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A New Efficient Synthesis of Long-Chain Di- and Triaminopolyols

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The asymmetric synthesis of long-chain di- and triamino polyols is reported. The developed methodology is based on the functionalization of 3,3′-methylenebis{[6-(benzyloxy)-methoxy]cyclohept-3-en-1-ol} derivatives that allows the selective introduction of amine moieties at defined positions of polyketide fragments. The versatile strategy disclosed here requires few purification steps and may generate a large panel of stereoisomers.

Introduction

Aminopolyols belonging to the large family of amino sugars and deoxyamino sugars are molecules of high importance in medicinal chemistry and glycobiology,[1] therefore many synthetic efforts have been directed toward the design of efficient routes toward these derivatives.[2] Long-chain polyketides containing amino groups are rare natural compounds that display important biological properties. For example, linearmycins,[3] which have been isolated from the mycelial extracts of *Streptomyces sp*, display antifungal and antibacterial activities, zwittermycin A,[4] an aminopolyol antibiotic produced by *Bacillus cereus* UW 85, suppresses certain plant diseases and is highly active against various eukaryotes (Figure 1), and galantinic acid,[5] a nonproteinogenic amino acid, has attracted much synthetic attention due to its unique structure and biological properties. Nevertheless, few synthetic routes toward linear aminopolyols have been reported thus far and are mostly limited to short sequences.[6]

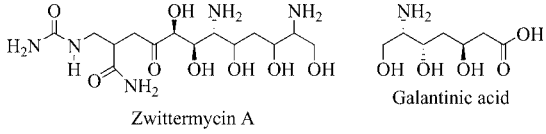
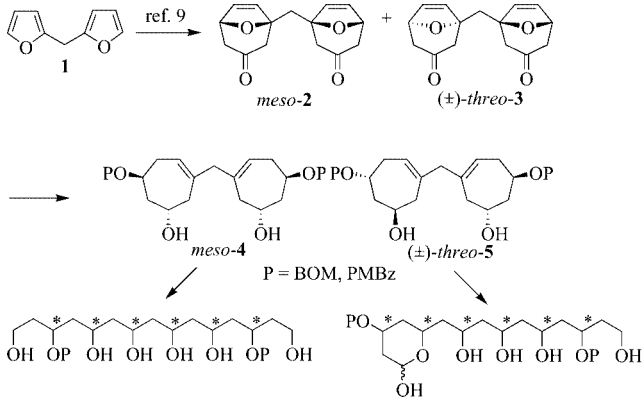


Figure 1. Natural long-chain aminopolyols.

Vogel's group has developed a non-iterative asymmetric synthesis of fifteen-carbon 1,3-polyols and heptahydroxypentadecanals based on the stereoselective functionalization of dialkenes of type *meso*-**4**[7] and (±)-*threo*-**5**,[8] which are readily obtained from the bicyclo adducts resulting from the double [4+3] cycloaddition of 2,2′-methylenedifuran to 1,1,3-trichloro-2-oxyallyl cation (Scheme 1).[9] In previous studies, we demonstrated that *meso*-**4** can be desymmetrized and transformed into polyketides containing amino groups at the terminal positions of the systems.[7c] Nevertheless, the synthetic route requires a large number of steps and does not allow the selective introduction of amino groups at internal positions of the polyketide chain. We report here a further development of the non-iterative functionalization of diolefin *threo*-**5** for the efficient preparation of long-chain di- and triamino polyols. In particular, pathways have been developed for the selective protection of some alcohol moieties of long-chain polyols[10] in order to introduce amino groups at defined positions of the skeleton. Linear flexible systems as well as diketal derivatives can be readily produced.



Scheme 1.

Results and Discussion

Based on our previous results on the synthesis of heptahydroxypentadecanals, diolefin (–)-**5** was submitted to ozonolysis followed by reductive treatment with Me_2S and then with an excess of Et_2BOMe and $NaBH_4$ at –30 °C[11] to afford a mixture of bis(hemiacetals) **6** in 55% yield. Re-

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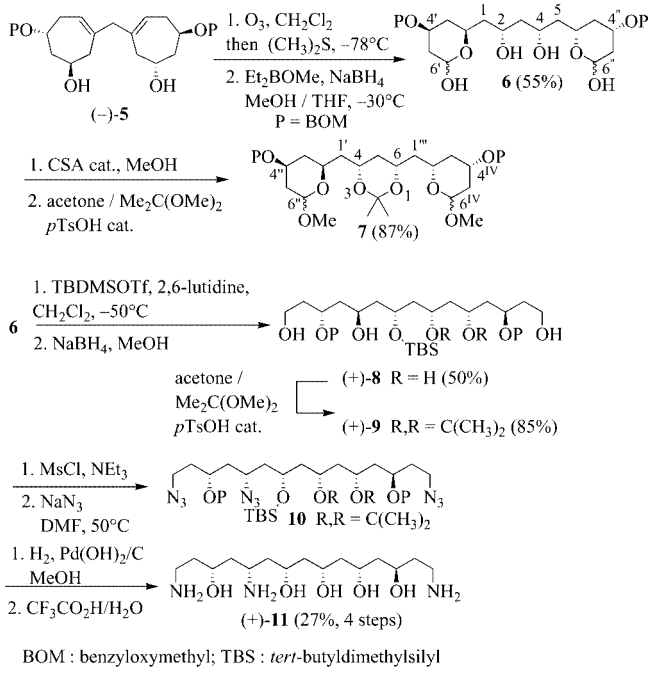
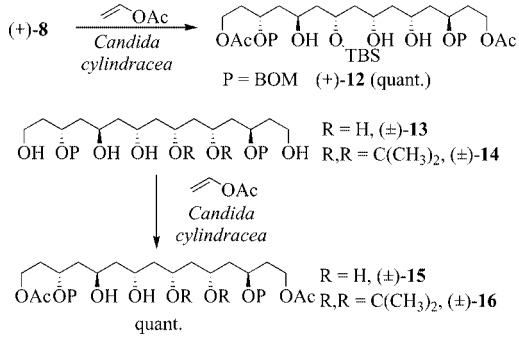
action with camphorsulfonic acid in methanol, followed by protection of the diol moiety as an acetonide, provided pyranosides **7** as a mixture of four isomers (87% yield, 2 steps) due to the presence of two anomers at each hemiketal moiety. Only two sets of signals (corresponding to anomers, 2:1 ratio) can be distinguished in the NMR spectra of this derivative as a result of the quasi-symmetry of the molecule. Moreover, typical ^{13}C NMR signals[12] were observed for the acetonide at C-4 and C-6 (δ_{Me} = 31.6 and 21.3 ppm), thus establishing the *syn* relative configuration of the corresponding diol (Scheme 2).



Scheme 2.

Treatment of bis(hemiacetals) **6** with *tert*-butyldimethylsilyl trifluoromethanesulfonate (1.5 equiv.) under dilute conditions at –50 °C led to the highly regioselective silylation of the alcohol at C-2, which is directed by intramolecular hydrogen bonding between the hydroxy moiety at C-4 and the intracyclic oxygen atom at C-2′′.[13] Subsequent reduction of the hemiacetal moieties afforded the monosilylated polyol (+)-**8** in 50% yield (2 steps). The 1,3-*syn*-diol (+)-**8** was converted into the corresponding acetonide [acetone/$Me_2C(OMe)_2$, *p*-TsOH cat.] to provide the semi-protected polyol (+)-**9**, which was used for the introduction of three amino groups on the polyketide skeleton. The remaining alcohols were esterified with CH_3SO_2Cl, and displacement of the resulting trimesylate with NaN_3 provided triazide **10**. This intermediate was directly submitted to catalytic hydrogenation [H_2, $Pd(OH)_2$/C, MeOH] followed by acidic removal of the protecting groups to deliver triaminopentol (+)-**11** in 27% yield (four steps).

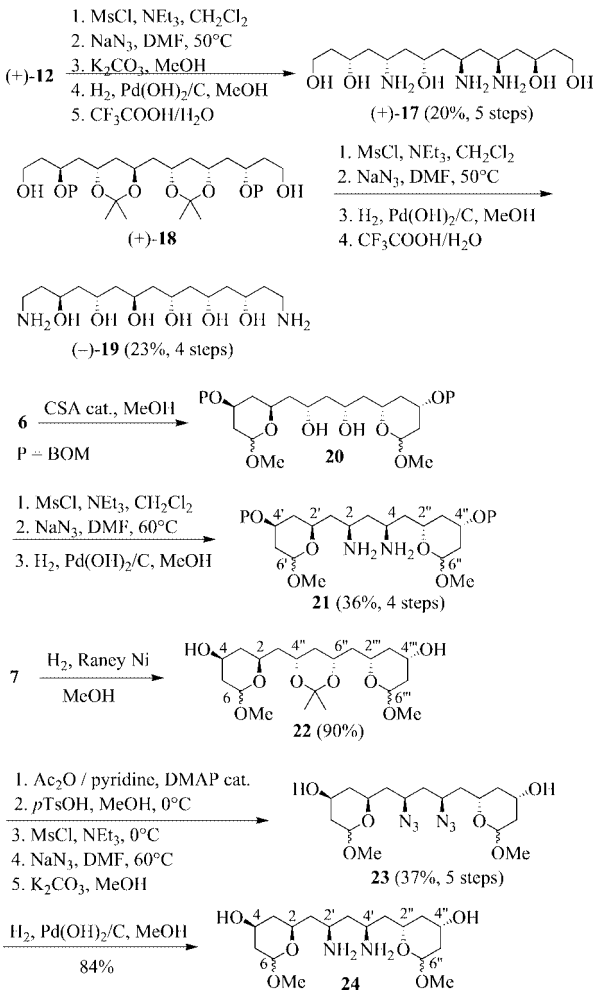
We next targeted the introduction of amino groups at three internal positions of the polyolic system. For this purpose, we studied the selective protection of the primary alcohols of polyketide chains without affecting internal secondary alcohols (Scheme 3). Treatment of the monosilylated derivative (+)-**8** with vinyl acetate in the presence of *Candida cylindracea* lipase (4800 U mmol^{-1}) allowed the selective transacetylation of the primary alcohols with quantitative yield. Interestingly, we found that this procedure could be applied to other semi-protected polyketides [(±)-**13**[8b] and (±)-**14**[10]], thus providing a simple and efficient method for the selective acetylation of primary alcohols in the presence of free secondary hydroxy moieties. In all cases, the corresponding diacetates [(±)-**15** and (±)-**16**] were obtained in quantitative yields.



Scheme 3.

Derivative (+)-**12** was then converted into an intermediate triazide as above (Scheme 4). The acetyl groups of this compound were methanolyzed directly under classical conditions (K_2CO_3, MeOH), without intermediate purification, and the azido groups were reduced by catalytic hydrogenation. The remaining protective moieties were finally removed by acidic hydrolysis (CF_3COOH/H_2O). This sequence afforded pentol (+)-**17**, with amino groups selectively introduced at internal positions of the linear backbone, in 20% yield (five steps). In the course of our study, amino groups were also easily introduced at the terminal positions of linear polyols. For instance, diol (+)-**18** [prepared from (+)-**5**[8b]] was submitted to a sequence of esterification with CH_3SO_2Cl followed by treatment with NaN_3 to afford an intermediate diazido derivative, which was subsequently reduced by catalytic hydrogenation and deprotected under acidic conditions to afford diaminohexol (–)-**19** in 23% yield (4 steps). Interestingly, bis(hemiacetals) **6** could also be directly derivatized into semi-protected diaminopolyols. Treatment with camphorsulfonic acid in methanol afforded a mixture of bis(methyl pyranosides) **20** (same isomeric ratio as **6** and **7**). At this stage, esterification of the secondary alcohols in the presence of CH_3SO_2Cl followed by displacement of the resulting dimesylate with NaN_3 and selective reduction of the azido groups [H_2, $Pd(OH)_2$/C, MeOH] provided derivative **21**, which is functionalized with two amino groups at positions C-2 and C-4. All our attempts to remove the benzyloxymethyl ethers from **21** were unsuccessful. Acetyl groups were thus envisaged for the protection of the alcohols at C-4′ and C-4′′. Catalytic hydrogenation of **7** in the presence of Raney nickel led to **22** by reduction of the benzyloxymethyl ethers. Acetylation of the resulting diol (Ac_2O/pyridine, DMAP cat.), followed by acidic removal of the acetonide moiety, allowed intro-

duction of azido groups at C-2 and C-4, as above. Methanolysis of the acetates delivered **23** in 37% yield (5 steps). Finally, catalytic hydrogenation in the presence of Pd(OH)$_2$/C provided diamino bis(methyl pyranosides) **24** in 84% yield.



Scheme 4.

Conclusions

An asymmetric synthesis of long-chain polyketides containing amino groups has been developed by the functionalization of 3,3′-methylenebis{[6-(benzyloxy)methoxy]cyclohept-3-en-1-ol} [(–)-**5**]. While very few methods have been reported for the preparation of linear aminopolyols, the methodology disclosed here gives access to the selective introduction of amino groups at various positions of polyketide fragments. Furthermore, the synthetic pathways require few purification steps, as exemplified by the conversion of (–)-**5** into triaminopentol (+)-**11**, which was performed with the isolation of only three intermediates over nine steps.

Experimental Section

General: Commercial reagents (Fluka, Aldrich) were used without purification. Solvents were filtered prior to use (Innovative Technology). Light petroleum ether refers to the fraction boiling at 40–60 °C. Solutions after reaction and extraction were concentrated at reduced pressure in a rotary evaporator. Liquid/solid flash chromatography (FC): columns of silica gel (0.040–0.63 mm, Merck no. 9385 silica gel 60, 240–400 mesh). TLC for reaction monitoring: Merck silica gel 60F$_{254}$ plates; detection by UV light; Pancaldi reagent [$(NH_4)_6MoO_4$, $Ce(SO_4)_2$, H_2SO_4, H_2O] or $KMnO_4$. IR spectra: Perkin–Elmer 1420 spectrometer. ^{1}H NMR spectra: Bruker ARX-400 spectrometer (400 MHz); δ_H in ppm relative to the solvent's residual ^{1}H signal [$CHCl_3$: δ_H = 7.27 ppm; CH_3OD: δ_H = 3.34 ppm; C_6H_6: δ_H = 7.3 ppm] as internal reference; all ^{1}H assignments were confirmed by 2D COSY-45 spectra. ^{13}C NMR spectra: same instrument as above (100.6 MHz); δ_C in ppm relative to solvent's C signal [$CDCl_3$: δ_C = 77.0 ppm; CD_3OD: δ_C = 48.5 ppm; C_6D_6: δ_C = 128.5 ppm] as internal reference; coupling constants are given in Hz. MS: Nermag R-10-10C, chemical ionization (NH_3) mode. MALDI-TOF, ESI and HR-MALDI-MS mass spectra were measured at the Swiss Institute of Technology Mass Spectral Facility. Elemental analyses: Ilse Beetz, 96301 Kronach, Germany.

Synthesis of 7: A stream of ozone was passed through a solution of diolefin (–)-**5** (500 mg, 0.861 mmol) in 26 mL of dichloromethane at –78 °C for 5 min. A stream of dry O_2 was then passed through the solution for 2 min, and Me_2S (250 μL, 3.45 mmol, 4 equiv.) was added dropwise. After stirring at –78 °C for 10 min, the solvent was evaporated at 0 °C. The residue was taken up in THF/MeOH (3:1; 16 mL) at 0 °C and Et_2BOMe (1 M in THF; 5.2 mL, 5.17 mmol, 6 equiv.) was added. The resulting mixture was stirred at 0 °C for an additional 1 h. The solution was cooled to –30 °C and $NaBH_4$ (260 mg, 6.891 mmol, 8 equiv.) was added portionwise. The temperature was kept below –20 °C for 2 h. The reaction mixture was poured into water (25 mL) and extracted with EtOAc (20 mL, 3 times). The combined organic extracts were dried with $MgSO_4$ and concentrated in vacuo. Purification of the residue by flash chromatography (5% to 10% of MeOH in CH_2Cl_2) afforded the intermediate bis(hemiketal) **6** as a colourless oil (274 mg, 55%). Camphorsulfonic acid (5 mg, 0.023 mmol, 0.2 equiv.) was added to a solution of **6** (65 mg, 0.113 mmol) in MeOH (3 mL) and the mixture was stirred at 25 °C for 2 h. The solution was then poured into a satd. aq. solution of $NaHCO_3$ (10 mL) and extracted with EtOAc (10 mL, 3 times). The combined organic extracts were washed with brine (20 mL), dried with $MgSO_4$ and concentrated in vacuo. The resulting diol was dissolved in a mixture of acetone and dimethoxypropane (0.3/3 mL), and treated with *p*-toluenesulfonic acid (8 mg, 0.042 mmol, 0.4 equiv.) at 0 °C. The resulting mixture was stirred at 0 °C for 1 h. The solution was poured into a satd. aq. solution of $NaHCO_3$ (10 mL) and extracted with EtOAc (10 mL, 3 times). The combined organic extracts were dried with $MgSO_4$ and concentrated in vacuo. Purification of the residue by flash chromatography (3% MeOH in CH_2Cl_2) afforded **7** as a colourless oil (63 mg, 87%, 2:1 ratio for two distinct sets of signals). IR (film): $\tilde{\nu}$ = 2940, 1450, 1380, 1260, 1200, 1160, 1115, 1045, 980, 740, 700 cm^{-1}. ^{1}H NMR (400 MHz, MeOD): δ = 7.35–7.25 (m, 10 $H_{arom.}$), 4.82 (s, 1.34 H, 6′′$_{maj}$-H, 6$^{IV}_{maj}$-H), 4.81, 4.78 [2 d, $^2J_{H,H}$ = 5.6, 6.9 Hz, 4 H, 2×CH_2(BOM)], 4.60 (s, 4 H, 2×CH_2Ph), 4.27 (m, 0.66 H, 6′′$_{min}$-H, 6$^{IV}_{min}$-H), 4.13–3.97 (m, 2 H, 2′′-H, 2^{IV}-H), 4.23–3.84 (2 m, 4 H, 4-H, 4′′-H, 4^{IV}-H, 6-H), 3.40, 3.30 (2 s, 6 H, 2×-OMe), 2.30–1.90, 1.60–1.40 (2 m, 10 H, 5-H_2, 3′′-H_2, 3^{IV}-H_2, 5′′-H_2, 5^{IV}-H_2), 1.70–1.50, 1.30–1.10 (2 m, 4 H, 1′-H_2, 1′′′-H_2),

1.26, 1.16 (2 s, 6 H, 2×2-Me) ppm. ^{13}C NMR (100 MHz, MeOD): δ = 140.4 (s, 2 $C_{arom.}$), 130.4, 130.0, 129.7 (3 d, $^1J_{C,H}$ = 160, 159, 160 Hz, 10 $C_{arom.}$), 103.6, 103.5 (2 d, $^1J_{C,H}$ = 160 Hz, C-6′′$_{min.}$, C-6$^{IV}_{min.}$), 101.5, 101.2 (2 d, $^1J_{C,H}$ = 160, 162 Hz, C-6′′$_{maj.}$, C-6$^{IV}_{maj.}$), 100.8 (s, C-2), 95.0, 94.8 [2 t, $^1J_{C,H}$ = 163 Hz, 2×CH_2(BOM)$_{maj.}$], 95.1, 94.9 [2 t, $^1J_{C,H}$ = 163 Hz, 2×CH_2(BOM)$_{min.}$], 74.5, 74.4 (2 d, $^1J_{C,H}$ = 148, 146 Hz, C-2′′$_{min.}$, C-2$^{IV}_{min.}$), 72.0, 71.8 (2 d, $^1J_{C,H}$ = 148, 144 Hz, C-2′′$_{maj.}$, C-2$^{IV}_{maj.}$), 71.5, 71.4 (2 t, $^1J_{C,H}$ = 144 Hz, 2×CH_2Ph), 70.6, 70.0, 68.3, 67.5 (4 d, C-4$_{min.}$, C-6$_{min.}$, C-4′′$_{min.}$, C-4$^{IV}_{min.}$), 68.2, 67.4, 66.4, 65.7 (4 d, $^1J_{C,H}$ = 140, 139, 145, 144 Hz, C-4$_{maj.}$, C-6$_{maj.}$, C-4′′$_{maj.}$, C-4$^{IV}_{maj.}$), 57.8, 57.7 (2 q, $^1J_{C,H}$ = 148 Hz, 2×OMe$_{min.}$), 56.2, 55.9 (2 q, $^1J_{C,H}$ = 147, 142 Hz, 2×OMe$_{maj}$), 45.3, 44.4 (2 t, $^1J_{C,H}$ = 127, 128 Hz, C-1′$_{maj.}$, C-1′′′$_{maj.}$), 44.6, 44.0 (2 t, $^1J_{C,H}$ = 127, 128 Hz, C-1′$_{min.}$, C-1′′′$_{min.}$), 41.2, 40.6, 39.1 (3 t, $^1J_{C,H}$ = 128, 130, 126 Hz, C-5, C-3′′, C-3^{IV}, C-5′′, C-5^{IV}), 31.6, 21.3 (2 q, $^1J_{C,H}$ = 123, 127 Hz, 2×Me-2) ppm. MALDI-MS: *m*/*z* = 667.35 [M + Na], 683.38 [M + K]. $C_{36}H_{52}O_{10}$ (644.792): calcd. C 67.06, H 8.13; found C 67.06, H 8.16.

Synthesis of (+)-8: 2,6-Lutidine (100 μL, 0.855 mmol, 3 equiv.) and a solution of *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.5 M in CH_2Cl_2; 900 μL, 0.456 mmol, 1.6 equiv.) were added to a solution of **6** (165 mg, 0.285 mmol) in CH_2Cl_2 (2.8 mL) at –50 °C. The resulting mixture was stirred for 1.5 h and then poured into a satd. aq. solution of $NaHCO_3$ (15 mL) and extracted with EtOAc (10 mL, 3 times). The combined organic extracts were washed with brine (30 mL), dried with $MgSO_4$ and concentrated in vacuo. The crude residual oil was dissolved in MeOH (3 mL) and treated with $NaBH_4$ (90 mg, 2.28 mmol, 8 equiv.) at 25 °C for 1 h. The reaction mixture was poured into water (20 mL) and extracted with EtOAc (20 mL, 3 times). The combined organic extracts were washed with brine (50 mL), dried with $MgSO_4$ and concentrated in vacuo. Purification of the residue by flash chromatography (4% MeOH in CH_2Cl_2) afforded (+)-**8** as a pale-yellow oil (99 mg, 50% over 2 steps). $[\alpha]^{23}_{405}$ = +31; $[\alpha]^{23}_{435}$ = +26; $[\alpha]^{23}_{577}$ = +13 (*c* = 1.4, MeOH). IR (film): $\tilde{\nu}$ = 3445, 2930, 1645, 1450, 1255, 1100 cm^{-1}. ^{1}H NMR (400 MHz, MeOD): δ = 7.35–7.22 (m, 10 $H_{arom.}$), 4.86 [br. s, 4 H, 2×CH_2(BOM)], 4.67 (br. s, 4 H, 2×CH_2Ph), 4.20–4.12 (m, 1 H, 9-H), 4.09–3.92 (m, 4 H, 3-H, 5-H, 7-H, 13-H), 3.89–3.81 (m, 1 H, 11-H), 3.70–3.62 (m, 4 H, 1-H_2, 15-H_2), 1.91–1.77 (m, 4 H, 2-H_2, 14-H_2), 1.77–1.44 (m, 10 H, 4-H_2, 6-H_2, 8-H_2, 10-H_2, 12-H_2), 0.92 [s, 9 H, C(CH_3)$_3$], 0.13 [2 s, 6 H, Si(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, MeOD): δ = 138.3 (s, 2 $C_{arom.}$), 128.4, 128.0, 127.7 (3 d, $^1J_{C,H}$ = 159, 160, 159 Hz, 10 $C_{arom.}$), 94.5 [2 t, $^1J_{C,H}$ = 163 Hz, 2×CH_2(BOM)], 73.5, 73.3 (d, $^1J_{C,H}$ = 142 Hz, C-3, C-13), 69.8, 69.3 (2 t, $^1J_{C,H}$ = 140, 142 Hz, 2×CH_2Ph), 67.8 (d, $^1J_{C,H}$ = 146 Hz, C-11), 67.5 (d, $^1J_{C,H}$ = 140 Hz, C-9), 67.1, 64.9 (2 d, $^1J_{C,H}$ = 143, 144 Hz, C-5, C-7), 58.5, 58.3 (2 t, $^1J_{C,H}$ = 148, 147 Hz, C-1, C-15), 45.9, 45.4, 44.6, 44.0, 43.4 (5 t, $^1J_{C,H}$ = 127, 125, 125, 124, 128 Hz, C-4, C-6, C-8, C-10, C-12), 38.4, 38.3 (2 t, $^1J_{C,H}$ = 126 Hz, C-2, C-14), 25.4 [q, $^1J_{C,H}$ = 129 Hz, C(CH_3)$_3$], 17.8 (s, *C*Me$_3$), –4.5, –5.0 [2 q, $^1J_{C,H}$ = 118 Hz, Si(CH_3)$_2$] ppm. MALDI-MS: *m*/*z* = 716.75 [M + Na], 732.71 [M + K]. $C_{37}H_{62}O_{10}Si$ (694.97): calcd. C 63.94, H 8.99, Si 4.04; found C 64.05, H 8.83, Si 3.90.

Synthesis of (+)-9: *p*-Toluenesulfonic acid (5 mg, 0.026 mmol, 0.3 equiv.) was added to a solution of (+)-**8** (60 mg, 0.086 mmol) in a mixture of acetone and dimethoxypropane (0.3/3 mL) and the mixture was stirred at 0 °C for 1 h. The solution was poured into a satd. aq. solution of $NaHCO_3$ (10 mL) and extracted with EtOAc (10 mL, 3 times). The combined organic extracts were washed with brine (30 mL), dried with $MgSO_4$ and concentrated in vacuo. Purification of the residue by flash chromatography (3% MeOH in CH_2Cl_2) afforded (+)-**9** as a pale-yellow oil (54 mg, 85%). $[\alpha]^{23}_{405}$ = +61; $[\alpha]^{23}_{435}$ = +52; $[\alpha]^{23}_{577}$ = +27; $[\alpha]^{23}_{589}$ = +26 (*c* = 0.95, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3440, 2945, 1460, 1430, 1380, 1255, 1200, 1160, 1040, 835, 780, 740, 700 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43–7.27 (m, 10 $H_{arom.}$), 4.86 [2 d, $^2J_{H,H}$ = 7.6, 8.4 Hz, 4 H, 2×CH_2(BOM)], 4.67 (2 d, $^2J_{H,H}$ = 10.2, 11.4 Hz, 4 H, 2×CH_2Ph), 4.17–4.04 (2 m, 4 H, 3-H, 5-H, 7-H, 2′′-H), 4.02–3.87 (2 m, 2 H, 4′-H, 6′-H), 3.86–3.77, 3.76–3.69 (2 m, 4 H, 1-H_2, 4′′-H_2), 1.89–1.72 (2 m, 6 H, 2-H_2, 1′′-H_2, 3′′-H_2), 1.68–1.52 (m, 8 H, 4-H_2, 6-H_2, 8-H_2, 5′-H_2), 1.35, 1.33 (2 s, 6 H, 2×CH_3-2′), 0.89 [s, 9 H, C(CH_3)$_3$], 0.08 [2 s, 6 H, Si(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, CDCl): δ = 137.9, 137,8 (2 s, 2 $C_{arom.}$), 128.9, 128.2 (2 d, $^1J_{C,H}$ = 160 Hz, 10 $C_{arom.}$), 98.9 (s, C-2′), 95.3, 95.1 [2 t, $^1J_{C,H}$ = 163 Hz, 2×CH_2(BOM)], 74.2, 74.0 (2 d, $^1J_{C,H}$ = 149 Hz, C-3, C-2′′), 70.4 (t, $^1J_{C,H}$ = 141 Hz, 2×CH_2Ph), 68.3 (d, $^1J_{C,H}$ = 140 Hz, C-7), 66.1, 65.9 (2 d, $^1J_{C,H}$ = 137, 141 Hz, C-4′, C-6′), 65.2 (d, $^1J_{C,H}$ = 143 Hz, C-5), 59.9, 59.8 (2 t, $^1J_{C,H}$ = 146 Hz, C-1, C-4′′), 43.8, 43.2, 42.9, 42.6 (4 t, $^1J_{C,H}$ = 127, 124, 126 Hz, C-4, C-6, C-8, C-5′), 38.3, 38.1, 38.0 (3 t, $^1J_{C,H}$ = 126 Hz, C-2, C-1′′, C-3′′), 30.5, 20.1 (2 q, $^1J_{C,H}$ = 123, 128 Hz, 2×CH_3-2′), 26.2 [q, $^1J_{C,H}$ = 126 Hz, C(CH_3)$_3$], 18.3 (s, *C*Me$_3$), –4.2, –4.3 [2 q, $^1J_{C,H}$ = 118 Hz, Si(CH_3)$_2$] ppm. MALDI-MS: *m*/*z* = 757.40 [M + Na], 773.39 [M + K]. $C_{40}H_{66}O_{10}Si$ (735.03): calcd. C 65.36, H 9.03, Si 3.82; found C 65.33, H 9.02, Si 3.79.

General Procedure for the Lipase-Catalyzed Transacetylation of Polyol Derivatives: A 0.1 M solution of polyol in vinyl acetate was vigorously stirred in the presence of lipase from *Candida Cylindracea* (5000 U mmol^{-1}, 3.85 U mg^{-1}) at 25 °C for 6 h. The suspension was then filtered through a pad of Celite. The filtrate was concentrated in vacuo and the resulting oil was purified by flash chromatography (CH_2Cl_2/MeOH, 97:3 to 95:5) in almost quantitative yields.

Synthesis of (+)-12: The general procedure applied to (+)-**8** (60 mg, 0.086 mmol) provided (+)-**12** as a pale-yellow oil (67 mg, quant.). $[\alpha]^{23}_{405}$ = +56; $[\alpha]^{23}_{435}$ = +47; $[\alpha]^{23}_{589}$ = +24 (*c* = 2.5, MeOH). IR (film): $\tilde{\nu}$ = 3460, 2945, 2860, 1740, 1460, 1430, 1370, 1250, 1100, 1040, 835, 780, 740, 700 cm^{-1}. ^{1}H NMR (400 MHz, MeOD): δ = 7.35–7.24 (m, 10 $H_{arom.}$), 4.83, 4.79 [2 d, $^2J_{H,H}$ = 6.7, 6.4 Hz, 4 H, 2×CH_2(BOM)], 4.62 (d, $^2J_{H,H}$ = 8.8 Hz, 4 H, 2×CH_2Ph), 4.18 (t, $^3J_{H,H}$ = 6.24 Hz, 4 H, 1-H_2, 15-H_2), 4.18–4.15 (m, 1 H, 11-H), 4.11–3.95 (m, 4 H, 3-H, 5-H, 7-H, 13-H), 3.91–3.78 (m, 1 H, 9-H), 2.0 [s, 6 H, 2×CH_3(OAc)], 1.93–1.85 (m, 4 H, 2-H_2, 14-H_2), 1.75–1.47 (m, 10 H, 4-H_2, 6-H_2, 8-H_2, 10-H_2, 12-H_2), 0.90 [s, 9 H, C(CH_3)$_3$], 0.11 [2 s, 6 H, Si(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, MeOD): δ = 171.9 [s, 2×C=O(OAc)], 138.2 (s, 2 $C_{arom.}$), 128.4, 127.9, 127.7 (3 d, $^1J_{C,H}$ = 159, 160, 159 Hz, 10 $C_{arom.}$), 94.5, 94.4, [2 t, $^1J_{C,H}$ = 163 Hz, 2×CH_2(BOM)], 72.8 (d, $^1J_{C,H}$ = 142 Hz, C-3, C-13), 69.9, 69.7 (t, $^1J_{C,H}$ = 140 Hz, 2×CH_2Ph), 67.6 (d, $^1J_{C,H}$ = 146 Hz, C-11), 67.3 (d, $^1J_{C,H}$ = 140 Hz, C-9), 66.9, 64.8 (2 d, $^1J_{C,H}$ = 143, 144 Hz, C-5, C-7), 61.4 (t, $^1J_{C,H}$ = 148 Hz, C-1, C-15), 46.0, 45.4, 44.4, 43.8, 43.2 (5 t, $^1J_{C,H}$ = 127, 125, 125, 124, 128 Hz, C-4, C-6, C-8, C-10, C-12), 34.4, 34.3 (t, $^1J_{C,H}$ = 126 Hz, C-2, C-14), 25.4 [q, $^1J_{C,H}$ = 129 Hz, C(CH_3)$_3$], 19.9 (s, *C*Me$_3$), –4.9, –5.3 [2 q, $^1J_{C,H}$ = 118 Hz, Si(CH_3)$_2$] ppm. CI-MS (NH_3): *m*/*z* = 780 [M + H]. $C_{41}H_{66}O_{12}Si$ (779.041): calcd. C 63.21, H 8.54, Si 3.61; found C 63.27, H 8.60, Si 3.51.

Synthesis of (±)-15: The general procedure applied to (±)-**13** (30 mg, 0.052 mmol) provided (±)-**15** as a colourless oil (35 mg, quant.). IR (film): $\tilde{\nu}$ = 3440, 2940, 1735, 1455, 1370, 1245, 1100, 1090, 740, 700 cm^{-1}. ^{1}H NMR (400 MHz, MeOD): δ = 7.37–7.25 (m, 10 $H_{arom.}$), 4.84, 4.81 [2 d, $^2J_{H,H}$ = 7.0, 6.9 Hz, 4 H, 2×CH_2(BOM)], 4.63 (s, 4 H, 2×CH_2Ph), 4.18 (t, $^3J_{H,H}$ = 6.8 Hz, 4 H, 1-H_2, 15-H_2), 4.04–3.98 (m, 6 H, 3-H, 5-H, 7-H, 9-H, 11-H, 13-H), 2.01 [s, 6 H, 2×CH_3(OAc)], 1.90 (t, $^3J_{H,H}$ = 5.5 Hz, 4 H, 2-H_2, 14-H_2), 1.64–1.50 (m, 10 H, 4-H_2, 6-H_2, 8-H_2, 10-H_2, 12-H_2) ppm. ^{13}C NMR (100 MHz, MeOD): δ = 172.9 [s, 2×C=O(OAc)],

139.3 (s, $C_{arom.}$), 129.4, 128.9, 128.7 (3 d, $^1J_{C,H}$ = 160, 159, 160 Hz, $C_{arom.}$), 95.5 [t, $^1J_{C,H}$ = 164 Hz, 2×CH_2(BOM)], 74.1, 73.9, 70.1, 68.1, 67.8, 65.8 (6 d, $^1J_{C,H}$ = 143, 144, 140, 142, 140, 146 Hz, C-3, C-5, C-7, C-9, C-11, C-13), 70.9 (t, $^1J_{C,H}$ = 144 Hz, 2×CH_2Ph), 62.4 (t, $^1J_{C,H}$ = 151 Hz, C-1, C-15), 46.6, 46.4, 45.9, 44.5, 44.2 (5 t, $^1J_{C,H}$ = 120, 123, 127, 125, 126 Hz, C-4, C-6, C-8, C-10, C-12), 35.5 (t, $^1J_{C,H}$ = 127 Hz, C-2, C-14), 20.9 [q, $^1J_{C,H}$ = 129 Hz, 2×Me(OAc)] ppm. ESI-MS: *m/z* = 665.29 [M + H]. MALDI HRMS: calcd. for [$C_{35}H_{52}O_{12}$ + Na] 687.3356; found 687.3359.

Synthesis of (±)-16: The general procedure applied to (±)-**14** (45 mg, 0.078 mmol) provided (±)-**16** as a colourless oil (55 mg, quant.). IR (film): $\tilde{\nu}$ = 3500, 2940, 1735, 1450, 1375, 1245, 1040 cm^{-1}. ^1H NMR (400 MHz, MeOD): δ = 7.37–7.15 (m, 10 $H_{arom.}$), 4.83, 4.80 [2 d, $^2J_{H,H}$ = 7.2, 7.4 Hz, 4 H, 2×CH_2(BOM)], 4.63 (s, 4 H, 2×CH_2Ph), 4.19 (t, $^3J_{H,H}$ = 6.6 Hz, 4 H, 1-H_2, 8′′-H_2), 4.17–4.07 (m, 2 H, 2′′-H, 4′′-H), 4.05–3.95 (m, 4 H, 3-H, 4′-H, 6′-H, 6′′-H), 2.00 [s, 6 H, 2×CH_3(OAc)], 1.90–1.87 (m, 4 H, 2-H_2, 7′′-H_2), 1.70–1.47, 1.55–1.47 (2 m, 10 H, 4-H_2, 5′-H_2, 1′′-H_2, 3′′-H_2, 5′′-H_2), 1.43, 1.29 (2 s, 6 H, 2×Me-2′) ppm. ^{13}C NMR (100 MHz, MeOD): δ = 171.9 [s, 2×C=O(OAc)], 138.0 (s, 2 $C_{arom.}$), 128.4, 127.9, 127.7 (3 d, 10 $C_{arom.}$), 98.9 (s, C-2′), 94.6, 94.5, [2 t, 2×CH_2(BOM)], 73.5, 73.4, (2 d, C-3, C-6′′), 69.8 (t, 2×CH_2Ph), 67.5, 66.4, 65.3, 64.4 (4 d, C-4′, C-6′, C-2′′, C-4′′), 61.4 (t, C-1, C-8′′), 44.8, 44.5, 43.6, 43.0, 37.6 (5 t, C-4, C-5′, C-1′′, C-3′′, C-5′′), 34.5, 34.4 (2 t, C-2, C-7′′), 29.6, 19.9 (2 q, 2×Me-2′), 19.2 [q, 2×Me(OAc)] ppm. ESI-MS: *m/z* = 705.33 [M + H]. MALDI HRMS: calcd. for [$C_{38}H_{56}O_{12}$ + Na] 727.3669; found 727.3665.

General Procedure for the Conversion of Semi-Protected Polyols (+)-9, (+)-12 and (+)-18 into Di- and Triaminopolyols: Triethylamine (4.5 equiv. per free alcohol group) and methanesulfonyl chloride (1.5 equiv. per free alcohol group) were added to a solution of the semi-protected polyol in CH_2Cl_2 (0.1 M) at 0 °C. The solution was stirred at 0 °C for 2 h and then poured into a satd. aq. solution of NH_4Cl and extracted with EtOAc (3 times). The combined organic extracts were washed with brine, dried with $MgSO_4$ and concentrated in vacuo. The residual oil was dissolved in DMF (0.75 M) and treated with sodium azide (5 equiv. per mesylate group) at 60 °C for 12 h. The mixture was poured into water and extracted with EtOAc (3 times). The combined organic extracts were washed with brine, dried with $MgSO_4$ and concentrated in vacuo. The residual oil was dissolved in MeOH (0.1 M). A catalytic amount of $Pd(OH)_2$ was added and the resulting mixture was vigorously stirred under hydrogen (1 atm.). At the end of the reaction (monitored by TLC: CH_3CN/NH_4OH), the mixture was filtered through a pad of Celite and concentrated in vacuo. The crude intermediate was dissolved in CF_3COOH/H_2O (4:1) and vigorously stirred at 25 °C. After completion of the reaction (monitored by TLC: CH_3CN/NH_4OH), the solvents were removed under vacuo. The crude oil was purified by flash chromatography (CH_3CN/NH_4OH, 2:1 to 1:2) to afford the aminopolyols as white foams.

Synthesis of (+)-11: The general procedure applied to compound (+)-**9** (200 mg, 0.272 mmol) afforded (+)-**11** (40 mg, 27% yield over four steps). $[\alpha]_{435}^{23}$ = +5.5; $[\alpha]_{589}^{23}$ = +3 (*c* = 0.19, MeOH). IR (KBr): $\tilde{\nu}$ = 3405, 1740, 1650, 1560, 1515, 1070 cm^{-1}. ^1H NMR (400 MHz, D_2O): δ = 4.1–3.88 (m, 5 H, 3-H, 5-H, 7-H, 9-H, 13-H), 3.46–3.34 (m, 1 H, 11-H), 3.19–3.00 (m, 4 H, 1-H_2, 15-H_2), 1.95–1.54 (m, 14 H, 2-H_2, 4-H_2, 6-H_2, 8-H_2, 10-H_2, 12-H_2) ppm. ^{13}C NMR (100 MHz, D_2O): δ = 70.2, 69.8, 68.4, 68.3 (4 d, C-3, C-5, C-7, C-9, C-13), 46.4, 46.3, 46.0, 43.8 (4 t, C-4, C-6, C-8, C-10, C-12), 40.1, 39.9, 39.7, 39.6, 39.4 (C-1, C-2, C-11, C-14, C-15) ppm. MALDI-MS: *m/z* = 338.483 [M + H], 360.445 [M + Na]. MALDI HRMS: calcd. for [$C_{15}H_{35}N_3O_5$ + H] 338.2653; found 338.2664.

Synthesis of (+)-17: The general procedure was applied to compound (+)-**12** (150 mg, 0.193 mmol). In this case, the intermediate triazide was treated with K_2CO_3 (2 equiv.) in methanol prior to catalytic hydrogenation. Compound (+)-**17** was obtained as a white foam (13 mg, 20% yield over 5 steps). $[\alpha]_{435}^{23}$ = +3.5; $[\alpha]_{589}^{23}$ = +1 (*c* = 0.11, MeOH). IR (KBr): $\tilde{\nu}$ = 3405, 1740, 1650, 1560, 1515, 1070 cm^{-1}. ^1H NMR (400 MHz, D_2O): δ = 3.99–3.82 (m, 3 H, 3-H, 7-H, 13-H), 3.73–3.52 (m, 7 H, 5-H, 9-H, 11-H, 1-H_2, 15-H_2), 1.97–1.43 (m, 14 H, 2-H_2, 4-H_2, 6-H_2, 8-H_2, 10-H_2, 12-H_2, 14-H_2) ppm. ^{13}C NMR (100 MHz, D_2O): δ = 69.5, 69.2, 69.0 (C-3, C-7, C-13), 61.2, 60.9, 60.6, 60.3 (C-1, C-5, C-9, C-11, C-15), 41.6, 41.5, 40.3, 39.5, 39.4, 39.3, 38.9 (C-2, C-4, C-6, C-8, C-10, C-12, C-14) ppm. CI-MS (NH_3): *m/z* = 338 [M + H]. MALDI HRMS: calcd. for [$C_{15}H_{35}N_3O_5$ + Na] 360.2474; found 360.2477.

Synthesis of (–)-19: The general procedure applied to (+)-**18** (380 mg, 0.592 mmol) afforded (–)-**19** (46 mg, 23% yield over four steps). $[\alpha]_{589}^{23}$ = –4 (*c* = 0.16, MeOH). IR (KBr): $\tilde{\nu}$ = 3040, 1655, 1565, 1435, 1075, 795 cm^{-1}. ^1H NMR (400 MHz, D_2O): δ = 4.02–3.94 (m, 6 H, 3-H, 5-H, 7-H, 9-H, 11-H, 13-H), 3.11–3.01 (m, 4 H, 1-H_2, 15-H_2), 1.82–1.60 (m, 14 H, 2-H_2, 4-H_2, 6-H_2, 8-H_2, 10-H_2, 12-H_2, 14-H_2) ppm. ^{13}C NMR (100 MHz, D_2O): δ = 68.05, 66.6, 66.5, 66.3, 64.8 (C-3, C-5, C-7, C-9, C-11, C-13), 45.1, 44.9, 44.6, 44.4, 43.8 (C-4, C-6, C-8, C-10, C-12), 38.2, 37.5 (C-1, C-15), 38.0, 37.9 (C-2, C-14) ppm. MALDI-MS: *m/z* = 339.10 [M + H], 361.050 [M + Na]. MALDI HRMS: calcd. for [$C_{15}H_{34}N_2O_6$ + Na] 361.2315; found 361.2328.

Synthesis of 21: Camphorsulfonic acid (15 mg, 0.060 mmol, 0.2 equiv.) was added to a solution of **6** (175 mg, 0.302 mmol) in MeOH (3 mL) and the mixture was stirred at 25 °C for 2 h. The solution was poured into a satd. aq. solution of $NaHCO_3$ (20 mL) and extracted with EtOAc (20 mL, 3 times). The combined organic extracts were washed with brine (30 mL), dried with $MgSO_4$ and concentrated in vacuo. The crude residual oil was dissolved in CH_2Cl_2 (3 mL) and treated at 0 °C with triethylamine (380 µL, 2.72 mmol, 9 equiv.) and methanesulfonyl chloride (110 µL, 0.907 mmol, 3 equiv.). After stirring at 0 °C for 1 h, the mixture was poured into a satd. aq. solution of NH_4Cl (20 mL) and extracted with EtOAc (20 mL, 3 times). The combined organic extracts were washed with brine (30 mL), dried with $MgSO_4$ and concentrated in vacuo. The resulting dimesylate was dissolved in DMF (6 mL) and treated with sodium azide (200 mg, 3.02 mmol, 10 equiv.) at 60 °C for 12 h. The mixture was poured into water (20 mL) and extracted with EtOAc (20 mL, 3 times). The combined organic extracts were washed with brine (30 mL), dried with $MgSO_4$ and concentrated in vacuo. The residue was dissolved in MeOH (2 mL). A catalytic amount of 10% $Pd(OH)_2$/C was added and the resulting mixture was vigorously stirred under hydrogen (1 atm.). After 4 h, the mixture was filtered through a pad of Celite and concentrated in vacuo. Purification of the residue by flash chromatography (5–10% of NH_4OH in CH_3CN) afforded **21** as a colourless oil (66 mg, 36% over 4 steps, 2:1 ratio for two distinct sets of signals). IR (film): $\tilde{\nu}$ = 3370, 3295, 2935, 1670, 1450, 1385, 1165, 1115, 1040, 970, 740, 700 cm^{-1}. ^1H NMR (400 MHz, C_6D_6): δ = 7.33–7.22 (m, 10 $H_{arom.}$), 4.84–4.80 (m, 2 H, 6′-H, 6′′-H), 4.86, 4.82 [2 d, $^3J_{H,H}$ = 6.8, 6.5 Hz, 4 H, 2×CH_2(BOM)], 4.68, 4.67 (s, 4 H, 2×CH_2Ph), 4.43–4.34 (m, 2 H, 2′-H, 2′′-H), 4.11–4.06, 3.96–3.88 (2 m, 2 H, 4′-H, 4′′-H), 3.35, 3.30 (2 s, 6 H, 2×OMe), 3.40–3.24 (m, 2 H, 2-H, 4-H), 2.43–2.26, 2.12–2.03 (2 m, 4 H, 5′-H_2, 5′′-H_2), 1.87–1.64, 1.61–1.33 (2 m, 10 H, 1-H_2, 3-H_2, 5-H_2, 3′-H_2, 3′′-H_2) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 138.7, 138.6 (2 s, 2 $C_{arom.}$), 128.6, 128.2, 128.0 (3 d, $^1J_{C,H}$ = 160, 158, 163 Hz, 10 $C_{arom.}$), 99.3 (2 d, $^1J_{C,H}$ = 156 Hz, C-6′, C-6′′), 92.9, 92.8 [2 t, $^1J_{C,H}$ = 163 Hz, 2×CH_2(BOM)], 69.9, 69.6 (2 d, $^1J_{C,H}$ = 140 Hz, 142, C-

2′, C-2′′), 69.4, 69.3 (2 t, $^1J_{C,H}$ = 143 Hz, 2×CH_2Ph), 66.7, 64.5 (2 d, $^1J_{C,H}$ = 142 Hz, C-4′, C-4′′), 54.6, 54.5 (2 q, $^1J_{C,H}$ = 147, 142 Hz, 2×OMe), 49.4, 47.6 (2 t, $^1J_{C,H}$ = 127, 128 Hz, C-2, C-4), 45.8, 45.5, 45.1 (3 t, $^1J_{C,H}$ = 128, 130, 126 Hz, C-1, C-3, C-5), 39.7, 39.4, 37.6, 37.5 (4 t, $^1J_{C,H}$ = 123, 127 Hz, C-3′, C-3′′, C-5′, C-5′′) ppm. MALDI-HR-MS: calcd. for [$C_{33}H_{50}N_2O_8$ + H] 603.3645; found 603.3698.

Synthesis of 22: A catalytic amount of Raney nickel was added to a solution of **7** (95 mg, 0.147 mmol) in MeOH (1.5 mL), and the resulting mixture was vigorously stirred under hydrogen (1 atm.). After 4 h, the mixture was filtered through a pad of Celite and concentrated in vacuo. Purification of the residue by flash chromatography (5% MeOH in CH_2Cl_2) afforded **22** as a colourless oil (53 mg, 90%, 2:1 ratio for two distinct sets of signals). IR (film): $\tilde{\nu}$ = 3390, 3350, 2920, 1605, 1450, 1370, 1105, 1025, 960, 925, 870, 735 cm^{-1}. ^{1}H NMR (400 MHz, MeOD): δ = 4.83–4.78 (m, 1.34 H, 6_{maj}-H, $6'_{maj}$-H), 4.32–4.28 (m, 0.66 H, 6_{min}-H, $6'_{min}$-H), 4.23–4.08 (m, 2 H, 4′′-H, 6′′-H), 4.03–3.07 (m, 4 H, 2-H, 4-H, 2′-H, 4′-H) 3.29 (s, 4.02 H, 2×OMe_{maj}), 3.46, 3.45 (2 s, 1.98 H, 2×$OMe_{min.}$), 2.10–1.77, 1.28–1.07 (2 m, 8 H, 3-H_2, 5-H_2, 3′-H_2, 5′-H_2), 1.63–1.52, 1.51–1.42 (2 m, 6 H, 5′′-H_2, 2×1′′′-H_2), 1.23, 1.17 (2 s, 6 H, 2×Me-2′′) ppm. ^{13}C NMR (100 MHz, MeOD): δ = 99.9 (s, C-2′′), 101.7, 101.6 (2 d, $^1J_{C,H}$ = 142 Hz, $C\text{-}6_{min.}$, $C\text{-}6'_{min.}$), 99.5, 99.3 (2 d, $^1J_{C,H}$ = 141 Hz, $C\text{-}6_{maj.}$, $C\text{-}6'_{maj.}$), 66.3 (d, $^1J_{C,H}$ = 140 Hz, C-2, C-2′), 65.4, 64.5 (2 d, $^1J_{C,H}$ = 136 Hz, C-4′′, C-6′′), 63.5, 63.3 (2 d, $^1J_{C,H}$ = 137 Hz, C-4, C-4′), 55.8, 55.7 (2 q, $^1J_{C,H}$ = 145 Hz, 2×$OMe_{min.}$), 54.2, 53.9 (2 q, $^1J_{C,H}$ = 145 Hz, 2×OMe_{maj}), 43.3, 42.5, 41,4 (3 t, $^1J_{C,H}$ = 129, 127, 128 Hz, C-1′′, C-5′′), 40.7, 39.1, 37.8, 39.0 (4 t, $^1J_{C,H}$ = 128, 129, 129, 126 Hz, C-3, C-5, C-3′′, C-5′′), 29.6, 19.2 (2 q, $^1J_{C,H}$ = 117, 121 Hz, 2×Me-$2''_{maj.}$), 29.5, 19.1 (2 q, $^1J_{C,H}$ = 120, 121 Hz, 2×Me-$2''_{min.}$) ppm. ESI-MS: *m*/*z* = 405 [M + H]. $C_{20}H_{36}O_8$ (404.50): calcd. C 59.39, H 8.97; found C 58.45, H 9.02.

Synthesis of 24: Diol **22** (174 mg, 0.432 mmol) was dissolved in 4 mL of pyridine/Ac_2O (1:1) and treated with 10 mg of DMAP (0.086 mmol, 0.2 equiv.). The resulting mixture was stirred at 25 °C for 1 h. The mixture was concentrated in vacuo and filtered through silica gel (3% of MeOH in CH_2Cl_2) to afford a pale-orange oil. The resulting diacetate (160 mg, 0.328 mmol) was dissolved in 3 mL of MeOH and treated with 12 mg of *p*-toluenesulfonic acid (0.065 mmol, 0.2 equiv.) at 25 °C for 2 h. The mixture was poured into a satd. aq. solution of $NaHCO_3$ (10 mL) and extracted with CH_2Cl_2 (10 mL, 3 times). The combined organic extracts were dried with $MgSO_4$ and concentrated in vacuo. The crude oil was dissolved in CH_2Cl_2 (2 mL) and treated at 0 °C with triethylamine (266 μL, 1.906 mmol, 9 equiv.) and methanesulfonyl chloride (62 μL, 0.635 mmol, 3 equiv.). After stirring at 0 °C for 1 h, the mixture was poured into a satd. aq. solution of NH_4Cl (20 mL) and extracted with EtOAc (20 mL, 3 times). The combined organic extracts were washed with brine (30 mL), dried with $MgSO_4$ and concentrated in vacuo. The crude dimesylate was dissolved in DMF (3.5 mL). Sodium azide (137 mg, 2.118 mmol, 10 equiv.) was added and the mixture was heated at 60 °C for 12 h. The solution was poured into water (20 mL) and extracted with EtOAc (20 mL, 3 times). The combined organic extracts were washed with brine (30 mL), dried with $MgSO_4$ and concentrated in vacuo. The crude diazide was dissolved in MeOH (3 mL) and treated at 25 °C with 125 mg of K_2CO_3 (0.903 mmol, 3 equiv.) for 4 h. The mixture was poured into water (20 mL) and extracted with EtOAc (20 mL, 3 times). The combined organic extracts were washed with brine (30 mL), dried with $MgSO_4$ and concentrated in vacuo. Purification by flash chromatography (3% of MeOH in CH_2Cl_2) afforded **23** as a colourless oil (66 mg, 37%, 5 steps). Diol **23** (60 mg, 0.145 mmol) was dissolved in MeOH (1.5 mL). A catalytic amount of $Pd(OH)_2$ was added and the resulting mixture was vigorously stirred under hydrogen (1 atm.). After 4 h, the mixture was filtered through a pad of Celite and concentrated in vacuo. Purification of the residue by flash chromatography (20% of NH_4OH in CH_3CN) afforded **24** as a colourless oil (44 mg, 84%, 2:1 ratio for two distinct sets of signals). IR (film): $\tilde{\nu}$ = 3350, 2925, 2505, 1450, 1385, 1115, 1040, 965 cm^{-1}. ^{1}H NMR (400 MHz, D_2O): δ = 4.84 (br. s, 1.34 H, 6_{maj}-H, $6'_{maj}$-H), 4.42–4.35 (m, 0.66 H, 6_{min}-H, $6'_{min}$-H), 3.96–3.80 (m, 2.68 H, 2_{maj}-H, 4_{maj}-H, $2''_{maj}$-H, $4''_{maj}$-H), 3.58–3.54 (m, 1.34 H, 2_{min}-H, 4_{min}-H, $2''_{min}$-H, $4''_{min}$-H), 3.41, 3.40 (2 s, 1.98 H, 2×$OMe_{min.}$), 3.27, 3.25 (2 s, 4.02 H, 2×$OMe_{maj.}$), 3.03–2.98 (m, 0.66 H, $2'_{min}$-H, $4'_{min}$-H), 2.83–2.74 (m, 1.34 H, $2'_{maj}$-H, $4'_{maj}$-H), 2.1–1.8 (m, 4 H, 3-H_2, 3′′-H_2), 1.75–1.30 (m, 6 H, 1′-H_2, 3′-H_2, 5′-H_2), 1.22–1.08 (m, 4 H, 5-H_2, 5′′-H_2) ppm. ^{13}C NMR (100 MHz, D_2O): δ = 101.4, 101.3 (2 d, $^1J_{C,H}$ = 171 Hz, $C\text{-}6_{min.}$, $C\text{-}6'_{min.}$), 99.4, 99.3 (2 d, $^1J_{C,H}$ = 172 Hz Hz, $C\text{-}6_{maj.}$, $C\text{-}6'_{maj.}$), 66.0, 65.4, 63.3 (4 d, $^1J_{C,H}$ = 140, 142, 141, 141, $C\text{-}2_{maj.}$, $C\text{-}4_{maj.}$, $C\text{-}2''_{maj.}$, $C\text{-}4''_{maj.}$), 65.9, 65.8, 63.3, 63.1 (4 d, $C\text{-}2_{min.}$, $C\text{-}4_{min.}$, $C\text{-}2''_{min.}$, $C\text{-}4''_{min.}$), 56.6 (q, $^1J_{C,H}$ = 140 Hz, 2×$OMe_{min.}$), 54.9 (q, $^1J_{C,H}$ = 143 Hz, 2×$OMe_{maj.}$), 51.8, 51.6 (2 d, $^1J_{C,H}$ = 138 Hz, $C\text{-}2'_{maj.}$, $C\text{-}4'_{maj.}$), 46.2, 45.0 (2 d, $^1J_{C,H}$ = 139 Hz, $C\text{-}2'_{min.}$, $C\text{-}4'_{min.}$), 42.3, 41.9 (3 t, C-1′, C-3′, C-5′), 40.2, 40.1 (2 t, $C\text{-}3_{min.}$, $C\text{-}3''_{min.}$), 39.9, 39.7 (2 t, $C\text{-}3_{maj.}$, $C\text{-}3''_{maj.}$), 38.9 (t, $C\text{-}5_{min.}$, $C\text{-}5''_{min.}$), 37.9 (t, $^1J_{C,H}$ = 123 Hz, $C\text{-}5_{maj.}$, $C\text{-}5''_{maj.}$) ppm. ESI-MS: *m*/*z* = 363 [M + H]. MALDI-HR-MS: calcd. for [$C_{17}H_{34}N_2O_6$ + H] 363.2495; found 363.2485.

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