the target molecule **2** in 71% yield (Scheme 4). The optical rotation of the synthetic **2** agreed



Scheme 3 Synthesis of segment **5**. *Reagents and conditions*: (a) Ph_3P=$CHCO_2Et$, CH_2Cl_2, 0 °C to r.t., 2 h, 88%; (b) DIBAL-H, CH_2Cl_2, 0 °C to r.t., 30 min, 70%; (c) (+)-DIPT, Ti(*i*-PrO)$_4$, CHP, CH_2Cl_2, powdered 4 Å MS, –20 °C, 14 h, 86%; (d) (–)-DIPT, Ti(*i*-PrO)$_4$, CHP, CH_2Cl_2, powdered 4 Å MS, –20 °C, 14 h, 90%; (e) I_2, Ph_3P, imidazole, THF, 0 °C to r.t., 20 min; (f) Zn, NaI, MeOH, reflux, 12 h.



Scheme 4 Synthesis of target molecule **2**. *Reagents and conditions*: (a) MOMCl, DIPEA, DMAP, CH_2Cl_2, 0 °C to r.t., 12 h, 78%; (b) 70% aq AcOH, 55 °C, 8 h; (c) $Ph_3P^+MeBr^-$, *n*-BuLi, THF, 0 °C to r.t., 2 h, 65%; (d) Grubbs II catalyst, toluene, r.t., 2 h, 76%; (e) BzCl, py, CH_2Cl_2, 0 °C to r.t., 8 h; (f) TFA, CH_2Cl_2, 0 °C to r.t., 2 h, 70%; (g) $TiCl_4$, CH_2Cl_2, 0 °C to r.t., 2 h, 71%.

well with that of the natural product {$[\alpha]_D^{22}$ –58.1 (*c* 0.12, $CHCl_3$); Lit.[1b] $[\alpha]_D^{22}$ –59.7 (*c* 0.39, $CHCl_3$)}.

Thus, a synthesis of **2** from diacetone glucose (**7**) was achieved in which the quaternary carbon center was created by a crossed aldol–Cannizzaro reaction, and the cyclohexene ring core was formed by an efficient RCM reaction.

Crude products were purified by column chromatography on 60–120 mesh silica gel. ^{1}H NMR spectra were recorded at 300 and 500 MHz, and ^{13}C NMR spectra were recorded at 50 and 75 MHz on Bruker Avance 300 and Varian Inova 500 spectrometers. NMR spectra (^{1}H and ^{13}C) were recorded in $CDCl_3$ and chemical shifts are reported with respect to internal TMS as a reference. FTIR spectra were measured with a Thermo Nicolet Nexus 670 spectrometer. Optical rotations were measured with a JASCO DIP 300 digital polarimeter. Mass spectra were recorded with a Finnigan MAT 1210 double-focusing mass spectrometer operating with a direct inlet system.

3-*O*-Benzyl-5-*O*-[*tert*-butyl(dimethyl)silyl]-4-(hydroxymethyl)-1,2-*O*-(1-methylethylidene)-β-L-arabinofuranose (6)[7b]

A 37% aq solution of HCHO (40 mL) and 1 M aq NaOH (120 mL) were added sequentially at 0 °C to a stirred solution of aldehyde **7a** (20.0 g, 71.94 mmol) in a mixture of H_2O (100 mL) and THF (100 mL) at 0 °C, and the mixture was stirred at r.t. for 16 h. The solvent (THF) was evaporated under reduced pressure and the residue was extracted with EtOAc (3 × 250 mL). The organic layers were combined, washed with brine (100 mL), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography (silica gel, 40% EtOAc–PE) to give **7b** as a white solid; yield: 17.40 (78%);[7a] mp 101–103 °C.

TBSCl (8.27 g, 54.84 mmol) and imidazole (11.19 g, 164.52 mmol) were added to a solution of compound **7b** (17.0 g, 54.84 mmol) in CH_2Cl_2 (255 mL) at –20 °C. The mixture was stirred for 1 h at –20 °C and then warmed r.t.; CH_2Cl_2 (100 mL) was added, and the mixture was washed successively with H_2O (3 × 150 mL) and brine (150 mL) then dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography (silica gel, 10% EtOAc–PE) to give a white solid; yield: 13.49 (58%);[7b] mp 52–53 °C.

3-*O*-Benzyl-5-*O*-[*tert*-butyl(dimethyl)silyl]-4-[(methoxymethoxy)methyl]-1,2-*O*-(1-methylethylidene)-β-L-arabinofuranose (8)

DIPEA (13.07 mL, 75.47 mmol), MOMCl (2.87 mL, 37.74 mmol), and a catalytic amount of DMAP were added successively to a stirred and cooled (0 °C) solution of alcohol **6** (8.0 g, 18.87 mmol) in CH_2Cl_2 (40 mL) at 0 °C, and the mixture was stirred to r.t. for 8 h. H_2O (40 mL) was added, and the mixture was extracted with CH_2Cl_2 (2 ´ 50 mL). The organic layer was separated, washed with brine (40 mL), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography (silica gel, 7% EtOAc–PE) to give a pale-yellow oil; yield: 8.12 (92%); $[\alpha]_D^{27}$ –57.9 (*c* 0.16, $CHCl_3$).

IR ($CHCl_3$): 2930, 2885, 2857, 1466, 1378, 1254, 1212, 1048, 838, 779, 749, 698 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.37–7.26 (m, 5 H, Ar-H), 5.98 (d, *J* = 4.2 Hz, 1 H, C-1 H), 4.75–4.67 (m, 2 H, OCHPh, C-2 H), 4.65 (d, *J* = 6.3 Hz, 1 H, OCHO), 4.62 (d, *J* = 6.3 Hz, 1 H, OCH′O), 4.53 (d, *J* = 11.5 Hz, 1 H, OCH′Ph), 4.14 (br s, 1 H, C-3 H), 3.77 (d, *J* = 9.9 Hz, 1 H, OCH), 3.72 (d, *J* = 10.5 Hz, 1 H, OC*H*), 3.66 (d, *J* = 10.5 Hz, 1 H, OC*H*′), 3.63 (d, *J* = 9.9 Hz, 1 H, OCH′), 3.33 (s, 3 H, OCH_3), 1.55 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3), 0.86 [s, 9 H, $(CH_3)_3$], 0.03 (s, 3 H, CH_3), 0.02 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.6, 128.4 (2 C), 127.7, 127.5 (2 C), 112.7, 105.1, 96.8, 89.2, 86.1, 84.2, 72.3, 67.3, 63.1, 55.2, 27.3, 26.8, 25.9 (3 C), 18.2, –5.4, –5.5.

HRMS (ESI+): *m/z* $[M + Na]^+$ calcd for $C_{24}H_{40}NaO_7Si$: 491.24355; found: 491.24300.

3-*O*-Benzyl-4-[(methoxymethoxy)methyl]-1,2-*O*-(1-methylethylidene)-β-L-arabinofuranose (9)

A 1 M solution of TBAF in THF (18.80 mL) was added to a solution of furanose **8** (8.0 g, 17.09 mmol) in THF (16 mL) at 0 °C, and the mixture was stirred at r.t. for 4 h. THF was removed under reduced pressure and the residue was purified by column chromatography (silica gel, 20% EtOAc–PE) to give a colorless syrup; yield: 4.96 (82%); $[\alpha]_D^{27}$ –34.9 (*c* 0.22, $CHCl_3$).

IR ($CHCl_3$): 3480, 3031, 2987, 2935, 1456, 1379, 1246, 1213, 1150, 1110, 1045, 917, 864, 739, 700 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.41–7.27 (m, 5 H, Ar-H), 5.97 (d, *J* = 4.5 Hz, 1 H, C-1 H), 4.77 (dd, *J* = 2.0, 4.5 Hz, 1 H, C-2 H), 4.74 (d, *J* = 11.7 Hz, 1 H, OCHPh), 4.64 (d, *J* = 6.6 Hz, 1 H, OCHO), 4.61 (d, *J* = 6.6 Hz, 1 H, OCH′O), 4.57 (d, *J* = 11.7 Hz, 1 H, OCH′Ph), 4.09 (d, *J* = 2.0 Hz, 1 H, C-3 H), 3.72 (d, *J* = 10.2 Hz, 1 H, OCH), 3.70 (s, 2 H, OCH_2), 3.62 (d, *J* = 10.2 Hz, 1 H, OCH′), 3.32 (s, 3 H, OCH_3), 2.40–2.20 (br s, 1 H, OH), 1.55 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.5, 128.4 (2 C), 127.8, 127.5 (2 C), 113.0, 105.0, 96.8, 89.1, 85.9, 83.8, 72.5, 67.4, 63.0, 55.4, 27.3, 26.8.

HRMS (ESI+): *m/z* $[M + Na]^+$ calcd for $C_{18}H_{26}NaO_7$: 377.15707; found: 377.15645.

3-*O*-Benzyl-4-[(methoxymethoxy)methyl]-1,2-*O*-(1-methylethylidene)-β-L-*arabino*-pentodialdo-1,4-furanose (10)

DMSO (2.94 mL, 41.53 mmol) was added dropwise to a stirred solution of oxalyl chloride (1.81 mL, 20.76 mmol) in CH_2Cl_2 (25 mL) at –78 °C. After 20 min, a solution of **9** (4.90 g, 13.84 mmol) in CH_2Cl_2 (15 mL) was added and the mixture was stirred at –78 °C for 2 h. Et_3N (11.55 mL, 83.05 mmol) was added and the mixture was stirred and warmed to r.t. The mixture was then diluted with CH_2Cl_2 (60 mL) and washed successively with H_2O (40 mL) and brine (40 mL) then dried (Na_2SO_4). Evaporation of the solvent at a low temperature (10 °C) gave a pale-yellow solid; yield: 4.80 (98%); mp 78–80 °C; $[\alpha]_D^{27}$ –203.1 (*c* 0.26, $CHCl_3$).

IR ($CHCl_3$): 3019, 2988, 2938, 1734, 1455, 1380, 1214, 1159, 1107, 1070, 1043, 1016, 917, 747, 667 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.80 (s, 1 H, CHO), 7.42–7.27 (m, 5 H, Ar-H), 6.07 (d, *J* = 3.6 Hz, 1 H, C-1 H), 4.71–4.52 (m, 5 H, C-2 H, OCH_2Ph, OCH_2O), 4.30 (s, 1 H, C-3 H), 3.95 (d, *J* = 10.6 Hz, 1 H, OCH), 3.86 (d, *J* = 10.6 Hz, 1 H, OCH′), 3.29 (s, 3 H, OCH_3), 1.43 (s, 3 H, CH_3), 1.29 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 203.3, 136.8, 128.5 (2 C), 128.1, 127.6 (2 C), 112.0, 105.9, 96.6, 93.5, 84.6, 82.5, 72.9, 68.9, 55.3, 25.9, 25.5.

HRMS (ESI+): *m/z* $[M + Na]^+$ calcd for $C_{18}H_{24}NaO_7$: 375.14142; found: 375.14349.

3-*O*-Benzyl-6,7-dideoxy-4-[(methoxymethoxy)methyl]-1,2-*O*-(1-methylethylidene)-α-D-*galacto*-hept-6-enofuranose (5) and 3-*O*-Benzyl-6,7-dideoxy-4-[(methoxymethoxy)methyl]-1,2-*O*-(1-methylethylidene)-β-L-*altro*-hept-6-enofuranose (*ent*-5)

A 1 M solution of CH_2=CHMgBr in THF (4.26 mL, 4.26 mmol) was added to a stirred solution of aldehyde **10** (0.50 g, 1.42 mmol) in THF (5 mL) at 0 °C, and the mixture was stirred for 20 min. Sat. aq NH_4Cl (5 mL) was added, and the mixture was diluted with EtOAc (20 mL), washed successively with H_2O (20 mL) and brine (20 mL), and dried (Na_2SO_4). The solvent was evaporated and the residue was purified by column chromatography (silica gel, 15%

EtOAc–PE) to give an inseparable mixture of allylic alcohols **5** and *ent*-**5** (1:5 ratio; ^{1}H NMR) as a colorless oil; yield: 0.41 g (76%).

Ethyl (5*E*)-3-*O*-Benzyl-5,6-dideoxy-4-[(methoxymethoxy)methyl]-1,2-*O*-(1-methylethylidene)-β-L-*arabino*-hept-5-enofuranuronate (11)

EtO_2CCH_2=PPh_3 (5.25 g, 14.66 mmol) was added to a stirred solution of aldehyde **10** (4.30 g, 12.22 mmol) in CH_2Cl_2 at 0 °C, and the mixture was stirred and warmed to r.t. over 2 h. The mixture was concentrated and the residue was purified by column chromatography (silica gel, 8% EtOAc–PE) to give a colorless oil; yield: 4.53 (88%); $[\alpha]_D^{27}$ –82.7 (*c* 0.33, $CHCl_3$).

IR ($CHCl_3$): 3019, 2984, 2936, 1718, 1454, 1372, 1304, 1266, 1214, 1111, 1075, 1043, 923, 746, 668 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.43–7.28 (m, 5 H, Ar-H), 7.0 (d, *J* = 15.9 Hz, 1 H, olefinic), 6.17 (d, *J* = 15.9 Hz, 1 H, olefinic), 6.04 (d, *J* = 4.5 Hz, 1 H, C-1 H), 4.81–4.72 (m, 2 H, C-2 H, OCHPh), 4.65–4.53 (m, 3 H, OCH′Ph, OCH_2O), 4.19 (q, *J* = 7.2 Hz, 2 H, OCH_2), 4.03 (d, *J* = 1.9 Hz, 1 H, C-3 H), 3.74 (d, *J* = 10.0 Hz, 1 H, OCH), 3.57 (d, *J* = 10.0 Hz, 1 H, OCH′), 3.29 (s, 3 H, OCH_3), 1.45 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 1.28 (t, *J* = 7.2 Hz, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.1, 146.6, 137.2, 128.4 (2 C), 127.9, 127.6 (2 C), 121.6, 113.4, 105.3, 96.6, 87.4, 87.3, 85.7, 72.6, 69.6, 60.5, 55.4, 27.1, 26.9, 14.2.

MS (ESI): *m/z* = 445 $[M + Na]^+$.

(5*E*)-3-*O*-Benzyl-5,6-dideoxy-4-[(methoxymethoxy)methyl]-1,2-*O*-(1-methylethylidene)-β-L-*arabino*-hept-5-enofuranose (12)

A 25% solution of DIBAL-H in toluene (11.59 mL, 20.38 mmol) was added to a stirred solution of **11** (4.30 g, 10.19 mmol) in anhydrous CH_2Cl_2 (22 mL) at 0 °C, and the mixture was stirred for 30 min. MeOH (25 mL) was added at 0 °C, and the mixture was stirred for 10 min. Sat. aq sodium potassium tartrate (5 mL) was added and the mixture was filtered through a pad of Celite that was then washed with EtOAc (3 × 30 mL). The solvent was evaporated and the residue was purified by column chromatography (silica gel, 20% EtOAc–PE) to give a colorless oil; yield: 2.71 (70%); $[\alpha]_D^{27}$ –57.4 (*c* 0.25, $CHCl_3$).

IR ($CHCl_3$): 3423, 2929, 1454, 1377, 1213, 1105, 1028, 918, 867, 750, 700, 667 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.28 (m, 5 H, Ar-H), 6.03 (d, *J* = 4.5 Hz, 1 H, C-1 H), 5.97 (dt, *J* = 4.9, 15.9 Hz, 1 H, olefinic), 5.82 (d, *J* = 15.9 Hz, 1 H, olefinic), 4.80 (dd, *J* = 2.6, 4.5 Hz, 1 H, C-2 H), 4.78 (d, *J* = 11.7 Hz, 1 H, OCHPh), 4.64–4.53 (m, 3 H, OCH′Ph, OCH_2O), 4.17–4.09 (m, 2 H, allylic OCH_2), 4.01 (d, *J* = 2.6 Hz, 1 H, C-3 H), 3.73 (d, *J* = 10.2 Hz, 1 H, OCH), 3.47 (d, *J* = 10.2 Hz, 1 H, OCH′), 3.30 (s, 3 H, OCH_3), 1.49 (s, 3 H, CH_3), 1.39 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.5, 130.1, 129.8, 128.3 (2 C), 127.8, 127.6 (2 C), 113.4, 104.9, 96.6, 88.4, 86.9, 86.6, 72.4, 70.4, 62.8, 55.3, 27.6, 27.4.

HRMS (ESI+): *m/z* $[M + Na]^+$ calcd for $C_{20}H_{28}NaO_7$: 403.17272; found: 403.17151.

5,6-Anhydro-3-*O*-benzyl-4-[(methoxymethoxy)methyl]-1,2-*O*-(1-methylethylidene)-L-*glycero*-α-D-*galacto*-heptofuranose (13a)

Ti(*i*-PrO)$_4$ (0.17 g, 0.61 mmol) was added to a solution of (+)-DIPT (0.28 g, 1.21 mmol) in anhydrous CH_2Cl_2 (10 mL) containing powdered 4 Å MS at –20 °C, and the mixture was stirred for 20 min. Cumene hydroperoxide (1.86 mL, 12.11 mmol) was added dropwise, and the mixture was stirred for 20 min. A solution of allylic alcohol **12** (2.30 g, 6.05 mmol) in anhydrous CH_2Cl_2 (7 mL) was then added and the mixture was stirred at –20 °C for 140 min, then kept at –20 °C for 14 h. The reaction was quenched with 10% NaOH in brine (11.5 mL) and the mixture was stirred for 3 h. It was then filtered through a pad of Celite that was subsequently washed with EtOAc. The solvent was evaporated, and the residue was purified by column chromatography (silica gel, 20% EtOAc–PE) to give a colorless oil; yield: 2.06 (86%); $[\alpha]_D^{27}$ –42.6 (*c* 0.21, $CHCl_3$).

IR ($CHCl_3$): 3467, 2988, 2938, 2887, 1455, 1378, 1242, 1214, 1150, 1110, 1071, 1040, 1017, 909, 866, 750, 700, 667 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.40–7.28 (m, 5 H, Ar-H), 5.95 (d, *J* = 4.5 Hz, 1 H, C-1 H), 4.82–4.76 (m, 2 H, C-2 H, OCHPh), 4.65–4.56 (m, 3 H, OCH′Ph, OCH_2O), 4.17 (d, *J* = 2.5 Hz, 1 H, C-3 H), 3.92–3.86 (m, 1 H, CHOH), 3.74 (d, *J* = 10.0 Hz, 1 H, OCH), 3.66–3.59 (m, 1 H, CH′OH), 3.51 (d, *J* = 10.0 Hz, 1 H, OCH′), 3.39–3.35 (m, 1 H, epoxy CH), 3.31 (s, 3 H, OCH_3), 3.08–3.04 (d, *J* = 2.0 Hz, 1 H, epoxy CH′), 1.56 (s, 3 H, CH_3), 1.40 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.4, 128.3 (2 C), 127.8, 127.6 (2 C), 114.1, 104.6, 96.6, 86.9, 85.7, 84.3, 72.6, 68.0, 60.6, 56.2, 55.3, 55.2, 27.9, 27.8.

HRMS (ESI+): *m/z* $[M + Na]^+$ calcd for $C_{20}H_{28}NaO_8$: 419.16764; found: 419.16508.

3-*O*-Benzyl-6,7-dideoxy-4-[(methoxymethoxy)methyl]-1,2-*O*-(1-methylethylidene)-α-D-*galacto*-hept-6-enofuranose (5) from 13a

Ph_3P (2.0 g, 7.65 mmol), imidazole (1.04 g, 15.30 mmol), and I_2 (1.94 g, 7.65 mmol) were added sequentially to a solution of **13a** (2.02 g, 5.10 mmol) in anhydrous THF (20 mL) at 0 °C, and the mixture as stirred for 20 min. The mixture was then washed with sat. aq $Na_2S_2O_3$ (30 mL) and extracted with EtOAc (50 mL). The extracts were washed with brine (30 mL) and concentrated to give the iodo derivative **13b**, which was used directly in the next reaction.

Zn (1.33 g, 20.40 mmol) and NaI (0.77 g, 5.10 mmol) were added to a solution of the iodide **13b** (2.58 g, 5.10 mmol) in MeOH (20 mL), and the mixture was stirred at the reflux for 12 h. The solvent was evaporated and the residue was purified by column chromatography (silica gel, 15% EtOAc–PE) to give **5** as a colorless oil; yield: 1.67 (86%); $[\alpha]_D^{27}$ +61.9 (*c* 0.37, $CHCl_3$).

IR ($CHCl_3$): 3473, 2988, 2937, 2884, 1455, 1376, 1241, 1214, 1149, 1109, 1068, 1016, 919, 864, 748, 699, 667 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.28 (m, 5 H, Ar-H), 6.0 (d, *J* = 4.5 Hz, 1 H, C-1 H), 5.82 (ddd, *J* = 6.4, 10.6, 17.0 Hz, 1 H, olefinic), 5.28 (d, *J* = 17.0 Hz, 1 H, olefinic), 5.18 (d, *J* = 10.6 Hz, 1 H, olefinic), 4.83 (dd, *J* = 3.0, 4.5 Hz, 1 H, C-2 H), 4.76 (d, *J* = 11.7 Hz, 1 H, OCHPh), 4.60 (d, *J* = 6.8 Hz, 1 H, OCHO), 4.58 (d, *J* = 6.8 Hz, 1 H, OCH′O), 4.54 (d, *J* = 11.5 Hz, 1 H, OCH′Ph), 4.15 (d, *J* = 6.4 Hz, 1 H, CHOH), 4.12 (d, *J* = 3.0 Hz, 1 H, C-3 H), 3.69 (d, *J* = 10.6 Hz, 1 H, OCH), 3.59 (d, *J* = 10.6 Hz, 1 H, OCH′), 3.29 (s, 3 H, OCH_3), 2.60 (d, *J* = 6.8 Hz, 1 H, OH), 1.57 (s, 3 H, CH_3), 1.39 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.4, 135.2, 128.3 (2 C), 127.8, 127.7 (2 C), 117.4, 113.9, 104.8, 96.7, 89.7, 86.9, 85.0, 75.2, 72.3, 67.7, 55.3, 27.9, 27.7.

HRMS (ESI+): *m/z* $[M + Na]^+$ calcd for $C_{20}H_{28}NaO_7$: 403.17272; found: 403.17178.

5,6-Anhydro-3-*O*-benzyl-4-[(methoxymethoxy)methyl]-1,2-*O*-(1-methylethylidene)-D-*glycero*-β-L-*altro*-heptofuranose (14a)

Ti(*i*-PrO)$_4$ (0.03 g, 0.10 mmol) was added to a solution of (–)-DIPT (0.05 g, 0.02 mmol) in anhydrous CH_2Cl_2 (2 mL) containing powdered 4 Å MS at –20 °C and the mixture was stirred for 20 min. Cumene hydroperoxide (0.30 g, 1.95 mmol) was added dropwise and the mixture was stirred for an additional 20 min. A solution of allylic alcohol **12** (0.37 g, 0.97 mmol) in anhydrous CH_2Cl_2 (1 mL) was added, and the mixture was stirred at –20 °C for 20 min, then kept at –20 °C for 14 h. Workup as described for **13a** and purification of the residue by column chromatography (silica gel, 20% EtOAc–PE) gave a colorless oil; yield: 0.35 (90%); $[\alpha]_D^{27}$ +40.0 (*c* 0.10, $CHCl_3$).

IR ($CHCl_3$): 3481, 2988, 2938, 2886, 1455, 1379, 1243, 1213, 1152, 1110, 1019, 916, 867, 814, 753, 700, 667 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.44–7.30 (m, 5 H, Ar-H), 6.0 (d, *J* = 4.7 Hz, 1 H, C-1 H), 4.82 (dd, *J* = 3.2, 4.7 Hz, 1 H, C-2 H), 4.77 (d, *J* = 11.5 Hz, 1 H, OCHPh), 4.62 (dd, *J* = 6.4, 8.3 Hz, 2 H, OCH_2O), 4.52 (d, *J* = 11.5 Hz, 1 H, OCH′Ph), 3.95 (d, *J* = 3.2 Hz, 1 H, C-3 H), 3.91–3.80 (m, 1 H, C*H*OH), 3.75 (d, *J* = 10.2 Hz, 1 H, OCH), 3.65–3.55 (m, 1 H, C*H*′OH), 3.54 (d, *J* = 10.2 Hz, 1 H, OCH′), 3.31 (s, 3 H, OCH_3), 3.22 (d, *J* = 2.7 Hz, 1 H, epoxy CH), 3.03–2.98 (m, 1 H, epoxy CH′), 1.57 (s, 3 H, CH_3), 1.42 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.1, 128.2 (2 C), 127.7, 127.6 (2 C), 113.7, 104.5, 96.5, 86.9, 85.7, 83.1, 72.0, 68.0, 60.8, 55.1, 55.0 (2 C), 27.7 (2 C).

HRMS (ESI+): *m/z* $[M + Na]^+$ calcd for $C_{20}H_{28}NaO_8$: 419.16764; found: 419.16601.

3-*O*-Benzyl-6,7-dideoxy-4-[(methoxymethoxy)methyl]-1,2-*O*-(1-methylethylidene)-β-L-*altro*-hept-6-enofuranose (*ent*-5) from 14a

Ph_3P (0.30 g, 1.14 mmol), imidazole (0.15 g, 2.27 mmol), and I_2 (0.29 g, 1.14 mmol) were added sequentially to a solution of **14a** (0.30 g, 0.76 mmol) in anhydrous THF (5 mL) at 0 °C, and the mixture was stirred for 20 min. Workup as described for **13b** gave iodide **14b**, which was used directly in the next reaction.

To a solution of **14b** (0.38 g, 0.76 mmol) in MeOH (6 mL), Zn (0.20 g, 3.03 mmol) and NaI (0.11 g, 1.14 mmol) were added and the mixture was stirred at the reflux for 10 h. The solvent was evaporated and the residue was purified by column chromatography (silica gel, 15% EtOAc–PE) to give *ent*-**5a** as a colorless oil; yield: 0.21 (72%); $[\alpha]_D^{27}$ +33.8 (*c* 0.25, $CHCl_3$).

IR ($CHCl_3$): 3481, 2987, 2935, 2886, 1455, 1376, 1214, 1151, 1108, 1074, 1039, 922, 865, 749, 700, 667 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.39–7.27 (m, 5 H, Ar-H), 5.96 (d, *J* = 4.3 Hz, 1 H, C-1 H), 5.81 (ddd, *J* = 6.2, 10.5, 16.8 Hz, 1 H, olefinic), 5.39 (d, *J* = 16.8 Hz, 1 H, olefinic), 5.21 (d, *J* = 10.5 Hz, 1 H, olefinic), 4.83–4.78 (m, 1 H, C-2 H), 4.71 (d, *J* = 11.5 Hz, 1 H, OCHPh), 4.60 (d, *J* = 6.2 Hz, 1 H, OCHO), 4.57 (d, *J* = 6.2 Hz, 1 H, OCH′O), 4.53 (d, *J* = 11.5 Hz, 1 H, OCH′Ph), 4.30–4.25 (m, 2 H, C-3 H, CHOH), 3.75 (d, *J* = 10.5 Hz, 1 H, OCH), 3.51 (d, *J* = 10.5 Hz, 1 H, OCH′), 3.29 (s, 3 H, OCH_3), 2.83 (d, *J* = 2.4 Hz, 1 H, OH), 1.58 (s, 3 H, CH_3), 1.37 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.5, 134.6, 128.3 (2 C), 127.7, 127.6 (2 C), 117.6, 113.7, 104.6, 96.7, 90.6, 87.0, 82.8, 73.0, 72.1, 68.1, 55.4, 27.9, 27.6.

HRMS (ESI+): *m/z* $[M + Na]^+$ calcd for $C_{20}H_{28}NaO_7$: 403.17272; found: 403.17189.

3-*O*-Benzyl-6,7-dideoxy-4-[(methoxymethoxy)methyl]-5-*O*-(methoxymethyl)-1,2-*O*-(1-methylethylidene)-α-D-*galacto*-hept-6-enofuranose (15)

DIPEA (2.73 mL, 15.79 mmol) MOMCl (0.60 mL, 7.89 mmol), and a catalytic amount of DMAP were added sequentially to a stirred and cooled (0 °C) solution of **5** (1.50 g, 3.95 mmol) in CH_2Cl_2 (8 mL) at 0 °C, and the mixture was warmed to r.t. with stirring for 12 h. Workup as described for **8** and purification of the residue by column chromatography (silica gel, 15% EtOAc–PE) gave a pale-yellow oil; yield: 1.31 (78%); $[\alpha]_D^{27}$ –39.7 (*c* 0.48, $CHCl_3$).

IR ($CHCl_3$): 3016, 2988, 2938, 2888, 1455, 1379, 1240, 1214, 1147, 1075, 1024, 918, 865, 748, 699, 667 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.27 (m, 5 H, Ar-H), 6.02 (d, *J* = 4.5 Hz, 1 H, C-1 H), 5.72 (ddd, *J* = 7.9, 10.6, 17.0 Hz, 1 H, olefinic), 5.29 (d, *J* = 10.6 Hz, 1 H, olefinic), 5.27 (d, *J* = 17.0 Hz, 1 H, olefinic), 4.84 (dd, *J* = 3.4, 4.5 Hz, 1 H, C-2 H), 4.76 (d, *J* = 11.3 Hz, 1 H, OCHPh), 4.68 (d, *J* = 6.8 Hz, 1 H, OCHO), 4.62–4.50 (m, 4 H, OCH′Ph, OCH′O, OCH_2O), 4.17 (d, *J* = 3.4 Hz, 1 H, C-3 H), 4.08 (d, *J* = 7.9 Hz, 1 H, allylic OCH), 3.74 (d, *J* = 10.2 Hz, 1 H, OCH), 3.58 (d, *J* = 10.2 Hz, 1 H, OCH′), 3.34 (s, 3 H, OCH_3), 3.26 (s, 3 H, OCH_3), 1.61 (s, 3 H, CH_3), 1.41 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.7, 133.4, 128.2 (2 C), 127.7 (2 C), 127.6, 119.9, 113.9, 104.9, 96.6, 93.8, 88.7, 87.3, 85.2, 78.6, 72.2, 68.0, 55.6, 55.2, 28.1, 27.8.

HRMS (ESI+): *m/z* $[M + Na]^+$ calcd for $C_{22}H_{32}NaO_8$: 447.19894; found: 447.19805.

4-*O*-Benzyl-1,2-dideoxy-5-*C*-[(1*R*)-1-(methoxymethoxy)prop-2-en-1-yl]-6-*O*-(methoxymethyl)-D-*xylo*-hex-1-enitol (4)

A solution of furanose **15** (1.20 g, 2.83 mmol) in 70% aq AcOH (12 mL) was stirred at 55 °C for 8 h. The mixture was neutralized with solid $NaHCO_3$ and then extracted with EtOAc (3 × 40 mL). The organic layer was dried (Na_2SO_4) and concentrated to give a residue that was purified by column chromatography (silica gel, 40% EtOAc–PE) to give **16** [yield: 0.69 g (63%)] as a colorless oil, along with trace amounts of triol **17**.

A suspension of $Ph_3P^+MeBr^-$ (2.23 g, 6.25 mmol) in anhydrous THF (4 mL) at 0 °C was treated with a 2.5 M solution of *n*-BuLi in hexane (2.09 mL, 5.21 mmol), and the mixture was stirred for 25 min. A solution of **16** (0.40 g, 1.04 mmol) in anhydrous THF (3 mL) was added, and the resulting mixture was stirred while it warmed to r.t. for 2 h. The mixture was then diluted with ice-cold H_2O (15 mL) and extracted with EtOAc (2 × 20 mL). The organic phases were combined, washed with brine (10 mL), and dried (Na_2SO_4). The solvent was evaporated under reduced pressure and the residue was purified by column chromatography (silica gel, 30% EtOAc–PE) to give **4** as a colorless oil; yield: 0.26 (65%); $[\alpha]_D^{27}$ –86.4 (*c* 0.40, $CHCl_3$).

IR ($CHCl_3$): 3546, 3395, 3017, 2932, 2892, 1451, 1404, 1215, 1149, 1105, 1026, 920, 746, 667 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.36–7.27 (m, 5 H, Ar-H), 6.12–5.87 (m, 2 H, olefinic), 5.45–5.27 (m, 3 H, olefinic), 5.19 (ddd, *J* = 1.5, 3.2, 10.6 Hz, 1 H, olefinic), 4.78–4.58 (m, 7 H, OCH_2Ph, 2 × OCH_2O, allylic CH), 4.21 (d, *J* = 8.1 Hz, 1 H, allylic CH′), 3.84 (d, *J* = 1.5 Hz, 1 H, CHOBn), 3.83 (d, *J* = 10.2 Hz, 1 H, OCH), 3.63 (d, *J* = 10.2 Hz, 1 H, OCH′), 3.39 (s, 3 H, OCH_3), 3.36 (s, 3 H, OCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.8, 138.2, 133.7, 128.2 (2 C), 127.6 (3 C), 120.2, 114.7, 97.2, 94.3, 81.4, 80.2, 77.3, 75.0, 70.9, 68.9, 56.1, 55.7.

HRMS (ESI+): *m/z* $[M + Na]^+$ calcd for $C_{20}H_{30}NaO_7$: 405.18837; found: 405.18718.

(1*S*,2*R*,3*S*,6*R*)-2-(Benzyloxy)-6-(methoxymethoxy)-1-[(methoxymethoxy)methyl]cyclohex-4-ene-1,3-diol (18)

Grubbs II catalyst (10 mol%) was added to a solution of hexenitol **4** (0.20 g, 0.52 mmol) in anhydrous toluene (32 mL), and the mixture was stirred at r.t. under N_2 for 2 h. The mixture was then evaporated to dryness to give a brown residue that was purified by column chromatography (silica gel, 35% EtOAc–PE) to give a colorless oil; yield: 0.14 (76%); $[\alpha]_D^{27}$ –3.6 (*c* 0.25, $CHCl_3$).

IR ($CHCl_3$): 3436, 3032, 2927, 2889, 2852, 2825, 1453, 1400, 1215, 1146, 1096, 1029, 958, 915, 772, 746, 700, 668 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.42–7.29 (m, 5 H, Ar-H), 5.84 (d, *J* = 11.7 Hz, 1 H, olefinic), 5.80 (d, *J* = 11.7 Hz, 1 H, olefinic), 4.84–4.61 (m, 6 H, OCH_2Ph, 2 × OCH_2O), 4.47 (d, *J* = 6.0 Hz, 1 H, allylic CH), 4.08 (s, 1 H, allylic CH′), 3.93 (d, *J* = 10.6 Hz, 1 H, OCH), 3.85 (d, *J* = 10.6 Hz, 1 H, OCH), 3.67 (d, *J* = 6.0 Hz, 1 H, CHOBn), 3.39 (s, 6 H, 2 × OCH_3), 3.15–3.00 (br s, 1 H, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.1, 130.9, 128.5 (2 C), 128.0 (2 C), 127.9, 127.0, 97.6, 97.0, 81.6, 75.6 (2 C), 74.6, 70.6, 69.7, 55.7, 55.5.

HRMS (ESI+): *m/z* $[M + Na]^+$ calcd for $C_{18}H_{26}NaO_7$: 377.15707; found: 377.15648.

(1*S*,4*R*,5*S*,6*R*)-6-(Benzyloxy)-5-hydroxy-4-(methoxymethoxy)-5-[(methoxymethoxy)methyl]cyclohex-2-en-1-yl Benzoate (19)

BzCl (0.07 mL, 0.56 mmol) was added to a stirred solution of diol **18** (0.10 g, 0.28 mmol) and pyridine (0.09 mL, 1.13 mmol) in CH_2Cl_2 (2 mL), and the mixture was stirred at r.t. for 8 h. The reaction was quenched with MeOH (0.3 mL), and the mixture was stirred for 15 min. H_2O (10 mL) was added and the aqueous phase was extracted with CH_2Cl_2 (3 × 5 mL). The organic layers were combined, washed sequentially with 1.0 M aq NaOH (2 × 5 mL) and brine (5 mL), dried ($NaSO_4$), and concentrated. The residue was purified by column chromatography (silica gel, 15% EtOAc–PE) to give a colorless oil; yield: 0.11 (85%); $[\alpha]_D^{27}$ +239.9 (*c* 0.22, $CHCl_3$).

IR ($CHCl_3$): 3486, 3432, 3032, 2929, 2889, 2852, 2824, 1715, 1602, 1452, 1397, 1316, 1263, 1214, 1147, 1097, 1038, 956, 916, 771, 749, 712, 667 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 7.2 Hz, 2 H, Ar-H), 7.57 (dd, *J* = 7.2, 7.6 Hz, 1 H, Ar-H), 7.44 (t, *J* = 7.6 Hz, 2 H, Ar-H), 7.34–7.19 (m, 5 H, Ar-H), 6.01–5.92 (m, 1 H, CHOBz), 5.90–5.82 (m, 2 H, olefinic), 4.87 (d, *J* = 6.4 Hz, 1 H, OCHO), 4.85 (d, *J* = 11.7 Hz, 1 H, OCHPh), 4.72 (d, *J* = 6.4 Hz, 1 H, OCH′O), 4.69 (d, *J* = 11.7 Hz, 1 H, OCH′Ph), 4.59 (d, *J* = 6.4 Hz, 1 H, OC*H*O), 4.55 (d, *J* = 6.4 Hz, 1 H, OC*H*′O), 4.22 (d, *J* = 3.0 Hz, 1 H, allylic CH), 4.09 (d, *J* = 5.3 Hz, 1 H, CHOBn), 3.96 (d, *J* = 11.0 Hz, 1 H, OCH), 3.83 (d, *J* = 11.0 Hz, 1 H, OCH′), 3.42 (s, 3 H, OCH_3), 3.30 (s, 3 H, OCH_3), 3.14–3.06 (br s, 1 H, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.9, 137.8, 133.0, 130.1, 130.0, 129.6 (2 C), 128.3 (4 C), 127.9 (2 C), 127.7, 126.4, 97.6, 97.0, 78.0, 75.6, 75.5, 74.3, 72.1, 69.8, 55.6, 55.5.

HRMS (ESI+): *m/z* $[M + Na]^+$ calcd for $C_{25}H_{30}NaO_8$: 481.18329; found: 481.18353.

(1*S*,4*R*,5*S*,6*R*)-6-(Benzyloxy)-4,5-dihydroxy-5-(hydroxymethyl)cyclohex-2-en-1-yl Benzoate (20)

A solution of **19** (0.10 g, 0.22 mmol) and TFA (0.2 mL) in CH_2Cl_2 (2 mL) was stirred at 0 °C to r.t. for 2 h. The reaction was then quenched with DIPEA and H_2O (5 mL) was added. The mixture was extracted with CH_2Cl_2 (2 × 10 mL), and the organic layers were combined, washed with brine (5 mL), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography (silica gel, 60% EtOAc–PE) to give a pale-yellow syrup; yield: 0.055 (70%); $[\alpha]_D^{27}$ +238.0 (*c* 0.15, $CHCl_3$).

IR ($CHCl_3$): 3430, 3020, 2925, 2854, 1713, 1451, 1317, 1214, 1109, 1027, 746, 667 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 7.4 Hz, 2 H, Ar-H), 7.59 (dd, *J* = 7.3, 7.5 Hz, 1 H, Ar-H), 7.46 (dd, *J* = 7.7, 7.6 Hz, 2 H, Ar-H), 7.33–7.21 (m, 5 H, Ar-H), 5.96 (dd, *J* = 2.9, 8.7 Hz, 1 H, CHOBz), 5.87–5.77 (m, 2 H, olefinic), 4.85 (d, *J* = 11.2 Hz, 1 H, OCHPh), 4.68 (d, *J* = 11.2 Hz, 1 H, OCH′Ph), 4.38 (d, *J* = 2.6 Hz, 1 H, allylic CH), 4.06 (d, *J* = 5.6 Hz, 1 H, CHOBn), 3.94 (d, *J* = 11.8 Hz, 1 H, OCH), 3.83 (d, *J* = 11.8 Hz, 1 H, OCH′), 3.12–2.45 (br s, 1 H, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.9, 137.4, 133.3, 130.7, 129.8, 129.7 (2 C), 128.5 (4 C), 128.1 (3 C), 126.5, 78.4, 75.0, 74.2, 72.2, 71.4, 65.0.

HRMS (ESI+): *m/z* $[M + Na]^+$ calcd for $C_{21}H_{22}NaO_6$: 393.13086; found: 393.13151.

(1*S*,4*R*,5*S*,6*R*)-5-[(Benzoyloxy)methyl]-6-(benzyloxy)-5-hydroxycyclohex-2-ene-1,4-diyl Dibenzoate (21)

BzCl (0.04 mL, 0.32 mmol) was added to a stirred solution of diol **20** (0.03 g, 0.08 mmol) and pyridine (0.04 mL, 0.49 mmol) in CH_2Cl_2 (1 mL), and the mixture was stirred at r.t. for 8 h. Workup as described for **19** and purification of the residue by column chromatography (silica gel, 20% EtOAc–PE) gave a colorless oil; yield: 0.04 (81%); $[\alpha]_D^{27}$ –22.6 (*c* 0.13, $CHCl_3$).

IR ($CHCl_3$): 3592, 3020, 2927, 1719, 1452, 1316, 1262, 1214, 1095, 1069, 1026, 749, 667 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.03 (dd, *J* = 1.5, 8.5 Hz, 2 H, Ar-H), 7.89 (dd, *J* = 1.3, 8.5 Hz, 2 H, Ar-H), 7.67 (dd, *J* = 1.3, 8.5 Hz, 2 H, Ar-H), 7.62–7.55 (m, 1 H, Ar-H), 7.50–7.21 (m, 13 H, Ar-H), 6.09–5.85 (m, 4 H, olefinic, 2 × CHOBz), 5.02 (d, *J* = 11.5 Hz, 1 H, CHOBz), 4.85 (d, *J* = 11.5 Hz, 1 H, CH′OBz), 4.77 (d, *J* = 12.1 Hz, 1 H, OCHPh), 4.58 (d, *J* = 12.1 Hz, 1 H, OCH′Ph), 4.35 (d, *J* = 3.6 Hz, 1 H, CHOBn), 2.92–2.86 (br s, 1 H, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.3, 165.8, 165.7, 137.1, 133.4, 133.2, 132.8, 129.7 (2 C), 129.6, 129.5 (3 C), 129.3 (2 C), 129.2, 129.1, 128.6 (2 C), 128.5 (4 C), 128.3 (3 C), 128.0 (2 C), 126.6, 76.7, 74.0, 73.5, 72.6, 70.2, 65.3.

HRMS (ESI+): *m/z* $[M + Na]^+$ calcd for $C_{35}H_{30}NaO_8$: 601.18329; found: 601.18451.

(1*S*,4*R*,5*R*,6*R*)-5-(Benzoyloxymethyl)-5,6-dihydroxy cyclohex-2-ene-1,4-diyl Dibenzoate (2; 6-*O*-Benzoylzeylenol)

$TiCl_4$ (0.02 g, 0.09 mmol) in CH_2Cl_2 (1 mL) was added to a solution of tribenzoate **21** (0.03 g, 0.04 mmol) in CH_2Cl_2 (1.5 mL) at 0 °C under N_2, and the mixture was stirred at r.t. for 3 h. Sat. aq $NaHCO_3$ (5 mL) was added and the mixture was extracted with $CHCl_3$ (2 × 15 mL). The organic layers were combined, washed successively with H_2O (5 mL) and brine (5 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 30% EtOAc–PE) to give a white solid; yield: 0.02 (71%); mp 137–139 °C; $[\alpha]_D^{27}$ –58.1 (*c* 0.12, $CHCl_3$) {lit.[1b] $[a]^{22}_D$ –59.7 (*c* 0.39, $CHCl_3$)}.

IR ($CHCl_3$): 3485, 2924, 2853, 1720, 1452, 1318, 1267, 1217, 1111, 1070, 1027, 964, 772, 710, 668 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 7.7 Hz, 2 H, Ar-H), 8.03 (d, *J* = 8.3 Hz, 2 H, Ar-H), 7.86 (d, *J* = 7.7 Hz, 2 H, Ar-H), 7.61–7.53 (m, 2 H, Ar-H), 7.50 (dd, *J* = 7.2, 7.7 Hz, 1 H, Ar-H), 7.47–7.37 (m, 4 H, Ar-H), 7.33 (t, *J* = 7.7 Hz, 2 H, Ar-H), 6.09 (dd, *J* = 2.8, 9.9 Hz, 1 H, CHOBz), 6.02 (dd, *J* = 1.7, 9.9 Hz, 1 H, CH′OBz), 5.84–5.76 (m, 2 H, olefinic), 4.92 (d, *J* = 12.1 Hz, 1 H, C*H*OBz), 4.63 (d, *J* = 12.1 Hz, 1 H, C*H*′OBz), 4.35 (d, *J* = 5.0 Hz, 1 H, OCH), 3.64–3.57 (br s, 1 H, OH), 3.36–3.27 (br s, 1 H, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.1, 167.0, 165.7, 133.42, 133.39, 133.1, 129.8 (2 C), 129.7 (2 C), 129.6 (2 C), 129.4, 129.3, 129.2, 128.7, 128.5 (2C), 128.4 (2 C), 128.3 (2 C), 126.6, 74.9, 73.4, 71.6, 71.3, 66.7.

HRMS (ESI+): *m/z* $[M + Na]^+$ calcd for $C_{28}H_{24}NaO_8$: 511.13634; found: 511.13675.

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Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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(5) Note that in ref. 4b, the zeylenol isolated from *Uvaria rufa* is depicted as the (–)-**1** enantiomer, although no chiroptical data are presented. A subsequent report on this same species assigned the isolate as (+)-**1** on the basis of its positive $[\alpha]_D$ value; see ref. 2b.
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