Nucleophilic opening of epoxyazepanes: expanding the family of polyhydroxyazepane-based glycosidase inhibitors†

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A range of new tetra- and pentahydroxylated seven-membered iminoalditols has been efficiently synthesized from epoxyazepane precursors *via* nucleophilic opening with hydride or oxygenated species and subsequent hydrogenolysis. One tetrahydroxylated azepane, a ring homologue of deoxymannojirimycin, displays a selective and fairly good inhibition of α-L-fucosidase.

Introduction

Glycosidases, which are known to increase the rate of glycosidic bond hydrolysis by a factor of 10^{17}, making them among the most proficient enzymes in Nature,[1] play many fundamental roles in biochemistry and metabolism. As a consequence, iminosugar-based glycosidase inhibitors have been the subject of extensive interest in the past three decades due to their therapeutic potential.[2] Some of them have already been tested or approved in the treatment of diabetes,[3] Gaucher's disease,[4] HIV infection,[5] viral infection[6] or cancer[7] and they are now expected to find an increasing number of therapeutic applications.[8] Extensive synthetic work has been devoted to five- and six-membered iminosugars,[9] which mimic the ring size of the naturally occuring sugars. Despite promising biological results[10] and conformational flexibility that could match the unusual conformation encountered in the glycosidase transition state,[11] the synthesis of seven-membered azasugars[12] has received only limited attention. As part of an ongoing project on the design of new carbohydrate mimetics based on conformational flexibility, we have previously reported the synthesis and biological evaluation of an α-nojirimycin homologue **1**, a β-mannojirimycin homologue **2**[12a] and an α-galactonojirimycin analogue **3**[12b] (Fig. 1). In order to establish a structure–activity relationship (SAR) for this new class of compounds and design new structures with potent glycosidase activity, we wanted to develop a versatile strategy enabling access to all stereoisomers at pseudo C-1 and C-2 positions of the polyhydroxylated azepane, such positions being crucial for glycosidase inhibition and selectivity. In this paper, we report, starting from key epoxyazepanes, the efficient synthesis of new 1,6-dideoxy-1,6-iminoheptitols. All the tetra- and pentahydroxylated azepanes synthesized were then evaluated as glycosidase inhibitors. For clarity reasons, the numbering used for these compounds follows the numbering of the parent sugar thus emphasizing the analogy between the azepanes and the corresponding monosaccharides.

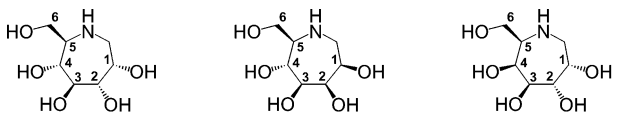

Fig. 1 Structure of analogues **1–3**.

Results and discussion

Our strategy takes advantage of our previously reported epoxyazepanes **4–7**, obtained by *m*-CPBA epoxidation of an azacycloheptene produced by ring-closing metathesis (RCM) of the corresponding iminodiene.[13] Epoxyazepane derivatives have been previously used in the synthesis of a) the optically active constituent of the antifungal antibiotic ophiocordin,[14] b) azepanone-based inhibitors of human and rat cathepsin K,[15] c) azepane–glycoside antibiotics targeting the bacterial ribosome,[16] d) protein kinase C inhibitor balanol.[17] The stereochemistry of the oxirane ring in epoxides **4–7** was deduced from the ^{1}H-NMR $J_{1,2}$ and $J_{2,3}$ coupling constants (Fig. 2) and was compared to those obtained for tricyclic epoxides **8** and **9** (Fig. 3).

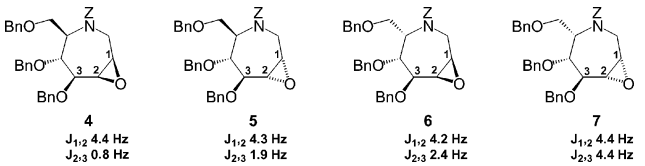

Fig. 2 Structure and ^{1}H-NMR $J_{1,2}$ and $J_{2,3}$ coupling constants of epoxides **4–7**.

Compound **8** has previously been reported by us and its crystal structure solved.[13] We were also able to solve the crystal structure of compound **9**[18] available in our laboratory (Fig. 4).

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† Dedicated to Professor Walter Szarek on the occasion of his 65th birthday.

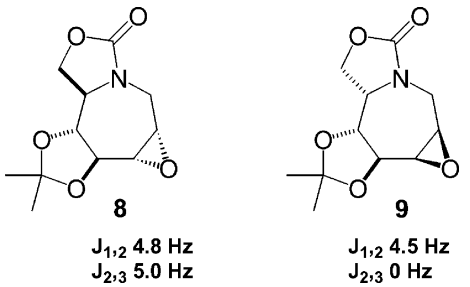


Fig. 3 Structure and ^{1}H-NMR $J_{1,2}$ and $J_{2,3}$ coupling constants of epoxides **8** and **9**.

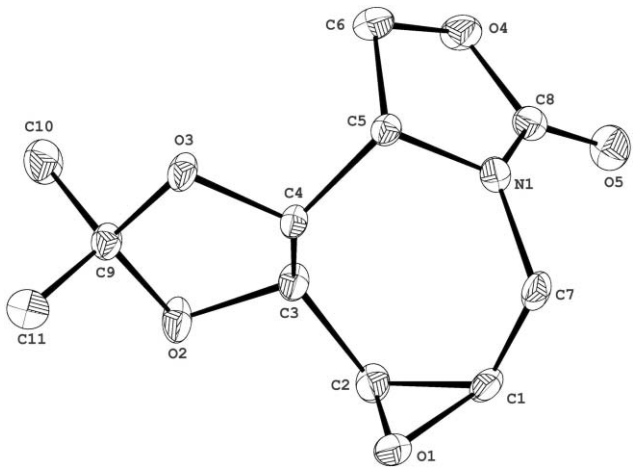


Fig. 4 Crystal structure of epoxyazepane **9**.

Discriminating $J_{2,3}$ coupling constants were observed for the oxirane rings *cis* and *trans* to the neighbouring C-3 substituent, *trans* epoxides **5** and **7** displaying always higher $J_{2,3}$ values than the corresponding *cis* epoxides **4** and **6**, a trend also observed with tricyclic epoxides **8** and **9**.

Oxirane ring opening with Super-Hydride®

Regarding the previously reported polyhydroxylated azepanes, we were particularly interested in the deoxygenation of the azepane ring at C-1 to afford compounds which, for two of them, can be seen as seven-membered analogues of the canonical inhibitors deoxynojirimycin (DNJ)[19] and deoxymannojirimycin (DMJ)[20] (Fig. 5).

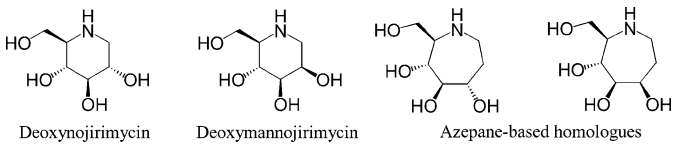
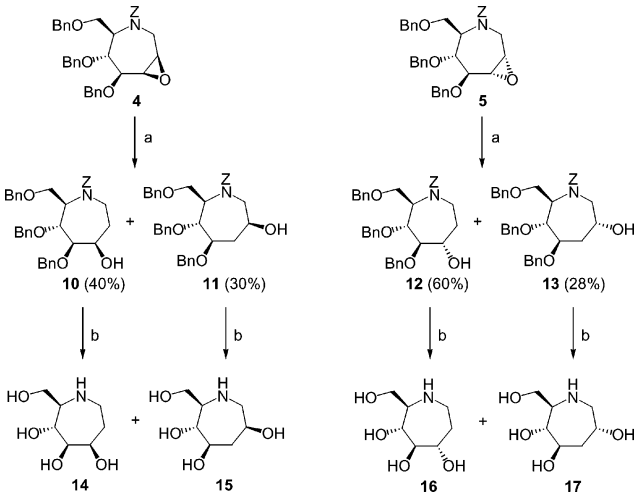


Fig. 5 Analogy between DNJ, DMJ and azepane-based homologues.

Such compounds should be easily accessible from epoxyazepanes **4–7** *via* regioselective epoxide opening with hydride species. Such an approach has been described in the case of piperidine derivatives to have access to fagomine and congeners.[21] Epoxides **4** and **5**[13] were treated with Super-Hydride® in THF to give the corresponding separable alcohols **10–11** and **12–13** respectively in good yield (70–88%), the 1-deoxy derivatives **10** and **12** being the major products indicating a preferred nucleophilic attack of the epoxide at C-1.[22] Nucleophilic opening of simple epoxyazepanes has been studied by the group of Tanner.[23] They observed a remarkable C-2 regioselective opening of these systems invoking both a nitrogen substituent steric effect and a charge control. We have previously obtained such selectivity during azide opening of our epoxyazepanes,[13] albeit with a lower degree of regiocontrol. The opposite regioselectivity obtained for azide and hydride oxirane ring opening of epoxyazepanes **4** and **5** is difficult to rationalize due to the flexibility of the seven-membered ring. Finally, hydrogenolysis of compounds **10–13** quantitatively afforded the corresponding tetrahydroxyazepanes **14–17** (Scheme 1), compounds **14** and **16** being the exact homologues of deoxymannojirimycin and deoxynojirimycin, respectively.



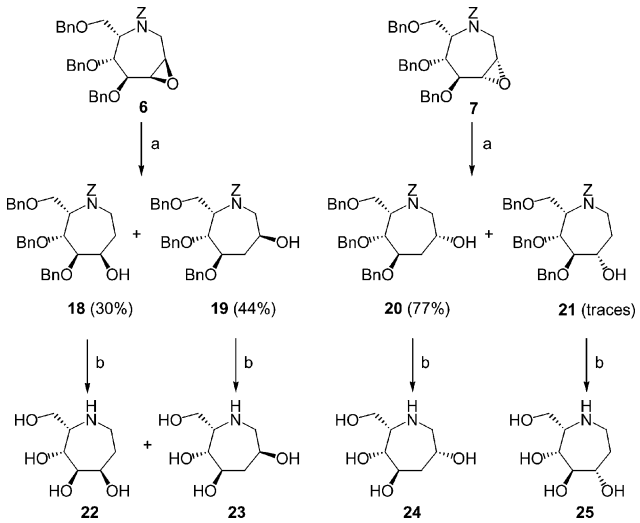
Scheme 1 Synthesis of tetrahydroxyazepanes **14–17**. Reagents and conditions: a) Super-Hydride®, THF, 70–88% yield; b) H_2, 10% Pd/C, MeOH/1M HCl quant.

The same sequence was uneventfully applied to diastereomeric epoxides **6** and **7** to afford alcohols **18–21**. Interestingly, alcohol **21** was only observed as traces.[24] The corresponding tetrahydroxyazepanes **22–25** were obtained after hydrogenolysis (Scheme 2).

Some similar iminocyclitols displaying other stereochemistries have been reported by Lin's group.[25]

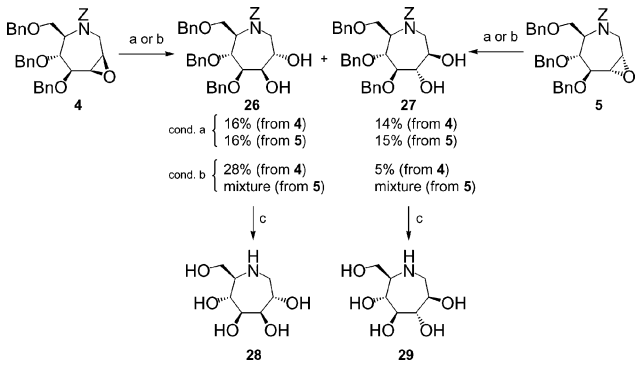
Oxirane ring opening with sodium nitrite

We have previously described the synthesis and inhibitory activity of α-D-nojirimycin homologue **1** and β-D-mannojirimycin homologue **2** in which a *cis* diol functionality is present at positions C-1 and C-2 of the ring. Both compounds displayed potent and selective glycosidase inhibition on α- and β-galactosidases respectively.[12a] These biological results encouraged us to investigate the synthesis and the biological evaluation of the corresponding *trans* 1,2-diols, in particular the β-D-nojirimycin and α-D-mannonojirimycin homologues. These latter should bring useful insights into the role of the two hydroxyl groups present at these positions in terms of selectivity and potency. Such structures should be rapidly accessible from epoxides **4** and **5** *via* nucleophilic opening with oxygenated species. We first envisioned the epoxide opening with nucleophiles such as caesium acetate and potassium



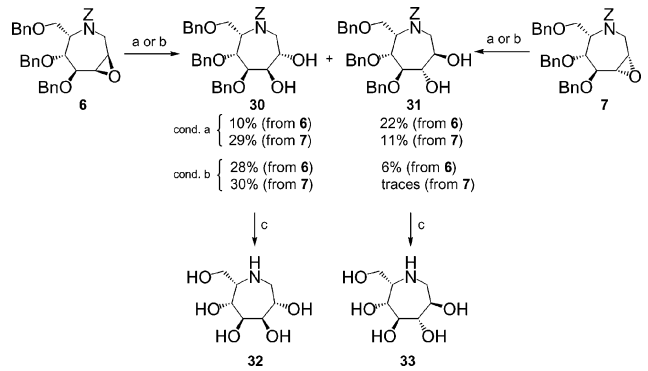
Scheme 2 Synthesis of tetrahydroxyazepanes **22–25**. Reagents and conditions: a) Super-Hydride®, THF, 74–77% yield; b) H_2, 10% Pd/C, MeOH/1M HCl quant.

hydroxide, but no *trans* diol was isolated and only starting material was recovered. These results led us to evaluate the opening of these epoxides under acidic conditions. Treatment of epoxide **4** with aq. sulfuric acid in DMF afforded the expected diols **26** and **27** albeit in low yield.[26] Unfortunately epoxide **5**, under the same conditions, yielded a complex mixture of compounds. Milder conditions were thus needed that could be applied to each epoxide and afford all the possible stereoisomers. A known procedure using sodium nitrite proved to be successful.[27] Treatment of epoxide **4** with sodium nitrite in aqueous DMF gave the corresponding *trans* 1,2-diols **26** and **27** in a low unoptimized 30% yield and 1 : 1 ratio. The same conditions were applied to epoxide **5** to yield compounds **26** and **27** in very similar yield and ratio. Subsequent hydrogenolysis furnished the corresponding α-homomannonojirimycin **28** and β-homonojirimycin **29** in quantitative yield (Scheme 3).



Scheme 3 Synthesis of α-D-homomannonojirimycin **28** and β-D-homonojirimycin **29**. Reagents and conditions: a) $NaNO_2$, DMF/H_2O; b) 15% aq. H_2SO_4, DMF (1 : 10); c) H_2, 10% Pd/C, MeOH, 1M aq. HCl, quant.

The same conditions were uneventfully applied to epoxides **6** and **7** to afford the β-L-homogulonojirimycin **32** and α-L-homoidonojirimycin **33** (Scheme 4).



Scheme 4 Synthesis of β-L-homogulonojirimycin **32** and α-L-homoidonojirimycin **33**. Reagents and conditions: a) $NaNO_2$, DMF/H_2O; b) 15% aq. H_2SO_4, DMF (1 : 10); c) H_2, 10% Pd/C MeOH, 1M aq. HCl, quant.

Inhibition on glycosidases

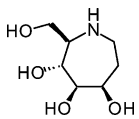
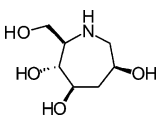
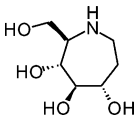
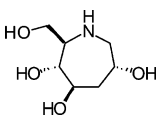
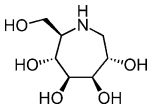
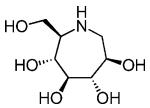
Iminoheptitols **14–17**, **22–25**, **28**, **29**, **32**, **33** were assayed towards a range of commercially available glycosidases.[28] They did not inhibit β-galactosidases from *Escherichia coli* and *Aspergillus oryzae* at 1 mM. For the other enzymes assayed, the results are shown in Tables 1 and 2. Pentahydroxylated azepanes **28**, **29**, **32**, **33** bearing a *trans* diol at position C-1 and C-2 were found to be only weak glycosidase inhibitors. This disappointing result is in marked contrast with our previously reported pentahydroxylated azepanes. The fact that these compounds do not significantly inhibit glycosidases can be tentatively attributed to an important conformational change imposed by the *trans* 1,2-diol in these structures making these molecules unable to interact favorably with the active site of the glycosidase. Work is now in progress to determine the predominant conformation of these structures that could explain the biological results.

Tetrahydroxylated azepanes **14–17** and **22–25** were also assayed on several glycosidases. Unfortunately we were not able to test these compounds against α-galactosidase from coffee beans which was strongly inhibited by some of our previous compounds. Again and as previously observed, compounds **14–17** with an *R* configured hydroxymethyl group are better inhibitors than the corresponding *S* configured compounds **22–25**. While most of the tetrahydroxylated compounds synthesized herein show only weak inhibition on glycosidases, compound **14**, a D-manno configured azepane, does not inhibit the corresponding mannosidase but displays a competitive inhibition towards bovine kidney α-L-fucosidase (*Ki* 10 μM). Similar inhibition values have been reported for this enzyme with other hydroxylated azepanes.[10,29] Compound **16**, the ring homologue of deoxynojirimycin, did not show significant inhibition of glycosidases while its azocane analogue was found to be a fairly good inhibitor of α-L-rhamnosidase (IC_{50} 110 μM).[30] Having now in hand many structures and biological results, work is now in progress to establish a SAR for this class of compounds towards glycosidases.

Conclusion

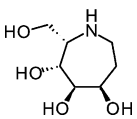
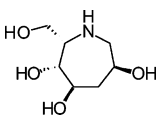
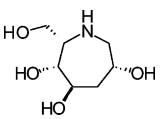
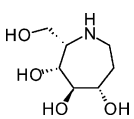
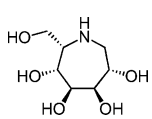
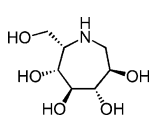
In conclusion, using a straightforward strategy based on nucleophilic opening of previously reported epoxyazepanes, we have obtained twelve new seven-membered ring iminoheptitols. Eight tetrahydroxylated azepanes **14–17** and **22–25** were synthesized *via*

Table 1 Inhibitory activity of compounds **14–17**, **28** and **29** towards glycosidases[a]

						
Compound/enzyme	**14**	**15**	**16**	**17**	**28**	**29**
α-L-Fucosidase						
Bovine kidney	93% (10 μM)	30%	NI	NI	40%	31%
α-Galactosidase						
Coffee bean	ND	ND	ND	ND	35%	29%
β-Galactosidase						
Bovine liver	52%	56%	40%	29%	24%	22%
α-Glucosidase						
Yeast	NI	NI	NI	NI	NI	NI
Rice	NI	NI	NI	NI		40%
Amyloglucosidase						
Aspergillus niger	NI	57%	NI	NI	NI	NI
Rhizopus mold	20%	55%	NI	NI	ND	ND
β-Glucosidase						
Sweet almonds	NI	40%	NI	NI	NI	28%
α-Mannosidase						
Jack bean	NI	NI	16%	NI	NI	38%
β-Mannosidase						
Snail	ND	ND	ND	ND	NI	NI
β-Xylosidase						
Aspergillus niger	NI	NI	NI	NI	27%	67%
β-*N*-Acetylglucosaminidase						
Jack bean	NI	NI	NI	20%	41%	NI
Bovine kidney	NI	NI	NI	NI	38%	NI

[a] % of inhibition at 1 mM concentration, optimal pH, 35 °C, ND = not determined, NI = no inhibition at 1 mM concentration of the inhibitor.

Table 2 Inhibitory activity of compounds **22–25**, **32** and **33** towards glycosidases[a]

						
Compound/enzyme	**22**	**23**	**24**	**25**	**32**	**33**
α-L-Fucosidase						
Bovine kidney	51%	NI	NI	NI	21%	24%
α-Galactosidase						
Coffee bean	ND	ND	ND	ND	NI	NI
β-Galactosidase						
Bovine liver	33%	NI	NI	24%	19%	30%
α-Glucosidase						
Yeast	NI	NI	NI	NI	NI	16%
Rice	NI	NI	NI	NI	NI	NI
Amyloglucosidase						
Aspergillus niger	NI	NI	NI	NI	NI	NI
Rhizopus mold	NI	NI	NI	NI	ND	ND
β-Glucosidase						
Sweet almonds	NI	NI	NI	NI	NI	NI
α-Mannosidase						
Jack bean	NI	NI	NI	NI	NI	NI
β-Xylosidase						
Aspergillus niger	NI	NI	NI	NI	17%	NI
β-*N*-Acetylglucosaminidase						
Jack bean	NI	NI	NI	NI	NI	NI

[a] % of inhibition at 1 mM concentration, optimal pH, 35 °C, ND = not determined, NI = no inhibition at 1 mM concentration of the inhibitor.

Super-Hydride® oxirane opening and hydrogenolysis. Two of them can be seen as ring homologues of classic DNJ (deoxynojirimycin) and DMJ (deoxymannojirimycin), the latter displaying a good and selective inhibition on α-L-fucosidase. Four pentahydroxylated azepanes **28**, **29**, **32**, **33** were also synthesized *via* sodium nitrite oxirane opening and hydrogenolysis. These compounds, albeit similar to previously reported pentahydroxylated azepanes and only differing by the presence of a *trans* 1,2-diol on the ring, do not show significant inhibition of glycosidases.

Experimental

General

Solvents were freshly distilled from Na/benzophenone (THF, toluene), or P_2O_5 (CH_2Cl_2). Reactions were carried under Ar, unless otherwise stated. Melting points were recorded on a Büchi 535 and are uncorrected. Optical rotations were measured on a Perkin Elmer 241 digital polarimeter with a path length of 1 dm. Mass spectra were recorded on a JMS-700 spectrometer, using chemical ionisation with ammonia or methane. NMR spectra were recorded on a Brüker DRX-400 (400 MHz and 100.6 MHz, for ^{1}H and ^{13}C, respectively). TLC was performed on silica gel 60 F254 (Merck) and developed by charring with conc. H_2SO_4. Flash column chromatography was performed using silica gel 60 (230–400 mesh, Merck).

NOTE: For compounds **4–7**, **10–13**, **18–20**, **26–27**, **30–31** bearing a benzyloxycarbonyl group on nitrogen, NMR spectra are provided for the mixture of rotamers.

Typical procedure for epoxidation

Azacycloheptene (330 mg, 0.586 mmol) was dissolved in dry CH_2Cl_2 (10 mL) under argon and *m*-CPBA (560 mg, 3.256 mmol, 5.6 eq.) was added to the solution cooled at 0 °C. The reaction mixture was stirred at RT for 48 h and then cooled to 0 °C and quenched with Me_2S (0.5 mL) stirring for 15 min at RT. The reaction mixture was then diluted with AcOEt, washed with a saturated aq. Na_2CO_3 solution and brine. The organic layer was dried over $MgSO_4$ and concentrated. Purification by flash column chromatography (cyclohexane/AcOEt 4 : 1) afforded epoxide **4** (99 mg, 29% yield) as a colorless oil. Further elution afforded epoxide **5** (181 mg, 53% yield) as a colorless oil.

Compound 4. $[\alpha]_D$ −63 (c = 1 in $CHCl_3$);^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.39–7.30 (m, 40H, 8 × Ph), 5.24–5.10 (m, 4H, 4 × NCOOCHPh), 4.97–4.37 (12 × d, 12H, 12 × CHPh), 4.36 (dd, 1H, J = 6.3 Hz, J = 15.8 Hz, H-7a), 4.27 (m, 1H, H-5′), 4.22 (dd, 1H, J = 6.8 Hz, J = 17.0 Hz, H-7′a), 4.11 (m, 1H, H-5), 3.91–3.80 (m, 5H, H-3, H-3′, H-4, H-4′, H-6′a), 3.78 (dd, 1H, J = 4.8 Hz, J = 9.9 Hz, H-6a), 3.62 (dd, 1H, J = 2.8 Hz, J = 10.0 Hz, H-6′b), 3.58–3.52 (m, 2H, H-6b, H-1), 3.44–3.38 (m, 2H, H-7′b, H-1′), 3.36 (dd, 1H, J = 3.8 Hz, J = 16.2 Hz, H-7b), 3.30 (dd, 1H, J = 0.7 Hz, J = 4.5 Hz, H-2), 3.23 (dd, 1H, J = 0.8 Hz, J = 4.4 Hz, H-2′); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.10, 155.79 (2 × C=O), 138.30, 138.24, 138.19, 138.02, 138.01, 137.90, 136.42, 136.25 (C_{ipso}), 128.39–127.51 (40 × aromatic C), 80.01 (C-3, C-3′), 75.26, 74.95 (2 × CH_2Ph), 74.44, 74.41 (C-4, C-4′), 74.33, 74.18, 73.05, 72.99 (4 × CH_2Ph), 69.47, 69.41 (C-6, C-6′), 67.65, 67.47 (2 × NCOOCH_2Ph), 57.21, 57.00 (C-5, C-5′), 56.10, 55.97 (C-2, C-2′), 55.25, 55.22 (C-1′, C-1), 43.17, 42.94 (C-7′, C-7); m/z (CI, NH_3): 580 (M + H$^+$, 100%), 597 (M + NH_4^+, 60%); HRMS (CI, NH_3): Calcd for $C_{36}H_{38}O_6N$ (M + H$^+$): 580.2699, Found 580.2695.

Compound 5. $[\alpha]_D$ −43 (c = 1 in $CHCl_3$);^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.42–7.33 (m, 40H, 8 × Ph), 5.25–5.11 (m, 4H, 4 × NCOOCHPh), 5.05– 4.76 (m, 6H, 6 × CHPh), 4.62 (app. d, 1H, J = 16.0 Hz, H-7′a), 4.55–4.34 (m, 8H, 6 × CHPh, H-5, H-7a), 4.25 (ddd, 1H, J = 2.5 Hz, J = 4.7 Hz, J = 8.0 Hz, H-5′), 3.88 (t, 1H, J = 9.8 Hz, H-4), 3.86–3.76 (m, 5H, H-3, H-4′, H-6a, H-6′a, H-7b), 3.74 (dd, 1H, J = 1.9 Hz, J = 9.7 Hz, H-3′), 3.73 (d, 1H, J = 15.8 Hz, H-7′b), 3.64 (dd, 1H, J = 2.4 Hz, J = 10.2 Hz, H-6b), 3.58 (dd, 1H, J = 2.5 Hz, J = 10.0 Hz, H-6′b), 3.26 (dd, 1H, J = 1.9 Hz, J = 4.4 Hz, H-2′), 3.25 (dd, 1H, J = 1.9 Hz, J = 4.4 Hz, H-2), 3.13 (dd, 1H, J = 1.7 Hz, J = 4.3 Hz, H-1′), 3.07 (dd, 1H, J = 1.7 Hz, J = 4.3 Hz, H-1); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.69, 156.34 (2 × C=O), 138.25, 138.12, 137.97, 137.94, 137.81, 136.61 (C_{ipso}), 128.41–127.58 (40 × aromatic C), 80.55, 80.43 (C-3, C-3′), 76.06, 76.05 (C-4, C-4′), 75.20, 74.89, 73.59, 73.12, 73.08, 73.04 (6 × CH_2Ph), 69.76, 69.62 (C-6, C-6′), 67.65, 67.49 (2 × NCOOCH_2Ph), 57.66, 57.09 (C-5′, C-5), 57.43 (C-2, C-2′), 53.88, 53.80 (C-1′, C-1), 40.69, 40.62 (C-7, C-7′); m/z (CI, NH_3): 580 (M + H$^+$, 30%), 597 (M + NH_4^+, 100%); HRMS (CI, NH_3): Calcd for $C_{36}H_{38}O_6N$ (M + H$^+$): 580.2699, Found 580.2703.

Compound 6. $[\alpha]_D$ −1 (c = 1.1 in $CHCl_3$);^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.43–7.34 (m, 40H, 8 × Ph), 5.32–5.15 (m, 4H, 4 × NCOOCHPh), 4.87–4.73 (m, 8H, 6 × CHPh, H-5, H-7′a), 4.65–4.48 (m, 8H, 6 × CHPh, H-5′, H-7a), 4.04 (dd, 1H, J = 2.4 Hz, J = 8.9 Hz H-3), 4.00 (dd, 1H, J = 2.8 Hz, J = 8.6 Hz, H-3′), 3.97 (dd, 1H, J = 3.9 Hz, J = 8.9 Hz, H-4), 3.86 (dd, 1H, J = 3.8 Hz, J = 8.3 Hz, H-4′), 3.85 (dd, 1H, J = 4.9 Hz, J = 10.2 Hz, H-6a), 3.78 (dd, 1H, J = 5.2 Hz, J = 10.2 Hz, H-6′a), 3.71 (t, 1H, J = 9.5 Hz, H-6b), 3.61 (t, 1H, J = 9.5 Hz, H-6′b), 3.54 (d, 1H, J = 16.2 Hz, H-7b), 3.48 (d, 1H, J = 15.9 Hz, H-7′b), 3.23 (dd, 2H, J = 2.6 Hz, J = 4.2 Hz, H-2, H-2′), 3.17 (t, 1H, J = 4.1 Hz, H-1′), 3.09 (t, 1H, J = 4.1 Hz, H-1); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.29, 156.15 (2 × C=O), 138.30, 138.29, 138.17, 138.14, 137.66, 137.58, 136.58, 136.30 (C_{ipso}), 128.35–127.40 (40 × aromatic C), 78.72, 78.23 (C-4′, C-4), 77.13, 76.72 (C-3, C-3′), 73.43, 73.41, 72.95, 72.89, 72.86, 72.71 (6 × CH_2Ph), 67.65, 67.31 (2 × NCOOCH_2Ph), 64.74, 64.52 (C-6′, C-6), 54.89, 54.24 (C-2, C-2′), 54.52, 54.15 (C-1′, C-1), 52.99, 52.66 (C-5′, C-5), 38.91, 38.88 (C-7′, C-7); m/z (CI, NH_3): 580 (M + H$^+$, 100%), 597 (M + NH_4^+, 65%); HRMS (CI, NH_3): Calcd for $C_{36}H_{38}O_6N$ (M + H$^+$): 580.2699, Found 580.2696.

Compound 7. $[\alpha]_D$ +56 (c = 1 in $CHCl_3$);^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.46–7.30 (m, 40H, 8 × Ph), 5.28–5.16 (m, 4H, 4 × NCOOCHPh), 5.06 (dt, 1H, J = 4.2 Hz, J = 8.1 Hz, H-5), 4.96–4.43 (m, 14H, 12 × CHPh, H-5′, H-7′a), 4.39 (dd, 1H, J = 5.5 Hz, J = 15.3 Hz, H-7a), 3.91 (dd, 1H, J = 4.1 Hz, J = 10.7 Hz, H-6a), 3.90–3.75 (m, 6H, H-3, H-3′, H-4, H-4′, H-6′a, H-6b), 3.72 (dd, 1H, J = 8.7 Hz, J = 10.2 Hz, H-6′b), 3.48 (dt, 1H, J = 5.6 Hz, J = 7.4 Hz, H-1′), 3.35 (dt, 1H, J = 5.3 Hz, J = 8.2 Hz, H-1), 3.13 (t, 2H, J = 4.4 Hz, H-2, H-2′), 2.94 (dd, 1H, J = 8.2 Hz, J = 15.2 Hz, H-7b), 2.93 (d, 1H, J = 7.4 Hz, J = 14.6 Hz, H-7′b); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 155.99, 155.69 (2 × C=O), 138.14, 137.99, 137.90, 137.86, 137.82, 136.39, 136.23 (C_{ipso}), 128.50–127.38 (40 × aromatic C), 78.59, 78.23 (C-3, C-3′), 77.15, 76.79 (C-4, C-4′),

74.31, 74.05, 72.84, 72.78, 72.72 (6 × CH_2Ph), 67.57, 67.44 (2 × $NCOOCH_2Ph$), 65.44, 65.22 (C-6, C-6′), 57.03, 56.86 (C-2, C-2′), 55.15, 54.15 (C-5′, C-5), 51.77, 51.40 (C-1′, C-1), 43.58, 43.36 (C-7, C-7′); *m/z* (CI, NH_3): 580 ($M + H^+$, 100%), 597 ($M + NH_4^+$, 10%); HRMS (CI, NH_3): Calcd for $C_{36}H_{38}O_6N$ ($M + H^+$): 580.2699, Found 580.2698.

Compound 9. $[a]_D$ −101 (*c* = 1 in $CHCl_3$); mp 175–176 °C (ethyl acetate/cyclohexane); ^1H NMR ($CDCl_3$, 400 MHz): δ 4.43–4.37 (m, 3H, H-6a, H-6b, H-7a), 4.24–4.16 (m, 3H, H-3, H-4, H-5), 3.53 (d, 1H, *J* = 4.5 Hz, H-2), 3.49 (ddd, 1H, *J* = 1.4 Hz, *J* = 4.5 Hz, *J* = 5.8 Hz, H-1), 3.29 (dd, 1H, *J* = 1.4 Hz, *J* = 16.6 Hz, H-7b), 1.50 (s, 3H, CH_3), 1.48 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 157.57 (C=O), 111.25 ($C(CH_3)_2$), 75.00 (C-3), 72.00 (C-4), 62.15 (C-6), 54.79 (C-2), 53.45 (C-1), 52.48 (C-5), 41.99 (C-7), 26.84 (CH_3), 26.63 (CH_3); *m/z* (CI, NH_3): 242 ($M + H^+$, 55%), 259 ($M + NH_4^+$, 100%); HRMS (CI, CH_4): Calcd for $C_{11}H_{16}O_5N$ ($M + H^+$): 242.1028, Found 242.1026.

Typical procedure for epoxide ring opening with Super-Hydride®

Epoxide **4** (50 mg, 0.086 mmol) was dissolved in dry THF (0.4 mL) and the solution was cooled to 0 °C. Super-Hydride® (0.6 mL, 0.6 mmol, 1M solution in THF) was added and the reaction mixture was stirred at RT for 16 h by which time TLC (cyclohexane/AcOEt 2:1) showed a complete reaction. The reaction mixture was diluted with AcOEt and washed with 1 M aq. HCl solution, water and brine. The organic layer was dried over $MgSO_4$ and concentrated. Purification by flash column chromatography (cyclohexane/AcOEt 4 : 1) afforded alcohol **10** (20 mg, 40% yield) as a colorless oil. Further elution afforded alcohol **11** (15 mg, 30% yield) as a colorless oil.

Compound 10. $[a]_D$ −27 (*c* = 1 in $CHCl_3$);^1H NMR ($CDCl_3$, 400 MHz): δ 7.39–7.28 (m, 40H, 8 × Ph), 5.20–5.08 (m, 4H, 4 × NCOOCHPh), 4.93–4.37 (m, 12H, 12 × CHPh), 4.29 (t, 1H, *J* = 9.4 Hz, H-4), 4.26 (t, 1H, *J* = 9.3 Hz, H-4′), 4.25–4.18 (m, 3H, H-2, H-2′, H-5), 4.09 (dt, 1H, *J* = 3.5 Hz, *J* = 9.2 Hz, H-5′), 3.85 (dd, 1H, *J* = 4.3 Hz, *J* = 9.8 Hz, H-6a), 3.79 (m, 1H, H-7′a), 3.76 (dd, 1H, *J* = 4.3 Hz, *J* = 9.8 Hz, H-6′a), 3.68 (dd, 1H, *J* = 2.8 Hz, *J* = 9.8 Hz, H-6b), 3.65 (m, 1H, H-7a), 3.63 (dd, 1H, *J* = 1.5 Hz, *J* = 8.6 Hz, H-3), 3.59 (dd, 1H, *J* = 2.8 Hz, *J* = 9.8 Hz, H-6′b), 3.58 (dd, 1H, *J* = 1.8 Hz, *J* = 9.8 Hz, H-3′), 3.35 (ddd, 1H, *J* = 1.6 Hz, *J* = 11.5 Hz, *J* = 13.7 Hz, H-7b), 3.27 (ddd, 1H, *J* = 3.2 Hz, *J* = 10.7 Hz, *J* = 14.2 Hz, H-7′b), 2.51 (s, 2H, OH, OH′), 1.92–1.71 (m, 4H, H-1a, H-1′a, H-1b, H-1′b); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 155.88, 155.67 (2 × C=O), 138.34, 138.25, 138.20, 138.11, 136.70, 136.58 (C_{ipso}), 128.46–127.45 (40 × aromatic C), 84.05, 83.99 (C-3, C-3′), 75.07, 74.72, 74.15, 74.04, 72.97, 72.92 (6 × CH_2Ph), 73.71, 73.55 (C-4′, C-4), 69.93, 69.69 (C-6′, C-6), 69.58, 69.47 (C-2, C-2′), 67.21, 67.10 (2 × $NCOOCH_2Ph$), 58.01, 57.76 (C-5′, C-5), 39.44, 39.24 (C-7, C-7′), 32.84, 32.04 (C-1, C-1′); *m/z* (CI, CH_4): 582 ($M + H^+$, 100%); HRMS (CI, CH_4): Calcd for $C_{36}H_{40}O_6N$ ($M + H^+$): 582.2856, Found 582.2849.

Compound 11. $[a]_D$ −20 (*c* = 1 in $CHCl_3$);^1H NMR ($CDCl_3$, 400 MHz): δ 7.38–7.28 (m, 40H, 8 × Ph), 5.19–5.07 (m, 4H, 4 × NCOOCHPh), 4.86–4.37 (m, 12H, 12 × CHPh), 4.31 (m, 1H, H-5′), 4.23 (dt, 1H, *J* = 4.4 Hz, *J* = 8.1 Hz, H-5), 4.00–3.88 (m, 5H, H-1, H-1′, H-4′, H-6′a, H-7a), 3.85 (dd, 1H, *J* = 4.7 Hz, *J* = 14.6 Hz, H-7′a), 3.81–3.72 (m, 3H, H-3, H-3′, H-6a), 3.68 (dd, 1H, *J* = 3.8 Hz, *J* = 9.8 Hz, H-6′b), 3.65 (m, 1H, H-4), 3.59 (dd, 1H, *J* = 3.7 Hz, *J* = 9.8 Hz, H-6b), 3.31 (dd, 1H, *J* = 8.7 Hz, *J* = 14.5 Hz, H-7′b), 3.13 (dd, 1H, *J* = 10.8 Hz, *J* = 15.0 Hz, H-7b), 2.48 (s, 2H, OH, OH′), 2.41 (m, 1H, H-2a), 2.30 (dd, 1H, *J* = 3.9 Hz, *J* = 14.1 Hz, H-2′a), 1.94 (ddd, 1H, *J* = 7.3 Hz, *J* = 8.7 Hz, *J* = 14.1 Hz, H-2′b), 1.86 (dt, 1H, *J* = 9.0 Hz, *J* = 14.0 Hz, H-2b); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.15, 155.94 (2 × C=O), 138.19, 138.15, 138.04, 137.98, 137.95, 136.59, 136.35 (C_{ipso}), 128.47–127.56 (40 × aromatic C), 79.84, 79.40 (C-3′, C-3), 78.93, 78.72 (C-4, C-4′), 74.34, 73.62, 73.13, 73.01, 72.97 (6 × CH_2Ph), 69.50, 69.12 (C-6′, C-6), 68.40, 66.82 (C-1, C-1′), 67.51, 67.20 (2 × $NCOOCH_2Ph$), 58.70, 58.19 (C-5, C-5′), 50.88, 50.26 (C-7′, C-7), 39.15, 37.56 (C-2, C-2′); *m/z* (CI, CH_4): 582 ($M + H^+$, 100%); HRMS (CI, CH_4): Calcd for $C_{36}H_{40}O_6N$ ($M + H^+$): 582.2856, Found 582.2853.

Compound 12. $[a]_D$ −4 (*c* = 1 in $CHCl_3$);^1H NMR ($CDCl_3$, 400 MHz): 7.43–7.31 (m, 40H, 8 × Ph), 5.27–5.16 (m, 4H, 4 × NCOOCHPh), 5.14–4.35 (m, 12H, 12 × CHPh), 4.31 (dt, 1H, *J* = 2.6 Hz, *J* = 9.8 Hz, H-5), 4.14 (dt, 1H, *J* = 2.6 Hz, *J* = 9.6 Hz, H-5′), 4.04 (dt, 1H, *J* = 3.3 Hz, *J* = 15.0 Hz, H-7′a), 3.91 (dt, 1H, *J* = 3.3 Hz, *J* = 15.4 Hz, H-7a), 3.88–3.79 (m, 4H, H-4, H-4′, H-6a, H-6′a), 3.75–3.67 (m, 2H, H-2, H-2′), 3.69 (dd, 1H, *J* = 2.6 Hz, *J* = 9.8 Hz, H-6b), 3.60 (dd, 1H, *J* = 2.5 Hz, *J* = 9.7 Hz, H-6′b), 3.50 (t, 1H, *J* = 9.0 Hz, H-3), 3.44 (t, 1H, *J* = 9.0 Hz, H-3′), 3.24 (s, 1H, OH), 3.20–3.07 (m, 3H, H-7b, H-7′b, OH′), 2.12–2.05 (m, 2H, H-1a, H-1′a), 1.78–1.63 (m, 2H, H-1b, H-1′b); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 155.87, 155.42 (2 × C=O), 138.14, 138.10, 138.02, 137.98, 137.84, 136.55, 136.48 (C_{ipso}), 128.58–127.49 (40 × aromatic C), 86.09, 85.91 (C-3′, C-3), 77.50, 77.34 (C-4′, C-4), 76.13, 76.07, 75.56, 75.31, 73.12, 73.06 (6 × CH_2Ph), 73.29, 73.04 (C-2′, C-2), 70.06, 69.83 (C-6′, C-6), 67.34, 67.33 (2 × $NCOOCH_2Ph$), 57.82, 57.78 (C-5′, C-5), 40.10, 39.95 (C-7′, C-7), 33.06, 32.44 (C-1, C-1′); *m/z* (CI, CH_4): 582 ($M + H^+$, 100%); HRMS (CI, CH_4): Calcd for $C_{36}H_{40}O_6N$ ($M + H^+$): 582.2856, Found 582.2850.

Compound 13. $[a]_D$ −43 (*c* = 1 in $CHCl_3$);^1H NMR ($CDCl_3$, 400 MHz): δ 7.39–7.28 (m, 40H, 8 × Ph), 5.24–5.06 (m, 4H, 4 × NCOOCHPh), 4.88–4.36 (m, 12H, 12 × CHPh), 4.27 (m, 1H, H-5′), 4.25 (dt, 1H, *J* = 4.0 Hz, *J* = 7.8 Hz, H-5), 4.16–4.05 (m, 3H, H-1, H-1′, H-7a), 3.95 (dd, 1H, *J* = 5.3 Hz, *J* = 9.9 Hz, H-6′a), 3.91 (dd, 1H, *J* = 1.9 Hz, *J* = 7.9 Hz, H-3), 3.87 (dd, 1H, *J* = 2.1 Hz, *J* = 6.9 Hz, H-3′), 3.84–3.79 (m, 2H, H-4′, H-7′a), 3.78 (dd, 1H, *J* = 4.4 Hz, *J* = 9.8 Hz, H-6a), 3.71 (dd, 1H, *J* = 4.5 Hz, *J* = 10.0 Hz, H-6′b), 3.70 (t, 1H, *J* = 7.8 Hz, H-4), 3.61 (dd, 1H, *J* = 3.6 Hz, *J* = 9.8 Hz, H-6b), 3.58 (dd, 1H, *J* = 2.8 Hz, *J* = 14.1 Hz, H-7′b), 3.47 (s, 1H, OH), 3.41 (dd, 1H, *J* = 2.6 Hz, *J* = 15.9 Hz, H-7b), 2.27 (ddd, 1H, *J* = 1.7 Hz, *J* = 6.2 Hz, *J* = 14.2 Hz, H-2a), 2.15 (ddd, 1H, *J* = 1.6 Hz, *J* = 6.5 Hz, *J* = 14.2 Hz, H-2′a), 2.06 (s, 1H, OH′), 1.98 (ddd, 1H, *J* = 4.0 Hz, *J* = 8.6 Hz, *J* = 14.3 Hz, H-2′b), 1.92 (ddd, 1H, *J* = 4.1 Hz, *J* = 9.6 Hz, *J* = 14.1 Hz, H-2b); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.04 (2 × C=O), 138.52, 138.20, 138.11, 137.95, 136.15, 136.09 (C_{ipso}), 128.64–127.50 (40 × aromatic C), 80.43, 79.61 (C-4, C-4′), 77.73, 77.46 (C-3, C-3′), 74.24, 73.76, 73.04, 73.01, 72.97, 72.63 (6 × CH_2Ph), 69.42, 69.16 (C-6, C-6′), 67.98, 67.53 (2 × $NCOOCH_2Ph$), 67.68, 66.70 (C-1, C-1′), 58.79, 57.68 (C-5′, C-5), 50.33, 49.02 (C-7′, C-7), 38.50, 38.00 (C-2, C-2′); *m/z* (CI, CH_4): 582 ($M + H^+$, 100%); HRMS (CI, CH_4): Calcd for $C_{36}H_{40}O_6N$ ($M + H^+$): 582.2856, Found 582.2851.

Compound 18. $[a]_D$ +25 (c = 1 in $CHCl_3$);^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38–7.29 (m, 40H, 8 × Ph), 5.29–5.03 (m, 4H, 4 × NCOOCHPh), 4.76 (dt, 1H, J = 5.2 Hz, J = 10.2 Hz, H-5′), 4.71–4.40 (m, 13H, 12 × CHPh, H-5), 4.25 (dd, 1H, J = 5.2 Hz, J = 7.4 Hz, H-4′), 4.21 (m, 2H, H-2, H-2′), 4.17 (dd, 1H, J = 5.1 Hz, J = 7.4 Hz, H-4), 4.08 (dd, 1H, J = 2.7 Hz, J = 7.5 Hz, H-3), 4.05 (dd, 1H, J = 2.6 Hz, J = 7.4 Hz, H-3′), 3.83–3.76 (m, 1H, H-7a), 3.79 (t, 1H, J = 9.0 Hz, H-6′a), 3.74 (t, 1H, J = 9.2 Hz, H-6a), 3.69 (m, 1H, H-7′a), 3.59 (dd, 1H, J = 5.5 Hz, J = 8.9 Hz, H-6′b), 3.48 (dd, 1H, J = 5.5 Hz, J = 8.9 Hz, H-6b), 3.19–3.10 (m, 2H, H-7b, H-7′b), 1.97–1.76 (m, 4H, H-1a, H-1′a, H-1b, H-1′b), 1.71 (s, 2H, OH, OH′); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 155.71, 155.49 (2 × C=O), 138.34, 138.18, 138.02, 137.98, 137.92, 137.84, 137.00, 136.88 (C_{ipso}), 128.48–127.49 (40 × aromatic C), 81.07, 80.96 (C-3, C-3′), 74.78, 74.62 (C-4′, C-4), 74.16, 74.03, 73.85, 73.11, 73.06 (6 × CH_2Ph), 69.66, 69.39 (C-2, C-2′), 67.80, 67.38 (C-6, C-6′), 67.03, 66.93 (2 × NCOOCH_2Ph), 54.92, 54.84 (C-5′, C-5), 39.51, 39.12 (C-7, C-7′), 34.10, 33.36 (C-1′, C-1); m/z (CI, CH_4): 582 (M + H$^+$, 100%); HRMS (CI, CH_4): Calcd for $C_{36}H_{40}O_6N$ (M + H$^+$): 582.2856, Found 582.2853.

Compound 19. $[a]_D$ +16 (c = 1 in $CHCl_3$);^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.39–7.27 (m, 40H, 8 × Ph), 5.25–5.06 (m, 4H, 4 × NCOOCHPh), 4.81 (dt, 1H, J = 5.0 Hz, J = 9.9 Hz, H-5′), 4.71 (dt, 1H, J = 5.4 Hz, J = 10.0 Hz, H-5), 4.78–4.43 (m, 12H, 12 × CHPh), 4.29 (dd, 1H, J = 4.9 Hz, J = 7.0 Hz, H-4′), 4.24 (m, 1H, H-7′a), 4.22 (dd, 1H, J = 5.1 Hz, J = 6.9 Hz, H-4), 4.18 (dd, 1H, J = 5.4 Hz, J = 15.5 Hz, H-7a), 4.17–4.10 (m, 2H, H-1, H-3), 4.06 (ddd, 1H, J = 2.0 Hz, J = 5.0 Hz, J = 6.8 Hz, H-3′), 4.00 (m, 1H, H-1′), 3.87 (t, 1H, J = 8.8 Hz, H-6′a), 3.81 (t, 1H, J = 9.2 Hz, H-6a), 3.73 (dd, 1H, J = 5.2 Hz, J = 8.7 Hz, H-6′b), 3.59 (dd, 1H, J = 5.6 Hz, J = 8.9 Hz, H-6b), 3.51 (d, 1H, J = 6.7 Hz, OH), 3.42 (d, 1H, J = 13.8 Hz, H-7′b), 3.38 (d, 1H, J = 14.1 Hz, H-7b), 3.08 (d, 1H, J = 9.9 Hz, OH′), 2.27 (m, 1H, H-2a), 2.13 (m, 1H, H-2′a), 2.07–1.98 (m, 2H, H-2b, H-2′b); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 157.82, 156.52 (2 × C=O), 138.36, 138.09, 138.08, 138.02, 137.91, 137.56, 136.92, 136.55 (C_{ipso}), 128.35–127.49 (40 × aromatic C), 77.16, 76.95 (C-3′, C-3), 76.59, 76.09 (C-4, C-4′), 73.83, 73.72, 73.09, 73.06, 72.16, 71.61 (6 × CH_2Ph), 70.35, 69.43 (C-1, C-1′), 67.52, 67.11 (2 × NCOOCH_2Ph), 67.51, 67.01 (C-6, C-6′), 55.26, 55.18 (C-5, C-5′), 47.64, 47.51 (C-7′, C-7), 33.21, 32.49 (C-2′, C-2); m/z (CI, CH_4): 582 (M + H$^+$, 100%); HRMS (CI, CH_4): Calcd for $C_{36}H_{40}O_6N$ (M + H$^+$): 582.2856, Found 582.2861.

Compound 20. $[a]_D$ −1 (c = 1 in $CHCl_3$);^{1}H NMR ($CDCl_3$, 400 MHz): 7.39–7.30 (m, 40H, 8 × Ph), 5.30–5.03 (m, 4H, 4 × NCOOCHPh), 4.81 (dt, 1H, J = 5.5 Hz, J = 10.2 Hz, H-5′), 4.66–4.40 (m, 13H, 12 × CHPh, H-5), 4.25 (dd, 1H, J = 5.4 Hz, J = 6.9 Hz, H-4′), 4.19 (dd, 1H, J = 5.4 Hz, J = 6.8 Hz, H-4), 4.14 (m, 1H, H-1), 4.05 (ddd, 1H, J = 1.6 Hz, J = 5.1 Hz, J = 6.8 Hz, H-3), 4.02 (m, 1H, H-1′), 3.99 (ddd, 1H, J = 1.7 Hz, J = 5.0 Hz, J = 6.9 Hz, H-3′), 3.89–3.78 (m, 4H, H-6a, H-6′a, H-7a, H-7′a), 3.69 (dd, 1H, J = 5.8 Hz, J = 8.9 Hz, H-6′b), 3.58 (dd, 1H, J = 5.7 Hz, J = 8.9 Hz, H-6b), 3.39 (dd, 1H, J = 9.2 Hz, J = 13.1 Hz, H-7b), 3.37 (dd, 1H, J = 9.9 Hz, J = 13.8 Hz, H-7b′), 3.18 (s, 1H, OH), 2.34 (m, 1H, H-2a), 2.29–2.20 (m, 2H, H-2′a, OH′), 2.05–1.92 (m, 2H, H-2b, H-2′b); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.10, 155.63 (2 × C=O), 138.30, 138.25, 138.12, 138.06, 137.93, 136.87, 136.56 (C_{ipso}), 128.35–127.09 (40 × aromatic C), 76.35, 76.21 (C-4′, C-4), 73.94, 73.82 (C-3, C-3′), 73.75, 73.61, 73.00, 72.97, 71.28, 71.12 (6 × CH_2Ph), 67.84, 67.39 (C-6, C-6′), 67.37, 66.23 (C-1′, C-1), 67.16, 66.92 (2 × NCOOCH_2Ph), 54.38, 54.31 (C-5′, C-5), 50.18, 49.46 (C-7′, C-7), 34.43, 33.29 (C-2′, C-2); m/z (CI, CH_4): 582 (M + H$^+$, 100%); HRMS (CI, CH_4): Calcd for $C_{36}H_{40}O_6N$ (M + H$^+$): 582.2856, Found 582.2847.

Typical procedure for *trans* diol formation

Epoxide opening with sodium nitrite. Epoxide **4** (90 mg, 0.155 mmol) and $NaNO_2$ (381 mg, 5.52 mmol) were suspended in a DMF/water (1.3 mL/0.4 mL) solution and the suspension was stirred at 90 °C for 48 h by which time TLC (cyclohexane/AcOEt 1 : 1) showed a complete reaction. The reaction mixture was then diluted with AcOEt, washed with water and brine. The organic layer was dried over $MgSO_4$ and concentrated. Purification by flash column chromatography (cyclohexane/AcOEt 3 : 2) afforded diol **26** (19 mg, 16% yield) as a colorless oil. Further elution afforded diol **27** (13 mg, 14% yield) as a colorless oil.

Epoxide opening with sulfuric acid. Epoxide **4** (9 mg, 0.015 mmol) was dissolved in 15% aq. H_2SO_4/DMF (0.08 mL, 0.5 mL) and the solution was stirred at RT for 48 h. The reaction mixture was then diluted with AcOEt, washed with aq. saturated $NaHCO_3$, water and brine. The organic layer was dried over $MgSO_4$ and concentrated. Purification by flash column chromatography (cyclohexane/AcOEt 3 : 2) afforded diol **26** (3 mg, 28% yield) as a colorless oil. Further elution afforded diol **27** (traces) as a colorless oil.

Compound 26. $[a]_D$ −39 (c = 0.95 in $CHCl_3$);^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.39–7.22 (m, 40H, 8 × Ph), 5.22–5.01 (m, 4H, 4 × CHPh), 4.82–4.36 (m, 12H, 12 × CHPh), 4.21 (dt, 1H, J = 4.3 Hz, 7.3 Hz, H-5), 4.16 (app. d, 1H, J = 3.8 Hz, H-2), 4.09 (m, 1H, H-5′), 4.07 (t, 1H, J = 7.8 Hz, H-4), 4.01 (app. dd, 1H, J = 3.0 Hz, J = 15.7 Hz, H-7a), 4.01–3.89 (m, 6H, H-1, H-1′, H-2′, H-3′, H-4′, H-7′a), 3.88 (dd, 1H, J = 1.3 Hz, J = 8.1 Hz, H-3), 3.77 (dd, 1H, J = 4.7 Hz, J = 9.8 Hz, H-6a), 3.75 (s, 1H, OH-1), 3.74–3.69 (m, 2H, H-6′a, H-6′b), 3.63 (m, 1H, H-7′b), 3.60 (dd, 1H, J = 3.8 Hz, J = 9.8 Hz, H-6b), 3.54 (dd, 1H, J = 1.7 Hz, J = 15.4 Hz, H-7b), 2.66 (s, 1H, OH-2), 2.62 (s, 1H, OH-1′), 2.42 (d, 1H, J = 3.3 Hz, OH-2′); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.22 (2 × C=O), 138.20, 138.13, 137.93, 137.90, 135.96 (C_{ipso}), 128.62–127.50 (40 × aromatic C), 81.56, 81.40 (C-3, C-3′), 74.24, 73.94, 73.48, 72.93, 72.91 (6 × CH_2Ph), 73.82 (C-4, C-4′), 73.61, 73.39 (C-2, C-2′), 72.41, 70, 77 (C-1, C-1′), 68.97, 68.89 (C-6, C-6′), 68.06, 67.50 (2 × NCOOCH_2Ph), 59.58, 57.71 (C-5, C-5′), 46.94, 44.91 (C-7, C-7′); m/z (CI, NH_3): 598 (M + H$^+$, 100%); HRMS (CI, CH_4): Calcd for $C_{36}H_{40}O_7N$ (M + H$^+$): 598.2805, Found 598.2798.

Compound 27. $[a]_D$ +3 (c = 1 in $CHCl_3$);^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.42–7.30 (m, 40H, 8 × Ph), 5.27–5.12 (m, 4H, 4 × NCOOCHPh), 5.11–4.32 (m, 12H, 12 × CHPh), 4.25 (dt, 1H, J = 2.5 Hz, J = 9.8 Hz, H-5), 4.08 (dt, 1H, J = 2.5 Hz, J = 9.6 Hz, H-5′), 4.03 (dd, 1H, J = 3.7 Hz, J = 14.5 Hz, H-7′a), 3.93 (dd, 1H, J = 3.6 Hz, J = 14.9 Hz, H-7a), 3.87 (t, 1H, J = 9.5 Hz, H-4′), 3.84 (t, 1H, J = 9.4 Hz, H-4), 3.79 (dd, 1H, J = 3.1 Hz, J = 9.9 Hz, H-6a), 3.74 (dd, 1H, J = 3.3 Hz, J = 9.7 Hz, H-6′a), 3.68 (m, 1H, H-1′), 3.64 (dd, 1H, J = 2.4 Hz, J = 9.8 Hz, H-6b), 3.62 (m, 1H, H-1), 3.56 (dd, 1H, J = 2.5 Hz, J = 9.7 Hz, H-6′b), 3.51 (t, 1H, J = 9.0 Hz, H-2′), 3.51–3.44 (m, 2H, H-2, H-3), 3.42 (t, 1H, J = 9.2 Hz, H-3′), 3.25 (s, 1H, OH-2), 3.22 (dd, 1H, J = 10.3 Hz, J =

14.8 Hz, H-7b), 3.21 (s, 1H, OH-2′), 3.16 (dd, 1H, J = 11.5 Hz, J = 14.5 Hz, H-7′b), 2.79 (d, 1H, J = 2.0 Hz, OH-1′), 2.69 (d, 1H, J = 1.5 Hz, OH-1); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 155.85, 155.64 (2 × C=O), 137.97, 137.95, 137.85, 137.83, 137.68, 136.33, 136.30 (C_{ipso}), 128.63–127.56 (40 × aromatic C), 82.42, 82.24 (C-3′, C-3), 79.01, 78.94 (C-2′, C-2), 77.34, 77.25 (C-4′, C-4), 76.31, 76.22, 75.69, 75.44, 73.17, 73.11 (6 × CH_2Ph), 71.80, 70.98 (C-1, C-1′), 69.72, 69.51 (C-6′, C-6), 67.63, 67.50 (2 × NCOOCH_2Ph), 58.14, 58.05 (C-5′, C-5), 45.17, 44.90 (C-7′, C-7); m/z (CI, CH_4): 598 (M + H$^+$, 100%); HRMS (CI, CH_4): Calcd for $C_{36}H_{40}O_7N$ (M + H$^+$): 598.2805, Found 598.2797.

Compound 30. $[a]_D$ +7 (c = 1 in $CHCl_3$);^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38–7.28 (m, 40H, × Ph), 5.28–5.00 (m, 4H, 4 × NCOOCHPh), 4.73–4.40 (m, 14H, H-5, H-5′, 12 × CHPh), 4.25 (dd, 1H, J = 5.3 Hz, J = 7.3 Hz, H-4′), 4.13 (m, 2H, H-3, H-4), 4.04 (dd, 1H, J = 2.8 Hz, J = 7.3 Hz, H-3′), 3.99 (app. dd, 1H, J = 2.0 Hz, J = 8.0 Hz, H-2), 3.94–3.86 (m, 2H, H-1, H-2′), 3.84–3.70 (m, 5H, H-1′, H-6a, H-6′a, H-7a, H-7′a), 3.61 (dd, 1H, J = 5.5 Hz, J = 8.8 Hz, H-6′b), 3.51 (dd, 1H, J = 5.5 Hz, J = 8.9 Hz, H-6b), 3.39 (s, 1H, OH-1), 3.28 (dd, 1H, J = 10.3 Hz, J = 13.8 Hz, H-7′b), 3.27 (dd, 1H, J = 10.2 Hz, J = 13.9 Hz, H-7b), 2.72 (s, 2H, OH-1′, OH-2), 2.44 (d, 1H, J = 9.1 Hz, OH-2′); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 155.97, 155.61 (2 × C=O), 138.18, 138.09, 138.04, 137.69, 137.63, 137.57, 136.76, 136.47 (C_{ipso}), 128.48–127.45 (40 × aromatic C), 78.54, 78.26 (C-3′, C-3), 74.93, 74.82 (C-2′, C-2), 74.59, 74.33 (C-4, C-4′), 74.16, 74.10, 73.91, 73.86, 73.11, 73.00 (6 × CH_2Ph), 72.21, 71.02 (C-1, C-1′), 67.64, 67.19 (C-6, C-6′), 67.33, 67.06 (2 × NCOOCH_2Ph), 54.10, 53.84 (C-5′, C-5), 44.58, 44.40 (C-7, C-7′); m/z (CI, CH_4): 598 (M + H$^+$, 100%); HRMS (CI, CH_4): Calcd for $C_{36}H_{40}O_7N$ (M + H$^+$): 598.2805, Found 598.2800.

Compound 31. $[a]_D$ +15 (c = 1 in $CHCl_3$);^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.39–7.26 (m, 40H, 8 × Ph), 5.26–5.13 (m, 4H, 4 × NCOOCHPh), 4.75–4.48 (m, 14H, H-5, H-5′, 12 × CHPh), 4.23 (app. t, 1H, J = 4.8 Hz, H-4′), 4.15 (app. t, 1H, J = 4.6 Hz, H-4), 4.07 (m, 1H, H-7′a), 4.04 (m, 1H, H-7a), 3.93–3.73 (m, 10H, H-1, H-1′, H-2, H-2′, H-3, H-3′, H-6a, H-6′a, H-6′b, H-7b), 3.69 (m, 1H, H-7′b), 3.60 (m, 2H, H-6b, OH), 3.22 (s, 1H, OH), 2.77 (d, 1H, J = 6.1 Hz, OH), 1.85 (s, 1H, OH); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 157.48, 156.18 (2 × C=O), 137.95, 137.76, 137.28, 136.91, 136.52, 136.27 (C_{ipso}), 128.54–127.57 (40 × aromatic C), 79.06, 78.94 (C-3, C-3′), 77.99, 77.89 (C-4, C-4′), 75.14, 74.18 (C-1, C-1′), 74.46, 74.33 (2 × CH_2Ph), 73.82, 72.88 (C-2, C-2′), 73.29, 73.12, 73.09, 72.95 (4 × CH_2Ph), 67.75, 67.39 (2 × NCOOCH_2Ph), 66.93, 66.37 (C-6, C-6′), 54.73, 54.68 (C-5′, C-5), 45.58, 44.62 (C-7, C-7′); m/z (CI, NH_3): 598 (M + H$^+$, 100%), 615 (M + NH_4^+, 20%); HRMS (CI, CH_4): Calcd for $C_{36}H_{40}O_7N$ (M + H$^+$): 598.2805, Found 598.2803.

Typical procedure for hydrogenolysis

Compound **10** (20 mg, 0.034 mmol) was dissolved in CH_3OH (2 mL) and a 1 M HCl aq. solution (0.08 mL) was added followed by 10% Pd/C (20 mg). The suspension was hydrogenated for 16 h, filtered through a 0.45 μM rotilabo® filter eluted with CH_3OH and concentrated to afford the corresponding polyhydroxylated azepane **14** as an oil.

Compound 14. $[a]_D$ +4 (c = 0.6 in CH_3OH);^{1}H NMR (D_2O, 400 MHz): δ 4.31 (ddd, 1H, J = 2.0 Hz, J = 2.7 Hz, J = 9.3 Hz, H-2), 4.02 (dd, 1H, J = 3.9 Hz, J = 12.2 Hz, H-6a), 3.93 (t, 1H, J = 7.5 Hz, H-4), 3.88 (dd, 1H, J = 2.0 Hz, J = 7.5 Hz, H-3), 3.84 (dd, 1H, J = 7.5 Hz, J = 12.2 Hz, H-6b), 3.53 (ddd, 1H, J = 5.3 Hz, J = 7.7 Hz, J = 13.5 Hz, H-7a), 3.35 (ddd, 1H, J = 3.9 Hz, J = 7.5 Hz, J = 7.5 Hz, H-5), 3.22 (ddd, 1H, J = 5.0 Hz, J = 7.7 Hz, J = 13.5 Hz, H-7b), 2.24 (dddd, 1H, J = 5.3 Hz, J = 7.5 Hz, J = 9.3 Hz, J = 15.5 Hz, H-1a), 2.07 (dddd, 1H, J = 2.8 Hz, J = 5.0 Hz, J = 7.7 Hz, J = 15.5 Hz, H-1b); ^{13}C NMR (D_2O, 100 MHz): δ 77.04 (C-3), 68.41 (C-4), 68.30 (C-2), 62.24 (C-5), 60.27 (C-6), 42.35 (C-7), 26.45 (C-1); m/z (CI, NH_3): 178 (M + H$^+$, 100%); HRMS (CI, NH_3): Calcd for $C_7H_{16}O_4N$ (M + H$^+$): 178.1079, Found 178.1074.

Compound 15. $[a]_D$ +5 (c = 0.45 in CH_3OH);^{1}H NMR (D_2O, 400 MHz): δ 4.36 (app. tt, 1H, J = 4.7 Hz, J = 9.3 Hz, H-1), 4.06 (dd, 1H, J = 3.6 Hz, J = 12.3 Hz, H-6a), 3.86 (dd, 1H, J = 7.5 Hz, J = 12.3 Hz, H-6b), 3.84 (ddd, 1H, J = 2.9 Hz, J = 8.7 Hz, J = 9.2 Hz, H-3), 3.71 (t, 1H, J = 8.7 Hz, H-4), 3.42 (dd, 1H, J = 4.7 Hz, J = 14.3 Hz, H-7a), 3.37 (dd, 1H, J = 4.2 Hz, J = 14.3 Hz, H-7b), 3.26 (ddd, 1H, J = 3.6 Hz, J = 7.5 Hz, J = 8.8 Hz, H-5), 2.37 (ddd, 1H, J = 2.9 Hz, J = 5.1 Hz, J = 14.8 Hz, H-2a), 1.94 (dt, 1H, J = 9.3 Hz, J = 14.8 Hz, H-2b); ^{13}C NMR (D_2O, 100 MHz): δ 72.39 (C-4), 70.49 (C-3), 63.35 (C-1), 62.76 (C-5), 59.96 (C-6), 51.84 (C-7), 37.08 (C-2); m/z (CI, NH_3): 178 (M + H$^+$, 100%); HRMS (CI, NH_3): Calcd for $C_7H_{16}O_4N$ (M + H$^+$): 178.1079, Found 178.1082.

Compound 16. $[a]_D$ +20 (c = 1 in CH_3OH);^{1}H NMR (D_2O, 400 MHz): δ 3.99 (dd, 1H, J = 3.8 Hz, J = 12.5 Hz, H-6a), 3.93 (dd, 1H, J = 6.3 Hz, J = 12.5 Hz, H-6b), 3.80 (ddd, 1H, J = 3.4 Hz, J = 7.6 Hz, J = 9.3 Hz, H-2), 3.75 (dd, 1H, J = 8.4 Hz, J = 9.4 Hz, H-4), 3.58 (t, 1H, J = 8.1 Hz, H-3), 3.50 (ddd, 1H, J = 3.8 Hz, J = 6.3 Hz, J = 9.4 Hz, H-5), 3.42 (ddd, 1H, J = 3.7 Hz, J = 6.6 Hz, J = 13.9 Hz, H-7a), 3.31 (ddd, 1H, J = 3.6 Hz, J = 9.6 Hz, J = 13.9 Hz, H-7b), 2.14 (ddt, 1H, J = 3.6 Hz, J = 6.6 Hz, J = 15.8 Hz, H-1a), 2.06 (dddd, 1H, J = 3.7 Hz, J = 9.5 Hz, J = 9.5 Hz, J = 15.8 Hz, H-1b); ^{13}C NMR (D_2O, 100 MHz): δ 78.87 (C-3), 71.33 (C-2), 69.28 (C-4), 59.15 (C-6), 58.56 (C-5), 40.76 (C-7), 27.86 (C-1); m/z (CI, NH_3): 178 (M + H$^+$, 100%); HRMS (CI, NH_3): Calcd for $C_7H_{16}O_4N$ (M + H$^+$): 178.1079, Found 178.1074.

Compound 17. $[a]_D$ +17 (c = 0.6 in CH_3OH);^{1}H NMR (D_2O, 400 MHz): δ 4.37 (app. tt, 1H, J = 3.4 Hz, J = 6.5 Hz, H-1), 4.06 (ddd, 1H, J = 2.6 Hz, J = 8.5 Hz, J = 9.9 Hz, 1H, H-3), 4.04 (dd, 1H, J = 3.6 Hz, J = 12.5 Hz, H-6a), 3.89 (dd, 1H, J = 7.6 Hz, J = 12.5 Hz, H-6b), 3.67 (t, 1H, J = 8.3 Hz, H-4), 3.51 (dd, 1H, J = 3.5 Hz, J = 13.9 Hz, H-7a), 3.41 (ddd, 1H, J = 3.7 Hz, J = 7.8 Hz, J = 7.8 Hz, H-5), 3.19 (dd, 1H, J = 6.6 Hz, J = 13.9 Hz, H-7b), 2.27 (ddd, 1H, J = 2.7 Hz, J = 6.3 Hz, J = 14.9 Hz, H-2a), 1.98 (ddd, 1H, J = 3.2 Hz, J = 9.9 Hz, J = 14.9 Hz, H-2b); ^{13}C NMR (D_2O, 100 MHz): δ 71.66 (C-4), 68.24 (C-3), 62.46 (C-1), 61.87 (C-5), 59.61 (C-6), 49.21 (C-7), 37.71 (C-2); m/z (CI, NH_3): 178 (M + H$^+$, 100%); HRMS (CI, NH_3): Calcd for $C_7H_{16}O_4N$ (M + H$^+$): 178.1079, Found 178.1076.

Compound 22. $[a]_D$ −1 (c = 0.65 in CH_3OH);^{1}H NMR (D_2O, 400 MHz): δ 4.09–4.05 (m, 2H, H-2, H-3), 3.97 (d, 1H, J = 4.9 Hz, H-4), 3.87–3.71 (m, 3H, H-5, H-6a, H-6b), 3.40 (dt, 1H, J = 4.6 Hz, J = 13.6 Hz, H-7a), 3.33 (ddd, 1H, J = 3.6 Hz, J = 10.8 Hz, J = 13.6 Hz, H-7b), 2.30 (dddd, 1H, J = 4.4 Hz, J = 10.8 Hz, J = 10.8 Hz, J = 15.4 Hz, H-1a), 1.87 (m, 1H, H-1b); ^{13}C NMR (D_2O, 100 MHz): δ 72.58 (C-3), 69.46 (C-2), 67.92 (C-4), 60.97 (C-6),

54.78 (C-5), 41.81 (C-7), 25.56 (C-1); *m/z* (CI, NH_3): 178 ($M + H^+$, 100%); HRMS (CI, NH_3): Calcd for $C_7H_{16}O_4N$ ($M + H^+$): 178.1079, Found 178.1077.

Compound 23. $[a]_D$ −13 ($c = 1$ in CH_3OH);^{1}H NMR (D_2O, 400 MHz): δ 4.34 (tt, 1H, $J = 3.0$ Hz, $J = 8.7$ Hz, H-1), 4.12 (ddd, 1H, $J = 4.4$ Hz, $J = 5.5$ Hz, $J = 6.7$ Hz, H-3), 4.01 (d, 1H, $J = 4.4$ Hz, H-4), 3.88 (dd, 1H, $J = 8.9$ Hz, $J = 15.6$ Hz, H-6a), 3.79 (dd, 1H, $J = 8.7$ Hz, $J = 15.6$ Hz, H-6b), 3.78 (ddd, 1H, $J = 0.6$ Hz, $J = 8.8$ Hz, $J = 8.8$ Hz, H-5), 3.50 (ddd, 1H, $J = 1.1$ Hz, $J = 3.0$ Hz, $J = 13.2$ Hz, H-7a), 3.18 (dd, 1H, $J = 8.7$ Hz, $J = 13.2$ Hz, H-7b), 2.38 (dddd, 1H, $J = 1.1$ Hz, $J = 3.0$ Hz, $J = 5.5$ Hz, $J = 15.0$ Hz, H-2a), 2.00 (ddd, 1H, $J = 6.8$ Hz, $J = 8.7$ Hz, $J = 15.0$ Hz, H-2b); ^{13}C NMR (D_2O, 100 MHz): δ 70.80 (C-4), 69.83 (C-3), 64.05 (C-1), 60.80 (C-6), 58.34 (C-5), 51.57 (C-7), 38.91 (C-2); *m/z* (CI, NH_3): 178 ($M + H^+$, 100%); HRMS (CI, NH_3): Calcd for $C_7H_{16}O_4N$ ($M + H^+$): 178.1079, Found 178.1074.

Compound 24. $[a]_D$ +4 ($c = 1$ in CH_3OH);^{1}H NMR (D_2O, 400 MHz): δ 4.37 (m, 1H, H-1), 4.11 (ddd, 1H, $J = 3.0$ Hz, $J = 5.3$ Hz, $J = 5.3$ Hz, H-3), 3.97 (d, 1H, $J = 4.9$ Hz, H-4), 3.84 (dd, 1H, $J = 5.3$ Hz, $J = 11.9$ Hz, H-6a), 3.79 (dd, 1H, $J = 8.8$ Hz, $J = 11.9$ Hz, H-6b), 3.62 (ddd, 1H, $J = 0.6$ Hz, $J = 5.3$ Hz, $J = 8.8$ Hz, H-5), 3.47 (dd, 1H, $J = 4.2$ Hz, $J = 13.3$ Hz, H-7a), 3.28 (dd, 1H, $J = 7.8$ Hz, $J = 13.3$ Hz, H-7b), 2.22 (ddd, 1H, $J = 2.9$ Hz, $J = 9.4$ Hz, $J = 15.0$ Hz, H-2a), 2.13 (ddd, 1H, $J = 3.0$ Hz, $J = 5.6$ Hz, $J = 15.0$ Hz, H-2b); ^{13}C NMR (D_2O, 100 MHz): δ 69.74 (C-4), 68.00 (C-3), 61.91 (C-1), 60.77 (C-6), 57.98 (C-5), 51.47 (C-7), 37.27 (C-2); *m/z* (CI, NH_3): 178 ($M + H^+$, 100%); HRMS (CI, NH_3): Calcd for $C_7H_{16}O_4N$ ($M + H^+$): 178.1079, Found 178.1081.

Compound 25. $[a]_D$ −18 ($c = 0.5$ in CH_3OH);^{1}H NMR (D_2O, 400 MHz): δ 3.89 (d, 1H, $J = 2.8$ Hz, H-4), 3.88 (ddd, 1H, $J = 1.8$ Hz, $J = 6.5$ Hz, $J = 10.1$ Hz, H-2), 3.82 (dd, 1H, $J = 5.3$ Hz, $J = 11.8$ Hz, H-6a), 3.79 (dd, 1H, $J = 2.8$ Hz, $J = 6.5$ Hz, H-3), 3.73 (dd, 1H, $J = 8.9$ Hz, $J = 11.8$ Hz, H-6b), 3.53 (ddd, 1H, $J = 2.6$ Hz, $J = 6.4$ Hz, $J = 13.6$ Hz, H-7a), 3.50 (dd, 1H, $J = 5.3$ Hz, $J = 8.9$ Hz, H-5), 3.18 (ddd, 1H, $J = 2.2$ Hz, $J = 11.1$ Hz, $J = 13.6$ Hz, H-7b), 2.17 (dddd, 1H, $J = 2.5$ Hz, $J = 10.8$ Hz, $J = 10.8$ Hz, $J = 15.6$ Hz, H-1a), 1.90 (ddt, 1H, $J = 2.1$ Hz, $J = 6.4$ Hz, $J = 15.6$ Hz, H-1b); ^{13}C NMR (D_2O, 100 MHz): δ 77.80 (C-3), 74.57 (C-2), 69.79 (C-4), 61.15 (C-6), 57.84 (C-5), 44.12 (C-7), 28.47 (C-1); *m/z* (CI, NH_3): 178 ($M + H^+$, 100%); HRMS (CI, NH_3): Calcd for $C_7H_{16}O_4N$ ($M + H^+$): 178.1079, Found 178.1077.

Compound 28. $[a]_D$ +15 ($c = 1$ in CH_3OH);^{1}H NMR (D_2O, 400 MHz): δ 4.16 (ddd, 1H, $J = 3.6$ Hz, $J = 7.2$ Hz, $J = 7.2$ Hz, H-1), 4.09 (dd, 1H, $J = 1.7$ Hz, $J = 7.2$ Hz, H-2), 4.07 (dd, 1H, $J = 1.7$ Hz, $J = 8.6$ Hz, H-3), 3.98 (dd, 1H, $J = 4.0$ Hz, $J = 12.4$ Hz, H-6a), 3.96 (t, 1H, $J = 7.5$ Hz, H-4), 3.81 (dd, 1H, $J = 8.2$ Hz, $J = 12.4$ Hz, H-6b), 3.54 (dd, 1H, $J = 3.6$ Hz, $J = 14.1$ Hz, H-7a), 3.37 (ddd, 1H, $J = 4.0$ Hz, $J = 6.8$ Hz, $J = 8.2$ Hz, H-5), 3.15 (dd, 1H, $J = 7.2$ Hz, $J = 14.1$ Hz, H-7b); ^{13}C NMR (D_2O, 100 MHz): δ 72.48 (C-2), 72.23 (C-3), 66.76 (C-1), 66.56 (C-4), 62.89 (C-5), 60.16 (C-6), 45.96 (C-7); *m/z* (CI, NH_3): 194 ($M + H^+$, 100%); HRMS (CI, NH_3): Calcd for $C_7H_{16}O_5N$ ($M + H^+$): 194.1028, Found 194.1026.

Compound 29. $[a]_D$ +17 ($c = 0.62$ in CH_3OH);^{1}H NMR (D_2O, 400 MHz): δ 4.09 (ddd, 1H, $J = 3.2$ Hz, $J = 6.2$ Hz, $J = 6.2$ Hz, H-1), 4.04 (dd, 1H, $J = 3.7$ Hz, $J = 12.5$ Hz, H-6a), 3.89 (dd, 1H, $J = 7.3$ Hz, $J = 12.5$ Hz, H-6b), 3.87 (t, 1H, $J = 9.1$ Hz, H-4), 3.74 (t, 1H, $J = 6.9$ Hz, H-2), 3.67 (dd, 1H, $J = 6.9$ Hz, $J = 8.8$ Hz, H-3), 3.43 (dd, 1H, $J = 3.2$ Hz, $J = 14.1$ Hz, H-7a), 3.39 (dd, 1H, $J = 6.2$ Hz, $J = 14.1$ Hz, H-7b), 3.37 (ddd, 1H, $J = 3.7$ Hz, $J = 7.3$ Hz, $J = 9.4$ Hz, H-5); ^{13}C NMR (D_2O, 100 MHz): δ 76.04 (C-3), 75.57 (C-2), 68.81 (C-4), 67.95 (C-1), 60.93 (C-5), 59.36 (C-6), 46.34 (C-7); *m/z* (CI, NH_3): 194 ($M + H^+$, 100%); HRMS (CI, NH_3): Calcd for $C_7H_{16}O_5N$ ($M + H^+$): 194.1028, Found 194.1029.

Compound 32. $[a]_D$ +1 ($c = 1$ in CH_3OH);^{1}H NMR (D_2O, 400 MHz): δ 4.16 (dd, 1H, $J = 2.3$ Hz, $J = 6.2$ Hz, H-3), 4.10 (ddd, 1H, $J = 3.6$ Hz, $J = 6.5$ Hz, $J = 8.2$ Hz, H-1), 4.07 (dd, 1H, $J = 1.8$ Hz, $J = 6.2$ Hz, H-4), 3.98 (dd, 1H, $J = 2.3$ Hz, $J = 8.2$ Hz, H-2), 3.84 (dd, 1H, $J = 5.3$ Hz, $J = 12.1$ Hz, H-6a), 3.79 (dd, 1H, $J = 8.6$ Hz, $J = 12.1$ Hz, H-6b), 3.64 (ddd, 1H, $J = 1.8$ Hz, $J = 5.3$ Hz, $J = 8.6$ Hz, H-5), 3.45 (dd, 1H, $J = 3.6$ Hz, $J = 13.9$ Hz, H-7a), 3.35 (dd, 1H, $J = 6.5$ Hz, $J = 13.9$ Hz, H-7b); ^{13}C NMR (D_2O, 100 MHz): δ 73.03 (C-2), 72.30 (C-3), 68.02 (C-4), 66.55 (C-1), 60.36 (C-6), 58.59 (C-5), 48.79 (C-7); *m/z* (CI, NH_3): 194 ($M + H^+$, 100%); HRMS (CI, NH_3): Calcd for $C_7H_{16}O_5N$ ($M + H^+$): 194.1028, Found 194.1030.

Compound 33. $[a]_D$ −19 ($c = 1$ in CH_3OH);^{1}H NMR (D_2O, 400 MHz): δ 4.18 (ddd, 1H, $J = 2.4$ Hz, $J = 8.7$ Hz, $J = 10.0$ Hz, H-1), 3.99 (d, 1H, $J = 4.6$ Hz, H-4), 3.93 (app. t, 1H, $J = 4.6$ Hz, H-3), 3.82 (dd, 1H, $J = 5.2$ Hz, $J = 11.9$ Hz, H-6a), 3.75 (dd, 1H, $J = 8.8$ Hz, $J = 11.9$ Hz, H-6b), 3.68 (dd, 1H, $J = 4.6$ Hz, $J = 8.7$ Hz, H-2), 3.58 (dd, 1H, $J = 5.2$ Hz, $J = 8.8$ Hz, H-5), 3.46 (dd, 1H, $J = 2.4$ Hz, $J = 13.6$ Hz, H-7a), 3.16 (dd, 1H, $J = 10.0$ Hz, $J = 13.6$ Hz, H-7b); ^{13}C NMR (D_2O, 100 MHz): δ 79.09 (C-2), 75.58 (C-3), 69.00 (C-4), 67.61 (C-1), 60.75 (C-6), 57.78 (C-5), 48.14 (C-7); *m/z* (CI, NH_3): 194 ($M + H^+$, 100%); HRMS (CI, NH_3): Calcd for $C_7H_{16}O_5N$ ($M + H^+$): 194.1028, Found 194.1026.

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