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Conduramine F-1 epoxides: synthesis and their glycosidase inhibitory activities

Robert Łysek, Sylvain Favre and Pierre Vogel*

Laboratoire de glycochimie et de synthèse asymétrique (LGSA), Ecole Polytechnique Fédérale de Lausanne (EPFL), Batochime, CH-1015 Lausanne, Switzerland

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Dedicated to Professor Marek Chmielewski on the occasion of his 65th birthday

Abstract—Starting from (±)-7-oxanorbornenone ((±)-**14**), (±)-(1*RS*,2*RS*,3*SR*,6*SR*)-6-azidocyclohex-4-en-1,2,3-triol ((±)-**24**) and (±)-(1*RS*,2*RS*,3*SR*,6*RS*)-6-azidocyclohex-4-en-1,2,3-triol ((±)-**26**) were obtained. Epoxidation of the latter cyclohexene derivative gave two epoxides (±)-**30** and (±)-**31** that were converted into (±)-conduramine F-1 epoxides (±)-**10** and (±)-**11** and *N*-substituted derivatives (±)-**12** and (±)-**13**. Compound (±)-(1*RS*,2*SR*,3*RS*,4*SR*,5*RS*,6*SR*)-5-({[4-(trifluoromethyl)phenyl]methyl}amino)-7-oxabicyclo[4.1.0]-heptane-2,3,4-triol ((±)-**12c**) is a good, non-competitive inhibitor of β-xylosidase from *Aspergillus niger* (K_i=2.2 μM), and (±)-(1*RS*,2*RS*,3*SR*,4*RS*,5*SR*,6*SR*)-5-{[(biphenyl-4-yl)methyl]amino}-7-oxabicyclo[4.1.0]heptane-2,3,4-triol ((±)-**13d**) is a good inhibitor of α-glucosidase from brewer's yeast (K_i=2.8 μM, non-competitive).

1. Introduction

Oligosaccharides were first recognized as biologically important for their role in metabolism and energy storage. More recently, it became clear that complex oligosaccharides also regulate a large number of additional biological processes. Most important are the oligosaccharides formed on the surfaces of cells and their role in protein and glycoprotein conformations. The cell-surface oligosaccharides are the 'words' used by cells to communicate with the outer world.[1–4] They guide the social behavior of cells with their environment including cell/cell interactions and cell/invader interactions.[5] Glycosidation and deglycosidation of proteins contribute to their folding,[6] their fate, and cell localization.[7]

Targeting glycosyltransferases and glycosidases, the enzymes intervening in the biosynthesis of the glycoproteins, has led to a better understanding of cell functions.[8] Glycosidase inhibitors arouse great interest as potential therapeutic agents for the treatment of diabetes,[9] obesity,[9] viruses,[10] cancer,[11] and genetic disorders.[12] Inhibitors of α-D-glucosidase such as Miglitol (*N*-(2-hydroxyethyl-1-deoxynojirimycin: Glyset®, Diastabol®) have found application in type II (non-insulino-dependent mellitus) diabetes,[13] and Miglustat (*N*-butyl-1-deoxynojirimycin: Zavesca®) in Gaucher's disease.[14] Acarbose (**1**: Glucor®, Precose®, Glucobay®) is a mimic of the non-reductive tetrasaccharide end of amylase[15] that contains valienamine **2** (Fig. 1).[16] It has shown long-term efficacy and tolerability in patients with type II diabetes.[17] It has been approved in medications as adjunct therapy for weight loss in patients with obesity.[18] Inhibitors of α-D-glucosidases and α-L-fucosidases have manifested moderate in vitro anti-HIV activities.[19] Selective inhibitors of influenza neuraminidase have been developed into effective drugs against influenza.[20] Zanamivir (Relenza®, GG167)[21] (from GlaxoSmithKline and Biota) and Oseltamivir Phosphate (GS4104, Tamiflu®, Ro 64-0796/002)[22] (from Gilead Sciences and Hoffman La Roche) play dominant roles in this fight. Tamiflu® is foreseen to be used in the event of an influenza pandemic[23].

Norvalienamine (*ent*-conduramine F-1) ((+)-**3**)[24] is almost as active as valienamine **2** in inhibiting α-glucosidase from yeast (IC_{50} (**2**)=170 μM, IC_{50} ((+)-**3**)=250 μM).[25] The inhibitory activity and selectivity toward this enzyme both are enhanced upon N-benzylation[25,26] of **2** and (+)-**3**. Glycosidase inhibitory activities of 2-(aminomethyl)pyrrolidine-3,4-diols (α-mannosidase inhibitors[27]) and conduramines B-1 (β-glucosidase inhibitors[28]) are also significantly improved upon N-benzylation.[29] Cyclophellitol (**4**)[30] and 1,6-*epi*-cyclophellitol (**5**)[31] are inhibitors of β-glucosidase from almond (IC_{50}=5 μM) and α-glucosidase from yeast (IC_{50}=64 μM), respectively[32] (Fig. 2).

Keywords: Azidocyclohexenetriols; Aminoconduritol epoxides; Mitsunobu azidation; α-Glucosidase; β-Xylosidase inhibitor.
* Corresponding author. Tel.: +41 21 693 93 71; fax: +41 21 693 93 75; e-mail: pierre.vogel@epfl.ch

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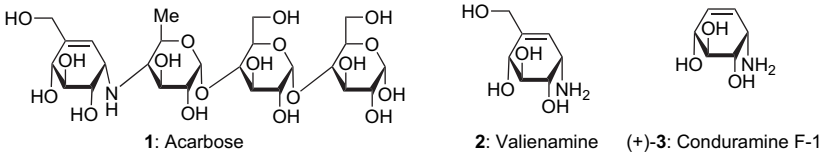


Figure 1. Examples of medically useful glycosidase inhibitors.

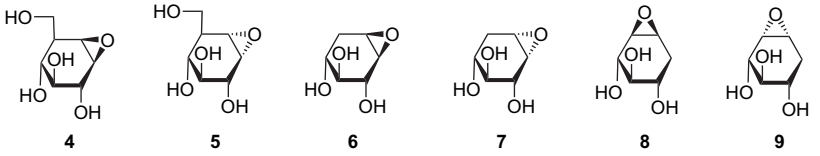


Figure 2. Examples of epoxides derived from carbasugars.

The simpler analogs **6** and **7** have been made by the Ogawa's group,[33] whereas **8** and **9** have not been described yet. No data have been reported for the inhibitory activities of **6** and **7** toward α- or β-glucosidase. Nevertheless, **6** (not **7**) was found to be a good inhibitor of glucocerebrosidase (IC_{50}=0.96 μM).[33] As *N*-benzyl derivatives of (+)-**3** were found to be selective and potent inhibitors of α-glucosidase from brewer's yeast, an enzyme presenting high functional analogy with the glycoprotein processing α-glucosidase I,[34] we embarked in the synthesis of the yet unknown racemic conduramine F-1 epoxides **10**, **11** and their *N*-benzylated derivatives **12**, **13**. Because there are two carboxylic groups (usually aspartate or glutamate residues) in the active site of the inverting α-glucosidases,[35] which imply nucleophilic assistance,[36] we hoped that **10**–**13** might represent interesting inhibitors of these enzymes. Indeed, we envisioned that while one of the two carboxylic groups of the α-glucosidases protonates the amino moieties of **10** and **12**, the second carboxylic group would bind with the epoxy ring through hydrogen bridging. In the case of **11** and **13**, the second carboxylic group would interact with the inhibitor in the form of its carboxylate anion, mainly in an attractive electrostatic interaction with the electrophilic oxirane ring. As we shall see, both amino epoxides (±)-**10** and (±)-**11** are poor inhibitors of glycosidases, but some of their *N*-benzylated derivatives (±)-**12** and (±)-**13** are much more interesting inhibitors (Fig. 3).

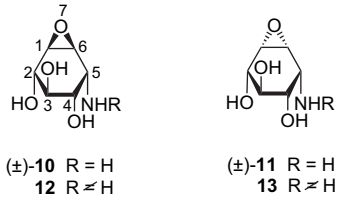
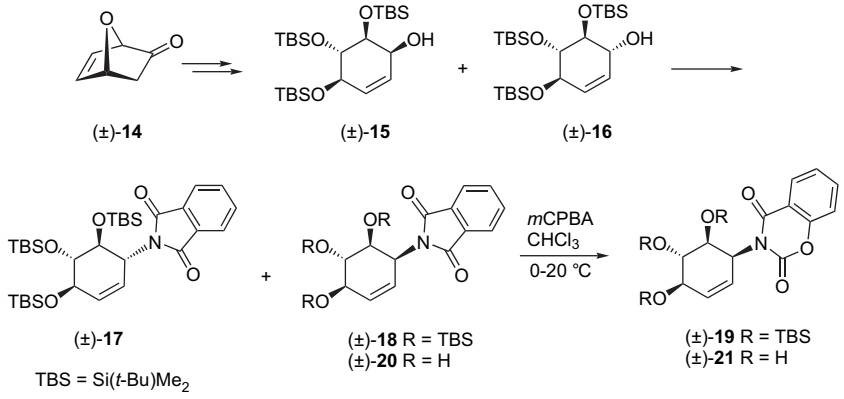


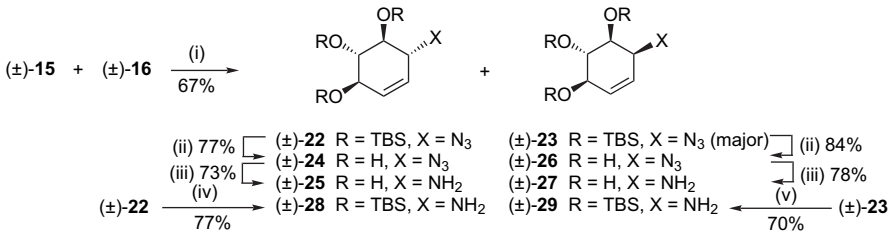
Figure 3.

2. Results and discussion

The synthesis of our targeted compounds relies on the 'naked sugar' methodology developed by our group.[37] Our studies started with racemic 7-oxanorbornenone ((±)-**14**), which was converted into a 1:5.1 mixture of semi protected conduritols (±)-**15** and (±)-**16**[38] that reacted under Mitsunobu conditions with phthalimide to produce a separable 1:2.5 mixture of protected conduramines (±)-**17** and (±)-**18**.[25] Attempts to epoxidize the alkene moiety of (±)-**18** with *m*CPBA (metachloroperbenzoic acid) in $CHCl_3$ led to a complex mixture containing the product of Baeyer–Villiger oxidation (±)-**19**. Similarly, treatment of the desilylated conduramine derivative (±)-**20** with *m*CPBA (AcOH/$CHCl_3$, 20 °C, 2 days) did not give the expected epoxides but a complex mixture also containing a product of Baeyer–Villiger rearrangement (±)-**21** (Scheme 1).



Scheme 1. Attempted epoxidations.

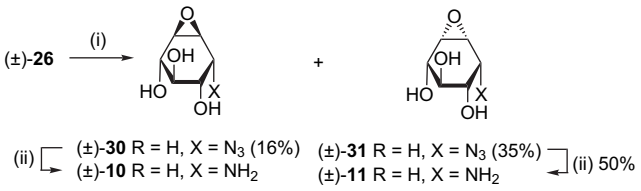


Scheme 2. Synthesis of (±)-conduramine B-1 and (±)-conduramine F-1 and derivatives. Reagents and conditions: (i) DPPA, DEAD, PhMe, −10 to 5 °C; (ii) (1) TBAF·3H_2O, rt; (2) AcOH, rt; (iii) (1) PPh_3; (2) NH_3/MeOH; (iv) H_2/Lindlar catalyst, EtOH; (v) (1) PPh_3/THF; (2) 2 N NaOH.

We thus decided to modify our synthesis of conduramines F-1[25] and explored the reaction of the 1:5.1 mixture of (±)-**15** and (±)-**16** with diphenylphosphoryl azide (DPPA) in the presence of diethyl azodicarboxylate (DEAD) and PPh_3.[39] We found the conditions under which a 1:2.5 mixture of azides (±)-**22** and (±)-**23** was obtained in 67% yield. The two azides were separated readily by column chromatography on silica gel (Scheme 2).

Desilylation of (±)-**22** with $Bu_4NF·3H_2O$ and work-up with AcOH gave (±)-**24** (77%), the reduction of which with PPh_3 and work-up with NH_3/MeOH[40] provided the known (±)-conduramine B-1 ((±)-**25**)[28,29,41] in 73% yield. The same reaction sequence applied to (±)-**23** gave first (±)-**26** (84%) and then conduramine F-1 ((±)-**27**)[25] in 78% yield. Its spectral data were identical to those reported for this compound.[25] Selective reduction of azide (±)-**22** with hydrogen in the presence of Lindlar's catalyst[42] in EtOH gave (±)-**28** (77%). Reduction of azide (±)-**23** with PPh_3/THF and work-up with 2 N aqueous NaOH gave (±)-**29** (70%).

Probably because of the bulk of the silyl ether groups of (±)-**23**, its reaction with *m*CPBA failed to provide the desired epoxides. Treatment of azidotriol (±)-**26** with *m*CPBA in excess in 4:1 AcOH/$CHCl_3$ gave a separable ~1:2 mixture of epoxides (±)-**30** (16%) and (±)-**31** (35%) (Scheme 3). The structures of these compounds were deduced from their spectral data and confirmed by single crystal diffraction studies of (±)-**30** (Fig. 4).



Scheme 3. Synthesis of (±)-conduramine F-1 epoxides. Reagents and conditions: (i) *m*CPBA, AcOH/$CHCl_3$, rt, 4 days; (ii) H_2/10% Pd/C, MeOH/EtOAc (1:2), 20 °C, 3.5 h.

Reduction of (±)-**31** with H_2/Pd/C in MeOH/AcOEt gave the desired conduramine F-1 epoxide (±)-**11** in 50% yield only. With other reducing agents such as SmI_2,[43] *N*,*N*-dimethylhydrazine in the presence of $FeCl_3$,[44] $NaBH_4$,[45] thiols,[46] the Staudinger reduction,[40] or with $LiAlH_4$ in THF[47] the yields were poorer. The diastereoselectivity of the epoxidation of (±)-**26** in favor of (±)-**31** can be explained by involving a lateral control by the allylic hydroxy group.[48]

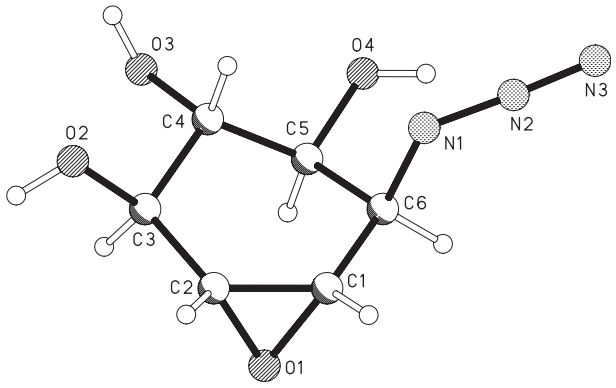
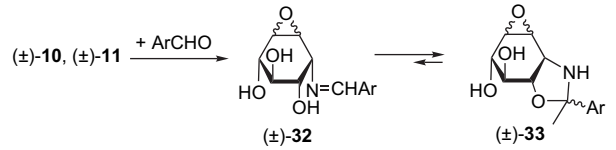


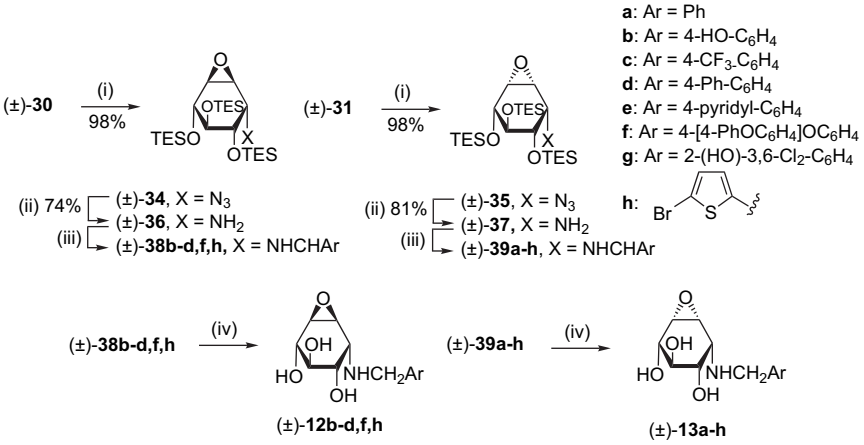
Figure 4. Molecular structure of (±)-**30** by single crystal X-ray diffraction studies.

Attempts to carry out reductive amination of aromatic aldehydes with (±)-**10** and (±)-**11** failed as the corresponding imines (±)-**32** equilibrated with the corresponding stable oxazolidines (±)-**33** (by ^1H NMR studies) (Scheme 4), the latter resisting reduction with $NaBH_4$ or $NaB(CN)H_3$ in AcOH/THF/H_2O.[25] We thus protected triols (±)-**30** and (±)-**31** as their tris(triethylsilyl)ethers (±)-**34** (98%) and (±)-**35** (98%) by treatment with Et_3SiCl/imidazole in DMF. Catalytic hydrogenation (Pd/C) of azides (±)-**34** and (±)-**35** gave primary amines (±)-**36** (74%) and (±)-**37** (81%), respectively (Scheme 5). Desilylation of these compounds furnished (±)-**10** (85%) and (±)-**11** (95%). The structures of the conduramine F-1 epoxides were given by their mode of formation and confirmed by their spectral data, especially the COSY-45 and 2D-HMQC spectra.



Scheme 4. Competitive oxazolidine formation.

N-Benzylation of the triethylsilyl protected conduramine F-1 epoxides (±)-**36** with five different aromatic aldehydes **b**–**d**,**f**,**h** under standard conditions ($NaBH(OAc)_3$, $ClCH_2CH_2Cl$, 20 °C, 3–5 h) generated the corresponding benzylated amines (±)-**38b**–**d**,**f**,**h**. Subsequent desilylation (AcOH/THF/H_2O) furnished the conduramine F-1 epoxide derivatives (±)-**12b**–**d**,**f**,**h** that were purified by column chromatography on silica gel. Similarly, N-benzylation of (±)-**37** with eight aldehydes **a**–**h** furnished (±)-**39a**–**h** that were desilylated into (±)-**13a**–**h** (Scheme 5).



Scheme 5. Synthesis of *N*-benzylated derivatives of conduramine F-1 epoxides. Reagents and conditions: (i) Et_3SiCl, imidazole, DMF, 20 °C, 15 h (98% yield); (ii) H_2/10% Pd/C, MeOH/EtOAc (1:2), 20 °C, 3.5 h; (iii) ArCHO, $NaBH(OAc)_3$ (1.4 equiv), $ClCH_2CH_2Cl$, 20 °C, 2–5 h; (iv) AcOH/THF/H_2O (3:4:3), 20 °C, 5–10 h. Overall yields for two last steps: **12b** (33%), **12c** (59%),**12f** (48%), **12h** (41%), **13a** (72%), **13b** (60%), **13c** (70%), **13d** (62%), **13e** (51%), **13f** (76%), **13g** (46%), **13h** (44%).

3. Enzyme inhibitory assays

Apart from (±)-**12d**, (±)-**12f**, (±)-**12h**, (±)-**13f**, and (±)-**13h** that were little soluble in H_2O (with up to 20% of MeOH or DMSO), all our conduramines F-1 epoxides (±)-**10**, (±)-**11** and their *N*-substituted derivatives (±)-**12b**, (±)-**12c**, (±)-**13a**, (±)-**13b**, (±)-**13c**, and (±)-**13d** have been assayed for their inhibitory activities toward 14 commercially available glycosidase inhibitors, under standard conditions.[49] At 1 mM concentration and optimal pH of the enzymes, none of these amines did inhibit α-galactosidase from coffee beans (EC 3.2.1.22), β-galactosidase from *Escherichia coli* and *Aspergillus oryzae* (EC 3.2.1.23), α-glucosidase from rice, β-glucosidase from almonds (EC 3.2.1.21), β-mannosidase from snail (EC 3.2.1.25), β-*N*-acetylglucosaminidases (EC 3.2.1.30) from jack beans and from bovine kidney. For the other glycosidases our results are summarized in Table 1.

Table 1. Inhibitory activities of conduramine F-1 epoxide (±)-**10** and its derivatives (±)-**12b**, (±)-**12c**, and of conduramine F-1 epoxide (±)-**11** and its derivatives (±)-**13a**–**e**. Percentage of inhibition at 1 mM concentration. IC_{50} values (μM) in italics and K_i values (μM) in bold[c]

Enzyme inhibitor	α-Fuc	β-Gal	α-Glc	Amyloglu	α-Man	β-Xyl[a]
(±)-**10**	ni	ni	16	18	ni	76
(±)-**12b**[b]	ni	ni	87(*120*)	54	ni	86 (6.9) **K_i=48 (NC)**
(±)-**12c**	ni	30	40	38	46	93 (2.6) **K_i=2.2 (NC)**
(±)-**11**	ni	18	18	ni	27	ni
(±)-**13a**[b]	ni	ni	72	ni	ni	21
(±)-**13b**	ni	36	81(*136*)	16	ni	ni
(±)-**13c**	ni	ni	71	16	ni	42
(±)-**13d**	ni	61	91(*47*) **K_i=2.8 (NC)**	16	ni	42
(±)-**13e**	19	47	82(*159*)	ni	29	ni

[a] α-Fuc=α-L-fucosidase from bovine kidney (EC 3.2.1.51), β-Gal=β-D-galactosidase from bovine liver (EC 3.2.1.23), α-Glc=α-glucosidase from brewer's yeast (EC 3.2.1.20), amyloglu=amyloglucosidase from *Aspergillus niger* (EC 3.2.1.3), α-Man=α-D-mannosidase from jack beans (EC 3.2.1.24), β-Xyl=β-D-xylosidase from *A. niger* (EC 3.2.1.37).

[b] a: Ar=Ph; b: Ar=4-(HO)C_6H_4; c: Ar=4-(CF_3)C_6H_4; d: Ar=4-(Ph)C_6H_4; e: Ar=4-(4-pyridyl)phenyl.

[c] ni=no inhibition detected at 1 mM concentration; NC=non-competitive.

Contrary to our expectations, the conduramine F-1 epoxides (±)-**10** and (±)-**11** are poor inhibitors of α-glucosidase from yeast. Compound (±)-**10** is recognized by the β-xylosidase not unexpectedly, as it contains three hydroxy groups that can occupy in the enzyme active site the position of xylose. It remains unexplained why the isomeric epoxide (±)-**11** does not inhibit this enzyme. On N-substitution with 4-hydroxybenzyl and 4-(trifluoromethyl)benzyl groups both the inhibitory activities of (±)-**10** toward α-glucosidase and β-xylosidase are increased. In fact, (±)-**12c** is an excellent inhibitor of β-xylosidase from *Aspergillus niger* and a much weaker inhibitor of α-glucosidase from brewer's yeast. Interestingly, with epoxide (±)-**11** the N-substitution effect is different as it improves the inhibitory activity toward α-glucosidase more than toward β-xylosidase. Thus (±)-**13d** ((1*RS*,2*RS*,3*SR*,4*RS*,5*SR*,6*SR*)-5-[4-phenylbenzyl]-amino-7-oxabicyclo[4.1.0]heptane-2,3,4-triol) is a good inhibitor of α-glucosidase from brewer's yeast. The difference in the N-substitution effects disclosed for (±)-**10** and (±)-**11** can be attributed to the mode of inhibition, which is non-competitive in the three cases where K_i have been measured (Table 1).

4. Conclusion

The two diastereomeric conduramine F-1 epoxides (±)-**10** and (±)-**11** have been obtained as racemic mixtures starting from (±)-7-oxabicyclo[2.2.1]hept-5-en-2-one ((±)-**14**). Whereas (±)-**10** (with *trans* epoxy and amino moieties) is a moderate inhibitor of β-D-xylosidase from *A. niger*, and (±)-**11** (with *cis* epoxy and amino moieties) is a weak inhibitor of α-D-glucosidase from brewer's yeast and α-D-mannosidase from jack beans. N-Benzylation of these conduramine epoxides generates much more interesting inhibitors. For instance (+)-**12c** (*trans* epoxy and 4-$CF_3C_6H_4CH_2NH$ groups) is a good, non-competitive inhibitor of β-D-xylosidase (K_i=2.2 μM) and (+)-**13d** (*cis* epoxy and 4-Ph–$C_6H_4CH_2NH$ groups) is a good, non-competitive inhibitor of α-D-glucosidase from brewer's yeast (K_i=2.8 μM).

5. Experimental section

5.1. General comments

All commercially available reagents (Fluka, Aldrich, Acros Organics) were used without further purification. Solvents were dried by standard methods. Light petroleum ether used refers to the fraction boiling between 40–60 °C. Liquid/solid flash chromatography (FC): silica gel *60* (*Merck* no. 9385, 240–400 mesh) or neutral alumina. TLC (reaction monitoring): *Merck* silica gel 60 F_{254} plates; detection by UV light, *Pancaldi* reagent ($(NH_4)_6MoO_4$, $Ce(SO_4)_2$, H_2SO_4, H_2O), 1% $KMnO_4$ in H_2O, or 1% ninhydrin in MeOH. IR spectra: *Perkin–Elmer 1420* spectrometer, in cm^{-1}. Optical rotations: at 25 °C; *Jasco P-1020* polarimeter: $[\alpha]_D$ in 10^{-1} deg cm^2 g^{-1}. ^1H NMR spectra: *Bruker ARX-400* spectrometer (400 MHz); δ(H) in parts per million rel to the solvent's residual ^1H signal ($CDCl_3$, δ(H) 7.27; CD_3OD, δ(H) 3.31) as internal reference; ^1H assignments were confirmed by 2D-COSY-45 experiment. ^{13}C NMR spectra: same instrument as for ^1H (100.6 MHz); δ(H) in parts per million rel to the solvent's C-signal ($CDCl_3$, δ(C) 77.0; CD_3OD, δ(C) 49.0) as internal reference; ^{13}C assignments were confirmed by 2D-HMQC; coupling constants *J* in hertz. MS: *Nermag R 10-10C*, chemical-ionization (NH_3) mode; *m/z* (% rel to the base peak (=100%)). Elemental analyses: *Ilse Beetz*, D-96301 Kronach, Germany. Melting points: *BUCHI SMP-20* apparatus and are uncorrected.

5.2. General method for the cleavage of triethylsilyl ethers

A solution of protected *N*-benzyl derivatives of conduramine F-1 epoxides (±)-**38b–d**,**f**,**h** and (±)-**39a–h** in AcOH/THF/H_2O (3:4:3, v/v/v) was stirred at 20 °C for 5–10 h. After solvent evaporation in vacuo, the residue was purified by flash chromatography on silica gel or alumina (light petroleum ether/AcOEt (1:1)→AcOEt→25% aq NH_3 soln/MeCN (1:9→1:4)).

5.2.1. (±)-(1*RS*,2*SR*,3*RS*,4*SR*,5*RS*,6*SR*)-5-Amino-7-oxabicyclo[4.1.0]heptane-2,3,4-triol ((±)-10). Desilylation of (±)-**36** (0.067 g, 0.133 mmol) following the general procedure (see above) gave (±)-**10** (0.018 g, 85%). TLC: MeOH/$CHCl_3$/25% aq NH_3 soln (20:3:2). FC: SiO_2, light petroleum ether/AcOEt (1:1)→AcOEt→25% aq NH_3 soln/MeCN (1:4). Viscous solid. IR (KBr): 3344, 2915, 1561, 1410, 1253, 1100, 1049, 1002, 793 cm^{-1}. ^1H NMR (400 MHz, CD_3OD): 3.70 (d, 1H, *J*=6.5), 3.67 (br m, 1H), 3.48 (dd, 1H, *J*=10.4, 6.5), 3.45 (dd, 1H, *J*=10.4, 3.7), 3.33–3.30 (m, 1H), 3.12 (d, 1H, *J*=3.3). ^{13}C NMR (100.6 MHz, CD_3OD): 72.8 (d, *J*=142), 72.6 (d, *J*=144), 68.1 (d, *J*=146), 57.6 (d, *J*=180), 56.4 (d, *J*=178), 51.3 (d, *J*=143). CIMS (NH_3): 163 (7, $[M+2H^+]$), 162 (100, $[M+H^+]$), 114 (2), 105 (3), 88 (1), 77 (17), 70 (2). HR-MALDI-TOF-MS, found: 162.0776 ($C_6H_{12}NO_4^+$, $[M+H]^+$); calcd: 162.0766.

5.2.2. (±)-(1*SR*,2*SR*,3*RS*,4*SR*,5*RS*,6*RS*)-5-Amino-7-oxabicyclo[4.1.0]heptane-2,3,4-triol ((±)-11). *Procedure 1*: a stirred solution of (±)-**31** (0.053 g, 0.26 mmol) in MeOH/AcOEt (1:1) (4 mL) was hydrogenated over 10% Pd/C (0.01 g) for ~1 h. Subsequently, the solution was passed through Celite and evaporated. The residue was purified on a silica gel column to afford (±)-**11** (0.023 g) as an oil (50%). TLC: MeOH/$CHCl_3$/25% aq NH_3 soln (20:3:2). FC: light petroleum ether/AcOEt (1:1)→AcOEt→25% aq NH_3 soln/MeCN (1:4).

Procedure 2: desilylation of (±)-**37** (0.067 g, 0.133 mmol) following the general procedure (see above) gave (±)-**11** (0.020 g, 95%). Viscous oil. IR (KBr): 3359, 2924, 1661, 1563, 1409, 1061, 925, 656 cm^{-1}. ^1H NMR (400 MHz, CD_3OD): 3.83 (br d, 1H, *J*=7.6), 3.73–3.70 (m, 1H), 3.55–3.44 (m, 4H). ^{13}C NMR (100.6 MHz, CD_3OD): 73.0 (d, *J*=141), 70.8, 70.2 (2d, *J*=143), 59.1 (d, *J*=181), 53.3 (d, *J*=183), 50.3 (d, *J*=140).

^1H NMR (400 MHz, pyridine-d_5): 4.26 (ddd, 1H, *J*=7.8, 1.8, 1.8), 4.10 (dd, 1H, *J*=9.7, 7.5), 3.70 (ddd, 1H, *J*=9.7, 6.2, 1.5), 3.68–3.65 (m, 1H), 3.64 (dd, 1H, *J*=6.2, 4.5), 3.54–3.51 (m, 1H). ^{13}C NMR (100.6 MHz, pyridine-d_5): 73.4 (d, *J*=136), 72.4 (d, *J*=138), 70.1 (d, *J*=143), 59.1 (d, *J*=177), 55.7 (d, *J*=179), 49.6 (d, *J*=136). CIMS (NH_3): 163 (14, $[M+2H]^+$), 162 (100, $[M+H]^+$), 161 (2, $[M]^+$), 148 (13), 114 (3), 88 (3), 84 (2), 77 (58), 72 (10). HR-MALDI-TOF-MS, found: 184.0527 ($C_6H_{11}NNaO_4^+$, $[M+Na]^+$); calcd: 184.0586.

5.2.3. (±)-(1*RS*,2*SR*,3*RS*,4*SR*,5*RS*,6*SR*)-5-{[(4-Hydroxyphenyl)methyl]amino}-7-oxabicyclo[4.1.0]heptane-2,3,4-triol ((±)-12b). Desilylation of (±)-**38b** (0.041 g, 0.065 mmol) following the general procedure (see above) gave (±)-**12b** (0.016 g, 91%). TLC: MeOH/AcOEt (1:4). Solid foam. IR (KBr): 3391, 2925, 1610, 1558, 1517, 1446, 1251, 1054, 831, 662 cm^{-1}. ^1H NMR (400 MHz, CD_3OD): 7.23 (d, 2H, *J*=8.4), 6.78 (d, 2H, *J*=8.4), 3.94 (d, 1H, *J*=12.9), 3.84 (d, 1H, *J*=12.9), 3.68 (d, 1H, *J*=6.3), 3.52–3.45 (m, 2H), 3.44–3.42 (m, 1H), 3.32–3.30 (m, 1H), 3.08 (d, 1H, *J*=3.3). ^{13}C NMR (100.6 MHz, CD_3OD): 158.3 (s), 132.5 (s), 131.2 (d, *J*=157), 116.4 (d, *J*=158), 73.6 (d, *J*=143), 72.4 (d, *J*=143), 68.1 (d, *J*=147), 57.7 (d, *J*=178), 57.0 (d, *J*=141), 55.4 (d, *J*=177), 53.2 (t, *J*=136). CIMS (NH_3): 270 (2, $[M+3H^+]$), 269 (12, $[M+2H^+]$), 268 (88, $[M+H^+]$), 222 (11), 198 (15), 162 (22), 124 (10), 108 (13), 107 (100), 94 (3), 78 (11), 70 (2). HR-MALDI-TOF-MS, found: 290.1375 ($C_{13}H_{17}NNaO_5^+$, $[M+Na]^+$); calcd: 290.1004.

5.2.4. (±)-(1*RS*,2*SR*,3*RS*,4*SR*,5*RS*,6*SR*)-5-({[4-(Trifluoromethyl)phenyl]methyl}amino)-7-oxabicyclo[4.1.0]heptane-2,3,4-triol ((±)-12c). Desilylation of (±)-**38c** (0.080 g, 0.120 mmol) following the general procedure (see above) gave (±)-**12c** (0.031 g, 81%). TLC: MeOH/AcOEt (15:85). White foam. IR (KBr): 3391, 2923, 1621, 1565, 1419, 1329, 1120, 1066, 828, 643 cm^{-1}. ^1H NMR (400 MHz, CD_3OD): 7.64 (d, 2H, *J*=8.4), 7.61 (d, 2H, *J*=8.4), 4.07 (d, 1H, *J*=13.9), 3.98 (d, 1H, *J*=13.9), 3.68 (d, 1H, *J*=7.0), 3.53 (dd, 1H, *J*=10.3, 7.0), 3.47 (dd, 1H, *J*=10.3, 4.4), 3.38–3.36 (br m, 1H), 3.35–3.33 (m, 1H), 3.06 (d, 1H, *J*=3.2). ^{13}C NMR (100.6 MHz, $CDCl_3$): 145.8 (s), 136.6 (q, *J*=33), 130.0 (d, *J*=163), 126.4 (dd, *J*=163, 4), 123.5 (d, *J*=273), 73.7 (d, *J*=144), 72.7 (d, *J*=146), 68.6 (d, *J*=146), 57.7 (d, *J*=178), 57.4 (d, *J*=135), 56.2 (d, *J*=177), 53.2 (t, *J*=136). CIMS (NH_3): 322 (2, $[M+3H^+]$), 321 (15, $[M+2H^+]$), 320 (100, $[M+H^+]$), 230 (2), 200 (2), 176 (8), 174 (9), 159 (8), 72 (1). HR-MALDI-TOF-MS, found:

320.1154 ($C_{14}F_3H_{17}NO_4^+$, $[M+H]^+$); calcd: 320.1110. Anal. Calcd for $C_{14}F_3H_{16}NO_4$ (319.276): C 52.67, H 5.05, N 4.39; found: C 52.30, H 5.22, N 4.15.

5.2.5. (±)-(1*RS*,2*SR*,3*RS*,4*SR*,5*RS*,6*SR*)-5-[(Biphenyl-4-ylmethyl)amino]-7-oxabicyclo[4.1.0]heptane-2,3,4-triol ((±)-12d). Desilylation of (±)-**38d** (0.068 g, 0.101 mmol) following the general procedure (see above) gave (±)-**12d** (0.025 g, 76%). TLC: MeOH/AcOEt (1.5:8.5). White crystals. Mp 147–150 °C (MeOH). IR (KBr): 3384, 2923, 1565, 1485, 1406, 1257, 1053, 831, 761, 697 cm^{-1}. ^1H NMR (400 MHz, CD_3OD): 7.63–7.60 (m, 4H), 7.48 (d, 2H, *J*=8.2), 7.43 (t, 2H, *J*=7.4), 7.32 (t, 1H, *J*=7.1), 4.03 (d, 1H, *J*=13.2), 3.92 (d, 1H, *J*=13.2), 3.68 (d, 1H, *J*=6.6), 3.51(dd, 1H, *J*=10.1, 6.6), 3.47 (dd, 1H, *J*=10.1, 4.7), 3.43–3.41 (br m, 1H), 3.38–3.36 (m, 1H), 3.07 (d, 1H, *J*=3.4). ^{13}C NMR (100.6 MHz, CD_3OD): 142.1 (s), 141.6 (s), 139.7 (s), 130.1 (d, *J*=158), 129.9 (d, *J*=159), 128.3 (d, *J*=161), 128.2 (d, *J*=159), 127.9 (d, *J*=160), 73.7 (d, *J*=144), 72.7 (d, *J*=140), 68.5 (d, *J*=143), 57.8 (d, *J*=178), 57.3 (d, *J*=138), 56.1 (d, *J*=177), 53.5 (t, *J*=136). CIMS (NH_3): 329 (21, $[M+2H^+]$), 328 (100, $[M+H^+]$), 237 (4), 182 (11), 167 (41), 165 (6), 72 (2). HR-MALDI-TOF-MS, found: 328.1557 ($C_{19}H_{22}NO_4^+$, $[M+H]^+$); calcd: 328.1549.

5.2.6. (±)-(1*RS*,2*SR*,3*RS*,4*SR*,5*RS*,6*SR*)-5-{[(4-{[4-(Phenyloxy)phenyl]oxy}phenyl)methyl]amino}-7-oxabicyclo[4.1.0]heptane-2,3,4-triol ((±)-12f). Desilylation of (±)-**38f** (0.043 g, 0.055 mmol) following the general procedure (see above) gave (±)-**12f** (0.014 g, 58%). TLC: MeOH/AcOEt (1:4). White crystals. Mp 135–137 °C (MeOH/Et_2O). IR (KBr): 3316, 2921, 1592, 1495, 1223, 1073, 1045, 872, 840, 695 cm^{-1}. ^1H NMR (400 MHz, CD_3OD): 7.39 (d, 2H, *J*=8.5), 7.34 (t, 2H, *J*=8.4), 7.08 (t, 1H, *J*=7.4), 7.02–6.96 (m, 8H), 3.96 (d, 1H, *J*=13.1), 3.84 (d, 1H, *J*=13.1), 3.67 (d, 1H, *J*=6.5), 3.49 (dd, 1H, *J*=10.2, 6.5), 3.44 (dd, 1H, *J*=10.2, 2.7), 3.39–3.37 (br m, 1H), 3.35–3.33 (m, 1H), 3.06 (d, 1H, *J*=3.4). ^{13}C NMR (100.6 MHz, CD_3OD): 154.3 (s), 154.0 (s), 152.7 (s), 151.9 (s), 131.2 (d, *J*=159), 130.9 (d, *J*=159), 124.2 (d, *J*=160), 121.5 (d, *J*=163), 119.3 (d, *J*=160), 73.8 (d, *J*=144), 72.7 (d, *J*=145), 68.5 (d, *J*=145), 57.8 (d, *J*=178), 57.2 (d, *J*=135), 56.1 (d, *J*=178), 53.3 (t, *J*=136). CIMS (NH_3): 437 (27, $[M+2H^+]$), 436 (98, $[M+H^+]$), 435 (12, $[M]^+$), 345 (5), 292 (8), 291 (21), 276 (26), 275 (100), 222 (2), 186 (18), 162 (20), 141 (13), 115 (12), 106 (22), 105 (20), 94 (25), 91 (23), 78 (22), 70 (4). HR-MALDI-TOF-MS, found: 458.1631 ($C_{25}H_{25}NNaO_6^+$, $[M+Na]^+$); calcd: 458.1580.

5.2.7. (±)-(1*RS*,2*SR*,3*RS*,4*SR*,5*RS*,6*SR*)-5-{[(5-Bromo-2-thienyl)methyl]amino}-7-oxabicyclo[4.1.0]heptane-2,3,4-triol ((±)-12h). Desilylation of (±)-**38h** (0.063 g, 0.093 mmol) following the general procedure (see above) gave (±)-**12h** (0.018 g, 58%). TLC: MeOH/AcOEt (0.5:4.5). White powder. Mp 158–160 °C (MeOH). IR (KBr): 3388, 3299, 2893, 1446, 1366, 1257, 1088, 1043, 976, 831, 794 cm^{-1}. ^1H NMR (400 MHz, CD_3OD): 6.97 (d, 1H, *J*=3.7), 6.86 (d, 1H, *J*=3.7), 4.09 (d, 1H, *J*=14.4), 4.04 (d, 1H, *J*=14.4), 3.66 (d, 1H, *J*=6.6), 3.49–3.42 (m, 2H), 3.38–3.36 (br m, 1H), 3.31–3.29 (m, 1H), 3.04 (d, 1H, *J*=3.3). ^{13}C NMR (100.6 MHz, CD_3OD): 147.4 (s), 130.8 (d, *J*=172), 127.1 (d, *J*=168), 111.9 (s), 73.7 (d, *J*=143), 72.7 (d, *J*=141), 68.7 (d, *J*=146), 57.7 (d, *J*=178), 57.0 (d, *J*=140), 56.0 (d, *J*=177), 48.7 (t, *J*=139). CIMS (NH_3): 338 (100, $[M+2H^+]$), 337 (10, $[M+H^+]$), 336 (99, $[M]^+$), 258 (5), 192 (26), 190 (25), 177 (41), 175 (40), 112 (7), 96 (5), 84 (1), 70 (2). HR-MALDI-TOF-MS, found: 335.9996 ($BrC_{11}H_{15}NO_4S^+$, $[M+H]^+$); calcd: 335.9905.

5.2.8. (±)-(1*RS*,2*RS*,3*SR*4*RS*,5*SR*,6*SR*)-5-[(Benzyl)-amino]-7-oxabicyclo[4.1.0]heptane-2,3,4-triol ((±)-13a). Desilylation of (±)-**39a** (0.057 g, 0.096 mmol) following the general procedure (see above) gave (±)-**13a** (0.022 g, 92%). TLC: MeOH/AcOEt (2:3). Solid foam. IR (KBr): 3364, 2936, 1601, 1456, 1401, 1259, 1066, 924, 751, 702 cm^{-1}. ^1H NMR (400 MHz, CD_3OD): 7.53–7.51, 7.44–7.36 (2m, 5H), 4.27 (d, 1H, *J*=13.2), 4.20 (d, 1H, *J*=13.2), 3.83 (dd, 1H, *J*=7.2, 2.2), 3.66 (dd, 1H, *J*=6.2, 4.3), 3.59 (dd, 1H, *J*=9.6, 6.2), 3.52 (dd, 1H, *J*=9.6, 7.2), 3.49 (dd, 1H, *J*=4.0, 2.2), 3.42 (dd, 1H, *J*=4.2, 4.1). ^{13}C NMR (100.6 MHz, CD_3OD): 137.8 (s), 130.6 (d, *J*=158), 130.0 (d, *J*=160), 129.8 (d, *J*=161), 72.3 (d, *J*=141), 71.5 (d, *J*=138), 69.8 (d, *J*=142), 59.3 (d, *J*=180), 55.6 (d, *J*=142), 52.4 (d, *J*=184), 51.7 (t, *J*=135). CIMS (NH_3): 253 (15, $[M+H^+]$), 252 (100, $[M]^+$), 200 (4), 162 (14), 148 (6), 120 (4), 108 (78), 106 (62), 91 (55), 78 (7), 72 (6). HR-MALDI-TOF-MS, found: 252.1238 ($C_{13}H_{18}NO_4^+$, $[M+H]^+$); calcd: 252.1236.

5.2.9. (±)-(1*RS*,2*RS*,3*SR*,4*RS*,5*SR*,6*SR*)-5-{[(4-Hydroxyphenyl)methyl]amino}-7-oxabicyclo[4.1.0]heptane-2,3,4-triol ((±)-13b). Desilylation of (±)-**39b** (0.046 g, 0.075 mmol) following the general procedure (see above) gave (±)-**13b** (0.017 g, 85%). TLC: MeOH/AcOEt (2:3). Viscous oil. IR (KBr): 3225, 2937, 1561, 1518, 1405, 1257, 1174, 1064, 837, 660 cm^{-1}. ^1H NMR (400 MHz, CD_3OD): 7.40 (d, 2H, *J*=8.5), 6.86 (d, 2H, *J*=8.5), 4.27 (d, 1H, *J*=13.2), 4.19 (d, 1H, *J*=13.2), 3.84 (dd, 1H, *J*=7.6, 1.9), 3.74 (dd, 1H, *J*=6.3, 4.5), 3.61 (dd, 1H, *J*=10.0, 6.4), 3.52 (dd, 1H, *J*=10.0, 7.6), 3.52–3.50 (m, 1H), 3.42 (dd, 1H, *J*=4.3, 4.2). ^{13}C NMR (100.6 MHz, CD_3OD): 159.7 (s), 132.5 (d, *J*=157), 124.0 (s), 116.9 (d, *J*=159), 72.4 (d, *J*=141), 71.2 (d, *J*=145), 69.3 (d, *J*=146), 59.5 (d, *J*=181), 55.4 (d, *J*=144), 51.5 (d, *J*=185), 50.7 (t, *J*=138). CIMS (NH_3): 269 (4, $[M+2H^+]$), 268 (22, $[M+H^+]$), 198 (24), 162 (7), 124 (44), 107 (100), 103 (42), 102 (92), 100 (12), 86 (98), 72 (9). HR-MALDI-TOF-MS, found: 268.1173 ($C_{13}H_{18}NO_5^+$, $[M+H]^+$); calcd: 268.1185.

5.2.10. (±)-(1*RS*,2*RS*,3*SR*,4*RS*,5*SR*,6*SR*)-5-({[4-(Trifluoromethyl)phenyl]methyl}amino)-7-oxabicyclo[4.1.0]heptane-2,3,4-triol ((±)-13c). Desilylation of (±)-**39c** (0.067 g, 0.086 mmol) following the general procedure (see above) gave (±)-**13c** (0.026 g, 93%). TLC: MeOH/AcOEt (1:4). White viscous solid. IR (KBr): 3376, 2926, 1620, 1567, 1418, 1328, 1164, 1121, 1067, 923, 825 cm^{-1}. ^1H NMR (400 MHz, CD_3OD): 7.67 (br s, 4H), 4.17 (d, 1H, *J*=13.7), 4.09 (d, 1H, *J*=13.7), 3.80 (br d, 1H, *J*=5.7), 3.51–3.33 (m, 5H). ^{13}C NMR (100.6 MHz, CD_3OD): 144.5 (s), 134.8 (q, *J*=31), 130.3 (d, *J*=162), 126.4 (d, *J*=163), 125.4 (d, *J*=260), 73.0 (d, *J*=141), 71.9, 71.0 (2d, *J*=146), 59.0, 54.1 (2d, *J*=178), 55.3 (d, *J*=139), 52.0 (t, *J*=138).

^1H NMR (400 MHz, pyridine-d_5): 7.39 (d, 2H, *J*=8.3), 7.54 (d, 2H, *J*=8.3), 4.31 (dd, 1H, *J*=7.2, 1.9), 4.25 (dd, 1H, *J*=9.0, 7.2), 4.14 (d, 1H, *J*=13.9), 4.04 (d, 1H, *J*=13.9), 3.86 (dd, 1H, *J*=9.0, 5.6), 3.71 (br m, 1H), 3.51–3.48 (m,

2H). ^{13}C NMR (100.6 MHz, pyridine-d_5): 146.2 (s), 129.0 (d, J=161), 125.5 (d, J=163), 73.1 (d, J=140), 71.9 (d, J=141), 71.8 (d, J=141), 58.5 (d, J=177), 54.9 (d, J=134), 54.3 (d, J=177), 51.8 (t, J=131).† CIMS (NH_3): 321 (17, [M+2H$^+$), 320 (100, [M]+H$^+$), 230 (8), 218 (9), 202 (6), 193 (7), 177 (11), 176 (88), 174 (56), 163 (13), 141 (11), 136 (14), 130 (11), 126 (28), 124 (16), 122 (15), 118 (10), 116 (10), 112 (21), 108 (20), 102 (69), 96 (20), 88 (47), 80 (11), 74 (56), 72 (44). HR-MALDI-TOF-MS, found: 320.1153 ($C_{14}F_3H_{17}NO_4^+$, [M+H]$^+$); calcd: 320.1110. Anal. Calcd for $C_{14}F_3H_{16}NO_4$ (319.276): C 52.67, H 5.05, N 4.39; found: C 52.33, H 4.80, N 4.60.

5.2.11. (±)-(1*RS*,2*RS*,3*SR*,4*RS*,5*SR*,6*SR*)-5-{[(Biphenyl-4-yl)methyl]amino}-7-oxabicyclo[4.1.0]heptane-2,3,4-triol ((±)-13d). Desilylation of (±)-**39d** (0.058 g, 0.086 mmol) following the general procedure (see above) gave (±)-**13d** (0.026 g, 93%). TLC: MeOH/AcOEt (3:7). White crystals. Mp 174–176 °C (MeOH). IR (KBr): 3254, 3025, 1576, 1405, 1346, 1210, 1138, 1067, 962, 762 cm^{-1}. ^{1}H NMR (400 MHz, CD_3OD): 7.74 (d, 2H, J=8.2), 7.67–7.64 (m, 4H), 7.48 (t, 2H, J=7.8), 7.39 (t, 2H, J=7.4), 4.38 (d, 1H, J=13.3), 4.29 (d, 1H, J=13.3), 3.84 (dd, 1H, J=7.5, 1.9), 3.74 (dd, 1H, J=6.1, 4.5), 3.59 (dd, 1H, J=10.0, 6.2), 3.55–3.50 (m, 1H), 3.52 (dd, 1H, J=4.1, 2.0), 3.47 (dd, 1H, J=4.2, 4.1). ^{13}C NMR (100.6 MHz, CD_3OD): 143.3 (s), 141.5 (s), 133.4 (s), 131.4 (d, J=159), 130.0 (d, J=161), 128.8 (d, J=161), 128.6 (d, J=160), 128.0 (d, J=160), 72.5 (d, J=142), 71.3 (d, J=146), 69.6 (d, J=147), 59.5 (d, J=181), 55.7 (d, J=146), 51.8 (d, J=184), 51.0 (t, J=137). CIMS (NH_3): 330 (4, [M]+3H$^+$), 329 (22, [M]+2H$^+$), 328 (100, [M]+H$^+$), 327 (4, [M]$^+$), 238 (8), 184 (11), 182 (12), 167 (34), 163 (12), 128 (3), 114 (3), 102 (54), 86 (17), 74 (13), 72 (12), 70 (2). HR-MALDI-TOF-MS, found: 350.1390 ($C_{19}H_{21}NNaO_4^+$, [M+Na]$^+$); calcd: 350.1368.

5.2.12. (±)-(1*RS*,2*RS*,3*SR*,4*RS*,5*SR*,6*SR*)-5-{[(4-Pyridin-4-ylphenyl)methyl]amino}-7-oxabicyclo[4.1.0]heptane-2,3,4-triol ((±)-13e). Desilylation of (±)-**39e** (0.050 g, 0.076 mmol) following the general procedure (see above) gave (±)-**13e** (0.022 g, 90%). TLC: MeOH/AcOEt (1:1). White foam. IR (KBr): 3233, 1602, 1560, 1406, 1264, 1067, 811, 670 cm^{-1}. ^{1}H NMR (400 MHz, CD_3OD): 8.56 (d, 2H, J=6.3), 7.75 (d, 2H, J=8.2), 7.69 (d, 2H, J=6.3), 7.58 (d, 2H, J=8.2), 4.04 (d, 1H, J=13.5), 4.00 (d, 1H, J=13.5), 3.91 (dd, 1H, J=5.7, 2.9), 3.62 (dd, 1H, J=8.3, 5.5), 3.57 (dd, 1H, J=8.3, 5.8), 3.54–3.51 (m, 1H), 3.49 (dd, 1H, J=3.8, 3.7) 3.33 (dd, 1H, J=5.6, 3.7). ^{13}C NMR (100.6 MHz, CD_3OD): 150.6 (d, J=179), 150.4 (s), 142.7 (s), 137.8 (s), 130.5 (d, J=160), 128.2 (d, J=160), 123.0 (d, J=163), 71.9, 71.8 (2d, J=143), 70.6 (d, J=139), 58.4 (d, J=181), 55.9 (d, J=180), 54.1 (d, J=134), 52.1 (t, J=135). CIMS (NH_3): 331 (3, [M]+3H$^+$), 330 (19, [M]+2H$^+$), 329 (100, [M]+H$^+$), 239 (2), 185 (5), 168 (7), 102 (70), 86 (13), 72 (3). HR-MALDI-TOF-MS, found: 329.1563 ($C_{18}H_{21}N_2O_4^+$, [M+H]$^+$); calcd: 329.1501.

5.2.13. (±)-(1*RS*,2*RS*,3*SR*,4*RS*,5*SR*,6*SR*)-5-{[(4-{[4-(Phenyloxy)phenyl]oxy}phenyl)methyl]amino}-7-oxabicyclo-[4.1.0]heptane-2,3,4-triol ((±)-13f). Desilylation of (±)-**39f** (0.076 g, 0.098 mmol) following the general procedure (see above) gave (±)-**13f** (0.040 g, 93%). TLC: MeOH/AcOEt (3:7). White solid. IR (KBr): 3380, 3146, 3044, 2817, 1591, 1493, 1406, 1225, 1070, 864 cm^{-1}. ^{1}H NMR (400 MHz, CD_3OD): 7.52 (d, 2H, J=8.2), 7.38 (t, 2H, J=7.5), 7.11 (t, 1H, J=7.1), 7.05–6.99 (m, 8H), 4.26 (d, 1H, J=13.3), 4.18 (d, 1H, J=13.3), 3.84 (br d, 1H, J=7.4), 3.67 (dd, 1H, J=5.7, 4.6), 3.56 (dd, 1H, J=9.8, 6.0), 3.52–3.50 (m, 2H), 3.46–3.44 (m, 1H). ^{13}C NMR (100.6 MHz, CD_3OD): 159.8 (s), 159.1 (s), 154.8 (s), 151.7 (s), 132.3 (d, J=159), 131.3 (s), 130.9 (d, J=160), 124.8 (d, J=160), 121.6 (d, J=162), 121.5 (d, J=162), 119.5 (d, J=162), 119.4 (d, J=162), 72.6 (d, J=141), 71.5, 70.0 (2d, J=146), 59.3 (d, J=181), 55.6 (d, J=140), 52.5 (d, J=183), 51.2 (t, J=140). CIMS (NH_3): 437 (29, [M]+2H$^+$), 436 (100, [M]+H$^+$), 313 (3), 290 (5), 275 (22), 198 (3), 180 (10), 163 (9), 130 (4), 126 (8), 112 (8), 102 (25), 98 (13), 97 (10), 96 (12), 88 (21), 77 (12), 72 (22), 70 (7). HR-MALDI-TOF-MS, found: 458.1530 ($C_{25}H_{25}NNaO_6^+$, [M+Na]$^+$); calcd: 458.1580.

5.2.14. (±)-(1*RS*,2*RS*,3*SR*,4*RS*,5*SR*,6*SR*)-5-{[(3,6-Dichloro-2-hydroxyphenyl)methyl]amino}-7-oxabicyclo[4.1.0]heptane-2,3,4-triol ((±)-13g). Desilylation of (±)-**39g** (0.040 g, 0.059 mmol) following the general procedure (see above) gave (±)-**13g** (0.018 g, 91%). TLC: MeOH/AcOEt (3:7). White solid. IR (KBr): 3372, 2905, 1565, 1457, 1384, 1277, 1073, 926, 741 cm^{-1}. ^{1}H NMR (400 MHz, CD_3OD): 7.25 (d, 1H, J=2.1), 7.11 (d, 1H, J=1.7), 4.18 (d, 1H, J=13.8), 4.09 (d, 1H, J=13.8), 3.81 (br d, 1H, J=6.7), 3.56–3.44 (m, 5H). ^{13}C NMR (100.6 MHz, $CDCl_3$): 154.9 (s), 129.6 (d, J=169), 128.7 (d, J=162), 127.0 (s), 123.8 (s), 123.1 (s), 73.1, 71.4, 70.8 (3d, J=143), 58.9 (d, J=181), 55.6 (d, J=141), 53.3 (d, J=183), 50.1 (t, J=138).

^{1}H NMR (400 MHz, pyridine-d_5): 7.42 (br s, 1H), 6.97 (br s, 1H), 4.35–4.31 (m, 2H), 4.25 (d, 1H, J=13.8), 4.05 (d, 1H, J=13.8), 3.93 (dd, 1H, J=8.7, 6.2), 3.76–4.74 (m, 1H), 3.60 (dd, 1H, J=6.3, 4.1), 3.54 (dd, 1H, J=4.3, 4.0). ^{13}C NMR (100.6 MHz, pyridine-d_5): 128.5 (d, J=169), 127.8 (s), 127.3 (d, J=164), 73.3 (d, J=140), 71.5, 71.2 (2d, J=141), 58.8 (d, J=180), 55.3 (d, J=137), 53.3 (d, J=179), 50.6 (t, J=137).‡ CIMS (NH_3): 338 (13, [M]+2H$^+$), 336 (21, [M]$^+$), 302 (3), 192 (5), 180 (23), 174 (9), 162 (100), 144 (13), 130 (10), 126 (35), 115 (89), 110 (13), 102 (15), 95 (24), 89 (15), 74 (12), 72 (37). HR-MALDI-TOF-MS, found: 336.0472 ($C_{13}Cl_2H_{16}NO_5^+$, [M+H]$^+$); calcd: 336.0406.

5.2.15. (±)-(1*RS*,2*RS*,3*SR*,4*RS*,5*SR*,6*SR*)-5-{[(5-Bromo-2-thienyl)methyl]amino}-7-oxabicyclo[4.1.0]heptane-2,3,4-triol ((±)-13h). Desilylation of (±)-**39h** (0.053 g, 0.078 mmol) following the general procedure (see above) gave (±)-**13h** (0.019 g, 73%). TLC: MeOH/AcOEt (1:4). White foam. IR (KBr): 3382, 2922, 1634, 1442, 1258, 1060, 921, 882, 800 cm^{-1}. ^{1}H NMR (400 MHz, CD_3OD): 6.97 (d, 1H, J=3.7), 6.85 (d, 1H, J=3.7), 4.14 (d, 1H, J=14.4), 4.07 (d, 1H, J=14.4), 3.81–3.76 (m, 1H), 3.47–3.40, 3.34–3.30 (2m, 5H). ^{13}C NMR (100.6 MHz, $CDCl_3$): 147.3 (s), 130.8 (d, J=173), 127.2 (d, J=169), 111.9 (s), 73.0, 72.1, 71.3 (3d, J=144), 58.8, 55.0 (2d, J=179), 54.3 (d, J=136), 47.6 (t, J=139).

† Signals for arom. C–CF_3 and CF_3 are omitted because they are masked by pyridine-d_5 signals.

‡ Some of aromatic signals are omitted because they are masked by pyridine-d_5 signals.

^{1}H NMR (400 MHz, pyridine-d_5): 6.96 (d, 1H, J=3.7), 6.75 (d, 1H, J=3.7), 4.32 (dd, 1H, J=6.6, 1.8), 4.27–4.23 (m, 1H), 4.23 (d, 1H, J=14.5), 4.15 (d, 1H, J=14.5), 3.90 (dd, 1H, J=8.6, 5.1), 3.70–4.68 (m, 1H), 3.56 (dd, 1H, J=5.8, 4.2), 3.50 (dd, 1H, J=4.1, 4.0). ^{13}C NMR (100.6 MHz, pyridine-d_5): 148.1 (s), 130.1 (d, J=170), 125.5 (d, J=167), 110.9 (s), 72.6 (d, J=138), 71.8, 71.6 (2d, J=139), 58.2 (d, J=177), 54.5 (d, J=185), 54.0 (d, J=132), 47.2 (t, J=137). CIMS (NH_3): 338 (26, $[M]+2H^+$), 336 (26, $[M]^+$), 298 (8), 281 (11), 258 (7), 234 (11), 211 (6), 197 (11), 192 (58), 182 (18), 177 (35), 168 (12), 163 (63), 152 (18), 148 (13), 138 (20), 126 (28), 120 (52), 112 (100), 104 (16), 97 (46), 88 (57), 84 (40), 74 (56), 72 (53), 70 (12). HR-MALDI-TOF-MS, found: 357.9729 ($BrC_{11}H_{14}NNaNO_4S^+$, $[M+Na]^+$); calcd: 357.9725.

5.2.16. (±)-[(1*RS*,2*RS*,3*SR*,6*SR*)-6-Azidocyclohex-4-en-1,2,3-triyl]tris(oxy)tris-*tert*-butyl(dimethyl)silane ((±)-22) and (±)-[(1*RS*,2*RS*,3*SR*,6*RS*)-6-azidocyclohex-4-en-1,2,3-triyl]tris(oxy)tris-*tert*-butyl(dimethyl)silane ((±)-23). To a chilled (−10 °C) solution of (±)-**15**/(±)-**16** (ca. 1:5.3) (4.30 g, 8.8 mmol, 1.0 equiv) and PPh_3 (3.0 g, 11.43 mmol, 1.3 equiv) in dry toluene (40 mL) were sequentially added diphenylphosphoryl azide (DPPA, 2.47 mL, 11.43 mmol, 1.3 equiv) and diethyl azodicarboxylate (DEAD, 1.77 mL, 11.43 mmol, 1.3 equiv). The resulting mixture was allowed to reach +5 °C in 2 h and stirred at this temperature for additional 2 h (TLC monitoring). Then it was poured into H_2O (100 mL) and aqueous phase was extracted with Et_2O (3×). The combined organic extracts were washed with brine, dried ($MgSO_4$), evaporated, and the residue was subjected to FC (silica gel, light petroleum ether/AcOEt, 98:2). The obtained oily mixture (ca. 1:2.46) (3.0 g, 67%) was resubjected to CC (light petroleum ether/AcOEt (99.5:0.5)→(99:1)): (±)-**22** (0.75 g) and (±)-**23** (2.0 g).

*Data of (±)-**22***: oil that solidifies at +4 °C. UV ($CHCl_3$): 240 (393). IR (KBr): 2928, 2856, 2101, 1471, 1258, 1093, 908, 835, 775 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 6.07 (dd, 1H, J=10.2, 3.9), 5.79 (dd, 1H, J=10.2, 4.6), 4.08 (br m, 1H), 3.95–3.83 (m, 2H), 3.60 (br m, 1H), 0.93, 0.91, 0.89 (3s, 27H), 0.15, 0.14, 0.12, 0.115, 0.11, 0.10 (6s, 18H). ^{13}C NMR (100.6 MHz, $CDCl_3$): 132.9 (d, J=160), 121.3 (d, J=161), 74.6, 72.2 (2d, J=146), 69.9 (d, J=142), 59.1 (d, J=147), 26.0, 25.9, 25.8 (3q, J=125), 18.1 (s), −4.2, −4.3, −4.4, −4.6, −4.9 (5q, J=118). CIMS (NH_3): 471 (2), 401 (6), 339 (9), 288 (11), 149 (11), 147 (47), 133 (17), 115 (18), 103 (5), 85 (5), 73 (100). HR-MALDI-TOF-MS, found: 536.3131 ($C_{24}H_{51}N_3NaO_3Si_3^+$, $[M+Na]^+$); calcd: 536.3136. Anal. Calcd for $C_{24}H_{51}N_3O_3Si_3$ (513.3241): C 56.09, H 10.00, N 8.18; found: C 56.17, H 9.89, N 8.14.

*Data of (±)-**23***: oil that solidifies at +4 °C. UV ($CHCl_3$): 277 (384). IR (KBr): 2927, 2857, 2099, 1471, 1463, 1361, 1257, 1186, 1083, 900, 834, 775 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 5.81 (dt, 1H, J=10.4, 2.0, 2.0), 5.66 (br d, 1H, J=10.4), 3.96–3.87 (2m, 4H), 0.94, 0.92, 0.89 (3s, 27H), 0.17, 0.13, 0.12, 0.11, 0.10 (5s, 18H). ^{13}C NMR (100.6 MHz, $CDCl_3$): 131.3 (d, J=163), 127.7 (d, J=163), 74.4, 71.2, 70.9 (3d, $J\approx$145), 57.3 (d, J=143), 26.1, 26.0, 25.8 (3q, J=125), 18.3, 18.24, 17.8 (3s), −4.28, −4.35, −4.36, −4.39, −4.5, −4.9 (6q, J=118). CIMS (NH_3): 471 (2), 428 (4), 339 (4), 288 (13), 231 (4), 147 (16), 140 (10), 115 (5), 99 (3), 75 (22), 70 (100). HR-MALDI-TOF-MS, found: 536.3102 ($C_{24}H_{51}N_3NaO_3Si_3^+$, $[M+Na]^+$); calcd: 536.3136. Anal. Calcd for $C_{24}H_{51}N_3O_3Si_3$ (513.3241): C 56.09, H 10.00, N 8.18; found: C 56.12, H 9.93, N 8.19.

5.2.17. (±)-(1*RS*,2*RS*,3*SR*,6*SR*)-6-Azidocyclohex-4-en-1,2,3-triol ((±)-24). To a soln of (±)-**22** (1.18 g, 2.29 mmol) in THF (25 mL), $Bu_4NF\cdot 3H_2O$ (1.45 g, 4.59 mmol, 2 equiv) was added. The mixture was stirred at 20 °C for 2 h (TLC control). Subsequently, AcOH (0.52 mL, 9.16 mmol, 4 equiv) was added, the solvent was evaporated to dryness, and the crude product was separated by FC (light petroleum ether/AcOEt (1:1)→AcOEt→MeOH/AcOEt (5:95)): 0.3 g (77%) of (±)-**24**. Colorless crystals. Mp 113–115 °C (AcOEt/MeOH). UV (MeOH): 270 (297), 208 (1950). IR (KBr): 3344, 2105, 1379, 1282, 1123, 1017, 893 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 5.71 (dt, 1H, J=10.3, 2.2, 2.2), 5.54 (dt, 1H, J=10.3, 2.2, 2.2), 4.10–4.06 (m, 1H), 4.01–3.97 (m, 1H), 3.51 (dd, 1H, J=10.3, 8.3), 3.44 (dd, 1H, J=10.3, 7.6). ^{13}C NMR (100.6 MHz, $CDCl_3$): 133.2 (d, J=164), 125.9 (d, J=166), 77.5 (d, J=142), 75.9 (d, J=144), 73.2 (d, J=139), 65.8 (d, J=144). CIMS (NH_3): 167 (14), 149 (70), 129 (5), 124 (18), 111 (100), 104 (7), 99 (55), 96 (59), 83 (84), 81 (45), 80 (60), 70 (66). HR-MALDI-TOF-MS, found: 194.0501 ($C_6H_9N_3NaO_3^+$, $[M+Na]^+$); calcd: 194.0542). Anal. Calcd for $C_6H_9N_3O_3$ (171.064): C 42.10, H 5.30, N 24.55; found: C 42.05, H 5.37, N 24.50.

5.2.18. (±)-(1*RS*,2*RS*,3*SR*,6*SR*)-6-Aminocyclohex-4-ene-1,2,3-triol, *rac*-conduramine B-1 ((±)-25). Compound (±)-**25** was obtained according to a known procedure[40a] starting from (±)-**24** (0.1 g, 0.58 mmol); (±)-**25**: 0.062 g, 73%. FC: SiO_2, light petroleum ether/AcOEt (1:1)→AcOEt→25% aq NH_3 soln/MeCN (1:4). All analytical data were identical to those reported in the literature.[28,29]

5.2.19. (±)-(1*RS*,2*RS*,3*SR*,6*RS*)-6-Azidocyclohex-4-en-1,2,3-triol ((±)-26). Compound (±)-**26** (0.28 g, 84%) was obtained according to the procedure described for (±)-**24** using (±)-**23** (1.0 g, 1.94 mmol). White solid. Mp 76–78 °C (MeOH/AcOEt). UV (MeOH): 208 (2395). IR (KBr): 3264, 2145, 2095, 1384, 1332, 1266, 1093, 1044, 798 cm^{-1}. ^{1}H NMR (400 MHz, MeOH): 5.82 (dd, 1H, J=10.0, 2.0), 5.75 (ddd, 1H, J=10.0, 4.9, 1.8), 4.16 (dd, 1H, J=4.7, 4.6), 3.95 (m, 1H), 3.70 (dd, 1H, J=10.3, 4.5), 3.60 (dd, 1H, J=10.3, 7.5). ^{13}C NMR (100.6 MHz, $CDCl_3$): 135.3 (d, J=162), 124.3 (d, J=166), 74.3 (d, J=144), 73.8 (d, J=142), 72.7 (d, J=144), 62.1 (d, J=147). CIMS (NH_3): 167 (26), 149 (97), 129 (4), 124 (11), 111 (88), 104 (12), 96 (54), 83 (100), 78 (14), 70 (43). HR-MALDI-TOF-MS, found: 194.0578 ($C_6H_9N_3NaO_3^+$, $[M+Na]^+$); calcd: 194.0542. Anal. Calcd for $C_6H_9N_3O_3$ (171.064): C 42.10, H 5.30, N 24.55; found: C 41.94, H 5.20, N 24.70.

5.2.20. (±)-(1*SR*,2*SR*,3*RS*,6*SR*)-6-Aminocyclohex-4-ene-1,2,3-triol, *rac*-conduramine F-1 ((±)-27). Compound (±)-**27** was obtained according to a known procedure[40a] starting from (±)-**26** (0.05 g, 0.29 mmol); (±)-**27** (0.033 g, 78%). FC: SiO_2, light petroleum ether/AcOEt (1:1)→AcOEt→25% aq NH_3 soln/MeCN (1:4). Analytical data are identical to those described in the literature.[25]

5.2.21. (±)-(1*RS*,4*RS*,5*SR*,6*SR*)-4,5,6-Tris-{[(*tert*-butyl)-dimethylsilyl]oxy}cyclohex-2-en-1-amine ((±)-28). Compound (±)-**28** (0.073 g, 77%) was obtained according to the Corey's procedure[42] starting from (±)-**22** (0.1 g, 0.194 mmol). FC: 5–20% AcOEt in light petroleum ether. Yellowish oil. UV (MeOH): 284 (820), 207 (3795). IR (film): 3385, 2929, 2857, 1673, 1472, 1389, 1361, 1256, 1082, 1006, 836, 775 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): 5.87 (dd, 1H, *J*=10.0, 4.4), 5.72 (dd, 1H, *J*=10.2, 3.7), 3.97 (br d, 1H, *J*=3.4), 3.91 (br s, 1H), 3.87 (br s, 1H), 3.12 (br d, 1H, *J*=4.2), 0.90 (s, 27H), 0.14, 0.10, 0.09 (3s, 18H). ^{13}C NMR (100.6 MHz, $CDCl_3$): 129.8 (d, *J*=160), 125.2 (d, *J*=160), 75.8 (d, *J*=146), 74.1 (d, *J*=140), 69.8 (d, *J*=140), 52.0 (d, *J*=144), 26.0, 25.9 (3q, *J*=125), 18.3, 18.2, 17.9 (s), −4.2, −4.35, −4.4, −4.8 (4q, *J*=118). CIMS (NH_3): 488 (2, $[M+H]^+$), 431 (6), 225 (5), 200 (89), 199 (100), 147 (3), 167 (3), 73 (6). HR-MALDI-TOF-MS, found: 488.5018 ($C_{24}H_{54}NO_3Si_3^+$, $[M+H]^+$); calcd: 488.3412.

5.2.22. (±)-(1*RS*,4*SR*,5*RS*,6*RS*)-4,5,6-Tris-{[(*tert*-butyl)-dimethylsilyl]oxy}cyclohex-2-en-1-amine ((±)-29). *Procedure 1*: compound (±)-**29** (0.1 g, 70%) was obtained according to the Paulsen's method[40a] starting from (±)-**23** (0.15 g, 0.29 mmol).

Procedure 2: to a soln of (±)-**18** (0.292 g, 0.47 mmol) in MeOH (6 mL) was added $N_2H_4 \cdot H_2O$ (0.115 mL, 2.36 mmol, 5.0 equiv). The reaction mixture was stirred under reflux for 4 h, treated with aq 1 N HCl (15 mL), and made alkaline with NaOH solution. The mixture was extracted with AcOEt (3×). The combined organic extracts were washed with brine, dried (Na_2SO_4), filtered, and evaporated under reduced pressure. The crude product was purified by FC (5–15% AcOEt/hexane): 0.13 g of (±)-**29** (56%). Yellowish oil. IR (KBr): 3286, 2950, 2857, 1471, 1389, 1361, 1256, 1078, 1006, 775 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): 5.62–5.52 (br m, 2H), 3.98 (br s, 1H), 3.84 (br m, 1H), 3.69–3.65 (br m, 1H), 3.48 (br s, 1H), 0.93, 0.92, 0.90 (3s, 27H), 0.132, 0.126, 0.121, 0.112, 0.098 (5s, 18H). ^{13}C NMR (100.6 MHz, $CDCl_3$): 130.2, 128.3 (2d, $J \approx 162$), 74.4 (d, *J*=147), 72.3 (d, *J*=144), 71.6 (d, *J*=142), 48.0 (d, *J*=136), 26.2, 26.1, 25.9 (3q, *J*=125), 18.3, 18.2, 17.9 (s), −3.7, −4.25, −4.31, −4.35, −4.7 (5q, *J*=118). CIMS (NH_3): 442 (42), 430 (38), 340 (4), 488 (1), 444 (9), 340 (4), 277 (3), 199 (100), 149 (7), 147 (13), 73 (79). HR-MALDI-TOF-MS, found: 488.3437($C_{24}H_{54}NO_3Si_3^+$, $[M+H]^+$); calcd: 488.3412.

5.2.23. (±)-(1*RS*,2*SR*,3*RS*,4*SR*,5*RS*,6*SR*)-5-Azido-7-oxabicyclo[4.1.0]heptane-2,3,4-triol ((±)-30) and (±)-(1*RS*,2*SR*,3*SR*,4*RS*,5*SR*,6*SR*)-5-azido-7-oxabicyclo[4.1.0]heptane-2,3,4-triol ((±)-31). A solution of (±)-**26** (2.0 g, 11.65 mmol, 1 equiv) in AcOH (85 mL) and $CHCl_3$ (44 mL) was treated with *m*-chloroperbenzoic acid (7.46 g, 30.29 mmol, 2.6 equiv, ~70% (FLUKA)) for 4 days at rt. The solution was concentrated in vacuo to about 15 mL. The obtained mixture was subjected to FC (SiO_2, light petroleum ether→light petroleum ether/AcOEt (1:1)→AcOEt→MeOH/AcOEt (5:95)): (±)-**30** (0.35 g, 16%) and (±)-**31** (0.76 g, 35%). Recovered starting material: 0.48 g.

*Data of (±)-**30***: colorless crystals. Mp 137–139 °C (MeOH/AcOEt). UV (MeOH): 209 (984), 203 (619). IR (KBr): 3331, 2919, 2106, 1374, 1337, 1254, 1057, 1004, 809 cm^{-1}. ^1H NMR (400 MHz, CD_3OD): 4.36 (br m, 1H), 3.70 (br d, 1H, *J*=7.5), 3.61 (dd, 1H, *J*=10.5, 3.6), 3.54 (dd, 1H, *J*=10.5, 7.5), 3.37–3.24 (br m, 1H), 3.07 (br d, 1H, *J*=3.2). ^{13}C NMR (100.6 MHz, CD_3OD): 73.4 (d, *J*=146), 72.6 (d, *J*=139), 69.6 (d, *J*=145), 62.6 (d, *J*=146), 57.3 (d, *J*=168), 55.6 (d, *J*=139). CIMS (NH_3): 205 (31, $[M+NH_4^+]$), 188 (1, $[M+H^+]$), 162 (100), 160 (50), 142 (9), 126 (10), 114 (5), 102 (8), 100 (69), 72 (32), 70 (6). HR-MALDI-TOF-MS, found: 210.0462 ($C_6H_9N_3NaO_4^+$, $[M+Na]^+$); calcd: 210.0491. Anal. Calcd for $C_6H_9N_3O_4$ (187.153): C 38.51, H 4.85, N 22.45; found: C 38.20, H 4.68, N 22.50.

*Data of (±)-**31***: colorless crystals. Mp 143–146 °C (MeOH/AcOEt). UV (MeOH): 209 (648). IR (KBr): 3278, 2154, 2102, 1456, 1327, 1255, 1070, 924, 881, 864, 739 cm^{-1}. ^1H NMR (400 MHz, CD_3OD): 4.11 (dd, 1H, *J*=4.9, 4.8), 3.76 (dd, 1H, *J*=7.1, 1.6), 3.60–3.52 (m, 2H), 3.46 (dd, 1H, *J*=4.7, 4.0), 3.35–3.32 (m, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$): 73.4 (d, *J*=141), 73.1, 71.2 (d, *J*=144), 60.5 (d, *J*=145), 57.6 (d, *J*=180), 53.8 (d, *J*=184). CIMS (NH_3): 205 (13, $[M+NH_4^+]$), 180 (6), 160 (12), 139 (7), 126 (7), 117 (6), 110 (16), 102 (18), 100 (100), 96 (7), 86 (21), 84 (22), 72 (54), 70 (6). HR-MALDI-TOF-MS, found: 210.3390 ($C_6H_9N_3NaO_4^+$, $[M+Na]^+$); calcd: 210.0491. Anal. Calcd for $C_6H_9N_3O_4$ (187.153): C 38.51, H 4.85, N 22.45; found: C 38.64, H 4.80, N 22.40.

5.2.24. (±)-{[(1*RS*,2*SR*,3*RS*,4*SR*,5*RS*,6*SR*)-5-Azido-7-oxabicyclo[4.1.0]heptane-2,3,4-triyl]tris(oxy)}tris(triethylsilane) ((±)-34). Azide (±)-**30** (0.94 g, 5.02 mmol, 1.0 equiv) was dissolved in anhyd DMF (12 mL) at 0 °C and imidazole (1.74 g, 25.6 mmol, 5.1 equiv) followed by triethylchlorosilane (3.54 mL, 21.10 mmol, 4.2 equiv) was added. After stirring overnight at rt, the solution was dissolved in *t*-BME and washed with a brine. The organic phase was collected and the aqueous phase extracted with *t*-BME (3×). The combined organic extracts were dried (Na_2SO_4), evaporated, and the residue was submitted to FC (light petroleum ether→5–10% AcOEt/light petroleum ether): 2.60 g (98%) of (±)-**34**. Yellowish oil. IR (film): 2955, 2881, 2104, 1462, 1413, 1241, 1164, 1084, 1010, 860, 734 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): 4.13 (br m, 1H), 3.76 (dd, 1H, *J*=9.2, 7.1), 3.70 (br d, 1H, *J*=7.1), 3.64 (dd, 1H, *J*=9.2, 3.3), 3.16 (br m, 1H), 2.99 (br d, 1H, *J*=2.9), 1.02–0.96 (m, 27H), 0.73–0.62 (m, 18H). ^{13}C NMR (100.6 MHz, $CDCl_3$): 73.4 (d, *J*=143), 73.0 (d, *J*=146), 70.3 (d, *J*=143), 61.7 (d, *J*=145), 57.1 (d, *J*=179), 54.3 (d, *J*=182), 7.0, 6.9, 6.9 (3q, *J*=126), 5.3, 5.0, 5.0 (t, *J*=116). CIMS (NH_3): 531 (28, $[M+2H^+]$), 530 (68, $[M+H^+]$), 502 (86), 472 (18), 370 (12), 308 (10), 291 (85), 261 (22), 234 (13), 220 (30), 205 (53), 165 (19), 132 (100), 120 (16), 115 (21), 104 (43), 91 (21), 74 (24), 70 (1). HR-MALDI-TOF-MS, found: 552.3092 ($C_{24}H_{51}N_3NaO_4Si_3^+$, $[M+Na]^+$); calcd: 552.3085.

5.2.25. (±)-{[(1*RS*,2*RS*,3*SR*,4*RS*,5*SR*,6*SR*)-5-Azido-7-oxabicyclo[4.1.0]heptane-2,3,4-triyl]tris(oxy)}tris(triethylsilane) ((±)-35). Compound (±)-**35** (5.2 g, 98%) was obtained from (±)-**31** (1.88 g, 10.04 mmol) as described for (±)-**34**. Yellowish oil. IR (film): 2955, 2881, 2101, 1462, 1413, 1241, 1164, 1092, 1009, 887, 736 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): 3.79 (dd, 1H, *J*=6.2, 2.4),

3.77–3.75 (m, 1H), 3.73 (dd, 1H, *J*=8.4, 6.2), 3.59 (dd, 1H, *J*=8.4, 5.1), 3.36 (dd, 1H, *J*=3.9, 3.8), 3.22 (dd, 1H, *J*=3.4, 2.7), 1.03–0.94 (m, 27H), 0.72–0.62 (m, 18H). ^{13}C NMR (100.6 MHz, $CDCl_3$): 74.8 (d, *J*=139), 73.6 (d, *J*=142), 71.3 (d, *J*=148), 58.9 (d, *J*=141), 55.6 (d, *J*=178), 52.5 (d, *J*=183), 7.0, 6.9, 6.8 (3q, *J*=124), 5.2, 5.1, 4.9 (3t, *J*=116). CIMS (NH_3): 547 (13, $[M+NH_4^+]$), 532 (18, $[M+3H^+]$), 531 (44, $[M+2H^+]$), 530 (100, $[M+H^+]$), 504 (25), 502 (75), 472 (13), 370 (12), 354 (20), 288 (11), 214 (23), 174 (7), 132 (56), 120 (11), 115 (17), 102 (10), 87 (18), 74 (16), 70 (3). HR-MALDI-TOF-MS, found: 552.3037 ($C_{24}H_{51}N_3NaO_4Si_3^+$, $[M+Na]^+$); calcd: 552.3085.

5.2.26. (±)-(1*RS*,2*SR*,3*RS*,4*SR*,5*RS*,6*SR*)-3,4,5-Tris[(triethylsilyl)oxy]-7-oxabicyclo[4.1.0]heptane-2-amine ((±)-36). A stirred solution of (±)-**34** (0.45 g, 0.85 mmol) in MeOH/AcOEt (1:2, v/v) mixture (15 mL) was hydrogenated over 10% Pd/C (0.03 g) for 2 h. Subsequently, the solution was passed through Celite and evaporated. The residue was purified on a silica gel column using AcOEt/light petroleum ether (10–40% AcOEt) as an eluant to afford (±)-**36** as a yellowish oil (0.32 g, 74%). IR (film): 3388, 2954, 2879, 1462, 1413, 1239, 1143, 1070, 887, 805, 735 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 3.77 (br d, 1H, *J*=6.5), 3.68 (dd, 1H, *J*=8.8, 6.5), 3.50–3.47 (m, 2H), 3.17 (br m, 1H), 3.02 (br d, 1H, *J*=3.4), 1.03–0.95 (m, 27H), 0.74–0.63 (m, 18H). ^{13}C NMR (100.6 MHz, $CDCl_3$): 73.9 (d, *J*=144), 73.0 (d, *J*=141), 70.6 (d, *J*=140), 57.0, 56.9 (2d, *J*=178), 51.3 (d, *J*=139), 7.0, 6.9, 6.8 (3q, *J*=126), 5.4, 5.2, 5.1 (t, *J*=116). CIMS (NH_3): 506 (19, $[M+3H^+]$), 505 (41, $[M+2H^+]$), 504 (100, $[M+H^+]$), 474 (5), 391 (40), 215 (6), 205 (2), 163 (4), 132 (13), 120 (8), 104 (12), 91 (6), 74 (7), 70 (1). HR-MALDI-TOF-MS, found: 504.3369 ($C_{24}H_{54}NO_4Si_3^+$, $[M+H]^+$); calcd: 504.3361.

5.2.27. (±)-(1*RS*,2*RS*,3*SR*,4*RS*,5*SR*,6*SR*)-3,4,5-Tris[(triethylsilyl)oxy]-7-oxabicyclo[4.1.0]heptane-2-amine ((±)-37). Compound (±)-**37** was prepared from (±)-**35** (1.1 g, 2.08 mmol) as described for (±)-**36** (0.85 g, 81%). Yellowish solid. Mp 46–49 °C. IR (KBr): 3384, 2956, 2880, 1581, 1462, 1414, 1240, 1164, 1082, 1010, 857, 738 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 3.79 (dd, 1H, *J*=7.5, 1.6), 3.53–3.47 (m, 1H), 3.36 (dd, 1H, *J*=4.1, 4.0), 3.28–3.21 (m, 3H), 1.03–0.93 (m, 27H), 0.73–0.62 (m, 18H). ^{13}C NMR (100.6 MHz, $CDCl_3$): 74.9 (d, *J*=141), 73.5 (d, *J*=139), 70.0 (d, *J*=145), 58.0 (d, *J*=177), 54.3 (d, *J*=181), 50.3 (d, *J*=142), 7.1, 7.0, 6.9 (3q, *J*=124), 5.4, 5.2, 5.0 (3t, *J*=116). CIMS (NH_3): 506 (20, $[M+3H^+]$), 505 (44, $[M+2H^+]$), 504 (100, $[M+H^+]$), 474 (8), 342 (5), 174 (3), 132 (10), 104 (12), 87 (8), 74 (6). HR-MALDI-TOF-MS, found: 542.2918 ($C_{24}H_{53}KNO_4Si_3^+$, $[M+K]^+$); calcd: 542.2919.

5.3. General method for the reductive amination

$NaBH(OAc)_3$ (1.4 equiv) was added portionwise to a stirred amino derivatives (±)-**36** and (±)-**37** (0.12 mmol) and an appropriate aromatic aldehyde (0.12 mmol) in abs $ClCH_2CH_2Cl$ (1.5 mL) at 20 °C. After complete disappearance of (±)-**36** and (±)-**37** (TLC control, 2–5 h), the solution was poured into a satd aq soln of NaCl. The organic phase was collected and the aqueous phase extracted with *t*-BME (three times×10 mL). The combined organic extracts were dried (Na_2SO_4). Solvent evaporation in vacuo and FC on silica gel gave pure amines (±)-**38b–d**,**f**,**h** and (±)-**39a–h** (light petroleum ether→AcOEt/light petroleum ether 0.5:99.5 up to 3:7).

5.3.1. (±)-4-[({(1*RS*,2*SR*,3*RS*,4*SR*,5*RS*,6*SR*)-3,4,5-Tris-[(triethylsilyl)oxy]-7-oxabicyclo[4.1.0]hept-2-yl}amino)-methyl]phenol ((±)-38b). This compound (0.026 g, 36%) was obtained according to the general procedure described above using (±)-**36** (0.06 g) and 4-hydroxybenzaldehyde (0.015 g). TLC: light petroleum ether/AcOEt (8.5:1.5). Yellowish oil. IR (film): 3330, 2955, 2879, 1612, 1516, 1460, 1240, 1100, 1011, 886, 805, 736 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 7.16 (d, 1H, *J*=8.5), 6.70 (d, 1H, *J*=8.5), 3.86 (d, 1H, *J*=12.9), 3.79 (dd, 1H, *J*=8.9, 6.6), 3.75 (d, 1H, *J*=12.9), 3.72 (br d, 1H, *J*=6.6), 3.57 (dd, 1H, *J*=8.9, 4.2), 3.28–3.26 (br m, 1H), 3.23–3.21 (br m, 1H), 3.04 (br d, 1H, *J*=3.6), 1.04–0.90 (m, 27H), 0.75–0.57 (m, 18H). ^{13}C NMR (100.6 MHz, $CDCl_3$): 155.2 (s), 131.4 (s), 129.5 (d, *J*=157), 115.4 (d, *J*=158), 73.5 (d, *J*=144), 73.0 (d, *J*=145), 69.6 (d, *J*=141), 57.6 (d, *J*=178), 57.1 (d, *J*=133), 55.5 (d, *J*=176), 52.5 (t, *J*=136), 7.1, 7.0, 6.9 (3q, *J*=126), 5.3, 5.0, 4.9 (t, *J*=116). CIMS (NH_3): 612 (23, $[M+2H^+]$), 611 (48, $[M+H^+]$), 610 (100, $[M]^+$), 504 (14), 391 (13), 321 (13), 279 (6), 205 (5), 161 (2), 122 (44), 107 (63), 104 (16), 87 (9), 74 (3). HR-MALDI-TOF-MS, found: 610.3811 ($C_{31}H_{60}NO_5Si_3^+$, $[M+H]^+$); calcd: 610.3779.

5.3.2. (±)-(1*RS*,2*SR*,3*RS*,4*SR*,5*RS*,6*SR*)-3,4,5-Tris[(triethylsilyl)oxy]-*N*-{[4-(trifluoromethyl)phenyl]methyl}-7-oxabicyclo[4.1.0]heptan-2-amine ((±)-38c). This compound (0.058 g, 73%) was obtained according to the general procedure described above using (±)-**36** (0.06 g) and 4-(trifluoromethyl)benzaldehyde (0.016 mL). TLC: light petroleum ether/AcOEt (9.4:0.6). Yellowish oil. IR (film): 3323, 2955, 2881, 1620, 1462, 1415, 1325, 1239, 1164, 1127, 1072, 1012, 807, 736 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 7.60 (d, 2H, *J*=8.1), 7.49 (d, 2H, *J*=8.1), 4.00 (d, 1H, *J*=14.0), 3.93 (d, 1H, *J*=14.0), 3.82 (dd, 1H, *J*=8.8, 6.4), 3.74 (br d, 1H, *J*=6.4), 3.58 (dd, 1H, *J*=8.8, 4.1), 3.25–3.22 (br m, 1H), 3.18–3.16 (br m, 1H), 3.02 (br d, 1H, *J*=3.0), 1.03–0.89 (m, 27H), 0.74–0.53 (m, 18H). ^{13}C NMR (100.6 MHz, $CDCl_3$): 144.5 (s), 135.0 (q, *J*=33), 128.2 (d, *J*=161), 125.3 (dd, *J*=164, 4), 124.2 (d, *J*=280), 73.4 (d, *J*=144), 73.1 (d, *J*=144), 69.8 (d, *J*=143), 57.3 (d, *J*=178), 57.1 (d, *J*=137), 55.4 (d, *J*=177), 52.3 (t, *J*=134), 7.0, 6.9 (2q, *J*=126), 5.3, 5.0, 4.9 (t, *J*=117). CIMS (NH_3): 665 (22, $[M+3H^+]$), 664 (48, $[M+2H^+]$), 663 (100, $[M+H^+]$), 662 (27, $[M]^+$), 391 (23), 373 (15), 238 (5), 200 (20), 115 (12), 104 (13), 87 (13), 76 (4). HR-MALDI-TOF-MS, found: 662.3725 ($C_{32}F_3H_{59}NO_4Si_3^+$, $[M+H]^+$); calcd: 662.3704.

5.3.3. (±)-(1*RS*,2*SR*,3*RS*,4*SR*,5*RS*,6*SR*)-*N*-(Biphenyl-4-ylmethyl)-3,4,5-tris[(triethylsilyl)oxy]-7-oxabicyclo[4.1.0]heptan-2-amine ((±)-38d). This compound (0.072 g, 90%) was obtained according to the general procedure described above using (±)-**36** (0.06 g) and 4-biphenylcarboxaldehyde (0.022 g). TLC: light petroleum ether/AcOEt (9.4:0.6). Yellowish oil. IR (film): 3323, 2954, 2879, 1704, 1605, 1461, 1412, 1239, 1074, 1010, 807, 735 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 7.63–7.57 (m, 4H), 7.49–7.44 (m, 4H), 7.37 (d, 1H, *J*=7.3), 4.01 (d, 1H, *J*=13.5), 3.92 (d, 1H, *J*=13.5), 3.87 (dd, *J*=9.0, 6.7), 3.75

(br d, 1H, *J*=6.7), 3.60 (dd, *J*=9.0, 4.1), 3.34–3.32 (br m, 1H), 3.26–3.24 (br m, 1H), 3.05 (br d, 1H, *J*=3.5), 1.06–0.94 (m, 27H), 0.76–0.55 (m, 18H). ^{13}C NMR (100.6 MHz, $CDCl_3$): 141.0 (s), 140.0 (s), 139.4 (s), 128.7 (d, *J*=159), 128.5 (d, *J*=158), 127.2 (d, *J*=160), 127.1 (d, *J*=159), 127.0 (d, *J*=158), 73.6 (d, *J*=145), 73.0 (d, *J*=144), 69.7 (d, *J*=142), 57.5 (d, *J*=178), 57.0 (d, *J*=134), 55.6 (d, *J*=176), 52.5 (t, *J*=134), 7.1, 7.0, 6.9 (3q, *J*=126), 5.1, 5.0, 4.9 (t, *J*=117). CIMS (NH_3): 671 (12, $[M]+H^+$), 670 (22, $[M]^+$), 391 (100), 279 (19), 246 (10), 184 (42), 174 (12), 167 (82), 152 (26), 132 (39), 120 (51), 104 (25), 91 (17), 87 (8), 70 (2). HR-MALDI-TOF-MS, found: 670.4157 ($C_{37}H_{64}NO_4Si_3^+$, $[M+H]^+$); calcd: 670.4143.

5.3.4. (±)-(1*RS*,2*SR*,3*RS*,4*SR*,5*RS*,6*SR*)-*N*-[(4-{[4-(Phenyloxy)phenyl]oxy}phenyl)methyl]-3,4,5-tris[(triethylsilyl)oxy]-7-oxabicyclo[4.1.0]heptan-2-amine ((±)-38f). This compound (0.076 g, 82%) was obtained according to the general procedure described above using (±)-**36** (0.06 g) and 4-(4-phenoxyphenoxy)benzaldehyde (0.035 g). TLC: light petroleum ether/AcOEt (9.4:0.6). Yellowish oil. IR (film): 3324, 2954, 2878, 1699, 1596, 1492, 1225, 1156, 1073, 1011, 864, 738 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 7.37–7.28 (m, 4H), 7.13 (t, 1H, *J*=7.4), 7.07–6.98 (m, 8H), 3.94 (d, 1H, *J*=13.4), 3.83 (d, 1H, *J*=13.4), 3.84–3.82 (m, 1H), 3.74 (br d, 1H, *J*=6.6), 3.59 (dd, 1H, *J*=8.9, 4.1), 3.30–3.28 (br m, 1H), 3.24–3.22 (br m, 1H), 3.03 (br d, 1H, *J*=3.6), 1.05–0.95 (m, 27H), 0.75–0.56 (m, 18H). ^{13}C NMR (100.6 MHz, $CDCl_3$): 157.8 (s), 156.7 (s), 152.8 (s), 152.6 (s), 135.1 (s), 129.7 (d, *J*=159), 129.4 (d, *J*=158), 123.0 (d, *J*=160), 120.5 (d, *J*=162), 120.3 (d, *J*=163), 118.3 (d, *J*=160), 118.2 (d, *J*=160), 73.6 (d, *J*=143), 73.1 (d, *J*=144), 69.7 (d, *J*=143), 57.4 (d, *J*=178), 57.0 (d, *J*=136), 55.6 (d, *J*=176), 52.2 (t, *J*=134), 7.1, 7.0, 6.9 (3q, *J*=126), 5.3, 5.0, 4.9 (t, *J*=117). CIMS (NH_3): 780 (22, $[M]+3H^+$), 779 (30, $[M]+2H^+$), 778 (40, $[M]+H^+$), 777 (6, $[M]^+$), 489 (18), 391 (16), 291 (25), 290 (82), 275 (100), 258 (5), 238 (3), 115 (10), 87 (9), 74 (4). HR-MALDI-TOF-MS, found: 778.4351 ($C_{43}H_{68}NO_6Si_3^+$, $[M+H]^+$); calcd: 778.4354.

5.3.5. (±)-(1*RS*,2*SR*,3*RS*,4*SR*,5*RS*,6*SR*)-*N*-[(5-Bromo-2-thienyl)methyl]-3,4,5-tris[(triethylsilyl)oxy]-7-oxabicyclo[4.1.0]heptan-2-amine ((±)-38h). This compound (0.057 g, 70%) was obtained according to the general procedure described above using (±)-**36** (0.06 g) and 5-bromothiophene-2-carboxaldehyde (0.014 mL). TLC: light petroleum ether/AcOEt (9.6:0.4). Yellowish oil. IR (film): 3323, 2954, 2878, 1459, 1413, 1239, 1104, 1073, 1010, 799, 734 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 6.89 (d, 1H, *J*=3.6), 6.70 (d, 1H, *J*=3.5), 4.02 (br s, 2H), 3.77 (dd, 1H, *J*=8.3, 6.3), 3.73 (br d, 1H, *J*=6.2), 3.58 (dd, 1H, *J*=8.3, 4.0), 3.27–3.25 (br m, 1H), 3.15 (br m, 1H), 3.02 (br d, 1H, *J*=3.6), 1.04–0.91 (m, 27H), 0.73–0.55 (m, 18H). ^{13}C NMR (100.6 MHz, $CDCl_3$): 146.3 (s), 129.4 (d, *J*=173), 124.8 (d, *J*=168), 111.0 (s), 73.2, 73.2 (2d, $J\approx146$), 69.8 (d, *J*=140), 57.2 (d, *J*=178), 56.6 (d, *J*=136), 55.4 (d, *J*=176), 47.7 (t, *J*=136, Ar*C*H$_2$N), 7.1, 7.0, 6.9 (3q, *J*=126), 5.2, 5.0, 4.9 (3t, *J*=117). CIMS (NH_3): 681 (25, $[M]+3H^+$), 680 (58, $[M]+2H^+$), 679 (25, $[M]+H^+$), 678 (47, $[M]^+$), 677 (10), 598 (1), 432 (3), 391 (100), 389 (25), 279 (22), 254 (6), 200 (14), 192 (69), 190 (70), 184 (10), 177 (37), 175 (36), 132 (27), 115 (13), 104 (29), 87 (12), 76 (6). HR-MALDI-TOF-MS, found: 700.2325 ($BrC_{29}H_{56}NNaO_4SSi_3^+$, $[M+Na]^+$); calcd: 700.2319.

5.3.6. (±)-(1*RS*,2*RS*,3*SR*,4*RS*,5*SR*,6*SR*)-*N*-Benzyl-3,4,5-tris[(triethylsilyl)oxy]-7-oxabicyclo[4.1.0]heptan-2-amine ((±)-39a). This compound (0.055 g, 78%) was obtained according to the general procedure described above using (±)-**37** (0.06 g) and benzaldehyde (0.012 mL). TLC: light petroleum ether/AcOEt (9.5:0.5). Light yellowish oil. IR (film): 3340, 2953, 2878, 1460, 1413, 1238, 1162, 1086, 1010, 897, 799, 736 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 7.38–7.23 (m, 5H), 4.06 (d, 1H, *J*=13.5), 3.87 (d, 1H, *J*=13.5), 3.84–3.78 (m, 2H), 3.45 (dd, 1H, *J*=6.5, 6.2), 3.27–3.25 (br m, 2H), 3.16–3.14 (br m, 1H), 1.05–0.93 (m, 27H), 0.74–0.55 (m, 18H). ^{13}C NMR (100.6 MHz, $CDCl_3$): 140.8 (s), 128.2 (d, *J*=159), 128.2 (d, *J*=159), 126.8 (d, *J*=160), 74.8, 71.7 (2d, *J*=142), 72.7 (d, *J*=139), 56.3, 53.3 (2d, *J*=177), 54.2 (d, *J*=134), 51.6 (t, *J*=134), 7.0, 6.9, 6.8 (3q, *J*=125), 5.3, 5.2, 5.0 (3t, *J*=117). CIMS (NH_3): 596 (22, $[M]+2H^+$), 595 (50, $[M]+H^+$), 594 (100, $[M]^+$), 564 (4), 392 (7), 391 (27), 305 (7), 170 (4), 106 (29), 91 (18), 87 (10), 74 (3). HR-MALDI-TOF-MS, found: 594.3847 ($C_{31}H_{60}NO_4Si_3^+$, $[M+H]^+$); calcd: 594.3830.

5.3.7. (±)-4-[({(1*RS*,2*RS*,3*SR*,4*RS*,5*SR*,6*SR*)-3,4,5-Tris[(triethylsilyl)oxy]-7-oxabicyclo[4.1.0]hept-2-yl}amino)methyl]phenol ((±)-39b). This compound (0.051 g, 70%) was obtained according to the general procedure described above using (±)-**37** (0.06 g) and 4-hydroxybenzaldehyde (0.015 g). TLC: light petroleum ether/AcOEt (4:1). Light yellowish oil. IR (KBr): 3423, 2955, 2879, 1613, 1516, 1460, 1240, 1164, 1088, 1010, 893, 737 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 7.13 (d, 2H, *J*=8.4), 6.71 (d, 1H, *J*=8.4), 3.93 (d, 1H, *J*=12.9), 3.82–3.74 (m, 3H), 3.45 (dd, 1H, *J*=6.8, 6.7), 3.28–3.27 (br m, 2H), 3.17–3.15 (br m, 1H), 1.03–0.91 (m, 27H), 0.72–0.53 (m, 18H). ^{13}C NMR (100.6 MHz, $CDCl_3$): 155.1 (s), 136.6 (s), 129.5 (d, *J*=157), 115.5 (d, *J*=158), 74.7 (d, *J*=138), 72.4 (d, *J*=140), 71.3 (d, *J*=147), 56.7, 53.2 (2d, *J*=177), 54.3 (d, *J*=134), 51.1 (t, *J*=133), 7.1, 7.0, 6.9 (3q, *J*=125), 5.3, 5.2, 5.0 (3t, *J*=117). CIMS (NH_3): 611 (3, $[M]+H^+$), 610 (7, $[M]^+$), 504 (21), 391 (13), 174 (5), 132 (9), 124 (17), 107 (100), 100 (4), 91 (6), 78 (6), 70 (1). HR-MALDI-TOF-MS, found: 610.3720 ($C_{31}H_{60}NO_5Si_3^+$, $[M+H]^+$); calcd: 610.3779.

5.3.8. (±)-(1*RS*,2*RS*,3*SR*,4*RS*,5*SR*,6*SR*)-3,4,5-Tris[(triethylsilyl)oxy]-*N*-{[4-(trifluoromethyl)phenyl]methyl}-7-oxabicyclo[4.1.0]heptan-2-amine ((±)-39c). This compound (0.059 g, 75%) was obtained according to the general procedure described above using (±)-**37** (0.06 g) and 4-(trifluoromethyl)benzaldehyde (0.016 mL). TLC: light petroleum ether/AcOEt (9.4:0.6)). Yellowish oil. IR (KBr): 3340, 2955, 2880, 1619, 1461, 1415, 1326, 1239, 1164, 1127, 1088, 1012, 896, 736 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 7.58 (d, 2H, *J*=8.2), 7.51 (d, 2H, *J*=8.2), 4.09 (d, 1H, *J*=14.0), 3.95 (d, 1H, *J*=14.0), 3.84 (dd, 1H, *J*=5.8, 2.0), 3.80 (dd, 1H, *J*=7.8, 5.8), 3.50 (dd, 1H, *J*=7.8, 5.1), 3.28–3.25 (br m, 2H), 3.15–3.12 (br m, 1H), 1.05–0.94 (m, 27H), 0.74–0.56 (m, 18H). ^{13}C NMR (100.6 MHz, $CDCl_3$): 145.0 (s), 134.8 (q, *J*=32), 128.3 (d, *J*=160), 125.2 (dd, *J*=163, 4), 124.1 (d, *J*=278), 74.6 (d, *J*=140), 72.6 (d, *J*=139), 71.7 (d, *J*=145), 56.3, 53.3 (2d, *J*=178), 54.4 (d, *J*=135), 51.1 (t, *J*=134), 7.0, 6.9, 6.8 (3q,

J=125), 5.3, 5.1 (2t, J=117). CIMS (NH_3): 664 (24, [M]+2H$^+$), 663 (51, [M]+H$^+$), 662 (100, [M]$^+$), 529 (7), 391 (72), 373 (10), 279 (6), 200 (6), 174 (8), 132 (14), 115 (9), 104 (20), 87 (14), 76 (7), 74 (6). HR-MALDI-TOF-MS, found: 684.3970 ($C_{32}F_3H_{58}NNaO_4Si_3^+$, [M+Na]$^+$); calcd: 684.3523.

5.3.9. (±)-(1*RS*,2*RS*,3*SR*,4*RS*,5*SR*,6*SR*)-*N*-[(Biphenyl-4-yl)methyl]-3,4,5-tris[(triethylsilyl)oxy]-7-oxabicyclo[4.1.0]heptan-2-amine ((±)-39d). This compound (0.053 g, 67%) was obtained according to the general procedure described above using (±)-**37** (0.06 g) and 4-biphenylcarboxaldehyde (0.022 g). TLC: light petroleum ether/AcOEt (9:1). Yellowish oil. IR (film): 3339, 2953, 2878, 1703, 1604, 1459, 1412, 1238, 1162, 1085, 1010, 896, 733 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 7.60 (d, 2H, J=8.0), 7.57 (d, 2H, J=8.5), 7.47–7.42 (m, 4H), 7.36 (t, 1H, J=7.4), 4.11 (d, 1H, J=13.7), 3.89 (d, 1H, J=13.7), 3.82–3.78 (m, 2H), 3.50 (ddd, 1H, J=7.3, 5.1, 1.5), 3.31–3.27 (br m, 2H), 3.17 (dd, 1H, J=5.1, 4.2), 1.04–0.91 (m, 27H), 0.73–0.52 (m, 18H). ^{13}C NMR (100.6 MHz, $CDCl_3$): 141.1 (s), 139.8 (s), 139.6 (s), 128.7 (d, J=159), 128.6 (d, J=160), 127.1 (d, J=159), 127.0 (d, J=159), 74.9, 71.2 (2d, J=141), 52.6 (d, J=136), 56.7, 53.1 (2d, J=177), 54.0 (d, J=134), 51.1 (t, J=134), 7.1, 7.0, 6.9 (3q, J=125), 5.3, 5.2, 5.0 (3t, J=117). CIMS (NH_3): 673 (8, [M]+3H$^+$), 672 (26, [M]+2H$^+$), 671 (55, [M]+H$^+$), 670 (100, [M]$^+$), 640 (4), 381 (9), 246 (3), 182 (47), 168 (6), 167 (31), 132 (12), 104 (16), 87 (13), 74 (9). HR-MALDI-TOF-MS, found: 670.4136 ($C_{37}H_{64}NO_4Si_3^+$, [M+H]$^+$); calcd: 670.4143.

5.3.10. (±)-(1*RS*,2*RS*,3*SR*,4*RS*,5*SR*,6*SR*)-*N*-[(4-Pyridin-4-ylphenyl)methyl]-3,4,5-tris[(triethylsilyl)oxy]-7-oxabicyclo[4.1.0]heptan-2-amine ((±)-39e). This compound (0.046 g, 57%) was obtained according to the general procedure described above using (±)-**37** (0.06 g) and 4-(4-formylphenyl)pyridine (0.022 g). TLC: light petroleum ether/AcOEt (3:2). Yellowish oil. IR (film): 3338, 2955, 2880, 1597, 1461, 1411, 1238, 1162, 1086, 1011, 897, 803, 731 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 8.65 (d, 2H, J=6.0), 7.61 (d, 2H, J=8.1), 7.51 (d, 2H, J=6.2), 7.49 (d, 2H, J=8.3), 4.11 (d, 1H, J=13.8), 3.91 (d, 1H, J=13.8), 3.82–3.76 (m, 2H), 3.43 (dd, 1H, J=7.5, 5.8), 3.28–3.26 (br m, 2H), 3.16–3.14 (br m, 1H), 1.03–0.91 (m, 27H), 0.72–0.54 (m, 18H). ^{13}C NMR (100.6 MHz, $CDCl_3$): 150.2 (d, J=178), 148.1 (s), 141.8 (s), 136.6 (s), 128.9 (d, J=159), 126.9 (d, J=159), 121.5 (d, J=162), 74.8, 71.2 (2d, J=140), 72.5 (d, J=137), 56.6, 53.1 (2d, J=178), 54.3 (d, J=134), 51.1 (t, J=134), 7.1, 7.0, 6.9 (3q, J=126), 5.2, 5.1, 4.9 (3t, J=116). CIMS (NH_3): 674 (23, [M]+3H$^+$), 672 (55, [M]+H$^+$), 671 (100, [M]$^+$), 509 (3), 504 (18), 391 (39), 382 (8), 279 (4), 183 (23), 168 (12), 132 (12), 104 (16), 87 (12), 72 (1). HR-MALDI-TOF-MS, found: 671.4061 ($C_{36}H_{63}N_2O_4Si_3^+$, [M+H]$^+$); calcd: 671.4096.

5.3.11. (±)-(1*RS*,2*RS*,3*SR*,4*RS*,5*SR*,6*SR*)-*N*-[(4-{[4-(Phenyloxy)phenyl]oxy}phenyl)methyl]-3,4,5-tris[(triethylsilyl)oxy]-7-oxabicyclo[4.1.0]heptan-2-amine ((±)-39f). This compound (0.076 g, 82%) was obtained according to the general procedure described above using (±)-**37** (0.06 g) and 4-(4-phenoxyphenoxy)benzaldehyde (0.035 g). TLC: light petroleum ether/AcOEt (9.4:0.6). Light yellowish oil. IR (film): 3340, 2954, 2879, 1699, 1595, 1492, 1415, 1224, 1160, 1087, 1011, 863, 737 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 7.37–7.27 (m, 4H), 7.09–6.96 (m, 9H), 4.04 (d, 1H, J=13.5), 3.84–3.76 (m, 3H), 3.42 (dd, 1H, J=8.2, 5.1), 3.28–3.26 (br m, 2H), 3.15 (dd, 1H, J=5.0, 4.3), 1.04–0.91 (m, 27H), 0.73–0.52 (m, 18H). ^{13}C NMR (100.6 MHz, $CDCl_3$): 157.8 (s), 156.5 (s), 153.0 (s), 152.4 (s), 135.3 (s), 129.7 (d, J=159), 129.5 (d, J=158), 122.9 (d, J=160), 120.4 (d, J=162), 120.1 (d, J=162), 118.3 (d, J=160), 118.2 (d, J=161), 74.8, 71.2 (2d, J=140), 72.5 (d, J=135), 56.7, 53.1 (2d, J=176), 54.1 (d, J=133), 50.8 (t, J=134), 7.1, 7.0, 6.9 (3q, J=126), 5.2, 5.2, 4.9 (3t, J=116). CIMS (NH_3): 781 (22, [M]+3H$^+$), 780 (42, [M]+2H$^+$), 779 (66, [M]+H$^+$), 778 (20, [M]$^+$), 504 (16), 391 (4), 308 (18), 292 (20), 291 (100), 290 (63), 275 (32), 144 (2), 132 (18), 120 (14), 115 (13), 104 (21), 91 (10), 87 (14), 76 (9), 72 (2). HR-MALDI-TOF-MS, found: 778.4357 ($C_{43}H_{68}NO_6Si_3^+$, [M+H]$^+$); calcd: 778.4354.

5.3.12. (±)-3,6-Dichloro-2-[({(1*RS*,2*RS*,3*SR*,4*RS*,5*SR*,6*SR*)-3,4,5-tris[(triethylsilyl)oxy]-7-oxabicyclo[4.1.0]hept-2-yl}amino)methyl]phenol ((±)-39g). This compound (0.04 g, 50%) was obtained according to the general procedure described above using (±)-**37** (0.06 g) and 3,5-dichlorosalicylaldehyde (0.023 g). TLC: light petroleum ether/AcOEt (9.4:0.6). Yellowish oil. IR (KBr): 3318, 2956, 2880, 1640, 1463, 1380, 1237, 1165, 1087, 1011, 898, 735 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 7.27 (d, 1H, J=2.1), 6.89 (d, 1H, J=4.0), 4.15 (d, 1H, J=13.8), 3.96 (d, 1H, J=13.8), 3.84 (dd, 1H, J=5.8, 1.2), 3.63 (dd, 1H, J=8.2, 5.8), 3.53 (dd, 1H, J=8.2, 5.2), 3.34–3.32 (br m, 2H), 3.14 (br m, 1H), 1.04–0.88 (m, 27H), 0.72–0.57 (m, 18H). ^{13}C NMR (100.6 MHz, $CDCl_3$): 153.1 (s), 128.8 (d, J=169), 126.5 (d, J=163), 125.0 (s), 123.1 (s), 122.1 (s), 73.8 (d, J=138), 71.3, 71.2 (d, J=140), 56.9, 52.3 (2d, J=178), 54.2 (d, J=134), 50.0 (t, J=136), 7.1, 7.0, 6.9 (3q, J=125), 5.1, 4.9 (2t, J=116). CIMS (NH_3): 681 (27, [M]+3H$^+$), 680 (58, [M]+2H$^+$), 678 (79, [M]$^+$), 504 (31), 391 (100), 372 (4), 371 (13), 279 (8), 192 (4), 132 (15), 104 (26), 87 (12), 76 (8), 72 (1). HR-MALDI-TOF-MS: 678.3052 ($C_{31}Cl_2H_{58}NO_5Si_3^+$, [M+H]$^+$); calcd: 678.3000.

5.3.13. (±)-(1*RS*,2*RS*,3*SR*,4*RS*,5*SR*,6*SR*)-*N*-[(5-Bromo-2-thienyl)methyl]-3,4,5-tris[(triethylsilyl)oxy]-7-oxabicyclo[4.1.0]heptan-2-amine ((±)-39h). This compound (0.048 g, 60%) was obtained according to the general procedure described above using (±)-**37** (0.06 g) and 5-bromothiophene-2-carboxaldehyde (0.014 mL). TLC: light petroleum ether/AcOEt (9.4:0.6). Yellowish oil. IR (film): 3337, 2954, 2878, 1675, 1459, 1415, 1238, 1163, 1088, 1010, 896, 796, 736 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 6.88 (d, 1H, J=3.7), 6.69 (d, 1H, J=3.7), 4.14 (d, 1H, J=14.4), 4.02 (d, 1H, J=14.4), 3.83 (dd, 1H, J=5.6, 1.9), 3.75 (dd, 1H, J=7.9, 5.6), 3.49 (dd, 1H, J=7.9, 5.0), 3.26–3.24 (br m, 2H), 3.21–3.19 (br m, 1H), 1.05–0.89 (m, 27H), 0.74–0.55 (m, 18H). ^{13}C NMR (100.6 MHz, $CDCl_3$): 146.8 (s), 129.3 (J=172), 124.8 (d, J=169), 110.7 (s), 74.3 (d, J=138, C(5)), 72.5 (d, J=136), 71.9 (d, J=146), 56.0, 53.2 (2d, J=177), 53.5 (d, J=135), 46.4 (t, J=136), 6.9, 6.8 (2q, J=125), 5.3, 5.1 (2t, J=116). CIMS (NH_3): 679 (2, [M]+H$^+$), 678 (4, [M]$^+$), 567 (4), 391 (100), 371 (20), 313 (8), 279 (48), 261 (6), 258 (14), 252 (10), 241 (13), 234 (14), 224 (17), 219 (17), 210 (18), 207 (22), 202 (20), 193 (29), 184 (51), 180 (44), 174 (41), 167 (59), 163 (30),

152 (40), 138 (31), 132 (97), 120 (96), 109 (24), 102 (32), 91 (39), 84 (28), 78 (14), 72 (19). HR-MALDI-TOF-MS, found: 700.2384 ($BrC_{29}H_{56}NNaO_4SSi_3^{\ddagger}$, $[M+Na]^+$); calcd: 700.2319.

5.4. Crystallographic data

Crystallographic data for the structure (±)-**30** have been deposited at the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 634190. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

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