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Total synthesis of calystegine A_7

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ABSTRACT

A straightforward chiral pool synthesis for the glycosidase inhibitor calystegine A_7 (isolated from *Lycium chinense*) from methyl α-D-glucopyranoside is described. Keysteps of this synthesis include a ultrasound assisted Zn-mediated tandem ring opening reaction followed by a *Grubbs'* catalyst mediated ring closure metathesis.

1. Introduction

Calystegines[1] are a family of polyhydroxylated nortropane alkaloids that were first isolated from *Calystegia sepium*[2,3] in 1988. They are believed to function as nutritional mediators[4] in the plant rhizosphere. Since calystegines exhibit strong or specific glyosylhydrolase competitive inhibitory activity[5–7] they were considered as ideal probes for enzymatic mechanism[8–10] as well as chemotherapeutic drugs for the treatment of metabolic disorders[11,12] (e.g., diabetes), cancer[13] or for the treatment[14,15] of viral diseases.

Calystegine A_7 has previously been isolated from the root of *Lycium chinense* and has been shown to act as a competitive inhibitor[5] against trehalase. Unfortunately, the amount of isolated calystegine A_7 remained small since from the extraction and exhaustive chromatography of 5 kg roots of *L. chinense* only 8 mg of the desired compound could be isolated. Thus, its structure has been proposed from NMR spectroscopic data.

In order to prove the structure as well as to obtain larger amounts of this calystegine, a total synthesis seemed to be called for.

2. Results and discussion

There has been considerable interest in the synthesis of calystegines and more or less elaborate routes for the synthesis of calystegines A_3,[16,17] B_2,[18–23] B_3 and B_4[24–28] have been described so far.

For the synthesis of calystegine A_7 we planned a chiral pool approach starting from well accessible methyl α-D-glucopyranoside using a zinc mediated tandem ring opening reaction followed by a ring closure metathesis using 2nd generation *Grubb's* catalyst.

Thus, methyl α-D-glucopyranoside (**1**) (Scheme 1) was transformed into well known methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-mannopyranoside (**2**)[29,30] that was reduced with lithium tetrahydrido aluminate to afford the corresponding 3-deoxy hexopyranoside **3** in 96% isolated yield. Deprotection of **3** with 0.1 M sulfuric acid[31] gave **4** whose regioselective tritylation afforded **5**. Compound **5** was benzylated (→**6**) followed by detritylation to yield the corresponding 2,4-di-*O*-benzylated 3-deoxy monosaccharide **7** that was subsequently iodinated using triphenyl phosphane/iodine[32,33] to yield 96.5% of the 6-iodo-derivative **8**.

An ultrasound assisted Zn-mediated tandem reaction[19,27,34] furnished 1,8-nonadiene **9** as the main product (81.8% yield) together with minor amounts of its diastereomeric analogue **16** and traces of **10**. Carbobenzoxylation of **9** gave 64% of fully protected **11** that was subjected to a ring closure metathesis[19,34] using *Grubbs'* catalyst. The corresponding cycloheptene derivative **12** was hydroxylated using $BH_3 \cdot THF/H_2O_2$[35] to furnish the diastereomeric alcohols **13**/**14** that were smoothly oxidized with PCC to yield the cycloheptanone **15**. Hydrogenolysis of **15** in the presence of Pd/C finally resulted in the formation of calystegine A_7 being undistinguishable from authentic material from *L. chinense* in each aspect.

The synthesis of analogues is presently under investigation in our laboratories. In a preliminary test, calystegine A_7 shows a K_i value (β-glycosidase from almonds) of 2.1 mM as compared to a K_i for calystegine B_2 of 5.9 μM.

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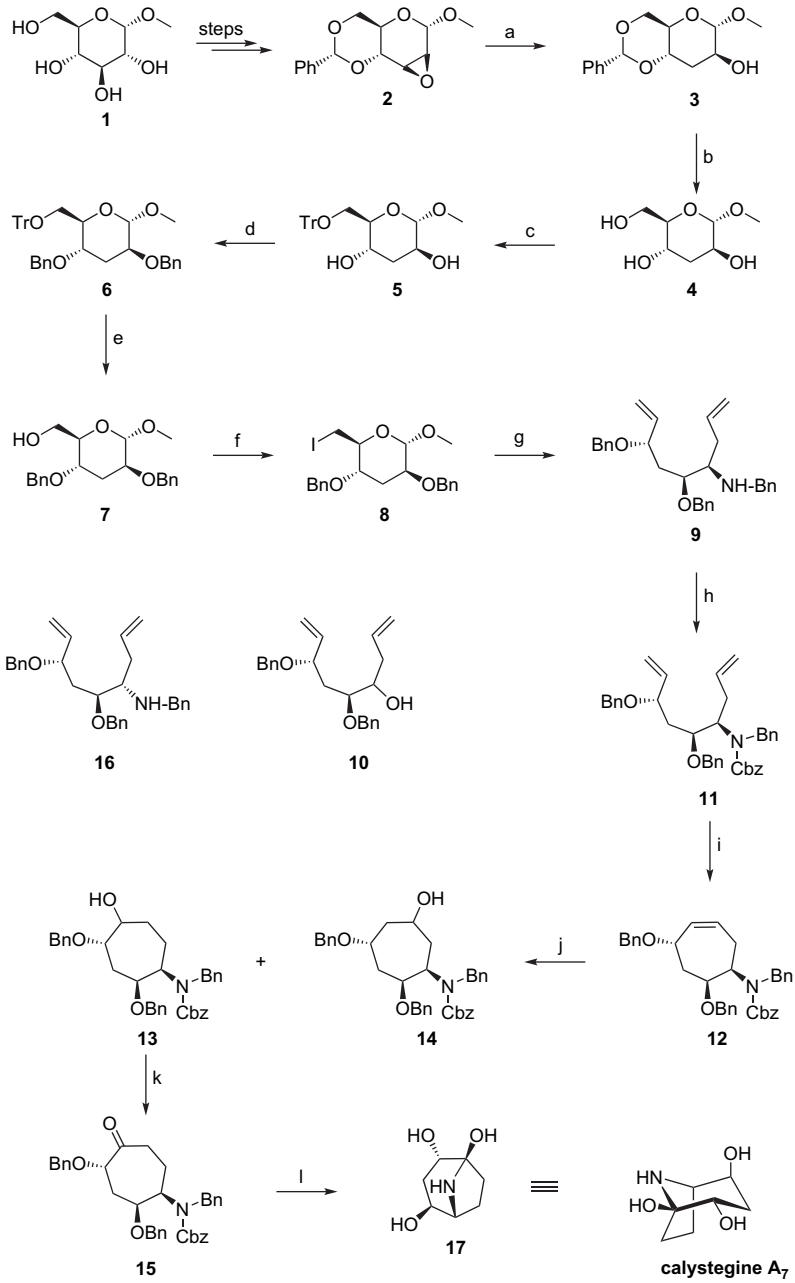

Scheme 1. (a) $LiAlH_4$ (96%); (b) 0.1 M H_2SO_4 (quant.); (c) Ph_3CCl (=TrCl), pyridine, DMAP (87%); (d) BnBr, NaOH (quant.); (e) *p*-TsOH (quant.); (f) Ph_3P, imidazole, iodine (97%); (g) Zn*, $BnNH_2$, allylbromide, (82%); (h) CbzCl, $NaHCO_3$ (64%); (i) *Grubbs'* catalyst (80%); (j) BH_3·THF, H_2O_2/NaOH (27% of **14** and 45% of **13**); (k) PCC (86%); (l) Pd/C, H_2 (92%).

3. Experimental

3.1. General

Melting points are uncorrected (*Leica* hot stage microscope), optical rotations were obtained using a Perkin–Elmer 341 polarimeter (1 cm micro cell), NMR spectra were recorded using the Varian spectrometers Gemini 200, Gemini 2000 or Unity 500 (δ given in ppm, *J* in Hz, internal Me_4Si or internal CCl_3F), IR spectra (film or KBr pellet) on a Perkin–Elmer FT-IR spectrometer Spectrum 1000, MS spectra were taken on a Intectra GmbH AMD 402 (electron impact, 70 eV) or on a Finnigan MAT TSQ 7000 (electrospray, voltage 4.5 kV, sheath gas nitrogen) instrument; for elemental analysis a Foss-Heraeus Vario EL instrument was used; TLC was performed on silica gel (Merck 5554, detection by UV absorption or by treatment with a solution of 10% sulfuric acid, ammonium molybdate and cerium(IV) sulfate) followed by gentle heating. The solvents were dried according to usual procedures.

3.2. Methyl (*R*)-4,6-*O*-benzylidene-3-deoxy-α-D-*arabino*-hexopyranoside (3)

To an ice-cold solution of **2** (15.63 g, 59 mmol) in dry diethylether (150 ml) $LiAlH_4$ (8.98 g, 237 mmol) was added in small portions. The reaction mixture was allowed to warm to room temperature and then refluxed for another 16 h. After cooling, a satd aq solution of magnesium sulfate (40 ml) was carefully added, the mixture filtered, the residue washed with hot ethyl acetate (3×100 ml) and the combined organic phases were evaporated. The residue was subjected to chromatography (silica gel, hexane/ethyl acetate 1:1) to afford **3** (15.2 g, 96.4%) as colourless crystals. Mp 109 °C (lit.[30] 108–110 °C), $[\alpha]_D^{20}$ 88.35 (*c* 0.82, $CHCl_3$)

(lit.[36] $[\alpha]_D^{20}$ 95.5 (*c* 2, $CHCl_3$)); R_f 0.42 (hexane/ethyl acetate 1:1); UV–vis (methanol): λ_{max1}=267.13 nm, *A*=0.23, λ_{max2}=272.84 nm, *A*=0.28, λ_{max3}=278.50 nm, *A*=0.24, λ_{max4}=282.89 nm, *A*=0.14; IR (KBr): ν=3406 (s), 3007 (m), 2962 (s), 2937 (s), 2859 (m), 1624 (w), 1462 (m), 1452 (m), 1385 (s), 1368 (m), 1336 (m), 1320 (m), 1294 (m), 1242 (m), 1194 (m), 1133 (s), 1101 (s), 1060 (s), 1043 (s), 1016 (s), 1002 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ=7.39–7.16 (m, 5H, phenyl-H), 5.48 (s, 1H, H-8), 4.47 (s, 1H, H-1), 4.14 (dd, 1H, *J*=9.4, 3.9 Hz, H-6′), 3.90 (dd, 1H, *J*=3.1, 4.2 Hz, H-2), 3.86 (ddd, 1H, *J*=3.6, 4.3, 12.4 Hz, H-4), 3.74 (ddd, 1H, *J*=3.9, 4.3, 10.2 Hz, H-5), 3.70 (dd, 1H, *J*=9.4, 10.2 Hz, H-6), 3.32 (s, 3H, OCH_3), 2.01 (ddd, 1H, *J*=12.9, 3.6, 4.2 Hz, H-3′), 1.97 (ddd, 1H, *J*=12.9, 3.1, 12.4 Hz, H-3); ^{13}C NMR (125 MHz, $CDCl_3$): δ=137.79 (C_i of benzylidene), 129.31 (C_{ar}), 128.57 (C_{ar}), 126.41 (C_{ar}), 102.40 (CH of benzylidene), 101.06 (C(1)), 74.15 (C(4)), 69.57 (C(6)), 68.10 (C(2)), 65.21 (C(5)), 55.16 (OCH_3), 32.24 (C(3)); MS (EI, 70 eV): *m*/*z* (%)=266 (9), 235 (2), 223 (6), 205 (7), 189 (2), 175 (1), 162 (16), 149 (3), 145 (12), 129 (5), 117 (100); MS (ESI): *m*/*z* (%)=266.9 (M+H, 100), 289.1 (M+Na, 55), 554.9 (M_2+Na, 40), 275.4 (M+Li, 28), 292.2 (M+LiH_2O, 70), 305.9 (M+LiMeOH, 100). Anal. Calcd for $C_{14}H_{18}O_5$ (266.30): C, 63.15; H, 6.81. Found: C, 62.92; H, 6.96.

3.3. Methyl 3-deoxy-α-D-*arabino*-hexopyranoside (4)

A suspension of **3** (15.94 g, 60 mmol) in water (100 ml) was heated at 60 °C in the presence of sulfuric acid (10 ml, 0.1 M) for 4 h. After cooling to room temperature barium oxide (0.16 g, 1.044 mmol) was added, the mixture was filtered and the filtrate was extracted with ethyl acetate (50 ml). The aqueous layer was concentrated under diminished pressure and the residue dried over potassium hydroxide to afford **4** (10.7 g, quantitative) as colourless crystals. Mp 122–123 °C (lit.[31] 123.5–124 °C); $[\alpha]_D^{20}$ 108.02 (*c* 0.54, MeOH) (lit.[36] $[\alpha]_D^{20}$ 126.5 (*c* 1, MeOH)); R_f 0.0 (hexane/ethyl acetate 1:1); IR (KBr): ν=3382 (s), 3002 (m), 2981 (s), 2966 (s), 2939 (s), 2903 (s), 2880 (s), 2842 (m), 2509 (s), 1560 (s), 1454 (s), 1414 (s), 1391 (s), 1366 (m), 1348 (s), 1292 (s), 1256 (m), 1195 (s), 1140 (s), 1124 (s), 1104 (s), 1046 (s), 1021 (s) cm^{-1}; ^1H NMR (500 MHz, D_2O): δ=4.51 (s, 1H, H-1), 3.34 (s, 3H, OCH_3), 3.84 (dd, 1H, *J*=3.0, 3.9 Hz, H-2), 3.78 (dd, 1H, *J*=12.1, 2.3 Hz, H-6′), 3.70 (ddd, 1H, *J*=4.8, 10.1, 11.1 Hz, H-4), 3.64 (dd, 1H, *J*=12.1, 6.5 Hz, H-6), 3.52 (ddd, 1H, *J*=2.3, 6.5, 10.1 Hz, H-5), 1.98 (ddd, 1H, *J*=13.6, 3.0, 4.9 Hz, H-3′), 1.71 (ddd, 1H, *J*=13.6, 3.1, 11.1 Hz, H-3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=99.53 (C(1)), 73.58 (C(5)), 67.08 (C(2)), 61.46 (C(4)), 61.13 (C(6)), 54.58 (OCH_3), 33.57 (C(3)); MS (EI, 70 eV): *m*/*z* (%)=147 (1), 130 (6), 129 (13), 115 (7), 111 (1), 101 (3), 100 (6), 87 (3), 82 (3), 74 (100), 71 (13); MS (ESI): *m*/*z* (%)=201.5 (M+Na, 65), 185.5 (M+Li, 100), 217.5 (M+Li (MeOH), 35). Anal. Calcd for $C_7H_{14}O_5$ (178.19): C, 47.19; H, 7.92. Found: C, 46.94; H, 7.97.

3.4. Methyl 3-deoxy-6-*O*-triphenylmethyl-α-D-*arabino*-hexopyranoside (5)

To a solution of **4** (11.1 g, 62.0 mmol) and dimethylaminopyridine (DMAP) (1.28 g, 10.5 mmol) in dry pyridine (100 ml) trityl chloride (21.92 g, 78.6 mmol) was added in several portions. Stirring at room temperature was continued for another day, then additional DMAP (1.28 g, 10.5 mmol) was added and the reaction mixture stirred at 40 °C for 2 h. The solvents were removed under reduced pressure and the residue was dissolved in dichloromethane (200 ml). The organic phase was washed with water (150 ml), dried ($MgSO_4$), the solvent was removed and the residue was subjected to chromatography (silica gel, hexane/ethyl acetate 1:1) to afford **5** (22.8 g, 87%) as colourless crystals. Mp 84–85 °C; $[\alpha]_D^{20}$ 23.47 (*c* 0.75, $CHCl_3$); R_f 0.26 (methanol/ethyl acetate=1:8); IR (KBr): ν=3425 (s), 3058 (m), 3032 (m), 2932 (s), 1962 (w), 1718 (w), 1596 (m), 1490 (s), 1448 (s), 1374 (m), 1326 (m), 1222 (s), 1188 (s), 1132 (s), 1055 (s), 983 (s), 958 (s), 901 (m), 877 (m), 845 (m), 819 (m), 764 (s), 748 (s), 708 (s), 654 (m), 643 (m), 633 (s), 536 (m), 503 (m) cm^{-1}; UV–vis (methanol): λ_{max}=275.89 nm, *A*=0.46; ^1H NMR (500 MHz, $CDCl_3$): δ=7.48–7.25 (ddd, 15H, phenyl-H), 4.51 (s, 1H, H-1), 3.85 (m, 2H, H-2, H-4), 3.69 (ddd, 1H, *J*=4.8, 6.4 Hz, H-5), 3.48 (dd, 1H, *J*=9.8, 4.8 Hz, H-6′), 3.40 (s, 3H, OCH_3), 3.38 (dd, 1H, *J*=9.8, 6.4 Hz, H-6), 2.60 (d, 1H, *J*=2.9 Hz, OH), 2.06 (ddd, 1H, *J*=13.3 Hz, H-3′), 1.83 (ddd, 1H, *J*=13.3 Hz, H-3), 1.77 (d, 1H, *J*=7.0 Hz, OH); ^{13}C NMR (125 MHz, $CDCl_3$): δ=143.51 (C_i of trityl), 128.58 (C_{ar}), 128.00 (C_{ar}), 127.25 (C_{ar}), 99.97 (C(1)), 87.59 (C(CPh_3)), 70.99 (C(5)), 68.04 (C(4)), 65.73 (C(6)), 65.18 (C(2)), 54.85 (OCH_3), 34.15 (C(3)); MS (ESI): *m*/*z* (%)=443.3 (M+Na, 100), 862.9 (M_2+Na, 30), 427.5 (M+Li, 100), 847.1 (M_2+Li, 7), 953.1 (M_2+Li_2ClO_4, 5). Anal. Calcd for $C_{26}H_{28}O_5$ (420.51): C, 74.27; H, 6.71. Found: 74.11; H, 6.91.

3.5. Methyl 2,4-di-*O*-benzyl-3-deoxy-6-*O*-triphenylmethyl-α-D-*arabino*-hexopyranoside (6) and methyl 2,4-di-*O*-benzyl-3-deoxy-α-D-*arabino*-hexopyranoside (7)

To an ice-cold solution of **5** (6.97 g, 16.6 mmol) in dry DMF (150 ml) sodium hydride (65–65% in mineral oil, 4.77 g, 99.4 mmol) was slowly added in several portions. Stirring at 0 °C followed by stirring at room temperature was continued for another hour, then at 0 °C benzyl bromide (5.95 ml, 49.7 mmol) was slowly added. After stirring at room temperature for another 3 h, methanol (100 ml) was carefully added and the solvents were removed under diminished pressure. The oily residue was dissolved in diethylether (250 ml) and washed with water and brine (100 ml each) and dried ($MgSO_4$); the solvents were evaporated and **6** (15.59 g) was directly used for the next step. To a solution of crude **6** (15.59 g) in methanol (200 ml) and dichloromethane (100 ml) catalytic amounts of *p*-TsOH were added and the mixture was stirred at room temperature for 1 day. After neutralization (triethylamine), the solvents were removed in vacuo, the residue was dissolved in ether (250 ml) and washed with water and brine (150 ml each). After drying ($MgSO_4$) the solvent was removed and the residue was subjected to chromatography (silica gel, hexane/ethyl acetate 85:15) to afford **7** (5.94 g, quant.) as a highly viscous, colourless oil. R_f 0.38 (hexane/ethyl acetate 5:3); $[\alpha]_D^{20}$ 70.08 (*c* 0.63, $CHCl_3$); IR (film): ν=3474 (m), 3063 (m), 3030 (m), 2930 (s), 1605 (w), 1497 (m), 1455 (s), 1371 (s), 1317 (m), 1186 (s), 1145 (s), 1050 (s), 981 (s), 909 (w), 834 (w), 739 (s), 699 (s), 613 (m), 542 (m), 510 (m) cm^{-1}; UV–vis (methanol): λ_{max1}=269.12 nm, *A*=0.33, λ_{max2}=274.91 nm, *A*=0.39, λ_{max3}=280.75 nm, *A*=0.30; ^1H NMR (500 MHz, $CDCl_3$): δ=7.35–7.24 (m, 10H, phenyl-H), 4.61 (s, 1H, H-1), 4.52 (s, 2H, CH_2 (C4-Bn)), 4.55 (d, 1H, *J*=11.5 Hz, CH_2 (C2-Bn)), 4.46 (d, 1H, *J*=11.5 Hz, CH_2' (C2-Bn)), 3.83 (dd, 1H, *J*=7.4, 4.0 Hz, H-6′), 3.76 (ddd, 1H, *J*=3.7, 9.7, 10.6 Hz, H-4), 3.69 (dd, 1H, *J*=2.9, 3.7 Hz, H-2), 3.67 (dd, 1H, *J*=7.4, 3.7 Hz, H-6), 3.58 (ddd, 1H, *J*=3.7, 4.0, 9.7 Hz, H-5), 3.35 (s, 3H, H-OCH_3), 2.23 (ddd, 1H, *J*=13.2, 3.8, 3.8 Hz, H-3′), 1.74 (ddd, 1H, *J*=13.2, 2.9, 10.6 Hz, H-3); ^{13}C NMR (125 MHz, $CDCl_3$): δ=138.20 (C_i (C4-Bn)), 138.07 (C_i (C2-Bn)), 128.40 (C_{ar}), 127.78 (C_{ar}), 127.73 (C_{ar}), 127.60 (C_{ar}), 98.26 (C(1)), 74.76 (C(5)), 71.80 (C(2)), 71.07 (CH_2 (C2-Bn)), 71.03 (CH_2 (C4-Bn)), 70.17 (C(4)), 62.92 (C(6)), 54.62 (OCH_3), 29.03 (C(3)); MS (ESI): *m*/*z* (%)=376.9 (M+NH_4, 3), 381.4 (M+Na, 100), 739.0 (M_2+Na, 5). Anal. Calcd for $C_{21}H_{26}O_5$ (358.44): C, 70.37; H, 7.31. Found: C, 70.12; H, 7.49.

3.6. Methyl 2,4-di-*O*-benzyl-3,6-dideoxy-6-iodo-α-D-*arabino*-hexopyranoside (8)

To a solution of **7** (5.9 g, 16.5 mmol) in toluene (100 ml) containing triphenylphosphane (9.83 g, 76.7 mmol) under argon iodine (8.65 g, 34.1 mmol) was added in several portions. After stirring at 90 °C for 2 h the reaction mixture was decanted and the remaining oil washed with ether (3×100 ml). The combined organic phases

were evaporated and the remaining residue was subjected to chromatography (silica gel, hexane/ethyl acetate 85:15) to afford **8** (7.52 g, 97.5%) as colourless crystals. R_f 0.40 (hexane/ethyl acetate 85:15); $[\alpha]_D^{20}$ 81.94 (*c* 1.01, $CHCl_3$); IR (KBr): ν=3446 (m), 3028 (m), 2928 (m), 2869 (m), 1498 (w), 1454 (m), 1389 (w), 1354 (w), 1340 (w), 1316 (w), 1245 (w), 1228 (w), 1201 (m), 1184 (m), 1174 (m), 1143 (m), 1105 (m), 1069 (m), 1035 (m), 972 (m), 924 (w), 890 (w), 867 (w), 768 (w), 751 (m), 739 (m), 696 (m), 622 (w), 609 (w), 538 (w), 489 (w) cm^{-1}; UV–vis (methanol): λ_{max1}=269.82 nm, *A*=0.58, λ_{max2}=274.85 nm, *A*=0.63; ^1H NMR (500 MHz, $CDCl_3$): δ=7.37–7.24 (d, 10H, phenyl-H), 4.67 (s, 1H, H-1), 4.58 (d, 1H, *J*=6.8 Hz, CH_2 (C2-Bn)), 4.57 (d, 1H, *J*=6.8 Hz, CH_2' (C2-Bn)), 4.53 (d, 1H, *J*=11.4 Hz, CH_2 (C4-Bn)), 4.45 (d, 1H, *J*=11.4 Hz, CH_2' (C4-Bn)), 3.62 (dd, 1H, *J*=10.2 Hz, H-6′), 3.59 (m, 3H, $J_{2;H,H}$=2.9, 3.4 Hz, $^3J_{4;H,H}$=3.4, 10.5 Hz, $^3J_{5;H,H}$=7.5 Hz, H-2, H-4, H-5), 3.44 (s, 3H, H-OCH_3), 3.30 (dd, 1H, *J*=10.2, 7.5 Hz, H-6), 2.25 (ddd, 1H, *J*=13.0, 3.4, 3.4 Hz, H-3′), 1.75 (ddd, 1H, *J*=13.0, 2.9, 10.5 Hz, H-3); ^{13}C NMR (125 MHz, $CDCl_3$): δ=138.18 (C_i (C4-Bn)), 138.04 (C_i (C2-Bn)), 128.46 (C_{ar}), 128.40 (C_{ar}), 127.86 (C_{ar}), 127.83 (C_{ar}), 127.69 (C_{ar}), 127.57 (C_{ar}), 98.33 (C(1)), 74.90 (C(2)), 73.62 (C(4)), 71.62 (C(5)), 71.11 (CH_2 (C2-Bn)), 71.00 (CH_2 (C4-Bn)), 54.95 (OCH_3), 29.34 (C(3)), 7.68 (C(6)); MS (ESI): *m*/*z* (%)=486.6 (M+NH_4, 45), 491.5 (M+Na, 100), 769.0 (cluster (M+278) Na, 13); 475.9 (M+Li, 85), 493.9 (M+Li+H_2O, 40), 507.3 (M+LiMeOH, 100), 753.3 (cluster (M+278) Li, 75). Anal. Calcd for $C_{21}H_{25}O_4I$ (468.34): C, 53.86; H, 5.38. Found: C, 53.61; H, 5.55.

3.7. (3*S*,5*S*,6*R*) 6-(*N*-Benzylamino)-3,5-bis(benzyloxy)-1,8-nonadiene (9), (3*S*,5*S*,6*S*)- 6-(*N*-benzylamino)-3,5-bis(benzyloxy)-1,8-nonadiene (16) and (3*S*,5*S*) 3,5-bis(benzyloxy)-6-hydroxy-1,8-nonadiene (10)

To a solution of **8** (2.32 g, 4.95 mmol) in dry THF (100 ml) acid activated Zn powder (4.5 g, 68.8 mmol) was added and put in an ultrasound cleaning bath for 20 min. At a temperature of 38 °C benzylamine (2.71 ml, 24.8 mmol) was slowly added and the treatment with microwaves was continued for another 6 h. Then allylbromide (1.28 ml, 14.9 mmol) was added, microwaves were applied for another 45 min, the mixture was cooled to room temperature and filtered over a small pad of silica gel. The solvents were removed and the residue partioned between dichloromethane and water (50 ml each), the aq phase was extracted with dichloromethane (3×50 ml), the combined organic layers were dried and the solvents evaporated. The residue was subjected to chromatography (silica gel, hexane/ethyl acetate 75:25) to afford **9** (1.79 g, 81.8%) and **16** (0.21 g, 9.6%); the formation of traces of **10** was observed on several occasions.

Data for **9**: colourless oil; R_f 0.2 (hexane/ethyl acetate 85:15); $[\alpha]_D^{20}$ −33.70 (*c* 0.98, $CHCl_3$); IR (film): ν=3321 (m), 3064 (m), 3029 (m), 2929 (m), 1949 (w), 1640 (m), 1605 (m), 1496 (m), 1454 (m), 1360 (m), 1206 (m), 1068 (m), 1028 (m), 995 (m), 919 (m), 735 (m), 697 (m), 608 (w), 462 (w) cm^{-1}; UV–vis (methanol): λ_{max}=275.26 nm, *A*=0.80; ^1H NMR (500 MHz, $CDCl_3$): δ=7.32–7.18 (m, 15H, phenyl-H), 5.76 (m, 2H, $^3J_{2;H,H}$=18.7 Hz, $^3J_{8;H,H}$=14.3 Hz, H-2, H-8), 5.20 (dd, 2H, *J*=10.3, 18.7 Hz, H-1), 5.06 (dd, 2H, *J*=10.2, 14.3 Hz, H-9), 4.53 (d, 1H, *J*=11.8 Hz, CH_2 (C3-Bn)), 4.42 (d, 1H, *J*=11.4 Hz, CH_2 (C5-Bn)), 4.21 (d, 1H, *J*=11.4 Hz, CH_2' (C5-Bn)), 4.18 (d, 1H, *J*=11.8 Hz, CH_2' (C3-Bn)), 3.95 (dd, 1H, H-3), 3.82 (d, 1H, *J*=13.4 Hz, CH_2 (N-Bn)), 3.79 (ddd, 1H, *J*=4.0 Hz, H-5), 3.79 (d, 1H, *J*=13.4 Hz, CH_2' (N-Bn)), 2.90 (ddd, 1H, *J*=4.0, 6.5, 6.7 Hz, H-6), 2.28 (m, 1H, *J*=6.5 Hz, H-7′), 2.18 (m, 1H, *J*=6.5 Hz, H-7), 1.77 (m, 2H, H-4); ^{13}C NMR (125 MHz, $CDCl_3$): δ=139.06 (C(2)), 138.78 (C_i (C3-Bn)), 138.78 (C_i (C5-Bn)), 138.78 (C_i of benzylamine), 135.85 (C(8)), 128.48 (C_{ar}), 128.33 (C_{ar}), 128.27 (C_{ar}), 128.28 (C_{ar}), 128.18 (C_{ar}), 127.84 (C_{ar}), 127.82 (C_{ar}), 127.73 (C_{ar}), 127.58 (C_{ar}), 127.48 (C_{ar}), 126.83 (C_{ar}), 117.19 (C(9)), 116.58 (C(1)), 77.27 (C(6)), 77.13 (C(5)), 71.87 (CH_2 (C5-Bn)), 70.10 (CH_2 (C3-Bn)), 57.75 (C(3)), 51.90 (CH_2 (N-Bn)), 36.68 (C(7)), 35.30 (C(4)); MS (ESI): *m*/*z* (%)=442.4 (M+H, 100). Anal. Calcd for $C_{30}H_{35}O_2N$ (441.62): C, 81.59; H, 7.99. Found: C, 81.64; H, 8.15.

Data for **16**: colourless oil; $[\alpha]_D^{20}$ −34.39 (*c* 0.69, $CHCl_3$); IR (film): ν=3317 (w), 3064 (m), 3029 (m), 2927 (m), 1640 (w), 1604 (w), 1496 (m), 1454 (m), 1360 (m), 1206 (m), 1065 (s), 1028 (m), 994 (m), 920 (m), 735 (m), 698 (s), 618 (w) cm^{-1}; UV–vis (methanol): λ_{max1}=264.00 nm, *A*=0.755; λ_{max2}=268.87 nm, *A*=0.771; λ_{max3}=274.91 nm, *A*=0.764; λ_{max4}=335.85 nm, *A*=0.206; ^1H NMR (400 MHz, $CDCl_3$): δ=7.33–7.17 (m, 15H, phenyl), 5.75 (m, 2H, *J*=19.3, 17.0 Hz, H-8), 5.16 (dd, 2H, *J*=11.2, 19.3 Hz, Hz, H-), 5.10 (dd, 2H, *J*=10.5, 17.0 Hz, H-9), 3.93 (dd, 1H, H-3), 4.52 (d, 1H, *J*=11.4 Hz, CH_2' (C3-Bn)), 4.40 (d, 1H, *J*=10.9 Hz, CH_2' (C5-Bn)), 4.17 (d, 1H, *J*=10.9 Hz, CH_2 (C5-Bn)), 4.17 (d, 1H, *J*=11.4 Hz, CH_2 (C3-Bn)), 3.79 (ddd, 1H, H-5), 3.81 (d, 1H, *J*=13.4 Hz, CH_2' (N-Bn)), 3.79 (d, 1H, *J*=13.4 Hz, CH_2 (N-Bn)), 2.89 (ddd, 1H, *J*=2.9, 6.5, 6.8 Hz, H-6), 2.27 (m, 1H, *J*=6.8 Hz, H-7′), 2.17 (m, 1H, *J*=6.5 Hz, H-7), 1.80 (ddd, 2H, H-4); ^{13}C NMR (100 MHz, $CDCl_3$): δ=140.60 (C_i (C3-Bn)), 139.01 (C(2)), 139.80 (C_i (C5-Bn)), 138.72 (C_i of benzylamine), 135.80 (C_{ar}), 128.46 (C_{ar}), 128.33 (C_{ar}), 128.23 (C_{ar}), 128.17 (C_{ar}), 128.14 (C_{ar}), 128.08 (C_{ar}), 127.73 (C_{ar}), 127.57 (C_{ar}), 127.52 (C_{ar}), 127.37 (C_{ar}), 127.29 (C_{ar}), 126.94 (C_{ar}), 126.87 (C_{ar}), 126.72 (C_{ar}), 117.04 (C(9)), 116.45 (C(1)), 77.19 (C(6)), 77.06 (C(5)), 71.90 (CH_2 (C5-Bn)), 70.13 (CH_2 (C3-Bn)), 53.13 (C(3)), 51.99 (CH_2 (N-Bn)), 36.82 (C(7)), 35.41 (C(4)). Anal. Calcd for $C_{30}H_{35}O_2N$ (441.62): C, 81.59; H, 7.99. Found: C, 81.62; H, 8.11.

Data for **10**: viscous oil; R_f 0.26 (hexane/ethyl acetate 85:15); $[\alpha]_D^{20}$ −19.85 (*c* 0.67, $CHCl_3$); IR (film): ν=3418 (m), 3064 (m), 3029 (m), 2926 (m), 2863 (m), 1678 (m), 1640 (m), 1604 (m), 1496 (m), 1455 (s), 1353 (m), 1206 (m), 1069 (s), 1028 (s), 994 (m), 923 (m), 735 (s), 698 (s), 618 (m) cm^{-1}; UV–vis (methanol): λ_{max1}=268.92 nm, *A*=0.748; λ_{max2}=274.90 nm, *A*=0.749; λ_{max3}=332.04 nm, *A*=0.276; ^1H NMR (500 MHz, $CDCl_3$): δ=7.35–7.19 (m, 10H, phenyl-H), 5.73 (m, 2H, H-2, H-8), 5.01 (m, 2H, H-1, H-9), 4.44 (d, 1H, *J*=11.5 Hz, CH_2 (C5-Bn)), 4.44 (d, 1H, *J*=11.8 Hz, CH_2 (C3-Bn)), 4.29 (d, 1H, *J*=11.5 Hz, CH_2' (C5-Bn)), 4.19 (d, 1H, *J*=11.8 Hz, CH_2' (C3-Bn)), 3.89 (ddd, 1H, H-7), 3.76 (ddd, 1H, H-5), 2.74 (ddd, 1H, H-4), 2.06 (ddd, 1H, H-3′), 1.96 (ddd, 1H, H-3), 1.65 (ddd, 1H, H-6); ^{13}C NMR (100 MHz, $CDCl_3$): δ=140.64 (C(2)), 139.09 (C_i (C7-Bn)), 138.79 (C_i (C5-Bn)), 136.43 (C(8)), 128.31 (C_{ar}), 128.19 (C_{ar}), 128.18 (C_{ar}), 128.16 (C_{ar}), 128.09 (C_{ar}), 127.73 (C_{ar}), 127.63 (C_{ar}), 127.44 (C_{ar}), 127.29 (C_{ar}), 127.29 (C_{ar}), 126.86 (C_{ar}), 126.72 (C_{ar}), 116.88 (C(1)), 116.59 (C(9)), 77.51 (C(7)), 76.68 (C(5)), 76.42 (C(4)), 72.35 (CH_2 (C7-Bn)),70.64 (CH_2 (C5-Bn)), 36.87 (C(3)), 34.61 (C(6)). Anal. Calcd for $C_{23}H_{28}O_3$ (352.47): C, 78.38; H, 8.01. Found: C, 78.11; H, 8.24.

3.8. (3*S*,5*S*,6*R*) 6-[*N*-Benzyl-*N*-(benzyloxy-carbonyl)amino]-3,5-bis(benzyloxy)-1,8-nonadiene (11)

To a solution of **9** (2.16 g, 4.88 mmol) in dichloromethane (100 ml) water (20 ml) and $NaHCO_3$ (4.10 g, 48.8 mmol) were added, then benzyl chloroformate (2.04 ml, 12.2 mmol) was added dropwise and stirring at room temperature continued for another 18 h. The layers were separated, the organic layer was washed with water (100 ml), the aq layer with dichloromethane (3×100 ml) and the combined organic layers were dried ($MgSO_4$) and the solvents were evaporated. The residue was subjected to chromatography (silica gel, hexane/ethyl acetate 85:15) to afford **11** (1.8 g, 64%) as a colourless, viscous oil. R_f 0.48 (hexane/ethyl acetate 85:15); $[\alpha]_D^{20}$ −16.72 (*c* 0.62, $CHCl_3$); IR (film): ν=3065 (m), 3031 (s), 2929 (m), 1951 (w), 1702 (s), 1643 (m), 1606 (m), 1586 (m), 1496 (s), 1454 (s), 1415 (s), 1366 (s), 1236 (s), 1178 (m), 1097 (s), 1028 (s), 994 (s), 920 (s), 821 (m), 769 (s), 735 (s), 697 (s), 598 (m), 458 (m) cm^{-1}; UV–vis (methanol): λ_{max1}=267.19 nm, *A*=0.20, λ_{max2}=272.86 nm, *A*=0.25, λ_{max3}=228.25 nm, *A*=0.23, λ_{max4}=282.96 nm, *A*=0.16; ^1H NMR

(500 MHz, $CDCl_3$): δ=7.46–7.07 (m, 20H, phenyl), 5.56 (m, 2H, H-2, H-8), 5.03–4.77 (m, 6H, H-1, H-1′, H-9, H-9′, CH_2-Cbz), 4.42 (m, 2H, CH_2′ (N-Bn), CH_2 (CBz-Bn)), 4.24 (m, 1H, H-6), 4.16 (m, 4H, CH_2-Bn), 3.75 (m, 2H, H-3, H-5), 2.44 (m, 1H, H-7′), 2.30 (ddd, 1H, H-7), 1.77 (m, 1H, H-4′), 1.68 (m, 1H, H-4); ^{13}C NMR (125 MHz, $CDCl_3$): δ=156.46 (CO (CBz)), 138.83 (C(2)), 138.62 (C_i (C3-Bn)), 138.46 (C_i (C5-Bn)), 137.57 (C_i, CBn), 136.70 (C_i of benzylamine), 135.55 (C(8)), 128.51 (C_{ar}), 128.42 (C_{ar}), 128.26 (C_{ar}), 127.92 (C_{ar}), 127.81 (C_{ar}), 127.73 (C_{ar}), 127.67 (C_{ar}), 127.57 (C_{ar}), 127.44 (C_{ar}), 126.81 (C_{ar}), 117.11 (C(9)), 116.97 (C(1)), 77.99 (C(3)), 77.84 (C(5)), 73.10 (CH_2 (C3-Bn)), 72.44 (CH_2 (C5-Bn)), 69.87 (CH_2 (CBz-Bn)), 60.48 (C(6)), 49.10 (CH_2 (N-Bn)), 38.76 (C(4)), 32.86 (C(7)); MS (ESI): *m*/*z* (%)=598.9 (M+Na, 100), 1173.1 (M_2+Na, 5), 582.7 (M+Li, 100), 1157.1 (M_2+Li, 3). Anal. Calcd for $C_{38}H_{41}O_4N$ (575.75): C, 79.27; H, 7.18. Found: C, 79.14; H, 7.44.

3.9. (3*S*,5*S*,6*R*) 6-[*N*-Benzyl-*N*-(benzyloxy-carbonyl)amino]-3,5-bis(benzyloxy)-cycloheptene (12)

To a solution of **11** (1.77 g, 3.07 mmol) in dry dichloromethane (100 ml) under argon *Grubbs*' catalyst (20 mg) was added and stirring at room temperature was continued for 24 h. The mixture was filtered through a short pad of silica gel, the filtrate evaporated and the remaining residue subjected to chromatography (silica gel, hexane/ethyl acetate (9:1)) to afford **12** (1.35 g, 80.4%) as a highly viscous oil and unreacted **11** (0.22 g). R_f 0.26 (hexane/ethyl acetate 85:15); $[\alpha]_D^{20}$ 60.34 (*c* 0.86, $CHCl_3$); IR (film): ν=3366 (m), 3031 (m), 2934 (m), 1694 (s), 1606 (m), 1496 (m), 1455 (s), 1411 (m), 1358 (m), 1254 (s), 1206 (m), 1175 (m), 1101 (s), 1028 (m), 772 (m), 735 (m), 697 (s), 600 (w), 458 (m) cm^{-1}; UV–vis (methanol): λ_{max1}=268.96 nm, *A*=0.46, λ_{max2}=274.79 nm, *A*=0.46; ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.70–7.06 (m, 20H, phenyl-H), 5.91 (m, 1H, H-1), 5.64 (m, 1H, H-2), 5.06 (dd, 1H, H-3), 4.63 (d, 1H, CH_2 (Bn)), 4.52 (d, 1H, *J*=12.0 Hz, CH_2′ (Bn)), 4.47 (m, 3H, CH_2 (Bn)), 4.41 (d, 1H, *J*=12.0 Hz, CH_2 (Bn)), 4.26 (d, 1H, CH_2 (Bn)), 4.19 (d, 1H, CH_2 (Bn)), 4.06 (m, 1H, H-5), 2.82 (dd, 1H, H-6), 2.33 (m, 2H, H-4), 1.83 (m, 2H, H-7); ^{13}C NMR (125 MHz, $CDCl_3$): δ=156.46 (CO (CBz)), 140.19 (C_i (C3-Bn)), 140.02 (C_i (C5-Bn)), 138.38 (C_i of benzylamine), 138.19 (C_i (CBz)), 128.37 (C(2)), 128.28 (C(1)), 128.23 (C_{ar}), 127.83 (C_{ar}), 127.71 (C_{ar}), 127.63 (C_{ar}), 127.54 (C_{ar}), 126.31 (C_{ar}), 126.06 (C_{ar}), 125.81 (C_{ar}), 79.08 (C(5)), 72.07 (C(3)), 70.82 (CH_2 (C5-Bn)), 70.68 (CH_2 (C3-Bn)), 67.09 (CH_2 (CBz-Bn)), 57.19 (C(6)), 47.70 (CH_2 (N-Bn)), 35.88 (C(4)), 25.95 (C(7)); MS (ESI): *m*/*z* (%)=548.5 (M+H, 30), 570.5 (M+Na, 100), 1117.0 (M_2+Na, 50). Anal. Calcd for $C_{36}H_{37}O_4N$ (547.68): C, 78.95; H, 6.81. Found: C, 78.72; H, 7.05.

3.10. (2*S*,4*S*,5*R*)-5-[*N*-benzyl-(benzyloxy-carbonyl) amino]2,4-bis(benzyloxy)cycloheptanol (13) and (3*R*,5*S*,6*R*)-6-[*N*-benzyl-*N*-(benzyloxy-carbonyl)amino]3,5-bis(benzyloxy)-cycloheptanol (14)

To a −78 °C cold solution of **12** (0.80 g, 1.47 mmol) in dry THF (80 ml) BH_3·THF (1 M, 5.87 ml, 5.87 mmol) was slowly added and stirring at room temperature was continued for another 12 h. After completion of the reaction aq sodium hydroxide (2 N, 10.5 ml) and aq hydrogenperoxide (30%, 1.5 ml) was slowly added. After stirring for 5 h at room temperature the phases were separated, the aq phase was extracted with ether (3×50 ml), the combined organic phases were dried ($MgSO_4$) and the solvent was evaporated. The residue was subjected to chromatography (silica gel, hexane/ethyl acetate 9:1) to afford **13** (0.37 g, 44.75%) and **14** (0.22 g, 26.5%) as colourless oils.

Data for **13**: R_f 0.44 (hexane/ethyl acetate 85:15); $[\alpha]_D^{20}$ 45.76 (*c* 0.49, $CHCl_3$); IR (film): ν=3440 (m), 3100 (m), 3060 (m), 3030 (m), 2980 (m), 2860 (m), 1570 (s), 1610 (m), 1570 (m), 1500 (m), 1455 (s), 1410 (m), 1245 (m), 1200 (s), 1140 (m), 1100 (s), 1080 (s), 1070 (s), 1030 (s), 1110 (m), 990 (m), 980 (m), 920 (w), 805 (w), 760 (s), 745 (s), 690 (s), 630 (w), 610 (w) cm^{-1}; UV–vis (methanol): λ_{max1}=268.50 nm, *A*=0.635; λ_{max2}=274.65 nm, *A*=0.582; ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.36–7.08 (m, 20H, phenyl-H), 5.07 (d, 1H, *J*=12.4 Hz, CH_2 (CBz-Bn)), 5.05 (d, 1H, *J*=12.4 Hz, CH_2 (CBz-Bn)), 4.54 (d, 1H, J_H=10.9 Hz, CH_2′ (N-Bn)), 4.50 (d, 1H, *J*=10.9 Hz, CH_2 (N-Bn)), 4.46 (d, 1H, *J*=11.6 Hz, CH_2′ (C2-Bn)), 4.44 (d, 1H, *J*=11.6 Hz, CH_2 (C2-Bn)), 4.27 (m, 1H, H-1), 4.22 (d, 2H, *J*=11.3 Hz, CH_2 (C4-Bn)), 4.00 (m, 1H, H-4), 3.82 (m, 1H, H-5), 3.66 (m, 1H, H-2), 2.93 (s, 1H, OH (C5-OH)), 2.01 (m, 1H, H-6′), 2.01 (m, 1H, H-6), 1.83 (m, 2H, H-3), 1.61 (m, 1H, H-7′), 1.53 (m, 1H, H-7); ^{13}C NMR (125 MHz, $CDCl_3$): δ=156.51 (CO (CBz)), 140.01 (C_i (C2-Bn)), 138.17 (C_i (C4-Bn)), 137.77 (C_i of benzylamine), 136.50 (C_i (CBz)), 128.49 (C_{ar}), 128.43 (C_{ar}), 128.23 (C_{ar}), 127.85 (C_{ar}), 127.79 (C_{ar}), 127.75 (C_{ar}), 126.37 (C_{ar}), 125.89 (C_{ar}), 79.81 (C(2)), 77.99 (C(4)), 73.05 (C(5)), 71.67 (CH_2 (C2-Bn)), 71.50 (CH_2 (C4-Bn)), 67.13 (CH_2 (CBz-Bn)), 60.49 (C(1)), 47.57 (CH_2 (N-Bn)), 32.15 (C(6)), 29.44 (C(3)), 21.68 (C(7)); MS (ESI): *m*/*z* (%)=567.4 (M+H, 10), 589.6 (M+Na, 100), 1153.5 (M_2+Na, 55). Anal. Calcd for $C_{36}H_{39}O_5N$ (565.72): C, 76.43; H, 6.95. Found: C, 76.31; H, 7.06.

Data for **14**: R_f 0.22 (hexane/ethyl acetate 85:15); $[\alpha]_D^{20}$ 32.77 (*c* 0.67, $CHCl_3$); IR (film): ν=3446 (s), 3088 (m), 3063 (s), 3030 (s), 2935 (s), 1953 (m), 1694 (s), 1606 (m), 1586 (m), 1496 (s), 1455 (s), 1415 (s), 1254 (s), 1207 (s), 1111 (s), 914 (m), 845 (m), 772 (s), 735 (s), 967 (s), 596 (m), 459 (m) cm^{-1}; UV–vis (methanol): λ_{max1}=234.96 nm, *A*=2.895; λ_{max2}=269.18 nm, *A*=0.489; λ_{max3}=274.95 nm, *A*=0.5404; ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.34–7.08 (m, 20H, phenyl), 5.05 (d, 2H, *J*=7.2 Hz, CH_2 (CBz-Bn)), 4.55 (d, 1H, *J*=12.4 Hz, CH_2 (N-Bn)), 4.39 (d, 1H, *J*=12.4 Hz, CH_2 (N-Bn)), 4.52 (d, 1H, *J*=10.8 Hz, CH_2 (C2-Bn)), 4.38 (d, 1H, *J*=10.8 Hz, CH_2 (C2-Bn)), 4.46 (m, 1H, H-1), 4.22 (d, 2H, *J*=12.0 Hz, CH_2 (C4-Bn)), 4.09 (m, 1H, H-4), 3.93 (m, 1H, H-6), 3.80 (m, 1H, H-2), 2.45 (m, 1H, H-5′), 2.09 (m, 1H, H-5), 1.94 (m, 2H, H-3), 1.74 (m, 1H, H-7′), 1.65 (m, 1H, H-7); ^{13}C NMR (125 MHz, $CDCl_3$): δ=155.92 (CO (CBz)), 141.21 (C_i (C2-Bn)), 138.78 (C_i (C4-Bn)), 137.49 (C_i of benzylamine), 136.94 (C_i (CBz)), 128.48 (C_{ar}), 128.39 (C_{ar}), 128.30 (C_{ar}), 127.85 (C_{ar}), 127.64 (C_{ar}), 127.57 (C_{ar}), 126.40 (C_{ar}), 125.83 (C_{ar}), 78.65 (C(2)), 77.69 (C(4)), 71.15 (C(5)), 70.54 (CH_2 (C2-Bn)), 70.32 (CH_2 (C4-Bn)), 67.25 (CH_2 (CBz-Bn)), 65.79 (C(1)), 41.22 (CH_2 (N-Bn)), 36.51 (C(6)), 29.12 (C(3)), 21.94 (C(7)); MS (ESI): *m*/*z* (%)=566.7 (M+H, 10), 589.4 (M+Na, 15), 1153.6 (M_2+Na, 100), 573.5 (M+Li, 100), 1137.5 (M_2+Li, 95), 1243.3 (M_2+Li_2ClO_4, 10). Anal. Calcd for $C_{36}H_{39}O_5N$ (565.72): C, 76.43; H, 6.95. Found: 76.37; H, 7.09.

3.11. (2*S*,4*S*,5*R*) 5-[*N*-benzyl-*N*-(benzyloxy-carbonyl)amino]2,4-bis(benzyloxy)-cycloheptanone (15)

To a solution of **13** (0.33 g, 0.59 mmol) in dry dichloromethane (50 ml) PCC (0.19 g, 0.59 mmol) was added and stirring at room temperature was continued for another 24 h; more PCC (0.2 g, 0.93 mmol) was added and after 24 h of stirring the mixture was decanted and the residue extracted with dichloromethane (3×50 ml). The combined organic layers were washed with water (50 ml), dried ($MgSO_4$), filtered through a pad of silica gel, the filtrate was evaporated and the residue subjected to chromatography (silica gel, hexane/ethyl acetate 85:15) to afford **15** (0.28 g, 86%) as a colourless viscous oil. R_f 0.58 (hexane/ethyl acetate 85:15); $[\alpha]_D^{20}$ 1.691 (*c* 0.28, $CHCl_3$); IR (film): ν=3418 (m), 2926 (m), 1694 (m), 1496 (m), 1456 (m), 1260 (m), 1111 (m), 736 (m), 699 (m) cm^{-1}; UV–vis (methanol): λ_{max1}=231.79 nm, *A*=2.857; λ_{max2}=260.81 nm, *A*=0.673; ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.39–6.98 (m, 20H, phenyl-H), 5.00 (d, 1H, *J*=12.0 Hz, CH_2′ (CBz-Bn)), 4.97 (d, 1H, *J*=12.0 Hz, CH_2 (CBz-Bn)), 4.59 (d, 1H, *J*=11.8 Hz, CH_2′ (C4-Bn)), 4.49 (d, 1H, *J*=10.6 Hz, CH_2′ (N-Bn)), 4.43 (d, 1H, *J*=11.2 Hz, CH_2′ (C2-Bn)), 4.33 (d, 1H, *J*=10.6 Hz, CH_2 (N-Bn)), 4.33 (m, 1H, CH_2, H-2), 4.27 (d, 1H, *J*=11.8 Hz, CH_2 (C4-Bn)), 4.17 (m, 1H, H-1), 4.13 (d, 1H, *J*=11.2 Hz,

CH_2 (C2-Bn)), 3.97 (m, 1H, H-4), 2.48 (m, 1H, H-6′), 2.38 (m, 1H, H-6), 2.25 (ddd, 1H, H-7′), 1.83 (m, 1H, H-7), 1.49 (ddd, 2H, H-3); ^{13}C NMR (125 MHz, $CDCl_3$): δ=209.33 (CO (C(5))), 171.09 (CO (CBz)), 139.85 (C_i (C4-Bn)), 138.01 (C_i (C2-Bn)), 137.71 (C_i of benzylamine), 136.38 (C_i (CBz)), 128.44 (C_{ar}), 128.36 (C_{ar}), 127.91 (C_{ar}), 127.86 (C_{ar}), 126.53 (C_{ar}), 125.75 (C_{ar}), 79.38 (C(2)), 77.56 (C(4)), 71.93 (CH_2 (C4-Bn)), 71.24 (CH_2 (C2-Bn)), 67.30 (CH_2 (CBz-Bn)), 60.50 (C(1)), 47.80 (CH_2 (N-Bn)), 39.04 (C(7)), 33.70 (C(6)), 21.16 (C(3)); MS (ESI): *m*/*z* (%)=587.0 (M+Na, 10), 1149.1 (M_2+Na, 10). Anal. Calcd for $C_{36}H_{37}O_5N$ (563.70): C, 76.71; H, 6.62. Found: 76.51; H, 6.92.

3.12. (1*R*,2*S*,4*S*,5*R*) 8-Azabicyclo[3.2.1]octane-1,2,4-triol (calystegine A_7) (17)

A solution of **15** (0.18 g, 0.32 mmol) in ethyl acetate (20 ml) and acetic acid (80 ml) was hydrogenated in the presence of Pd/C (0.2 g, 10% Pd) at a pressure of 2.38 atm for 24 h. The solvents were removed under reduced pressure and the residue subjected to chromatography (silica gel, methanol/water/concd ammonium hydroxide 95:5:1) to afford **17** (0.047 g, 92.1%) as a viscous oil. R_f 0.2 (methanol/water/ammonium hydroxide 95:5:1); $[\alpha]_D^{20}$ −1.87 (*c* 0.97, MeOH); $[\alpha]_D^{20}$ −10.83 (*c* 0.3, H_2O) (lit.[5] $[\alpha]_D^{20}$ −10.8 (*c* 0.27, H_2O)); IR (film): ν=3355 (s), 2926 (s), 2498 (m), 1652 (m), 1456 (m), 1085 (m) cm^{-1}; ^1H NMR (400 MHz, D_2O): δ=3.85 (ddd, 1H, $^3J_{2,3ax}$=9.5 Hz, $^3J_{2,3eq}$=5.5 Hz, $^4J_{2,7exo}$=1.8 Hz, H2), 3.81 (m, 1H, H4), 3.35 (m, 1H, H5), 2.09 (m, 1H, H6$_{endo}$), 2.06 (m, 1H, H7$_{endo}$), 2.00 (dddd, 1H, $^3J_{2,3eq}$=5.5 Hz, $^3J_{3eq,4}$=2.2 Hz, $^2J_{3ax,3eq}$=14.7 Hz, $^4J_{3eq,5}$=1.8 Hz, H3$_{eq}$), 1.61 (ddd, 1H, $^3J_{2,3ax}$=9.5 Hz, $^3J_{3ax,4}$=4.0 Hz, $^2J_{3ax,4}$=4.0 Hz, $^2J_{3ax,3eq}$=14.7 Hz, H3$_{ax}$), 1.55 (m, 1H, H7$_{exo}$), 1.42 (m, 1H, H6$_{endo}$); ^{13}C NMR (125 MHz, CD_3OD): δ=92.04 (C(5)), 72.51 (C(4)), 71.60 (C(2)), 60.00 (C(1)), 35.84 (C(3)), 27.60 (C(6)), 24.96 (C(7)); MS (ESI): *m*/*z* (%)=160.4 (M+H, 100), 182.3 (M+Na, 8). Anal. Calcd for $C_7H_{14}O_3N$ (160.19): C, 52.49; H, 8.81. Found: C, 52.31; H, 8.95.

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