Synthesis of Several Members of a New Family of Carbasugars: The Cyclooctane Mimetics

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The TIBAL-promoted Claisen rearrangement of carbohydrates, developed in our group, has been applied to vinyl glycosides derived from D-glucose to afford highly functionalized cyclooctene derivatives in a stereospecific manner. Subsequent manipulation of these compounds gave access to a new family of carbasugars: the glucose and idose cyclooctanic mimetics.

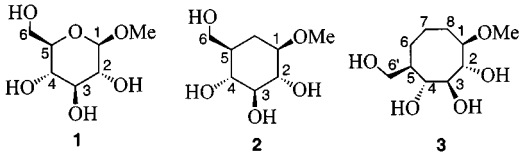
Introduction

The TIBAL-promoted Claisen rearrangement of 2-methylene-6-vinyl-tetrahydropyrans to afford cyclooctane derivatives has been elegantly developed by Paquette et al.[1] for the synthesis of a variety of natural products possessing eight-membered rings as a structural feature. In the context of a general program on TIBAL-promoted rearrangements in the field of carbohydrates,[2] we recently observed the same rearrangement in a glucopyranoside derivative.[3] We would now like to give a full account of this reaction and of the transformation of the resulting cyclooctenes into some members of a new family of carbasugars: the cyclooctane carbohydrate mimetics.[4] The concept of mimicking pyranosides with polyhydroxylated cyclooctanes,[5] offering a new alternative to conventional carbohydrates, gradually came to us out of the two following considerations:

1. A possible drawback in the use of synthetic oligosaccharides as therapeutic agents is their potential vulnerability towards in vivo degradation by various glycosidases. This is the main stimulus behind the search for nonhydrolysable oligosaccharide mimetics. One approach is based on the replacement of the endocyclic oxygen atom of aldopyranosyl residues by a methylene group, thus generating the so-called 5a-carbasugars, which are hydrolytically stable analogues.[6]

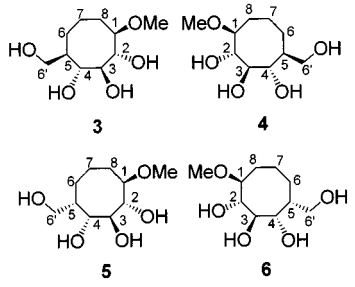
2. The conformational behaviour of cyclooctane derivatives[7] is different from that of their cyclohexane counterparts. Cyclooctane sugars may thus offer new distributions of hydroxy groups compared to those available through the classical chair, boat and skew-boat forms of the classical pseudorotational itinerary of pyranoid rings.

From these two premises, a mimetic, such as **3**, of the authentic methyl β-D-glucopyranoside **1** should combine the chemical stability of the 5a-carbasugar **2** with a different conformational behaviour (Scheme 1).



Scheme 1. Cyclohexane and cyclooctane mimetics **2** and **3** of methyl β-D-glucopyranoside **1**

We would like to describe here the chemical synthesis of four members of this new class of compounds: the cyclooctane mimetic **3**, its enantiomer **4** and their diastereoisomers at their respective 5-positions (compounds **5** and **6**), which are mimetics of methyl α-L-idopyranoside and methyl α-D-idopyranoside, respectively (Scheme 2).



Scheme 2. Cycloctane mimetics **3**−**6**

Results and Discussion

We first investigated the synthesis of the D-gluco and L-ido mimetics **3** and **5**, because of the relevance of D-glucose and L-idose as natural compounds. The starting material was the unsaturated derivative **10**, which was prepared uneventfully from the known[8] glucopyranoside derivative **7**, as shown in the self-explanatory Scheme 3. TIBAL-promoted Claisen rearrangement of **10** provided the cyclooctane derivative **11** in almost quantitative yield, as shown in the key Scheme 4. An X-ray analysis of the peracetate derivative **12** confirmed the structural assignment for compound **11**, in particular the absolute configuration at C-1[9] (Figure 1).

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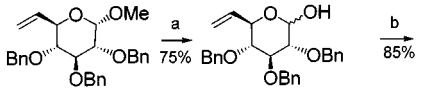
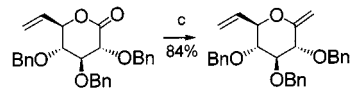
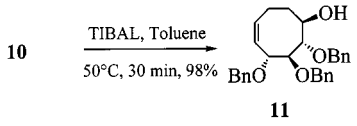




Scheme 3. Reagents and conditions: a) TfOH/AcOH/H_2O (1:28:5), 80 °C, 2.5 h, 75%; b) PCC, 4 Å molecular sieves, dry CH_2Cl_2, 0 °C to room temp., 3 h, 85%; c) Tebbe reagent, Py/THF (1:1), −78 °C to room temp., 30 min, 84%



Scheme 4. Claisen rearrangement of an unsaturated monosaccharide derivative, promoted by triisobutylaluminium (TIBAL), see ref.[3]

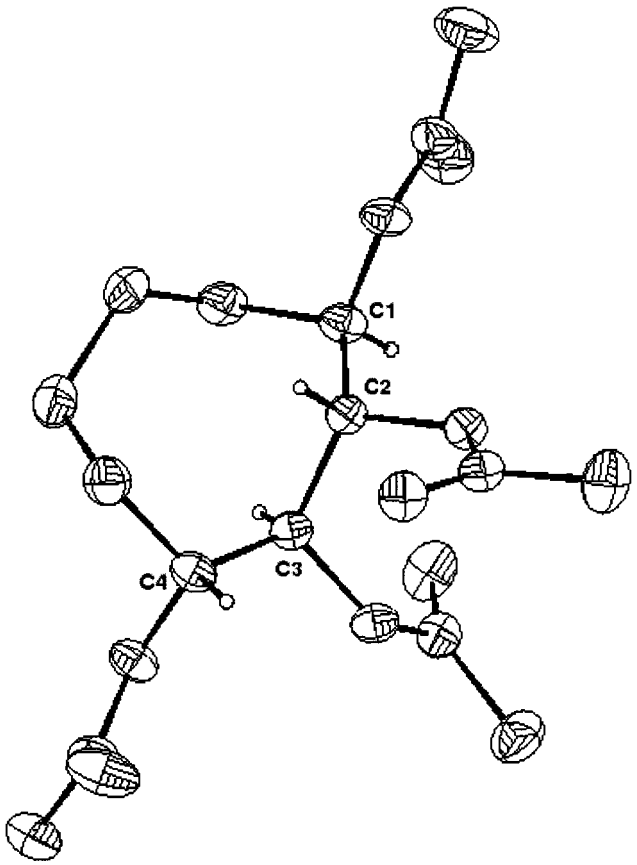
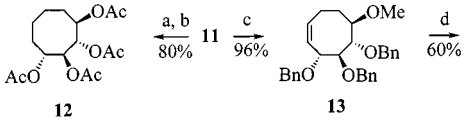
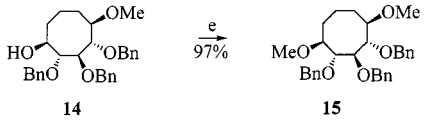


Figure 1. Crystallographic structure of compound **12**

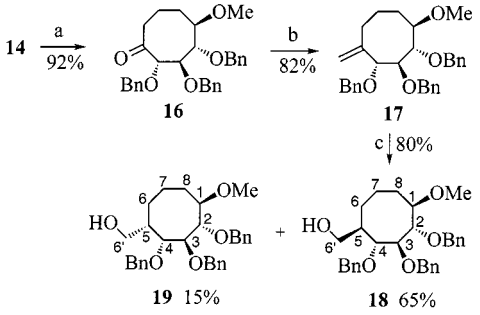
Methylation of **11** using iodomethane in DMF gave **13** (96%), which was then subjected to hydroboration using BH_3−THF. Subsequent oxidation by alkaline hydrogen peroxide afforded cyclooctanol **14** as the major isomer, in 60% yield (Scheme 5). The structure of the cyclooctanol derivative **14** was established by ^{1}H (COSY, NOESY) and ^{13}C NMR and further confirmed by spectroscopic study of the dimethylated derivative **15**. Both ^{1}H and ^{13}C NMR spectra confirmed a symmetrical structure for **15**, thus demonstrating the *cis* relationship between the two methoxy groups.



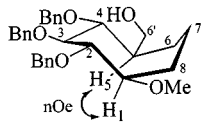


Scheme 5. Reagents and conditions: a) H_2, Pd/C, THF, room temp., 1.5 h; b) Ac_2O, Py, DMAP, room temp., 18 h; c) NaH, MeI, DMF, room temp., 2 h; d) BH_3−THF, THF, Ar, room temp., 1 h then NaOH (11%), H_2O_2 (35%), 0 °C to room temp., 1.5 h; e) NaH, MeI, DMF, room temp., 3 h

As shown in Scheme 6, oxidation of **14** with PCC gave cyclooctanone **16** (92%); subsequent treatment of **16** with Tebbe reagent afforded compound **17** in 82% yield (Scheme 6). Hydroboration/oxidation of **17** gave the two separable diastereomers **18** and **19**, in 80% overall yield. The structure and boat-chair conformation of compound **18** were determined on the basis of ^3J coupling constants and NOE experiments (Scheme 7).



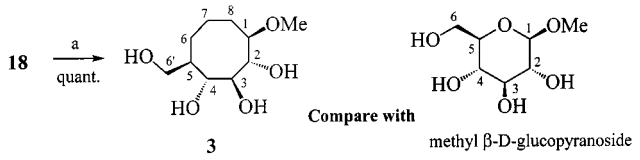
Scheme 6. Reagents and conditions: a) PCC, 4 Å molecular sieves, dry CH_2Cl_2, Ar, 0 °C, 2 h, 92%; b) Tebbe reagent, Py-THF (1:1), Ar, −78 °C to room temp., 20 min; c) BH_3−THF, THF, Ar, room temp., 1 h, then aq. NaOH (11%), H_2O_2 (35%), 0 °C to room temp., 2 h



Scheme 7. The boat-chair conformation assigned to compound **18**

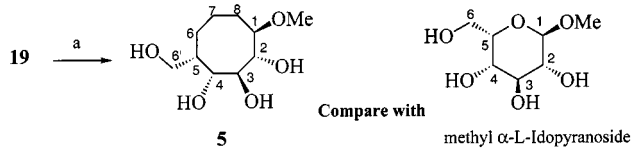
Hydrogenolysis of **18** in the presence of 10% Pd/C afforded the corresponding D-*gluco* mimetic **3** (Scheme 8). As expected, the ^{1}H NMR spectrum of **3** (see Exp. Sect.) shows a close analogy with that of methyl β-D-glucopyranoside, particularly for the coupling constants between 1-H, 2-H, 3-H, 4-H, 5-H and 6-H (6′-H), a feature which fully quali-

fies **3** as a cyclooctane mimetic of methyl β-D-glucopyranoside.



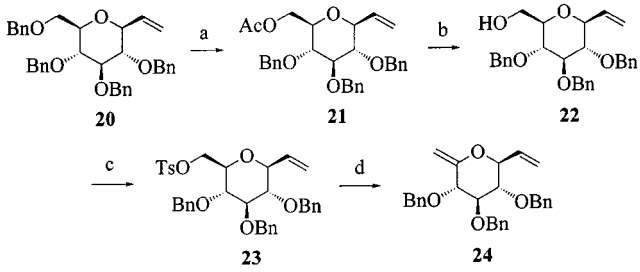
Scheme 8. D-Gluco mimetic preparation; reagents and conditions: a) H_2, 10% Pd/C, EtOAc/MeOH (1:1), room temp., 2 h

Hydrogenolysis of **19** as described above for **18** afforded **5**, a mimetic of methyl α-L-idopyranoside, in quantitative yield (Scheme 9). A conformational analysis of this compound has not been achieved.

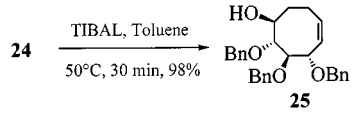


Scheme 9. L-Ido mimetic preparation; reagents and conditions: a) H_2 (170 kPa), Pd/C, EtOAc/MeOH (1:1), room temp., 2 h

For the preparation of the corresponding L-*gluco* and D-*ido* mimetics **4** and **6**, we started from the *C*-vinyl glycoside **24**,[3] the enantiomer of **10**. It was synthesized from the known compound **20**,[10] according to the sequence described in Scheme 10. TIBAL-catalysed rearrangement of **24** gave **25**, the enantiomer of **11** (Scheme 11).

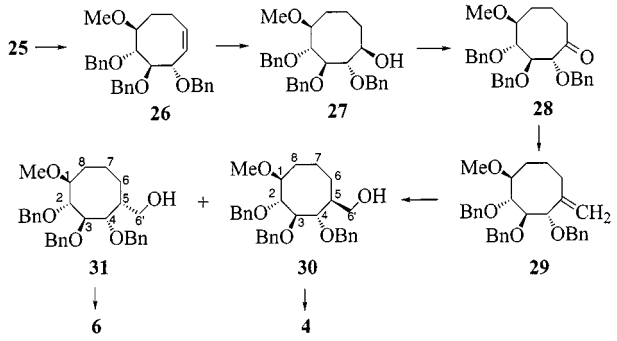


Scheme 10. Reagents and conditions: a) TMSOTf, Ac_2O, dry CH_2Cl_2, −40 °C, 1.5 h; b) NaOMe/MeOH (pH = 9), 2 h; c) TsCl/Py, 2 h; d) NaI, nBu$_4$NI, 4 Å molecular sieves, DMSO, 80 °C, 3 h then DBU, 80 °C, 1 h



Scheme 11. Claisen rearrangement of diene derivative **24**, promoted by triisobutylaluminium (TIBAL)

According to the same reaction sequence described in Schemes 6 and 8 for the preparation of compounds **3** and **5**, compounds **26**, **27**, **28**, **29**, **30** and **31** − mirror images of compounds **13**, **14**, **16**, **17**, **18** and **19**, respectively − were obtained. Debenzylation of **30** and **31** afforded the target compounds **4** and **6** (Scheme 12).



Scheme 12. Preparation of compounds **26**, **27**, **28**, **29**, **30**, **31**, **4** and **6**

In summary, we have synthesized the first members of a new class of carbasugars. The potential biological activity of these compounds is currently under investigation.

Experimental Section

General Methods: Melting points were determined with a Büchi model 535 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 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 the 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 $CDCl_3$, CD_3OD or D_2O at ambient temperature. Assignment was aided by COSY experiments. − ^{13}C NMR spectra were recorded at 62.9 MHz with a Bruker AC 250, at 100.6 MHz with a Bruker DRX 400 or at 150.9 MHz with a Bruker DRX 600 spectrometer, for solutions in $CDCl_3$ and adopting δ = 77.00 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 precoated plate of 60 F_{254} silica gel (layer thickness 0.2 mm; E. Merck, Darmstadt, Germany), and viewed by charring with sulfuric acid. − Flash column chromatography was performed on silica gel 60 (230−400 mesh, E. Merck).

2,3,4-Tri-*O*-benzyl-6,7-dideoxy-D-*gluco*-hept-6-enopyranose (8): Aq. TfOH (2 M, 3.2 mL) was added to a solution of compound **7** (726 mg, 1.6 mmol) in 16 mL of AcOH, and the mixture was heated at 80 °C for 2.5 h. TLC (cyclohexane/EtOAc, 4:1) indicated no trace of starting material, and the reaction mixture was cooled to room temp. CH_2Cl_2 was added to the system and the mixture was poured into cold sat. aq. $NaHCO_3$ (50 mL). Stirring was continued for 1 h. The organic layer was separated, dried with $MgSO_4$ and the solvent co-evaporated with toluene to remove the excess of acid. The residue was subjected to flash chromatography (cyclohexane/EtOAc, 8:1) to give **8** (α/β, 7:4) in 75% yield. Crude compound **8** was used directly in the next step.

2,3,4-Tri-*O*-benzyl-6,7-dideoxy-D-*gluco*-hept-6-eno-1,5-lactone (9): A suspension of PCC (292 mg, 3 equiv.) and 4 Å molecular sieves (300 mg) in dry CH_2Cl_2 (10 mL) was stirred at room temp. for 1 h and cooled to 0 °C under argon. A solution of **8** (200 mg,

0.45 mmol) in dry CH_2Cl_2 (10 mL) was added to the suspension at 0 °C under argon. The reaction mixture was then stirred for another 2 h at room temp., after which TLC (cyclohexane/EtOAc, 4:1) showed completion of the reaction. The reaction mixture was filtered through a silica plug, eluting with EtOAc. The filtrate was concentrated and subjected to flash chromatography (cyclohexane/EtOAc, 10:1) to give lactone **9** (170 mg, 85% yield) as an oil. − $[\alpha]_D^{20}$ = +82 (*c* = 0.5, $CHCl_3$). − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.57 (dd, $J_{3,4}$ = 4.8 Hz, $J_{4,5}$ = 7.3 Hz, 1 H, 4-H), 3.86 (dd, $J_{2,3}$ = 5.6 Hz, $J_{3,4}$ = 4.8 Hz, 1 H, 3-H), 4.12 (d, $J_{2,3}$ = 5.6 Hz, 1 H, 2-H), 4.55, 4.47 (2 d, *J* = 11.2 Hz, 2 H, $PhCH_2$), 4.58, 4.47 (2 d, *J* = 11.2 Hz, 2 H, $PhCH_2$), 4.89, 4.56 (2 d, *J* = 11.4 Hz, 2 H, $PhCH_2$), 4.90−4.83 (m, 1 H, 5-H), 5.29 (br. d, $J_{6,7b}$ = 10.6 Hz, 1 H, 7-H_b), 5.42 (br. d, $J_{6,7a}$ = 17.1 Hz, 1 H, 7-H_a), 5.84 (ddd, $J_{6,7a}$ = 17.1 Hz, $J_{6,7b}$ = 10.6 Hz, $J_{5,6}$ = 5.4 Hz, 1 H, 6-H), 7.36−7.14 (m, 15 H, aromatic H). − ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 72.9, 73.1, 73.4 (3 $PhCH_2$), 77.2 (C-2), 78.5 (C-5), 79.5 (C-4), 81.2 (C-3), 119.2 (C-7), 127.9−128.5 (15 C-aromatic), 132.7 (C-6), 136.8, 137.1, 137.3 (3 C-*ipso*), 169.0 (C-1). − MS (CI; NH_3); *m*/*z*: 462.5 [M^+ + NH_3 + H]. − $C_{28}H_{28}O_5$ (444.5): calcd. C 75.66, H 6.35; found C 75.68, H 6.38.

2,6-Anhydro-3,4,5-tri-*O*-benzyl-1,7,8-trideoxy-D-*gluco*-octa-1,7-dienitol (10): Compound **9** (140 mg, 0.32 mmol) was dissolved in dry THF (2 mL) and dry pyridine (2 mL), and the solution was cooled to −78 °C under argon. Tebbe reagent (2 mL, 3 equiv., 0.5 M solution) was added dropwise to the solution at −78 °C over 10 min under argon. The reaction mixture was then allowed to warm to room temp. and stirred for another 20 min. TLC monitoring indicated no trace of starting material. The mixture was cooled to 0 °C and aq. NaOH (0.6 mL, 11%) was added carefully to the solution to quench the reaction. The reaction mixture was filtered and the filtrate was washed with CH_2Cl_2. The extracts were dried with $MgSO_4$ and concentrated. The residue was subjected to flash chromatography (cyclohexane/EtOAc, 20:1) to afford compound **10** (116 mg, 84% yield) as an oil. − $[\alpha]_D^{20}$ = +51 (*c* = 3.5, $CHCl_3$). − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.35 (dd, $J_{3,4}$ = 7.7 Hz, $J_{4,5}$ = 9.8 Hz, 1 H, 2-H), 3.64 (t, *J* = 7.5 Hz, 1 H, 3-H), 3.87 (br. d, *J* = 7.4 Hz, 1 H, 4-H), 4.03 (dd, $J_{4,5}$ = 9.8 Hz, $J_{5,6}$ = 6.3 Hz, 1 H, 1-H), 4.56, 4.69 (2 s, 2 H, 6-H_a, 6-H_b), 4.54, 4.65 (2 d, *J* = 11.2 Hz, 2 H, $PhCH_2$), 4.58, 4.70 (2 d, *J* = 11.6 Hz, 2 H, $PhCH_2$), 4.68, 4.77 (2 d, *J* = 11.2 Hz, 2 H, $PhCH_2$), 5.25 (br. d, $J_{6,7b}$ = 10.5 Hz, 1 H, 8-H_b), 5.42 (br. d, $J_{6,7a}$ = 17.1 Hz, 1 H, 8-H_a), 5.87 (ddd, $J_{6,7a}$ = 17.1 Hz, $J_{6,7b}$ = 10.5 Hz, $J_{5,6}$ = 6.3 Hz, 1 H, 7-H), 7.16−7.32 (m, 15 H, aromatic H). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 72.6, 74.3, 74.4 (3 $PhCH_2$), 78.7 (C-4), 79.2 (C-1), 81.7 (C-2), 84.3 (C-3), 94.7 (C-6), 118.4 (C-8), 127.6−128.4 (15 C-aromatic), 134.8 (C-7), 137.8, 137.9, 138.2 (3 C-*ipso*), 155.9 (C-5). − MS (CI; NH_3): *m*/*z* = 460.5 [M^+ + NH_3 + H]. − $C_{29}H_{30}O_4$ (442.6): calcd. C 78.71, H 6.83; found C 78.60, H 6.69.

(1*R*,6*R*,7*S*,8*S*)-6,7,8-Tribenzyloxycycloocta-4-en-1-ol (11): TIBAL (0.9 mL, 0.9 mmol, 1 M in toluene) was added at room temp. to a stirred solution of compound **10** (100 mg, 0.23 mmol) in anhydrous toluene (7.5 mL) under argon. The reaction mixture was heated at 50 °C for 15 min., after which TLC indicated the absence of starting material. The mixture was cooled to 0 °C and ice-cold water (2 mL) was added. The mixture was filtered and the filtrate was extracted with EtOAc (3 × 5 mL). The combined organic extracts were dried and the solvent was removed under vacuum. The residue was purified by flash chromatography (cyclohexane/EtOAc, 4:1) to afford product **11** (98 mg, 98% yield) as an oil. − $[\alpha]_D^{20}$ = +12 (*c* = 1.9, $CHCl_3$). − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.59−1.73 (m, 1 H, 2-H_b), 1.80−1.95 (m, 1 H, 2-H_a), 1.92−2.06 (m, 1 H, 3-H_b), 2.26−2.45 (m, 1 H, 3-H_a), 3.23 (br. s, 1 H, OH-H), 3.60−3.69 (m, 2 H, 7-H, 8-H), 3.93−4.03 (m, 1 H, 1-H), 4.51−4.62 (m, 1 H, 6-H), 4.35, 4.60 (2 d, *J* = 11.6 Hz, 2 H, $PhCH_2$), 4.42, 4.60 (2 d, *J* = 11.6 Hz, 2 H, $PhCH_2$), 4.62, 4.76 (2 d, *J* = 11.1 Hz, 2 H, $PhCH_2$), 5.48 (ddd, *J* = 1.7, 7.2, 10.8 Hz, 1 H, 5-H), 5.73−5.86 (m, 1 H, H-4), 7.12−7.30 (m, 15 H, aromatic H). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 22.1 (C-3), 32.1 (C-2), 70.2 (C-1), 71.5, 74.1, 75.0 (3 $PhCH_2$), 78.6 (C-6), 81.5, 84.7 (C-8, 7), 127.6−128.5 (15 C-aromatic), 129.4 (C-5), 133.3 (C-4), 138.6, 138.8, 138.9 (3 C-*ipso*). − MS (CI; NH_3); *m*/*z*: 462 [M^+ + NH_3 + H]. − $C_{30}H_{34}O_4$ (444.6): calcd. C 78.35, H 7.26; found C 78.22, H 7.24.

(1*R*,2*R*,3*S*,4*R*)-Tetraacetoxycyclooctane (12): Compound **11** (50 mg, 0.112 mmol) was dissolved in THF (5 mL), 10% Pd/C (10 mg) was added and the suspension was stirred under hydrogen for 90 min at room temp. The solution was filtered through Celite, eluting with CH_3OH. The solvent was removed under reduced pressure. The crude tetrol was dissolved in anhydrous pyridine (4 mL) and the solution was cooled to 0 °C. Ac_2O (1 mL) and DMAP (5 mg) were added and the solution was stirred at room temp. for 18 h. The solvent was removed under reduced pressure and co-evaporated with toluene. Purification by column chromatography (EtOAc/cyclohexane, 1:2 then 1:1) afforded the tetraacetate **12** (31 mg, 80% yield) as a crystalline solid. Recrystallisation from EtOH, m.p.107−108 °C. − ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.65 (m, 4 H, 6-H, 7-H), 1.98 (m, 4 H, 5-H, 8-H), 2.04 (s, 6 H, 2 × OAc), 5.08 (m, 2 H, 1-H, 4-H), 5.28 (m, 2 H, 2-H, 3-H) − ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.3 (2 × OAc), 21.0 (2 × OAc), 21.6 (C-6, C-7), 28.5 (C-5, C-8), 67.0 (C-2, C-3), 73.2 (C-1, C-4), 169.9, 169.8 (4 × C=O). − MS (CI; NH_3); *m*/*z*: 362 [M^+ + NH_3 + H]. − $C_{16}H_{24}O_8$ (344.36): calcd. C 55.80, H 7.02; found C 55.91, H 7.09.

(3*R*,4*S*,5*S*,6*R*)-3,4,5-Tribenzyloxy-6-methoxycyclooct-1-ene (13): NaH (60%, 17 mg) was added at 0 °C under argon to a solution of compound **11** (65 mg, 0.15 mmol) in DMF (3 mL). MeI (25 μL) was then added to the solution. The reaction mixture was allowed to warm to room temp. and stirred for 2 h. After addition of methanol (100 μL), DMF was evaporated. Water was added and the mixture was extracted with dichloromethane. The organic layer was dried ($MgSO_4$) and concentrated. The residue was purified by flash chromatography (cyclohexane/AcOEt, 4:1) to afford compound **13** (66 mg, 96% yield) as an oil. − $[\alpha]_D^{20}$ = +13 (*c* = 2.7, $CHCl_3$). − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.68−1.88 (m, 3 H, 8-H_b, 7-$H_{a,b}$), 2.20−2.41 (m, 1 H, 8-H_a), 3.28 (s, 3 H, OCH_3), 3.47−3.57 (m, 1 H, 6-H), 3.54 (dd, *J* = 2.9, 8.9 Hz, 1 H, 4-H), 3.75 (dd, *J* = 2.9, 7.7 Hz, 1 H, 5-H), 4.12, 4.28 (2 d, *J* = 12.0 Hz, 2 H, $PhCH_2$), 4.42, 4.51 (2 d, *J* = 11.7 Hz, 2 H, $PhCH_2$), 4.64 (bt, *J* = 8.5 Hz, 1 H, 3-H), 4.57, 4.71 (2 d, *J* = 11.8 Hz, 2 H, $PhCH_2$), 5.30−5.43 (m, 1 H, 2-H), 5.66−5.83 (m, 1 H, 1-H), 7.03−7.30 (m, 15 H, aromatic H). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.6 (C-7), 29.1 (C-8), 58.6 (OCH_3), 71.4, 72.5, 74.6 (3 $PhCH_2$), 78.2 (C-3), 80.6 (C-4), 80.6 (C-5), 84.8 (C-6), 127.3−128.3 (15 C-aromatic), 130.0, 132.9 (C-1, 2), 138.9, 139.3, 139.3 (3 C-*ipso*). − MS (CI; NH_3); *m*/*z*: 476 [M^+ + NH_3 + H]. − $C_{30}H_{34}O_4$(458.6): calcd. C 78.57, H 7.47; found C 78.51, H 7.51.

(1*S*,2*R*,3*S*,4*S*,5*R*)-2,3,4-Tribenzyloxy-5-methoxycyclooctan-1-ol (14): Compound **13** (60 mg, 0.13 mmol) was dissolved in dry THF (2 mL) under argon at room temp., and the solution was cooled to 0 °C. BH_3−THF (0.26 mL, 1 M solution) was then added dropwise to the solution, and the system was warmed to room temp. The mixture was stirred at room temp. for 1 h, after which TLC indicated the complete disappearance of the starting material. Ethanol (0.2 mL) was added dropwise at room temp., followed by aq.

NaOH (0.22 mL, 3 M). The reaction mixture was cooled to 0 °C, and H_2O_2 (0.16 mL, 35%) was added dropwise. The reaction mixture was then allowed to warm to room temp. and stirred for another 1.5 h. Ice-cold water was added to the mixture, which was then extracted six times with CH_2Cl_2. The organic layers were combined, washed with brine and dried with $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by flash chromatography (cyclohexane/EtOAc, 3:1) to give **14** (37 mg, 60% yield) as an oil. − $[\alpha]_D^{20}$ = +49 (*c* = 0.8, $CHCl_3$). − ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.45−1.56 (m, 1 H, 7-H_b), 1.60−1.76 (m, 2 H, 6-H_b, 8-H_b), 1.78−1.88 (m, 1 H, 7-H_a), 1.97−2.06 (m, 1 H, 8-H_a), 2.08−2.18 (m, 1 H, 6-H_a), 2.79 (s, 1 H, OH-H), 3.42 (s, 3 H, OCH_3), 3.59 (br. dd, *J* = 4.8, 6.5 Hz, 1 H, 5-H), 3.66 (dd, $J_{2,3}$ = 8.1 Hz, $J_{3,4}$ = 6.2 Hz, 1 H, 3-H), 3.79−3.84 (m, 1 H, 1-H), 3.82 (dd, $J_{1,2}$ = 4.8 Hz, $J_{2,3}$ = 8.1 Hz, 1 H, 4-H), 4.04 (dd, $J_{3,4}$ = 6.2 Hz, $J_{4,5}$ = 9.3 Hz, 1 H, 2-H), 4.67−4.84 (2 d, *J* = 11.2 Hz, 2 H, $PhCH_2$), 4.73−4.84 (2 d, *J* = 11.2 Hz, 2 H, $PhCH_2$), 4.52−5.01 (2 d, *J* = 11.0 Hz, 2 H, $PhCH_2$), 7.30−7.40 (m, 15 H, aromatic H). − ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 16.3 (C-7), 27.6 (C-6), 30.9 (C-8), 57.0 (OCH_3), 73.3 (C-1), 74.2, 74.5, 74.6 (3 $PhCH_2$), 80.4 (C-3), 80.9 (C-2), 81.5 (C-5), 83.7 (C-4), 127.4−128.4 (15 C-aromatic), 138.4, 138.6, 138.7 (3 C-*ipso*). − MS (CI; NH_3); *m*/*z*: 494 [M^+ + NH_3 + H]. − $C_{30}H_{36}O_5$ (476.6): calcd. C 75.60, H 7.61; found C 75.59 H 7.70.

(1*R*,2*R*,3β,4*S*,5*S*)-2,3,4-Tribenzyloxy-1,5-dimethoxycyclooctane (15): MeI (20 μL) was added to a mixture of compound **14** (8 mg, 0.017 mmol) and NaH (3 mg, 60%) in dry DMF (1.5 mL) at 0 °C. The mixture was stirred for 3 h at room temp. After addition of methanol (2 drops), DMF was evaporated. Water was added and the mixture was extracted with dichloromethane. The organic layer was dried ($MgSO_4$) and concentrated. The residue was flash-chromatographed (cyclohexane/AcOEt, 10:1 then 4:1) to afford product **15** (8 mg, 97% yield) as a syrup. − $[\alpha]_D^{20}$ = 0 (*c* = 0.9, $CHCl_3$). − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.23−1.41 (m, 1 H, 7-H_b), 1.42−1.56 (m, 2 H, 6-H_b, 8-H_b), 1.62−1.78 (m, 1 H, 7-H_a), 1.88−2.03 (m, 2 H, 6-H_a, 8-H_a), 3.30 (s, 6 H, 2 OCH_3), 3.33−3.40 (m, 2 H, 1-H, 5-H), 3.52 (t, $J_{2,3}$ = $J_{3,4}$ = 7.3 Hz, 1 H, 3-H), 3.82 (t, $J_{1,2}$ = $J_{2,3}$ = $J_{3,4}$ = $J_{4,5}$ = 7.3 Hz, 2 H, 2-H, 4-H), 4.62 (s, 2 H, $PhCH_2$), 4.56, 4.74 (2 d, *J* = 11.2 Hz, 4 H, 2 $PhCH_2$), 7.17−7.35 (m, 15 H, aromatic H). − ^{13}C NMR (150.9 MHz, $CDCl_3$): δ = 16.3 (C-7), 29.7, 29.7 (C-6, 8), 57.4, 57.4 (2 OCH_3), 74.5, 74.5, 74.7 (3 $PhCH_2$), 81.0 (C-2, 4), 81.8 (C-3), 83.0 (C-1, 5), 127.3−128.1 (15 C-aromatic), 138.9, 139.1, 139.1 (3 C-aromatic). − MS (CI; NH_3); *m*/*z*: 508 [M^+ + NH_3 + H]. − $C_{31}H_{39}O_5$: calcd. 491.2797; found 491.2799 [M^+ + H] (HRMS).

(2*S*,3*R*,4*R*,5*R*)-2,3,4-Tribenzyloxy-5-methoxycyclooctan-1-one (16): A suspension of PCC (256 mg, 3 equiv.) and 4 Å molecular sieves (260 mg) in dry CH_2Cl_2 (3 mL) was stirred at room temp. for 1 h and cooled to 0 °C under argon. A solution of compound **14** (186 mg, 0.38 mmol) in dry CH_2Cl_2 (3 mL) was added to the above solution at 0 °C under argon. The reaction mixture was then stirred for another 2 h at 0 °C. The reaction mixture was directly filtered through a silica plug, eluting with EtOAc. The filtrate was concentrated and subjected to column chromatography (cyclohexane/EtOAc, 2:1) to give compound **15** (170 mg, 92% yield) as an oil. − $[\alpha]_D^{20}$ = −14 (*c* = 1.7, $CHCl_3$). − ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.80−1.93 (m, 3 H, 7-$H_{a,b}$, 6-H_b), 2.00−2.10 (m, 1 H, 6-H_a), 2.30−2.40 (m, 1 H, 8-H_b), 2.64−2.71 (m, 1 H, 8-H_a), 3.32 (s, 3 H, OCH_3), 3.52 (br. t, $J_{1,2}$ = 6.3 Hz, 1 H, 5-H), 3.68 (dd, $J_{2,3}$ = 7.3 Hz, $J_{1,2}$ = 6.3 Hz, 1 H, 4-H), 3.95 (dd, $J_{3,4}$ = 8.5 Hz, $J_{2,3}$ = 7.3 Hz, 1 H, 3-H), 4.01 (d, $J_{3,4}$ = 8.5 Hz, 1 H, 2-H), 4.56−4.63 (2 d, *J* = 11.4 Hz, 2 H, $PhCH_2$), 4.59−4.73 (2 d, *J* = 11.3 Hz, 2 H, $PhCH_2$), 4.81, 4.86 (2 d, *J* = 10.9 Hz, 2 H, $PhCH_2$), 7.20−7.37 (m, 15 H, aromatic H). − ^{13}C NMR (100.9 MHz, $CDCl_3$): δ = 20.3, 26.9 (C-6, 7), 39.6 (C-8), 57.4 (OCH_3), 72.8, 74.1, 75.8 (3 $PhCH_2$), 78.9, 81.2, 81.6, 85.9 (C-2, 3, 4, 5), 127.6−128.3 (15 C-aromatic), 137.6, 138.4, 138.5 (3 C-*ipso*), 207.4 (C-1). − MS (CI; NH_3); *m*/*z*: 492 [M^+ + NH_3 + H]. − $C_{30}H_{34}O_5$ (474.6): calcd. C 75.92, H 7.22; found C 75.80, H 7.30.

(1*R*,2*S*,3*S*,4*S*)-2,3,4-Tribenzyloxy-1-methoxy-5-methylenecyclooctane (17): Compound **16** (170 mg, 0.36 mmol) was dissolved in dry THF (1.5 mL) and dry pyridine (0.8 mL), and the solution was cooled to − 78 °C under argon. Tebbe reagent (0.5 M, 2.16 mL, 3 equiv.) was added dropwise to the solution over 10 min, at − 78 °C under argon. The reaction mixture was then allowed to warm to room temp. and stirred for another 20 min. The mixture was cooled to 0 °C and aq. NaOH (0.6 mL, 11%) was carefully added dropwise to the solution to quench the reaction. The reaction mixture was filtered and washed with CH_2Cl_2. The filtrate was concentrated and the residue was subjected to flash chromatography (cyclohexane/EtOAc, 8:1) to give **17** (139 mg, 82% yield) as a syrup. − $[\alpha]_D^{20}$ = −13 (*c* = 2.15, $CHCl_3$). − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.80−1.94 (m, 1 H, 8-H_a), 1.44−2.20 (m, 5 H, 6-$H_{a,b}$, 7-$H_{a,b}$, 8-H_b), 3.27−3.38 (m, 1 H, 1-H), 3.37 (s, 3 H, OCH_3), 3.44 (t, $J_{2,3}$ = $J_{1,2}$ = 7.8 Hz, 1 H, 2-H), 3.53 (t, $J_{2,3}$ = $J_{3,4}$ = 7.8 Hz, 1 H, 3-H), 3.91 (d, $J_{3,4}$ = 7.8 Hz, 1 H, 4-H), 4.28, 4.44 (2 d, *J* = 11.8 Hz, 2 H, $PhCH_2$), 4.50, 4.76 (2 d, *J* = 11.0 Hz, 2 H, $PhCH_2$), 4.55, 4.83 (2 d, *J* = 11.4 Hz, 2 H, $PhCH_2$), 5.00 (d, $J_{5,6'b}$ = 1.7 Hz, 1 H, 6′-H_b), 5.10 (d, $J_{5,6'a}$ = 1.2 Hz, 1 H, 6′-H_a), 7.16−7.34 (m, 15 H, aromatic H). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 23.1 (C-7), 29.7 (C-8), 31.9 (C-6), 58.4 (OCH_3), 70.3, 74.7, 74.9 (3 $PhCH_2$), 80.3, 81.6, 84.2, 88.8 (C-1, 2, 3, 4), 120.0 (C-6′), 127.2−128.2 (15 C-aromatic), 138.7, 139.1, 139.2 (3 C-aromatic), 146.3 (C-5). − MS (CI; NH_3); *m*/*z*: 490 [M^+ + NH_3 + H]. − $C_{31}H_{36}O_4$ (472.6): calcd. C 78.78, H 7.68; found C 78.75, H 7.84.

Cyclooctane 18: Compound **17** (116 mg, 0.25 mmol) was dissolved in dry THF (3 mL) under argon at room temp., and the solution was cooled to 0 °C. BH_3−THF (0.5 mL, 1 M solution) was then added dropwise to the solution, and the system was allowed to warm to room temp. The mixture was stirred at room temp. for 2 h. Ethanol (0.26 mL) was added dropwise at room temp., followed by aq. NaOH (0.42 mL, 3 M). The reaction mixture was cooled to 0 °C, and H_2O_2 (0.31 mL, 35%) was added dropwise. The system was allowed to warm to room temp. and stirred for another 1 h. Ice-cold water was added to the mixture, which was then extracted six times with CH_2Cl_2. The organic layers were combined and dried with $MgSO_4$. After concentration, the residue was flash-chromatographed (cyclohexane/EtOAc, 4:1 then 3:1) to give **18** (64 mg, 65% yield) as an oil. Using the same procedure, compounds **29** and **30** were obtained. Further elution afforded **19** (17 mg, 15% yield) as an oil. − **18:** $[\alpha]_D^{20}$ = +30 (*c* = 0.14, $CHCl_3$). − ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.45−1.60 (m, 2 H, 6-H_b, 7-H_b), 1.61−1.78 (m, 3 H, 6-H_a, 7-H_a, 8-H_b), 1.97−2.09 (m, 2 H, 5-H, 8-H_a), 2.86 (br. d, *J* = 6.5 Hz, 1 H, OH-H), 3.42 (s, 3 H, OCH_3), 3.52−3.61 (m, 1 H, 6′-H_b), 3.62 (br.dd, *J* = 4.6, 7.5 Hz, 1 H, 1-H), 3.77 (dd, *J* = 7.8, 10.6 Hz, 1 H, 6′-H_a), 3.80−3.86 (m, 2 H, 2-H, 3-H), 4.02 (dd, *J* = 5.5, 9.1 Hz, 1 H, 4-H), 4.71, 4.79 (2 d, *J* = 11.4 Hz, 2 H, $PhCH_2$), 4.72, 4.80 (2 d, *J* = 11.3 Hz, 2 H, $PhCH_2$), 4.51, 4.92 (2 d, *J* = 10.9 Hz, 2 H, $PhCH_2$), 7.30−7.38 (m, 15 H, aromatic H). − ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 19.1 (C-7). 27.67 (C-6), 27.70 (C-8), 43.5 (C-5), 57.4 (OCH_3), 67.5 (C-6′), 76.7, 77.0, 77.3 (3 $PhCH_2$), 80.7 (C-4), 82.0 (C-1), 82.5 (C-3), 83.1 (C-2), 127.5−128.4 (15 C-aromatic), 138.1, 138.6, 138.7 (3 C-aromatic). − MS (CI; NH_3); *m*/*z*: 508.5 [M^+ + NH_3 + H]. − $C_{31}H_{38}O_5$ (490.6):

calcd. C 75.89, H 7.81; found C 75.77, H 7.90. − **19:** $[\alpha]_D^{20} = -20$ (c = 0.5, $CHCl_3$). − ^1H NMR (600 MHz, $CDCl_3$): δ = 1.36−1.44 (m, 1 H, 6-H_b), 1.45−1.55 (m, 2 H, 6-H_a, 7-H_b), 1.60−1.68 (m, 1 H, 7-H_a), 1.76−1.86 (m, 1 H, 8-H_b), 1.86−1.93 (m, 1 H, 5-H), 1.95−2.00 (m, 1 H, 8-H_a), 3.44 (s, 3 H, OCH_3), 3.47−3.57 (m, 3 H, 1-H, 6-H_a, 6-H_b), 3.60 (t, $J_{1,2} = J_{2,3}$ = 7.2 Hz, 1 H, 2-H), 3.79 (t, $J_{2,3} = J_{3,4}$ = 7.2 Hz, 1 H, 3-H), 3.94 (dd, $J_{3,4}$ = 7.2 Hz, $J_{4,5}$ = 1.7 Hz, 1 H, 4-H), 4.68, 4.83 (2 d, J = 11.0 Hz, 2 H, $PhCH_2$), 4.60, 4.86 (2 d, J = 10.9 Hz, 2 H, $PhCH_2$), 4.57, 4.88 (2 d, J = 11.4 Hz, 2 H, $PhCH_2$), 7.24−7.38 (m, 15 H, aromatic H). − ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 21.4 (C-7), 25.3 (C-6), 28.8 (C-8), 41.9 (C-5), 58.0 (OCH_3), 66.6 (C-6′), 74.2, 74.4, 74.8 (3 $PhCH_2$), 81.2 (C-4), 81.7 (C-3), 82.6 (C-2), 83.5 (C-1), 127.4−128.4 (15 C-aromatic), 138.6, 138.8, 139.0 (3 C-aromatic). − MS (CI; NH_3); m/z: 508 [$M^+ + NH_3 + H$]. − $C_{31}H_{38}O_5$ (490.6): calcd. C 75.89, H 7.81; found C 75.88, H 8.00.

2,6-Anhydro-3,4,5-tri-*O*-benzyl-1,7,8-trideoxy-L-*gluco*-octa-1,7-dienitol (24): A solution of compound **23** (200 mg, 0.34 mmol), NaI (260 mg, 1.7 mmol), Bu_4NI (62.8 mg, 0.17 mmol) and 4 Å molecular sieves in dry DMSO (5 mL) was stirred at 80 °C for 3 h. DBU (1.2 eq, 0.062 mL) was then added to the system and stirring was continued for 1 h at 80 °C. The mixture was cooled to room temp. and water (10 mL) was added. The reaction mixture was extracted with CH_2Cl_2 (2 × 20 mL), and the organic layers were combined and dried with $MgSO_4$. The solvent was evaporated and the residue was flash-chromatographed (cyclohexane/EtOAc, 20:1) to give compound **24** (130 mg, 87%) as an oil. − $[\alpha]_D^{20} = -43$ (c = 2.6, $CHCl_3$). − NMR spectroscopic data are the same as those obtained for compound **10**. − MS (CI; NH_3); m/z: 460.5 [$M^+ + NH_3 + H$]. − $C_{29}H_{30}O_4$ (442.5): calcd. C 78.71, H 6.83; found C 78.66; H 6.88.

(1*S*,6*S*,7*R*,8*R*)-6,7,8-Tribenzyloxycycloocta-4-en-1-ol (25): This product was synthesized from **24** as previously described for **11**; oil. $[\alpha]_D^{20} = -11$ (c = 6.3, $CHCl_3$). − NMR spectroscopic data are the same as those obtained for compound **11**. − MS (CI; NH_3); m/z: 462.5 [$M^+ + NH_3 + H$]. − $C_{29}H_{32}O_4$ (444.6): calcd. C 78.35, H 7.26; found C 78.22, H 7.44.

(3*S*,4*R*,5*R*,6*S*)-3,4,5-Tribenzyloxy-6-methoxycyclooct-1-ene (26): This product was synthesized as previously described for **13**; oil. − $[\alpha]_D^{20} = -13$ (c = 2.1, $CHCl_3$). − NMR spectroscopic data are the same as those obtained for compound **13**. − MS (CI; NH_3); m/z: 476 [$M^+ + NH_3 + H$]. − $C_{30}H_{34}O_4$ (458.6): calcd. C 78.57, H 7.47; found C 78.67, H 7.54.

(1*R*,2*S*,3*R*,4*R*,5*S*)-2,3,4-Tribenzyloxy-5-methoxycyclooctan-1-ol (27): This product was synthesized as previously described for **14**; oil. − $[\alpha]_D^{20} = -48$ (c = 1.0, $CHCl_3$). − NMR spectroscopic data are the same as those obtained for compound **14**. − MS (CI; NH_3); m/z: 494 [$M^+ + NH_3 + H$]. − $C_{30}H_{36}O_5$ (476.6): calcd. C 75.60, H 7.61; found C 75.50, H 7.73.

(2*R*,3*S*,4*S*,5*S*)-2,3,4-Tribenzyloxy-5-methoxycyclooctan-1-one (28): This product was synthesized from **27** by the method previously described for **16**; oil. − $[\alpha]_D^{20} = +14$ (c = 1.5, $CHCl_3$). − NMR spectroscopic data are the same as those obtained for compound **16**. − MS (CI; NH_3); m/z: 492 [$M^+ + NH_3 + H$]. − $C_{30}H_{34}O_5$ (474.6): calcd. C 75.92, H 7.22; found C 75.83, H 7.36.

(1*S*,2*R*,3*R*,4*R*)-2,3,4-Tribenzyloxy-1-methoxy-5-methylenecyclooctane (29): This product was synthesized as previously described for **17**; oil. − $[\alpha]_D^{20} = +16$ (c = 1.3, $CHCl_3$). − NMR spectroscopic data are the same as those obtained for compound **17**. − MS (CI; NH_3); m/z: 490 [$M^+ + NH_3 + H$]. − $C_{31}H_{36}O_4$ (472.6): calcd. C 78.78, H 7.68; found C 78.70, H 7.81.

Cyclooctane 30: This product was synthesized as previously described for **18**; oil. − $[\alpha]_D^{20} = -32$ (c = 1.46, $CHCl_3$). − NMR spectroscopic data are the same as those obtained for compound **18**. − MS (CI; NH_3); m/z: 508.5 [$M^+ + NH_3 + H$]. − $C_{31}H_{38}O_5$ (490.6): calcd. C 75.89, H 7.81; found C 75.83, H 7.91.

Cyclooctane 31: This product was synthesized as previously described for **19**. − Oil. − $[\alpha]_D^{20} = +19$ (c = 1.0, $CHCl_3$). − NMR spectroscopic data were the same as those obtained for compound **19**. − MS (CI; NH_3): m/z = 508.5 [$M^+ + NH_3 + H$]. − $C_{31}H_{38}O_5$(490.6): calcd. C 75.89, H 7.81; found C 75.89, H 7.98.

Cyclooctane 3: Pd/C (20 mg) was added at room temp. to a solution of compound **18** (28 mg, 0.057 mmol) in ethyl acetate/methanol (1:1) (3 mL), and the system was stirred under H_2 for 3 h. The reaction mixture was filtered through Celite and the filtrate was concentrated to a solid, which was subjected to flash chromatography (EtOAc/MeOH, 5:1) to afford product **3** (12 mg, 96% yield) as an amorphous solid. A crystal (white needle) was obtained from ethyl acetate; m.p. 101.5 °C. − $[\alpha]_D^{20} = -28$ (c = 1.5, MeOH). − ^1H NMR (400 MHz, D_2O): δ = 1.31−1.45 (m, 2 H, 6-H_b, 7-H_b), 1.56−1.72 (m, 4 H, 5-H, 6-H_a, 7-H_a, 8-H_b), 1.83−1.93 (m, 1 H, 8-H_a), 3.37 (s, 3 H, OCH_3), 3.34−3.39 (m, 1 H, 1-H), 3.40 (dd, $J_{3,4}$ = 8.6 Hz, $J_{4,5}$ = 10.3 Hz, 1 H, 4-H), 3.52 (t, $J_{2,3} = J_{3,4}$ = 8.6 Hz, 1 H, 3-H), 3.65 (dd, $J_{6'a,6'b}$ = 10.8 Hz, $J_{5,6'b}$ = 6.7 Hz, 1 H, 6′-H_b), 3.68 (t, $J_{1,2} = J_{2,3}$ = 8.6 Hz, 1 H, 2-H), 3.76 (dd, $J_{5,6'a}$ = 4.0 Hz, $J_{6'a,6'b}$ = 10.8 Hz, 1 H, 6′-H_a). − ^{13}C NMR (100.6 MHz, CD_3OD): δ = 22.4 (C-7), 25.1 (C-8), 26.3 (C-6), 44.3 (C-5), 57.4 (OCH_3), 66.7 (C-6′), 74.6 (C-3), 75.4 (C-2), 77.5 (C-4), 86.6 (C-1). − MS (CI; NH_3); m/z: 238 [$M^+ + NH_3 + H$]. − $C_{10}H_{21}O_5$: calcd. 221.1389; found 221.1392 [$M^+ + H$] (HRMS).

Cyclooctane 4: This product was synthesized as previously described for **3**. A crystal (yellowish needle) was obtained from ethyl acetate; m.p. 101.5−102.2 °C. − $[\alpha]_D^{20} = +28$ (c = 1.2, MeOH). − NMR spectroscopic data are the same as those obtained for compound **3**. − MS (CI; NH_3); m/z: 238 [$M^+ + NH_3 + H$]. − $C_{10}H_{21}O_5$: calcd. 221.1389; found 221.1390 [$M^+ + H$] (HRMS).

Cyclooctane 5: This compound was obtained as an amorphous solid using the method previously described for **3**. − $[\alpha]_D^{20} = -7$ (c = 0.3, MeOH). − ^1H NMR (400 MHz, D_2O, 25 °C): δ = 1.31−1.48 (m, 3 H, 6-H_a, 6-H_b, 7-H_b), 1.55−1.65 (m, 2 H, 7-H_a, 8-H_b), 1.80−1.88 (m, 1 H, 5-H), 1.95−2.04 (m, 1 H, 8-H_a), 3.23−3.29 (m, 1 H, 1-H), 3.38 (s, 3 H, OCH_3), 3.45 (dd, $J_{6'a,6'b}$ = 10.8 Hz, $J_{5,6'b}$ = 6.5 Hz, 1 H, 6′-H_b), 3.52 (dd, $J_{1,2}$ = 8.6 Hz, $J_{2,3}$ = 7.0 Hz, 1 H, 2-H), 3.57 (dd, $J_{5,6'a}$ = 7.4 Hz, $J_{6'a,6'b}$ = 10.8 Hz, 1 H, 6′-H_a), 3.67−3.74 (m, 2 H, 3-H, 4-H). − ^{13}C NMR (150.9 MHz, D_2O, 25 °C): δ = 22.33 (C-7), 26.22 (C-8), 28.91 (C-6), 41.37 (C-5), 59.03 (OCH_3), 66.95 (C-6′), 73.80 (C-3), 75.01 (C-2), 77.48 (C-4), 87.93 (C-1). − MS (CI; NH_3); m/z: 238 [$M^+ + NH_3 + H$]. − $C_{10}H_{21}O_5$: calcd. 221.1389; found 221.1388 [$M^+ + H$] (HRMS).

Cyclooctane 6: This compound was obtained as an amorphous solid using the method previously described for **3**. − $[\alpha]_D^{20} = +7$ (c = 0.5, MeOH). − NMR spectroscopic data are the same as those obtained for compound **5**. − MS (CI; NH_3); m/z: 238 [$M^+ + NH_3 + H$]. − $C_{10}H_{21}O_5$: calcd. 221.1389; found 221.1384 [$M^+ + H$] (HRMS).

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[9] Selected crystal structure data for **12**; crystal system monoclinic; space group $P2_1$; $Z = 4$; cell parameters: $a = 7.903(5)$, $b = 14.497(6)$, $c = 8.909(5)$ Å, $\beta = 111.80°$; radiation Mo-K_α ($\lambda = 0.710690$ Å); 219 variables for 1383 reflections; final $R = 0.0377$, $R_w = 0.05122$; Crystallographic data (excluding structure factors) have been deposited at the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-150180. 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].

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