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Cycloheptanic sugar mimetics, bridging the gap in the homologous series of carbocyclic analogues

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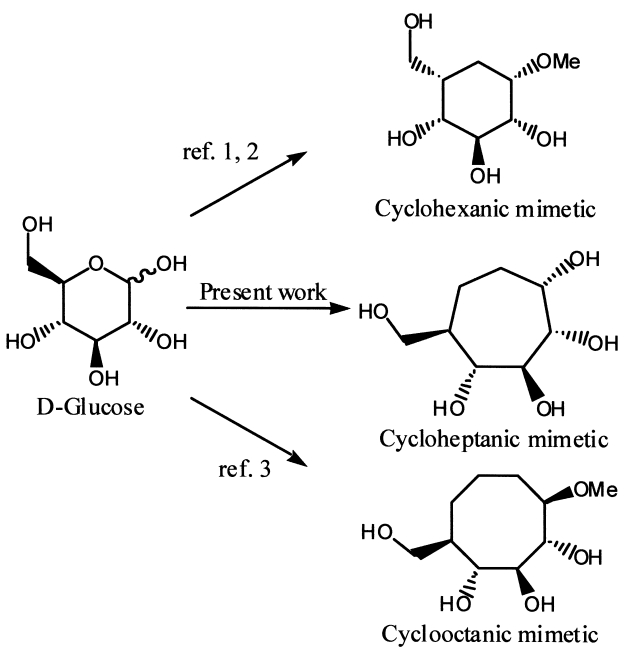
Abstract—The cycloheptanic analogues of α-D-glucopyranose and β-D-mannopyranose have been synthesized. These two members of a new class of carbocyclic sugar mimetics are filling the gap between already existing cyclohexanic and cyclooctanic classes of sugar mimetics. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

Carbasugars are a class of sugar mimetics in which the ring oxygen has been replaced by a methylene group. We have recently described the synthesis of such cyclohexanic compounds[1] using the triisobutylaluminium (TIBAL)-promoted carbocyclisation developed by us.[2] During a study of the scope of this reaction, we have synthesized cyclooctanic mimetics of sugars using a TIBAL-mediated Claisen rearrangement.[3,4] We now want to bridge the gap between these two families of carbocycles, describing the synthesis of cycloheptanic sugar mimetics, as shown in Scheme 1.

Various methods have been used for the conversion of sugars into seven-membered carbocycles including ring-closing metathesis,[5,6] free radical-mediated cyclization,[5,7] 1,3-dipolar cycloadditions,[8] intramolecular nucleophilic attack,[9] and ring enlargement of cyclohexanones.[10] Although the Claisen rearrangement has been extensively studied in sugar chemistry,[11] it has not been used for cycloheptane synthesis from sugars. Similarly, TIBAL promoted Claisen rearrangement has been widely used for cyclooctane formation,[12] but only one report of such a reaction has been found for a cycloheptane synthesis.[13] As we previously developed a TIBAL promoted reductive Claisen rearrangement for cyclooctene formation from pyranic rings,[3,4] we assumed that a similar reaction could be used for the construction of a cycloheptene ring from furanic compounds (Scheme 2).



Scheme 1. Carbocyclic sugar mimetics.

2. Results and discussion

The synthesis of the key diene **1** was achieved as shown in Scheme 3. The known alcohol **2**,[14] was paramethoxy benzylated to afford **3** in almost quantitative yield. Compound **3** was then hydrolysed in the presence of silver nitrate in an acetone/water mixture; Wittig olefination on the resulting hexose **4** gave the unsaturated alcohol **5** in 66% yield and this alcohol was converted into the corresponding triflate using triflic anhydride and pyridine in dichloromethane at −40°C. On heating, this triflate was displaced by nucleophilic attack of O-2, and subsequent debenzylation

Keywords: carbohydrates; carbasugars; cycloheptanes; Claisen rearrangement; triisobutylaluminium.

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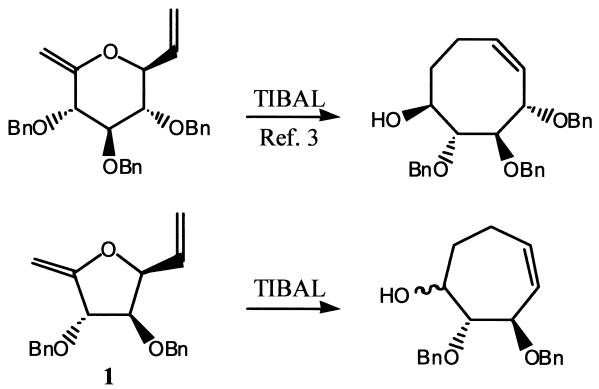


Scheme 2. TIBAL promoted reductive Claisen rearrangement on sugars.

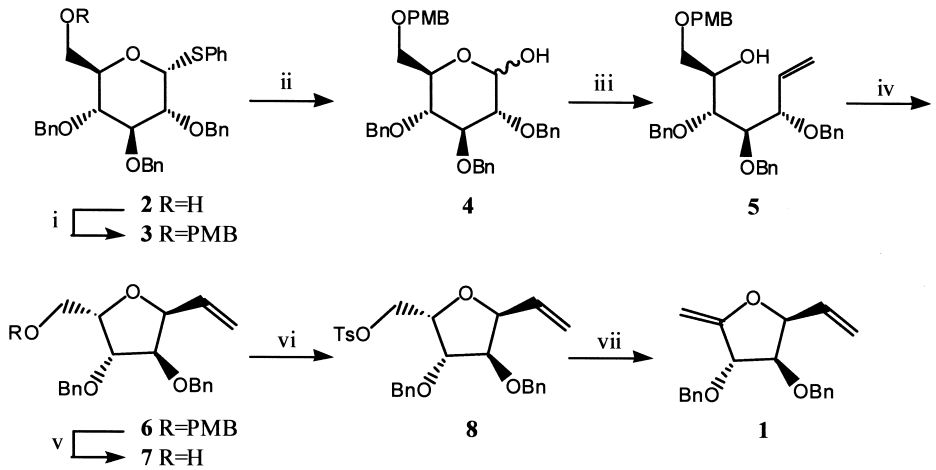
afforded **6** in 68% yield.[15] Selective deprotection of C-7, followed by tosylation, iodination and elimination[16] uneventfully afforded the expected diene **1** in 30% overall yield from the starting alcohol **2**.

Not unexpectedly, diene **1** underwent a smooth Claisen rearrangement catalyzed by TIBAL affording **9** and **10** in 76% yield as a 2:1 unseparable mixture, a side open-chain product **11** being also isolated in 7% yield (Scheme 4). Product **11** is the result of an hydroalumination–elimination process, that has already been reported in related cases.[3] The Claisen rearrangement into cycloheptene is not quite as efficient as for cyclooctene, probably due to the strain induced by the furanic ring.

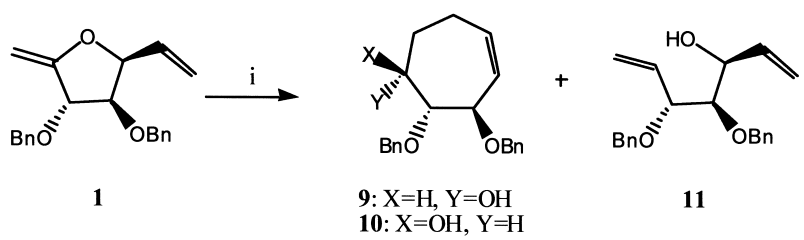
Dihydroxylation of the mixture of **9** and **10** with osmium tetroxide, followed by conventional acetonide protection of the resulting diol, and oxidation of the resulting alcohol with pyridinium chlorochromate, afforded **12** and **13** in 55% overall yield as a 5:4 separable mixture. Ketones **12** and **13** were then converted into cycloheptanic mimetics using the same sequence: Tebbe olefination of the carbonyl, hydroboration/oxidation of the resulting alkene, and final deprotection. (Scheme 5)

The hydroboration/oxidation step afforded a mixture of isomers for both compounds **14** and **19**. Assignment of the stereochemistry of the cycloheptanic compounds was achieved at this point by NMR spectroscopy. The coupling constants: $J_{1,2}\approx J_{2,3}\approx J_{3,4}\approx 9$ Hz for α-D-glucopyranose mimic **15** and $J_{1,2}\approx J_{2,3}\approx 8$ Hz and $J_{3,4}\approx 2$ Hz for β-D-mannopyranose mimic **20** were consistent with the data for similar compounds[17] and in agreement with the twist chair conformation described for seven-membered rings.[18] **15** and **20** were then fully deprotected: acetonide removal with TFA in a dioxane/water mixture, and benzyl removal by hydrogenolysis afforded **18** (75%) and **23** (82%), respectively. (Scheme 6)

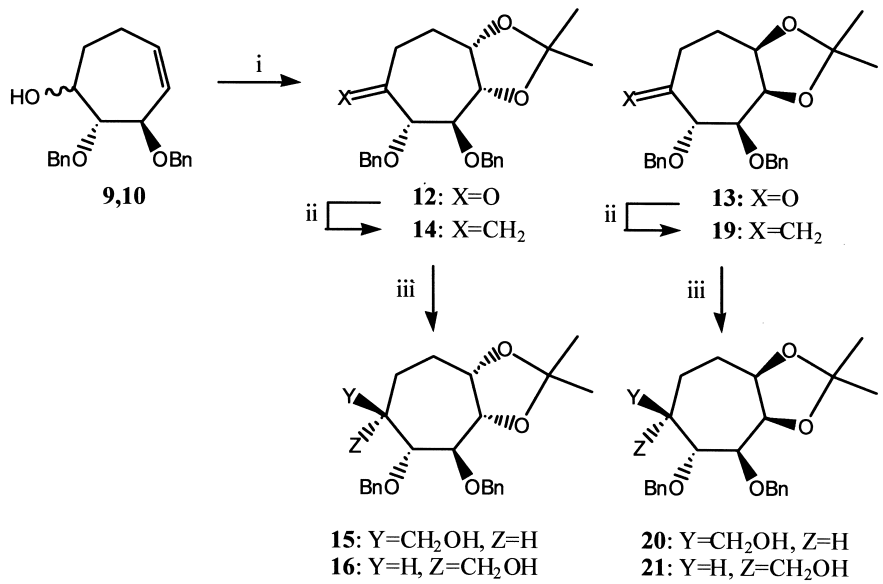
As expected, the ^{1}H NMR spectrum of **18** and **23** has a close analogy with that of α-D-glucopyranose[19] and β-D-mannopyranose,[20] respectively, a feature which fully qualifies **18** and **23** as cycloheptanic mimetics of their related sugars (Table 1). Compounds **18** and **23** represent the first two members of a new class of homologous carbasugars, which



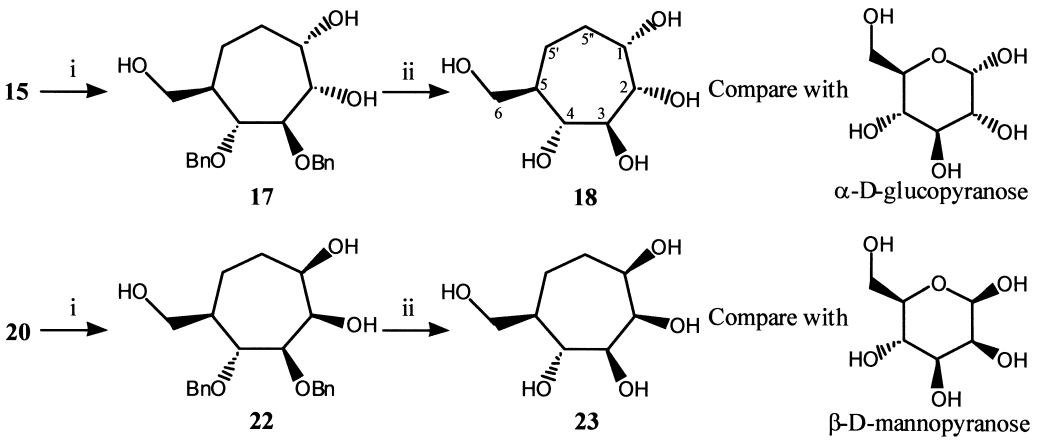
Scheme 3. Synthesis of the key diene **1**. *Reagents and conditions*: (i) PMBCl, NaH, DMF, rt, 12 h, (99%); (ii) $AgNO_3$, acetone, H_2O, rt, 48 h, (98%); (iii) Ph_3PMeBr/BuLi, DME, rt→80°C, 25 min, (66%); (iv) Tf_2O, Pyr, dichloromethane, −40°C→rt, 6 h, (68%); (v) DDQ, dichloromethane, H_2O, rt, 4 h, (87%); (vi) TsCl, DMAP, Pyr, dichloromethane, rt, 8 h, (87%); (vii) (a) NaI, Bu_4NI, DMSO, MS 4 Å, 80°C, 12 h; (b) DBU, DMSO, 4 Å MS, 80°C, 6 h, (93%, two steps).



Scheme 4. Action of TIBAL on diene **1**. *Reagents and conditions*: (i) *i*Bu_3Al, toluene, 60°C, 12 h, (**9/10/11**, 62:30:8, 83%).



Scheme 5. Chain elongation of cycloheptanes **9** and **10**. *Reagents and conditions*: (i) (a) OsO_4, NMO, MeCOMe/H_2O, rt, 24 h; (b) $Me_2C(OMe)_2$, CSA CH_2Cl_2, rt, 15 h; (c) PCC, 4 Å MS, CH_2Cl_2, rt, 2 h (**12/13**, 55:45, 56%, 3 steps); (ii) Tebbe reagent, THF/pyr. −40°C→rt, 36 h, (**14**, 63%; **19**, 71%); (iii) BH_3.THF, rt, 5 h then H_2O_2, aq NaOH, 50°C, 3 h, (**15/16**, 75:25, 69%; **20/21**, 7:3, 65%).



Scheme 6. Final deprotection in the synthesis of cycloheptanic sugar mimetics. Reagents and conditions: (i) TFA, dioxane/H_2O, rt, 24 h, (**17**, 82%; **22** 89%); (ii) H_2, Pd/C, EtOH/MeOH, rt, 5 h, (**18**, 92%; **23**, 92%).

Table 1. Comparison of the coupling constants between the sugars and their analogues

Coupling constants (Hz)	α-D-glucopyranose[19]	**18**	β-D-mannopyranose[20]	**23**
$J_{1,2}$	3.6	2.6	1.5	2
$J_{2,3}$	9.5	7.8	3.8	2
$J_{3,4}$	9.5	7.8	10.0	8.8
$J_{4,5}$	9.5	9.3	9.8	8.6

We used carbasugar numbering for the cycloheptanic mimetic as shown on Scheme 6.

fills the gap between previously described cyclohexanic and cyclooctanic sugar mimetics.

3. Experimental

3.1. General

Melting points were determined with a Büchi model 535 mp apparatus and are uncorrected. Optical rotations were measured at 20±2°C with a Perkin–Elmer Model 241 digital polarimeter, using a 10 cm, 1 mL cell. Chemical Ionization Mass Spectra (CI-MS ammonia) and Fast Atom Bombardment Mass Spectra (FAB-MS) were obtained with a JMS-700 spectrometer. Elemental analyses were performed by Service de Microanalyse de l'Université Pierre et Marie Curie, 4 Place Jussieu, 75005 Paris, France. ^{1}H NMR spectra were recorded with a Bruker AC 250 or a Bruker DRX 400 or a Bruker Avance 600 spectrometer for solutions in $CDCl_3$ or CD_3OD or D_2O at ambient

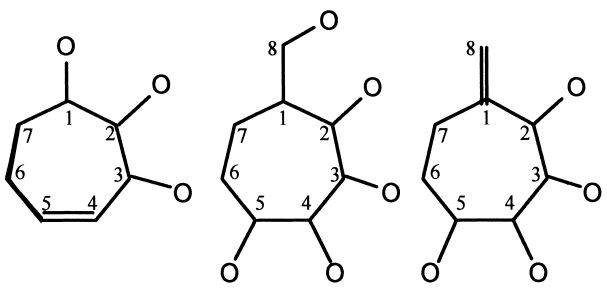


Figure 1. Cycloheptane numbering for NMR assignment.

temperature. Assignment were aided by COSY experiments. ^{13}C NMR spectra were recorded at 62.9 MHz with a Bruker AC 250 or at 100.6 MHz with a Bruker DRX 400 or at 150.9 MHz with a Bruker DRX 600 spectrometer for solutions in $CDCl_3$ adopting 77.00 ppm for the central line of $CDCl_3$. Assignments were aided by J-mod technique and proton–carbon correlation. Numbering of cycloheptanic compounds is indicated on Fig. 1 (for compounds **18** and **23** see Scheme 6). Reactions were monitored by thin-layer chromatography (TLC) on a precoated plate of silica gel 60 F_{254} (layer thickness 0.2 mm; E. Merck, Darmstadt, Germany) and detection by charring with sulfuric acid. Flash column chromatography was performed on silica gel 60 (230–400 mesh, E. Merck).

3.1.1. Phenyl 2,3,4-tri-*O*-benzyl-6-*O*-(4-methoxybenzyl)-1-thio-β-D-glucopyranoside (3). Sodium hydride (60% in mineral oil, 0.9 g, 21.5 mmol) was added portionwise to a cooled (0°C) solution of **2** (5.3 g, 9.77 mmol) and *p*-methoxybenzyl chloride (2.9 mL, 21.5 mmol) in DMF (100 mL). The reaction mixture was stirred at rt overnight. MeOH (5 mL) was added. The reaction mixture was stirred for 1 h then concentrated. A solution of the residue in dichloromethane was washed with water, dried ($MgSO_4$) and concentrated. The residue was chromatographed (cyclohexane/AcOEt=5:1) to give **3** (6.4 g, 99%). Mp 65–66°C, $[\alpha]_D$=+6 (c=0.75, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz): 7.70–6.90 (m, 24H, H-arom); 4.93 (d, 1H, J=11 Hz, CH_2Ph); 4.91 (d, 1H, J=10.2 Hz, CH_2Ph); 4.89 (d, 1H, J=11 Hz, CH_2Ph); 4.85 (d, 1H, J=10.8 Hz, CH_2Ph); 4.78 (d, 1H, J=10.3 Hz, CH_2Ph); 4.72 (d, 1H, $J_{1,2}$=9.8 Hz, H-1); 4.61 (d, 1H, J=10.8 Hz, CH_2Ph); 4.60 (d, 1H, J=11.6 Hz, CH_2Ph); 4.52 (d, 1H, J=11.6 Hz, CH_2Ph); 3.85 (s, 3H, OCH_3); 3.80 (dd, 1H, $J_{6a,6b}$=11 Hz, $J_{6a,5}$=2 Hz, H-6a); 3.78 (dd, 1H, $J_{6a,5}$=4 Hz, H-6b); 3.75 (t, 1H, $J_{3,4}$=$J_{3,2}$=9 Hz, H-3); 3.68 (t, 1H, $J_{4,5}$=9 Hz, H-4); 3.55 (dd, 1H, H-2); 3.53 (ddd, 1H, H-5). MS (CI): m/z=680 (M+NH_4). Anal. calcd for $C_{41}H_{42}O_6S$: C%=74.29, H%=6.38; found C%=74.29, H%=6.39.

3.1.2. 2,3,4-Tri-*O*-benzyl-6-*O*-(4-methoxybenzyl)-α,β-D-glucopyranose (4). Silver nitrate (5 g, 29.4 mmol) was added to a solution of **3** (6.4 g, 11.5 mmol) in acetone/water (120 mL, v/v 5:1). The mixture was stirred for 3 days, filtered and concentrated. A solution of the residue in dichloromethane was washed with water, aq. $NaHCO_3$, dried ($MgSO_4$) and concentrated. Chromatography of the residue on silica gel (cyclohexane/AcOEt 2:1), gave **4** (5.24 g, 98%). ^1H NMR ($CDCl_3$, 400 MHz): 7.50–6.70 (m, 19H, H-arom); 5.27 (d, 1H, $J_{1,2}$=3.4 Hz, H-1α); 4.99 (d, 1H, J=11 Hz, CH_2Ph); 4.98 (d, 1H, J=10.9 Hz, CH_2Ph); 4.97 (d, 1H, J=11 Hz, CH_2Ph); 4.88 (d, 1H, J=11 Hz, CH_2Ph); 4.85 (d, 1H, J=10.8 Hz, CH_2Ph); 4.84 (d, 1H, J=10 Hz, CH_2Ph); 4.81 (d, 1H, J=11.7 Hz, CH_2Ph); 4.77 (d, 1H, $J_{1,2}$=8 Hz, H-1β); 4.73 (d, 1H, J=11.9 Hz, CH_2Ph); 4.60 (d, 1H, J=11.9 Hz, CH_2Ph); 4.57 (d, 1H, J=11 Hz, CH_2Ph); 4.50 (d, 1H, J=11.4 Hz, CH_2Ph); 4.48 (d, 1H, J=10.8 Hz, CH_2Ph); 4.45 (d, 1H, J=11.9 Hz, CH_2Ph); 4.07 (ddd, 1H, H-5α); 4.01 (t, 1H, $J_{3,2}$=9.2 Hz, H-3α); 3.82 (s, 3H, OCH_3β); 3.80 (s, 3H, OCH_3α); 3.72 (dd, 1H, $J_{6b,5}$=3.8 Hz, H-6bα); 3.65 (dd, 1H, $J_{5,6a}$=2 Hz, $J_{6a,6b}$=10 Hz, H-6aα); 3.64 (t, 1H, $J_{4,3}$=$J_{4,5}$=9.2 Hz, H-4α); 3.63 (dd, 1H, $J_{1,2}$=3.5 Hz, H-2α); 3.44 (dd, 1H, $J_{1,2}$=8 Hz, $J_{2,3}$=7.8 Hz, H-2β); 3.21 (bs, 1H, OH). MS (CI): m/z=588 (M+NH_4). Anal. calcd for $C_{35}H_{38}O_7$: C%=73.66, H%=6.71; found C%=73.55, H%=6.68.

3.1.3. 7-*O*-(4-Methoxybenzyl)-3,4,5-tri-*O*-benzyl-D-*gluco*-hept-1-enitol (5). A solution of $Ph_3P{=}CH_2$ in DME (prepared by mixing Ph_3PMeBr (9.8 g, 27.6 mmol), BuLi (1.6 M in hexane, 17.25 mL, 27.6 mmol) in dry DME (25 mL) at −20°C and then stirring for 3 h at room temperature) was added dropwise at 0°C to a solution of **4** (5.1 g, 9.2 mmol) and BuLi (1.6 M in hexane, 5.75 mL, 9.2 mmol) in dry DME (25 mL). The temperature was raised to 80°C for 20 min then cooled to 0°C. The reaction mixture was quenched with acetone (15 mL), filtered, concentrated. Chromatography (toluene/AcOEt=9:1) of the residue gave **5** (3.38 g, 66%). $[\alpha]_D$=+24 (c=1, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz): 7.75–7.30 (m, 14H, H-arom.); 5.90 (ddd, 1H, $J_{2,1a}$=10 Hz, $J_{2,1b}$=17.2 Hz, $J_{2,3}$=7.3 Hz, H-2); 5.37 (dd, 1H, $J_{1a,1b}$=1.8 Hz, H-1a); 5.32 (dd, 1H, H-1b); 4.89 (d, 1H, J=11.3 Hz, CH_2Ph); 4.75 (d, 1H, J=11.3 Hz, CH_2Ph); 4.74 (d, 1H, J=11.7 Hz, CH_2Ph); 4.68 (d, 1H, J=11.6 Hz, CH_2Ph); 4.64 (d, 1H, J=11.5 Hz, CH_2Ph); 4.59 (d, 1H, J=11.5 Hz, CH_2Ph); 4.51 (d, 1H, J=11.5 Hz, CH_2Ph); 4.48 (d, 1H, J=11.6 Hz, CH_2Ph); 4.27 (dd, 1H, $J_{4,3}$=6.2 Hz, H-3); 4.08 (quin, 1H, $J_{6,7a}$=$J_{6,7b}$=$J_{6,5}$=$J_{6,OH}$=5 Hz, H-6); 3.85 (s, 1H, OCH_3); 3.82 (dd, 1H, $J_{4,5}$=3.6 Hz, H-4); 3.78 (dd, 1H, H-5); 3.67–3.60 (m, 2H, H-7a, H-7b); 2.91 (d, 1H, OH). MS (CI): m/z=586 (M+NH_4). Anal. calcd for $C_{36}H_{40}O_6$: C%=76.03, H%=7.09; found C%=75.97, H%=7.18.

3.1.4. 7-*O*-(4-Methoxybenzyl)-4,5-di-*O*-benzyl-3,6-anhydro-L-*ido*-hept-1-enitol (6). Triflic anhydride (2.2 mL, 13 mmol) was added dropwise at −40°C to a solution of **5** (1.91 g, 3.46 mmol) in a mixture of dichloromethane (25 mL) and pyridine (5 mL). The temperature was maintained at −40 to −20° C for 4 h, then slowly raised to room temperature over night. MeOH (10 mL) was added at 0°C. The reaction mixture was concentrated. A solution of the residue in dichloromethane was washed with water, aq $NaHCO_3$, dried ($MgSO_4$) and concentrated. Chromatography on silica gel (cyclohexane/AcOEt=5:1) of the residue gave **6** (1.08 g, 68%). $[\alpha]_D$=+37 (c=1.5, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz): 7.40–7.60 (m, 14H, H-arom); 6.11 (ddd, 1H, $J_{2,1a}$=17 Hz, $J_{2,1b}$=10 Hz, $J_{2,3}$=7.7 Hz, H-2); 5.43 (dt, 1H, $J_{1a,1b}$=$J_{1a,3}$=1.6 Hz, H-1a); 5.33 (dddd, 1H, $J_{1b,3}$=0.8 Hz, H-1b); 4.65 (dd, 1H, $J_{3,4}$=4 Hz, H-3); 4.66 (d, 1H, J=11.5 Hz, CH_2Ph); 4.62 (d, 1H, J=12.2 Hz, CH_2Ph); 4.60 (d, 1H, J=12.3 Hz, CH_2Ph); 4.56 (d, 1H, J=12 Hz, CH_2Ph); 4.55 (d, 1H, J=12.2 Hz, CH_2Ph); 4.52 (d, 1H, J=11.5 Hz, CH_2Ph); 4.50 (dt, 1H

$J_{6,7}$=6.2 Hz, $J_{6,5}$=4 Hz, H-6); 4.15 (dd, 1H, $J_{5,4}$=1.5 Hz, H-5); 4.01 (dd, 1H, H-4); 3.86 (s, 3H, OCH_3); 3.82 (dd, 1H, $J_{7a,7b}$=9.7 Hz, H-7a); 3.77 (dd, 1H, H-7b). MS (CI): *m*/*z*=478 ($M+NH_4$). Anal. calcd for $C_{29}H_{32}O_5$: C%=75.62, H%=7.00; found C%=75.62, H%=6.95.

3.1.5. 4,5-Di-*O*-benzyl-3,6-anhydro-L-*ido*-hept-1-enitol (7). A solution of DDQ (518 mg, 2.28 mmol), **6** (700 mg, 1.52 mmol) in dichloromethane/water (21 mL, 20:1 v/v) was stirred overnight, diluted with dichloromethane (25 mL), washed with 20% aq NaOH, water, dried ($MgSO_4$) and concentrated. Column chromatography (cyclohexane/AcOEt=3:1) of the residue gave **7** (450 mg, 87%). $[\alpha]_D$=+41 (*c*=0.65 $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz): 7.20–7.40 (m, 10H, H-arom); 6.10 (ddd, 1H, $J_{2,1a}$=10 Hz, $J_{2,1b}$=17 Hz, $J_{2,3}$=7 Hz, H-2); 5.46 (dt, 1H, $J_{1b,1a}$=$J_{1a,3}$=1.2 Hz, H-1a); 5.35 (dt, 1H, $J_{1b,3}$=1.2 Hz, H-1b); 4.67 (dd, 1H, $J_{3,4}$=4 Hz, H-3); 4.63 (d, 1H, *J*=11.9 Hz, CH_2Ph); 4.62 (d, 1H, *J*=12.2 Hz, CH_2Ph); 4.58 (d, 1H, *J*=12.2 Hz, CH_2Ph); 4.48 (d, 1H, *J*=11.9 Hz, CH_2Ph); 4.36 (q, 1H, $J_{6,5}$=$J_{6,7a}$=$J_{6,7b}$=5 Hz, H-6); 4.19 (dd, 1H, $J_{5,4}$=2 Hz, H-5); 4.05 (dd, 1H, H-4); 3.92 (dd, 1H, $J_{7a,7b}$=11.8 Hz, H-7a); 3.84 (dd, 1H, H-7b); 2.40 (s, 1H, OH). MS (CI): *m*/*z*=358 ($M+NH_4$). Anal. calcd for $C_{21}H_{24}O_4$: C%=74.09, H%=7.10; found C%=73.94, H%=7.13.

3.1.6. 7-*O*-Tosyl-4,5-di-*O*-benzyl-3,6-anhydro-L-*ido*-hept-1-enitol (8). A solution of **7** (450 mg, 1.32 mmol), tosyl chloride (1.26 g) and DMAP (cat.) in dry pyridine (5 mL) was stirred 24 h at rt, diluted with MeOH (5 mL) and concentrated. Column chromatography (cyclohexane/AcOEt=4:1) of the residue gave **8** (570 mg, 87%). Mp 50–51°C $[\alpha]_D$=+14 (*c*=1.7, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz): 7.90 (d, 2H, Ts); 7.20–7.40 (m, 12H, H-arom); 6.01 (ddd, 1H, $J_{2,1a}$=10 Hz, $J_{2,1b}$=17.5 Hz, $J_{2,3}$=7 Hz H-2); 5.37 (dt, 1H, $J_{1b,1a}$=$J_{1a,3}$=1.5 Hz, H-1a); 5.30 (dt, 1H, $J_{1b,3}$=1.5 Hz, H-1b); 4.53 (d, 1H, *J*=12.2 Hz, CH_2Ph); 4.52 (d, 1H, *J*=11.8 Hz, CH_2Ph); 4.51 (dd, 1H, H-3); 4.50 (d, 1H, *J*=12.2 Hz, CH_2Ph); 4.45 (d, 1H, *J*=11.8 Hz, CH_2Ph); 4.44 (td, 1H, $J_{6,7a}$=$J_{6,7b}$=6.5 Hz, $J_{6,5}$=4.2 Hz, H-6); 4.32 (dd, 1H, $J_{7a,7b}$=9.7 Hz, H-7b); 4.20 (dd, 1H, H-7a); 4.09 (dd, 1H, $J_{5,6}$=4.1 Hz, $J_{5,4}$=1.4 Hz, H-5); 3.92 (dd, 1H, $J_{4,3}$=3.7 Hz, H-4); 2.50 (s, 3H, Tos). MS (CI): *m*/*z*=512 ($M+NH_4$). Anal. calcd for $C_{28}H_{30}O_6S$: C%=67.99, H%=6.11; found C%=67.91, H%=5.78.

3.1.7. (3*S*,4*R*,5*S*)-3,4-Di-benzyloxy-2-methylene-5-vinyl-tetrahydrofurane (1). A mixture of **8** (560 mg, 1.13 mmol), 4 Å molecular sieve (0.5 g), NaI (1.1 g, 6.78 mmol) and Bu_4NI (6.30 mg, 1.69 mmol) in anhydrous DMSO (6 mL) was stirred at 80°C for 7 h. The mixture was cooled to room temperature, and DBU (0.7 mL, 2.26 mmol) was added, the mixture was then stirred overnight at 90°C, cooled to room temperature, diluted with AcOEt (25 mL), filtered through Celite, concentrated. Chromatography (cyclohexane/AcOEt=95:5) of the residue gave **1** (340 mg, 93%). $[\alpha]_D$+3 (*c*=1.3, $CHCl_3$). ^1H NMR ($CDCl_3$, 250 MHz): 7.50–7.20 (m, 10H, H-arom); 6.00 (ddd, 1H, $J_{6,7a}$=17 Hz, $J_{6,7b}$=10.3 Hz, $J_{5,6}$=7.6 Hz, H-6); 5.35 (dt, 1H, $J_{7a,7b}$=$J_{7a,5}$=1.5 Hz, H-7a); 5.25 (ddd, 1H, $J_{7b,5}$=1.5 Hz, H-7b); 4.75 (dd, 1H, $J_{4,5}$=3.8 Hz, H-5); 4.63 (d, 1H, *J*=11.8 Hz, CH_2Ph); 4.51 (d, 1H, *J*=12.2 Hz, CH_2Ph); 4.50 (d, 1H, $J_{1a,1b}$=1.7 Hz, H-1a); 4.44 (d, 1H, *J*=12.2 Hz, CH_2Ph); 4.43 (d, 1H, *J*=11.8 Hz, CH_2Ph); 4.20 (d, 1H, $J_{3,4}$=1.5 Hz, H-3); 4.10 (d, 1H, H-1b); 3.90 (dd, 1H, H-4). MS (CI): *m*/*z*=340 ($M+NH_4$). Anal. calcd for $C_{21}H_{22}O_3$: C%=78.23, H%=6.88; found C%=78.11, H%=7.08.

3.1.8. (1*R* and 1*S*,2*R*,3*S*)-1-Hydroxy-2,3-dibenzyloxy-cyclohept-4-ene (9) and (10). A mixture of a triisobutyl-aluminum (1 M solution in toluene, 6.5 mL, 6.5 mmol), **1** (600 mg, 1.85 mmol) in dry dichloromethane (8 mL) was stirred in a Schlenk tube under argon for 12 h at 60°C, then cooled (0°C) and diluted with ethyl acetate (10 mL) and water (2 mL), filtered dried ($MgSO_4$) and concentrated. The residue was chromatographed (toluene/AcOEt/MeCOMe=95:4:1) to give a mixture of **9** and **10** (430 mg, 76%, 9/10=2:1 from ^1H NMR), **11** (40 mg, 7%) and **1** (40 mg, 7%). **9**+**10** (′): ^1H NMR ($CDCl_3$, 400 MHz): 7.30–7.50 (m, 20H, H-arom); 6.02–5.95 (m, 2H, H-5, H-5′); 5.80 (ddd, 1H, $J_{4',5'}$=11.5 Hz, $J_{4',3'}$=3.4 Hz, $J_{4',6a'}$=2 Hz, H-4′); 5.75 (dd, 1H, $J_{4,5}$=11.4 Hz, $J_{4,3}$=4 Hz, H-4); 5.12 (d, 1H, *J*=11.2 Hz, CH_2Ph'); 4.90 (d, 1H, *J*=11.5 Hz, CH_2Ph); 4.79 (d, 1H, *J*=11.7 Hz, CH_2Ph'); 4.72 (d, 1H, *J*=11.7 Hz, CH_2Ph); 4.70 (d, 1H, *J*=11.7 Hz, CH_2Ph'); 4.69 (d, 1H, *J*=11.6 Hz, CH_2Ph); 4.66 (d, 1H, *J*=11.7 Hz, CH_2Ph); 4.65 (d, 1H, *J*=11.2 Hz, CH_2Ph'); 4.50 (dd, 1H, $J_{3,2}$=8.5 Hz, H-3); 4.23–4.18 (m, 2H, H-3′, H-1); 3.70 (td, 1H, $J_{1',7a'}$=$J_{1',2'}$=8.5 Hz, $J_{1',7b'}$=3.5 Hz, H-1′); 3.67 (dd, 1H, $J_{2,1}$=3.1 Hz, H-2); 3.40 (t, 1H, $J_{2',1'}$=$J_{2',3'}$=8.5 Hz, H-2′); 3.10 (s br, 1H, OH′); 2.70 (s br, 1H, OH); 2.41–2.31 (m, 1H, H-6a); 2.30–2.21 (m, 1H, H-6a′); 2.08–1.97 (m, 3H, H-7a′, H-6b′, H-6b); 1.87 (dtd, 1H, $J_{7a,7b}$=13.6 Hz, *J*=8.2, 8.2, 2.4 Hz, H-7a); 1.76 87 (ddt, 1H, *J*=10.5, 3, 3 Hz, H-7b); 1.60–1.50 (m, 1H, H-7′b). MS (CI): *m*/*z*=342 ($M+NH_4$). Anal. calcd for $C_{21}H_{24}O_3$: C%=77.74, H%=7.45; found C%=77.61, H%=7.61.

3.1.9. (3*S*,4*S*,5*R*)-3,4-Dibenzyloxy-5-hydroxy hepta-1,6-diene (11). $[\alpha]_D$=−23 (*c*=1.3, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz): 7.35 (m, 10H, H-arom); 5.95 (ddd, 1H, $J_{2,1a}$=17.5 Hz, $J_{2,1b}$=10 Hz, $J_{2,3}$=7.5 Hz, H-2); 5.90 (ddd, 1H, $J_{6,7a}$=17.2 Hz, $J_{6,7b}$=10.4 Hz, $J_{6,5}$=5.3 Hz, H-6); 5.46–5.39 (m, 2H, H-1); 5.32 (dt, 1H, $J_{7a,7b}$=$J_{7a,5}$=1.6 Hz, H-7a); 5.19 (dt, 1H, $J_{7b,6}$=1.5 Hz, H-7b); 4.88 (d, 1H, *J*=11.1 Hz, CH_2Ph); 4.69 (d, 1H, *J*=10.9 Hz, CH_2Ph); 4.43 (d, 1H, *J*=11.7 Hz, CH_2Ph); 4.33–4.29 (m, 1H, H-5); 4.10 (dd, 1H, $J_{3,4}$=6 Hz, H-3); 3.47 (dd, 1H, $J_{4,5}$=3.5 Hz, H-4); 2.54 (d, 1H, $J_{OH,5}$=6.9 Hz, OH); MS (CI): *m*/*z*=342 ($M+NH_4$); Anal. calcd for $C_{21}H_{24}O_3$: C%=77.74, H%=7.45; found C%=77.70, H%=7.64.

3.1.10. (2*R* and 2*S*,3*R*,4*S*,5*S*)-4,5-Dihydroxy-4,5-*O*-isopropylidene-2,3-di-benzyloxy-cylohept-1-one (12 and 13). A solution of *N*-morpholin-oxide (130 mg, 0.96 mmol) and OsO_4 (2.5% solution in tertbutanol, 0.048 mL, 0.005 mmol) and (**9**+**10**, 155 mg) in acetone/water (20 mL, 8:1=v/v) was stirred for 24 h at room temperature, diluted with dichloromethane (20 mL) and 1 M aq HCl (3 mL), stirred for 30 min. The organic layer was separated, concentrated to 5 mL treated for 1 h with 1.5 mL 10% aq. $Na_2S_2O_5$, washed with water, dried ($MgSO_4$) and concentrated. Column chromatography (cyclohexane/AcOEt=1:2) gave to an mixture of diols (95 mg) directly engaged in the next step.

A solution of diols (95 mg, 0.27 mmol), 2,2-dimethoxy propane (3.5 mL) and CSA (cat) in dry dichloromethane (3.5 mL) was stirred overnight at room temperature, diluted with dichloromethane (25 mL), washed with sat. aq. $NaHCO_3$, dried ($MgSO_4$) and concentrated. Chromatography (cyclohexane/AcOEt=3.5:1) gave a mixture of isopropylidene derivatives (90 mg, 85%).

A mixture of isopropylidene derivatives (90 mg, 0.226 mmol), PCC (155 mg, 0.7 mmol), 4 Å molecular sieve (150 mg) in anhydrous dichloromethane (5 mL) under argon was stirred for 2 h., diluted with dichloromethane (25 mL) and ether (10 mL), filtered through Celite. The organic phase was dried ($MgSO_4$), concentrated and the residue was chromatographed (cyclohexane/AcOEt=5:1) to give **12** and **13** (58 mg, 65% ratio **12/13**=5/4).

12: $[\alpha]_D$=+10 (c=0.5, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.30–7.50 (m, 10H, H-arom); 4.71 (d, 1H, J=11.6 Hz, CH_2Ph); 4.70 (d, 1H, J=11.8 Hz, CH_2Ph); 4.64 (d, 1H, J=11.8 Hz, CH_2Ph); 4.41 (d, 1H, J=11.6 Hz, CH_2Ph); 4.40 (dt, 1H, $J_{5,4}$=6.8 Hz, $J_{5,6}$=3.5 Hz, H-5); 4.34 (t, 1H, $J_{4,3}$=7.1 Hz, H-4); 4.29 (d, 1H, $J_{2,3}$=3.4 Hz, H-2); 4.01 (dd, 1H, H-3); 2.85 (ddd, 1H, $J_{7a,6b}$=5.2 Hz, $J_{7a,6a}$=8.5 Hz, $J_{7a,7b}$=16.5 Hz, H-7a); 2.35 (ddd, 1H, $J_{7b,6a}$=4.6 Hz, $J_{7b,6b}$=7.5 Hz, H-7b); 2.22–2.10 (m, 2H, H-6a, H-6b); 1.46, 1.25 (2 s, 6H, $C(CH_3)_2$). ^{13}C NMR ($CDCl_3$, 150 MHz): 206.7 (1C, CO); 137.6, 137.1 (2C, Cquat. CH_2Ph); 128.4, 128.3, 128.2, 128.0, 127.9, 127.8 (10C, CH_2Ph); 108.5 (1C, C $(CH_3)_2$); 87.2 (1C, C2); 80.2 (1C, C3); 76.6 (1C, C4); 74.4 (1C, C5); 72.8, 72.1 (2C, 2×CH_2Ph); 36.6 (1C, C7); 25.9, 24.6 (2C, $C(CH_3)_2$); 23.7 (1C, C6). MS (CI): m/z=414 (M+NH_4). Anal. calcd for $C_{24}H_{28}O_5$: C%=72.70, H%=7.11; found C%=72.58, H%=7.31.

13: $[\alpha]_D$=−28 (c=0.8, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.40 (m, 10H, H-arom); 4.75 (d, 1H, J=12 Hz, CH_2Ph); 4.69 (dd, 1H, $J_{4,3}$=2.5 Hz, $J_{4,5}$=7.7 Hz, H-4); 4.69 (d, 1H, J=12 Hz, CH_2Ph); 4.55 (d, 1H, J=11.6 Hz, CH_2Ph); 4.50 (ddd, 1H, $J_{5,6a}$=9.4 Hz, $J_{5,6b}$=4 Hz, H-5); 4.43 (d, 1H, J=11.6 Hz, CH_2Ph); 4.15 (dd, 1H, $J_{2,3}$=6.6 Hz, $J_{2,7b}$= 1.2 Hz, H-2); 4.09 (dd, 1H, H-3); 2.70 (ddd, 1H, $J_{7a,7b}$=14.2 Hz, $J_{7a,6a}$=10.8 Hz, $J_{7a,6b}$=3.3 Hz, H-7a); 2.53 (dddd, 1H, $J_{7b,6a}$=2.6 Hz, $J_{7b,6b}$=8.6 Hz, $J_{7b,2}$=1.2 Hz, H-7b); 2.26 (dddd, 1H, $J_{6a,6b}$=13.8 Hz, H-6a); 2.10 (dddd, 1H, H-6b); 1.52, 1.40 (2s, 1H, C $(CH_3)_2$). ^{13}C NMR ($CDCl_3$, 150 MHz): 208.0 (1C, CO); 137.8, 136.8 (2C, Cquat. CH_2Ph); 127.6, 127.5, 128.5, 128.2, 128.2, 128.1, (10C, 2×CH_2Ph); 107.8 (1C, CMe_2); 84.9 (1C, C2); 77.4 (1C, C3); 76.9 (1C, C4); 76.2 (1C, C5); 73.8 (1C, CH_2Ph); 72.5 (1C, CH_2Ph); 35.3 (1C, C7); 26.1 (1C, CH_3); 25.5 (1C, C6); 24.3 (1C, CH_3), MS (CI): m/z=414 (M+NH_4). Anal. calcd for $C_{24}H_{28}O_5$: C%=72.70, H%=7.11; found C%=72.78, H%=7.19.

3.1.11. (2*R*,3*R*,4*S*,5*S*)-2,3-Di-benzyloxy-4,5-*O*-isopropylidene-methylenecycloheptane (14). Tebbe reagent (1 M in toluene, 2, mL, 2 mmol) was added to a solution of **12** (150 mg, 0.378 mmol) in THF/Pyridine (2 mL 1:1 v/v) at −40°C. The reaction mixture was stirred at −40°C for 30 min, at rt for 1.5 day, cooled to -25°C and diluted with acetone (2 mL) and triethylamine (2 mL) then with ethyl ether (30 mL), filtered through Celite. The organic solution was concentrated. Flash chromatography (cyclohexane/AcOET/EtOH=6:1:0.1) of the residue gave **14** (126 mg, 63%). $[\alpha]_D$=+85 (c=0.8, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.50–7.30 (m, 10H, H-arom); 5.18 (t, 1H, $J_{8a,8b}$=$J_{8a,2}$=1.9 Hz, H-8a); 5.10 (t, 1H, $J_{8b,2}$=1.9 Hz, H-8b); 4.84 (d, 1H, J=11.9 Hz, CH_2Ph); 4.78 (d, 1H, J=11.9 Hz, CH_2Ph); 4.53 (d, 1H, J=11.8 Hz, CH_2Ph); 4.31 (d, 1H, J=11.8 Hz, CH_2Ph); 4.20 (dt, 1H, $J_{5,4}$= $J_{5,6a}$= 7.1 Hz, $J_{5,6b}$=8.7 Hz, H-5); 4.12 (dd, 1H, $J_{4,3}$=10 Hz, H-4); 4.10 (d, 1H, $J_{2,3}$=4 Hz, H-2); 3.85 (dd, 1H, H-3); 2.53–2.45 (m, 1H, H-7a); 2.24 (ddd, 1H, $J_{7a,7b}$=14.7 Hz, $J_{7b,6a}$= 10.8 Hz, $J_{7b,6b}$=8.2 Hz, H-7b); 2.04–1.97 (m, 2H, H-6a, H-6b). ^{13}C NMR ($CDCl_3$, 150 MHz): 144.1 (1C, C1); 138.6, 138.0 (2C, Cquat. CH_2Ph); 128.3, 128.1, 128.1, 127.9, 127.6, 127.3, (10C, 2×CH_2Ph); 108.2 (1C, CMe_2); 87.8 (1C, C2); 82.6 (1C, C3); 76.8 (1C, C4); 75.2 (1C, C5); 73.1 69.6 (2C, CH_2Ph); 27.6 (12C, C7); 27.1, 24.0 (2C, C $(CH_3)_2$); 26.2 (1C, C6). MS (CI): m/z=412 (M+NH_4). Anal. calcd for $C_{25}H_{30}O_4$: C%=76.11, H%=7.66; found C%=75.51, H%=7.89.

3.1.12. (1*R* and 1*S*,2*R*,3*S*,4*S*)-1-Hydroxymethyl-2,3-dibenzyloxy-4,5-isopropylidene-cycloheptane (15 and 16). BH_3 (1 M solution in THF 0.5 mL, 0.5 mmol) was added to solution of **14** (100 mg, 0.25 mmol) in THF (2 mL) at 0°C. The reaction mixture was stirred for 5 h at rt, quenched with water (0.2 mL). Aq 3N NaOH (0.17 mL, 0.5 mmol) and H_2O_2 (30%, 0.15 mL, 1.5 mmol) were added to the cooled (0°C) solution. The reaction mixture was stirred for 1 h at rt then 3 h at 45–50°C. The cooled (20°C) solution was extracted with ethyl ether (50 mL), dried ($MgSO_4$), and concentrated. Column chromatography (chloroform/AcOEt=9:1) of the residue gave **15** and **16** (73 mg, 69%), (**15/16**=11:3).

15: $[\alpha]_D$=+74 (c=0.3, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.40 (m, 10H, H-arom); 5.06 (d, 1H, J=10.9 Hz, CH_2Ph); 4.93 (d, 1H, J=11.2 Hz, CH_2Ph); 4.88 (d, 1H, J=11.2 Hz, CH_2Ph); 4.60 (d, 1H, J=10.9 Hz, CH_2Ph); 4.33 (dd, 1H, $J_{4,3}$=8.6 Hz, $J_{4,5}$=7 Hz, H-4); 4.15 (ddd, 1H, $J_{5,6a}$=11 Hz, $J_{5,6b}$=4 Hz, H-5); 3.72 (t, 1H, $J_{3,2}$=9 Hz, H-3); 3.63–3.58 (m, 2H, H-8a, H-8b); 3.29 (t, 1H, $J_{2,1}$=9.5 Hz, H-2); 2.50 (br s, 1H, OH); 1.95–1.88 (m, 1H, H-6a,); 1.88–1.75 (m, 2H, H-1, H-7a); 1.66–1.55 (m, 1H, H-6b); 1.50, 1.40 (2s, 2×CH_3); 1.21–1.10 (m, 1H, H-7b). ^{13}C NMR ($CDCl_3$, 100 MHz): 138.7, 137.8, (2C, Cquat. CH_2Ph); 128.5, 128.5, 128.2, 128.1, 127.9, 127.4, (10C, CH_2Ph); 107.9 (1C, $C(CH_3)_2$); 83.8 (1C, C3); 82.3 (1C, C2); 80.5 (1C, C4); 76.7 (1C, C1); 75.8 (1C, CH_2Ph); 75.5 (1C, CH_2Ph); 66.7 (1C, C8); 47.4 (1C, C1); 28.9 (1C, C6); 27.6, 24.8 (2C, $C(CH_3)_2$); 24.9 (1C, C7). MS (CI) m/z=413 (M+H). Anal. calcd for $C_{25}H_{32}O_5$: C%=72.79, H%=7.82; found C%=72.67, H%=8.00.

16: $[\alpha]_D$=+35 (c=0.5, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.50–7.20 (m, 10H, H-arom); 5.31 (d, 1H, J=11.4 Hz, CH_2Ph); 4.88 (d, 1H, J=11.8 Hz, CH_2Ph); 4.75 (d, 1H, J=11.4 Hz, CH_2Ph); 4.60 (d, 1H, J=11.8 Hz, CH_2Ph); 4.25 (dd, 1H, $J_{4,3}$=10 Hz, $J_{4,5}$=7 Hz, H-4); 4.10–4.00 (m, 3H, H-2, H-3, H-5); 3.55 (dd, 1H, $J_{8a,8b}$=10.4 Hz, $J_{8a,1}$=8 Hz, H-8a); 3.40 (dd, 1H, $J_{8b,1}$=4.8 Hz, H-8b); 2.05–1.98 (m, 2H, H-6a, H-6b); 1.73–1.63 (m, 1H, H-7a);

1.62, 1.38 (2s, 6H $C(CH_3)_2$); 1.5–1.42 (m, 1H, H-1); 1.21 (ddt, 1H, $J_{7a,7b}$=18.5 Hz, $J_{7b,6a}$=7.5 Hz, $J_{7b,6b}$=$J_{7b,5}$=5.3 Hz, H-7b). ^{13}C NMR ($CDCl_3$, 100 MHz): 140.3, 139.8 (2C, Cquat. CH_2Ph); (10C, 2×CH_2Ph); 107.7 (1C, CMe_2); 85.3 (1C, C3); 82.2 (1C, C2); 79.8 (1C, C4); 76.1 (1C, C5); 74.7 (1C, CH_2Ph); 73.2 (1C, CH_2Ph); 65.4 (1C, C8); 41.3 (1C, C1); 27.8, 24.4 (2C, CMe_2); 27.0 (1C, C6); 21.1 (1C, C7); MS (CI): *m*/*z*=430 (M+NH_4); Anal. calcd for for $C_{25}H_{32}O_5$: C%=72.79, H%=7.82; found C%=72.39, H%=8.20.

3.1.13. (1*R*,2*R*,3*S*,4*S*)-1-Hydroxymethyl-2,3-dibenzyloxy-4,5-dihydroxy-cycloheptane (17). Trifluoroacetic acid (2 mL) was added to a solution of **15** (38 mg, 0.09 mmol) in dioxane/water (0.1 mL, 4:1 v/v) at room temperature. After 24 h, the mixture is neutralized with concentrated aq NH_3 and concentrated, the residue was chromatographed (cyclohexane/AcOEt=1:2) to afford **17** (28 mg, 82%) as a an oil. ^{1}H NMR ($CDCl_3$, 400 MHz): 7.41–7.30 (m, 10H, H-arom); 4.84 (d, 1H, *J*=11.5 Hz, CH_2Ph); 4.80 (d, 1H, *J*=11.4 Hz, CH_2Ph); 4.67 (d, 1H, *J*=11.4 Hz, CH_2Ph); 4.62 (d, 1H, *J*=11.5 Hz, CH_2Ph); 4.07–4.02 (m, 1H, H-5); 3.92 (dd, $J_{2,1}$=$J_{2,3}$=7 Hz, H-2); 3.90 (dd, 1H, $J_{4,3}$=7 Hz, $J_{4,5}$=3 Hz, H-4); 3.65 (dd, 1H, H-3); 3.65 (dd, $J_{8a,1}$=7 Hz, $J_{8a,8b}$=11 Hz, H-8a); 3.58 (dd, $J_{8b,1}$=5 Hz, H-8b); 2.12–2.07 (m, 1H, H-1); 1.92–1.75 (m, 3H, H-6a, H-6b, H-7a); 1.50–1.39 (m, 1H, H-7b). ^{13}C NMR ($CDCl_3$, 100 MHz): 137.5, 137.4 (2C, Cquat. CH_2Ph); 128.6, 128.5, 128.079, 128.0, 127.9, (10C, 2×CH_2Ph); 82.1 (1C, C3); 80.6 (1C, C2); 74.7 (1C, C4); 74.3, 73.7 (2C, 2×CH_2Ph); 70.4 (1C, C5); 65.6 (1C, C8); 44.7 (1C, C1); 28.8 (1C, C6); 21.2 (1C, C7); HRMS, *m*/*z*=373.201 (M+H): calcd for $C_{22}H_{29}O_5$=373.472.

3.1.14. Cycloheptanic α-D-glucopyranose mimetic (18). A solution of **17** (33 mg) in EtOH/MeOH (0.3 mL, 1:1) was stirred under hydrogen for 5 h in the presence of 10% Pd/C (cat) at rt. The reaction mixture was filtered, concentrated to give **18** (19 mg, 92%). ^{1}H NMR (D_2O, 600 MHz): 3.99 (ddd, 1H, $J_{1,5''a}$=8 Hz, $J_{1,5''b}$=5 Hz, $J_{1,2}$=2.7 Hz, H-1); 3.69 (dd, 1H, $J_{6a,6b}$=11 Hz, $J_{6a,5}$=4.1 Hz, H-6a); 3.66 (t, 1H, $J_{3,2}$=$J_{3,4}$=7.8 Hz, H-3); 3.63 (dd, 1H, H-2); 3.57 (dd, 1H, $J_{6b,1}$=6.5 Hz, H-6b); 3.33 (dd, 1H, $J_{4,5}$=9.3 Hz, H-4); 1.90–1.84 (m, 1H, H-5″a); 1.79–1.75 (m, 1H, H-5′a); 1.74–1.68 (m, 1H, H-5); 1.64 (dddd, 1H, $J_{5''b,5''a}$=18.4 Hz, *J*=10.4 Hz, *J*=8 Hz, *J*=3.2 Hz, H-5″b); 1.35 (dddd, 1H, $J_{5'b,5'a}$=17.8 Hz, *J*=10.3 Hz, *J*=9.3 Hz, *J*=3.1 Hz, H-5′b). ^{13}C NMR (D_2O, 150 MHz): 74.9 (1C, C4); 74.7 (2C, C2, C3); 70.4 (1C, C1); 44.4 (1C, C6); 44.4 (1C, C5); 28.7 (1C, C5″); 22.4 (1C, C5′). HRMS, *m*/*z*=193.107 (M+H) calcd for $C_8H_{17}O_5$=193.221.

3.1.15. (2*R*,3*R*,4*R*,5*R*)-2,3-Di-benzyloxy-4,5-*O*-isopropylidene methylenecycloheptane (19). The ketone **13** (140 mg, 0.352 mmol) was treated with Tebbe reagent as described for **14**. Chromatography (cyclohexane/AcOEt=6:1) gave **19** (100 mg, 71%). $[\alpha]_D$=−42 (*c*=1.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.20–7.40 (m, 10H, H-arom); 5.16 (d, 1H, $J_{8a,8b}$=2 Hz, H-8a); 4.97 (d, 1H, H-8b); 4.79 (d, 1H, *J*=12.1 Hz, CH_2Ph); 4.74 (dd, 1H, $J_{4,5}$=7.8 Hz, $J_{4,3}$=2.5 Hz, H-4); 4.67 (d, 1H, *J*=12.1 Hz, CH_2Ph); 4.54 (d, 1H, *J*=12 Hz, CH_2Ph); 4.42 (ddd, 1H, $J_{5,6a}$=5.9 Hz, $J_{5,6b}$=9.3 Hz, H-5); 4.29 (d, 1H, *J*=12 Hz, CH_2Ph); 4.12 (d, 1H, $J_{2,3}$=6.3 Hz, H-2); 4.04 (dd, 1H, H-3); 2.35 (br dd, 1H, $J_{6a,7a}$=6.8 Hz, $J_{6a,6b}$=12 Hz, H-6a); 2.25–2.09 (m, 3H, H-6b, H-7a, H-7b); 1.53, 1.40 (2s, 6H, CMe_2). ^{13}C NMR ($CDCl_3$, 150 MHz): 145.6 (1C, C1); 139.9, 138.3 (2C, Cquat. CH_2Ph); 128.3, 128.0, 127.4, 127.4, 127.3, 127.1, (10C, 2×CH_2Ph); 117.5 (1C, C8); 107.6 (1C, CMe_2); 81.9 (1C, C2); 79.5 (1C, C3); 77.3 (1C, C4); 76.9 (1C, C5); 73.7, 69.9 (2C, 2×CH_2Ph); 29.4 (1C, C7); 27.3 (1C, C6); 26.5, 24.4 (2C, CMe_2); MS (CI): *m*/*z*=412 (M+NH_4); Anal. calcd for ($C_{25}H_{30}O_4$)·H_2O: C%=72.79, H%=7.82; found C%=72.99, H%=7.62.

3.1.16. (1*R* and 1*S*,2*R*,3*R*,4*R*)-1-Hydroxymethyl-2,3-dibenzyloxy-4,5-isopropylidene-cycloheptane (20 and 21). 19 (80 mg, 0.2 mmol) was treated with BH_3 as described for **15** and **16** to give after flash chromatography (cyclohexane/AcOEt=3:1) **20** and **21** (54 mg, 65%, **20/21**=2.7:1).

20: $[\alpha]_D$=+37 (*c*=0.5, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.40 (m, 10H, H-arom); 4.98 (d, 1H, *J*=11 Hz, CH_2Ph); 4.90 (d, 1H, *J*=12 Hz, CH_2Ph); 4.79 (d, 1H, *J*=12 Hz, CH_2Ph); 4.62 (d, 1H, *J*=11 Hz, CH_2Ph); 4.55 (dd, 1H, $J_{4,5}$=8.4 Hz, $J_{4,3}$=1.8 Hz, H-4); 4.30 (ddd, 1H, $J_{5,6a}$=2 Hz, $J_{5,6b}$=6 Hz, H-5); 3.88 (dd, 1H, $J_{1,2}$=8.3 Hz, $J_{2,3}$=8 Hz, H-2); 3.68 (dd, 1H, $J_{8a,8b}$=10.9 Hz, $J_{8a,1}$=6.2 Hz, H-8a); 3.63 (dd, 1H, H-3); 3.61 (dd, 1H, $J_{8b,1}$=4 Hz, H-8b); 2.60 (s, 1H, OH); 2.10 (m, 1H, $J_{6a,7b}$=6 Hz, $J_{6a,7a}$=4.7 Hz, $J_{6a,6b}$=10 Hz, H-6a); 1.78–1.69 (m, 1H, H-1); 1.45–1.58 (m, 3H, H-6b, H-7a, H-7b). ^{13}C NMR ($CDCl_3$, 100 MHz): 138.2, 137.9 (2C, Cquat. CH_2Ph); 128.5, 128.4, 128.3, 128.0, 127.8, 127.6 (10C, 2×CH_2Ph); 81.5 (1C, C3); 80.7 (1C, C2); 77.8 (1C, C4); 74.6 (1C, CH_2Ph); 74.5 (1C, CH_2Ph); 74.1 (1C, C5); 66.9 (1C, C8); 46.6 (1C, C1); 28.2 (1C, C6); 23.7, 25.9 (2×CH_3); 21.1 (1C, C7). MS (CI) *m*/*z*=413 (M+H). Anal. calcd for $C_{25}H_{32}O_5$: C%=72.78, H%=7.81; found C%=72.64, H%=8.00.

21: $[\alpha]_D$=−21 (*c*=0.4, $CHCl_3$). ^{1}H NMR (C_6D_6, 400 MHz): 7.40–7.20 (m, 10H, H-arom); 5.08 (d, 1H, *J*=11.9 Hz, CH_2Ph); 4.80 (dd, 1H, $J_{4,5}$=7.8 Hz, $J_{4,3}$=2.6 Hz, H-4); 4.65 (d, 1H, *J*=11.9 Hz, CH_2Ph); 4.45 (d, 1H, *J*=11.4 Hz, CH_2Ph); 4.40 (ddd, 1H, 4.28 (dd, 1H, $J_{3,2}$=6.8 Hz, H-3); 4.04 (dd, 1H, $J_{5,6a}$=11.1 Hz, $J_{5,6b}$=5.5 Hz, H-5); 4.38 (d, 1H, *J*=11.4 Hz, CH_2Ph); 4.28 (dd, 1H, $J_{3,2}$=6.8 Hz, H-3); 4.04 (dd, 1H, $J_{2,1}$=2.5 Hz, H-2); 3.55 (dd, 1H, $J_{8a,8b}$=10.4 Hz, $J_{8a,1}$=8 Hz, H-8a); 3.4 (dd, 1H, $J_{8b,1}$=5.1 Hz, H-8b); 2.48–2.38 (m, 1H, H-6a); 2.27–2.18 (m, 1H, H-6b); 2.18–2.10 (m, 1H, H-1); 1.71, 1.42 (2 s, 6H, CMe_2); 1.50–1.35 (m, 2H, H-7a, H-7b). ^{13}C NMR (C_6D_6, 100 MHz): 140.1, 139.1 (2C, Cquat. CH_2Ph); 129.1, 129.0, 128.8, 128.5, 128.1 (10C, 2×CH_2Ph); 108.3 (1C, CMe_2); 78.7 (1C, C5); 78.1 (1C, C3); 77.9 (1C, C4); 77.4 (1C, C2); 75.3 (1C, CH_2Ph); 73.2 (1C, CH_2Ph); 66.0 (1C, C8); 43.4 (1C, C1); 30.2 (1C, C6); 27.6, 24.9 (2C, CMe_2); 21.3 (1C, C7); MS (CI) *m*/*z*=413 (M+H). Anal. calcd for $C_{25}H_{32}O_5$: C%=72.79, H%=7.82; found C%=72.72, H%=8.13.

3.1.17. 1-Hydroxymethyl-2,3-dibenzyloxy-4,5-dihydroxy cycloheptane (22). 20 (35 mg, 0.084 mmol) was reacted with trifluoroacetic acid as described for **17** to give **22**

(28 mg, 89%). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.30–7.40 (m, 10H, H-arom); 4.78 (d, 1H, J=11.6 Hz, CH_2Ph); 4.68 (d, 1H, J=11.3 Hz, CH_2Ph); 4.66 (d, 1H, J=11.3 Hz, CH_2Ph); 4.49 (d, 1H, J=11.6 Hz, CH_2Ph); 4.10 (br d, 1H, $J_{3,2}$= 4.5 Hz, H-3); 4.04 (br m, 1H, H-5); 4.00 (br s, 1H, H-4); 3.68 (dd, 1H, $J_{2,1}$=6 Hz, H-2); 3.65 (dd, 1H, $J_{8a,8b}$= 10.5 Hz, $J_{8a,1}$=4.6 Hz, H-8a); 3.57 (dd, 1H, $J_{8b,1}$=5.2 Hz, H-8b); 2.12–2.05 (m, 1H, H-6a); 1.82–1.65 (m, 3H, H-7b, H-6b, H-1); 1.55–1.45 (m, 1H, H-7a). ^{13}C NMR ($CDCl_3$, 100 MHz): 137.7, 137.2 (2C, Cquat. CH_2Ph); 128.8, 128.7, 128.5, 128.3, 128.1, 127.9, 127.9 (10C, 2×CH_2Ph); 86.7 (1C, C3); 78.3 (1C, C2); 74.2 (1C, CH_2Ph); 73.7 (1C, C5); 72.5 (1C, CH_2Ph); 86.7 (1C, C3); 78.3 (1C, C2); 74.2 (1C, CH_2Ph); 73.7 (1C, C5); 72.5 (1C, CH_2Ph); 71.0 (1C, C4); 66.7 (1C, C8); 32.5 (1C, C6); 20.5 (1C, C7). HRMS, m/z=373.201 (M+H), calcd for $C_{22}H_{28}O_5$=373.472.

3.1.18. Cycloheptanic β-D-mannopyranose mimetic (23). Deprotection of **22** (26 mg) as described for **18** gave **23** (15 mg, 92%). ^{1}H NMR (D_2O, 600 MHz): 4.02 (t, 1H, $J_{2,1}$=$J_{2,3}$=2 Hz, H-2); 3.83 (td, 1H, $J_{1,5''b}$=7.4 Hz, H-1); 3.69 (dd, 1H, $J_{6a,6b}$=11 Hz, $J_{6a,5}$=4 Hz, H-6a); 3.60 (dd, 1H, $J_{3,4}$=8.8 Hz, H-3); 3.52 (dd, 1H, $J_{6b,5}$=7 Hz, H-6b); 3.50 (t, 1H, $J_{4,5}$=8.6 Hz, H-4); 1.88–1.65 (m, 2H, H-6a, H-7a); 1.61–1.55 (m, 3H, H-6b, H-7b, H-1). ^{13}C NMR (D_2O, 150 MHz): 76.2 (1C, C2); 75.7 (1C, C3); 75.2 (1C, C4); 71.8 (1C, C1); 64.3 (1C, C6); 43.5 (1C, C5); 27.5 (1C, C5′); 22.1 (1C, C5″); HRMS, m/z=193.107 (M+H): calcd for $C_8H_{16}O_5$=193.221.

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