Pergamon

Tetrahedron: *Asymmetry* 13 (2002) 2553–2565

TETRAHEDRON: *ASYMMETRY*

Synthesis of seven- and eight-membered carbasugar analogs via ring-closing metathesis and their inhibitory activities toward glycosidases

Yves Blériot,[a] André Girault,[a] Jean-Maurice Mallet,[a] Eliazar Rodriguez,[b] Pierre Vogel[b] and Pierre Sinaÿ[a,*]

[a]*Ecole Normale Supérieure, Département de Chimie, UMR 8642, 24 rue Lhomond, 75231 Paris Cedex 05, France*
[b]*Institut de Chimie Moléculaire et Biologique, Ecole Polytechnique Fédérale de Lausanne, BCH, CH-1015 Lausanne, Switzerland*

Received 24 September 2002; accepted 11 October 2002

Abstract—An expeditious and efficient synthesis of new enantiopure polyhydroxylated seven- and eight-membered carbocycles is described starting from 2,3,5-tri-*O*-benzyl-D-arabinose. The key cyclization step involves ring closing metathesis of 1,8- and 1,9-dienes using Grubbs' catalyst. All of the new carbasugar analogs synthesized were evaluated as glycosidase inhibitors. Contrary to our expectations, (1*S*,2*S*,3*R*,4*R*,5*R*)-1-(hydroxymethyl)-cyclohepta-1,2,3,4,5-pentol which has the β-D-mannopyranose configuration for C(1)–C(5) inhibits α- and β-glucosidases, whereas its diepimer (1*S*,2*S*,3*R*,4*S*,5*S*)-1-(hydroxymethyl)-cyclohepta-1,2,3,4,5-pentol, which has the α-D-glucopyranose configuration, is not recognised by these enzymes.

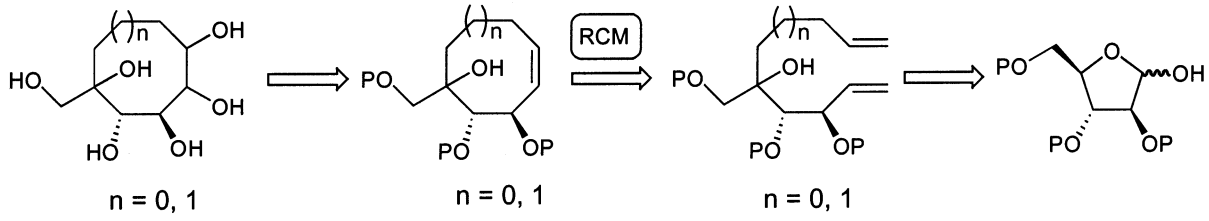
1. Introduction

The conversion of carbohydrates into carbocycles is a major task and has been the subject of many studies.[1] Interest in this class of compounds is high due to the fact that many biologically important molecules and natural products contain a polyhydroxylated carbocycle.[2] Various methods are already available for the construction of functionalized five- and six-membered rings from sugars[3] but only a few approaches have been reported for the synthesis of seven-[4] and eight-membered ring cyclitols.[5]

As part of our ongoing project on the synthesis of new carbohydrate carbocyclic mimetics,[6] we would like to disclose herein our approach for the synthesis of new cycloheptanic and cyclooctanic carbasugar analogs. The new spatial distribution of the hydroxyl groups and the increased flexibility of such structures should allow an enhanced adaptability of these carbocycles in the active site of the carbohydrate processing enzymes. Our route enables us to obtain various carbasugars to study their inhibitory activities towards glycosidases.

2. Results

The envisaged retrosynthetic approach starts from readily available 2,3,5-tri-*O*-benzyl-D-arabinose[7] and involves the carbocyclization of 1,8-diene or 1,9-diene using the ring-closing metathesis methodology (Scheme 1). A similar strategy has been reported by Eustache et



Scheme 1. Retrosynthetic analysis.

* Corresponding author. Tel.: +33(0)144323389; fax: +33(0)144323397; e-mail: pierre.sinay@ens.fr

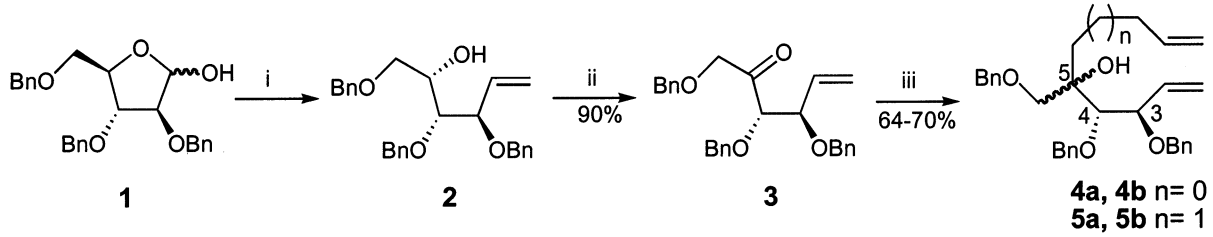
0957-4166/02/$ - see front matter
PII: S0957-4166(02)00654-7

al. for the synthesis of five-membered branched cyclitols and valiolamine.[8]

For some time we have been interested in the powerful ring-closing metathesis (RCM) methodology which has become the method of choice for carbon–carbon bond construction in particular in carbohydrate chemistry.[9] The main advantages of RCM are its wide applicability and its remarkable tolerance to functional groups.[10] Preparation of cycloheptanols using RCM is well documented.[4] To our knowledge, only a few examples describe the synthesis of cyclooctanols,[5] probably due to the unfavorable thermodynamic factors associated with cyclooctane chemistry.[11]

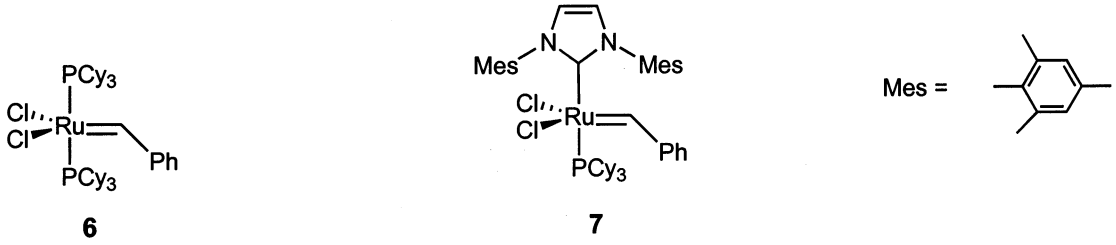
Our approach starts with the use of compound **2**[12] which could be prepared through Wittig olefination of 2,3,5-tri-*O*-benzyl-D-arabinose **1**.[7] The alcohol **2** was then oxidized with PCC to give the known ketone **3**[13] in 90% yield. Compound **3** was reacted with an excess of butenyl- or pentenylmagnesium bromide in THF at 0°C to furnish the 1,8-diene-ols **4a** and **4b** and 1,9-diene-ols **5a** and **5b**, respectively, in 64–70% yield as inseparable mixtures of diastereomers and in a 1/1 ratio (Scheme 2).

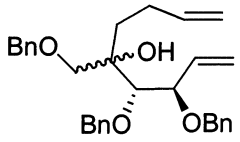
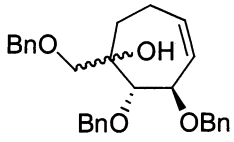
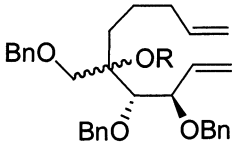
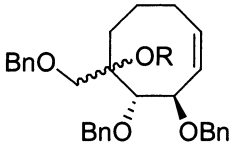
The key carbocyclization step was then examined, the results being summarized in Table 1. Cyclization of the 1,8-diene-ols **4a** and **4b** using Grubbs catalyst **6** in dichloromethane afforded cycloheptenes **8** and **9** in 60%



Scheme 2. Synthesis of dienes **4a**, **4b**, **5a** and **5b**. *Reagents and conditions*: (i) Reference 7; (ii) PCC, molecular sieves, DCM, ether; (iii) CH_2=$CH(CH_2)_3Br$ or CH_2=$CH(CH_2)_2Br$, Mg, Et_2O, THF.

Table 1. RCM of cycloheptenes **4a**, **4b** and cyclooctenes **5a**, **5b**, **12a**, **12b** using catalysts **6** and **7**



Entry	Diene	Catalyst (%mol), time	Cycloalkene	Yield (%)
				
1	**4a, 4b**	**6** (10%), 17 h	**8, 9**	60
2	**4a, 4b**	**7** (10%), 17 h	**8, 9**	97
				
3	**5a, 5b** R=H	**6** (10%), 72 h	**10, 11** R=H	29
4	**5a, 5b** R=H	**7** (10%), 72 h	**10, 11** R=H	0
5	**12a, 12b** R=TBDMS	**6** (10%), 72 h	**13, 14** R=TBDMS	86
6	**12a, 12b** R=TBDMS	**7** (10%), 72 h	**13, 14** R=TBDMS	0

yield (entry 1). When dienes **4a** and **4b** were subjected to RCM conditions using catalyst **7**,[14–16] the diastereomeric cycloheptenes **8** and **9** were obtained in almost quantitative yield (entry 2).

When the homologous 1,9-diene-ols **5a** and **5b** were subjected to the RCM procedure, disappointing results were obtained: cyclization using Grubbs' catalyst **6** under various conditions (temperature, solvent, dropwise addition of the catalyst) afforded diastereomeric cyclooctenes **10** and **11** in a modest 29% yield (entry 3) along with recovered starting material (40%). Similar results have been observed previously by Bourgeois et al. in their synthesis of the B–C ring system of taxol.[17] Surprisingly, use of catalyst **7** failed to effect any reaction (entry 4). We postulated that the low reactivity of the 1,9-diene-ols with the ruthenium-based catalysts **6** and **7** could be due to chelation of the oxygen of the free tertiary alcohol group with ruthenium as previously observed in others cases.[18] To overcome this problem, the tertiary alcohol in **5a** and **5b** was protected as its *tert*-butyldimethylsilyl ether to afford **12a** and **12b**. To our great satisfaction, when **12a** and **12b** were submitted to RCM reaction in the presence of Grubbs' catalyst **6** in toluene at 90°C for 3 days, cyclooctenes **13** and **14** were obtained in a 86% overall yield (entry 5). Subsequent desilylation with TBAF in THF afforded the corresponding cyclooctenes **10** and **11** in high yield. Thin layer chromatography monitoring of the RCM reaction indicated that the diastereomeric 1,8-dienes and 1,9-dienes cyclized at a comparable rate and 1:1 diastereomeric mixtures were obtained in each case. Use of the modified Grubbs' catalyst **7** with the fully protected dienes **12a** and **12b** was again unsuccessful (entry 6). The lack of reaction observed with cyclooctenes **5a**, **5b**, **12a** and **12b** in the presence of catalyst **7** is in marked contrast with previously reported results.[5b]

The next step was the functionalization of the ethylenic bond present in the cycloheptenes and cyclooctenes. *syn*-Dihydroxylation of cycloheptene **8** using OsO_4[19] afforded triols **15** and **16** in 82% yield and in a 3/7 ratio. Subsequent hydrogenolysis of the benzyl groups afforded cyclitols **19** and **20** in quantitative yield. The same sequence was uneventfully applied to cycloheptene **9** to give cyclitols **21** and **22** (Scheme 3).

The same sequence was then applied to cyclooctenes **10** and **11** affording cyclitols **27**–**30** (Scheme 4).

2.1. Structural assignments

The stereochemistry of the carbon C-5 of cycloheptenes **8** and **9** and cyclooctenes **10** and **11** was deduced from NOE measurements performed on each cycloalkene which indicated that compounds **8** and **10** had the 5*S* configuration and compounds **9** and **11** the 5*R* configuration (Fig. 1).

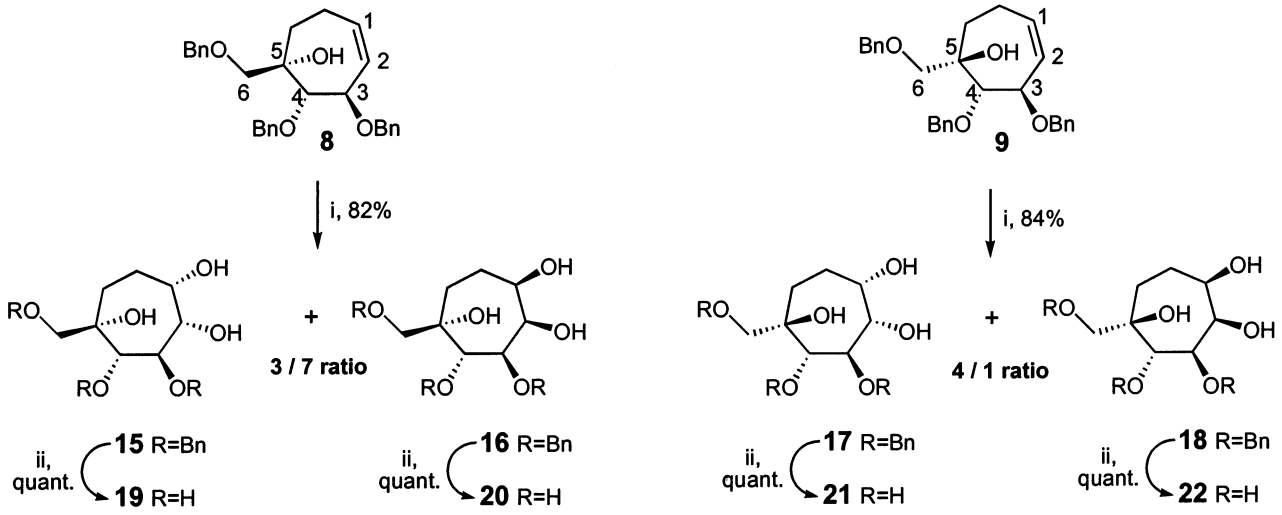
The stereochemistry of the *syn*-dihydroxylation performed on cycloheptenes and cyclooctenes was deduced from the coupling constants observed between H-1, H-2 and H-3 in compounds **15**, **16**, **17**, **18**, **23**, **24**, **25** and **26**.

To unambiguously confirm the structural assignment of our conformationally flexible carbocycles, their conformation was locked in order to obtain crystals suitable for X-ray crystallographic analysis. Thus, compound **25** was converted in three steps into the crystalline triacetonide **31**[20] (Scheme 5 and Fig. 2).

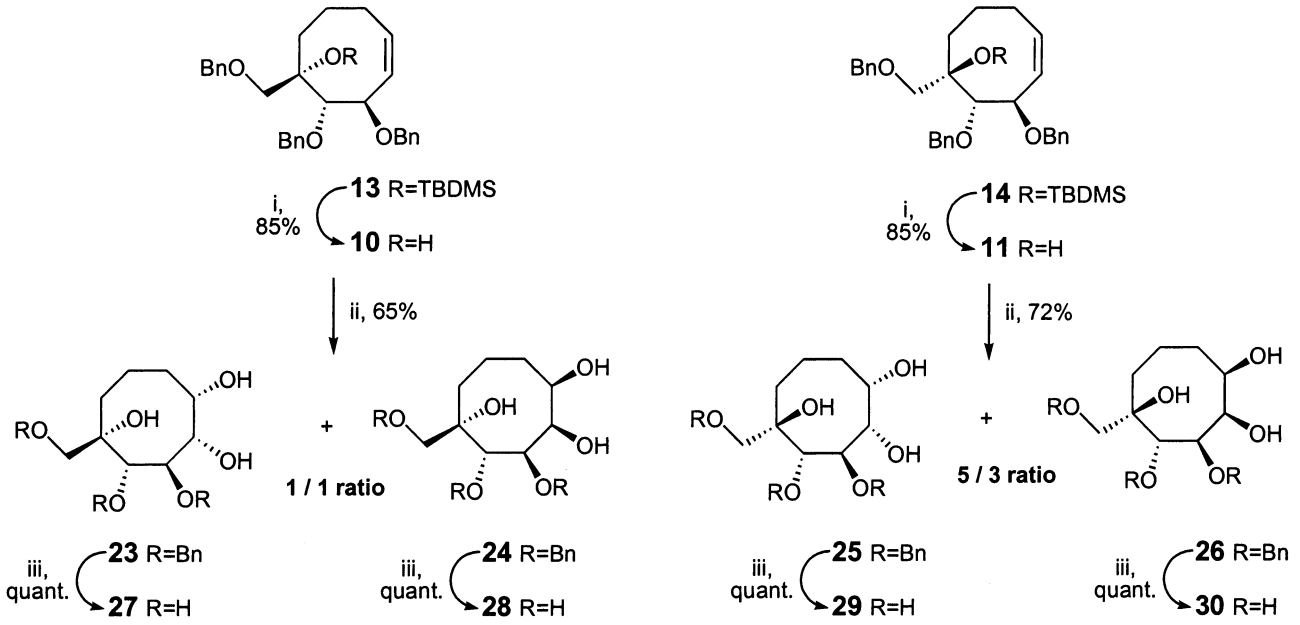
The new synthetic polyhydroxylated carbocycles were then evaluated as glycosidase inhibitors.

2.2. Glycosidase inhibition

Cyclic polyols such as epoxides of conduritols can be selective inhibitors of glycosidases.[21] Recently, it has



Scheme 3. Synthesis of the polyhydroxylated cycloheptanes **19**–**22**. *Reagents and conditions*: (i) OsO_4, NMO, *t*BuOH, acetone, H_2O; (ii) H_2, Pd/C, MeOH, AcOEt.



Scheme 4. Synthesis of the polyhydroxylated cyclooctanes **27**–**30**. *Reagents and conditions*: (i) TBAF, THF; (ii) OsO_4, NMO, *t*BuOH, acetone, H_2O; (iii) H_2, Pd/C, MeOH, AcOEt.

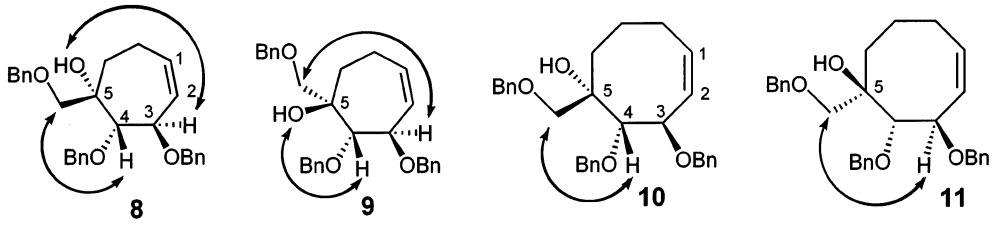
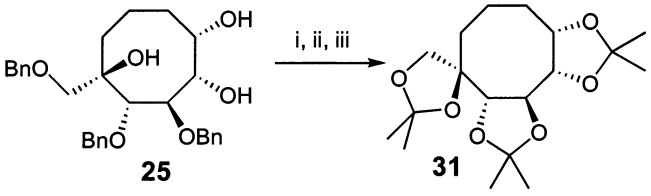


Figure 1. NOE observed for cycloheptenes **8** and **9** and cyclooctenes **10** and **11** (for reasons of commodity atom numbering does not follow IUPAC numbering rules).



Scheme 5. Synthesis of triacetonide **31**. *Reagents and conditions*: (i) acetone, 2,2-dimethoxypropane, CSA, 78%; (ii) H_2, 10% Pd/C, CH_3OH, EtOAc; (iii) acetone, 2,2-dimethoxypropane, CSA, 78%.

been shown that a bicyclo-[4.3.0]-nonane-2,3,4,5,6,7,8,9-heptol inhibits α-glucosidases.[22] Conduritol A, a cyclohex-5-ene-1,2,3,4-tetrol isolated from the leaves of *Gymnema sylvestre* is an hypoglycemia agent.[23] It has been proposed as an additive to food to control the metabolism of sugars in patients suffering from diabetes and obesity.[24] Conduritols A and B and analogs are able to modulate the release of insulin from isolated pancreatic islets in the presence of varying concentration of glucose, in both a stimulatory and inhibitory sense.[25] Cyclophellitol ((1*S*,2*R*,3*S*,4*R*,5*R*,6*R*)-5-hydroxymethyl-7-oxa-bicyclo-[4.1.0]-heptane-2,3,4-triol) is a weak inhibitor of fungal β-xylosidase and a strong inhibitor of β-glucosidase.[26] This discovery has stimulated the synthesis of several stereomers and analogs of cyclophellitol and their glycosidase inhibitory activities have been evaluated.[27]

By analogy with the above, we envisioned that polyols **19** and **27** with the α-D-glucopyranose configuration for C(1), C(2), C(3), C(4), C(5) could be potential α-glucosidase inhibitors. This was not the case. To our surprise, compound **20** with the β-D-mannopyranose configuration is a moderate inhibitor of α-glucosidase (maltase) from yeast (81% at 1 mM), isomaltase from baker's yeast (78% at 1 mM) and of β-glucosidase from almonds (79% at 1 mM). It is also a weak inhibitor of β-galactosidase from both *Aspergillus oryzae* and jack beans, and also inhibits β-glucosidase from *Caldocellum saccharolyticum* and β-xylosidase from *Aspergillus niger* (Table 2).

The polyhydroxylated cycloheptanes **19**–**22** and cyclooctanes **27**–**30** were assayed for their inhibitory activities towards 25 commercially available glycosidases. At 1 mM concentration (optimal pH, 35°C), they were found to be inactive toward α-fucosidase from human placenta, α-galactosidase from coffee beans and

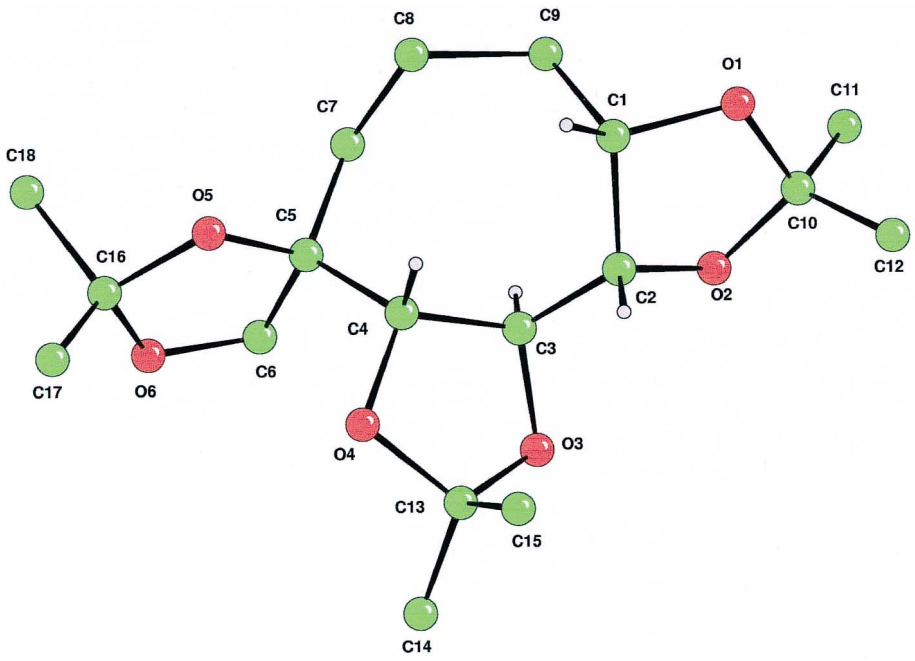
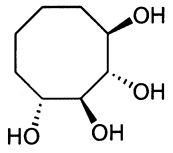


Figure 2. X-Ray structure of **31** (for reasons of commodity atom numbering does not follow IUPAC numbering rules).

from *A. niger*, β-galactosidase from *E. coli*, amyloglucosidases from *A. niger* and from *Rhizopus* mold, α-mannosidases from jack beans and from almonds, β-mannosidase from *Helix pomatia*, α-*N*-acetylgalactosaminidase from chicken liver and β-*N*-acetylgalactosaminidases from jack beans and from bovine epididymis A and B. Weak inhibitory activities were found for some of the compounds toward some glycosidases (Tables 2 and 3). In general, the cyclohepta-1,2,3,4,5-pentols were more active than the cycloocta-1,2,3,4,5-pentols. The presence of five contiguous hydroxy groups and a hydroxymethyl substituent is necessary for the inhibitory activity, as we found that (1*R*,2*S*,3*S*,4*R*)-cycloocta-1,2,3,4-tetrol **32**[6b] is completely inactive toward the 25 glycosidases assayed in this study.



32

The presence of a tertiary alcohol moiety at the position corresponding to C-5 of pyranosides might be responsible for the lack of activity. The geometry of the cyclooctapentols **27**–**30** departs from that of pyranosides more than the corresponding cycloheptapentols **19**–**22**. Although the high flexibility of seven-membered rings might introduce an entropic penalty, this factor could explain that the latter are better recognized by glycosidases than the former carbasugar analogs. The fact that **20** with the β-D-mannopyranose configuration is recognized by glucosidases and not its diepimer **19** that has the configuration of α-D-glucopyranose might also be attributed to a conformational factor (conjugation of seven-membered ring flexibility and gauche interactions between the substituents). It is interesting to note that **22**, the 1-epimer of **20**, is recognized by some galactosidases and only weakly by isomaltase from Baker's yeast (Table 2). The most striking outcome of this study is that carbasugar analogs that do not possess an amine or an electrophilic moiety (allylic alcohol, epoxide) can be moderate glycosidase inhibitors.

3. Conclusion

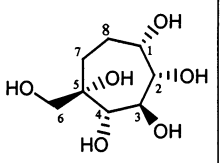
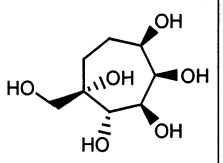
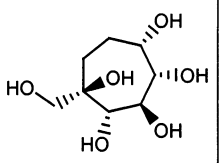
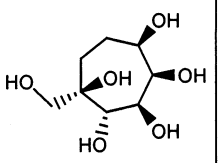
Eight new polyhydroxylated carbocycles have been prepared in six steps starting from commercially readily available 2,3,5-tri-*O*-benzyl-D-arabinose. The ring-closing metathesis key step proceeded smoothly in the case of cycloheptane derivatives but required the protection of the tertiary alcohol in the case of cyclooctane compounds. Further elaboration of the C=C bond and subsequent deprotection afforded the target compounds which showed some activity as glycosidase inhibitors despite the lack of nitrogen in the compounds. Further modifications of these compounds to improve their potency against glycosidases, such as introduction of nitrogen and/or deoxygenation of the tertiary alcohol are underway and will be reported in due course.

4. Experimental

4.1. General methods

Melting points were determined using a Büchi model 535 mp apparatus and are uncorrected. Optical rotations were measured at 20±2°C with a Perkin–Elmer

Table 2. Inhibitory activities of cycloheptapentols **19–22**. Percentage of inhibition at 1 mM concentration of the inhibitor. Optimal pH, 35°C[a] (NI = no inhibition)

				
Enzyme, Compound	**19**	**20**	**21**	**22**
α-fucosidase bovine epididymis	22%	NI	26%	NI
α-galactosidase *E. coli*	NI	NI	32%	NI
β-galactosidase				
bovine liver	NI	NI	NI	NI
Aspergillus niger	NI	NI	NI	60%
Aspergillus oryzae	NI	35%	NI	NI
Jack beans	NI	42%	NI	74%
α-glucosidase (maltase)				
yeast	NI	81%	NI	NI
rice	NI	NI	NI	NI
(isomaltase)				
Baker yeast	NI	81%	NI	50%
β-glucosidase				
almonds	NI	79%	22%	NI
Caldocellum saccharolyticum	NI	30%	NI	NI
β-xylosidase Aspergillus niger	NI	24%	NI	NI

[a] Methods of inhibitory activity evaluation, see ref. 28

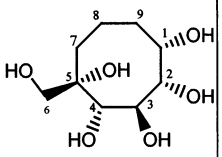
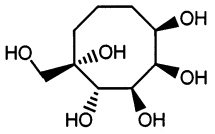
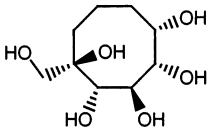
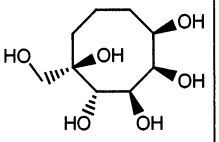
model 241 digital polarimeter, using a 10 cm, 1 mL cell. Chemical ionisation mass spectra (CI-MS ammonia) and fast atom bombardment mass spectra (FAB-MS) were obtained with a JMS-700 spectrometer. Elemental analyses were performed by Service de Microanalyse de l'Université Pierre et Marie Curie, 4 Place 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 temperature. Assignments 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. Reactions were monitored by thin-layer chromatography (TLC) on a pre-coated 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).

Note: for the assignment of the NMR spectra, the numbering of the compounds is based on the analogy with the corresponding sugar as shown for compounds **19** and **27** in Tables 2 and 3 and not on the IUPAC rules for commodity reasons.

4.2. (3*R*,4*S*,5*R*)-3,4-Dibenzyloxy-5-(benzyloxymethyl)-nona-1,8-dien-5-ol 4a and (3*R*,4*S*,5*S*)-3,4-dibenzyloxy-5-(benzyloxymethyl)nona-1,8-dien-5-ol, 4b

To a freshly prepared solution of butenylmagnesium bromide (0.3 M in dry Et_2O, 50 mL) was added dropwise under argon a solution of ketone **3** (3.75 g, 10.8 mmol) in anhydrous Et_2O (60 mL). The reaction mixture was stirred for 18 h at rt and quenched at 0°C by dropwise addition of a sat. aq. NH_4Cl solution (50 mL). The aqueous layer was extracted with AcOEt (3×50 mL). Organic extracts were combined, dried ($MgSO_4$), filtered and the solvent was evaporated. Purification by flash chromatography (AcOEt/cyclohexane, 1:8) afforded dienes **4a** and **4b** (3.26 g, 6.9 mmol, 64% yield) as an inseparable mixture of diastereomers.

Table 3. Inhibitory activities of cyclooctapentols **27**–**30**. Percentage of inhibition at 1 mM concentration of the inhibitor. Optimal pH, 35°C[a] (NI = no inhibition)[b]

				
Enzyme, Compound	**27**	**28**	**29**	**30**
β-galactosidase				
bovine liver	NI	NI	NI	54%
Aspergillus niger	67%	NI	NI	NI
Aspergillus oryzae	NI	NI	NI	NI
jack beans	NI	NI	NI	NI
β-glucosidase				
almonds	NI	25%	22%	NI

[a] Methods, see ref. 28

[b] No inhibition found toward α-fucosidase from bovine epididymis, α-galactosidase from *E. coli*, α-glucosidase (maltase) from yeast and from rice, isomaltase from baker yeast, β-glucosidase from *Caldocellum saccharolyticum* and β-xylosidase from *Aspergillus niger*.

^{1}H NMR ($CDCl_3$, 400 MHz): 7.39–7.30 (m, 30H, aromatic H), 6.05 (m, 2H, H-2a, H-2b), 5.78 (m, 1H, H-9a, H-9b), 5.30–5.37 (m, 4H, H-1a, H-1b, H-1′a, H-1′b), 4.99 (m, 2H, H-10a, H-10b), 4.93 (m, 2H, H-10′a, H-10′b), 4.23–4.82 (m, 12H, 6×CH_2Ph), 4.21 (dd, 1H, J = 3.1 Hz, 8.1 Hz, H-3a), 4.13 (dd, 1H, J = 3.4 Hz, 8.0 Hz, H-3b), 3.69 (s, 1H, OH), 3.62 (d, 2H, J = 3.3 Hz, H-4a, H-4b), 3.58 (d, 1H, J = 9.0 Hz, H-6a), 3.56 (d, 1H, J = 9.3 Hz, H-6b), 3.53 (s, 1H, OH), 3.35 (d, 1H, J = 9.0 Hz, H-6′a), 3.26 (d, 1H, J = 9.3 Hz, H-6′b), 1.95–2.30 (m, 4H, H-8a, H-8b, H-8′a, H-8′b), 1.75 (m, 2H, H-7a, H-7′a), 1.62 (m, 1H, H-7b), 1.43 (m, 1H, H-7′b); ^{13}C NMR ($CDCl_3$, 100 MHz): 139.20, 139.18 (C-9a, C-9b), 138.45, 138.26, 138.02, 137.98, 137.44, 137.22 (6×C_{ipso}), 136.30, 136.07 (C-2a, C-2b), 127.59–128.63 (aromatic C), 118.99, 118.47 (C-1a, C-1b), 114.07, 114.01 (C-10a, C-10b), 83.41, 82.54 (C-4a, C-4b), 80.98, 80.90 (C-3a, C-3b), 76.53, 76.30 (C-5a, C-5b), 76.14, 76.00 (2×CH_2Ph), 73.25, 73.13 (2×CH_2Ph), 72.45, 70.72 (C-6a, C-6b), 70.11, 69.96 (2×CH_2Ph), 34.26, 33.77 (C-7a, C-7b), 27.22 (C-8a, C-8b); m/z (CI, NH_3): 504 (M+NH_4^+, 100%). Anal. calcd for $C_{31}H_{36}O_4$: C, 78.78; H, 7.68. Found: C, 78.63; H, 7.79%.

4.3. (3*R*,4*S*,5*R*)-3,4-Dibenzyloxy-5-(benzyloxymethyl)-deca-1,9-dien-5-ol 5a and (3*R*,4*S*,5*S*)-3,4-dibenzyloxy-5-(benzyloxymethyl)deca-1,9-dien-5-ol 5b

To a freshly prepared solution of pentenylmagnesium bromide (0.3 M in Et_2O, 50 mL) was added dropwise under argon at 0°C a solution of ketone **3** (4.5 g, 10.8 mmol) in Et_2O (80 mL). The reaction mixture was stirred for 18 h at rt and quenched at 0°C by dropwise addition of a sat. aq. NH_4Cl solution (50 mL). The aqueous layer was extracted with AcOEt (3×50 mL). Organic extracts were combined, dried ($MgSO_4$), filtered and the solvent was evaporated. Purification by flash chromatography (AcOEt/cyclohexane, 1:10) afforded diene **5a** and **5b** (3.69 g, 7.6 mmol, 70% yield), as an inseparable mixture of diastereomers.

^{1}H NMR ($CDCl_3$, 400 MHz): 7.30–7.39 (m, 30H, aromatic H), 6.05 (m, 2H, H-2a, H-2b), 5.80 (m, 1H, H-10a, H-10b), 5.29–5.38 (m, 4H, H-1a, H-1b, H-1′a, H-1′b), 4.93–5.04 (m, 4H, H-10a, H-10b, H-10′a, H-10′b), 4.23–4.82 (m, 12H, 6×CH_2Ph), 4.21 (dd, 1H, J = 3.1 Hz, 8.1 Hz, H-3a), 4.12 (dd, 1H, J = 3.5 Hz, 8.1 Hz, H-3b), 3.64 (s, 1H, OH), 3.61 (d, 2H, J = 3.4 Hz, H-4a, H-4b), 3.57 (d, 2H, J = 8.8 Hz, H-6a, H-6b), 3.49 (s, 1H, OH), 3.37 (d, 1H, J = 9.0 Hz, H-6′a), 3.27 (d, 1H, J = 9.3 Hz, H-6′b), 1.93–2.03 (m, 4H, H-9a, H-9b, H-9′a, H-9′b), 1.30–1.70 (m, 8H, H-7a, H-7′a, H-7b, H-7′b, H-8a, H-8′a, H-8b, H-8′b); ^{13}C NMR ($CDCl_3$, 100 MHz): 138.90, 138.87 (C-10a, C-10b), 138.50, 138.30, 138.06, 138.03, 137.49, 137.31 (6×C_{ipso}), 136.37, 136.13 (C-2a, C-2b), 127.47–128.65 (aromatic C), 118.89, 118.38 (C-1a, C-1b), 114.20, 114.03 (C-11a, C-11b), 83.45, 82.60 (C-4a, C-4b), 81.06, 80.91 (C-3a, C-3b), 76.67, 76.44 (C-5a, C-5b), 76.13, 75.96 (2×CH_2Ph), 73.25, 73.14 (2×CH_2Ph), 72.61, 70.93 (C-6a, C-6b), 70.10, 69.95 (2×CH_2Ph), 34.50, 34.29, 34.21, 34.08 (C-7a, C-7b, C-9a, C-9b), 22.12, 22.03 (C-8a, C-8b); m/z (CI, NH_3): 504 (M+NH_4^+, 100%). Anal. calcd for $C_{32}H_{38}O_4$: C, 78.97; H, 7.87. Found: C, 78.57; H, 8.01%.

4.4. (1*R*,2*S*,3*R*)-2,3-Dibenzyloxy-1-(benzyloxymethyl)-cyclohept-4-en-1-ol, 8 and (1*S*,2*S*,3*R*)-2,3-dibenzyloxy-1-(benzyloxymethyl)cyclohept-4-en-1-ol, 9

Dienes **4a** and **4b** (100 mg, 0.212 mmol) were dissolved in dry CH_2Cl_2 (50 mL) under argon. The solution was degased for 10 min by bubbling argon through the

solution. Catalyst **7** (9 mg, 0.011 mmol, 5% mol) was added and the solution was stirred at rt under argon. After 24 h, some more catalyst **7** was added (9 mg, 0.011 mmol, 5% mol). After 45 h, the reaction was quenched by stirring the reaction mixture with $Pb(OAc)_4$ (20 mg, 0.033 mmol) for 5 h. The solvent was then evaporated and the residue purified by flash chromatography (EtOAc/cyclohexane, 1:20) to afford cycloheptene **8** (47 mg, 0.106 mmol, 48% yield) as a colorless oil.

$[\alpha]_D = +17$ (*c* 1 in $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): 7.27–7.39 (m, 15H, aromatic H), 5.93 (m, 1H, H-1), 5.80 (m, 1H, H-2), 5.05 (d, 1H, $J = 10.7$ Hz, CHPh), 4.75 (s, 2H, CH_2Ph), 4.63 (m, 1H, H-3), 4.55 (d, 1H, $J = 12.0$ Hz, CHPh), 4.53 (d, 1H, $J = 10.7$ Hz, CHPh), 4.48 (1H, $J = 12.0$ Hz, CHPh), 3.72 (d, 1H, $J = 9.6$ Hz, H-4), 3.62 (d, 1H, $J = 8.7$ Hz, H-6), 3.28 (d, 1H, $J = 8.7$ Hz, H-6′), 2.80 (s, 1H, OH), 2.37 (m, 1H, H-8), 2.10 (m, 1H, H-8′), 2.01 (m, 1H, H-7), 1.78 (m, 1H, H-7′); ^{13}C NMR ($CDCl_3$, 100 MHz): 138.77, 138.38, 138.12 ($3\times C_{ipso}$), 132.95 (C-2), 132.00 (C-1), 127.34–128.32 (aromatic C), 80.87 (C-4), 77.31 (C-3), 76.33 (CH_2Ph), 75.54 (C-6), 75.40 (C-5), 73.28 (CH_2Ph), 73.03 (CH_2Ph), 34.06 (C-7), 22.11 (C-8); *m*/*z* (CI, NH_3): 462 ($M+NH_4^+$, 100%); HRMS (CI, NH_3) calcd for $C_{29}H_{33}O_4$ (MH^+): 445.2379. Found: 445.2373.

Further elution afforded cycloheptene **9** (47 mg, 0.106 mmol, 49% yield) as a colorless oil; $[\alpha]_D = -50$ (*c* 0.1 in $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) 7.27–7.40 (m, 15H, aromatic H), 6.11 (ddd, 1H, $J = 4.5$ Hz, 7.4 Hz, 11.7 Hz, H-1), 5.73 (ddd, 1H, $J = 2.3$ Hz, 5.2 Hz, 11.5 Hz, H-2), 4.73 (d, 1H, $J = 11.6$ Hz, CHPh), 4.65 (m, 4H, $2\times CH_2Ph$), 4.52 (d, 1H, $J = 11.6$ Hz, CHPh), 4.27 (dd, 1H, $J = 5.6$ Hz, 6.8 Hz, H-3), 4.11 (s, 1H, OH), 3.98 (d, 1H, $J = 6.8$ Hz, H-4), 3.65 (d, 1H, $J = 9.6$ Hz, H-6), 3.43 (d, 1H, $J = 9.6$ Hz, H-6′), 2.53 (m, 1H, H-8), 2.11 (m, 1H, H-8′), 1.87 (ddd, 1H, H-7), 1.58 (ddd, 1H, H-7′); ^{13}C NMR ($CDCl_3$, 100 MHz): 138.62, 138.42, 137.73 ($3\times C_{ipso}$), 135.94 (C-1), 128.13 (C-2), 127.45–128.39 (aromatic C), 79.74 (C-4), 77.42 (C-5), 76.36 (C-3), 75.03 (C-6), 73.95, 73.58, 71.68 ($3\times CH_2Ph$), 31.70 (C-7), 22.18 (C-8); *m*/*z* (CI, NH_3): 462 ($M+NH_4^+$, 100%). Anal. calcd for $C_{29}H_{32}O_4$: C, 78.35; H, 7.25. Found: C, 78.16; H, 7.37%.

4.5. (1*R*,2*S*,3*R*)-2,3-Dibenzyloxy-1-(benzyloxymethyl)-cyclooct-4-en-1-ol, 10 and (1*S*,2*S*,3*R*)-2,3-dibenzyloxy-1-(benzyloxymethyl)cyclooct-4-en-1-ol, 11

The diene **5a** or **5b** (100 mg, 0.212 mmol) was dissolved in dry CH_2Cl_2 (50 mL) under argon. The solution was degased for 10 min by bubbling argon through the solution. Grubbs' catalyst **6** (9 mg, 0.011 mmol, 5% mol) was added and the solution was stirred at rt under argon. After 24 h, some more catalyst **6** was added (9 mg, 0.011 mmol, 5% mol). After 72 h, the reaction was quenched by stirring the reaction mixture with $Pb(OAc)_4$ (20 mg, 0.033 mmol) for 5 h. The solvent was then evaporated and the residue purified by flash chromatography (EtOAc/cyclohexane, 1:20) to afford cyclooctene **10** (13 mg, 0.029 mmol, 14% yield) as a colorless oil; $[\alpha]_D = +2$ (*c* 0.2 in $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): 7.39–7.27 (m, 15H, aromatic H), 5.77 (m, 1H, H-2), 5.71 (m, 1H, H-1), 5.11 (d, 1H, $J = 10.5$ Hz, CHPh), 4.73 (d, 1H, $J = 11.5$ Hz, CHPh), 4.53–4.61 (m, 5H, H-3, $2\times CH_2Ph$), 3.74 (d, 1H, $J = 9.8$ Hz, H-4), 3.64 (d, 1H, $J = 8.3$ Hz, H-6), 3.33 (d, 1H, $J = 8.3$ Hz, H-6′), 2.73 (s, 1H, OH), 2.35 (m, 1H, H-9), 2.17 (m, 1H, H-9′), 1.90 (m, 3H, H-7, H-7′, H-8), 1.43 (m, 1H, H-8′); ^{13}C NMR ($CDCl_3$, 100 MHz): 138.77, 138.55, 138.12 ($3\times C_{ipso}$), 132.49 (C-2), 131.01 (C-1), 127.31–128.44 (aromatic C), 82.90 (C-4), 77.51 (C-6), 77.47 (C-3), 75.78 (CH_2Ph), 74.88 (C-5), 73.32 (CH_2Ph), 71.66 (CH_2Ph), 31.00 (C-9), 26.57 (C-8), 21.94 (C-7); *m*/*z* (CI, NH_3): 462 ($M+NH_4^+$, 100%). Anal. calcd for $C_{30}H_{34}O_4$: C, 78.57; H, 7.47. Found: C, 78.50; H, 7.79%.

Further elution afforded cyclooctene **11** (14 mg, 0.031 mmol, 15% yield) as a colorless oil; $[\alpha]_D = -50$ (*c* 0.1 in $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) 7.40–7.27 (m, 15H, aromatic H), 6.11 (ddd, 1H, $J = 4.5$ Hz, 7.4 Hz, 11.7 Hz, H-1), 5.73 (ddd, 1H, $J = 2.3$ Hz, 5.2 Hz, 11.5 Hz, H-2), 4.73 (d, 1H, $J = 11.6$ Hz, CHPh), 4.65 (m, 4H, $2\times CH_2Ph$), 4.52 (d, 1H, $J = 11.6$ Hz, CHPh), 4.27 (dd, 1H, $J = 5.6$ Hz, 6.8 Hz, H-3), 4.11 (s, 1H, OH), 3.98 (d, 1H, $J = 6.8$ Hz, H-4), 3.65 (d, 1H, $J = 9.6$ Hz, H-6), 3.43 (d, 1H, $J = 9.6$ Hz, H-6′), 2.53 (m, 1H, H-8), 2.11 (m, 1H, H-8′), 1.87 (ddd, 1H, H-7), 1.58 (ddd, 1H, H-7′); ^{13}C NMR ($CDCl_3$, 100 MHz): 138.62, 138.42, 137.73 ($3\times C_{ipso}$), 135.94 (C-1), 128.13 (C-2), 127.45–128.39 (aromatic C), 79.74 (C-4), 77.42 (C-5), 76.36 (C-3), 75.03 (C-6), 73.95, 73.58, 71.68 ($3\times CH_2Ph$), 31.70 (C-7), 22.18 (C-8); *m*/*z* (CI, NH_3): 462 ($M+NH_4^+$, 100%). Anal. calcd for $C_{30}H_{34}O_4$: C, 78.57; H, 7.47. Found: C, 78.16; H, 7.37%.

4.6. (3*R*,4*S*,5*R*)-3,4-Dibenzyloxy-5-(benzyloxymethyl)-5-[(*tert*-butyl)dimethylsilyloxy]deca-1,9-diene, 12a and (3*R*,4*S*,5*S*)-3,4-dibenzyloxy-5-(benzyloxymethyl)-5-[(*tert*-butyl)dimethylsilyloxy]-deca-1,9-diene, 12b

To a solution of dienes **5a** and **5b** (500 mg, 1.03 mmol), triethylamine (360 μL, 2.57 mmol) in CH_2Cl_2 (10 mL) was added dropwise TBDMSOTf (435 mg, 1.65 mmol) under argon at 0°C. The reaction mixture was stirred for 18 h at rt. The solvent was evaporated and the residue partitioned between dichloromethane and water. Organic extracts was dried ($MgSO_4$), filtered and the solvent was evaporated. Purification by flash chromatography (AcOEt/cyclohexane, 1:30) afforded dienes **12a** and **12b** (552 mg, 0.926 mmol, 89% yield), as an inseparable mixture of diastereomers. ^1H NMR ($CDCl_3$, 400 MHz): 7.29–7.36 (m, 30H, aromatic H), 6.02 (m, 2H, H-2a, H-2b), 5.79 (m, 1H, H-10a, H-10b), 5.29 (m, 4H, H-1a, H-1b, H-1′a, H-1′b), 4.97 (m, 4H, H-11a, H-11b, H-11′a, H-11′b), 4.33–4.80 (m, 12H, $6\times CH_2Ph$), 4.25 (dd, 1H, $J = 3.1$ Hz, 8.1 Hz, H-3a), 4.22 (dd, 1H, $J = 3.5$ Hz, 8.1 Hz, H-3b), 3.74 (d, 1H, H-6b), 3.73 (d, 1H, H-4b), 3.62 (d, 1H, H-6a), 3.61 (d, 1H, H-6′b), 3.56 (d, 1H, H-4a), 3.51 (d, 1H, H-6′a), 1.76–2.05 (m, 4H, H-9a, H-9b, H-9′a, H-9′b), 1.36–1.61 (m, 8H, H-7a, H-7′a, H-7b, H-7′b, H-8a, H-8′a, H-8b, H-8′b); 0.88, 0.87 (2×s, *t*Bu a, *t*Bu b); 0.09 (s, CH_3Si b),

0.08 (s, CH_3Si a), 0.06 (s, CH_3Si b), –0.02 (s, CH_3Si a); ^{13}C NMR ($CDCl_3$, 100 MHz): 139.09 (C-10a), 139.02 (C-10b), 138.47 (C-2a), 138.28, 138.26, 137.94 (C_{ipso}), 138.15 (C-2b), 127.09–128.40 (aromatic C), 117.11 (C-1a), 116.92 (C-1b), 114.27 (C-11b), 114.26 (C-11a), 85.27 (C-4a), 84.54 (C-4b), 80.47 (C-5a), 80.22 (C-5b), 79.11 (C-3b), 79.02 (C-3a), 75.41, 75.28 (2×CH_2Ph), 73.88 (C-6a), 73.39 (C-6b), 73.02, 72.92, 70.18, 70.13 (4×CH_2Ph), 34.51, 34.49, 34.31, 33.59 (C-7a, C-7b, C-9a, C-9b), 26.31, 26.28 (*t*Bu a, *t*Bu b), 22.81, 22.57 (C-8a, C-8b), –2.70, –2.84, –3.02 (4×CH_3Si); *m*/*z* (CI, NH_3): 618 (M+NH_4^+, 100%); HRMS (CI, NH_3) calcd for $C_{38}H_{56}O_4NSi$ (M+NH_4^+): 618.3979. Found: 618.3984.

4.7. (1*R*,2*S*,3*R*)-2,3-Dibenzyloxy-1-(benzyloxymethyl)-1-[(*tert*-butyl)dimethylsilyloxy]-cyclooct-4-ene, 13 and (1*S*,2*S*,3*R*)-2,3-dibenzyloxy-1-(benzyloxymethyl)-1-[(*tert*-butyl)dimethylsilyloxy]-cyclooct-4-ene, 14

Dienes **12a** and **12b** (250 mg, 0.417 mmol) were dissolved in dry toluene (85 mL) under argon. The solution was degased for 10 min by bubbling argon through the solution. Grubbs' catalyst **6** (17 mg, 0.021 mmol, 5% mol) was added dropwise with a syringe pump over 10 h as a solution in dry toluene and the solution was stirred at rt under argon. After 24 h, some more catalyst **6** was added (17 mg, 0.021 mmol, 5% mol). After 72 h, the reaction was quenched by stirring the reaction mixture with $Pb(OAc)_4$ (23 mg, 0.11 mmol) for 4 h. The solvent was then evaporated and the residue purified by flash chromatography (EtOAc/cyclohexane, 1:200) to afford cyclooctenes **13** and **14** (207 mg, 0.36 mmol, 86% yield) as an inseparable mixture of diastereomers.

Spectroscopic data for 13: ^1H NMR ($CDCl_3$, 400 MHz): 7.34–7.26 (m, 15H, aromatic H), 5.90 (m, 1H, H-1), 5.66 (m, 1H, H-2), 5.11 (d, 1H, J=11.3 Hz, CHPh), 4.77 (d, 1H, J=11.3 Hz, CHPh), 4.63 (d, 1H, J=11.6 Hz, CHPh), 4.49 (m, 1H, H-3), 4.47 (d, 1H, J=11.6 Hz, CHPh), 4.40 (s, 2H, CH_2Ph), 3.82 (d, 1H, J=8.8 Hz, H-4), 3.71 (d, 1H, J=9.2 Hz, H-6), 3.35 (d, 1H, J=9.2 Hz, H-6′), 2.22 (m, 1H, H-9), 2.12 (m, 1H, H-9′), 1.81 (m, 1H, H-8), 1.65 (m, 2H, H-7, H-7′), 1.55 (m, 1H, H-8′), 1.30 (s, 9H, *t*Bu), 0.12 (s, 6H, $Si(CH_3)_2$); ^{13}C NMR ($CDCl_3$, 100 MHz): 139.98, 138.80, 137.74 (3×C_{ipso}), 132.33 (C-1), 131.41 (C-2), 126.87–128.24 (aromatic C), 86.77 (C-4), 81.48 (C-3), 79.15 (C-5), 77.00 (C-6), 75.81 (CH_2Ph), 73.22 (CH_2Ph), 71.89 (CH_2Ph), 31.78 (C-7), 26.26 (C-9), 26.11 (*t*BuSi), 22.22 (C-8), –2.12, –2.21 (2×$SiCH_3$); *m*/*z* (CI, NH_3): 590 (M+NH_4^+, 100%). Anal. calcd for $C_{36}H_{48}O_4Si$: C, 75.48; H, 8.45. Found: C, 74.92; H, 8.68%.

Spectroscopic data for 14: ^1H NMR ($CDCl_3$, 400 MHz): 7.39–7.30 (m, 15H, aromatic H), 5.81 (m, 1H, H-2), 5.64 (m, 1H, H-1), 5.12 (d, 1H, J=10.6 Hz, CHPh), 4.71 (d, 1H, J=11.5 Hz, CHPh), 4.61 (d, 1H, J=11.5 Hz, CHPh), 4.57 (m, 1H, H-3), 4.49 (s, 2H, CH_2Ph), 4.46 (d, 1H, J=10.6 Hz, CHPh), 3.83 (d, 1H, J=7.1 Hz, H-6), 3.53 (d, 1H, J=10.0 Hz, H-4), 3.15 (d, 1H, J=7.1 Hz, H-6′), 2.38 (m, 1H, H-9), 2.10 (m, 1H, H-9′), 1.95 (m, 1H, H-8), 1.82 (m, 2H, H-7, H-7′), 1.32 (m, 1H, H-8′), 0.91 (s, 9H, *t*Bu), 0.10 (s, 3H, $Si(CH_3)$), 0.04 (s, 3H, $Si(CH_3)$); ^{13}C NMR ($CDCl_3$, 100 MHz): 139.20, 139.07, 138.27 (3×C_{ipso}), 133.89 (C-1), 129.60 (C-2), 127.07–128.29 (aromatic C), 84.24 (C-4), 79.27 (C-5), 78.10 (C-6), 76.79 (C-3), 75.25 (CH_2Ph), 72.87 (CH_2Ph), 71.12 (CH_2Ph), 33.27 (C-7), 27.95 (C-9), 26.52 (*t*BuSi), 24.59 (C-8), –2.03, –2.27 (2×$SiCH_3$); *m*/*z* (CI, NH_3): 590 (M+NH_4^+, 100%).

4.8. (1*S*,2*S*,3*R*,4*S*,5*S*)-2,3-Dibenzyloxy-1-(benzyloxymethyl)cyclohepta-1,5,6-triol, 15 and (1*S*,2*S*,3*R*,4*R*,5*R*)-2,3-dibenzyloxy-1-(benzyloxymethyl)cyclohepta-1,5,6-triol, 16

Cycloheptene **8** (227 mg, 0.51 mmol) was dissolved in acetone/water (8/1, 9 mL). *N*-Methyl morpholine oxide (151 mg, 1.12 mmol) was added, followed by OsO_4 (10 μL, 2.5% wt in *t*BuOH). The reaction mixture was stirred for 5 days at rt and OsO_4 (10 μL, 2.5% wt in *t*BuOH) was added every day. The reaction mixture was then diluted with CH_2Cl_2 (10 mL) and H_2O (10 mL). The aqueous layer was extracted with CH_2Cl_2 (10 mL) and the organic extracts were combined, dried ($MgSO_4$) and the solvent removed under reduced pressure. Purification by careful flash chromatography (EtOAc/cyclohexane, 1:4) afforded triol **15** as a colorless oil (60 mg, 0.125 mmol, 25% yield); $[\alpha]_D$=+21 (*c* 0.1 in $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): 7.38–7.24 (m, 15H, aromatic H), 4.76 (d, 1H, J=11.3 Hz, CHPh), 4.72 (d, 1H, J=11.8 Hz, CHPh), 4.57 (d, 1H, J=11.8 Hz, CHPh), 4.52 (d, 1H, J=12.0 Hz, CHPh), 4.46 (d, 1H, J=12.0 Hz, CHPh), 4.45 (d, 1H, J=11.3 Hz, CHPh), 4.09 (m, 1H, H-2), 3.96 (m, 2H, H-3, H-4), 3.91 (m, 1H, H-1), 3.38 (d, 1H, J=8.7 Hz, H-6), 3.24 (d, 1H, J=8.7 Hz, H-6′), 3.22 (d, 1H, J=9.7 Hz, OH-1), 3.07 (s, 1H, OH-5), 2.94 (d, 1H, J=6.6 Hz, OH-2), 2.19 (m, 1H, H-7), 2.04 (m, 2H, H-8), 1.80 (m, 1H, H-8′), 1.52 (m, 1H, H-7′); ^{13}C NMR ($CDCl_3$, 100 MHz): 138.11, 137.49, 137.44 (3×C_{ipso}), 127.67–128.82 (aromatic C), 83.56 (C-2), 77.22 (C-5), 75.92 (C-1), 74.16 (CH_2Ph), 74.16 (CH_2Ph), 73.79 (C-6), 73.44 (C-3), 73.33 (CH_2Ph), 71.36 (C-4), 29.68 (C-7), 28.12 (C-8); *m*/*z* (CI, NH_3): 496 (M+NH_4^+, 100%); HRMS (CI, NH_3) calcd for $C_{29}H_{38}O_6N$ (M+NH_4^+): 496.2699. Found: 496.2701.

Further elution afforded triol **16** (140 mg, 0.293 mmol, 57% yield) as a colorless oil; $[\alpha]_D$=+41 (*c* 0.22 in $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): 7.39–7.22 (m, 15H, aromatic H), 4.90 (d, 1H, J=11.0 Hz, CHPh), 4.88 (d, 1H, J=11.3 Hz, CHPh), 4.62 (d, 1H, J=11.3 Hz, CHPh), 4.52 (d, 1H, J=12.0 Hz, CHPh), 4.48 (d, 1H, J=11.0 Hz, CHPh), 4.43 (d, 1H, J=12.0 Hz, CHPh), 4.08 (m, 1H, H-1), 3.97 (app t, 1H, J=7.7 Hz, H-3), 3.74 (m, 1H, H-2), 3.66 (d, 1H, J=7.3 Hz, H-4), 3.64 (d, 1H, OH-2), 3.48 (d, 1H, J=8.4 Hz, H-6), 3.28 (d, 1H, J=8.4 Hz, H-6′), 3.06 (s, 1H, OH-5), 2.84 (br s, 1H, OH-1), 1.97 (m, 2H, H-7, H-8), 1.85 (m, 2H, H-7′, H-8′); ^{13}C NMR ($CDCl_3$, 100 MHz): 137.86, 137.76, 137.66 (3×C_{ipso}), 127.65–128.58 (aromatic C), 82.05 (C-4), 78.23 (C-3), 76.15 (C-6), 75.10 (CH_2Ph), 74.69 (CH_2Ph), 74.36 (C-2), 73.73 (C-5), 73.30 (CH_2Ph), 68.27 (C-1), 27.87, 27.35 (C-7, C-8); *m*/*z* (CI, NH_3): 496 (M+NH_4^+, 100%). Anal. calcd for $C_{29}H_{34}O_6$: C, 72.78; H, 7.16. Found: C, 73.10; H, 7.54%.

4.9. (1*R*,2*S*,3*R*,4*S*,5*S*)-2,3-Dibenzyloxy-1-(benzyloxymethyl)cyclohepta-1,5,6-triol, 17 and (1*R*,2*S*,3*R*,4*R*,5*R*)-2,3-dibenzyloxy-1-(benzyloxymethyl)cyclohepta-1,5,6-triol, 18

Cycloheptene **9** (289 mg, 0.65 mmol) was dissolved in acetone/water (8/1, 9 mL). *N*-Methyl morpholine oxide (193 mg, 1.43 mmol) was added followed by OsO_4 (10 μL, 2.5% wt in *t*BuOH). The reaction mixture was stirred for 6 days at rt and OsO_4 (10 μL, 2.5% wt in *t*BuOH) was added every day. The reaction mixture was then diluted with CH_2Cl_2 (10 mL) and H_2O (10 mL). The aqueous layer was extracted with CH_2Cl_2 (10 mL) and the organic extracts were combined, dried ($MgSO_4$) and the solvent removed under reduced pressure. Purification by careful flash chromatography (EtOAc/cyclohexane, 1:3) afforded triol **17** as a colorless oil (208 mg, 0.435 mmol, 67% yield); $[\alpha]_D = +38.5$ (*c* 0.93 in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): 7.39–7.22 (m, 15H, aromatic H), 4.81 (d, 1H, $J = 11.6$ Hz, CHPh), 4.69 (d, 1H, $J = 11.6$ Hz, CHPh), 4.62 (d, 1H, $J = 11.2$ Hz, CHPh), 4.56 (d, 1H, $J = 11.9$ Hz, CHPh), 4.42 (d, 1H, $J = 11.9$ Hz, CHPh), 4.30 (d, 1H, $J = 11.2$ Hz, CHPh), 4.13 (ddd, 1H, $J = 1.7$ Hz, 5.4 Hz, H-2), 4.06 (m, 1H, H-1), 3.95 (d, 1H, $J = 3.1$ Hz, H-4), 3.87 (dd, 1H, $J = 3.1$ Hz, 7.1 Hz, H-3), 3.46 (d, 1H, $J = 9.1$ Hz, H-6), 3.43 (d, 1H, $J = 7.9$ Hz, OH-1), 3.26 (d, 1H, $J = 9.1$ Hz, H-6′), 2.89 (d, 1H, $J = 0.6$ Hz, OH-5), 2.79 (d, 1H, $J = 5.3$ Hz, OH-2), 1.97–2.03 (m, 2H, H-7, H-7′), 1.87 (m, 1H, H-8), 1.41 (1H, m, H-8′); ^{13}C NMR ($CDCl_3$, 100 MHz): 137.84, 137.79, 136.72 ($3\times C_{ipso}$), 127.68–128.52 (aromatic C), 82.96 (C-3), 79.33 (C-4), 78.52 (C-2), 75.50 (C-5), 75.20 (C-6), 73.36 (CH_2Ph), 73.35 (CH_2Ph), 73.18 (C-1), 73.12 (CH_2Ph), 26.79 (C-8), 24.87 (C-7); *m*/*z* (CI, NH_3): 496 ($M+NH_4^+$, 100%). Anal. calcd for $C_{29}H_{34}O_6$: C, 72.78; H, 7.16. Found: C, 72.61; H, 7.33%.

Further elution afforded triol **18** as a white solid (45 mg, 0.094 mmol, 15% yield); $[\alpha]_D = +4$ (*c* 1 in $CHCl_3$); mp 99–100°C; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.40–7.22 (m, 15H, aromatic H), 4.74 (d, 1H, $J = 11.5$ Hz, CHPh), 4.64 (d, 1H, $J = 11.5$ Hz, CHPh), 4.63 (d, 1H, $J = 11.3$ Hz, CHPh), 4.57 (d, 1H, $J = 11.9$ Hz, CHPh), 4.52 (d, 1H, $J = 11.9$ Hz, CHPh), 4.47 (d, 1H, $J = 11.3$ Hz, CHPh), 4.26 (m, 2H, H-2, OH), 3.91 (app d, 1H, $J = 4.3$ Hz, H-4), 3.88 (app d, 1H, $J = 4.3$ Hz, H-3), 3.82 (m, 1H, H-1), 3.65 (d, 1H, $J = 7.9$ Hz, OH-1), 3.59 (d, 1H, $J = 9.1$ Hz, H-6), 3.24 (d, 1H, $J = 9.1$ Hz, H-6′), 2.42 (s, 1H, OH-5), 2.06 (m, 1H, H-8), 1.88 (m, 1H, H-8′), 1.75 (m, 1H, H-7), 1.51 (1H, m, H-7′); ^{13}C NMR ($CDCl_3$, 100 MHz): 138.05, 137.65, 137.61 ($3\times C_{ipso}$), 127.68–128.57 (aromatic C), 82.98 (C-3), 81.77 (C-4), 75.39 (C-6), 75.32 (C-5), 73.45 (CH_2Ph), 73.39 (CH_2Ph), 72.99 (C-2), 72.27 (CH_2Ph), 71.84 (C-1), 26.74 (C-7), 26.03 (C-8); *m*/*z* (CI, NH_3): 496 ($M+NH_4^+$, 100%); HRMS (CI, NH_3) calcd for $C_{29}H_{35}O_6$ (MH^+): 479.2434. Found: 479.2439.

4.10. (1*S*,2*S*,3*R*,4*S*,5*S*)-1-(Hydroxymethyl)cyclohepta-1,2,3,4,5-pentol, 19

Triol **15** (67 mg, 0.140 mmol) was dissolved in EtOAc/MeOH (1:1, 10 mL) and 10% Pd/C (10 mg) was added. The suspension was stirred under H_2 for 1 h, filtered through Celite, eluted with MeOH. The solvent was removed under reduced pressure to afford pentol **19** as a colorless oil (29 mg, 0. 140 mmol, quant. yield); $[\alpha]_D = +11$ (*c* 0.35 in CH_3OH); ^{1}H NMR (D_2O, 400 MHz): 3.98 (m, 1H, H-1), 3.81 (app t, 1H, $J = 7.8$ Hz, H-3), 3.64 (dd, 1H, $J = 3.0$ Hz, 7.6 Hz, H-2), 3.59 (d, 1H, $J = 11.3$ Hz, H-6), 3.50 (d, 1H, $J = 11.3$ Hz, H-6′), 3.47 (d, 1H, $J = 8.3$ Hz, H-4), 1.67–1.87 (m, 4H, H-7, H-7′, H-8, H-8′); ^{13}C NMR (D_2O, 100 MHz): 75.76 (C-2), 75.02 (C-5), 74.80 (C-4), 72.00 (C-3), 70.02 (C-1), 66.92 (C-6), 28.28, 24.88 (C-7, C-8); *m*/*z* (ES+): 231 ($M+Na^+$, 100%), 247 ($M+K^+$, 5%).

4.11. (1*S*,2*S*,3*R*,4*R*,5*R*)-1-(Hydroxymethyl)cyclohepta-1,2,3,4,5-pentol, 20

Triol **16** was deprotected as described for **19** to afford compound **20**; $[\alpha]_D = +20$ (*c* 0.60 in CH_3OH); ^{1}H NMR (D_2O, 400 MHz): 4.11 (m, 1H, H-2), 3.83 (ddd, 1H, $J = 2.9$ Hz, 5.0 Hz, 9.9 Hz, H-1), 3.75 (m, 2H, H-3, H-4), 3.56 (d, 1H, $J = 11.5$ Hz, H-6), 3.51 (d, 1H, $J = 11.5$ Hz, H-6′), 2.05 (ddd, 1H, $J = 3.4$ Hz, 9.6 Hz, 15.1 Hz, H-7), 1.64 (2H, m, H-8, H-8′), 1.43 (ddd, 1H,, $J = 3.5$ Hz, 8.1 Hz, 15.1 Hz, H-7′); ^{13}C NMR (D_2O, 100 MHz): 75.41 (C-2), 74.82 (C-5), 72.03 (C-4), 69.88 (C-3), 69.20 (C-1), 66.90 (C-6), 28.71, 24.99 (C-7, C-8); *m*/*z* (ES+): 231 ($M+Na^+$, 100%), 247 ($M+K^+$, 5%).

4.12. (1*R*,2*S*,3*R*,4*S*,5*S*)-1-(Hydroxymethyl)cyclohepta-1,2,3,4,5-pentol, 21

Triol **17** was deprotected as described for **19** to afford **21**; $[\alpha]_D = +29$ (*c* 0.79 in CH_3OH); ^{1}H NMR (D_2O, 400 MHz): 4.07 (m, 1H, H-1), 3.81 (dd, 1H, $J = 2.2$ Hz, 7.7 Hz, H-2), 3.76 (dd, 1H, $J = 5.4$ Hz, 7.7 Hz, H-3), 3.64 (d, 1H, $J = 5.4$ Hz, H-4), 3.59 (d, 1H, $J = 11.8$ Hz, H-6), 3.47 (d, 1H, $J = 11.8$ Hz, H-6′), 1.75–1.92 (3H, m, H-7, H-7′, H-8), 1.43 (m, 1H, H-8); ^{13}C NMR (D_2O, 100 MHz): 77.22 (C-2), 76.24 (C-5, C-4), 75.04 (C-3), 71.86 (C-1), 66.71 (C-6), 25.86, 25.27 (C-7, C-8); *m*/*z* (ES+): 231 ($M+Na^+$, 100%), 247 ($M+K^+$, 5%).

4.13. (1*R*,2*S*,3*R*,4*R*,5*R*)-1-(Hydroxymethyl)cyclohepta-1,2,3,4,5-pentol, 22

Triol **18** was deprotected as described for **19** to afford **22**; $[\alpha]_D = +16$ (*c* 0.55 in CH_3OH); ^{1}H NMR (D_2O, 400 MHz): 4.03 (m, 1H, H-2), 3.83 (ddd, 1H, $J = 2.4$ Hz, 5.7 Hz, 12.3 Hz, H-1), 3.81 (d, 1H, H-4), 3.72 (dd, 1H, $J = 1.4$ Hz, 7.8 Hz, H-3), 3.64 (d, 1H, $J = 11.8$ Hz, H-6), 3.43 (d, 1H, $J = 11.8$ Hz, H-6′), 1.72–1.88 (2H, m, H-8, H-8′), 1.57–1.61 (m, 2H, H-7, H-7′); ^{13}C NMR (D_2O, 100 MHz): 77.77 (C-2), 76.97 (C-1 or C-4), 75.12 (C-5), 74.57 (C-3), 72.18 (C-1 or C-4), 66.86 (C-6), 27.19 (C-7), 24.42 (C-8); *m*/*z* (ES+): 231 ($M+Na^+$, 100%), 247 ($M+K^+$, 5%).

4.14. (1*S*,2*S*,3*R*,4*S*,5*S*)-2,3-Dibenzyloxy-1-(benzyloxymethyl)cycloocta-1,4,5-triol, 23 and (1*S*,2*S*,3*R*,4*R*,5*R*)-2,3-dibenzyloxy-1-(benzyloxymethyl)cycloocta-1,4,5-triol, 24

These products were synthesized as previously described for **15** and **16**.

Spectroscopic data for triol 23: $[\alpha]_D = +32$ (*c* 0.60 in $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): 7.39–7.30 (m, 15H, aromatic H), 5.00–4.89 (m, 2H, CH_2Ph), 4.64–4.46 (m, 4H, 2×CH_2Ph), 4.08 (dd, 1H, $J=7.2$ Hz, 9.4 Hz, H-3), 4.02 (m, 1H, $J=2.4$ Hz, 10.8 Hz, H-1), 3.83 (dd, 1H, $J=3.0$ Hz, 9.4 Hz, H-2), 3.70 (d, 1H, $J=7.2$ Hz, H-4), 3.58 (d, 1H, $J=8.5$ Hz, H-6), 3.39 (d, 1H, $J=8.5$ Hz, H-6′), 2.10–1.80 (m, 3H, H-9, H-9′, H-7), 1.70–1.42 (m, 3H, H-7′, H-8, H-8′); ^{13}C NMR ($CDCl_3$, 100 MHz): 138.21, 137.96, 137.74 (3×C_{ipso}), 128.34–127.51 (aromatic C), 78.04 (C-4), 77.05 (C-2), 76.86 (C-3), 74.92 (C-5), 74.67 (C-6), 74.52 (CH_2Ph), 74.12 (CH_2Ph), 73.38 (CH_2Ph), 69.39 (C-1), 31.00 (C-7), 29.19 (C-9), 17.81 (C-8); *m*/*z* (CI, NH_3): 510 ($M+NH_4^+$, 100%). Anal. calcd for $C_{30}H_{36}O_6$: C, 73.15; H, 7.37. Found: C, 73.39; H, 7.82%.

Spectroscopic data for triol 24: $[\alpha]_D = +12$ (*c* 0.75 in $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): 7.39–7.30 (m, 15H, aromatic H), 5.00–4.89 (m, 2H, CH_2Ph), 4.64–4.46 (m, 4H, 2×CH_2Ph), 4.28 (m, 1H, H-2), 4.17 (d, 1H, $J=7.4$ Hz, H-4), 3.91 (dd, 1H, $J=1.6$ Hz, 7.4 Hz, H-3), 3.69 (m, 1H, H-1), 3.49 (d, 1H, $J=9.3$ Hz, H-6), 3.38 (d, 1H, $J=9.3$ Hz, H-6′), 2.10–1.80 (m, 3H, H-9, H-9′, H-7), 1.70–1.42 (m, 3H, H-7′, H-8, H-8′); ^{13}C NMR ($CDCl_3$, 100 MHz): 138.41, 138.06, 138.05 (3×C_{ipso}), 127.51–128.34 (aromatic C), 76.63 (C-3′), 76.03 (C-6), 75.36 (C-5), 75.27 (C-2), 75.17 (CH_2Ph), 74.43 (C-4), 74.23 (CH_2Ph), 73.38 (CH_2Ph), 70.96 (C-1), 33.27 (C-7), 28.31 (C-9), 20.15 (C-8); *m*/*z* (CI, NH_3): 510 ($M+NH_4^+$, 100%). Anal. calcd for $C_{30}H_{36}O_6$: C, 73.15; H, 7.37. Found: C, 73.30; H, 7.70%.

4.15. (1*R*,2*S*,3*R*,4*S*,5*S*)-2,3-Dibenzyloxy-1-(benzyloxymethyl)cycloocta-1,4,5-triol, 25 and (1*R*,2*S*,3*R*,4*R*,5*R*)-2,3-dibenzyloxy-1-(benzyloxymethyl)cycloocta-1,4,5-triol, 26

These products were synthesized as previously described for **17** and **18**.

Spectroscopic data for triol 25: $[\alpha]_D = +37$ (*c* 1 in $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): 7.38–7.30 (m, 15H, aromatic H), 4.83 (d, 1H, $J=11.6$ Hz, CHPh), 4.80 (d, 1H, $J=11.0$ Hz, CHPh), 4.57 (d, 1H, $J=11.7$ Hz, CHPh), 4.50 (d, 1H, $J=11.0$ Hz, CHPh), 4.49 (d, 1H, $J=11.7$ Hz, CHPh), 4.46 (m, 1H, H-2), 4.43 (d, 1H, $J=11.6$ Hz, CHPh), 4.09 (m, 1H, H-1), 4.05 (d, 1H, $J=4.2$ Hz, H-4), 3.95 (dd, 1H, $J=8.7$ Hz, 4.2 Hz, H-3), 3.52 (d, 1H, $J=8.9$ Hz, H-6), 3.28 (d, 1H, $J=8.9$ Hz, H-6′), 3.12 (d, 1H, $J=1.6$ Hz, OH-2), 2.88 (s, 1H, OH-5), 2.61 (d, 1H, $J=3.0$ Hz, OH-1), 2.01 (m, 2H, H-9), 1.88 (m, 1H, H-7), 1.65 (m, 2H, H-8), 1.58 (m, 1H, H-7′); ^{13}C NMR ($CDCl_3$, 100 MHz): 137.98, 137.83, 137.48 (3×C_{ipso}), 127.78–128.57 (aromatic C), 79.63 (C-3, C-4), 76.16 (C-6), 75.91 (C-5), 73.71 (CH_2Ph), 73.58 (CH_2Ph), 73.31 (CH_2Ph), 72.79 (C-2), 71.25 (C-1), 33.14 (C-7, C-8), 29.20 (C-9); *m*/*z* (CI, NH_3): 510 ($M+NH_4^+$, 100%); HRMS (CI, NH_3) calcd for $C_{30}H_{37}O_6$ (MH^+): 493.2590. Found: 493.2589.

Spectroscopic data for triol 26: $[\alpha]_D = +11$ (*c* 1 in $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): 7.38–7.30 (m, 15H, aromatic H), 4.98 (d, 1H, $J=11.6$ Hz, CHPh), 4.86 (d, 1H, $J=11.2$ Hz, CHPh), 4.67 (d, 1H, $J=11.2$ Hz, CHPh), 4.66 (d, 1H, $J=11.6$ Hz, CHPh), 4.57 (s, 2H, CH_2Ph), 4.28 (m, 1H, H-2), 4.25 (d, 1H, $J=8.0$ Hz, H-4), 4.14 (dd, 1H, $J=2.3$ Hz, 8.0 Hz, H-3), 3.94 (m, 1H, H-1), 3.62 (d, 1H, $J=8.9$ Hz, H-6), 3.38 (d, 1H, $J=8.9$ Hz, H-6′), 3.18 (d, 1H, $J=7.3$ Hz, OH-2), 2.83 (d, 1H, $J=3.0$ Hz, OH-1), 2.65 (s, 1H, OH-5), 2.16 (m, 2H, H-7, H-9), 1.93 (m, 1H, H-8), 1.76 (m, 2H, H-7′, H-9′), 1.61 (m, 1H, H-8′); ^{13}C NMR ($CDCl_3$, 100 MHz): 138.50, 138.01, 137.84 (3×C_{ipso}), 127.45–128.58 (aromatic C), 83.36 (C-4), 81.51 (C-3), 75.77 (C-5), 75.15 (CH_2Ph), 75.12 (CH_2Ph), 74.55 (C-6), 74.11 (C-1), 73.47 (CH_2Ph), 73.07 (C-2), 31.71 (C-7), 31.65 (C-9), 17.60 (C-8); *m*/*z* (CI, NH_3): 510 ($M+NH_4^+$, 100%); HRMS (CI, NH_3) calcd for $C_{30}H_{40}O_6N$ (MNH_4^+): 510.2856. Found: 510.2858.

4.16. (1*S*,2*S*,3*R*,4*S*,5*S*)-1-(Hydroxymethyl)cycloocta-1,2,3,4,5-pentol, 27

This compound was obtained as a foam using the method previously described for **19**; $[\alpha]_D = -8$ (*c* 0.55 in CH_3OH); ^1H NMR (D_2O, 400 MHz): 4.06 (dd, 1H, $J=7.4$ Hz, 8.8 Hz, H-3), 3.91 (ddd, 1H, $J=2.5$ Hz, 2.8 Hz, 11.3 Hz, H-2), 3.75 (dd, 1H, $J=2.5$ Hz, 8.8 Hz, H-2), 3.65 (d, 1H, $J=11.3$ Hz, H-6), 3.62 (d, 1H, $J=7.4$ Hz, H-4), 3.48 (d, 1H, $J=11.3$ Hz, H-6′), 1.85–1.48 (m, 6H, H-7, H-7′, H-8, H-8′, H-9, H-9′); ^{13}C NMR (D_2O, 100 MHz): 78.43 (C-2), 75.64 (C-5), 68.88 (C-1, C-4), 68.74 (C-3), 67.36 (C-6), 31.40 (C-7), 29.40 (C-9), 16.52 (C-8); *m*/*z* (ES+): 245 ($M+Na^+$, 100%).

4.17. (1*S*,2*S*,3*R*,4*R*,5*R*)-1-(Hydroxymethyl)cycloocta-1,2,3,4,5-pentol, 28

This compound was obtained as a foam using the method previously described for **19**; $[\alpha]_D = -2$ (*c* 0.88 in CH_3OH); ^1H NMR (D_2O, 400 MHz): 4.12 (m, 1H, H-2), 3.90 (m, 2H, H-3, H-4), 3.87 (m, 1H, H-1), 3.73 (dd, 1H, $J=0.5$ Hz, 12.0 Hz, H-6), 3.61 (d, 1H, $J=12.0$ Hz, H-6′), 1.97–1.83 (m, 2H, H-9, H-7), 1.72–1.61 (m, 1H, H-8), 1.52–1.34 (m, 3H, H-7′, H-8′, H-9′); ^{13}C NMR (D_2O, 100 MHz): 76.70 (C-5), 75.79 (C-2), 70.67 (C-1), 67.34, 66.12 (C-3, C-4), 64.75 (C-6), 28.19 (C-7), 27.11 (C-9), 19.76 (C-8); *m*/*z* (ES+): 245 ($M+Na^+$, 100%).

4.18. (1*R*,2*S*,3*R*,4*S*,5*S*)-1-(Hydroxymethyl)cycloocta-1,2,3,4,5-pentol, 29

This compound was obtained as a foam using the method previously described for **19**; $[\alpha]_D = -15$ (*c* 0.30 in CH_3OH); ^1H NMR (D_2O, 400 MHz): 3.97 (dd, 1H, $J=3.0$ Hz, 10.3 Hz, H-1), 3.83 (dd, 1H, $J=3.0$ Hz, 7.3 Hz, H-2), 3.70 (dd, 1H, $J=5.8$ Hz, 7.3 Hz, H-3), 3.68 (d, 1H, $J=5.8$ Hz, H-4), 3.66 (d, 1H, $J=11.9$ Hz, H-6), 3.56 (d, 1H, $J=11.9$ Hz, H-6′), 1.84–1.52 (m, 6H, H-7, H-7′, H-8, H-8′, H-9, H-9′); ^{13}C NMR (D_2O, 100 MHz): 76.81 (C-5), 76.62 (C-2), 72.46 (C-3), 71.31 (C-1), 70.39 (C-4), 64.19 (C-6), 33.31 (C-7), 31.21 (C-9), 18.35 (C-8); *m*/*z* (ES+): 245 ($M+Na^+$, 100%).

4.19. (1*R*,2*S*,3*R*,4*R*,5*R*)-1-(Hydroxymethyl)cycloocta-1,2,3,4,5-pentol, 30

This compound was obtained as a foam using the method previously described for **19**; $[\alpha]_D = +3$ (*c* 0.25 in CH_3OH); ^1H NMR (D_2O, 400 MHz): 4.16 (d, 1H, $J = 7.6$ Hz, H-4), 4.06 (app t, 1H, $J = 2.2$ Hz, H-2), 3.93 (m, 1H, H-1), 3.81 (dd, 1H, $J = 2.2$ Hz, 7.6 Hz, H-3), 3.56 (m, 2H, H-6, H-6′), 2.00 (m, 1H, H-9′), 1.78–1.51 (m, 5H, H-7, H-7′, H-8, H-8′, H-9); ^{13}C NMR (D_2O, 100 MHz): 76.80 (C-5), 74.72 (C-2), 72.39 (C-1), 71.45 (C-4), 70.55 (C-3), 65.10 (C-6), 30.40, 29.47, 17.62 (C-7, C-8, C-9); *m*/*z* (ES+): 245 ($M+Na^+$, 100%).

4.20. Triacetonide 31

Diol **25** (96 mg, 0.194 mmol) was dissolved under argon in acetone (9 mL). Camphorsulfonic acid (10 mg) and 2,2-dimethoxypropane (1 mL) were added. The reaction mixture was stirred for 3 h at rt, quenched with triethylamine (0.2 mL) and concentrated under vacuum. The residue was dissolved in MeOH/AcOEt (10 mL, 1/1) and stirred under H_2 for 1 h in the presence of 10% Pd/C (10 mg). The reaction mixture was filtered through Celite, eluted with MeOH and the solvent was evaporated. The residue was dissolved under argon in acetone (9 mL). Camphorsulfonic acid (10 mg) and 2,2-dimethoxypropane (1 mL) were added. The reaction mixture was stirred for 5 h at rt, quenched with triethylamine (0.2 mL) and concentrated under vacuum. Purification by flash chromatography (EtOAc/cylohexane, 1:5) afforded the triacetonide **31** (40 mg, 0.116 mmol, 60% yield) as white crystals; $[\alpha]_D = +15$ (*c* 0.7 in $CHCl_3$); mp 127–128°C (EtOAc/cyclohexane); ^1H NMR ($CDCl_3$, 400 MHz): 4.30 (ddd, 1H, $J = 5.4$ Hz, 10.1 Hz, H-1), 4.19 (dd, 1H, $J = 5.4$ Hz, 9.3 Hz, H-2), 4.17 (d, 1H, $J = 8.6$ Hz, H-6), 3.93 (dd, 1H, $J = 8.1$ Hz, 9.3 Hz, H-3), 3.86 (d, 1H, $J = 8.1$ Hz, H-4), 3.78 (d, 1H, $J = 8.6$ Hz, H-6′), 1.93–1.68 (m, 6H, H-7, H-7′, H-8, H-8′, H-9, H-9′), 1.51 (3H, s, CH_3), 1.49 (6H, 2×s, 2×CH_3), 1.46 (3H, s, CH_3), 1.43 (3H, s, CH_3), 1.41 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): 82.15 (C-4), 81.66 (C-5), 78.38 (C-2), 77.57 (C-1), 76.45 (C-3), 71.08 (C-6), 35.77, 31.38 (C-7, C-9), 20.08 (C-8), 28.36, 27.53, 27.07, 26.91, 26.00, 25.88 (6×CH_3); *m*/*z* (CI, NH_3): 343 ($M+H^+$, 18%); 360 ($M+NH_4^+$, 100%). Anal. calcd for $C_{18}H_{30}O_6$: C, 63.14; H, 8.83. Found: C, 63.12; H, 8.95%.

Acknowledgements

We would like to thank Professor Aloïs Fürstner for the generous gift of the RCM catalyst **7**. We thank Dr. Carine Duhayon from the Centre de Résolution des Structures (Université Pierre et Marie Curie), for solving the X-ray structure of compound **31** and Dr. Denis Lesage (Université Pierre et Marie Curie) for recording the electrospray spectra. We thank also Miss Catherine Schütz for technical help and the Swiss National Science Foundation and the 'Office Fédéral de l'Education et de la Science' for financial support.

References

1. (a) Martinez-Grau, A.; Marco-Contelles, J. *Chem. Soc. Rev.* **1998**, *27*, 155 and references cited herein; (b) Dalko, P. I.; Sinaÿ, P. *Angew. Chem., Int. Ed.* **1999**, *38*, 773.
2. Ogawa, S. In *Carbohydrates in Drug Design*; Witczak, Z. J.; Nieforth, K. A., Eds.; Dekker: New York, 1997; p. 433.
3. For example, see: (a) Ackermann, L.; El Tom, D.; Fürstner, A. *Tetrahedron* **2000**, *56*, 2195–2202; (b) Hyldtoft, L.; Madsen, R. *J. Am. Chem. Soc.* **2000**, *122*, 8444–8452; (c) Callam, C. S.; Lowary, T. L. *Org. Lett.* **2000**, *2*, 167–169.
4. (a) Marco-Contelles, J.; de Opazo, E. *Tetrahedron Lett.* **1999**, *40*, 4445–4448; (b) Marco-Contelles, J.; de Opazo, E. *J. Org. Chem.* **2000**, *65*, 5416–5419; (c) Marco-Contelles, J.; de Opazo, E. *Tetrahedron Lett.* **2000**, *41*, 5341–5345; (d) Marco-Contelles, J.; de Opazo, E. *Tetrahedron Lett.* **2000**, *41*, 2439–2441; (e) Boyer, F.-D.; Hanna, I. *Tetrahedron Lett.* **2001**, *42*, 1275–1277; (f) Marco-Contelles, J.; de Opazo, E. *J. Org. Chem.* **2002**, *67*, 3705–3717 and references cited therein.
5. (a) Hanna, I.; Ricard, L. *Org. Lett.* **2000**, *2*, 2651–2654; (b) Boyer, F.-D.; Hanna, I.; Nolan, S. P. *J. Org. Chem.* **2001**, *66*, 4094–4096; (c) van Hooft, P. A. V.; van der Marel, G. A.; van Boeckel, C. A. A.; van Boom, J. H. *Tetrahedron Lett.* **2001**, *42*, 1769–1772; (d) van Hooft, P. A.; Litjens, R. E. J. N.; van der Marel, G. A.; van Boeckel, C. A. A.; van Boom, J. H. *Org. Lett.* **2001**, *3*, 731–733; (e) McNulty, J.; Grunner, V.; Mao, J. *Tetrahedron Lett.* **2001**, *42*, 5609–5612; (f) Gravier-Pelletier, C.; Andriuzzi, O.; Le Merrer, Y. *Tetrahedron Lett.* **2002**, *43*, 245–248.
6. (a) Wang, W.; Zhang, Y.; Sollogoub, M.; Sinaÿ, P. *Angew. Chem., Int. Ed.* **2000**, *39*, 2466–2467; (b) Wang, W.; Zhang, Y.; Zhou, H.; Blériot, Y.; Sinaÿ, P. *Eur. J. Org. Chem.* **2001**, 1053–1059.
7. Barker, R.; Fletcher, H. G., Jr. *J. Org. Chem.* **1961**, *26*, 4605–4609.
8. (a) Sellier, O.; Van de Weghe, P.; Le Nouen, D.; Strehler, C.; Eustache, J. *Tetrahedron Lett.* **1999**, *40*, 853–856; (b) Sellier, O.; Van de Weghe, P.; Eustache, J. *Tetrahedron Lett.* **1999**, *40*, 5859–5860.
9. Roy, R.; Das, S. K. *Chem. Commun.* **2000**, 519–529.
10. Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413–4450.
11. Kirkland, T. A.; Grubbs, R. H. *J. Org. Chem.* **1997**, *62*, 7310–7318.
12. (a) Freeman, F.; Robarge, R. D. *Carbohydr. Res.* **1986**, *154*, 270–274; (b) Pearson, W. H.; Hines, J. V. *Tetrahedron Lett.* **1991**, *32*, 5513–5516; (c) Sharma, G. V. M.; Subash Chander, A.; Krishnudu, K.; Radha Krishna, P. *Tetrahedron Lett.* **1997**, *38*, 9051–9054; (d) Tatibouët, A.; Rollin, P.; Martin, O. R. *J. Carbohydr. Chem.* **2000**, *19*, 641–645; (e) Pearson, W. H.; Hines, J. V. *J. Org. Chem.* **2000**, *65*, 5785–5793; (f) Postema, M. H. D.; Calimente, D.; Liu, L.; Behrmann, T. L. *J. Org. Chem.* **2000**, *65*, 6061–6068.
13. Chorghade, M. S.; Cseke, C. T.; Liu, P. S. *Tetrahedron: Asymmetry* **1994**, *5*, 2251–2254.
14. Catalyst **6** was purchased from Fluka and catalyst **7** was a generous gift from Professor A. Fürstner.
15. Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953–956.

16. (a) Scholl, M.; Trnka, T. M.; Morgan, J. P.; Grubbs, R. H. *Tetrahedron Lett*. **1999**, *40*, 2247–2250; (b) Briot, A.; Bujard, M.; Gouverneur, V.; Nolan, S. P.; Mioskowski, C. *Org. Lett*. **2000**, *2*, 1517–1519; (c) Maier, M. E. *Angew. Chem., Int. Ed*. **2000**, *39*, 2073–2077.
17. Bourgeois, D.; Mahuteau, J.; Pancrazi, A.; Nolan, S. P.; Prunet, J. *Synthesis* **2000**, *6*, 869–882.
18. (a) Johnson, L. K.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc*. **1993**, *115*, 8130–8145; (b) Johnson, L. K.; Frey, M.; Ulibarri, T. A.; Virgil, S. C.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc*. **1993**, *115*, 8167–8177; (c) Maughon, B. R.; Grubbs, R. H. *Macromolecules* **1997**, *30*, 3459–3469; (d) Kingsbury, J. S.; Harrity, J. P. A.; Bonitatebus, P. J., Jr.; Hoveyda, A. H. *J. Am. Chem. Soc*. **1999**, *121*, 791–799; (e) Lee, C. W.; Grubbs, R. H. *Org. Lett*. **2000**, *2*, 2145–2147.
19. Pearson, A. J.; Srinivasan, K. *J. Org. Chem*. **1992**, *57*, 3965–3973.
20. Selected crystal structure data for **31**; crystal system orthorhombic; space group $P2_12_12_1$; $Z=4$; cell parameters: $a=5.607(7)$, $b=17.258(11)$, $c=19.297(15)$ Å, $\alpha=90$, $\beta=90$, $\gamma=90°$; radiation (Mo-Kα) $\lambda=0.710690$ Å; 98 variables for 588 reflections; final $R=0.0820$, $R_w=0.0990$; crystallographic data (excluding structure factors) have been deposited at the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 183140. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: (internat.) +44-1223/336-033; e-mail: deposit@ccdc.cam.ac.uk].
21. (a) Legler, G.; Herrchen, M. *FEBS Lett*. **1981**, *135*, 139–144; (b) Cavanagh, K. J.; Fischer, R. A.; Legler, G.; Herrchen, M.; Jones, M. Z.; Julich, E.; Sewell-Alger, R. P.; Sinnott, M. L.; Wilkinson, F. E. *Enzyme* **1985**, *34*, 75–82; (c) El Ashry, E. S. H.; Rasked, N.; Shobier, A. H. S. *Pharmazie* **2000**, *55*, 403–415; (d) Ley, S. V.; Sternfeld, F.; Taylor, S. *Tetrahedron Lett*. **1987**, *28*, 225–228; (e) Legler, G. *Adv. Carbohydr. Chem. Biochem*. **1990**, *48*, 319–384; (f) Legler, G.; Bollhagen, R. *Carbohydr. Res*. **1992**, *233*, 113–123.
22. Mehta, G.; Ramesh, S. S. *Tetrahedron Lett*. **2001**, *42*, 1987–1990.
23. Kensho, I.; Yamashita, F.; Nagai, T.; Fujimoto, T.; Nakano, Y.; Fukimura, H. *Eur. Pat. Appl*. (1992), Appl. EP91-306919 19910729; *Chem. Abstr*. **1992**, *116*: 248434.
24. (a) Iwata, N.; Ishiwatari, K. *Jpn Kokai–Tokkyo Koho* (2001), Appl. JP99-287620 19991008; *Chem. Abstr*. **2001**, *134*: 279953; (b) Miyatake, K.; Kensho, G.; Fujimoto, T.; Noguchi, E.; Shinohara, M.; Takenaka, S.; Taira, T.; Upadhaya, S. P.; Ichimoto, I.; Nakano, Y. *Biosc. Biotechnol. Biochem*. **1994**, *58*, 756–757.
25. Billington, D. C.; Perron-Sierra, F.; Picard, I.; Beaubras, S.; Duhault, J.; Espinal, J.; Challal, S. *Bioorg. Med. Chem. Lett*. **1994**, *4*, 2307–2312.
26. (a) Atsumi, S.; Iinuma, H.; Nosaka, C.; Umezawa, K. *J. Antibiot*. **1990**, *43*, 1579–1585; (b) Withers, S. G.; Umezawa, K. *Biochem. Biophys. Res. Commun*. **1991**, *177*, 432–437.
27. (a) Tai, V. W.-F.; Fung, P.-H.; Wong, Y.-S.; Shing, T. K. M. *Tetrahedron: Asymmetry* **1994**, *5*, 1353–1362; (b) Marco-Contelles, J. *Eur. J. Org. Chem*. **2001**, 1607–1618; (c) Tatsuta, K.; Niwata, Y.; Umezawa, K.; Toshima, K.; Nakata, M. *J. Antibiot*. **1991**, *44*, 912–914; (d) Atsumi, S.; Nosaka, C.; Ochi, Y.; Iinuma, H.; Umezawa, K. *Cancer Res*. **1993**, *53*, 4896–4899; (e) Nakata, M.; Chong, C.; Niwata, Y.; Toshima, K.; Tatsuta, K. *J. Antibiot*. **1993**, *46*, 1919–1922.
28. (a) Tropea, J. E.; Molyneux, R. J.; Kaushal, G. P.; Pan, Y. T.; Mitchell, M.; Elbein, A. D. *Biochemistry* **1989**, *28*, 2027–2034; for details see: (b) Brandi, A.; Cicchi, S.; Cordero, F. M.; Frignoli, B.; Goti, A.; Picasso, S.; Vogel, P. *J. Org. Chem*. **1995**, *60*, 6806–6812; (c) Picasso, S.; Chen, Y.; Vogel, P. *Carbohydr. Lett*. **1994**, *1*, 1–8.