Diastereoselective Synthesis of 1,6-Diepicastanospermine from D-Glucono-δ-lactone

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Homochiral (−)-pipecolaldehyde **6** from D-glucono-δ-lactone underwent a highly diastereoselective addition upon treatment with vinylmagnesium bromide. Treatment with vinylmagnesium bromide produced *anti*-aminoalcohol **7a** which was easily converted into the synthesis of 1,6-diepicastanospermine **2**.

Key Words : 1,6-Diepicastanospermine, Diastereoselective nucleophilic addition, *anti*-Aminoalcohol, Vinylmagnesium bromide, D-Glucono-δ-lactone

Introduction

Diastereoselective nucleophilic addition is one of the most reliable synthetic protocols, capable of the selective formation of C-C bond and the introduction of chiral hydroxyl group.[1] Particularly, a transformation of aminoaldehyde from carbohydrate containing multiple stereogenic centers to aminoalcohol has attracted great interests among synthetic organic chemists because the resulting chiral aminoalcohol is a useful synthetic synthon for bioactive polyhydroxylated alkaloids.[2] The related asymmetric synthesis of aminoalcohol has also been applied to synthesis of complex molecular fragments.[3] Synthetic investigations concerning the nucleophilic addition to C=O bonds of aminoaldehyde with alkyl Grinard have demonstrated that ethynyl group offers much better selectivity rather than any other alkyl nucleophiles.[4] Herein we describe a highly diastereoselective synthesis of *anti*-aminoalcohol **7a** *via* a simple nucleophilic addition of vinylmagnesium bromide. This *anti*-aminoalcohol **7a** was applied to the synthesis of a castanospermine derivative that consists of piperidine and pyrrolidine rings. We have recently reported simple and convenient routes to piperidine and pyrrolidine alkaloids with chirospecific manners.[5] As an extension of our previous studies, we prepared 1,6-diepicastanospermine **2** *via* diastereoselective nucleophilic addition.

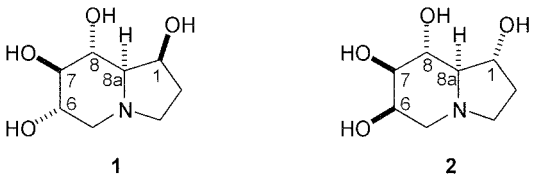

Figure 1. (+)-Castanospermine and its derivative.

Castanospermine **1** and its stereoisomers isolated from *Castanospermum australe*[6] and *Alexa leiopetala*[7] exhibit potent activities against diabetes, cancer, and viral infection due to their inhibition of glycosidases.

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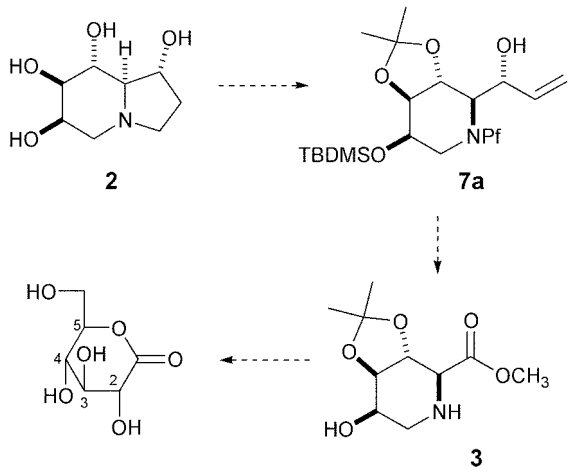
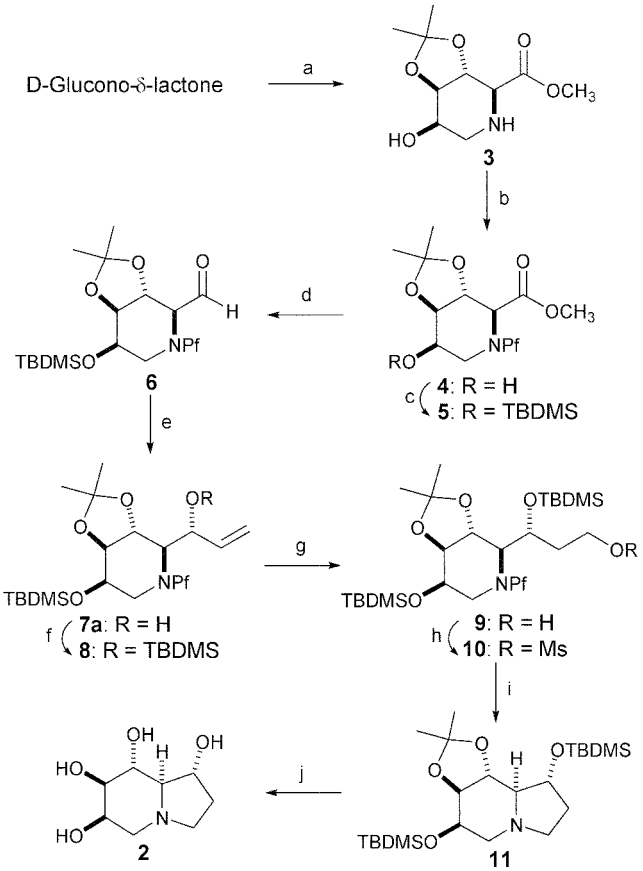


Figure 2. Retrosynthesis of target molecule **2**.

Results and Discussion

The stereochemistries of C6, C7, C8 and C8a in target molecule **2** were transferred from those of C2, C3, C4 and C5 in D-glucono-δ-lactone as the starting material. The formation of the two-carbon unit and introduction of the C1 hydroxy group for compound **2** were carried out *via* nucleophilic addition of vinylmagesium bromide.

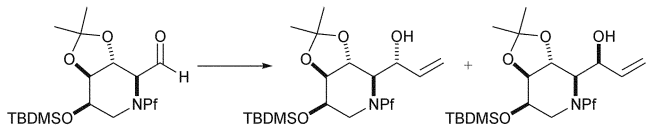
The known piperidine **3** was easily accessible *via* known procedures from D-glucono-δ-lactone.[5d] Piperidine **3** was sequentially protected with 9-phenylfluoren-9-yl (Pf) and TBDMS group to give the protected piperidine **5** in 82% overall yield. We chose the Pf group for amine protection since this protecting group has been shown to prevent deprotonation at α-position of α-amino aldehyde.[8] α-Aminoaldehydes protected with Pf group are stable to enolization under Grignard reaction condition.[9] Reduction of the ester **5** with DIBAL-H produced the aldehyde **6** in 84% yield. Pipecolaldehyde **6** was stable enough for the purification by silica gel column chromatography. The hydroxy group and the two-carbon unit should be introduced to aldehyde **6** for formation of pyrrolidine ring in the target molecule **2**. Pipecolaldehyde **6** was treated with vinylmagnesium bromide at -40 °C for 20 min to give *anti*-aminoalcohol **7a** *via* a diastereo-



Scheme 1. Reagents and conditions a. ref. 5d.; b. PfBr, $Pb(NO_3)_2$, Et_3N. CH_2Cl_2. rt. 85%; c. TBDMSCl. Imidazole. DMF. rt. 96%; d. DIBAL-H. Toluene. -78 °C. 84%; e. VinylMgBr. THF, -78 °C. 79%; f. TBDMSCl. Imidazole, DMF. rt. 98%; g. BH_3SMe_2, THF. 0 °C. 75%; h. MsCl. Et_3N, THF. 0 °C. 98%; i. H_2. 10% Pd/C. NaOAc, MeOH. 60 °C. 93%; j. Dowex 50W-X8. 90% MeOH. reflux. 91%.

selective addition. ^{1}H NMR spectroscopic analysis of the crude reaction mixture showed that the reaction afforded a 10 : 1 mixture of the *anti* and *syn* isomers, providing *anti*-aminoalcohol **7a** in 79% yield after chromatographic purification. The stereochemistry of product **7a** was deduced from 2D NOESY experiments of final product **2** (Figure 4).

Table 1. Stereoselective nucleophilic addition of aminoaldehyde[a]



Entry	Reagents	Conditions	Ratio[b] 7a : 7b	Yield (%)[c]
1	VinylMgBr	THF/-78 °C	10:1	90
2	VinylMgBr	THF/-40 °C	10:1	87
3	EthynylMgBr	THF/-78 °C	4:1	90
4	AllylMgBr	THF/-40 °C	1:2	92
5	AllylMgBr	THF/-78 °C	1:4	90

[a]All experiments were performed at least in duplicate. [b]The ratio was determined by ^{1}H NMR analysis of the reaction mixtures. [c]Isolated yield.

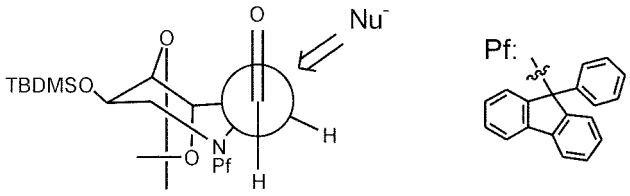


Figure 3.

As shown in Table 1, other nucleophiles were treated to polypipecolaldehyde **6** under the same reaction conditions to afford a less than 4 : 1 ratio of *anti* and *syn* isomers. Especially, ethynyl group showed worse selectivity than expected. The *anti* diastereoselectivity of nucleophilic addition could be explained by the Cram's rule[10a] which concisely accommodates favored formation of the *anti*-aminoalcohol. In contrast, the *syn*-diastereoselectivity of allylMgBr could be explained by the chelation control model.[10]

The hydroxyl functionality was protected as silyl ether using TBDMSCl and imidazole, giving silyl ether **8** in high yield. Hydroboration of the alkenyl group in **8** with BH_3SMe_2 in THF, followed by alkaline hydrogen peroxide oxidation, gave the primary alcohol **9** in 75% yield. Reaction of **9** with MsCl in the presence of triethylamine in THF yielded the mesylate **10** in quantitative yield. The mesylate **10** was hydrogenated in the presence of 10% Pd/C and NaOAc to remove Pf group. The concomitant intramolecular cyclization occurred to give indolizidine **11** in 93% yield. The indolizidine **11** protected with acid sensitive groups was refluxed with Dowex 50W-X8 in 90% MeOH for 5 h and filtered. The filterate was washed with MeOH, and then eluted with 3 N NH_3 solution to afford enantiomerically pure 1,6-diepicastanospermine **2** (91% yield) without further purification.

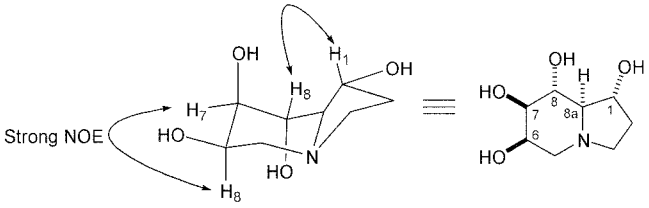


Figure 4. NOE experiments with 1,6-diepicastanospermine **2**.

The relatative stereochemistry of the target molecule **2** was determined from 2D NOESY experiments. Strong NOE cross peak were observed H6/H7, and H1/H8, but not H1/H8a in compound **2**. The spectral and physical properties of 1,6-diepicastanospermine **2** matched those reported in the literature {$[\alpha]_D^{20}$ -73.8 (*c* 0.60, H_2O); lit.,[11] $[\alpha]_D^{20}$ -72.0 (*c* 0.72, MeOH)}.

Experimental Section

General. All non-aqueous reaction was carried out under an inert nitrogen atmosphere. THF was distilled from Na/benzophenone; 2,2-dimethoxypropane, DMF, and methylene chloride were distilled from CaH_2. Column chromatography was carried out using 230-400 mesh silica gel. Final solution before evaporation was washed with brine and dried over

anhydrous Na_2SO_4. Melting points are uncorrected. ^{1}H-NMR and ^{13}C-NMR experiments were conducted on Brucker AW-500 spectrometer. HREIMS were obtained on a JEOLJMS-700 mass spectrometer. Optical rotations were measured on a JASCO DIP-1000 polarimeter and $[\alpha]_D$ values are given in units of 10^{-1} deg cm^{2}g^{-1}.

Methyl 2,6-imino-3,4-*O*-isopropylidene-D-mannonate (3). This was prepared as described.[5d] $[\alpha]_D^{20}$ -13.7 (*c* 0.90, $CHCl_3$); δ_H (500 MHz; $CDCl_3$) 1.43 (s, 3H), 1.46 (s, 3H), 2.73 (dd, *J* = 14.7, 2.4 Hz, 1H), 3.20 (dd, *J* = 14.7, 2.4 Hz, 1H), 3.43-3.49 (m, 2H), 3.73 (m, 1H), 3.80 (s, 3H) and 4.25 (m, 1H); δ_C (125 MHz; $CDCl_3$) 26.6, 26.8, 49.1, 52.5, 61.2, 67.5, 72.6, 80.7, 109.4, and 171.2 (Found: C, 51.93; H, 7.43; N, 6.05 $C_{10}H_{17}NO_5$ requires C, 51.94; H, 7.41; N, 6.06%).

Methyl 2,6-imino-3,4-*O*-isopropylidene-*N*-(9-phenylfluoren-9-yl)-D-mannonate (4). To a solution of piperidine **3** (2.07 g, 9.0 mmol) in CH_2Cl_2 (50 mL) was added 9-phenylfluoren-9-yl bromide (3.51 g, 10.9 mmol), $Pb(NO_3)_2$ (4.49 g, 13.6 mmol), and triethylamine (2.53 mL, 18.2 mmol) were added. The mixture was stirred for 48 h at room temperature, and then it was filtered and concentrated. The residue was chromatographed on silica gel [hexane-EtOAc (6 : 1)] to give **4** (3.61 g, 85%) as a solid. mp 68-69 °C; $[\alpha]_D^{20}$ -276.3 (*c* 2.00, $CHCl_3$); δ_H (500 MHz; $CDCl_3$) 1.38 (s, 3H), 1.44 (s, 3H), 3.03 (s, 3H), 3.46 (dd, *J* = 13.6, 6.4 Hz, 1H), 3.61 (m, 2H), 3.95 (dd, *J* = 9.9, 5.0 Hz, 1H), 4.17 (dd, *J* = 9.9, 8.7 Hz, 1H), 4.44 (m, 1H), and 7.20-7.66 (m, 13H); δ_C (125 MHz; $CDCl_3$) 26.7, 27.2, 50.6, 51.2, 61.7, 63.5, 74.2, 76.8, 77.0, 77.1, 113.0, 119.9, 120.1, 125.6, 126.3, 126.9, 127.5, 127.6, 127.9, 128.5, 128.6, 139.8, 140.8, 144.3, 145.8, 146.5, and 172.3 (Found: C, 73.88; H, 6.20; N, 2.96 $C_{29}H_{29}NO_5$ requires C, 73.87; H, 6.20; N, 2.97%).

Methyl 5-*O*-*t*-butyldimethylsilyl-2,6-imino-3,4-*O*-isopropylidene-*N*-(9-phenylfluoren-9-yl)-D-ma-nnonate (5). To a solution of **4** (3.88 g, 8.2 mmol) was dissolved in DMF (40 mL) were added imidazole (1.12 g, 16.5 mmol) and TBDMSCl (1.49 g, 9.9 mmol) at room temperature. After stirring of the mixture for 12 h, saturated aqueous $NaHCO_3$ (80 mL) was added and the mixture was extracted with EtOAc (50 mL × 5). After concentration of combined extracts, the residue was chromatographed on silica gel [hexane-EtOAc (8 : 1)] to give compound **5** (4.63 g, 96%) as a solid. mp 69-70 °C; $[\alpha]_D^{20}$ -15.2 (*c* 2.00, $CHCl_3$); δ_H (500 MHz; $CDCl_3$) -0.03 (s, 3H), 0.00 (s, 3H), 0.85 (s, 9H), 1.30 (s, 3H), 1.33 (s, 3H), 3.02 (s, 3H), 3.17 (dd, *J* = 13.3, 6.4 Hz, 1H), 3.30 (dd, *J* = 13.4, 5.4 Hz, 1H), 3.42 (d, *J* = 8.5 Hz, 1H), 3.69 (dd, *J* = 9.8, 4.3 Hz, 1H), 4.20 (dd, *J* = 9.7, 8.7 Hz, 1H), 4.28 (m, 1H), and 7.16-7.57 (m, 13H); δ_C (125 MHz; $CDCl_3$) -4.4, 12.7, 16.7, 16.8, 21.2, 24.1, 24.2, 24.4, 25.3, 25.8, 28.2, 29.5, 30.5, 49.8, 51.2, 61.4, 63.7, 72.5, 76.0, 76.8, 110.5, 118.3, 118.5, 124.3, 125.1, 125.9, 125.9, 126.0, 126.4, 126.9, 127.0, 138.3, 139.4, 142.4, 144.2, 145.6, and 170.7 (Found: C, 71.77; H, 7.41; N, 2.37 $C_{35}H_{43}NO_5Si$ requires C, 71.76; H, 7.40; N, 2.39%).

5-*O*-*t*-Butyldimethylsilyl-2,6-imino-3,4-*O*-isopropylidene-*N*-(9-phenylfluoren-9-yl)-D-mannose (6). To a solution of ester **5** (4.63 g, 7.9 mmol) in toluene (50 mL) was added DIBAL-H (1 M in toluene, 9.49 mL, 9.5 mmol) at -78 °C and then stirred for 5 min at same temperature. The reaction mixture was added 10% NaOH (5 mL), and the solution was allowed to reach room temperature, and then filtered. The filtrate was evaporated, and the residue was chromatographed on silica gel [hexane-EtOAc (10 : 1)] to give compound **6** (2.51 g, 84%, based on 68% conversion) as a solid and starting material **5** (1.48 g) as an oil; $[\alpha]_D^{20}$ -19.9 (*c* 1.00, $CHCl_3$); δ_H (500 MHz; $CDCl_3$) -0.03 (s, 3H), 0.00 (s, 3H), 0.93 (s, 9H), 1.18 (s, 3H), 1.24 (s, 3H), 2.43 (d, *J* = 12.2 Hz, 1H), 2.76 (dd, *J* = 15.2, 9.3 Hz, 1H), 3.19 (m, 2H), 4.04 (bs, 1H), 4.11 (t, *J* = 9.3 Hz, 1H), 7.10-7.62 (m, 13H), and 8.62 (d, *J* = 5.9 HZ, 1H); δ_C (125 MHz; $CDCl_3$) 0.0, 18.4, 25.9, 26.7, 26.9, 53.7, 66.2, 70.1, 71.3, 77.8, 79.8, 111.2, 120.1, 120.1, 120.6, 124.8, 125.4, 126.7, 127.3, 127.9, 128.1, 128.2, 128.5, 128.8, 129.1, 129.8, 141.0, 141.1, 142.7, 145.1, 145.7, 176.6, and 192.0 (Found: C, 73.47; H, 7.44; N, 2.54 $C_{34}H_{41}NO_4Si$ requires C, 73.48; H, 7.44; N, 2.52%).

2-(1'-Hydroxy-2'-propylenyl)-5-*O*-*t*-butyldimethylsilyl-3,4-*O*-isopropylidene-3,4,5-trihydroxy-*N*-(9-phenylfluoren-9-yl) piperidine (7a). To a solution of aldehyde **6** (2.74 g, 4.9 mmol) in dry THF (25 mL) at -78 °C was dropwised vinylmagnesium bromide (1 M in THF, 7.39 mL, 7.4 mmol) and stirred for 30 min at same temperature, and then quenched with saturated aqueous NH_4Cl (50 mL). The reaction mixture was extracted with EtOAc (50 mL). The organic phase was separated and the aqueous phase was extracted with EtOAc (40 mL × 3). After concentration of combined extracts, the resulting residue was chromatographed on silica gel [hexane-EtOAc (8 : 1)] to give **7a** (2.26 g, 79%) as a solid. mp 129-131 °C; $[\alpha]_D^{20}$ -336.0 (*c* 3.00, $CHCl_3$); δ_H (500 MHz; $CDCl_3$) -0.03 (s, 3H), 0.00 (s, 3H), 0.81 (s, 9H), 1.30 (s, 3H), 1.39 (s, 3H), 3.07 (dd, *J* = 8.0, 2.2 Hz, 1H), 3.44 (dd, *J* = 13.0, 6.1 Hz, 1H), 3.52-3.56 (m, 2H), 4.01 (dd, *J* = 10.0, 5.0 Hz, 1H), 4.30-4.37 (m, 2H), 4.56 (m, 1H), 4.75 (m, 1H), 5.45 (m, 1H), and 7.12-7.68 (m, 13H); δ_C (125 MHz; $CDCl_3$) -4.5, -4.0, 18.7, 26.3, 27.3, 28.1, 54.2, 64.0, 65.2, 70.5, 75.3, 77.2, 78.6, 111.7, 114.9, 120.7, 121.1, 126.0, 126.4, 126.7, 127.8, 128.3, 128.4, 128.7, 128.9, 129.3, 137.7, 139.3, 141.3, 146.1, 147.4, and 149.8 (Found: C, 74.06; H, 7.75; N, 2.41 $C_{36}H_{45}NO_4Si$ requires C, 74.06; H, 7.77; N, 2.40%).

2-(1'-*O*-*t*-Butyldimethylsilyl-1'-hydroxy-2'-propylenyl)-5-*O*-*t*-butyldimethylsilyl-3,4-*O*-isopropyli-dene-3,4,5-trihydroxy-*N*-(9-phenylfluoren-9-yl) piperidine (8). To a solution of **7a** (2.59 g, 4.4 mmol) in dry DMF (23 mL) was added imidazole (0.75 g, 11.1 mmol) and TBDMSCl (0.80 g, 5.3 mmol) at room temperature. After stirred for 10 h, saturated aqueous $NaHCO_3$ (60 mL) was added and the mixture was extracted with EtOAc (20 mL × 5). After concentration of the combined extracts, the residue was chromatographed on silica gel [hexane-EtOAc (10 : 1)] to give **8** (3.03 g, 98%) as a solid. mp 62-63 °C; $[\alpha]_D^{20}$ -57.0 (*c* 2.50, $CHCl_3$); δ_H (500 MHz; $CDCl_3$) -0.30 (s, 3H), -0.23 (s, 3H), 0.00 (2s, 9H), 0.83 (2s, 15H), 1.32 (s, 3H), 1.37 (s, 3H), 3.00 (d, *J* = 8.0 Hz, 1H), 3.48 (dd, *J* = 13.4, 6.2 Hz, 1H), 3.57 (dd, *J* = 13.3, 8.5 Hz, 1H), 3.74 (d, *J* = 9.1 Hz, 1H), 3.80 (dd, *J* = 10.2, 5.0 Hz, 1H), 4.09 (dd, *J* = 17.2, 1.4 Hz, 1H), 4.35 (m, 1H), 4.57 (dd, *J* = 10.1, 1.9 Hz, 1H), 4.66 (dd, *J* = 10.2, 8.0

Hz, 1H), 5.52 (m, 1H), and 7.12 -7.70 (m, 13H); δ_C (125 MHz; $CDCl_3$) 18.1, 18.3, 25.7, 25.8, 25.9, 26.2, 26.9, 27.7, 53.5, 65.0, 65.2, 69.9, 77.8, 77.9, 111.0, 114.5, 120.0, 120.0, 126.3, 126.9, 127.2, 127.8, 128.1, 128.3, 128.4, 139.5, 140.2, 140.6, 146.0, 147.5, and 149.8 (Found: C, 72.25; H, 8.53; N, 2.01 $C_{42}H_{59}NO_4Si_2$ requires C, 72.26; H, 8.52; N, 2.01%).

2-(1'-*O*-*t*-Butyldimethylsilyl-1',3'-dihydroxypropyl)-5-*O*-*t*-butyldimethylsilyl-3,4-*O*-isopropylidene-3,4,5-trihydroxy-*N*-(9-phenylfluoren-9-yl) piperidine (9). To a stirred solution of **8** (1.60 g, 2.3 mmol) in dry THF (15 mL) was added $BH_3(CH_3)_2S$ (3.2 mL, 6.9 mmol) at 0 °C. After stirring of the mixture for 10 h at room temperature, the reaction mixture was quenched by sequential addition of water (2.0 mL), 3 M NaOH (2.5 mL) and 30% H_2O_2 (4.5 mL). The mixture was extracted with EtOAc (15 mL × 3) and combined extracts was concentrated. The residue was chromatographed on silica gel [hexane-EtOAc (6 : 1)] to give **9** as an oil (1.22 g, 75%). $[\alpha]_D^{20}$ -33.4 (*c* 2.00, $CHCl_3$); δ_H (500 MHz; $CDCl_3$) -0.11 (s, 3H), -0.03 (s, 3H), -0.01 (s, 3H), 0.02 (s, 3H), 0.85 (s, 9H), 0.88 (s, 9H), 1.32 (s, 3H), 1.33 (s, 3H), 1.48 (m, 1H), 1.59 (m, 2H), 2.66 (m, 1H), 2.87 (m, 1H), 3.18 (d, J = 8.0 Hz, 1H), 3.39 (dd, J = 13.9, 6.1 Hz, 1H), 3.53 (dd, J = 10.3, 4.3 Hz, 1H), 3.61 (m, 1H), 4.36 (m, 1H), 4.53 (dd, J = 10.3, 8.1 Hz, 1H), and 7.22-7.68 (m, 13H); δ_C (125 MHz; $CDCl_3$) -4.5, -4.1, -3.8, -3.5, 0.39, 18.6, 18.7, 26.2, 26.6, 27.3, 27.8, 38.9, 54.1, 58.9, 62.2, 65.9, 70.2, 73.9, 77.9, 78.1, 111.4, 120.5, 120.6, 126.6, 127.3, 127.7, 128.0, 128.2, 128.7, 128.9, 128.9, 140.2, 140.7, 145.7, 148.2, and 150.1 (Found: C, 70.44; H, 8.57; N, 1.98 $C_{42}H_{61}NO_5Si_2$ requires C, 70.44; H, 8.59; N, 1.96%).

2-(1'-*O*-*t*-Butyldimethylsilyl-3'-*O*-methanesulfonyl-1',3'-dihydroxy-propyl)-5-*O*-*t*-butyldimethylsilyl-3,4-*O*-isopropylidene-3,4,5-trihydroxy-*N*-(9-phenylfluoren-9-yl) piperidine (10). To a solution of alcohol **9** (1.22 g, 1.7 mmol) in dry THF (10 mL) at 0 °C was added triethylamine (0.47 mL, 3.4 mmol) and MsCl (0.19 mL, 2.6 mmol). The reaction mixture was stirred for 30 min, and then was quenched with saturated aqueous $NaHCO_3$ (15 mL). The organic phase was separated and the aqueous phase was extracted with EtOAc (10 mL × 3). After concentration of combined extracts, the residue was chromatographed on silica gel [hexane-EtOAc (8 : 1)] to give **10** (1.33 g, 98%). $[\alpha]_D^{20}$ -67.3 (*c* 2.00, $CHCl_3$); δ_H (500 MHz; $CDCl_3$) -0.10 (s, 3H), -0.02 (s, 3H), 0.00 (s, 6H), 0.83 (s, 9H), 0.87 (s, 9H), 1.28 (s, 6H), 1.39 (m, 1H), 1.55 (m, 1H), 1.70 (m, 1H), 2.84 (s, 3H), 3.03 (m, 1H), 3.32 (dd, J = 14.0, 6.0 Hz, 1H), 3.45 (m, 2H), 3.51 (m, 1H), 3.59 (m, 1H), 4.33 (m, 1H), 4.47 (dd, J = 10.2, 8.1 Hz, 1H), and 7.19-7.72 (m, 13H); δ_C (125 MHz; $CDCl_3$) -4.9, -4.5, -4.1, -4.1, 18.2, 18.3, 25.8, 26.1, 26.9, 27.5, 29.7, 35.0, 37.1, 53.8, 62.4, 65.4, 66.6, 69.4, 71.9, 77.5, 77.6, 110.9, 120.2, 120.5, 126.1, 126.6, 126.8, 127.3, 127.9, 128.4, 128.7, 139.8, 140.3, 144.9, 147.7, and 149.5 (Found: C, 65.05; H, 8.01; N, 1.77 $C_{43}H_{63}NO_7SSi_2$ requires C, 65.03; H, 8.00; N, 1.76%).

1,6-Di-*O*-*t*-butyldimethylsilyl-7,8-*O*-isopropylidene-1,6-diepicastanospermine (11). A mixture of mesylate **10** (1.33 g, 1.7 mmol), NaOAc (0.68 g, 8.4 mmol) and 10% Pd/C (0.05 g) in MeOH (10 mL) was hydrogenated at atmospheric pressure for 10 h at 60 °C. The catalyst was filtered off, the filterate was refluxed for 1 h, the MeOH was evaporated and water was added. The mixture was extracted with EtOAc (10 mL × 3), and the combined organic phase was concentrated. The residue was chromatographed on silica gel [hexane-EtOAc (3 : 1)] to give **11** as a solid (0.71 g, 93%) mp 58-59 °C; $[\alpha]_D^{20}$ -36.5 (*c* 2.00, $CHCl_3$); δ_H (500 MHz; $CDCl_3$) 0.00 (s, 12H), 0.80 (s, 18H), 1.29 (s, 3H), 1.30 (s, 3H), 1.59 (m, 1H), 2.16 (m, 1H), 2.47 (dd, J = 9.7, 3.9 Hz, 1H), 2.52 (d, J = 12.2 Hz, 1H), 2.71 (m, 1H), 2.88 (dd, J = 13.4, 2.2 Hz, 1H), 3.02 (m, 1H), 3.17 (dd, J = 9.2, 2.4 Hz, 1H), 3.57 (dd, J = 18.9, 9.5 Hz, 1H), 4.14 (dd, J = 4.2, 2.0 Hz, 1H), and 4.23 (m, 1H); δ_C (125 MHz; $CDCl_3$) -4.6, -4.6, -4.5, -4.2, 18.7, 18.7, 26.2, 26.3, 27.0, 27.5, 35.5, 51.9, 55.6, 69.1, 72.3, 72.4, 75.5, 82.1, and 109.8 (Found: C, 60.34; H, 10.37; N, 3.05 $C_{23}H_{47}NO_4Si_2$ requires C, 60.34; H, 10.35; N, 3.06%).

1,6-Diepicastanospermine (2). A solution of **11** (0.71 g, 1.6 mmol) and Dowex 50W-X8 (100 mg) in MeOH was refluxed for 12 h. The mixture was filtered, and then was washed with MeOH. The remaining residue was eluted with 3 N NH_4OH. The solution evaporated, then co-evaporated with toluene to give **2** as an oil (0.26 g, 91%). $[\alpha]_D^{20}$ -73.8 (*c* 0.60, H_2O); δ_H (500 MHz; D_2O) 1.61 (m, 1H), 1.96 (dd, J = 9.3, 6.7 Hz, 1H), 2.27 (m, 1H), 2.40 (d, J = 12.5 Hz, 1H), 2.45 (dd, J = 18.4, 9.2 Hz, 1H), 2.89 (t, J = 8.3 Hz, 1H), 3.02 (dd, J = 12.6, 2.5 Hz, 1H), 3.49 (dd, J = 9.5, 3.6 Hz, 1H), 3.64 (t, J = 9.5 Hz, 1H), 3.99 (m, 1H), and 4.23 (m, 1H); δ_C (125 MHz; D_2O) 32.7, 51.5, 55.5, 69.2, 72.0, 73.8, 74.4, and 75.6 (Found: C, 50.77; H, 7.98; N, 7.40 $C_8H_{15}NO_4$ requires C, 50.78; H, 7.99; N, 7.40%).

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