A flexible synthesis of cyclopentitol derivatives based on ring-closing metathesis of carbohydrate-derived 1,6-dienes

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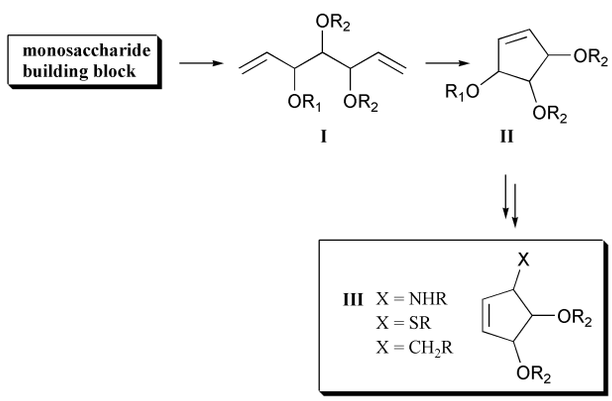
Four partially protected stereoisomeric cyclopentenetriols **5**, **10**, **15** and **21** have been prepared by ring-closing metathesis of carbohydrate-derived 1,6-dienes. The presence of a differentiated allylic alcohol in the cyclopentenetriols allows a variety of synthetic transformations, underlining the synthetic use of the prepared cyclopentenetriol derivatives as chiral building blocks.

Introduction

Cyclopentitols, hydroxylated cyclopentane derivatives of varying nature and complexity, form an integral part of a broad class of natural products. Relevant examples are the glycosidase inhibitors mannostatin A, allosamidin and trehalostatin,[1] the cancer therapeutic agent neplanocin[2] and the hypermodified nucleoside queuosine[3] (nucleoside Q). The remarkable biological activities exerted by cyclopentitol derivatives have inspired several research laboratories to explore their chemical synthesis, resulting in various successful total syntheses.[4] The target-oriented approaches generally applied, however, normally exclude the rapid generation of synthetic analogues of naturally occurring cyclopentitols. The development of methodologies that ensure an easy access to cyclopentitols varying in stereochemistry and substitution pattern should eventually lead to synthetic analogues of natural products with favourable properties in terms of activity, toxicity and bioavailability. In this respect, we have recently demonstrated the usefulness of carbohydrate-derived dienes, in combination with ring-closing metathesis (RCM),[5] in the construction of a variety of highly functionalised hetero- and carbocycles.[6,7,8] As an extension of these studies, we here present the results on the transformation of four easily accessible and cheap carbohydrate derivatives into the four partially protected cyclopentenetriols **5**, **10**, **15** and **21**, respectively. We further demonstrate the feasibility of a selected cyclopentenetriol (*i.e.* cyclopentene derivative **5**) for the ensuing introduction of additional hetero- (nitrogen, sulfur) and carbon functionalities through well-established synthetic procedures.

Results and discussion

The general synthetic strategy is outlined in Scheme 1. In the first step, a suitably protected monosaccharide is transformed into the corresponding, orthogonally protected 3,4,5-trihydroxy-1,6-diene **I**. Ensuing ring-closing metathesis affords 3,4,5-trihydroxycyclopentene **II**, the orthogonal functionalisation of which allows synthetic modifications leading to the introduction of additional functionalities onto the cyclopentene scaffold, as in **III**.



Scheme 1

In Scheme 2, the synthesis of partially protected cyclopentenetriols **5**, **10**, **15** and **21** is presented. Regioselective removal of the 5,6-isopropylidene group in benzoyl 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose (**1**),[9] followed by treatment with triethylorthoformate led, after acid catalysed thermal rearrangement[10] to the isolation of **2** in 93% yield over the three steps. Anomeric debenzoylation (**2** to **3**, 96%) and consecutive Wittig olefination gave, after purification by distillation, diene **4** in an overall yield of 84% based on **1**. RCM of **4** under the influence of Grubbs' ruthenium alkylidene catalyst ($Cl_2(PCy_3)_2Ru{=}CHPh$)[11] gave the homogeneous (3*R*,4*S*,5*R*)-3,4-*O*-isopropylidenecyclopentene-3,4,5-triol (**5**)[12] in 95% yield.

In a related sequence of transformations, (3*R*,4*S*,5*S*)-3,4-*O*-cyclohexylidenecyclopentene-3,4,5-triol (**10**) was prepared. The required key intermediate **8** proved to be readily accessible by adaptation of the literature procedure,[13] starting from 2,3-*O*-hexylidene-D-ribofuranose **6**. Treatment of **6** with excess vinyl magnesium bromide afforded (3*S*,4*S*,5*R*,6*R*)-4,5-*O*-cyclohexylidene-3,4,5,6,7-pentahydroxyhex-1-ene (**7**), which, upon reaction with sodium periodate, led to the formation of compound **8** in 78% yield over the two steps. Subjection of **8** to anomeric Wittig olefination and exposure of the resulting 1,6-diene **9** to Grubbs' catalyst afforded the desired partially protected cyclopentene **10** in 70% yield over the last two steps. The synthesis of (3*S*,4*S*,5*R*)-3,4-*O*-benzylcyclopentene-3,4,5-triol (**15**) was accomplished as follows. Treatment of the known[14] 3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hex-5-enofuranose (**11**) with ethanolic HCl followed by benzylation of the resulting free hydroxy function furnished the anomeric mixture of ethyl furanosides **12**. Subsequent liberation of the anomeric hydroxy was effected by treatment with acetic acid at 65 °C for three days, affording hemiacetal **13** in 79% over the three steps.

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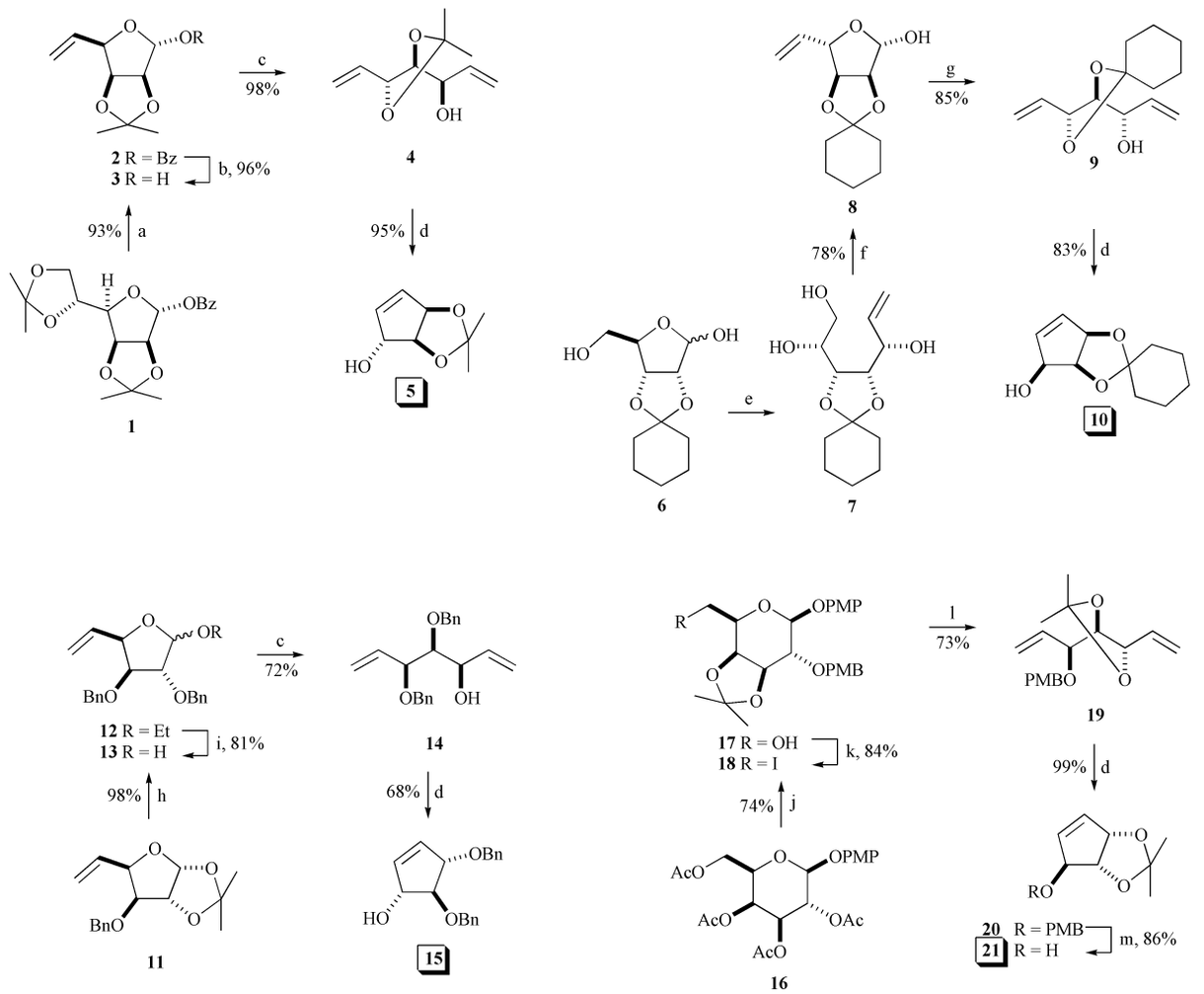


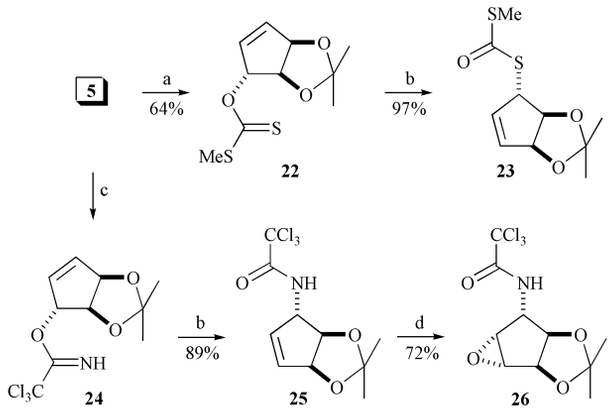
Scheme 2 *Reagents and conditions*: a) 1. 80% HOAc, 40 °C, 2. $HC(OEt_3)$, HOAc, 80 °C, 3. Ph_3CCO_2H (cat), neat, 170 °C; b) KO*t*Bu, MeOH; c) $Ph_3P^+CH_3Br^-$, *n*-BuLi, THF, −20 °C to rt; d) $Cl_2(PCy_3)_2Ru$=CHPh (0.5–5 mol%), CH_2Cl_2; e) vinylmagnesium bromide (5 eq.), THF, −50 °C to rt; f) $NaIO_4$ (2 eq.), MeOH–H_2O 85 : 15; g) $Ph_3P^+CH_3Br^-$ (2.1 eq.), KO*t*Bu (2.1 eq.), THF–HMPA, −78 °C to rt; h) 1. EtOH, HCl, 2. NaH, BnBr, DMF; i) HOAc–H_2O 3 : 1, 3 days; j) 1. KO*t*Bu, MeOH, 2. TBDPSCl, pyridine, 3. dimethoxypropane, *p*-TsOH (cat), 4. *p*MeOBnCl, NaH, DMF, 5. TBAF, THF; k) imidazole, triiodoimidazole, Ph_3P, toluene, reflux; l) 1. Zn, EtOH–H2O, reflux, 2. $Ph_3P^+CH_3Br^-$, *n*-BuLi, THF, −20 °C to rt; m) DDQ, CH_2Cl_2–H_2O.

Subjection of **13** to the two-step sequence as outlined for the conversion of **3** to **5** proceeded smoothly to give cyclopentene derivative **15** in 39% yield based on **11**.

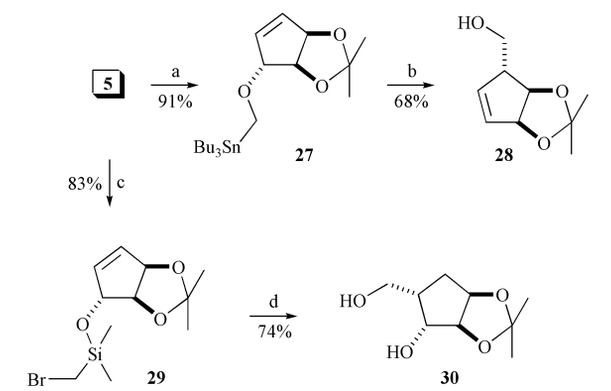
The results presented so far comprise the facile transformation of D-sugars to a set of three diastereoisomeric, orthogonally protected cyclopentenetriols **5**, **10** and **15**. The flexibility of our strategy is further illustrated by the conversion of D-galactose into (3*S*,4*R*,5*S*)-3,4-*O*-isopropylidenecyclopentene-3,4,5-triol (**21**) (the enantiomer of **5**). To this end, the known[15] peracetylated *p*-methoxyphenyl-α-D-galactopyranoside **16** was converted into the primary iodide **18** *via* the following six step sequence (see Scheme 2): Saponification of the acetate groups and subsequent regioselective silylation, introduction of the isopropylidene protective group, protection of the remaining hydroxy function as the *p*-methoxybenzyl ether, deprotection of the *t*-butyldiphenylsilyl group and treatment of the resulting **17** with 2,4,5-triiodoimidazole and triphenylphosphine according to the method of Garegg and Samuelsson.[16] Ensuing reductive rearrangement[17] of **18** proceeded smoothly to give the open-chain aldehyde, which was subjected to Wittig olefination to provide orthogonally protected 1,6-diene **19** in good yield (45% based on **16**). RCM and subsequent DDQ-mediated oxidative cleavage of the *p*-methoxybenzyl protecting group in **20** gave the desired partially protected cyclopentenetriol **21** ($[a]_D^{20}$ +110.4) in 85% over the last two steps. The NMR spectra of **21** (both proton and carbon) proved to be identical to those of enantiomeric **5** ($[a]_D^{20}$ −110.0).

At this stage, having easy access to partially protected cyclopentenetriols of different stereochemistry, we set out to demonstrate their potential usefulness as synthetic intermediates. To this end, we selected compound **5**, which we have subjected to various synthetic transformations. For instance, installation of a xanthate ester was readily accomplished by reaction of **5** with carbon disulfide followed by methylation to afford **22** (Scheme 3). Subsequent thermal rearrangement led to the stereoselective formation of mixed dithiocarbonate **23** in 62% yield over the two steps. In a related synthetic sequence of reactions, compound **5** was transformed into protected aminocyclopentenediol **25**. Reaction of **5** with trichloroacetonitrile in the presence of the base DBU afforded trichloroacetimidate **24**, which, upon heating in xylenes under reflux, rearranged to give target compound **25** in high yield.[18] The synthetic potential of **25** is further demonstrated by subsequent epoxidation (**25** to **26**) in good yield and excellent stereoselectivity. It is of interest to note that both (unprotected) aminocyclopentenediols **25** and **26** are found as an integral part of hypermodified nucleosides of the queuosine family.[19]

Apart from the successful [3,3]-sigmatropic rearrangements of compounds **22** and **24** to allow the introduction of heteroatoms onto the cyclopentene scaffold, it was realised that **5** would also be amenable to the stereoselective installation of a hydroxymethylene functionality. As a first example, attention was focused on the installation of a hydroxymethyl substituent *via* a [2,3]-Wittig–Still[20] rearrangement. Condensation of **5**



Scheme 3 *Reagents and conditions:* a) 1. NaH, CS_2, toluene, 2. MeI, DMF; b) xylenes, reflux; c) DBU, CCl_3CN, CH_2Cl_2, 0 °C; d) 3-methyl-3-trifluoromethyldioxirane, CH_3CN.



Scheme 4 *Reagents and conditions:* a) Bu_3SnCH_2I, KH, dibenzo-18-crown-6, THF, 0 °C; b) *n*-BuLi, THF, −78 °C; c) $ClSiMe_2CH_2Br$, CH_2Cl_2, Et3N; d) 1. Bu3SnH (1.5 eq.), AIBN (cat), benzene, reflux, 2. H_2O_2 (30%, aq.), Na_2CO_3, THF–MeOH, 5 °C.

with tributyliodomethylstannane (Scheme 4), followed by transmetallation of **27** with *n*-butyllithium afforded the expected hydroxymethylated species **28** in 68% yield, together with 20% recovery of **5**. Alternatively, introduction of an α-halosilylether provides a handle for radical cyclisation while the silylether functions as a masked hydroxy moiety. The latter Stork[21] radical cyclisation approach generates a hydroxymethyl substituent *cis* relative to the original alcohol.[22] Silylation of **5** with bromomethyldimethylsilyl chloride afforded **29** in 83% yield (Scheme 4). 5-Exo-*trig* radical cyclisation of **29** followed by *in situ* hydrogen peroxide-mediated oxidation afforded 1,2-*O*-isopropylidene-4a-carba-β-L-xylofuranose **30** in 73% yield over two steps.

In conclusion, partially protected 1,6-heptadiene-3,4,5-triols, which are easily accessible from suitably functionalised monosaccharides, proved to be excellent starting compounds for the RCM-mediated construction of partially protected, chiral cyclopentenetriols. The cyclopentenetriols are useful assets in the preparation of higher functionalised cyclopentane derivatives. The latter is demonstrated by the transformation of cyclopentenetriol **5** into highly versatile structural entities, including side-chain modifications of nucleoside Q (**25** and **26**) and the carba-L-xylofuranose derivative **30**.

Experimental

General methods and materials

^{1}H- and ^{13}C-NMR spectra were recorded on a Jeol JNM-FX-200 (200/50.1 MHz) or on a Bruker DPX-300 (300/75.1 MHz). NMR shifts are reported in ppm (δ) relative to tetramethylsilane, coupling constants *J* are given in Hz. Optical rotations were determined at 20 °C, in units of 10^{-1} deg cm^2 g^{-1}by means of a Propol automatic polarimeter at the sodium D-line. Mass spectrometry was performed on a PE/SCIEX API 165 equipped with an ion spray interface. Column chromatography was performed on Baker silica gel (0.063–0.200 mm) or on Merck silica gel (0.040–0.063 mm) column. TLC analysis was conducted on DC-fertigfolien (Schleicher and Schüll F1500 LS254) or Merck silica 60 F245 coated aluminum sheets. Toluene, CH_2Cl_2, triethylamine and xylenes were boiled under reflux with CaH_2 for 3 hours, distilled and stored over molecular sieves (4 Å). THF and Et_2O were distilled from $LiAlH_4$ prior to use. HMPA was distilled directly before use under high vacuum. All other solvents (Baker, *pro analysis*) were stored over molecular sieves (4 Å) except for methanol and acetonitrile (Rathburn, HPLC grade), which were stored over molecular sieves (3 Å). Methyl triphenylphosphonium bromide was dried over KOH under high vacuum at 140 °C for 24 hours prior to use. Grubbs' catalyst $Cl_2(PCy_3)_2Ru$=CHPh was prepared according to the literature procedure.[11] *n*-BuLi (1.6 M in hexanes, Aldrich) and vinylmagnesium bromide (1 M in THF, Aldrich), were used as received.

Benzoyl 2,3-*O*-isopropylidene-α-D-*lyxo*-hex-5-enofuranose (2)

Benzoyl 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose (**1**) (28.7 g, 78.76 mmol) was dissolved in HOAc (175 mL) and heated to 40 °C. Water (75 mL) was added and stirring was continued for 135 minutes after which time TLC analysis showed complete conversion (R_f 0.55, EtOAc). Solvents were evaporated and the remainder was coevaporated with toluene (2 × 50 mL). The residue was taken up in $(EtO)_3CH$, heated to 80 °C and HOAc was added (1.5 mL). The reaction was complete within 30 minutes (R_f 0.60, EtOAc–petroleum ether 30 : 70). The solution was concentrated and heated to 170 °C in an open flask. Triphenyl acetic acid (100 mg, 0.347 mmol, 0.44 mol%) was added and after 4 hours all starting material had been transformed into a higher running product (R_f 0.55, EtOAc–petroleum ether, 2 : 8). The resulting clear oil was allowed to cool to room temperature. Column chromatography (20% EtOAc in petroleum ether) gave the homogeneous title compound (21.5 g, 93%). ^{13}C-NMR (50.1 MHz, $CDCl_3$): δ 24.7, 25.9 (2 × CH_3, isopr.), 76.4, 77.0, 77.6 (C-2, C-3, C-4), 101.0 (C-1), 112.9 (C_q, isopr.), 119.6 (C-6), 128.2, 129.4, 131.3, 133.2 (CH_{arom} Bz, C-5), 164.7 (C=O). ^{1}H NMR (200 MHZ, $CDCl_3$): δ 1.36 (s, 3H, CH_3, isopr.), 1.39 (s, 3H, CH_3, isopr.), 4.64 (m, 1H), 4.86 (m, 2H) (H-2, H-3, H-4), 5.40 (m, 2H, H-6), 5.98 (m, 1H, H-5), 6.42 (s, 1H, H-1), 7.41–8.04 (m, 5H, CH_{arom} Bz).

2,3-*O*-Isopropylidene-α-D-*lyxo*-hex-5-enofuranose (3)

Compound **2** (21.0 g, 72.3 mmol) was dissolved in MeOH (100 mL), 100 mg KO*t*Bu was added and the solution was stirred for 24 h. TLC analysis revealed total conversion into a lower running product (R_f 0.65, EtOAc–petroleum ether 1 : 1). Dowex-W50X4-H^+ was added until neutral pH, the resin was filtered and the filtrate was concentrated under reduced pressure. Column chromatography (30% EtOAc in petroleum ether) gave pure **3** (12.95 g, 96%) as a clear oil. ^{13}C-NMR (50.1 MHz, $CDCl_3$): δ 24.7, 25.8 (2 × CH_3, isopr.), 81.2, 81.3, 85.7 (C-2, C-3, C-4), 100.7 (C-1), 112.5 (C_q isopr.), 119.2 (C-6), 132.0 (C-5). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.32 (s, 3H, CH_3 isopr.), 1.48 (s, 3H, CH_3 isopr.), 3.38 (br s, 1H, OH), 4.63 (m, 2H), 4.74 (m, 1H) (H-2, H-3, H-4), 5.31–5.45 (m, 2H, H-6), 5.95 (m, 1H, H-5).

(3*R*,4*S*,5*R*)-3,4-Isopropylidenehepta-1,6-diene-3,4,5-triol (4)

Methyltriphenylphosphonium bromide (4.22 g, 11.81 mmol) was dissolved in 50 mL of THF and cooled to −20 °C. *n*-BuLi (1.6 M in hexanes, 7 mL, 11.8 mmol) was added and the solution was allowed to warm to rt, stirred for 30 minutes, and

cooled to −20 °C. A solution of 998 mg (5.36 mmol) of **3** in THF (5 mL) was slowly added to the reaction mixture *via* the cold wall of the flask and the reaction mixture was allowed to warm to rt and stirred overnight. TLC analysis revealed the appearance of a higher running spot (R_f 0.60, EtOAc–petroleum ether 1 : 1). A little sat. aq. NH_4Cl was added and the solution was concentrated to a small volume. The residue was taken up in Et_2O (100 mL), extracted with sat. aq. NH_4Cl and water. The organic phase was dried ($MgSO_4$), filtered and concentrated. Little Et_2O and petroleum ether were added after which a white solid precipitated. The precipitate was filtered off over Celite, rinsed with ice-cold Et_2O and the filtrate was concentrated. Column chromatography (20% EtOAc in petroleum ether) gave pure **4** (0.96 g, 98%). ^{13}C-NMR (50.1 MHz, $CDCl_3$): δ 24.9, 27.3 (2 × CH_3, isopr.), 70.4, 78.8, 80.6 (C-3, C-4, C-5), 108.4 (C_q, isopr.), 116.9, 119.0 (C-1, C-7), 134.0, 136.5 (C-2, C-6). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.41 (s, 3H, CH_3, isopr.), 1.55 (s, 3H, CH_3, isopr.), 4.08 (m, 2H), 4.62 (dd, *J* 7.6, *J* 7.8 Hz, 1H) (H-3, H-4, H-5), 5.22–5.43 (m, 4H, H-1, H-7), 5.78–6.12 (m, 2H, H-2, H-6). MS (CI): *m*/*z* 207.0 $[M + Na]^+$.

(3*R*,4*S*,5*R*)-3,4-*O*-Isopropylidenecyclopentene-3,4,5-triol (5)

Compound **4** (3.10 g, 16.8 mmol) was dissolved in CH_2Cl_2 (50 mL), the solution was degassed by passing through a stream of argon for 15 min and 69 mg (0.5 mol%) of Grubbs' catalyst $(PCy_3)_2Cl_2Ru$=CHPh was added under an atmosphere of argon. After 5 hours TLC analysis revealed complete conversion (R_f 0.40, EtOAc–petroleum ether 4 : 6). The reaction mixture was exposed to air and purified by column chromatography (40% EtOAc in petroleum ether) to yield 2.61 g (95%) of homogeneous **5**. ^{13}C-NMR (75.1 MHz, $CDCl_3$): δ 25.3, 26.8 (2 × CH_3 isopr.), 80.0 (C-5), 83.9 (C-4), 85.4 (C-3),111.2 (C_q isopr.), 134.4, 134.6 (C-1, C-2). ^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.35 (s, 3H, CH_3 isopr.), 1.40 (s, 3H, CH_3 isopr.), 1.80 (br s, OH) 4.53 (d, H-3 *J* 5.5 Hz, 1H), 4.80 (s, 1H, H-5), 5.30 (m, 1H, H-4), 5.92 (m, 1H), 6.03 (m, 1H), (H-1, H-2). MS (ESI): *m*/*z* 157.2 $[M + H]^+$; $[\alpha]_D^{20}$ −110 (*c*=1, $CHCl_3$).

2,3-*O*-Cyclohexylidene-αβ-L-*ribo*-hex-5-enofuranose (8)

2,3-*O*-Cyclohexylidene-D-ribose (**6**) (3.47 g,15.1 mmol) was dissolved in THF (30 mL) and cooled to −50 °C. Vinylmagnesium bromide (75 mL, 1 M in THF) was slowly added *via* the cold wall of the flask maintaining the temperature at −50 °C. After addition the solution was allowed to warm to room temperature and stirred overnight after which all starting material had been transformed into a lower running product (R_f 0.60, EtOAc–petroleum ether 7 : 3). The solution was cooled to 0 °C, and 5 g of solid NH_4Cl was added, followed by the slow addition of sat. aq. NH_4Cl (20 mL). THF was evaporated under reduced pressure and EtOAc (200 mL) was added followed by saturated aqueous NH_4Cl (100 mL). The EtOAc layer was collected and concentrated, providing crude **7** as an oil which was used in the next step without further purification. Thus, **7** was dissolved in 85 mL of MeOH and cooled to 0 °C. Water (15 mL) was added followed by $NaIO_4$ (6.62 g, 31 mmol). The solution was allowed to warm to room temperature and was stirred for 45 minutes after which the reaction was complete (R_f 0.80, EtOAc–petroleum ether 6 : 4) as judged by TLC. Solids were filtered over Celite and the filtrate was washed with Et_2O. Solvents were removed under reduced pressure and the residue was taken up in Et_2O (200 mL) and washed with water (200 mL). The organic phase was dried ($MgSO_4$), filtered and concentrated. Column chromatography (20⟶40% EtOAc in petroleum ether) gave 2.64 g (78%) of homogeneous **8** as an oil. ^{13}C-NMR (50.1 MHz $CDCl_3$): δ 23.3, 23.6, 24.7, 34.1, 35.9 (5 : *C*H_2, Cy), 82.0, 84.4, 86.0 (C-2, C-3, C-4), 101.2 (C-1), 112.7 (C_q Cy), 116.4 (C-6), 142.3 (C-5). ^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.61 (m, 10H, 5 × CH_2, Cy), 4.65 (m, 3H, H-2, H-3, H-4), 5.15–5.43 (m, 2H, H-6), 5.49 (d, *J* 3.0 Hz, 1H, H-1), 5.92–6.10 (m, 1H, H-5).

(3*R*,4*S*,5*S*)-3,4-*O*-Cyclohexylidenehepta-1,6-diene-3,4,5-triol (9)

To methyl triphenylphosphonium bromide, 3.40 g (9.53 mmol) in THF (8 mL) and HMPA (2 mL) was added at −78 °C, KO*t*Bu (1.97 g, 9.5 mmol). The resulting solution was stirred for an additional hour at −20 °C. A solution of **8** (980 mg, 4.33 mmol) in THF (2 mL) was added and the solution was allowed to warm to room temperature. After 14 hours all starting material had been transformed into a slightly higher running product as indicated by TLC (R_f 0.60, EtOAc–petroleum ether 4 : 6). The reaction mixture was quenched with aq. sat. NH_4Cl (50 mL) and extracted with Et_2O (100 mL). The ether layer was dried ($MgSO_4$), filtered and concentrated. Column chromatography (5%⟶15% EtOAc–petroleum ether) gave homogeneous **9** (0.83 g, 85%). ^{13}C-NMR (50.1 MHz, $CDCl_3$): δ 23.6, 23.9, 25.0, 34.6, 37.4 (5 × CH_2, Cy), 70.8, 78.2, 80.2 (C-3, C-4, C-5), 109.4 (C_q, Cy), 115.9, 118.0 (C-1, C-7), 134.2, 137.7 (C-2, C-6). ^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.17–1.68 (m, 10H, 5 × CH_2, Cy), 1.81 (d, *J* 4.4 Hz, 1H, OH), 4.02 (m 1H), 4.18 (m, 1H), 4.80 (m,1H) (H-3, H-4, H-5), 5.21–5.49 (m, 4H, H-1, H-7), 5.97–6.15 (m, 2H, H-1, H-6).

(3*R*,4*S*,5*S*)-3,4-*O*-Cyclohexylidenecyclopentene-3,4,5-triol (10)

Compound **9** (275 mg, 1.23 mmol) was dissolved in CH_2Cl_2 (25 mL). This solution was degassed by bubbling through nitrogen for 10 minutes and 51 mg (5 mol%) of $Cl_2(PCy_3)_2$-Ru=CHPh was added. The reaction mixture was stirred overnight in a sealed flask, after which time TLC (EtOAc–petroleum ether 1 : 4) indicated total conversion of starting material into a lower running product (R_f 0.40, EtOAc–petroleum ether 1 : 4). The reaction mixture was exposed to air, concentrated and purified by column chromatography. Column chromatography (15% EtOAc in petroleum ether) gave 192 mg (80%) of homogeneous **10** as a colourless oil. ^{13}C-NMR (50.1 MHz, $CDCl_3$): δ 23.6, 23.8, 24.8, 35.9, 37.2 (5 × CH_2, Cy), 74.0, 76.5, 83.1 (C-3, C-4, C-5), 132.0, 136.2 (C-1, C-2). ^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.28–1.66 (m, 10H, CH_2 Cy), 2.77 (d, *J* 9.9 Hz, 1H), 4.53 (dd, *J* 5.9 Hz, *J* 9.9 Hz, 1H, H-5), 4.74 (t, *J* 5.9 Hz, 1H, H-3), 5.02 (dd, *J* 1 Hz, *J* 5.5 Hz, 1H, H-4), 5.88 (m, 2H, H-1, H-2). MS (CI): *m*/*z* $(M + Na)^+$ 219.0; $[\alpha]_D^{20}$ −9.6 (*c*=1, $CHCl_3$).

Ethyl 2,3-di-*O*-benzyl-αβ-D-*xylo*-hex-5-enofuranoside (12)

3-*O*-benzyl-5,6-dideoxy-αβ-D-*xylo*-hex-5-enofuranose[12] **11** (7.1 g, 29.6 mmol) was dissolved in absolute EtOH (100 mL) and cooled to 0 °C, then a 3 M HCl solution in EtOH (5 mL) was added and the mixture was allowed to warm to rt. After 3 hours all starting material had been transformed into two new spots (R_f 0.30 and 0.40, EtOAc–petroleum ether 7 : 3). Sat. aq. $NaHCO_3$ was added (3 mL) and the resulting suspension was reduced to a small volume, taken up in EtOAc (200 mL) and washed with water (2 × 100 mL). The EtOAc layer was dried ($MgSO_4$), filtered and concentrated to give 7.74 g (99%) of the ethyl glycosides as a mixture of anomers, which were used in the next reaction without further purification. Thus, the ethyl glycosides (7.28 g, 27.6 mmol) were dissolved in DMF (100 mL) and cooled to 0 °C. NaH (2.0 g, 50 mmol, 60% in mineral oil) was added followed by benzylbromide (4.75 mL, 40 mmol). After 1 hour TLC analysis revealed complete transformation into two higher running products (R_f 0.50 and 0.55, EtOAc–petroleum ether 1 : 9). Methanol (2 mL) was added and the solution was stirred for a further 30 minutes. The mixture was poured into Et_2O (300 mL) and washed with water (2 × 500 mL). The organic layers were dried ($MgSO_4$), filtered and concentrated. Column chromatography (EtOAc–

petroleum ether 15 : 85) gave 9.87 g (99%) of the title compound as an anomeric mixture. ^{13}C-NMR (50.1 MHz, $CDCl_3$): δ 14.8, 14.9 (2 × CH_3,,OEt), 63.1, 63.4 (2 × CH_2, OEt), 71.5, 71.7, 71.8, 72.1 (4 × CH_2, Bn), 78.2, 81.6, 82.3, 82.4, 83.4, 87.0 (C-2, C-3, C-4), 99.0, 106.3 (C-1), 117.8, 117.9 (C-6), 127.3, 127.4, 127.5, 127.7, 128.0, 128.1 (CH_{arom} Bn), 134.1, 134.9 (C-5), 137.6 (C_q Bn).

2,3-Di-*O*-benzyl-D-*xylo*-hex-5-enofuranose (13)

Compound **12** (0.65 g, 1.80 mmol) was dissolved in HOAc (7.5 mL), heated to 65 °C and water (2.5 mL) was slowly added. The solution was kept at 65 °C for three days. TLC analysis indicated complete conversion (R_f 0.40, EtOAc–petroleum ether 3 : 7). Toluene (10 mL) was added and the solution was evaporated to dryness, and coevaporated with toluene (2 × 3 mL). Column chromatography (EtOAc–petroleum ether 25 : 75) gave homogeneous **13** (0.48 g, 81%) as an anomeric mixture. ^{13}C-NMR (50.1 MHz, $CDCl_3$): δ 71.5, 71.8, 72.0, 72.5 (4 × CH_2Bn), 79.2, 81.6, 81.7, 82.2, 82.7, 85.2 (C-1, C-2, C-3), 95.3, 100.8 (C-1), 118.0, 118.2 (C-6), 127.3, 127.4, 127.6, 127.7, 127.8, 128.1, 128.2 (CH_{arom} Bn), 133.5, 134.0 (C-5), 136.9, 137.1, 137.4 (C_q Bn). ^{1}H-NMR (200 MHz, $CDCl_3$): δ 3.97 (m, 2H), 4.49–4.68 (m, 5H) (2 × CH_2Bn, H-2, H-3, H-4), 5.25–5.53 (m, 3H, H-6, H-1), 5.89–6.17 (m, 1H, H-5), 7.22–7.43 (m, 10H, CH_{arom} Bn).

(3*R*,4*S*,5*R*)-3,4-*O*-Benzylhepta-1,6-diene-3,4,5-triol (14)

A solution of 4.2 mmol of ylide was prepared by the addition of 1 eq. of *n*-BuLi in hexanes to methyl triphenylphosphonium bromide in THF (20 mL) at −78 °C until all solids had dissolved. The resulting solution was allowed to warm to −20 °C and was stirred for one hour. Compound **13** (0.45 g, 1.38 mmol) in THF (1 mL) was added by syringe *via* the cold wall of the flask at −20 °C. The resulting solution was allowed to warm to rt and was stirred overnight. TLC analysis revealed a higher running spot (R_f 0.85, EtOAc–petroleum ether 1 : 1). The solution was quenched with sat. aq. NH_4Cl (100 mL) and extracted with ether (100 mL). The ether layer was dried ($MgSO_4$), filtered and concentrated. Purification by column chromatography (10%⟶25% EtOAc in petroleum ether) gave homogeneous **14** (0.31g, 72%). ^{13}C-NMR (50.1 MHz, $CDCl_3$): δ 70.5, 75.0 (2 × CH_2Bn), 71.9, 81.6, 83.8 (C-3, C-4, C-5), 115.6, 119.2 (C-1, C-7), 127.4, 127.6, 127.7, 128.0 (CH_{arom} Bn), 135.2, 138.3 (C-2, C-6), 138.1 (C_q Bn). ^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.47 (d, *J* 7.3 Hz, 1H, OH), 3.43 (dd, *J* 3.7 *Hz*, *J* 6.2 Hz, 1H), 4.07 (dd, *J* 5.8, *J* 7.7 Hz, 1H) (H-3, H-4), 4.27 (m, 1H, H-5), 4.38 (d, *J* 11.7 Hz, 1H), 4.61 (d, *J* 11.7 Hz, 1H, CH_2 Bn), 4.66 (d, AB, *J* 11.3 Hz, 1H), 4.84 (d, AB, *J* 11.3 Hz, 1H, CH_2 Bn), 5.12–5.44 (m, 4H, H-1, H-7), 5.79–5.96 (m, 2H, H-2, H-6), 7.24–7.35 (m, 10H, CH_{arom} Bn).

(3*S*,4*S*,5*R*)-3,4-*O*-Benzylcyclopentene-3,4,5-triol (15)

Compound **14** (240 mg, 0.73 mmol) was dissolved in CH_2Cl_2 (75 mL). The solution was degassed by bubbling through nitrogen for 10 minutes, 31 mg (5 mol%) of $Cl_2(PCy_3)_2Ru$=CHPh was added and the reaction mixture was stirred for 3 days in a sealed flask. TLC analysis (25% EtOAc in petroleum ether) revealed total transformation of starting material into a lower running product and higher running, unidentified products. The lower running compound was isolated by column chromatography (10%⟶20% EtOAc in petroleum ether) to give 150 mg (68%) of homogeneous **15**. ^{13}C-NMR (50.1 MHz, $CDCl_3$): δ 71.3, 72.1 (2 × CH_2Bn), 79.7, 86.1, 93.8 (C-3, C-4, C-5), 127.7, 127.9, 128.3 (CH_{arom} Bn), 131.7, 134.5 (C-1, C-2), (138.1 C_q Bn). ^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.78 (d, *J* 8.1 Hz, 1H, OH), 4.01 (t, *J* 3.9 Hz, 1H, H-4), 4.45 (m, 1H, H-3), 4.58 (app. s, 2H, CH_2 Bn), 4.63 (m, 1H, H-5), 4.74 (d, AB, *J* 11.8 Hz, 2H, CH_2 Bn), 5.84–5.92 (m, 2H, H-1, H-2), 7.27–7.43 (m, 10H, CH_{arom} Bn); $[a]_D^{20}$ 29.5 (*c*=1, $CHCl_3$).

p-Methoxyphenyl 2-*O*-(*p*-methoxybenzyl)-3,4-*O*-isopropylidene-β-D-galactopyranoside (17)

A. Synthesis of *p*-methoxyphenyl 6-*O*-*tert*-butyldiphenylsilyl-β-D-galactopyranoside. To a solution of compound **16** (13.8 g, 30.4 mmol) in methanol (400 mL) was added 33.6 mg (0.3 mmol) KO*t*Bu. The solution was stirred for three hours, after which time the solution was brought to neutral pH with Dowex-H^+. The mixture was filtered and concentrated, coevaporated with pyridine and taken up in pyridine (300 mL). TBDPSCl (8.6 mL) was added, and the mixture was stirred for two hours. TLC analysis revealed the disappearance of starting compound and formation of a new product (R_f 0.90, EtOAc–EtOH 9 : 1). Methanol was added and the mixture was concentrated. The residue was taken up in EtOAc (400 mL) and washed with 1 M HCl and water. The organic layer was separated, dried on $MgSO_4$ to give the crude title compound, which was used in the next step without further purification. ^{13}C-NMR (50.1 MHz, in $CDCl_3$): δ 19.0 (Cq, *t*Bu), 26.7 (CH_3, *t*Bu), 55.5 (OMe), 63.6 (C-6), 69.2, 71.3, 73.7, 75.2 (C-2, C-3, C-4, C-5), 102.5 (C-1), 114.4, 118.6 (CH, MP), 127.7, 129.7, 135.5 (CH, Ph), 133.0 (Cq, Ph), 151.3, 155.2 (Cq, MP).

B. Synthesis of *p*-methoxyphenyl 6-*O*-*tert*-butyldiphenylsilyl-3,4-*O*-isopropylidene-β-D-galactopyranoside. The crude galactoside from the previous step was dissolved in acetone (250 mL), and dimethoxypropane (18.5 mL) and a catalytic amount of *p*-TsOH were added. The reaction was stirred for one hour, after which it was neutralised with a little sat. Na_2HCO_3 and concentrated *in vacuo*. The residue was taken up in EtOAc (250 mL), washed with water and dried on $MgSO_4$. Column chromatography (10⟶50% EtOAc in petroleum ether) gave the title compound (17.2 g) in 99% yield over the two steps. ^{13}C-NMR (50.1 MHz, in $CDCl_3$): δ 18.9 (Cq, *t*Bu), 26.0 (CH_3, isopr.), 26.5 (CH_3, *t*Bu), 27.8 (CH_3, isopr.), 55.2 (OMe), 62.7 (C-6), 72.9, 73.7, 78.8 (C-2, C-3, C-4, C-5), 101.7 (C-1), 109.9 (Cq, isopr.), 114.2, 118.4 (CH, MP), 127.4, 129.5, (CH, Ph), 132.9 (Cq, Ph), 151.1, 155.0 (Cq, MP).

C. Synthesis of *p*-methoxyphenyl 2-*O*-(*p*-methoxybenzyl)-6-*O*-*tert*-butyldiphenylsilyl-3,4-*O*-isopropylidene-β-D-galactopyranoside. The galactoside from the previous step (4.38 g, 7.76 mmol) was dissolved in DMF (100 mL), brought to 0 °C and NaH (466 mg, 60% in oil, 11.6 mmol) was added, followed by *p*-methoxybenzyl chloride (1.26 mL, 9.28 mmol). The solution was stirred for two days, after which time methanol was added and the solution was stirred for a further 30 minutes. Et_2O was added (250 mL) and the solution was washed with water (2 × 200 mL). The organic phase was dried on $MgSO_4$, filtered and concentrated. Column chromatography (0⟶30% EtOAc in petroleum ether) gave the title compound (4.25 g, 80%). ^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.08 (s, 9H, CH_3, *t*Bu), 1.34 (s, 3H, CH_3, isopr.), 1.41 (s, 3H, CH_3, isopr.), 3.76 (s, 3H, OMe), 3.80 (s, 3H, OMe), 3.65 (m, 1H), 3.95 (m, 3H), 4.24 (m, 2H) (H-2, H-3, H-4, H-5, H-6), 4.78 (m, 1H, H-1), 4.85 (s, 2H, CH_2, Bn), 6.68 (m, 2H, CH, MP), 6.88 (m, 2H, CH, MBn), 7.05 (m, 2H, CH, MP), 7.35–7.47 (m, 8H, CH, MBn, Ph), 7.69–7.72 (m, 4H, Ph).

D. Synthesis of *p*-methoxyphenyl 2-*O*-*p*-methoxybenzyl-3,4-*O*-isopropylidene-β-D-galactopyranoside (17). The galactoside from the previous step (2.49 g, 3.63 mmol) was dissolved in 40 mL THF, and 4.0 mL 1 M TBAF in THF was added. After 45 minutes the reaction was complete, Et_2O was added, and the mixture was washed with water, dried on $MgSO_4$ and concentrated *in vacuo*. Column chromatography yielded 1.53 g (94%) of the title compound. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.35 (s, 3H, CH_3, isopr.), 1.41 (s, 3H, CH_3, isopr.), 3.78 (s, 3H, OMe), 3.80 (s, 3H, OMe), 3.64 (dd, 1H, *J* 6.6 Hz, *J* 8.0 Hz), 3.81 (m, 1H), 3.93 (m, 2H), 4.23 (m, 2H) (H-2, H-3, H-4, H-5, H-6), 4.79

(d, AB, 1H, CH_2, MBn, *J* 11.7 Hz), 4.84 (d, 1H, H-1), 4.85 (d, AB, 1H, CH_2, MBn, *J* 11.7 Hz), 6.86 (m, 4H, CH, MP, MBn), 6.97 (m, 2H, CH, MP), 7.53 (m, 2H, CH, MBn).

p-Methoxyphenyl 6-deoxy-6-iodo-2-*O*-(*p*-methoxybenzyl)-3,4-*O*-isopropylidene-β-D-galactopyranoside (18)

Compound **17** (1.53 g, 3.42 mmol), imidazole (0.46 g, 6.8 mmol), and 1,4,5-triiodoimidazole (2.43 g, 5.45 mmol) were dissolved in toluene (50 mL). Triphenylphospine (3.58 g, 13.6 mmol) was added and the slurry solution was brought to reflux temperature. After one hour the reaction was complete, the mixture was cooled to rt, Et_2O (50 mL) was added and the mixture was washed with aqueous saturated $Na_2S_2O_3$ (50 mL), saturated aqueous $NaHCO_3$ (50 mL) and water (50 mL), dried on $MgSO_4$, and concentrated *in vacuo*. Et_2O (50 mL) was added and the mixture was filtered over Celite. Column chromatography (0⟶50% EtOAc in petroleum ether) yielded 1.53 g (95%) of iodide **18**. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.35 (s, 3H, CH_3, isopr.), 1.40 (s, 3H, CH_3, isopr.), 3.40 (m, 2H, H-6), 3.78 (s, 3H, OMe), 3.79 (s, 3H, OMe), 3.62 (dd, 1H, *J* 6.5 Hz, *J* 8.0 Hz), 3.97 (m, 1H), 4.26 (m, 2H) (H-2, H-3, H-4, H-5), 4.77 (d, 1H, H-1, $J_{1,2}$ 7.3 Hz), 4.78 (d, AB, 1H, CH_2, MBn, *J* 11.7 Hz), 4.85 (d, AB, 1H, CH_2, MBn, *J* 11.7 Hz), 6.85 (m, 4H, CH, MP, MBn), 7.08 (m, 2H, CH, MP), 7.33 (m, 2, CH, MBn).

(3*S*,4*R*,5*S*)-3,4-*O*-Isopropylidene-5-*O*-*p*-methoxybenzylhepta-1,6-diene-3,4,5-triol (19)

Iodide **18** (367 mg, 0.684 mmol) was dissolved in 96% EtOH (8 mL), 1 g of activated powdered zinc was added and the mixture was boiled under reflux. After 75 minutes, TLC indicated total conversion into a lower running product. The solution was filtered over Celite, washed with a little EtOH and concentrated. Sat. aq. $Na_2S_2O_3$ (1 ml) and CH_2Cl_2 (10 ml) were added. The organic phase was separated, dried ($MgSO_4$) and concentrated. The product was subjected directly to Wittig olefination as described for the synthesis of **14** (using 2.2 eq. of freshly prepared ylide) to give after column chromatography (5⟶10% EtOAc in petroleum ether) 152 mg (73%) of the title compound as an oil. ^{13}C-NMR (75.1 MHz, $CDCl_3$): δ 25.6, 27.4 (2 × CH_3 isopr.), 55.1 (CH_3, OMe MBn), 69.6 (CH_2 MBn), 78.3, 79.0, 80.6 (C-3, C-4, C-5), 109.0 (C_q isopr.), 113.5 (CH_{arom} MBn), 118.7, 119.4 (C-1, C-7), 128.9 (CH_{arom} MBn), 130.4 (C_q MBn), 134.3, 134.5 (C-2, C-6). ^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.39 (s, 3H, CH_3 isopr.), 1.52 (s, 3H, CH_3 isopr.), 3.81 (m, 4H), 4.17 (t, *J* 6.6 Hz, 1H), 4.48 (AB, *J* 11.7 Hz, 2H), 4.59 (d, *J* 7.3 Hz, 1H) (H-3, H-4, H-5, CH_2 MBn), 5.26 (m 4H, H-1, H-7), 5.86 (m, 2H, H-2, H-6), 6.86 (d, *J* 8.8 Hz, 2H, CH_{arom} MBn), 7.29 (d, *J* 8.8 Hz, 2H, CH_{arom} MBn).

(3*S*,4*R*,5*S*)-3,4-*O*-Isopropylidene-5-*O*-*p*-methoxybenzylcyclopentene-3,4,5-triol (20)

Compound **19** (92 mg, 0.30 mmol) was subjected to RCM using the same conditions as described for the synthesis of **15** to give 82 mg (99%) of the title compound. ^{13}C-NMR (75.1 MHz, $CDCl_3$): δ 25.5, 27.1 (2 × CH_3 isopr.), 55.1 (CH_3, OMe MBn), 71.2 (CH_2 MBn), 83.2, 84.1, 87.7 (C-3, C-4, C-5), 109.0 (C_q isopr.), 113.7 (CH_{arom} MBn), 129.3 (CH_{arom} MBn), 129.8 (C_q MBn), 133.1, 135.4 (C-1, C-2). ^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.37 (s, 3H, CH_3 isopr.), 1.41 (s, 3H, CH_3 isopr), 3.82 (m, 4H), 4.47 (m, 3H), 5.28 (m, 1H, H-3, H-4, H-5, CH_2 MBn), 5.91 (m, 1H), 6.03 (m, 1H) (H-1, H-2), 6.88 (m, 2H, CH_{arom} MBn), 7.29 (m, 2H, CH_{arom} MBn).

(3*S*,4*R*,5*S*)-3,4-*O*-Isopropylidenecyclopentene-3,4,5-triol (21)

Compound **20** (272 mg, 0.98 mmol) was dissolved in CH_2Cl_2 (8 mL), water (0.5 mL) was added and cooled to 0 °C. DDQ (446 mg, 1.97 mmol) was added. After 2 hours all starting material had been transformed into a lower running product according to TLC. The solution was filtered over Celite. The filtrate was washed subsequently with water (50 mL) and aqueous $NaHCO_3$. The organic phase was dried ($MgSO_4$) filtered and concentrated. Column chromatography (20%⟶50% EtOAc in petroleum ether) afforded 132 mg (86%) of **21**, the NMR spectra of which were identical to those of enantiomer **5**. MS (CI): *m*/*z* 157.2 $[M + H]^+$; $[\alpha]_D^{20}$ +110.4 (*c*=1, $CHCl_3$).

S-Methyl *O*-(3*R*,4*S*,5*R*)-4,5-*O*-isopropylidenedioxycyclopenten-3-yl dithiocarbonate (22)

Alcohol **5** (180 mg, 1.12 mmol) was dissolved in toluene (5 mL), NaH (60% in mineral oil, 90 mg, 2.25 mmol) was added and the solution was heated to 50 °C for 10 min and cooled to 0 °C. CS_2 (0.24 mL, 0.31 g, 4 mmol) was added and the solution was allowed to warm to rt and stirred for 3 hours. The solution was cooled to 0 °C and then MeI (0.25 mL, 0.45 mmol) was added, immediately followed by the addition of 5 mL of DMF. After an additional 15 min all starting material had been transformed into a higher running product according to TLC (R_f 0.80, EtOAc–petroleum ether 25 : 75). The reaction mixture was poured into Et_2O (50 mL) and washed with water (2 × 50 mL). The organic phase was dried ($MgSO_4$), filtered and concentrated. Column chromatography (0⟶25% EtOAc in petroleum ether) gave homogeneous **22** (177 mg, 64%). ^{13}C-NMR (75.1 MHz, $CDCl_3$): δ 19.2 (CH_3, SMe), 25.8, 27.3 (2 × CH_3 isopr), 82.5, 83.9 (C-4, C-5), 90.9 (C-3), 112.4 (C_q isopr.), 130.2, 139.1 (C-1, C-2). ^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.37 (s, 3H, CH_3 isopr), 1.44 (s, 3H, CH_3 isopr), 2.58 (s, 3H, SMe), 4.73 (d, *J* 5.8 Hz, 1H), 5.32 (m, 1H) (H-4, H-5), 6.03 (m, 1H), 6.23 (m, 1H) (H-1, H-2), 6.35 (m, 1H, H-3); $[\alpha]_D^{20}$ −248.6 (*c*=1, $CHCl_3$).

S-Methyl *S*-(3*S*,4*S*,5*S*)-4,5-*O*-isopropylidenedioxycyclopenten-3-yl dithiocarbonate (23)

Compound **22** (170 mg, 0.68 mmol) was dissolved in xylenes (5 mL) and brought to reflux for 20 minutes after which time the starting material had been transformed into a slightly higher running product (R_f 0.60, EtOAc–toluene 4 : 96). Solvents were removed under vacuum and column chromatography gave 165 mg (97%) of **23** as a clear oil. ^{13}C-NMR (75.1 MHz, $CDCl_3$): δ 13.0 (SMe), 25.9, 27.3 (2 × CH_3 isopr), 54.8, 84.6, 84.9 (C-3, C-4, C,5), 111.4 (C_q isopr.), 130.4, 135.3 (C-1, C-2), 188.6 (C=O). ^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.36 (s, 3H), 1.42 (s, 3H), 2.45 (s, 3H), 4.67 (d, *J* 5.8 Hz, 1H), 5.27 (m, 2H), 5.98 (m, 1H), 5.77 (m, 1H); $[\alpha]_D^{20}$ +188 (*c*=1, $CHCl_3$).

(3*R*,4*R*,5*R*)-3-*O*-Trichloroacetimidoyl-4,5-*O*-isopropylidene-cyclopentene-3,4,5-triol (24)

Compound **5** (917 mg, 5.87 mmol) was dissolved in CH_2Cl_2 (15 mL) and cooled to 0 °C. DBU, (1.05 mL, 6.8 mmol) was added followed by trichloroacetonitrile (0.88 mL, 8.8 mmol). The reaction was complete after 10 minutes as judged by TLC (R_f 0.90, EtOAc–petroleum ether 1 : 1). The reaction mixture was poured into sat. aq. NH_4Cl (10 mL). The organic layer was collected and washed with water (10 mL), dried (Na_2SO_4), filtered and concentrated. Column chromatography (30% EtOAc in petroleum ether) gave 1.74 g (99%) of pure **24** as white needles. ^{13}C-NMR (75.1 MHz, $CDCl_3$): δ 25.7, 27.2 (2 × CH_3, isopr.), 82.7, 83.9, 87.5 (C-3, C-4, C-5), 112.4 (C_q isopr.), 130.6, 138.3 (C-1, C-2), 161.9 (C=NH). ^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.38 (s, 3H, CH_3 isopr.), 1.45 (s, 3H, CH_3 isopr.), 4.70 (d, *J* 5.8 Hz, 1H, H-5), 5.33 (m, 1H, H-4), 5.76 (s, 1H, H-3), 6.04 (m, 1H), 6.22 (m, 1H), (H-1, H-2). MS (ESI): *m*/*z* 321.8 $[M + Na]^+$, *m*/*z* 323.8 $[M + Na + 2]^+$, *m*/*z* 325.9 $[M + Na + 4]$; $[\alpha]_D^{20}$ −121.0 (*c*=1, $CHCl_3$).

(3*S*,4*R*,5*S*)-5-(*N*-Trichloroacetylamino)-3,4-*O*-isopropylidene-cyclopentene-3,4-diol (25)

Compound **24** (1.45 g, 4.82 mmol) was dissolved in xylenes (25 mL) and heated until reflux. After 5 hours all starting

material had been transformed into a lower running product (R_f 0.25, EtOAc–petroleum ether, 0.75 : 0.25). Solvents were evaporated and column chromatography (20% EtOAc in petroleum ether) gave 1.29 g, 89% of homogeneous **24** as a white solid. ^{13}C-NMR (75.1 MHz, $CDCl_3$): δ 25.6, 27.2 (2 × CH_3, isopr.), 63.0 (C-5), 83.5 (C-4), 84.3 (C-3), 92.2 (C_q, CCl_3), 111.6 (C_q, isopr.), 130.4, 136.7 (C-1, C-2), 161.5 (C=O). ^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.36 (s, 3H, CH_3, isopr.), 1.44 (s, 3H, CH_3, isopr.), 4.57 (d, 1H, H-3, *J* 5.0 Hz), 4.84 (m, 1H, H-4), 5.33 (m, 1H, H-5), 5.58 (m, 1H), 6.15 (m, 1H), (H-1, H-2), 6.58 (bd, 1H, NH, *J* 6.0 Hz.). MS (CI): *m*/*z* 321.8 $[M + Na]^+$, *m*/*z* 323.8 $[M + Na + 2]^+$, *m*/*z* 325.9 $[M + Na + 4]^+$; $[a]_D^{20}$ +130.8 (*c*=1, $CHCl_3$).

(1*R*,2*R*,3*S*,4*R*,5*S*)-5-(*N*-Trichloroacetylamino)-1,2-epoxy-3,4-*O*-isopropylidenecyclopentanediol (26)

Compound **5** (100 mg, 0.33 mmol) was dissolved in acetonitrile and Na_2EDTA solution (0.83 mL, 8 M in H_2O) was added. The mixture was cooled to 0 °C and 1,1,1-trifluoroacetone (0.33 mL, 3.5 mmol) was added *via* a pre-cooled syringe. Subsequently, $NaHCO_3$ (217 mg, 2.55 mmol) and oxone (1.02 g, 1.66 mmol) were added in portions over a period of 1 h. H_2O (0.8 mL) and EtOH (5 mL) were added and the mixture was brought to pH 7 through the addition of $NaHCO_3$. After two days stirring at rt TLC analysis revealed the formation of a new product (R_f 0.40, EtOAc–petroleum ether 2 : 8). The mixture was filtered, taken up in dichloromethane and washed with water. The organic phase was separated, dried ($MgSO_4$), filtered and concentrated. After column chromatography (0⟶10% EtOAc in petroleum ether) the title compound was obtained (75 mg, 72%) as a white solid. ^{13}C-NMR (75.1 MHz, $CDCl_3$): δ 24.5, 26.8 (2 × CH_3, isopr.), 58.6 (C-5), 59.1 (C-1), 60.2 (C-2), 79.0 (C-3), 86.4 (C-4), 112.6 (C_q, isopr.), 161.5 (C=O). ^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.31 (s, 3H, CH_3, isopr.), 1.50 (s, 3H, CH_3, isopr.), 3.75 (m, 1H, H-2), 3.81 (m, 1H, H-1), 4.26 (m, 1H, H-4), 4.51 (m, 1H, H-5), 4.72 (m, 1H, H-3). MS (CI): *m*/*z* 338.0 $[M + Na]^+$, *m*/*z* 339.9 $[M + Na + 2]^+$, *m*/*z* 341.9 $[M + Na + 4]^+$.

(3*R*,4*S*,5*R*)-3,4-*O*-Isopropylidene-5-methyltributylstannyl-cyclopentene-3,4,5-triol (27)

Compound **5** (300 mg, 1.85 mmol) was dissolved in THF (5 mL) and cooled to 0 °C. Potassium hydride (165 mg, 4 mmol) was added followed by 5 mg of dibenzo-18-crown-6. Bu_3SnCH_2I (0.66 mL, 2.2 mmol) was added and the solution was allowed to warm to rt. Stirring was continued for 30 min after which time TLC indicated consumption of all starting material and that a new compound had been formed (R_f 0.8, EtOAc–light petroleum 1 : 9 v/v). Water (20 mL) was added followed by EtOAc (10 mL) and toluene (10 mL). The organic phase was separated, dried (Na_2SO_4), filtered and concentrated. Column chromatography (0⟶10% EtOAc in toluene) gave pure **27** (787 mg, 91%). ^{13}C-NMR (75.1 MHz, $CDCl_3$): δ 8.9 ($SnBu_3$), 13.6 ($SnBu_3$), 25.5 (2 × CH_3 isopr.), 27.2, 29.0 ($SnBu_3$), 60.2 (OCH_2Sn), 82.3, 84.2, 92.7 (C-3, C-4, C-5), 111.4 (C_q isopr.), 133.4, 134.9 (C-1, C-2). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.89 (m, 9H, CH_3 $SnBu_3$), 1.2–1.6 (m, 18H, CH_2 $SnBu_3$), 3.69 (d, *J* 10.0 Hz, 1H, OCH_2Sn), 3.89 (d, *J* 10.0 Hz, 1H, OCH_2Sn), 4.24 (s, 1H), 4.51 (d, *J* 6.0 Hz, 1H), 5.21 (dd, *J* 2.0 Hz, *J* 6.0 Hz, 1H) (H-3, H-4, H-5), 5.90 (m, 1H), 6.99 (m, 1H) (H-1, H-2).

(3*S*,4*R*,5*R*)-3,4-*O*-Isopropylidene-5-hydroxymethylcyclo-pentene-3,4-diol (28)

Compound **27** (250 mg, 0.54 mmol) was dissolved in THF (7.5 mL) and cooled to −78 °C. *n*-BuLi (0.50 mL, 1.6 M in hexanes, 0.81 mmol) was added dropwise *via* the cold wall of the flask. The solution was allowed to warm to rt and was stirred overnight after which a new compound had been formed (R_f 0.2, EtOAc–petroleum ether 7 : 3). The solution was poured into sat. aq. NH_4Cl (20 mL) and extracted with EtOAc (2 × 25 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated. Column chromatography (10⟶50% EtOAc in petroleum ether) gave 64 mg (0.38 mmol) of **28** (68%) yield and 16 mg recovery (20%) of **5**. ^{13}C-NMR (75.1 MHz, $CDCl_3$): δ 25.4, 27.2 (2 × CH_3 isopr.), 63.4 (CH_2OH), 54.6, 81.3, 84.2 (C-3, C-4, C-5), 109.9 (C_q isopr.), 132.9, 133.5 (C-1, C-2). ^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.36 (s, 3H, CH_3 isopr), 1.42 (s, 3H, CH_3 isopr), 2.08 (br s, 2H, 2 × OH), 2.99 (m, 1H, H-5), 3.55 (dd, *J* 6 Hz, *J* 11 Hz, 1H, CH_2OH), 3.75 (dd, *J* 5 Hz, *J* 11.0 Hz, 1H, CH_2OH), 4.59 (d, *J* 6 Hz, 1H, H-3), 5.15 (m, 1H, H-4), 5.76 (m, 1H, H-2), 5.92 (m, 1H, H-1).

(3*R*,4*R*,5*R*)-3-*O*-Bromomethyldimethylsilyl-4,5-*O*-isopropyl-idenecyclopentene-3,4,5-triol (29)

Alcohol **5** (123 mg, 0.79 mmol) was dissolved in CH_2Cl_2 (4 mL) and triethylamine (0.22 mL) was added followed by bromomethyldimethylsilylchloride (0.14 mL, 1.03 mmol). After 1 hour all starting material had been transformed into a higher running product (R_f 0.85, EtOAc–petroleum ether 4 : 6). The suspension was directly poured onto a silica gel column eluting with 25% EtOAc and 1% Et_3N in petroleum ether giving 0.201 g of pure **29** (83%). ^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.31 (s, 3H, CH_3Si), 0.32 (s, 3H, CH_3Si), 1.34 (s, 3H, isopr.), 1.40 (s, 3H, isopr.), 2.48 (s, 2H, -OCH_2Si), 4.47 (d, *J* 6 Hz, 1H), 4.81 (m, 1H), 5.27 (m, 1H) (H-3, H-4, H-5), 5.83 (m, 1H), 6.00 (m, 1H) (H-1, H-2).

1,2-*O*-Isopropylidene-4a-carba-β-L-xylofuranose (30)

Compound **29** (201 mg, 0.66 mmol) was dissolved in benzene (10 mL) and heated to reflux. A solution of AIBN (2.15 mg, 0.013 mmol, 2 mol%) and Bu_3SnH (286 mg, 0.98 mmol) in benzene (0.7 mL) was added using a syringe pump over a 3 hour period. By this time, all starting material had disappeared and volatiles were evaporated off. The resulting solution was taken up in THF (1 mL) and MeOH (1 mL), 79 mg of Na_2CO_3 was added followed by 1.18 mL 30% aqueous H_2O_2 and the mixture was heated at 50 °C overnight. The resulting suspension was evaporated to dryness, EtOAc was added and solids were crushed. The resulting suspension was poured onto a silica gel column using pure EtOAc as eluent giving 90 mg (74%) of **30**. ^{13}C-NMR (75.1 MHz, $CDCl_3$): δ 24.3, 26.6 (2 × CH_3 isopr.), 32.4 (C-4a), 42.2 (C-4), 61.8 (C-5), 77.6 (C-3), 80.2 (C-1), 86.8 (C-2), 110.4 (C_q isopr.). ^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.30 (s, 3H, CH_3 isopr.), 1.42 (s, 3H, CH_3 isopr), 1.74 (m, 1H), 1.92 (m, 1H) (H-4a), 2.39 (m, 1H, H-4), 3.86 (dd, *J* 5 Hz, *J* 11 Hz, 1H, H-5a), 4.08 (dd, *J* 4 Hz, *J* 11 Hz, 1H, H-5b), 4.24 (d, *J* 4 Hz, 1H, H-3), 4.37 (d, *J* 6 Hz, 1H, H-2), 4.79 (t, *J* 5 Hz, 1H, H-1); $[a]_D^{20}$ +16.08 (*c*=1, $CHCl_3$).

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