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Synthesis of (+)-goniothalesdiol and (+)-7-*epi*-goniothalesdiol

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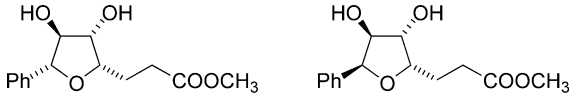
Dedicated to Prof. Peter Stanetty on his 60th birthday.

Abstract—A total synthesis of (+)-goniothalesdiol, a 3,4-dihydroxy-2,5-disubstituted tetrahydrofuran isolated from *Goniothalamus borneensis* (Annonaceae), and its 7-epimer is reported using oxycarbonylation methodology for construction of polyhydroxylated substituted heterocycles. Diastereoselectivity of addition of organometallic reagents to 2,3-*O*-isopropylidene-D-threose derivatives using theoretical calculations based on the semiempirical PM5 was studied.

1. Introduction

The palladium(II)-catalysed oxycarbonylation[1] of unsaturated polyols[2] or/and aminopolyols[3] represents a powerful methodology[4] for construction of 5-/6-membered saturated oxa/azaheterocycles. In our long term program directed towards the application of carbonylation methodology to natural product synthesis, we have described the syntheses of both enantiomers of cytotoxic styryl-lactones goniofufurone,[5a,b] 7-*epi*-goniofufurone,[5a,b] erythro-skyrine,[5c] homo-DLX,[5d] homo-DMDP,[5d] homo-DNJ[5e,f] and homo-L-ido-DNJ.[5e,f] Herein, we report experimental details of the optimised synthesis of goniothalesdiol **1** and 7-*epi*-goniothalesdiol **2** (Fig. 1) starting with D-mannitol.[6]



1 **2**

Figure 1. Goniothalesdiol **1** and 7-*epi*-goniothalesdiol **2**.

Goniothalesdiol was isolated from the bark of the Malaysian tree *Goniothalamus borneensis* (Annonaceae), and has been revealed to have significant cytotoxicity against P388 mouse leukaemia cells, and insecticidal activities.[7] The structure and relative stereochemistry of **1** was assigned on the basis of ^{1}H, ^{13}C NMR spectroscopy and the absolute configuration was confirmed by semi-synthesis from natural (+)-goniothalenol (altholactone).

Meanwhile, growing attention is given to this class of compounds, as demonstrated by development of new syntheses of unnatural enantiomer of goniothalesdiol (−)-**1**,[8] and its 7-epimer (+)-**2**.[9] Both syntheses started from chiral pool, D-glucuronolactone or D-tartaric acid, respectively, using Grignard addition followed by Lewis acid promoted hydrogenation of the corresponding lactone, the latter setting the *cis* configuration at C_6-C_7 of the epimer, and thus were not applicable for natural goniothalesdiol. Recently, preparation of 3,6-anhydro-2-deoxy-6-*C*-phenyl-D-*gluco*-1,4-hexonolactone **9**, an intermediate in our synthetic route,[6] was described from an erythrulose derivate[10] via an aldol reaction.

2. Results and discussion

We report herein details of the optimised synthesis[6] of natural goniothalesdiol (+)-**1** and its 7-epimer (+)-**2**. The strategy followed is shown in Scheme 1. In both routes the phenyl moiety is introduced by diastereoselective addition of organometallic reagents at C_1 of the aldose **6**, to allow for an entry into both diastereomers. For the second crucial step, oxycarbonylating bicyclisation of pentenitols, advantage is taken of recent progress in Pd(II)-catalysed carbonylations of unsaturated polyols or aminopolyols, that have turned out bicyclic lactones/lactams with high regio-control and excellent stereoselectivity, without necessity of OH-protection.[4,5]

Keywords: Palladium(II) catalysis; Stereoselective oxycarbonylation; Diastereoselective addition to carbonyl; Goniothalesdiol; Natural products; PM5 calculations.
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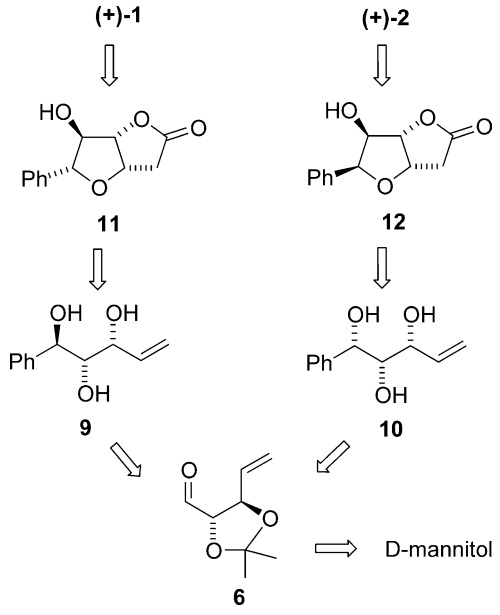
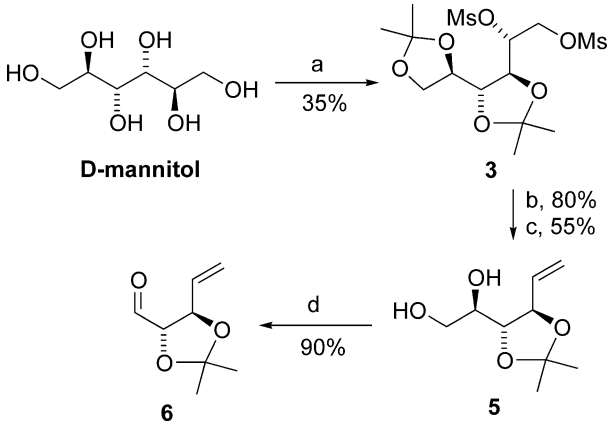


Scheme 1. Retrosynthetic analysis of **1** and **2**.

The first key intermediate, aldose **6**, was obtained from D-mannitol by a standard carbohydrate chemistry procedure.[11,12] Following the reaction sequence, acetonisation of D-mannitol,[13] selective hydrolysis of the terminal acetonide,[13] *O*-mesylation of both unprotected hydroxyl groups, reductive elimination with sodium iodide[14] and subsequent selective hydrolysis of the next terminal acetonide with HCl in ethanol, the diol **5** was readily prepared, however, in poor yield (3% overall[4a,6]).

In order to improve the efficiency of the synthesis of the requisite aldose **6** various reaction conditions for dioxolane ring hydrolysis and work up of reactions were examined. An effort that culminated in development of a four-step protocol for synthesis of C_5-aldose **6** with 14% yield, starting from cheap D-mannitol. (Scheme 2). The major improvement is the one pot conversion of D-mannitol to bismesylate **3**, which was isolated by simple crystallisation in 35% yield together with 30% of tris-*O*-acetonide-D-mannitol; the latter can be recycled. A selective hydrolysis

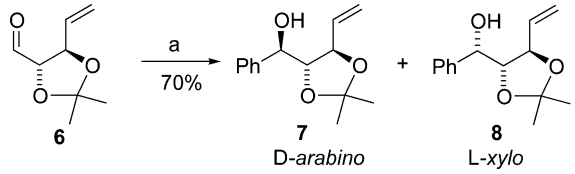


Scheme 2. Reagents and conditions: (a) 1, H_2SO_4, acetone; 2, H_2O; 3, NaOH; 4, MsCl, pyridine; (b) Lit.[14] NaI, acetone; (c) Lit.[15] $Zn(NO_3)_2 \cdot 6H_2O$, acetonitrile; (d) $NaIO_4$, H_2O.

of the second terminal acetonide was achieved with $Zn(NO_3)_2 \cdot 6H_2O$ in acetonitrile.[15]

With aldose **6** in our hands the synthesis was set up for the first key reaction of the sequence—Grignard addition with phenylmagnesium bromide (Scheme 3). A diastereomeric mixture of D-*arabino* **7** and L-*xylo* **8** partially protected pentenitols in the ratio 50:50 and 70% yield was obtained. The diastereomers could be readily separated by flash chromatography.

The unexpected lack of diastereocontrol observed in the



Scheme 3. Reagents and conditions: (a) PhMgBr, THF.

addition led us to study the reactions of organometallic reagents with aldehyde **6** in more detail.[16]

Generally, the design of addition of *C*-nucleophiles to aldehyde **6** could be based on models of either chelation-control: 1,2- (Cram) versus 1,3-asymmetric induction (Reetz) or non-chelation-control (Felkin-Anh), leading to alcohols **8** (1,2-*syn*, Cram) or **7** (1,2-*anti*, Reetz and Felkin-Anh).

Table 1 summarises the results of a series of micro scale experiments with several organometallics. The best results were noted with the Seebach reagent (entry 6, non-chelation control) and with $PhCeCl_2$ in diethyl ether at $-10\,^{\circ}C$, affording the requisite D-*arabino* diastereomer (1,2-*anti*) in 62% de (entry 1, chelation control). General *anti*-diastereoselectivity, observed in this set of reactions, in concert with literary references,[16] called for a new model of the transition state for these reactions. In the case of hard Lewis acids, such as $MgBr_2$ (entry 4), the convenient Cram's chelating model favored 1,2-*syn*-diastereomer (L-*xylo*, **8**), whereas dominance of 1,2-*anti*-diastereomer was found in practice. Our model considers a 1,2-chelation of the subsidiary Lewis acid along with the chelation of organometallic reagent, causing the *Re* face of carbonyl group to be the preferred one for a nucleophilic attack (model B, Fig. 2). The activation energy for this model of TS (model B, 4 kcal/mol), was considerably lower, than that predicted by the modified Cram's model (model A, ~8 kcal/mol) or classical Cram's model (15 kcal/mol). Transition state candidates were determined using saddle-point calculations and potential energy surfaces. PM5 semiempirical method was chosen as well balanced compromise between speed and accurancy,[17] even though it is still a novelty in the field of metal complex calculations.[18] Transition states were subsequently verified by vibrational and IRC analysis.

Predictions made by the suggested bis-chelation model of the transition state for addition of organometallic reagents to 2,3-*O*-isopropylidene-D-threose derivatives matched the

Table 1. Addition of organometallics to aldehyde **6**

Entry	Reagent	Temp °C	Solvent	*anti*-**7**:*syn*-**8**
1	$PhCeCl_2$	−10	Et_2O	81:19
2	PhMgBr/18-crown-6	rt	CH_2Cl_2	79:21
3	PhMgBr/LiCl	−80	THF	72:28
4	$PhMgBr/MgBr_2$	−80	THF	69:31
5	PhLi	rt	Et_2O	79:21
6	$PhTi(OiPr)_3$[a]	−80	CH_2Cl_2	>98:<2
7	$PhMgBr/SnCl_4$	−80	THF	68:32
8	$PhMgBr/TiCl_4$	−80	THF	44:56
9	$PhMgBr/ZnBr_2$	−80	THF	63:37
10	$PhMgBr/ZnBr_2$	−80	Et_2O	52:48

[a] Low conversion.

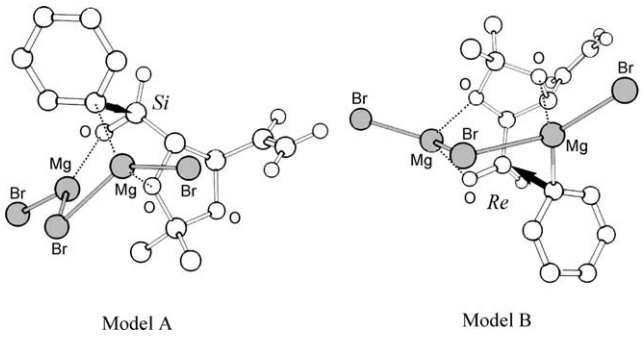


Figure 2. Models of transition states, calculated by PM5 method.

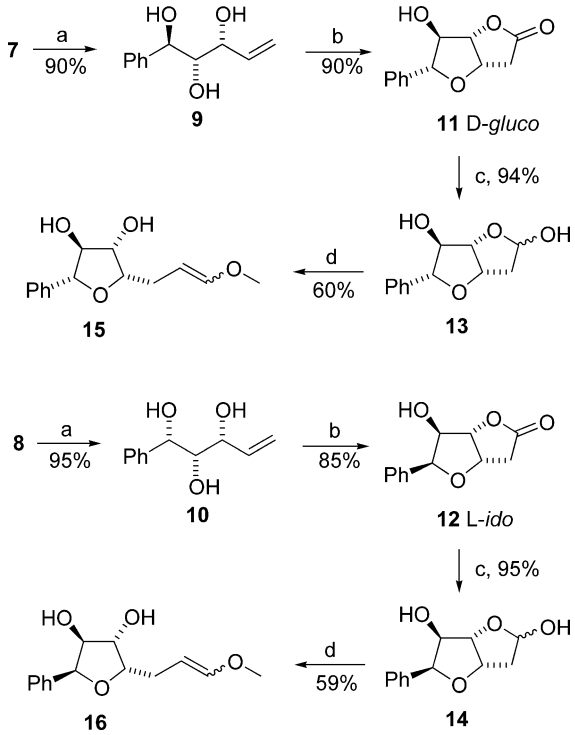
experimental results and clarified the discrepancies in stereochemical outcomes of additions to *erythro*-[19] versus *threo*-[16] configured aldehydes. In fact, the goniothalesdiol-precursor **7** was obtained by the addition of $PhCeCl_2$ to aldehyde **6** in 55% yield.

The second crucial step of both syntheses, which were run in parallel with the pure diastereomers **7** (D-*arabino*) and **8** (L-*xylo*) is oxycarbonylating bicyclisation. Firstly, the acetonide group was removed in acidic ethanol and pentenitols **9** and **10** were exposed to oxycarbonylation conditions (Scheme 4). The reaction was carried out under standard conditions with palladium(II) chloride as catalyst (0.1 equiv), copper(II) chloride as oxidant (3 equiv), sodium acetate (3 equiv) in acetic acid as buffer under a carbon monoxide atmosphere (balloon) at room temperature. As expected only the required lactones **11** and **12**, were formed with high regio- and *threo*-selectivity.[4,5] After work-up of the reaction mixture and flash chromatography the key intermediates were isolated, **11** in 90% and **12** in 85% yield, after recrystallisation. The configuration of both lactones, D-*gluco* for **11** (intermediate with correct stereochemistry for the natural product) and L-*ido* for **12** (precursor of **2**) was established by comparison of ^1H NMR data with the literature data of 3,6-anhydro-2-deoxy-1,4-heptonolactones of the same configuration.[4a] The final confirmation of the absolute stereochemistry came from the single crystal X-ray analysis of **12**.[20]

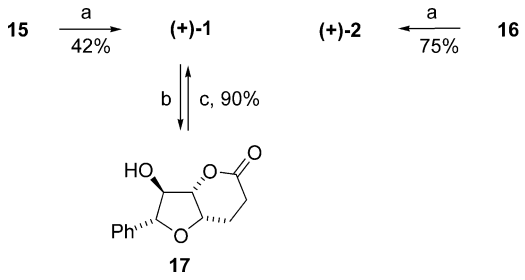
The syntheses continued with smooth partial reduction of the lactones using diisobutylaluminium hydride in CH_2Cl_2 affording a mixture of anomeric lactols **13** and **14** (*exo*:*endo*, 75:25) in very good yields, which were transformed to tetrahydrofuran derivatives **15** and **16** by the Wittig reaction with (methoxymethylene)-triphenylphosphonium chloride and *tert*-butyllithium in THF (60 and 59% as the mixtures of *E/Z*-isomers, 60:40).

Finally, the *E/Z*-isomeric mixtures of **15** and **16** were subjected to a three-step, in one-pot sequence to convert the vinyl ether to the methyl carboxylate (Scheme 5). Ether cleavage with sulphuric acid in THF–H_2O, followed by Ag_2O oxidation of the aldehyde and an acidic esterification with methanol afforded target compounds (+)-**1** and (+)-**2**, respectively. Final purification by Kugelrohr-distillation in vacuo (190 °C, 0.05 Torr), followed by repeated treatment with acidic Amberlyst in the case of (+)-**1**, because of lactonisation by heating to **17**, provided the target goniothalesdiol (+)-**1** and its 7-epimer (+)-**2** in 42 and 75% yields, respectively over three steps.

The NMR data, mp, and specific rotations of (+)-**1** and (+)-**2** were in good agreement with the reported data for the



Scheme 4. Reagents and conditions: (a) HCl, aqueous EtOH; (b) $PdCl_2$, $CuCl_2$, AcONa, AcOH, CO; (c) DIBAL-H, CH_2Cl_2; (d) $Ph_3PCH_2OCH_3Cl$, ^tBuLi, THF.



Scheme 5. Reagents and conditions: (a) 1, H_2SO_4, THF–H_2O; 2, Ag_2O, NaOH, THF–H_2O; 3, Amberlyst 15, MeOH; (b) distillation, 190 °C/0.05 Torr; (c) Amberlyst 15, MeOH.

natural product,[7] and/or unnatural antipode[8] {$[\alpha]_D^{27} = -7.1$ (*c* 0.15, EtOH)} and its 7-epimer.[9]

3. Conclusions

In conclusion, (+)-goniothalesdiol and (+)-7-*epi*-goniothalesdiol have been synthesised in 10 steps from cheap D-mannitol using an oxycarbonylation strategy for construction of tetrahydrofuran ring in two key steps, namely diastereoselective addition of organometallics to aldose **6** followed by a palladium(II)-catalysed oxycarbonylation of the appropriate unsaturated triols **9**, **10**. The synthesis of D-threose derivative, a very useful C_5-chiron, was developed from D-mannitol.

The diastereoselectivity of addition of organometallic reagent to aldose **6** was studied and model for transition state was designed using theoretical calculations based on the semiempirical PM5.

4. Experimental

4.1. General methods

Commercial reagents were used without further purification. All solvents were distilled before use. Hexanes refer to the fraction boiling at 60–65 °C. Lewis acids for diastereoselectivity studies were prepared as follows: $CeCl_3$, $ZnBr_2$ and LiCl as commercial hydrates (Fluka) were heated in tube oven at 150 °C under pressure of 2 Torr for 5 h, then stored under argon gas. $MgBr_2 \cdot THF$: 1 equiv of Mg turnings and few crystals of iodine were heated in the flask covered with reflux condenser and dropping funnel, cooled, charged with Ar and under vigorous stirring solution 1.05 equiv of 1,2-dibromoethane in THF was added and refluxed until no Mg remained. $Ti(O^iPr)_3Cl$: at −10 °C, 1 equiv of $TiCl_4$ was added dropwise to 3 equiv of $Ti(O^iPr)_4$ and stirred for 2 h, then distilled under reduced pressure (bp 65–70 °C/0.1 Torr). $TiCl_4$ and $SnCl_4$ were used without further treatment. Flash column liquid chromatography (FLC) was performed on silica gel Kieselgel 60 (40–63 μm, 230–400 mesh) and analytical thin-layer chromatography (TLC) was performed on aluminum plates pre-coated with either 0.2 mm (DC-Alufolien, Merck) or 0.25 mm silica gel 60 F_{254} (ALUGRAM® SIL G/UV$_{254}$, Macherey-Nagel). The compounds were visualised by UV fluorescence and by dipping the plates in an aqueous H_2SO_4 solution of cerium sulphate/ammonium molybdate followed by charring with a heat-gun. HPLC analyses were performed on Varian Dynamax system with variable wavelength UV detector. Melting points were obtained using a Boecius apparatus and are uncorrected. Optical rotations were measured with a POLAR L-μP polarimeter (IBZ Messtechnik) with a water-jacketed 10,000 cm cell at the wavelength of sodium line D ($\lambda = 589$ nm). Specific rotations are given in units of 10^{-1} deg cm^2 g^{-1} and concentrations are given in g/100 mL. Elemental analyses were run on FISONS EA1108 instrument, HRMS on Finnigan MAT 8230. Infrared spectra were recorded either on a Philips Analytical PU9800 FTIR spectrometer or a Perkin–Elmer 1750 FTIR spectrophotometer as KBr discs (KBr) or as thin films on KBr plates (film). NMR spectra were recorded on a Tesla BS 487 (80 MHz) and a Varian VXR-300 spectrometers. Chemical shifts (δ) are quoted in ppm and are either referenced to the tetramethylsilane (TMS) as internal standard. Compounds are numbered according to carbohydrate naming scheme.

4.1.1. 1,2:3,4-Di-*O*-isopropylidene-5,6-di-*O*-mesyl-D-mannitol (3). To the suspension of D-mannitol (25 g, 0.137 mol) in dry acetone (300 mL) was concd H_2SO_4 (3.5 mL) added dropwise and the mixture was stirred for 6 h at room temperature. At this point, the reaction could be scaled up by addition of discretionary amount of acetone solution of 1,2:3,4:5,6-tri-*O*-isopropylidene-D-mannitol (*c*, 13.8 g/100 mL). Water was added (3.3 mL/100 mL of reaction solution) and the mixture was additionally stirred for 1 h (TLC monitoring). The mixture was neutralised with 10% aqueous sol NaOH and boiled-down to half of volume in vacuo. Resulting aqueous slurry was extracted with CH_2Cl_2 (4×50 mL) and combined extracts were dried over Na_2CO_3 and evaporated in vacuo. Oily residue, containing mixture of 1,2:3,4-di-*O*-isopropylidene-D-mannitol and 1,2:3,4:5,6-tri-*O*-isopropylidene-D-mannitol was dissolved in pyridine (35 mL) and cooled to 0 °C. A solution of MsCl (6.4 mL, 9.6 g, 82 mmol) in pyridine (15 mL) was added dropwise with vigorous stirring, keeping the reaction temperature below 10 °C. After 10 h stirring at rt the mixture was poured on ice/water (350 mL) to form a brown-yellow precipitate, which was filtered and dissolved in boiling AcOEt (150 mL). The solution was dried over Na_2SO_4 an concentrated in vacuo. The residue was slurried in cold hexanes (100 mL) and filtered to provide crude product. The procedure was repeated twice and obtained white powder was recrystallised from MeOH; yield 20 g (35%) of **3**, colourless crystals, mp 120–122 °C, $[\alpha]_D^{25} = +22.5$ (*c* 2.3, CH_2Cl_2); {lit.[14]: mp 118–120 °C, $[\alpha]_D^{20} = +25.1$ (*c* 2.0, $CHCl_3$); lit.[4a]: mp 117–118 °C, $[\alpha]_D^{23} = +24.7$ (*c* 2.18, $CHCl_3$)}. Combined hexanes extracts were evaporated and the solid residue crystallised from Et_2O to give 1,2:3,4:5,6-tri-*O*-isopropylidene-D-mannitol (12 g, 30%), mp 68–70 °C, $[\alpha]_D^{25} = +16$ (*c* 1.4, MeOH); {lit.[4a]: mp 66–67 °C, $[\alpha]_D^{23} = +16.5$ (*c* 1.395, MeOH)}.

4.1.2. 3,4:5,6-Di-*O*-isopropylidene-D-*arabino*-1-hexenitol (4).[14] The dimesylate **3** (8 g, 16.6 mmol) and dry NaI (24 g, 160 mmol were dissolved in dry acetone (100 mL) and heated at 100 °C for 6 h in an autoclave. The resulting

brown suspension was distributed between $Na_2S_2O_3$ solution (10% in H_2O, 100 mL) and AcOEt (100 mL). Inorganic phase was extracted with AcOEt (3×50 mL) and combined organic phases were dried over Na_2SO_4. Concentrated crude mixture was distilled under reduced pressure on a microscale distillation apparatus equipped with 15 cm Vigreux column. Analytically pure product **4** was isolated (3.52 g, 80%) as a colourless oil, bp 40–45 °C/0.05 Torr, $[\alpha]_D^{25}=-4.8$ (*c* 3.25, CH_2Cl_2); {lit.[12]: $[\alpha]_D^{23}=-3.6$ (*c* 4.23, $CHCl_3$); lit.[14]: $[\alpha]_D^{21}=-5.5$ (*c* 2.4, $CHCl_3$); lit.[4a]: bp 70–80 °C/1 mbar, $[\alpha]_D^{21}=-5.3$ (*c* 2.98, $CHCl_3$)}.

4.1.3. 3,4-*O*-isoPropylidene-D-*arabino*-1-hexenitol (5). According to lit.[15] a solution of bisacetonide **4** (5 g, 26.6 mmol) and $Zn(NO_3)_2\cdot 6H_2O$ (39 g, 133 mmol) in acetonitrile (30 mL) was stirred at rt for 24 h. After concentration in vacuo the remainder was distributed between CH_2Cl_2 (200 mL) and water (200 mL) and separated water layer was extracted with CH_2Cl_2 (2× 50 mL). Combined organic extracts were dried over Na_2CO_3 and after solvent removal separated by flash column chromatography on silica (50% AcOEt in hexanes). Yield of **5** as a colourless oil: 2.3 g (55%), R_f 0.21 (50% AcOEt in hexanes), $[\alpha]_D^{25}=+6.4$ (*c* 0.47, CH_2Cl_2); {lit.[12]: $[\alpha]_D^{23}=+16.1$ (*c* 3.25, EtOH)}. IR (film, cm^{-1}): ν 3391 (bs), 2936 (s), 2985 (s), 1732 (s), 1647, 1559 (all m); ^1H NMR (300 MHz, $CDCl_3$): δ 1.42, 1.43 (2× s, 6H, $C(CH_3)_2$), 3.25 (broad s, 2H, OH), 3.64–3.90 (m, 4H, H-1, H-2, H-3), 4.42 ('t', 1H, $J_{4,5}=7$ Hz, $J_{3,4}=7$ Hz, H-4), 5.25 (d, 1H, $J_{5,6Z}=10.3$ Hz, H-6Z) 5.41 (d, 1H, $J_{5,6E}=17.5$ Hz, H-6E), 5.88 (ddd, 1H, $J_{4,5}=7$ Hz, $J_{5,6Z}=10.3$ Hz, $J_{5,6E}=17.5$ Hz, H-5); ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.9, 27.0 (all q, $C(CH_3)_2$), 63.5 (t, C-1), 72.1, 79.3, 81.0 (all d, C-2, C-3, C-4), 109.4 (s, $C(CH_3)_2$), 118.6 (t, C-6), 135.9 (d, C-5). Anal. calcd for $C_9H_{16}O_4$ (188.2): C, 57.43; H, 8.57. Found: C, 57.72; H, 8.55.

4.1.4. 2,3-*O*-isoPropylidene-D-*threo*-4-pentenose (6). A solution of $NaIO_4$ (3.4 g, 14.6 mmol) in water (35 mL) was added dropwise to the suspension of **5** (2.3 g, 12.2 mmol) in water (9 mL) at 0 °C. After 90 min (TLC monitoring) of vigorous stirring (white precipitate had been created) NaCl (3 g) was added and mixture was extracted with AcOEt (4× 50 mL). Extracts were dried over K_2CO_3 and concentrated. After removal of the traces of solvent (0.05 Torr for 30 min at rt) a colourless viscous oil of **6** (1.7 g, 90%) was obtained in satisfactory purity for the next reaction step. R_f 0.58 (50% AcOEt in hexanes), $[\alpha]_D^{25}=-24.1$ (*c* 0.21, $CHCl_3$). ^1H NMR (80 MHz, $CDCl_3$): δ 1.46 (s, 6H, $C(CH_3)_2$), 3.80–4.48 (m, 2H, H-2, H-3), 5.00–5.50 (m, 2H, H-5E, H-5Z), 5.65–6.20 (m, 1H, H-4), 9.72 (d, 1H, $J_{1,2}=2$ Hz, H-1). The aldose **6** can be stored for 1 month at 0–10 °C without loss of quality.

4.2. 2,3-*O*-isoPropylidene-5-*C*-phenyl-D-*arabino*-1-pentenitol (7) and 2,3-*O*-isopropylidene-5-*C*-phenyl-L-*xylo*-1-pentenitol (8)

Preparative procedure with PhMgBr: a dry flask was charged with Mg turnings (260 mg, 10.7 mmol) and a few particles of iodine, heated under Ar until the iodine started to sublime. The solution of PhBr (1.7 g, 10.8 mmol) in dry THF (20 mL) was added dropwise to start a vigorous exothermic reaction. Reaction was left to reflux for 1 h, until no Mg particles remained in the flask, and subsequently cooled to 0 °C. Aldehyde **6** (1.5 g, 9.6 mmol) in THF (15 mL) was added and solution was left to stand overnight (12 h), and then quenched with saturated solution of NH_4Cl (20 mL), Et_2O (30 mL) was added and the separated aqueous phase extracted with AcOEt (4×30 mL). Organic phases were dried over Na_2SO_4 and concentrated. Crude oil was separated on silica gel column (100 g, 4 cm i.d. of column, 4% AcOEt and 0.3% THF in hexanes) to afford **7** (750 mg, 33%), **8** (600 mg, 27%) and 200 mg fraction containing both isomers. Overall yield of isolated products was 70%.

Preparative procedure with $PhCeCl_2\cdot MgBrCl$: The aldehyde **6** (500 mg, 3.21 mmol) in Et_2O (10 mL) was added to the freshly prepared reagent [875 mg, 2.35 mmol of dry $CeCl_3$ was sonicated for 10 min in dry Et_2O (10 mL), then 2.35 mmol of freshly prepared PhMgBr in Et_2O (10 mL) was added and suspension was stirred for 2 h at −10 °C and the resulting suspension was left to stir overnight. Reaction was quenched by addition of 5% HCl (15 mL) and extracted with Et_2O. Organic phases were dried over Na_2SO_4 and concentrated. Crude oil was separated on silica gel column (25 g, 2.5 cm i.d. of column, 4% AcOEt and 0.3% THF in hexanes) to afford **7** (410 mg, 55%), **8** (105 mg, 14%) and 80 mg fraction containing both isomers. Overall yield of isolated products was 79%.

4.2.1. Compound 7. R_f 0.49 (23% AcOEt in hexanes), $[\alpha]_D^{21}=+4.4$ (*c* 0.21, CH_2Cl_2). IR (film, cm^{-1}): ν 3467 (s), 2987 (s), 1455, 1381, 1240, 1217, 1167, 1057, 701 (all s). ^1H NMR (300 MHz, $CDCl_3$): δ 1.43, 1.45 (all s, 6H, $C(CH_3)_2$), 2.68 (broad s, 2H, OH), 4.02 (dd, 1H, $J_{4,5}=4.0$ Hz, $J_{3,4}=8.1$ Hz, H-4), 4.42 (dd, 1H, $J_{2,3}=6.2$ Hz, $J_{3,4}=8.1$ Hz, H-3), 4.88 (ddd, 1H, $J_{1Z,2}=10.5$ Hz, H-1Z), 4.99 (d, 1H, $J_{1E,2}=17.3$ Hz, H-1E), 5.03 (bd, 1H, $J_{4,5}=4.0$ Hz, H-5), 5.28 (ddd, 1H, $J_{2,3}=6.2$ Hz, $J_{1Z,2}=10.5$ Hz, $J_{1E,2}=17.3$ Hz, H-2), 7.20–7.40 (m, 5H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.9 ('q', 2× q $C(CH_3)_2$), 71.8, 77.0, 84.2 (all d, C-3, C-4, C-5), 109.4 (s, $C(CH_3)_2$), 117.1 (t, C-1), 126.1, 128.3, 129.7 (all d, Ph), 135.7 (d, C-2), 138.5 (s, Ph). Anal. calcd for $C_{14}H_{18}O_3$ (234.3): C, 71.77; H, 7.74; Found: C, 72.12; H, 7.55.

4.2.2. Compound 8. R_f 0.57 (23% AcOEt/hexanes), $[\alpha]_D^{21}=+14.4$ (*c* 0.25, CH_2Cl_2). IR (film, cm^{-1}): ν 3466 (s), 2987 (s), 1458, 1381, 1240, 1218, 1166, 701 (all s). ^1H NMR (300 MHz, $CDCl_3$): δ 1.44, 1.48 (2× s, 6H, $C(CH_3)_2$), 2.81 (broad s, OH), 3.93 (dd, 1H, $J_{4,5}=5.3$ Hz, $J_{3,4}=8.1$ Hz, H-4), 4.31 (dd, 1H, $J_{2,3}=6.8$ Hz, $J_{3,4}=8.1$ Hz, H-3), 4.62 (bd, 1H, $J_{4,5}=5.3$ Hz, H-5), 5.00 (d, 1H, $J_{1Z,2}=10.5$ Hz, H-1Z), 5.08 (d, 1H, $J_{1E,2}=17.3$ Hz, H-1E), 5.44 (ddd, 1H, $J_{2,3}=6.2$ Hz, $J_{1Z,2}=10.5$ Hz, $J_{1E,2}=17.3$ Hz, H-2), 7.26–7.29 (m, 5H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.2, 27.1 (both q, $C(CH_3)_2$), 74.0, 79.1, 84.5 (all d, C-3, C-4, C-5), 109.7 (s, $C(CH_3)_2$), 118.1 (t, C-1), 125.3, 126.8, 128.4 (all d, Ph), 134.7 (d, C-2), 139.8 (s, Ph). Anal. calcd for $C_{14}H_{18}O_3$ (234.3): C, 71.77; H, 7.74; Found: C, 71.92; H, 7.95.

4.3. Typical procedure for addition of organometallics to aldehyde 6

Freshly prepared phenylating reagent (1.1 mmol PhMgBr, PhLi, $PhCeCl_2$) in 10 mL of corresponding solvent was set up to chosen temperature. Aldehyde **6** (156 mg, 1 mmol) was added dropwise in solvent (5 mL) and mixture was kept at initial temperature for additional 3 h, then kept to reach rt. Reaction was left until no **6** was observed, but no longer than 24 h (Table 1).

4.4. Typical procedure for addition of organometallics to aldehyde 6 in the presence of Lewis acid

Lewis acid (1.1 mmol) was dissolved or suspended in corresponding solvent (10 mL) and cooled to chosen temperature. Aldehyde **6** (156 mg, 1 mmol) in solvent (5 mL) was added and mixture was left to stir for 30 min. Phenylating agent (1.1 mL, 1.1 mmol PhLi or PhMgBr, 1 M soln) was added dropwise within 10 min, and mixture was stirred at initial temperature for 2 h, then left to reach rt; until no **6** was observed, but no longer than 24 h.

4.5. Procedure for addition of organometallics to aldehyde 6 in the presence of crown-ether

Freshly prepared PhMgBr in Et_2O (1.2 mmol in 10 mL) was concentrated under Ar. Syrupy brown residue was dissolved in CH_2Cl_2 (10 mL), 18-crown-6 (4 equiv) was added and mixture was left to stir until all crown-ether dissolved. Aldehyde **6** (156 mg, 1 mmol) in CH_2Cl_2 (5 mL) was added during 10 min and mixture was left overnight.

4.6. General workup procedure for all reactions above

Reactions were quenched with satd NH_4Cl (10 mL), extracted with Et_2O and dried over Na_2SO_4. Crude oils were analysed on *n*-phase HPLC (Separon SGX 250×4 mm column, $\lambda=254$ nm, 17% AcOEt in *i*-hexane, flow rate 0.7 mL/min, 25 °C); $T_r=7.8$ min for **7** and 11.7 min for **8**.

4.6.1. 5-*C*-Phenyl-D-*arabino*-1-pentenitol; [(1*R*, 2*S*, 3*R*)-1-phenyl-pent-4-ene-1,2,3-triol] (9). A suspension of protected triol **7** (600 mg, 2.56 mmol) in 70% EtOH (10 mL) and concd HCl (1 mL) was stirred for 3 h at rt. Solvents were removed in vacuo and residue was purified by flash chromatography on silica (50% AcOEt in hexanes). Yield of **9** (450 mg, 90%), colourless crystals; mp 143–144 °C, R_f 0.21 (50% AcOEt/hexanes), $[\alpha]_D^{21}=+11.9$ (*c* 0.08, MeOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.46 (broad s, 3H, OH), 3.67 (dd, 1H, $J_{3,4}=2.6$ Hz, $J_{4,5}=5.4$ Hz, H-4), 4.28 (dd, 1H, $J_{3,4}=2.6$ Hz, $J_{2,3}=5.4$ Hz, H-3), 4.88 (d, 1H, $J_{4,5}=5.4$ Hz, H-5), 5.21 (d, 1H, $J_{1Z,2}=10.6$ Hz, H-1Z), 5.30 (d, 1H, $J_{1E,2}=17.2$ Hz, H-1E), 5.90 (ddd, 1H, $J_{2,3}=5.4$ Hz, $J_{1Z,2}=10.6$ Hz, $J_{1E,2}=17.2$ Hz, H-2), 7.27–7.43 (m, 5H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ 71.4, 75.7, 75.9 (all d, C-3, C-4, C-5), 116.2 (t, C-1), 126.4, 127.7, 128.4 (all d, Ph), 137.4 (d, C-2), 140.8 (s, Ph). Anal. calcd for $C_{11}H_{14}O_3$ (194.2): C, 68.02; H, 7.27. Found: C, 68.22; H, 7.31.

4.6.2. 5-*C*-Phenyl-L-*xylo*-1-pentenitol; [(1*S*, 2*S*, 3*R*)-1-phenyl-pent-4-ene-1,2,3-triol] (10). Procedure as above; protected triol **8** (600 mg, 2.56 mmol). Flash column chromatography (50% AcOEt in hexanes) afforded pure **10** (472 mg, 95%) as colourless oil, R_f 0.15 (50% AcOEt/hexanes), $[\alpha]_D^{21}=+29.4$ (*c* 0.35, MeOH). IR (film, cm^{-1}): ν 3386 (s), 3064, 3032, 2914, 1718 (all m), 1494, 1454, 1401 (all s), 1198, 1042 (all m). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.96 (broad s, 3H, OH), 3.59 (dd, 1H, $J_{3,4}=3.3$ Hz, $J_{4,5}=5.5$ Hz, H-4), 4.04 (dd, 1H, $J_{3,4}=3.3$ Hz, $J_{2,3}=5.5$ Hz, H-3), 4.79 (d, 1H, $J_{4,5}=5.5$ Hz, H-5), 5.20 (d, 1H, $J_{1Z,2}=10.5$ Hz, H-1Z), 5.29 (d, 1H, $J_{1E,2}=17.2$ Hz, H-1E), 5.87 (ddd, 1H, $J_{2,3}=5.5$ Hz, $J_{1Z,2}=10.5$ Hz, $J_{1E,2}=17.2$ Hz, H-2), 7.26–7.40 (m, 5H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ 72.6, 74.5, 77.4 (all d, C-3, C-4, C-5), 116.8 (t, C-1), 126.6, 128.0, 128.5 (all d, Ph), 137.6 (d, C-2), 140.7 (s, Ph). Anal. calcd for $C_{11}H_{14}O_3$ (194.2): C, 68.02; H, 7.27. Found: C, 68.31; H, 7.52.

4.6.3. 3,6-Anhydro-2-deoxy-6-*C*-phenyl-D-*gluco*-1,4-hexonolactone; [(1*S*, 5*S*, 7*R*, 8*R*)-8-hydroxy-7-phenyl-2,6-dioxabicyclo[3.3.0]octan-3-one] (11). A 25 mL-flask with stopcock equipped side inlet was charged with $PdCl_2$ (9 mg, 0.05 mmol, 0.1 equiv), $CuCl_2$ (207 mg, 1.55 mmol, 3 equiv) and AcONa (127 mg, 1.55 mmol, 3 equiv). Alkenol **9** (100 mg, 0.52 mmol) in AcOH (10 mL) was added and the flask was purged with CO from balloon (residual air was removed through side inlet with water aspirator). The mixture was vigorously stirred at rt until colour of the mixture changed from green to pale brown (approx. 10 h). Inorganic material was removed on Cellite® pad and the filtrate was concentrated in vacuo. Residue was dissolved in AcOEt (25 mL) and washed with 10% $NaHCO_3$ (10 mL). Separated organic phase was dried over Na_2SO_4 and concentrated. Crude product was purified on silica gel column (50% AcOEt in hexanes). Spectroscopically pure lactone **11** was isolated as pale brown oil (102 mg, 90%), R_f 0.44 (50% AcOEt/hexanes), $[\alpha]_D^{21}=-75$ (*c* 0.38, CH_2Cl_2). IR (film, cm^{-1}) ν 3438, 2930, 1782, 1194, 1154, 1048, 1003, 760, 701. ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.64 (d, 1H, $J_{2A,2B}=18$ Hz, H-2), 2.97 (dd, 1H, $J_{2A,2B}=18$ Hz, $J_{2,3}=2.7$ Hz, H-2), 4.06 (dd, 1H, $J_{5,OH}=5.1$ Hz, $J_{4,5}=5.4$ Hz, H-5), 4.66 (d, 1H, $J_{4,5}=5.7$ Hz, H-4), 4.87 (bs, 2H, H-3, H-6), 5.97 (d, 1H, $J_{5,OH}=5.1$ Hz, OH), 7.26–7.40 (m, 5H, Ph); ^{13}C NMR (75 MHz, DMSO-d_6): δ 35.7 (t, C-2), 77.4 (d, C-5), 81.8 (d, C-3), 86.8 (d, C-4), 90.1 (d, C-6), 125.8, 127.7, 128.3 (all d, Ph), 139.4 (s, Ph), 175.5 (s, C-1). HR MS: 220.0733±5 ppm (calcd 220.0736 for $C_{12}H_{12}O_4$).

4.6.4. 3,6-Anhydro-2-deoxy-6-*C*-phenyl-L-*ido*-1,4-hexonolactone; [(1*S*, 5*S*, 7*S*, 8*R*)-8-hydroxy-7-phenyl-2,6-dioxabicyclo[3.3.0]octan-3-one] (12). Procedure as above; alkenol **10** (100 mg, 0.52 mmol). Lactone **12** was obtained in pure form by crystallisation of the crude product from AcOEt. Yield of **12** (97 mg, 85%), as colourless crystals, mp 177–180 °C, R_f 0.44 (50% AcOEt/hexanes), $[\alpha]_D^{21}=+38$ (*c* 0.31, CH_2Cl_2). IR (KBr, cm^{-1}): ν 3499, 1774, 1188, 1158, 1052, 1037, 742. ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.47 (d, 1H, $J_{2A,2B}=18.3$ Hz, H-2), 2.86 (dd, 1H, $J_{2A,2B}=18.3$ Hz, $J_{2,3}=6.6$ Hz, H-2), 4.20 (dd, 1H, $J_{5,OH}=5.1$ Hz, $J_{5,6}=3.6$ Hz, H-5), 4.88 (2× d, 2H, $J_{3,4}=3.8$ Hz, $J_{5,6}=3.6$ Hz, H-4, H-6), 4.94 (dd, 1H, $J_{2,3}=6.0$ Hz, $J_{3,4}=3.8$ Hz, H-3), 5.19 (d, 1H, $J_{5,OH}=5.4$ Hz, OH), 7.15–7.32 (m, 5H, Ph)); ^{13}C NMR (75 MHz, DMSO-d_6): δ 35.7 (t, C-2), 74.4 (d, C-5), 76.4 (d, C-3), 82.2 (d, C-4), 88.1 (d, C-6) 127.1, 127.3, 127.4 (all d, Ph), 136.7 (s, Ph), 176 (s, C-1)).

Anal. calcd for $C_{12}H_{12}O_4$ (220.2): C, 65.45; H, 5.49. Found: C, 65.28; H, 5.50.

4.6.5. 3,6-Anhydro-2-deoxy-6-*C*-phenyl-α/β-D-glucofuranose (13). A flame dried 25 mL-flask with stopcock equipped side inlet was flushed with Ar, charged with lactone **11** (130 mg, 0.6 mmol) in dry CH_2Cl_2 (5 mL) and cooled to −80 °C. Diisobutylaluminiumhydride solution (0.8 mL, 1.2 mmol, 2 equiv, 1.5 M soln in toluene) was added dropwise under vigorous stirring. The mixture was kept at −80 °C for 90 min and subsequently quenched with 1 M HCl (5 mL). Water phase was separated and extracted with AcOEt (3×10 mL). Combined organic extracts were washed with satd NaCl, dried over Na_2SO_4 and evaporated. Crude aldose **13** was isolated in 95% purity as colourless oil (125 mg, 94%) and therefore no purification was necessary, R_f 0.24 (50% AcOEt/hexanes). IR (KBr, cm^{-1}): ν 3455, 3410, 2938, 1247, 1101, 1074, 1059, 996, 958 (all s). ^{1}H NMR (300 MHz, DMSO-d_6, mixture of anomers in 1:8 ratio, following spectra are for major anomer): δ 2.03 (dd, 2H, $J_{1,2}$=3.6 Hz, $J_{2,3}$=4.5 Hz, H-2), 4.02 (dd, 1H, $J_{5,6}$=2.5 Hz, $J_{5,OH}$=5.1 Hz, H-5), 4.47 (d, 1H, $J_{3,4}$=4.5 Hz, H-4), 4.81 (d, 1H, $J_{5,6}$=2.4 Hz, H-6), 4.85 (d, 1H, $J_{5,OH}$=5.4 Hz, OH), 4.98 ('q', 1H, $J_{2,3}$=4.8 Hz, $J_{3,4}$=4.5 Hz, H-3), 5.51 ('q', 1H, $J_{1,2}$=3.6 Hz, $J_{1,OH}$=4.3 Hz, H-1), 6.24 (d, 1H, $J_{1,OH}$=4.8 Hz, OH), 7.14–7.37 (m, 5H, Ph); ^{13}C NMR (75 MHz, DMSO-d_6): δ 41.5 (t, C-2), 76.2 (d, C-5), 80.7 (d, C-3), 81.7 (d, C-6), 87.0 (d, C-4), 98.8 (d, C-1), 126.8, 127.3, 127.5 (3× d, Ph), 137.6 (s, Ph).

4.6.6. 3,6-Anhydro-2-deoxy-6-*C*-phenyl-α/β-D-idofuranose (14). The same procedure as above was used for the preparation of idofuranose **14** (127 mg, 95%), colourless oil, R_f 0.24 (50% AcOEt/hexanes). ^{1}H NMR (300 MHz, DMSO-d_6, only one anomer was detected): δ 1.85 (dt, 1H, $J_{2A,2B}$=9.0 Hz, $J_{1,2}$=$J_{2,3}$=4.5 Hz, H-2A), 2.23 (d, 1H, $J_{2A,2B}$=9.0 Hz, H-2B), 3.87 (dd, 1H, $J_{5,OH}$=5.1 Hz, H-5), 4.42 (d, 1H, $J_{5,6}$=2.4 Hz, H-6), 4.54 (d, 1H, $J_{3,4}$=5.7 Hz, H-4), 4.73 (dd, 1H, $J_{2,3}$=4.5 Hz, $J_{3,4}$=5.1 Hz, H-3), 5.49 (dd, 1H, $J_{1,2}$=4.5 Hz, $J_{1,OH}$=5.1 Hz, H-1), 5.61 (d, 1H, $J_{5,OH}$=5.1 Hz, OH), 6.25 (d, 1H, $J_{1,OH}$=5.4 Hz, OH), 7.14–7.38 (m, 5H, Ph); ^{13}C NMR (75 MHz, DMSO-d_6): δ 40.8 (t, C-2), 81.8 (d, C-5), 82.9 (d, C-3), 87.9 (d, C-6), 89.0 (d, C-4), 99.1 (d, C-1), 125.9, 127.4, 128.1 (3× d, Ph), 140.6 (s, Ph).

4.6.7. (*E*/*Z*)-4,7-Anhydro-2,3-dideoxy-1-*O*-methyl-7-*C*-phenyl-D-*gluco*-1-heptenitol (15). A flame dried 100 mL-flask with stopcock equipped side inlet was flushed with Ar, charged with methoxymethylene–triphenyl–phosphonium chloride (1.27 g, 3.78 mmol, 7 equiv) in dry THF (20 mL) and cooled to −80 °C. *tert*-Butyllithium (2.5 mL, 3.75 mmol, 6.9 equiv, 1.5 M in pentane) was added in two portions and the mixture was stirred at −80 °C for 1 h. Properly prepared reagent has bright red colour. Furanose **13** (120 mg, 0.54 mmol) in THF (5 mL) was added and the temperature was kept under −60 °C for additional 2 h. After overnight stirring at rt water (20 mL) and diethyl ether (50 mL) was added and separated water layer was extracted with diethyl ether. Combined organic layers were washed with water (30 mL) and dried over Na_2SO_4. Crude brown oil was purified by flash chromatography (20 g of silica-gel, 20%, then 35% and 50% ethyl acetate in toluene as eluent) to afford **15** (81 mg, 60%, pale yellow oil), as a mixture of *E*/*Z* isomers (*E*: *Z*=60:40).

E-**15**: ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.20 (dd, 2H, $J_{2,3}$=5.9 Hz, $J_{3,4}$=7.5 Hz, H-3), 3.45 (s, 3H, Me), 3.90–4.02 (m, 2H, H-5, H-6), 4.10 (dd, 1H, $J_{3,4}$=7.5 Hz, $J_{4,5}$=4.1 Hz, H-4), 4.38 (dd, 1H, $J_{1,2}$=13.0 Hz, $J_{2,3}$=5.9 Hz, H-2), 4.74 (s, 1H, H-7), 5.01 (d, 1H, $J_{5,OH}$=3.6 Hz, OH), 5.15 (d, 1H, $J_{6,OH}$=4.2 Hz, OH), 6.43 (d, 1H, $J_{1,2}$=12.9 Hz, H-1), 7.16–7.35 (m, 5H, Ph); ^{13}C NMR (75 MHz, DMSO-d_6): δ 27.2 (t, C-3), 55.5 (q, Me), 76.7 (d, C-5), 78.3 (d, C-6), 81.6 (d, C-4), 81.7 (d, C-7), 99.0 (d, C-2), 126.5, 127.2, 127.3 (all d, Ph), 139.3 (s, Ph), 148.2 (d, C-1).

Z-**15**: ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.15–2.26 (m, 2H, H-3), 3.55 (s, 3H, Me), 3.92 (m, 2H, H-5, H-6), 4.05–4.14 (m, 1H, $J_{6,7}$=7.5 Hz, H-7), 4.77 (d, 1H, $J_{4,5}$=4.2 Hz, H-4), 4.79 (d, 1H, $J_{1,2}$=6.3 Hz, H-2), 5.00 (d, 1H, $J_{5,OH}$=3.6 Hz, OH), 5.09 (d, 1H, $J_{6,OH}$=4.5 Hz, OH), 6.03 (d, 1H, $J_{1,2}$=6.3 Hz, H-1), 7.16–7.35 (m, 5H, Ph); ^{13}C NMR (75 MHz, DMSO-d_6): δ 23.9 (t, C-3), 59.0 (q, Me), 77.0 (d, C-5), 78.3 (d, C-6), 80.6 (d, C-4), 81.6 (d, C-7), 102.2 (d, C-2), 126.5, 127.2, 127.3 (3× d, Ph), 139.3 (s, Ph), 147.3 (d, C-1).

4.6.8. (*E*/*Z*)-4,7-Anhydro-2,3-dideoxy-1-*O*-methyl-7-*C*-phenyl-L-*ido*-1-heptenitol (16). Following the above procedure heptenitol **16** was obtained (80 mg, 59%) as a mixture of *E*/*Z* isomers (*E*: *Z*=62:38 by NMR) from idofuranose **14** (120 mg, 0.54 mmol).

E-**16**: ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.20–2.35 (m, 2H, H-3), 3.44 (s, 3H, Me), 3.80 (dd, 1H, $J_{5,OH}$=4.5 Hz, $J_{4,5}$=4.8 Hz, H-5), 3.84 (2× d, 2H, $J_{6,OH}$=3.6 Hz, $J_{6,7}$=3.6 Hz, H-6, H-7), 4.46 (d, 1H, $J_{3,4}$=5.7 Hz, $J_{4,5}$=4.2 Hz, H-4), 4.76 (dd, 1H, $J_{1,2}$=12.9 Hz, H-2), 4.90 (d, 1H, $J_{6,OH}$=3.6 Hz, OH), 5.40 (d, 1H, $J_{5,OH}$=4.5 Hz, OH), 6.43 (d, 1H, $J_{1,2}$=12.9 Hz, H-1), 7.20–7.44 (m, 5H, Ph); ^{13}C NMR (75 MHz, DMSO-d_6): δ 27.0 (t, C-3), 55.4 (q, Me), 77.9 (d, C-5), 82.0 (d, C-6), 84.8 (d, C-4), 86.7 (d, C-7), 99.0 (d, C-2), 126.4, 128.7, 128.8 (all d, Ph), 141.1 (s, Ph), 148.2 (d, C-1).

Z-**16**: ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.30–2.40 (m, 2H, H-3), 3.55 (s, 3H, Me), 3.80 (t, 1H, $J_{5,OH}$=4.5 Hz, $J_{4,5}$=4.8 Hz, H-5), 3.84 (2× d, 2H, $J_{6,OH}$=3.6 Hz, $J_{6,7}$=3.6 Hz, H-6, H-7), 4.46 (dd, 1H, $J_{3,4}$=5.7 Hz, $J_{4,5}$=4.2 Hz, H-4), 4.76 (d, 1H, $J_{1,2}$=6.3 Hz, H-2), 4.90 (d, 1H, $J_{6,OH}$=4.2 Hz, OH), 5.40 (d, 1H, $J_{5,OH}$=4.5 Hz, OH), 6.02 (d, 1H, $J_{1,2}$=6.3 Hz, H-1), 7.20–7.44 (m, 5H, Ph); ^{13}C NMR (75 MHz, DMSO-d_6): δ 23.7 (t, C-3), 59.1 (q, Me), 77.6 (d, C-5), 81.0 (d, C-6), 84.7 (d, C-4), 86.5 (d, C-7), 102.2 (d, C-2), 126.4, 127.9, 128.8 (all d, Ph), 141.7 (s, Ph), 147.4 (d, C-1).

4.6.9. (+)-Goniothalesdiol (1). A solution of D-*gluco*-heptenitol **15** (100 mg, 0.4 mmol) in THF (7 mL) and water (3 mL) was acidified with H_2SO_4 (96%, 1 mL) and left to stir at rt, until no starting material was detected by TLC (approx. 3 h). The mixture was carefully neutralised with 10% NaOH solution (pH=8) and the entire content of the reaction flask was introduced into the freshly prepared suspension of Ag_2O (250 mg, 1.5 mmol of $AgNO_3$ and 130 mg, 3.25 mmol of NaOH in 5 mL of deionised water, stirred for 30 min to prepare brown suspension). After 1 h of

vigorous stirring colour of the suspension turned to black and TLC detected no spots with Rf > 0.05 (50% AcOEt in hexanes). The precipitate of Ag/Ag_2O was filtered off (Cellite pad) and the filtrate neutralised with 1 M HCl. Solvents were replaced with dry MeOH (25 ml) and acidic catex (1 g, Amberlyst 15, previously washed three times with MeOH) was added. After 1 h of stirring at rt, catex and inorganic salts were removed by filtration on Celite® and the filtrate was concentrated. Crude yellow oil (100 mg), containing mixture of methylester **1**, nonesterified acid and impurities, was distilled on Kugelrohr apparatus (190 °C/ 0.05 Torr) to provide colourless oil (50 mg), a mixture of required product **1** and lactone **17** (50:50, determined by ^{1}H NMR). Another esterification this mixture (10 mL of dry MeOH, 300 mg of Amberlyst 15, 1 h at rt) afforded analytically pure goniothalesdiol **1** (45 mg, 42%) as a colourless oil, R_f 0.20 (50% AcOEt/hexanes), $[\alpha]_D^{21} = +6.9$ (*c* 0.38, MeOH) {lit.[7]:$[\alpha]_D^{25} = +7.5$ (*c* 0.23, EtOH), (−)-goniothalesdiol lit.[8]: $[\alpha]_D^{27} = -7.1$ (*c* 0.15, EtOH)}. IR (film, cm^{-1}): ν 3448 (bs), 2956 (m), 2929 (m), 1736, 1449, 1375, 1236, 1176, 1070, 757, 700 (all s). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.03–2.15 (m, 2H, H-3), 2.42–2.70 (m, 2H, H-2), 3.68 (s, 3H, OMe), 4.03–4.07 (m, 3H, H-4, H-5, H-6), 4.59 (d, 1H, $J_{6,7}$ = 4.5 Hz, H-7), 7.25 (d, 1H, J = 7.0 Hz, H-4′), 7.33 (t, 2H, J = 7.0 Hz, H-3′, H-5′), 7.41 (d, 2H, J = 7.0 Hz, H-2′, H-6′); ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.7 (t, C-3), 30.6 (t, C-2), 51.9 (q, OMe), 79.0 (d, C-5), 80.7 (d, C-4), 85.3 (d, C-6), 86.1 (d, C-7), 126.1 (d, C-3′, C-5′), 127.9 (d, C-4′), 128.7 (d, C-2′, C-6′), 139.9 (s, C-1′), 174.7 (s, C-1). Anal. calcd for $C_{14}H_{18}O_5$ (266.3): C, 63.15; H, 6.81. Found: C, 63.38; H, 6.60.

4.6.10. (+)-7-*epi*-Goniothalesdiol (2). Prepared as above from **16** (100 mg, 0.4 mmol). In this case the second esterification was not needed, because Kugelrohr distillation afforded pure target compound **2** (80 mg, 75%) as colourless oil, R_f 0.21 (50% AcOEt/hexanes), $[\alpha]_D^{21} = +70.3$ (*c* 0.23, EtOH) {lit.[9]:$[\alpha]_D^{25} = +66.6$ (*c* 0.74, EtOH)}. IR (film, cm^{-1}): ν 3456 (s), 2926 (m), 1717 (s), 1452, 1369, 1253, 1173, 1067, 742, 704 (all s). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.07 (dd, 2H, $J_{2,3} = J_{3,4}$ = 7.2 Hz, H-3), 2.40–2.65 (m, 2H, H-2), 3.70 (s, 3H, OMe), 4.16 (d, 1H, $J_{6,7}$ = 3.0 Hz, H-6), 4.21 (d, 1H, $J_{4,5}$ = 2.9 Hz, H-5), 4.31 (dt, 1H, $J_{3,4}$ = 7.2 Hz, $J_{4,5}$ = 2.9 Hz, H-4), 5.32 (d, 1H, $J_{6,7}$ = 3.0 Hz, H-7), 7.25–7.43 (m, 5H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.5 (t, C-3), 30.6 (t, C-2), 52.0 (q, OMe), 76.9 (d, C-5), 79.1 (d, C-4), 81.4 (d, C-6), 82.3 (d, C-7), 126.7 (d, C-3′, C-5′), 127.9 (d, C-4′), 128.6 (d, C-2′, C-6′), 136.8 (s, C-1′), 175.1 (s, C-1). Anal. calcd for $C_{14}H_{18}O_5$ (266.3): C, 63.15; H, 6.81. Found: C, 63.42; H, 6.93.

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