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Enantioselective Syntheses of Polyhydroxylated Nortropane Derivatives : Total Synthesis of (+) and (-)-Calystegine B_2

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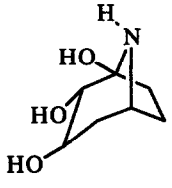
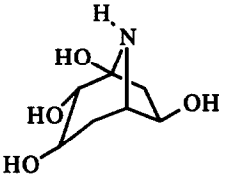
Abstract : *(+) and (-)-Calystegine B_2 were prepared from D-Glucose via Ferrier reaction followed by regiospecific ring enlargement of a polysubstituted cyclohexanone and intramolecular cyclisation of 4-aminocycloheptanone.*

Calystegines (**1-3**) have been discovered in the root secretions of *Calystegia sepium*, a member of the *Convolvulacae sepium*[1] and have been found to stimulate the growth of a nitrogen fixing bacterium, *Rhizobium meliloti 41* by serving as a source of carbon and nitrogen. Three Calystegines structures have been described (A_3: **1**, B_1: **2**, B_2: **3**), all of which exhibit a polyhydroxylated nortropane skeleton having an original aminoketal function at the bridgehead position[2]. These compounds have been recently reported as displaying an inhibitory activity toward β-glucosidase and α-galactosidase[3].



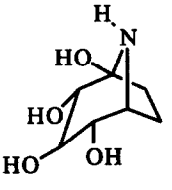
1

Calystegine A_3



2

Calystegine B_1

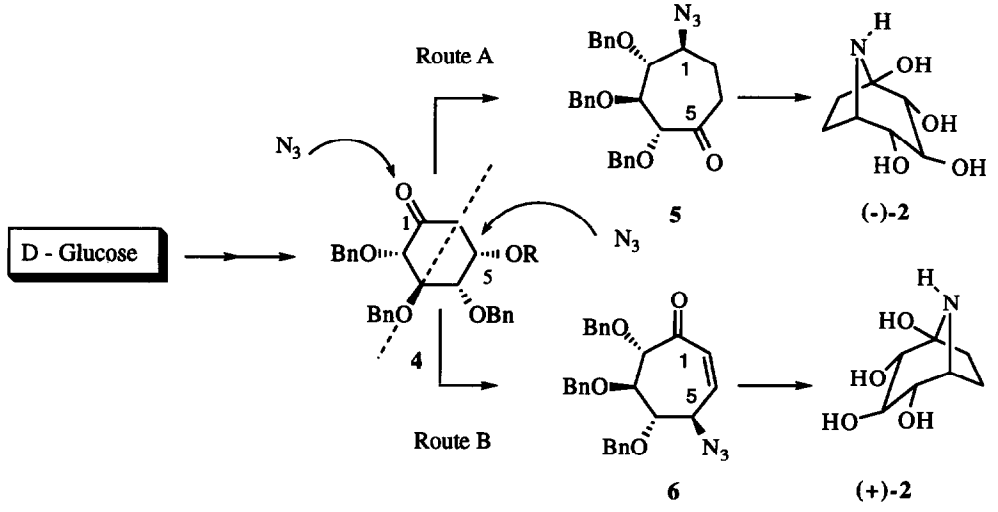


3

Calystegine B_2

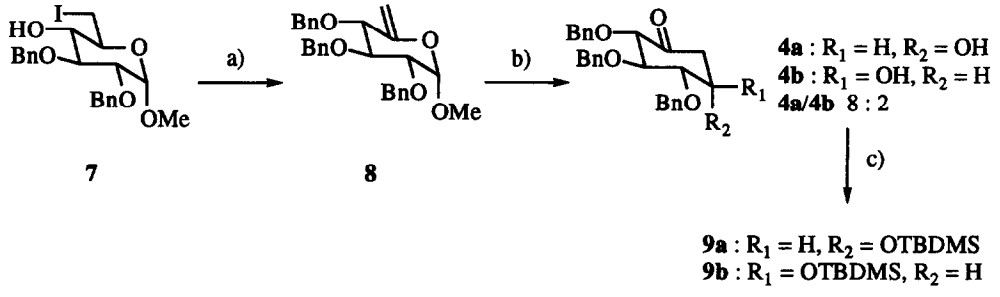
We have already reported a synthetic strategy for the 1-hydroxynortropane system, by spontaneous cyclisation of a 4-aminocycloheptanone. This method allowed us to prepare racemic Calystegine A_3 and analogous products[4]. We describe here an enantioselective preparation of (+) and (-)-Calystegine B_2[5], using D-

glucose as starting material. This methodology, depicted in scheme 1, is based on a ring enlargement of polysubstituted cyclohexanone **4**, followed by introduction of the nitrogen atom as an azide. It allowed to prepare both enantiomers of **2** by taking advantage of the pseudosymmetry of cyclohexanone **4**. The nitrogen atom can be introduced at either position C-1 (route A) to synthetize (-)-**2**, or at C-5 (route B) to synthetize (+)-**2**.



Scheme 1

Intermediate **4** was prepared as a mixture of C-5 epimers (8 : 2 ratio) from methyl-α-D-glucopyranoside by standard carbohydrate methods[6] (Scheme 2).

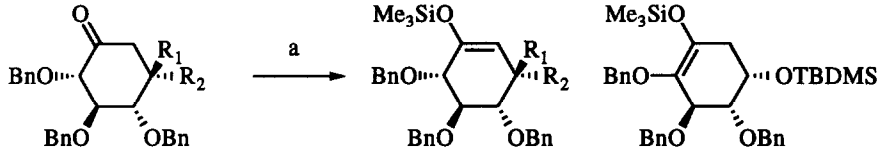


Scheme 2 : a) NaH, THF, then BnBr, *n*-Bu_4NI, (70%), b) $Hg(OAc)_2$, Acetone, H_2O, 1% AcOH, (90%), c) TBDMSOTf, 2,6-lutidine, CH_2Cl_2, (94%).

A two-step, one-pot reaction involving dehydroiodination by NaH[7] in THF and protection of the C-4 hydroxyl group as benzyl ether converted iodide **7** into **8**. The key step of our approach relied on the Ferrier rearrangement reaction[8] which afforded the polysubstituted cyclohexanone **4** intermediate from **8**. This reaction gave an 8 : 2 mixture of the two C-5 diastereoisomers which were easily separated by chromatography on silica gel (90% overall yield). Protection of the hydroxyl group of **4** (**a** or **b**) as its TBDMS ether[9] was necessary to

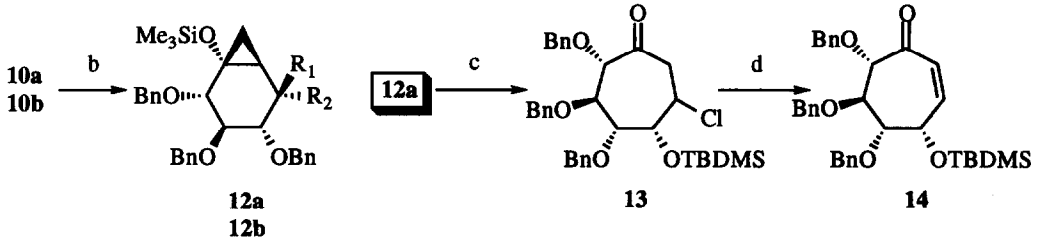
avoid β elimination and subsequent aromatization.

Treatment of **9a** with LDA at -70°C afforded the kinetic enol ether which was quenched with TMSCl giving **10a** as the major product, along with its regioisomer **11a** (**10a/11a** 8/2 from ^{1}H NMR). The ring enlargement was readily achieved by cyclopropanation of **10a** (Et_2Zn, CH_2I_2) followed by treatment of the resulting cyclopropane derivative **12a** with $FeCl_3$[10].



9a : R_1 = H, R_2 = OTBDMS
9b : R_1 = OTBDMS, R_2 =H

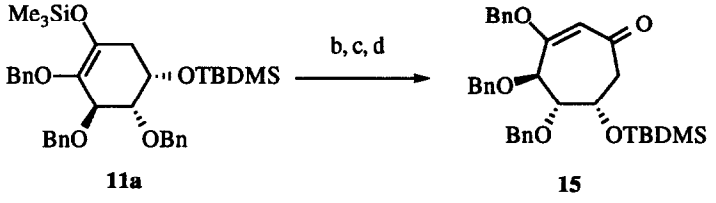
10a 8 : 2 **11a**
10b



12a
12b

13

14



11a

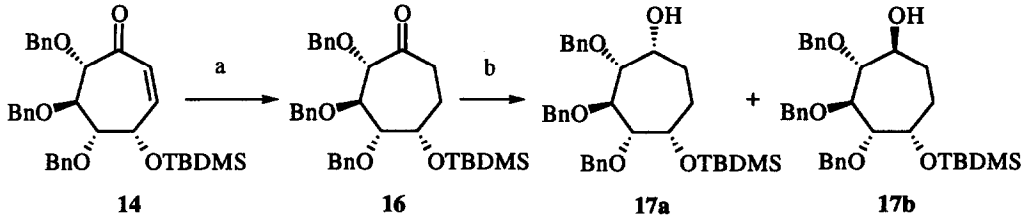
15

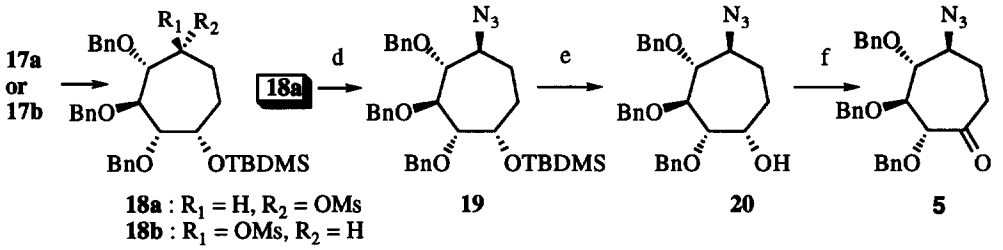
Scheme 3 : a) LDA, TMSCl, THF, -70°C, b) Et_2Zn, CH_2I_2, toluène, 0°C, c) $FeCl_3$, DMF, 70°C
d) AcO^-Na^+, MeOH, reflux (**14** : 49% from **9a**, **15** : 7% from **9a**).

Other standard methods based on the use of the zinc-silver couple gave poor yields due to cleavage of the trimethylsilyl enol ether. This sequence of reactions and subsequent dehydrochlorination, performed without purification, afforded unsaturated ketone **14** (49% from **9a** after chromatography on silica gel), and 7% of undesired isomer **15**. The regiospecific ring enlargement was also successful on **9b** *via* enol ether **10b** and cyclopropanation leading to **11b**. The stereochemistry of **11b** and consequently **11a** were assigned from nuclear Overhauser effect observed between H-2, H-4 and H-7a in ^{1}H NMR spectra.

Synthesis of (-)-Calystegine B_2

Selective hydrogenation of **14** (Pd/C 10%, EtOH) gave **16**. Reduction of the ketone with $NaBH_4$ in dioxane afforded a mixture of diastereoisomeric alcohols **17a** and **17b** (6 : 4) which were separated by chromatography on silica gel.

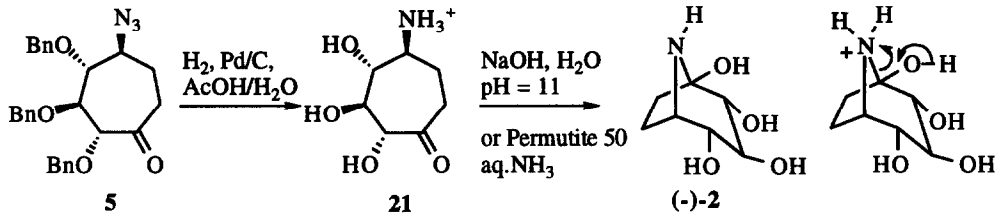




Scheme 4 : a) H_2, Pd/C 10%, EtOH, (90%), b) $NaBH_4$, dioxane, 20°C, (**17a** : **17b** 60/40, 83%) or DIBALH, ether, -60°C, (**17a** : **17b** >99/1, 79%), c) MsCl, DMAP, pyridine, d) NaN_3, DMF, 80°C, (80% from **17a**), e) *n*-Bu_4NF, THF, (90%), f) CH_2Cl_2, PCC, (94%).

Assignment of the stereochemistry of **17a** and **17b** was achieved using ^1H NMR data (400 MHz) of the corresponding mesylate derivatives **18a** and **18b**. In **18a** H-1 and H-5 display the same coupling patterns (broad doublet) in agreement with the pseudosymmetry of the molecule. In contrast, H-1 and H-5 display different patterns (triplet and doublet doublet) in **18b**. Reduction of ketone **16** by diisobutylaluminum hydride at low temperature in ether gave **17a** with a considerably high degree of stereocontrol. Subsequent displacement of mesylate by sodium azide (NaN_3, DMF, 80°C, 16h) then permited introduction of the nitrogen atom. After silyl ether deprotection (*n*-Bu_4NF, THF), the resulting alcohol was converted into the masked aminoprotected ketone **5** by oxidation (PCC, CH_2Cl_2) in 85% overall yield (Scheme 4). Finally, full deprotection was accomplished by hydrogenolysis on Pd/C 10% in aqueous AcOH. NMR spectra of the crude material only displayed broad signals and no aminoketal formation. This could be explained by the presence of an equilibrium between various forms of the molecule: open form, closed form and oligomers. However it was found that workup at high pH (addition of NaOH) led exclusively to Calystegine B_2.This can be understood as a general acid-base catalysis of the cyclisation process. Protonation of amine function in Calystegine can clearly trigger the opening of the system

into aminoketone **21** as displayed on scheme 5. (-)-Calystegine B_2 **2** ($[\alpha_D]$ = -17.5, c = 0.37, H_2O) thus obtained, was purified by HPLC on NH_2 μBondapak column. ^1H and ^{13}C NMR spectra are identical with those of the natural sample[2].

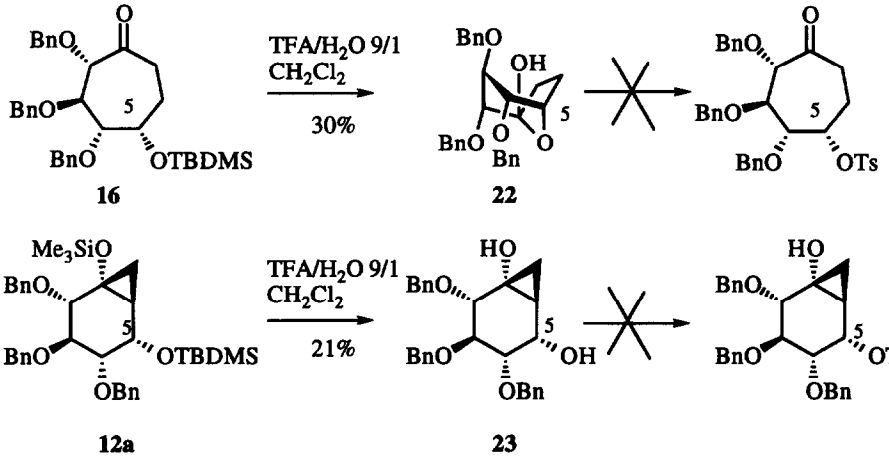


5 **21** **(-)-2**

Scheme 5

Synthesis of (+)-Calystegine B_2

Introduction of a nitrogen atom at the C-5 position (Scheme 1) appeared to be more difficult. Deprotection of the silyl ether in cycloheptanone **16** or cyclopropane derivative **12a** was carried out in acidic medium to avoid elimination of the benzyl group but led to hemiketal **22** by spontaneous cyclisation of intermediate keto-alcohol. Formation of the tosylate from this compound or selective tosylation of **23** at the C-5 position was unsuccessful.



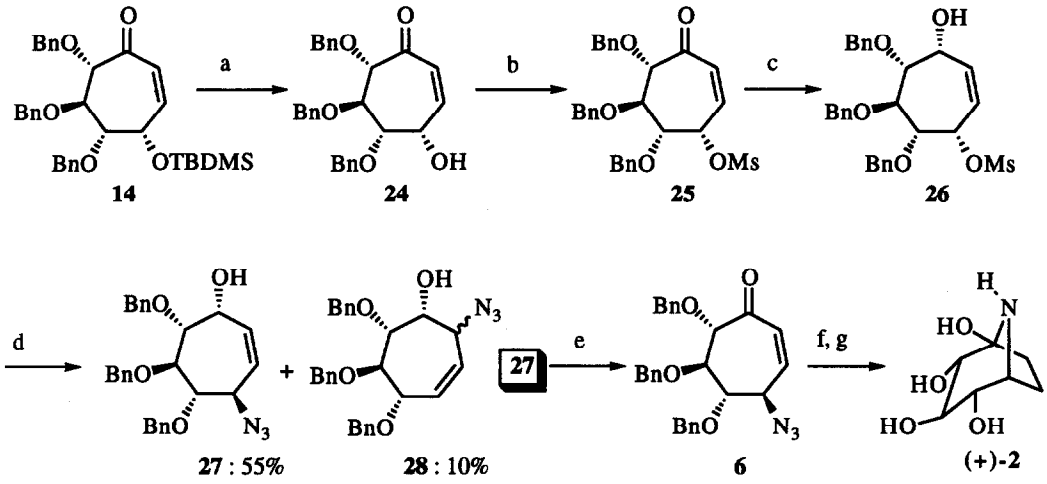
16 **22**

12a **23**

Scheme 6

However, deprotection of the silyl ether **14** with *n*-Bu_4NF in THF furnished the monocyclic derivative **24**, which was easily converted into **25**. Subsequent displacement of the mesylate by NaN_3 failed and we observed degradation of the starting material **25**. Similar observation was made on the hydrogenated derivative leading us to suggest that the keto group is involved in the failure of this approach. This problem was resolved by stereoselective reduction of the ketone group giving **26**, which allowed the substitution of the mesylate function by sodium azide at room temperature in DMF. The formation of a minor compound **28** by SN_2' reaction was also observed. Oxidation of **27** by the Dess-Martin triacetoxyperiodane reagent[11] afforded ketoazide **6**, which under

the conditions used for the preparation of (-)-2, gave the (+)-Calystegine B_2 **2** ($[\alpha_D]$ = +17.1, c = 0.41, H_2O).



Scheme 7 : a) *n*-Bu_4NF, THF, (73%), b) MsCl, pyridine, (72%), c) DIBALH, Et_2O, -60°C, d) NaN_3, DMF, r.t. (**27** : 55%, **28** : 10%), e) Dess-Martin reagent, Pyridine, CH_2Cl_2, r.t. (86%), f) H_2, Pd/C 10%, AcOH/H_2O, g) Permutite 50, aq.NH_3.

Biological tests showed that (+)-**2** is catabolized by *Rhizobium meliloti,* whereas (-)-**2** is not. These results confirmed that (+)-**2** is the natural molecule. The potent glycosidase inhibitory properties of these compounds are currently under study.

Experimental Section

Methyl 2,3,4-tri-*O*-benzyl-α-D-xylo-hex-5-enopyranoside 8.

To a suspension of NaH (60% in mineral oil) (5.3 g, 132.5 mmol) in THF (100 mL) under argon was added dropwise a solution of **7** (10.1 g, 20.8 mmol) in THF (200 mL) at -5°C. The reaction mixture was stirred at room temperature for 1h and heated at 60°C for 1h. To the resulting orange mixture was added at 15°C *n*-$Bu_4N^+I^-$ (0.8 g, 2.16 mmol), followed by benzylbromide (5 mL, 20 mmol) added dropwise. The reaction mixture was then stirred at room temperature for 1h, warmed at 40°C for 1h, hydrolysed at 0°C with saturated aqueous NH_4Cl, and diluted with AcOEt (100 mL). The aqueous phase was re-extracted with AcOEt (2 x 200 mL). The combined organic phases were washed with brine, dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give the crude product which was purified by column chromatography (petroleum ether/AcOEt 90:10 to 80:20) to give **8** (6.57 g, 70%) as a white solid. m.p. = 56-58°C (petroleum ether/AcOEt). $[\alpha]_D$ = +2.4 (c = 0.59 CH_2Cl_2). (Lit.[12] +2 (c = 1 CH_2Cl_2)).

(2S,3R,4S,5S) 5-Hydroxy-2,3,4-tris(benzyloxy) cyclohexane-1-one 4a.
(2S,3R,4S,5R) 5-Hydroxy-2,3,4-tris(benzyloxy) cyclohexane-1-one 4b.

To a solution of **8** (2.607 g, 5.8 mmol) in water (40 mL) and freshly distilled acetone (92 mL) was added $Hg(OAc)_2$ (2.096 g, 6.5 mmol) and AcOH (2 mL). The reaction mixture was stirred at reflux for 5h. After

cooling to room temperature, solvents were evaporated under reduced pressure and the aqueous phase was extracted with dichloromethane (3 x 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (petroleum ether/AcOEt 60:40) to give **4a** (1.892 g, 72%) and **4b** (0.473, 18%) as white solids.**4a** : m.p. = 121-122°C (petroleum ether/AcOEt) (Lit.[12] 122-124°C).$[\alpha]_D$ = -40.6 (c =1.2, CH_2Cl_2) (Lit.[12] -52 (c = 1, CH_2Cl_2)).**4b** : m.p. = 132-133°C (petroleum ether/AcOEt) (Lit.[12] 130-132°C), $[\alpha]_D$ = -43.0 (c = 1.4 CH_2Cl_2). (Lit.[12] -50).

(2S,3R,4R,5S) 5-[(*t*-Butyldimethylsilyl)oxy]-2,3,4-tris(benzyloxy) cyclohexane-1-one 9a.

To a solution of **4a** (2.37 g, 5.26 mmol) in dichloromethane (20 mL) was added at 0°C 2, 6-lutidine (2.79 mL, 12.1 mmol) followed by *tert*-butyldimethylsilyltriflate (2.79 mL, 12.1 mmol) added dropwise. The reaction mixture was stirred 1 h at room temperature and diluted with dichloromethane (100 mL). The mixture was washed with 1N HCl aqueous (100 mL) and brine (100 mL). The organic layer was dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (petroleum ether/AcOEt 70:30) to give **9a** (2.69 g, 94%) as a white solid. m. p. = 50-52°C (AcOEt/petroleum ether). $[\alpha]_D$ = -15.6 (c = 3.2 CH_2Cl_2), (Lit[9]. -14 (c = 1, $CHCl_3$)), ^1H NMR (400 MHz, $CDCl_3$) δ(ppm) = 7.27-7.45 (m, 15H, Ar-H), 5.0-4.6 (m, 6H, 3 AB syst. CH_2-Ph), 4.31 (m, 1H, $J_{4,5}$ = 2.1 Hz, $J_{5,6'}$ = 2.3 Hz, $J_{5,6}$ = 4.2 Hz, H-5), 4.13 (t, 1H, $J_{2,3} = J_{34}$ = 9.2 Hz, H-3), 4.05 (d, 1H, $J_{2,3}$ = 9.2 Hz, H-2), 3.71 (dd, 1H, $J_{3,4}$ = 9.2 Hz, $J_{4,5}$ = 2.1 Hz, H-4), 2.52 (dd, 1H, $J_{5,6b}$ = 2.3 Hz, $J_{6a,6b}$ = 14.1 Hz, H-6b), 2.46 (dd, 1H, $J_{5,6a}$ = 4.2 Hz, $J_{6a,6b}$ = 14.1 Hz, H-6), 0.95 (s, 9H, $(CH_3)_3$-C), 0.11 (s, 6H, $(CH_3)_2$-Si). ^{13}C NMR (50 MHz, $CDCl_3$) δ(ppm) = 203.6 (C-1), 138.5; 137.8 (arom.), 128.6; 128.4; 128.1; 128.0, 127.8; 127.7 (arom.), 87.7; 82.3; 81.8 (C-2, C-3, C-4), 75.7; 73.4; 73.0 (CH_2-Ph), 67.9 (C-5), 45.1 (C-6), 25.75 (($\underline{C}H_3)_3$-C), 18.1 (($CH_3)_3$-$\underline{C}$), -4.52; -5.0 (($\underline{C}H_3)_2$-Si). IR ($CDCl_3$) : 3087, 3063, 3030, 2952, 2927, 2889, 2855, 1736 cm^{-1}. Mass CI NH_3 : 564 (M+18) (40%), 455 (40%), 106 (100%). HREIMS (70 eV) calcd for $C_{33}H_{42}O_5Si$ 546.28015, found : 546.2796.

(2S,3R,4R,5R) 5-[(*t*-Butyldimethylsilyl)oxy]-2,3,4-tris(benzyloxy) cyclohexane-1-one 9b.

Colorless oil, 94% yield. Prepared from **4b** by the same procedure as for **9a**. $[\alpha]_D$ = -16.8 (c = 3.0 CH_2Cl_2), ^1H NMR (200 MHz, $CDCl_3$) δ(ppm) = 7.49-7.31 (m, 15H, Ar-H), 5.05-4.62 (m, 6H, 3 AB syst. CH_2-Ph), 4.35 (d, 1H, $J_{2,3}$ = 9.4 Hz, H-2), 3.97 (td, 1H, $J_{5,6a}$ = 9.4 Hz, $J_{5,6b}$ = 5.0 Hz, $J_{4,5}$ = 9.4 Hz, H-5), 3.86 (t, 1H, J = 9.4 Hz, H-3 or H-4), 3.72 (t, 1H, J = 9.4 Hz, H-3 or H-4), 2.73 (dd, 1H, $J_{5,6b}$ = 5.0 Hz, $J_{6a,6b}$ = 14.4 Hz, H-6b), 2.60 (dd, 1H, $J_{5,6a}$ = 9.4 Hz, $J_{6b,6a}$ = 14.4 Hz, H-6a), 0.96 (s, 9H, $(CH_3)_3$-C), 0.14 (s, 6H, $(CH_3)_2$-Si). ^{13}C NMR (50 MHz, $CDCl_3$) δ(ppm) = 204.1 (C-1), 138.4; 137.7 (arom.), 128.35; 128.3; 128.1; 127.9, 127.8; 127.5 (arom.), 85.1 (2C), 81.9; 81.8 (C-2, C-3, C-4), 75.3; 74.8; 73.5 (CH_2-Ph), 69.6 (C-5), 45.9 (C-6), 25.7 (($\underline{C}H_3)_3$-C), 17.9 (($CH_3)_3$-$\underline{C}$), -4.6; -5.8 (($\underline{C}H_3)_2$-Si). HREIMS (70 eV) calcd for $C_{33}H_{42}O_5Si$ 546.28015, found 546.280174.

(2S,3R,4S,5S) 5-[(*t*-Butyldimethylsilyl)oxy]-2,3,4-tris(benzyloxy)-1-[(trimethylsilyl)oxy]-1,6-cyclohexene 10a.

(3R,4S,5S) 5-[(*t*-Butyldimethylsilyl)oxy]-2,3,4-tris(benzyloxy)-1-[(trimethylsilyl)oxy]-1,2-cyclohexene 11a.

To a solution of **9a** (2.0 g, 3.60 mmol) in THF (20 ml) at -70°C under argon was added dropwise a

solution of LDA (diisopropylamine (0.92 mL, 7.2 mmol), BuLi (1.125 M in hexane) (6.4 mL, 7.20 mmol), THF (50 mL)).The enolate was immediately silylated with TMSCl (2 mL, 21.6 mmol) at -70°C. The reaction mixture was stirred and warmed to room temperature over 1h and then concentrated under reduced pressure. The residue was diluted with saturated aqueous $NaHCO_3$ (40 mL). The aqueous phase was extracted with CH_2Cl_2 (3 x 40 mL) and the combined organic phases were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give a crude product **10a** and **11a** (2.2 g) (8 : 2 ratio measured by ^1H NMR integration), which was used in the next step without further purification. **10a** ^1H NMR (400 MHz, $CDCl_3$) δ(ppm) = 7.3 (m, 15H, Ar-H), 5.0-4.6 (m, 7H, 3 AB syst. (CH_2-Ph), H-6), 4.35 (t, 1H, $J_{4,5} = J_{5,6} = 3.0$ Hz, H-5), 4.20 (dd, 1H, $J_{4,3} = 7.0$ Hz, $J_{2,3} = 10.0$ Hz, H-3), 4.05 (d, 1H, $J_{2,3} = 10.0$ Hz, H-2), 3.45 (dd, 1H, $J_{4,3} = 7.0$ Hz, $J_{4,5} = 3.0$ Hz, H-4), 0.9 (s, 9H, $(CH_3)_3$-C), 0.2-0.0 (m, 15H, $(CH_3)_2$-Si, $(CH_3)_3$-Si). ^{13}C NMR (50 MHz, $CDCl_3$) δ(ppm) = 152.7 (C-1), 139.1 (arom.), 128.3; 127.9; 127.7; 127.4 (arom.), 106.4 (C-6), 81.8; 80.3; 79.1 (C-2, C-3, C-4), 74.9; 72.9; 72.4 (CH_2-Ph), 65.6 (C-5), 26.0 ($(\underline{C}H_3)_3$-C), 18.3 ($(CH_3)_3$-$\underline{C}$), 0.5 ($(CH_3)_3$-Si) -4.2; -4.4 ($(\underline{C}H_3)_2$-Si). IR ($CDCl_3$) : 3089, 3065, 3032, 2955, 2929, 2856, 1654 cm^{-1}. **11a** ^1H NMR (400 MHz, $CDCl_3$) partial δ(ppm) = 2.45 (m, 2H, H-6a and H-6b).

(2S,3R,4S,5R) 5-[(*t*-Butyldimethylsilyl)oxy]-2,3,4-tris(benzyloxy)-1-[(trimethylsilyl)oxy]-1,6-cyclohexene 10b.

Prepared from **9a** by the same procedure as for **10a**. The crude product was used in the next step without further purification. ^1H NMR (200 MHz, $CDCl_3$) δ(ppm) = 7.28-7.13 (m, 15H, Ar-H), 4.91-4.62 (m, 7H, 3 AB syst. CH_2-Ph, H-6), 4.37 (br.d, 1H, $J_{4,5} = 10.5$ Hz, H-5), 4.09 (dd, 1H, $J_{2,3} = 7.5$ Hz, $J_{2,6} = 1.9$ Hz, H-2), 3.66 (dd, 1H, J = 10.5 Hz, J = 7.5 Hz, H-3 or H-4), 3.47 (dd, 1H, J = 10.5 Hz, J = 7.5 Hz, H-3 or H-4), 0.87 (s, 9H, $(CH_3)_3$-C), 0.21-0.06 (s, 15H, $(CH_3)_2$-Si, $(CH_3)_3$-Si). ^{13}C NMR (50 MHz, $CDCl_3$) δ(ppm) =149.2 (C-1), 139.0; 138.8(arom.), 128.3; 127.9 127.7; 127.5, 127.3 (arom.), 108.1 (C-6), 85.0; 82.8; 81.6 (C-2, C-3, C-4), 75.5 (2C), 74.5 (CH_2-Ph), 71.6 (C-5), 25.9 ($(\underline{C}H_3)_3$-C), 18.1 ($(CH_3)_3$-$\underline{C}$), 0.3 ($(\underline{C}H_3)_3$-Si), -4.4; -4.6 ($(\underline{C}H_3)_2$-Si).

(1R,2S,3R,4S,5S,6S) 5-[(*t*-Butyldimethylsilyl)oxy]-2,3,4-tris(benzyloxy)-1-[(trimethylsilyl)oxy] bicyclo[4.1.0]heptane 12a.

To a solution of the crude product **11a** (2.2 g) in toluene (46 mL) and CH_2I_2 (1.2 mL, 14.7 mmol) under argon was added dropwise at -10°C Et_2Zn (13.1 mL, 14.4 mmol, 1.1 M solution in toluene). The resulting mixture was stirred at 0°C for 1h during which time a white precipitate formed, and warmed for 2h to room temperature . The reaction mixture was hydrolysed at 5°C with saturated aqueous NH_4Cl. The organic phase was extracted with Et_2O (3 x 50 mL) and the combined organic phases were washed with saturated aqueous NH_4Cl (50 mL), brine (50 mL), dried (Na_2SO_4), filtered and concentrated under reduced pressure.The crude product **12a** (2.218 g) was used in the next step without further purification. ^1H NMR (400 MHz, $CDCl_3$) δ(ppm) = 7.24-7.41 (m, 15H, Ar-H), 4.60-4.96 (m, 6H, 3 AB syst. CH_2-Ph), 4.44 (dd, 1H, $J_{4,5} = 3.6$ Hz, $J_{5,6} = 8.1$ Hz, H-5), 4.10 (dd, 1H, $J_{2,3} = 7.9$ Hz, $J_{2,7} = 1.1$ Hz, H-2), 3.49 (dd, 1H, $J_{2,3} = 7.9$ Hz, $J_{3,4} = 10.1$ Hz, $J_{3,4} = 10.1$ Hz, H-3), 3.36 (t, 1H, $J_{4,5} = 3.6$ Hz, H-4), 1.50 (ddd, 1H, $J_{6,7a} = 6.4$ Hz, $J_{5,6} = 8.1$ Hz, $J_{6,7b} = 8.0$ Hz, H-6), 1.14 (t, 1H, $J_{7a,7b} = J_{6,7a} = 6.4$ Hz, H-7a), 0.93 (br.s, 10H, $(CH_3)_3$-C, H-7b), 0.16 (br.s, 15H, $(CH_3)_2$-Si, $(CH_3)_3$-Si). ^{13}C NMR (50 MHz, $CDCl_3$) δ(ppm) = 139.3; 138.9; 138.8 (arom.), 128.3; 127.9; 127.8; 127.4 (arom.), 87.1; 81.3; 78.3 (C-2; C-3, C-4), 75.2; 74.1; 72.7 (CH_2-Ph), 65.3 (C-5), 61.2

(C-1), 29.7 (C-6), 26.0 (($\underline{C}H_3)_3$-C), 18.4 (($CH_3)_3$-$\underline{C}$), 13.7 (C-7), 1.5; 1.1 (($\underline{C}H_3)_3$-Si), -4.5; -4.7 (($\underline{C}H_3)_2$-Si).

(1S,2S,3R,4S,5S,6R) 5-[(*t*-Butyldimethylsilyl)oxy]-2,3,4-tris(benzyloxy)-1-[(trimethylsilyl)oxy] bicyclo[4.1.0]heptane 12b.

Prepared from **10b** by the same procedure as for **12a.** ^1H NMR (200 MHz, $CDCl_3$) δ(ppm) = 7.40-7.20 (m, 15H, Ar-H), 5.02-4.73 (m, 6H, 3 AB syst. CH_2-Ph), 4.13 (dd, 1H, H-5), 3.66 (d, 1H, $J_{2\,3}$ = 10.5 Hz, H-2), 3.39 (t, 1H, $J_{2,\,3} = J_{3,\,4}$ = 10.5 Hz, H-3), 3.01 (dd, 1H, $J_{3,\,4}$ = 10.5 Hz, $J_{4,\,5}$ = 8.7 Hz, H-4), 1.27 (dd, 1H, $J_{7a,\,7b}$ = 6.8 Hz, $J_{6,\,7a}$ = 11.1 Hz, H-7b), 1.01 (ddd, 1H, $J_{5,\,6}$ = 1.4 Hz, $J_{6,\,7a}$ = 6.8 Hz, $J_{6,\,7b}$ = 11.1 Hz, H-6), 0.92 (s, 9H, $(CH_3)_3$-C), 0.57 (t, 1H, $J_{7a,\,7b} = J_{6,\,7}$ = 6.8 Hz, H-7), 0.14-0.07 (m, 15H, $(CH_3)_2$-Si, $(CH_3)_3$-Si). Stereochemistry was established through NOE enhancement beetween H-2, H-4 and H-7a. ^{13}C NMR (50 MHz, $CDCl_3$) δ(ppm) = 139.2; 138.9 (arom.), 128.3; 127.9; 127.8; 127.4(arom.), 85.6 (2C); 81.5 (C-2, C-3, C-4), 75.7; 75.5; 72.3 (CH_2-Ph), 74.2 (C-5), 61.5 (C-1), 28.6 (C-6), 25.9 (($\underline{C}H_3)_3$-C), 17.9 (($CH_3)_3$-$\underline{C}$), 15.9 (C-7), 1.35 (($\underline{C}H_3)_3$-Si), -4.4; -4.7 (($\underline{C}H_3)_2$-Si). Mass EI 70 eV : 632, 541, 301, 287, 277, 261, 181, 91. HRMS calcd for $C_{37}H_{52}O_5Si_2$ 632.335328, found 632.335552.

(2S,3R,4R,5R,6R ou S) 5-[(*t*-Butyldimethylsilyl)oxy]-6-chloro-2,3,4-tris(benzyloxy)-1-trimethylsilyloxy cycloheptane-1-one 13.

To a solution of $FeCl_3$ (3.48 g, 21.5 mmol) in DMF (30 mL) at 0°C under argon was added dropwise a solution of the crude product **12a** (2.218 g) in DMF (10 mL). The resulting reaction mixture was warmed at 70°C for 2h and hydrolysed at 0°C with 1N aqueous HCl (30 mL). The aqueous phase was extracted with CH_2Cl_2 (3 x 40 mL). The combined organic phases were washed with 1N aqueous HCl (30 mL), washed with saturated aqueous $NaHCO_3$ (30 mL), brine (30 mL) and dried (Na_2SO_4). Solvent was evaporated under reduced pressure to give the crude product **13** (1.480 g), which was used in the next step without further purification. ^1H NMR (400 MHz, $CDCl_3$) δ(ppm) = 7.29 (m, 15H, Ar-H), 4.90-4.38 (m, 6H, 3 AB syst. CH_2-Ph), 4.34 (br.d, 1H, $J_{4,\,5}$ = 1.6 Hz, H-5), 4.27 (br.dd, 1H, $J_{6,\,7b}$ = 6.3 Hz, $J_{6,\,7a}$ = 11.3 Hz, H-6), 4.03 (d, 1H, $J_{2,\,3}$ = 8.8 Hz, H-2), 3.75 (dd, 1H, $J_{2,\,3}$ = 8.8 Hz, $J_{3,\,4}$ = 8.7 Hz, H-3), 3.48 (dd, 1H, $J_{3,\,4}$ = 8.7 Hz, $J_{4,\,5}$ = 1.6 Hz, H-4), 3.04 (dd, 1H, J = 11.3 Hz, J = 15.8 Hz, H-7a or H-7b), 2.64 (dd, 1H, J = 11.3 Hz, J = 15.8 Hz, H-7a or H-7b), 0.95 (s, 9H, $(CH_3)_3$-C), 0.11 (s, 6H, $(CH_3)_2$-Si). ^{13}C NMR (50 MHz, $CDCl_3$) δ(ppm) = 203.2 (C-1), 138.5, 138.0, 137.4 (arom.), 128.6; 128.4; 128.3; 128.1; 128.0; 127.8, 127.8 (arom.), 106.4 (C-6), 85.3; 84.6; 80.6; 77.8 (C-2, C-3, C-4, C-5), 74.9; 76.4; 74.3, 73.0 (CH_2-Ph), 55.9 (C-6), 46.9 (C-7), 26.0 (($\underline{C}H_3)_3$-C), 18.6 (($CH_3)_3$-$\underline{C}$), -4.3; -5.0 (($\underline{C}H_3)_2$-Si). IR ($CDCl_3$) : 2953, 2932, 2850, 1726 cm^{-1}. Mass EI (70 eV) : 561 (M-Cl) (20%), 505 (100%), 91.

(2S,3R,4S,5S) 5-[(*t*-Butyldimethylsilyl)oxy]-2,3,4-tris(benzyloxy) cyclohept-6,7-en-1-one 14.
(4R,5R,6S) 6-[(*t*-Butyldimethylsilyl)oxy]-3,4,5-tris(benzyloxy) cyclohept-2,3-en-1-one 15.

The crude product **13** (1.480 g) was dissolved in a saturated AcONa methanolic solution (40 ml) and the mixture refluxed for 1h30. After cooling to room temperature, the solvent was evaporated under reduced pressure and the residue dissolved in H_2O (40 mL). The aqueous phase was extracted with CH_2Cl_2 (3 x 40 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (cyclohexane, AcOEt 90:10) to give **14** (0.994g, 49% from **9a**) as a white solid and **15** (0.101g, 7% from **9a**) as a yellow oil. **14** : m.p. = 78-79°C (petroleum ether/AcOEt).

$[\alpha]_D$ = +62.2 (c = 1.23 CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ(ppm) = 7.15-7.40 (m, 15H, Ar-H), 6.35 (dt, 1H, $J_{6,7}$ = 12.3 Hz, $J_{4,6} = J_{5,6}$ = 1.5 Hz, H-6), 6.10 (dd, 1H, $J_{6,7}$ = 12.3 Hz, $J_{5,7}$ = 3.0 Hz, H-7), 4.82 (dd, 1H, $J_{5,6}$ = 1.5 Hz, $J_{5,7}$ = 3.0 Hz, H-5), 4.75-4.35 (m, 6H, 3 AB syst. CH_2-Ph), 4.17 (d, 1H, $J_{2,3}$ = 6.4 Hz, H-2), 3.88 (br.s, 1H, H-4), 3.75 (dd, 1H, $J_{3,4}$ = 2.8, $J_{2,3}$ = 6.4 Hz, H-3), 0.85 (s, 9H, $(CH_3)_3$-C), 0.10 (s, 6H, $(CH_3)_2$-Si). ^{13}C NMR (100 MHz, $CDCl_3$) δ(ppm) = 198.5 (C-1),145.3 (C-3), 127.3 (C-2), 137.8 (arom.), 128.4; 128.3; 128.1; 128.0; 127.9; 127.8; 127.4; 127.3 (arom.), 89.1 (C-7); 81.6; 80.2 (C-5, C-6), 73.6; 72.7; 71.5 (CH_2-Ph), 71.3 (C-4), 46.9 (C-7), 25.8 (($\underline{C}H_3)_3$-C), 18.1 (($CH_3)_3$-$\underline{C}$), -4.7; -4.9 (($\underline{C}H_3)_2$-Si). IR ($CDCl_3$) : 3087, 3066, 3032, 2953, 2929, 2857, 1693, 1622 cm^{-1}. Mass EI (70 eV) : 559, 468, 396, 362, 331, 239. HRMS calcd for $C_{34}H_{42}O_5Si$ 558.28015, found : 558.27793. Anal. Calcd for $C_{34}H_{42}O_5Si$: C : 73.08, H : 7.58. Found : C : 72.80, H : 7.42.

15 : $[\alpha]_D$ = +62.2 (c = 0.53 CH_2Cl_2). ^1H NMR (200 MHz, $CDCl_3$) δ(ppm) = 7.21-7.42 (m, 15H, Ar-H), 5.58 (br.s, 1H, H-2), 4.94-4.55 (m, 7H, 3 AB syst. CH_2-Ph, H-6), 4.18 (dd, 1H, $J_{4,5}$ = 5.5 Hz, $J_{2,4}$ = 0.5, H-4), 3.93 (d, 1H, $J_{4,5}$ = 5.5 Hz, H-5), 3.28 (dd, 1H, $J_{6,7a}$ = 10.8 Hz, $J_{7a,7b}$ = 16.2 Hz, H-7a), 2.76 (dd, 1H, $J_{6,7b}$ = 3.8 Hz, $J_{7a,7b}$ = 16.2 Hz, H-7b), 0.94 (s, 9H, $(CH_3)_3$-C), 0.12 (s, 6H, $(CH_3)_2$-Si). ^{13}C NMR (50 MHz, $CDCl_3$) δ(ppm) = 197.5 (C-1), 165.6 (C-3), 138.4; 137.5; 135.4 (arom.), 128.7; 128.4; 128.1; 127.9; 127.7 (arom.), 107.8 (C-2), 80.9; 78.6 (C-4, C-5), 73.7 (2C), 70.5 (CH_2-Ph), 67.0 (C-7), 25.9 (($\underline{C}H_3)_3$-C), 18.1 (($CH_3)_3$-$\underline{C}$), -4.7 (($\underline{C}H_3)_2$-Si). IR ($CDCl_3$) : 3090, 3067, 3033, 2956, 2930, 2884, 2858, 1623 cm^{-1}. Anal. Calcd for $C_{34}H_{42}O_5Si$: C : 73.08, H : 7.58. Found : C : 73.30, H : 7.63.

(2S,3R,4S,5S) 5-[(*t*-Butyldimethylsilyl)oxy]-2,3,4-tris(benzyloxy) cycloheptane-1-one 16.

A solution of **14** (114 mg, 0.2 mmol) in ethanol (8 mL) was hydrogenated under atmospheric pressure in the presence of 10% palladium on charcoal. The suspension was filtered through Celite and the resulting solution concentrated under reduced pressure, yielding the crude product, which was purified by column chromatography (petroleum ether/AcOEt 90:10) to give **16** (101 mg, 90%) as a colorless oil. $[\alpha]_D$ = -3.1 (c = 5.5 CH_2Cl_2), ^1H NMR (400 MHz, $CDCl_3$) δ(ppm) = 7.3-7.6 (m, 15H, Ar-H), 4.7-4.4 (m, 6H, 3 AB syst. CH_2-Ph), 4.22 (m, 1H, $J_{5,6a}$ = 8.0 Hz, $J_{5,6b}$ = 2.8 Hz, H-5), 4.09 (d, 1H, $J_{2,3}$ = 5.1 Hz, H-2), 3.84 (dd, 1H, $J_{2,3}$ = 5.1 Hz, $J_{3,4}$ = 6.7 Hz, H-3), 3.41 (br.d, 1H, $J_{3,4}$ = 6.7 Hz, H-4), 2.55 (m, 1H), 2.28 (m, 1H), (H-7a and H-7b), 2.05 (m, 1H, $J_{5,6a}$ = 8.0 Hz, $J_{6a,6b}$ = 12 Hz, H-6a), 1.74 (m, 1H, $J_{5,6b}$ = 2.8 Hz, $J_{6a,6b}$ = 12 Hz, H-6b), 0.85 (s, 9H, $(CH_3)_3$-C), 0.10 (s, 6H, $(CH_3)_2$-Si). ^{13}C NMR (100 MHz, $CDCl_3$) δ(ppm) = 206.5 (C-1), 138.9; 138.5 (arom.), 128.5; 128.3; 128.1; 127.8; 127.7; 127.4 (arom.) 87.2; 83.4; 80.9 (C-2, C-3, C-4), 73.9; 73.7; 72.7 (CH_2-Ph), 71.3 (C-5), 36.7 (C-7), 27.9 (C-6), 26.0 (($\underline{C}H_3)_3$-C), 18.3 (($CH_3)_3$-$\underline{C}$), -4.5; -4.7 (($\underline{C}H_3)_2$-Si). IR ($CDCl_3$) : 3088, 3066, 3032, 2958, 2929, 2857, 1722 cm^{-1}. Mass EI (70 eV) : 561, 503, 469, 452, 428, 229, 181, 91. HRMS calcd for $C_{34}H_{44}O_5Si$ 560.295799, found (doublet): 560.28746 and 559.95837. Anal. Calcd for $C_{34}H_{44}O_5Si$: C : 72.82, H : 7.91, Si : 5.01. Found : C : 72.87, H : 8.07, Si : 5.14.

(1R,2R,3S,4R,5S) 5-[(*t*-Butyldimethylsilyl)oxy]-2,3,4-tris(benzyloxy) cycloheptane-1-ol 17a.
(1S,2R,3S,4R,5S) 5-[(*t*-Butyldimethylsilyl)oxy]-2,3,4-tris(benzyloxy) cycloheptane-1-ol 17b.

To a solution of **16** (296 mg, 0.53 mmol) in freshly distilled dioxane (33 mL) at room temperature was added $NaBH_4$ (30 mg, 0.79 mmol) in several portions. The reaction mixture was hydrolysed with H_2O (15 mL) and the dioxane evaporated under reduced pressure. The residue was extracted with CH_2Cl_2 (3 x 15 mL). The combined organic phases were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude

product was purified by column chromatography (petroleum ether/AcOEt 90:10) to give **17b** (101 mg, 33%) and **17a** (150 mg, 50%) as colorless oils. **17a** : $[\alpha]_D$ = +24.0 (c = 1.0 CH_2Cl_2), ^1H NMR (400 MHz, $CDCl_3$) δ(ppm) = 7.35-7.20 (m, 15H, Ar-H), 4.85-4.45 (m, 6H, 3 AB syst. CH_2-Ph), 3.95 (dd, 1H, $J_{7a,\ 1}$ = 4.0 Hz, $J_{1,\ 7b}$ = 10.6 Hz, H-1), 3.90 (td, 1H, $J_{4,\ 5}$ = $J_{5,\ 6b}$ = 9.2 Hz, $J_{5,\ 6a}$ = 2.1 Hz, H-5), 3.78 (m, 2H, H-2 and H-3), 3.32 (m, 1H, $J_{4,\ 5}$ = 9.2 Hz, H-4), 2.07 (m, 1H, H-7a or H-7b), 1.98 (m, 1H, $J_{6a,\ 6b}$ = 17.4 Hz, H-6a or H-6b), 1.74 (m, 1H, $J_{6a,\ 6b}$ = 17.4 Hz, H-6a or H-6b), 1.60 (m, 1H, $J_{7a,\ 7b}$ = 17.4 Hz, H-7a or H-7b), 0.90 (s, 9H, $(CH_3)_3$-C), 0.05 (s, 6H, $(CH_3)_2$-Si). ^{13}C NMR (100 MHz, $CDCl_3$) δ(ppm) = 138.9; 138.2; 137.8 (arom.), 128.5; 128.4; 128.3; 128.1; 127.9; 127.8; 127.6; 127.4 (arom.), 89.2; 83.2; 82.3 (C-2, C-3, C-4), 74.2; 73.5; 72.5 (CH_2-Ph), 72.0; 69.5 (C-1, C-5), 30.8; 28.2 (C-7, C-6), 25.9 (($\underline{C}H_3)_3$-C), 18.0 (($CH_3)_3$-$\underline{C}$), -4.8 (($\underline{C}H_3)_2$-Si). IR ($CDCl_3$) : 3545, 3087, 3066, 3032, 2955, 2930, 2887, 2858 cm^{-1}. Mass EI (70 eV) : 471, 413, 379, 365, 347, 253, 199, 181, 91. Anal. Calcd for $C_{34}H_{46}O_5Si$: C : 72.56, H : 8.24, Si : 4.63. Found : C : 72.64, H : 8.46, Si : 4.63. **17b** : $[\alpha]_D$ = -7.4 (c = 2.12 CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ(ppm) = 7.34-7.20 (m, 15H, Ar-H), 4.80-4.50 (m, 6H, 3 AB syst. CH_2-Ph), 4.10 (1H, OH), 4.08 (br.d, 1H, $J_{1,\ 7}$ = 5.6 Hz, H-1), 3.90 (dd, 1H, $J_{4,\ 5}$ = 3.0 Hz, $J_{5,\ 6a}$ = 11.1 Hz, H-5), 3.80 (dd, 1H, $J_{4,\ 3}$ = 6.2 Hz, $J_{4,\ 5}$ = 3.0 Hz, H-4), 3.77 (br.s, 1H, H-2), 3.40 (d, 1H, $J_{4,\ 3}$ = 6.2 Hz, H-3), 2.20 (m, 1H, H-6a or H-6b), 1.98 (m, 1H, H-7a or H-7b), 1.60 (m, 1H, H-6a or H-6b), 1.45 (m, 1H, H-7a or H-7b), 0.90 (s, 9H, $(CH_3)_3$-C), 0.05 (s, 6H, $(CH_3)_2$-Si). ^{13}C NMR (100 MHz, $CDCl_3$) δ(ppm) = 138.6; 138.1; 137.4 (arom.), 128.5; 128.3; 128.15; 128.0; 127.9; 127.5 (arom.) 87.8; 83.0; 82.8 (C-2, C-3; C-4), 74.0; 73.4; 72.4 (CH_2-Ph), 72.1; 70.4 (C-1, C-5), 30.2; 26.65 (C-7, C-6), 25.9 (($\underline{C}H_3)_3$-C), 18.1 (($CH_3)_3$-$\underline{C}$), -4.8 (($\underline{C}H_3)_2$-Si). IR ($CDCl_3$) : 3416, 3089, 3066, 3032, 2953, 2930, 2886, 2858 cm^{-1}.

(1R,2R,3S,4R,5S) 5-[(*t*-Butyldimethylsilyl)oxy]-2,3,4-tris(benzyloxy) cycloheptane-1-ol 17a.

To an etheral solution (40 mL) of **16** (447 mg, 0.79 mmol) under argon was added dropwise for 30 mn at -60°C DIBALH (2.55 mL, 1.5 M in toluene). After warming to room temperature the reaction mixture was hydrolysed with 1N aqueous HCl (40 mL). The resulting aqueous phase was reextracted with AcOEt (3 x 30 mL) and the combined organic phases were washed with brine (30 mL), dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (petroleum ether/AcOEt 90:10) to give **17a** (352 mg, 79%) as a colorless oil.

(1R,2S,3R,4R,5S) 5-[(*t*-Butyldimethylsilyl)oxy]-1-mesyloxy-2,3,4-tris(benzyloxy) cycloheptane 18a.

MsCl (0.2 mL, 3.02 mmol) was added to a solution of **17a** (108 mg, 0.19 mmol) with DMAP (5 mg) in pyridine (3 mL) at room temperature. The reaction mixture was stirred overnight at room temperature and concentrated under reduced pressure. The residue was dissolved into aqueous $CuSO_4$ and extracted with AcOEt (3 x 5 mL). The combined organic phases were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give the crude product **18a** (130 mg), which was used in the next step without further purification. ^1H NMR (400 MHz, $CDCl_3$) δ(ppm) = 7.33-7.24 (m, 15H, Ar-H), 4.98 (br.d, 1H, $J_{1,\ 7}$ = 8.5 Hz, H-1), 4.79-4.44 (m, 6H, 3 AB syst. CH_2-Ph), 4.00 (br.d, 1H, $J_{5,\ 6a}$ = 6.9 Hz, H-5), 3.78 (br.s, 1H), 3.63 (br.s, 2H, H-2, H-3, H-4), 2.83 (s, 3H, CH_3-SO_3), 2.39 (m, 1H, H-7a or H-7b), 2.25 (m, 1H, H-6a or H-6b),1.58 (m, 1H, H-7a or H-7b), 1.25 (m, 1H, H-6a or H-6b), 0.88 (s, 9H, $(CH_3)_3$-C), 0.06 (s, 3H, $(CH_3)_2$-Si), 0.04 (s, 3H, $(CH_3)_2$-Si). ^{13}C NMR (100 MHz, $CDCl_3$) δ(ppm) = 138.9; 138.0; 137.9 (arom.), 128.3; 128.1; 127.9; 127.7; 127.4; 127.2 (arom.), 84.5; 82.6; 80.7; 79.4 (C-1, C-2, C-3; C-4),73.4; 72.9; 72.7 (CH_2-Ph), 70.9 (C-5), 38.3

($\underline{C}H_3SO_3$), 27.4; 25.7 (C-7, C-6), 25.7 (($\underline{C}H_3)_3$-C), 17.9 (($CH_3)_3$-$\underline{C}$), -4.8; -5.0 (($\underline{C}H_3)_2$-Si).

(1S,2S,3R,4R,5S) 5-[(*t*-Butyldimethylsilyl)oxy]-1-mesyloxy-2,3,4-tris(benzyloxy) cycloheptane 18b.

Prepared from **17b** by the same procedure as for **18a**. ^1H NMR (400 MHz, $CDCl_3$) δ(ppm) = 7.32-7.20 (m, 15H, Ar-H), 4.93 (dd, 1H, $J_{1,\ 7a} = J_{1,\ 2}$ = 9.5 Hz, H-1), 4.83-4.46 (m, 6H, 3 AB syst. CH_2-Ph), 4.10 (dd, 1H, $J_{5,\ 6b}$ = 4.8, $J_{5,\ 6a}$ = 10.5 Hz, H-5), 3.86 (syst. AB, 2H, J = 6.7 Hz, H-3, H-4), 3.60 (d, 1H, $J_{1,\ 2}$ = 9.5 Hz, H-2), 2.75 (s, 3H, CH_3-SO_3), 2.10 (m, 1H, H-7a or H-7b), 1.96 (m, 1H, H-6a or H-6b), 1.83 (m, 1H, H-7a or H-7b), 1.70 (m, 1H, H-6a or H-6b), 0.89 (s, 9H, $(CH_3)_3$-C), 0.05 (s, 6H, $(CH_3)_2$-Si).

(1S,2R,3S,4R,5S) 1-Azido-5-[(*t*-butyldiméthylsilyl)oxy]-2,3,4-tris(benzyloxy) cycloheptane 19.

To a solution of the crude product **18a** (130 mg) in DMF (3 mL) under argon was added NaN_3 (60 mg, 0.9 mmol). The resulting mixture was stirred overnight at 90°C. After cooling to room temperature, DMF was evaporated under reduced pressure, the residue dissolved with H_2O (5 ml), and the aqueous phase extracted with CH_2Cl_2 (3 x 3 mL). The combined organic phases were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give the crude colorless oily product **19** (89 mg, 80% from **17a**), which was used in the next step without further purification. $[\alpha]_D$ = -14.5 (c = 2.3 CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ(ppm) = 7.35-7.21 (m, 15H, Ar-H), 4.77-4.45 (m, 6H, 3 AB syst. CH_2-Ph), 4.03 (dd, 1H, $J_{5,\ 6a}$ = 10.7 Hz, $J_{5,\ 6a}$ = 4.0 Hz, H-5), 3.95 (br.dd, 1H, $J_{1,\ 2}$ = 9.0 Hz, $J_{1,\ 7b}$ = 9.1 Hz, H-1), 3.81 (m, 2H, H-3, H-4), 3.43 (dd, 1H, $J_{1,\ 2}$ = 9.0 Hz, $J_{2,\ 3}$ = 2.8 Hz, H-2), 1.96 (m, 1H),1.80 (m, 1H), 1.65 (m, 1H), 1.50 (m, 1H) (H-6a, H-6b, H-7a, H-7b), 0.88 (s, 9H, $(CH_3)_3$-C), 0.05 (s, 6H, $(CH_3)_2$-Si). ^{13}C NMR (50 MHz, $CDCl_3$) δ(ppm) = 139.0; 138.0 (arom.), 128.5; 128.4; 128.3; 128.1; 127.9; 127.7; 127.5(arom.), 87.7; 82.3; 80.8 (C-2, C-3; C-4), 73.6 (2C); 72.6 (CH_2-Ph), 71.4 (C-5); 64.8 (C-1), 29.9; 27.7 (C-7, C-6), 26.0 (($\underline{C}H_3)_3$-C), 18.1 (($CH_3)_3$-$\underline{C}$), -4.6 (($\underline{C}H_3)_2$-Si). IR ($CDCl_3$) : 3089, 3066, 3032, 2953, 2930, 2886, 2856, 2105 cm^{-1}. Mass EI (70eV) : 560, 545, 502, 452, 410, 362, 230, 181, 91.

(1S,2R,3S,4S,5S) 1-Azido-5-hydroxy-2,3,4-tris(benzyloxy) cycloheptane 20.

To a solution of **20** (60 mg, 0.1 mmol) in THF (2 mL) under nitrogen was added dropwise at room temperature *n*-Bu_4NF (0.6 mL, 0.6 mmol, 1 M solution in THF). The reaction mixture was then hydrolysed at 0°C with saturated aqueous NH_4Cl (4 mL) and the aqueous phase extracted with CH_2Cl_2 (3 x 6 mL). The combined organic phases were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (petroleum ether/AcOEt 80:20) to give **20** (52 mg, 90%) as colorless oil. $[\alpha]_D$ = -11.8 (c = 1.9 CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ(ppm) = 7.36-7.24 (m, 15H, Ar-H), 4.75-4.40 (m, 6H, 3 AB syst. CH_2-Ph), 4.01 (br.s, 1H, H-5), 3.96 (dd, 1H, $J_{2,\ 3}$ = 2.5 Hz, $J_{3,\ 4}$ = 6.8 Hz, H-3), 3.95-3.88 (m, 2H, H-1, H-4), 3.53 (dd, 1H, $J_{1,\ 2}$ = 8.6 Hz, $J_{2,\ 3}$ = 2.5 Hz, H-2), 2.1 (br.s, 1H, OH), 1.86-1.61 (m, 4H, H-6a, H-6b, H-7a, H-7b). ^{13}C NMR (50 MHz, $CDCl_3$) δ(ppm) = 138.3; 138.2; 137.9 (arom.), 128.6; 128.5; 128.2; 128.0 (arom.), 85.8; 82.5; 78.8 (C-2, C-3, C-4), 73.5; 73.3; 73.0 (CH_2-Ph), 69.6 (C-5), 65.7 (C-1), 30.1; 25.6 (C-7, C-6). IR ($CDCl_3$) : 3577, 3089, 3066, 3032, 2932, 2869, 2104 cm^{-1}. Mass EI (70eV) : 445, 408, 382, 354, 248, 91. Anal. Calcd for $C_{28}H_{32}N_3O_4$: C : 70.86, H : 6.80, N : 8.85. Found : C : 70.77, H : 6.57, N : 8.92.

(2R,3S,4R,5S) 1-Azido-2,3,4-tris(benzyloxy) cycloheptane-1-one 5.

A solution of **20** (50 mg, 0.10 mmol) with PCC (50 mg, 0.23 mmol) and Celite (50 mg) in CH_2Cl_2 (5 mL) was stirred overnight at room temperature. The brown reaction mixture was filtered on silicagel to remove the chromium residues and the solvent concentrated under reduced pressure to give **5** (48 mg, 94%) as a colorless oil. $[\alpha]_D$ = -12.7 (c = 2.52 CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ(ppm) = 7.39-7.29 (m, 15H, Ar-H), 4.68-4.43 (m, 6H, 3 AB syst. CH_2-Ph), 4.35 (d, 1H, $J_{2,3}$ = 5.4 Hz, H-2), 3.94 (t, 1H, J = 5.4 Hz, H-3 or H-4), 3.88 (m, 1H, H-5), 3.70 (t, 1H,J = 5.4 Hz, H-3 or H-4), 2.67 (ddd, 1H, J = 5.2 Hz, J = 11.0 Hz,$J_{6a,6b}$ = 16.4 Hz, H-6a), 2.50 (ddd, 1H, J = 4.0 Hz, J = 3.8 Hz, $J_{6a,6b}$ = 16.4 Hz, H-6b), 2.07 (m, 2H, H-7a and H-7b). ^{13}C NMR (50 MHz, $CDCl_3$) δ(ppm) = 206.5 (C-1), 137.5 (arom.), 128.5; 128.1 (arom.), 86.1; 82.5; 80.2 (C-2, C-3, C-4), 73.4; 73.2; 72.6 (CH_2-Ph), 63.4 (C-5), 37.8 (C-7), 24.8 (C-6). IR ($CDCl_3$) : 2928, 2863, 2104, 1721 cm^{-1}. Mass EI (70eV) : 471, 443, 428, 408, 390, 380, 352, 279, 167, 149, 91. Anal. Calcd for $C_{28}H_{32}N_3O_4$: C : 71.16, H : 6.40, N : 8.89. Found : C : 70.88, H : 6.46, N : 8.14.

(-)-Calystegine B_2: (1S,2R,3S,4R,5S) 8-azabicyclo[3.2.1]octane-1,2,3,4-tetraol 2.

A solution of **7** (106 mg, 0.22 mmol) in a mixture AcOH (2 mL) and H_2O (2 mL) was hydrogenated at atmospheric pressure in the presence of 10% palladium on charcoal for 48h. TLC monitoring showed that the reduction was over. The suspension was filtered through Celite and the resulting solution concentrated under reduced pressure. This residue was purified on permutite 50 (elution : aq.NH_3) to give, after evaporation under reduced pressure, **(-)-2** (34 mg, 87%). Further purification was carried out by HPLC using a 8 x 10 mm column (μBondapak NH_2 10 μ and MeCN-H_2O, 4:1), 2 ml min^{-1} flow rate and RI detection. $[\alpha]_D$ = -17.5 (c = 0.37 H_2O). ^1H NMR (400 MHz, D_2O) δ(ppm) = 3.41 (dd, 1H, $J_{3,4}$ = 8.5 Hz, $J_{4,5}$ = 3.7 Hz, H-4), 3.25 (d, 1H, $J_{2,3}$ = 8.5 Hz, H-2), 3.17 (t, 1H, $J_{2,3} = J_{3,4}$ = 8.5 Hz, H-3), 3.13 (m, 1H, H-5), 1.79 (m, 2H, H-6a, H-6b), 1.58 (m, 1H, H-7a), 1.37 (m, 1H, H-7b). ^{13}C NMR (100 MHz, D_2O) δ(ppm) = 93.0 (C-1), 80.3; 77.5 (2C) (C-2, C-3, C-4), 58.4 (C-5), 31.4; 24.2 (C-6, C-7).

(1R,2S,3R,4S,5R) 1-Hydroxy-2,3,4-tris(benzyloxy)-8-oxabicyclo[3.2.1]octane 22.

A solution of **16** (50 mg, 0.08 mmol) in CH_2Cl_2 (1 mL) and TFA/H_2O (1/9, 2 mL) was stirred at room temperature for 48 h. The reaction mixture was neutralised with solid $NaHCO_3$ and extracted with CH_2Cl_2 (3 x 5 mL). The combined organic phases were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (petroleum ether/AcOEt 20:80) to give **23** (10.5 mg, 30%) as a colorless oil. $[\alpha]_D$ = -23.3 (c = 1.05 CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ(ppm) = 7.38-7.21 (m, 15H, Ar-H), 4.66-4.35 (m, 6H, 3 CH_2-Ph), 4.11 (br.s, 1H, OH), 3.73 (br.s, 1H), 3.41 (br.s, 1H), 3.20 (br.s, 1H) (H-2, H-3, H-4), 2.16-2.04 (m, 2H, H-7a, H-7b), 1.89 (dd, 1H, $J_{6b,7a}$ = 6.0 Hz, $J_{6a,6b}$ = 14.0 Hz, H-6b), 1.89 (dd, 1H, $J_{5,6}$ = 4.9 Hz, $J_{6a,6b}$ = 14.0 Hz, H-6a). ^{13}C NMR (50 MHz, $CDCl_3$) δ(ppm) = 138.3; 137.8; 137.4 (arom.), 128.7; 128.6; 128.5; 128.3; 128.0; 127.8; 127.6 (arom.), 102.3 (C-1), 79.4; 77.0; 76.5; 75.7 (C-2, C-3, C-4, C-5), 72.6; 71.9; 71.1 (CH_2-Ph), 30.2 (C-7), 24.6 (C-6). IR ($CDCl_3$) : 3532, 3087, 3065, 3031, 2960, 2927, 2870, 2858 cm^{-1}.

(1S,2S,3R,4S,5S,6R) 1,5-Bishydroxy-2,3,4-tris(benzyloxy) bicyclo[4.1.0]heptane 23.

A solution of **12a** (183 mg, 0.29 mmol) in CH_2Cl_2 (2 mL) and a mixture of TFA/H_2O (1/9, 4 mL) was stirred at room temperature for 48 h. The reaction mixture was neutralised with solid $NaHCO_3$ and extracted with

CH_2Cl_2 (3 x 10 mL). The combined organic phases were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (petroleum ether/AcOEt 20:80) to give **23** (28 mg, 21%) as a colorless oil. $[\alpha]_D$ = -11.4 (c = 0.36 CH_2Cl_2).^{1}H NMR (200 MHz, $CDCl_3$) δ(ppm) = 7.31-7.20 (m, 15H, Ar-H), 4.94-4.53 (m, 7H, 3 CH_2-Ph, H-5), 4.28 (dd, 1H, $J_{4,5}$ = 2.6 Hz, $J_{3,4}$ = 8.2 Hz, H-4), 4.04 (m, 1H, H-5), 3.37 (m, 2H, H-2, H-3), 2.44 (br.m, 2H, 2 OH), 1.51 (m, 1H, H-6), 1.07 (dd, 1H, $J_{6,7a}$ = 6.8 Hz, $J_{7a,7b}$ = 6.8 Hz, H-7a), 0.85 (m, 1H, H-7b). ^{13}C NMR (50 MHz, $CDCl_3$) partial δ(ppm) = 85.6; 80.9; 78.7 (C-2, C-3, C-4), 75.3; 74.5; 73.0 (CH_2-Ph), 64.1 (C-5), 60.1 (C-1), 24.9 (C-6), 14.2 (C-7). IR ($CDCl_3$) : 3582, 3089, 3066, 3032, 2929, 2885, 2857 cm^{-1}.

(2S,3R,4S,5S) 5-Hydroxy-2,3,4-tris(benzyloxy) cyclohept-6,7-en-1-one 24.

To a solution of **14** (1.254g, 2.2 mmol) in THF (62 mL) under argon was added dropwise *n*-Bu_4NF (2.2 ml, 2.2 mmol, 1M solution in THF). The resulting reaction mixture was stirred at room temperature for 2h, then hydrolysed at 0°C with saturated aqueous NH_4Cl (20 mL) and extracted with CH_2Cl_2 (3 x 40 mL). The combined organic phases were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (petroleum ether/AcOEt 50:50) to give **22** (0.720g, 73%) as a colorless oil. $[\alpha]_D$ = +48.2 (c = 0.5 CH_2Cl_2).^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm) = 7.36-7.12 (m, 15H, Ar-H), 6.33 (dt, 1H, $J_{5,6}$ = 1.8 Hz, $J_{4,6}$ = 1.8 Hz, $J_{6,7}$ = 12.4 Hz, H-6), 6.04 (dd, 1H, $J_{7,5}$ = 2.7 Hz, $J_{7,6}$ = 12.4 Hz, H-7), 4.74-4.29 (m, 7H, 3 CH_2-Ph, H-5), 4.19 (d, 1H, $J_{2,3}$ = 6.0 Hz, H-2), 3.86 (m, 1H, $J_{6,4}$ = 1.8 Hz, $J_{3,4}$ = 3.1 Hz, H-4), 3.80 (dd, 1H, $J_{2,3}$ = 6.0 Hz, $J_{3,4}$ = 3.1 Hz, H-3), 3.05 (br.d, 1H, J = 7.4 Hz, OH). ^{13}C NMR (50 MHz, $CDCl_3$) δ(ppm) = 196.3 (C-1), 144.2 (C-6), 137.8; 137.6; 137.5 (arom.), 129.1; 128.5; 128.2; 128.0; 127.9; 127.7 (arom., C-7), 88.3; 81.9; 79.0 (C-2, C-3, C-4), 73.5; 72.6; 71.8 (CH_2-Ph), 70.1 (C-5).IR (CCl_4) : 3579, 3089, 3066, 3032, 2869, 1734, 1699 cm^{-1}.

(2S,3R,4S,5S) 5-Mesyloxy-2,3,4-tris(benzyloxy) cyclohept-6,7-en-1-one 25.

To a solution of **24** (720 mg, 1.56 mmol) with DMAP (2 mg) in pyridine (9.2 mL) was added at room temperature MsCl (1.378 mL, 20.8 mmol). The reaction mixture was stirred overnight at room temperature and concentrated under reduced pressure. The orange residue was diluted into aqueous $CuSO_4$ and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic phases were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give the crude product which was purified by column chromatography to give **23** (592 mg, 72%) as a colorless oil. $[\alpha]_D$ = +46.3 (c = 0.7 CH_2Cl_2). ^{1}H NMR (200 MHz, $CDCl_3$) δ(ppm) = 7.34-7.10 (m, 15H, Ar-H), 6.34 (dt, 1H, $J_{7,6}$ = 12.6 Hz, $J_{6,4}$= 1.8 Hz, $J_{5,6}$ = 1.8 Hz, H-6), 6.18 (dd, 1H, $J_{7,5}$ = 2.9 Hz, $J_{7,6}$ = 12.6 Hz, H-7), 5.64 (br.m, 1H, H-5), 4.76-4.31 (m, 6H, 3 CH_2-Ph), 4.16 (d, 1H, $J_{2,3}$ = 6.0 Hz, H-2), 4.10 (br.m, 1H, H-4), 3.78 (dd, 1H, $J_{2,3}$ = 6.0 Hz, $J_{3,4}$ = 3.3 Hz, H-3), 2.83 (s, 3H, CH_3 (OMs)). ^{13}C NMR (50 MHz, $CDCl_3$) δ(ppm) = 194.4 (C-1), 137.5; 137.3 (arom.), 136.9 (C-6), 131.2 (C-7), 129.1; 128.5; 128.2; 128.0; 127.9; 127.7 (arom.), 88.5; 78.7; 78.5; 78.0 (C-2, C-3, C-4, C-5), 73.4; 72.7; 71.6 (CH_2-Ph), 38.3 (CH_3-SO_3). IR ($CDCl_3$) : 3089, 3066, 3032, 2872, 1699 cm^{-1}.

(1R,2S,3R,4S,5S) 5-Mesyloxy-2,3,4-tris(benzyloxy) cycloheptane-1-ol 26.

To an etheral solution (40 mL) of **25** (492 mg, 0.93 mmol) under argon was added dropwise at -60°C DIBALH (2.4 mL, 3.6 mmol, 1.5 M solution in toluene). The resulting mixture was stirred at -60°C for 2h, hydrolysed at -40°C with MeOH (20 mL), and warmed to room temperature. Brine (2 mL) and Na_2SO_4 were then

added, and the mixture was stirred for 1h and filtered. The salts were washed with CH_2Cl_2 and the combined organic phases concentrated under reduced pressure to give the crude product **26** (350 mg), which was used in the next step without further purification. ^1H NMR (200 MHz, $CDCl_3$) δ(ppm) = 7.34-7.20 (m, 15H, Ar-H), 6.00 (ddd, 1H, $J_{6,7}$ = 12.1 Hz, $J_{6,5}$ = 2.6 Hz, $J_{6,1}$ = 6.6 Hz, H-6), 5.68 (dt, 1H, $J_{6,7}$ = 12.1 Hz, $J_{1,7} = J_{5,7}$ = 1.9 Hz, H-7) , 5.51 (m, 1H, H-5), 4.69-4.49 (m, 6H, 3 AB syst. CH_2-Ph), 4.36 (br.m, 1H, H-1), 4.02 (m, 1H, H-4), 3.93 (dd, 1H, $J_{1,2}$ = 3.0 Hz, $J_{2,3}$ = 6.8 Hz, H-2), 3.55 (dd, 1H, $J_{2,3}$ = 6.8 Hz, $J_{3,4}$ = 1.7 Hz, H-3), 3.40 (br.s, 1H, OH), 2.90 (s, 3H, CH_3-SO_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ(ppm) = 138.2; 137.7; 136.6 (arom.), 131.8; 127.0 (C-6, C-7), 128.7; 128.5; 128.0, 127.8 (arom.), 83.7; 79.3; 79.0 (2C) (C-2; C-3, C-4, C-5), 73.5; 73.4; 73.0 (CH_2-Ph), 68.8 (C-1), 38.4 (CH_3-SO_3). IR ($CDCl_3$) : 3459, 3089, 3066, 3033, 2929, 2873 cm^{-1}.

(1R,2S,3R,4S,5R) 5-Azido-2,3,4-tris(benzyloxy) cyclohept-6,7-en-1-ol 27.
(1R,2S,3R,4S,7S et 7R) 7-Azido-2,3,4-tris(benzyloxy) cyclohept-5,6-en-1-ol 28.

To a solution of the crude product **24** (350 mg) in DMF (7.1 mL) under argon was added NaN_3 (164 mg, 2.5 mmol). The resulting mixture was stirred at room temperature for 1h. DMF was evaporated under reduced pressure, the residue dissolved with H_2O (10 mL) and extracted with Et_2O (3 x 10 mL). The combined organic layers were washed with brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography to give **27** (241 mg, 55% from **25**) and **28** (40 mg, 10% from **25**) as a colorless oils. **27** : $[\alpha]_D$ = -21.4 (c = 0.43 CH_2Cl_2), ^1H NMR (200 MHz, $CDCl_3$) δ(ppm) = 7.36-7.29 (m, 15H, Ar-H), 5.67 (dt, 1H, $J_{5,6} = J_{6,1}$ = 2.0 Hz, $J_{6,7}$ = 12.0 Hz, H-6), 5.59 (dt, 1H, $J_{6,7}$ = 12.0 Hz, $J_{1,7} = J_{7,5}$ = 2.0 Hz, H-7), 4.84-4.49 (m, 6H, 3 AB syst. CH_2-Ph), 4.50 (m, 1H, H-5), 4.43 (br.m, 1H, H-1), 3.93 (dd, 1H, $J_{2,3}$ = 4.7 Hz, $J_{3,4}$ = 6.9 Hz, H-3), 3.79 (br.d, 1H, $J_{2,3}$ = 4.7 Hz, H-2), 3.56 (dd, 1H, $J_{3,4}$ = 6.9 Hz, $J_{4,5}$ = 9.8 Hz, H-4), 2.25 (br.d, 1H, J = 9.7 Hz, OH). ^{13}C NMR (50 MHz, $CDCl_3$) δ(ppm) = 138.0; 137.8 (2C) (arom.), 131.2; 129.3 (C-6, C-7), 128.7; 128.6; 128.5, 128.3; 128.0 (arom.), 85.0; 82.1; 81.8 (C-2, C-3, C-4), 75.8; 74.1; 73.1 (CH_2-Ph), 68.3 (C-1), 61.9 (C-5). IR ($CDCl_3$) : 3573, 3089, 3067, 3033, 2872, 2108 cm^{-1}. Mass EI (70 eV) : 444, 415, 369, 352, 334, 308, 253, 246, 230, 181, 108, 91. Anal. Calcd for $C_{28}H_{29}N_3O_4$: C : 71.19, H : 6.01, N : 8.68, O : 13.43. Found C : 71.32, H : 6.20, N : 8.91, O : 13.57.
28 (7S/7R 75/25) 7S : ^1H NMR (200 MHz, $CDCl_3$) δ(ppm) = 7.40-7.28 (m, 15H, Ar-H), 5.94 (dd, 1H, $J_{5,6}$ = 12.2 Hz, $J_{5,4}$ = 3.0 Hz, H-5), 5.72 (ddd, 1H, $J_{5,6}$ = 12.2 Hz, $J_{4,6}$ = 2.1 Hz, $J_{6,7}$ =3.9 Hz, H-6), 4.98-4.61 (m, 6H, 3 AB syst. CH_2-Ph), 4.26-4.22 (m, 2H, H-4, H-7), 4.07 (br.m, 1H, H-1), 3.93 (dd, 1H, H-2), 3.75 (dd, 1H, $J_{2,3}$ = 4.1 Hz, $J_{3,4}$ = 8.7 Hz, H-3), 2.72 (br.d, 1H, J = 5.0 Hz, OH). ^{13}C NMR (50 MHz, $CDCl_3$) δ(ppm) = 138.1 (arom.), 133.6; 125.8 (C-5, C-6), 128.5; 128.1; 127.9 (arom.), 83.0; 82.3; 78.5 (C-2; C-3, C-4), 74.1; 73.7; 72.9 (CH_2-Ph), 72.4 (C-1), 63.3 (C-5). IR ($CDCl_3$) : 3572, 3089, 3066, 3032, 2868, 2105 cm^{-1}.

(2S,3R,4S,5S) 5-azido-2,3,4-tris(benzyloxy) cyclohept-6,7-en-1-one 6.

Dess-Martin triacetoxyperiodinane reagent[11] (395 mg, 0.92 mmol) was added in one portion to a stirred solution of the alcohol **27** (210 mg, 0.44 mmol) and pyridine (0.39 mL, 4.8 mmol) in CH_2Cl_2 (11.1 mL). After 20 mn, the mixture was poured into saturated aqueous $NaHCO_3/Na_2S_2O_3$ (1/1, 100 mL) and extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. Purification of the residue by flash chromatography (petroleum ether/AcOEt 70:30) afforded **8**

(180 mg, 86%) as a colorless oil. $[\alpha]_D$ = -56.1 (c = 0.28 CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ(ppm) = 7.38-7.23 (m, 15H, Ar-H), 6.44 (dd, 1H, $J_{6,7}$ = 12.4 Hz, $J_{6,5}$ = 2.8 Hz, H-6), 6.02 (ddd, 1H, $J_{6,7}$ = 12.4 Hz, $J_{2,7}$ = 1.4 Hz, $J_{5,7}$ = 2.8 Hz, H-7), 5.07 (ddd, 1H, $J_{4,5}$ = 9.3 Hz, $J_{5,7}$ = $J_{5,6}$ = 2.8 Hz, H-5), 4.74-4.41 (m, 6H, 3 AB syst. CH_2-Ph), 4.20 (dd, 1H, $J_{2,3}$ = 4.6 Hz, $J_{2,7}$ = 1.4 Hz, H-2), 4.02 (dd, 1H, $J_{2,3}$ = $J_{3,4}$ = 4.6 Hz, H-3), 3.72 (dd, 1H, $J_{4,5}$ = 9.3 Hz, $J_{3,4}$ = 4.6 Hz, H-4). ^{13}C NMR (50 MHz, $CDCl_3$) δ(ppm) = 198.2 (C-1), 144.7 (C-6), 137.5; 137.1; 136.7 (arom.), 129.1 (C-7), 128.6; 128.5, 128.3; 128.2; 128.1 (arom.), 85.6; 83.1; 80.1 (C-2; C-3, C-4), 74.6; 72.8 (2C) (CH_2-Ph), 62.3 (C-5). IR ($CDCl_3$) : 3090, 3067, 3033, 2870, 2109, 1677 cm^{-1}. Mass IE (70 eV) : 441, 378, 350, 292, 240, 201, 181, 144, 91. Anal. Calcd for $C_{28}H_{27}N_3O_4$: C : 71.62, H : 5.80, N : 8.95, O : 13.63. Found C : 71.35, H : 5.64, N : 8.69, O : 13.54.

(+)-Calystegine B_2(1R,2S,3R,4S,5R) 8-azabicyclo[3.2.1]octane-1,2,3,4-tetraol 2.

A solution of **6** (133 mg, 0.28 mmol) in a mixture AcOH (6 mL) and H_2O (6 mL) was hydrogenated for 96h under atmospheric pressure in the presence of 10% palladium on charcoal. The suspension was filtered through Celite and the resulting solution concentrated under reduced pressure. This residue was purified on permutite 50 (elution : aq.NH_3) to give, after evaporation under reduced pressure, **(+)-2** (47 mg, 96%). Further purification was carried out by HPLC using a 8 x 10 mm column (μBondapak NH_2 10 μ and MeCN-H_2O, 4:1), 2 ml min^{-1} flow rate and RI detection.$[\alpha]_D$ = +17.1 (c = 0.41 H_2O).

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