# SUPPORTING INFORMATION

# Carboxybenzyl Group as an *O*-Nucleophile in the C-H Allylic Oxidation: Total Synthesis of (–)-Castanospermine

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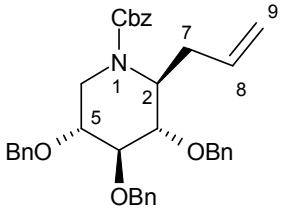
**Experimental**

NMR spectra were recorded with a Varian AM-600 (600 MHz $^{1}H$, 150 MHz $^{13}C$) or with a Varian AM-500 (500 MHz $^{1}H$, 125 MHz $^{13}C$) at room temperature. Chemical shifts (δ) are reported in ppm relative to TMS (δ 0.00) for $^{1}H$, residual chloroform (δ 77.0), benzene (δ 128.1) and methanol (49.2) for $^{13}C$, unless otherwise stated. All significant resonances (carbon skeleton) were assigned by COSY ($^{1}H$-$^{1}H$), HSQC ($^{1}H$-$^{13}C$) and HMBC ($^{1}H$-$^{13}C$) correlations. Relative stereochemistry was assigned based on the 1D-NOE or 2D-NOESY experiments. Mass spectra were recorded with a MALDISynapt G2-S HDMS (*Waters Inc.*), melting points were measured with an SRS OptiMelt and are uncorrected. Optical rotations were measured in $CH_2Cl_2$ or MeOH with a Jasco P 1020 apparatus using sodium light ($c$ = 1, $T$ = 23 ˚C); elemental analyses were performed with an Elementar vario ELIII. Reagents were purchased from Sigma-Aldrich, Alfa Aesar or ABCR, and used without further purification. Dry solvents were purchased from Sigma-Aldrich and used as obtained. Hexanes (65-80 ˚C fraction from petroleum) and EtOAc obtained from local suppliers were purified by distillation. Other solvents were purchased from Sigma-Aldrich and used without further purification. Thin-layer chromatography was carried out on silica gel 60 F-254 (Merck). TLC results were visualized with cerium ammonium molybdate stain. Organic solutions were dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. Flash chromatography was performed on Grace Resolv or Grace Reveleris cartridges, using Grace Reveleris X2 system (UV and ELSD detection).

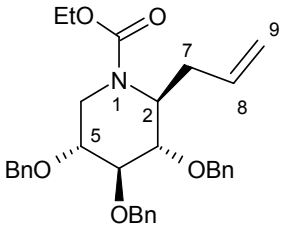
**(2*S*,3*S*,4*S*,5*R*)-1-benzyloxycarbonyl-2-allyl-3,4,5-tribenzyloxypiperidine (3a):**




To a stirred solution of **1** (980 mg, 2.21 mmol) in acetonitrile (50 mL), finely pulverized $K_2CO_3$ (1.5 g, 4.9 equiv) was added, followed by benzyl chloroformate (0.35 mL, 2.45 mmol, 1.1 equiv). The reaction was stirred for 30 min, the solid was filtered off and the solvent was evaporated. The residue was chromatographed (flash chromatography, linear gradient: 100% hexanes to 100% ethyl acetate in 3h) to yield **3a** as a colorless oil (1.22 g, 95%).

LRMS: *m*/*z*: 600.5 ([M + Na]$^+$); elem. anal.: found: C – 76.69, H –6.86, N – 2.49%; calcd. C – 76.92, H – 6.80, N – 2.42%; $[\alpha]_D^{23} = -7.1$; $R_f$ = 0.6 (hexanes: ethyl acetate 3:1). $^1$H NMR (600 MHz, $CDCl_3$) δ: 7.28 (m, arom.), 5.71 (m, 1H, H-8), 5.12 (m, 2H, OC*H*$_2$Ph), 4.98 (m, 2H, H-9, H-9'), 4.57 (m, 6H, OC*H*$_2$Ph), 4.32 (~bs, 1H, H-2), 4.05 (~bs, 1H, H-6), 3.73 (~t, 1H, *J* = 4.2 Hz, H-4), 3.65 (~d, 1H, *J* = 3.3 Hz, H-5), 3.55 (~t, 1H, *J* = 3.7 Hz, H-3), 3.31 (dd, 1H, *J* = 14.1, 3.0 Hz, H-6'), 2.45 ppm (m, 2H, H-7, H-7'). $^{13}$C NMR (150 MHz, $CDCl_3$) δ: 156.0 (*C*=O), 138.2, 138.0, 136.7 (4 × quat. benzyl), 134.5 (C-8), 128.4-127.5 (arom.), 117.7 (C-9), 79.5 (C-4), 75.9 (C-5), 75.3 (C-3), 72.5, 71.8, 70.7, 67.1 (4 × O*C*H$_2$Ph), 54.5 (C-2), 39.7 (C-6), 35.1 ppm (C-7).

**(2*S*,3*S*,4*S*,5*R*)-1-ethoxycarbonyl-2-allyl-3,4,5-tribenzyloxypiperidine (3b):**

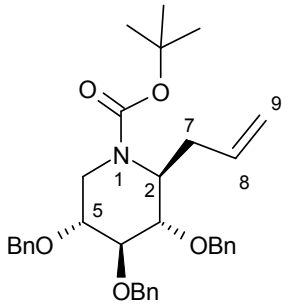



To a stirred solution of **1** (500 mg, 1.13 mmol) in acetonitrile (25 mL), finely pulverized $K_2CO_3$ (0.7 g, 5.1 equiv) was added, followed by ethyl chloroformate (0.24 mL, 2.51 mmol, 2.2 equiv). The reaction was stirred for 30 min, the solid was filtered off and the solvent was evaporated. The residue was chromatographed (flash chromatography, linear gradient: 100% hexanes to 100% ethyl acetate) to yield **3b** as a colorless oil (520 mg, 90%).

LRMS: *m*/*z*: 538.4 ([M + Na]$^+$); elem. anal.: found: C – 74.36, H – 7.16, N – 2.53%; calcd. C – 74.54, H – 7.23, N – 2.72%; $[\alpha]_D^{23} = -11.1$; $R_f$ = 0.5 (hexanes: ethyl acetate 4:1). $^1$H NMR (600 MHz, $CDCl_3$) δ: 7.29 (m, arom.), 5.74 (~ddt, 1H, *J* = 17.4, 10.4, 7.2 Hz, H-8), 5.01 (m, 2H, H-9, H-9'), 4.71

(d, 1H, $J$ = 11.9 Hz, OC$\underline{H}_2$Ph), 4.61 (m, 2H, OC$\underline{H}_2$Ph), 4.54 (m, 2H, OC$\underline{H}_2$Ph), 4.24 (~bs, 1H, H-2), 4.12 (m, 2H, $CH_3C\underline{H}_2$-), 4.00 (~d, 1H, $J$ = 12.0 Hz, H-6), 3.72 (~t, 1H, $J$ = 4.4 Hz, H-4), 3.65 (~dd, 1H, $J$ = 7.8, 4.2 Hz, H-5), 3.55 (~t, 1H, $J$ = 4.2 Hz, H-3), 3.30 (dd, 1H, $J$ = 14.1, 3.2 Hz, H-6'), 1.21 ppm (t, 3H, $J$ = 7.1 Hz, $C\underline{H}_3CH_2$-). $^{13}$C NMR (150 MHz, $CDCl_3$) δ: 156.2 ($\underline{C}$=O), 138.23, 138.19, 138.0 (3 × quat. benzyl), 134.6 (C-8), 128.4-127.5 (arom.), 117.6 (C-9), 80.0 (C-4), 76.2 (C-5), 75.5 (C-3), 72.5, 71.9, 70.7 (3 × O$\underline{C}H_2$Ph), 61.3 ($CH_3\underline{C}H_2$-), 54.4 (C-2), 39.7 (C-6), 35.2 (C-7), 14.6 ppm ($\underline{C}H_3CH_2$-).

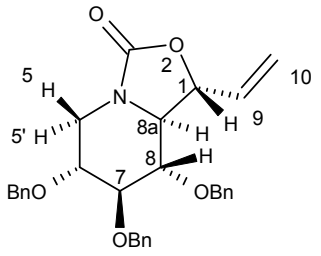
**(2*S*,3*S*,4*S*,5*R*)-1-(*tert*-butoxycarbonyl)-2-allyl-3,4,5-tribenzyloxypiperidine (3c):**




To a stirred solution of **1** (291 mg, 0.66 mmol) in acetonitrile (5 mL), finely pulverized $K_2CO_3$ (0.5 g, 5.5 equiv) was added, followed by $Boc_2O$ (2 M in DCM, 0.8 mL, 1.6 mmol, 2.4 equiv). The reaction was stirred for 24 h, the solid was filtered off and the solvent was evaporated. The residue was chromatographed (flash chromatography, linear gradient: 100% hexanes to 100% ethyl acetate) to yield **3c** as a colorless oil (348 mg, 97%).

LRMS: $m/z$: 566.5 ($[M + Na]^+$); elem. anal.: found: C – 74.97, H – 7.62, N – 2.55%; calcd. C – 75.11, H – 7.60, N – 2.58%; $[\alpha]_D^{23}$ = −10.8; $R_f$ = 0.5 (hexanes: ethyl acetate 5:1). $^1$H NMR (600 MHz, $CDCl_3$) δ: 7.29 (m, arom.), 5.75 (~ddt, 1H, $J$ = 16.0, 11.1, 7.2 Hz, H-8), 5.01 (m, 2H, H-9, H-9'), 4.73 (d, 1H, $J$ = 11.7, OC$\underline{H}_2$Ph), 4.57 (m, 5H, OC$\underline{H}_2$Ph), 4.18 (~bs, 1H, H-2), 3.96 (~d, 1H, H-6), 3.72 (~t, 1H, $J$ = 4.5 Hz, H-4), 3.66 (~dd, 1H, $J$ = 7.9, 4.3 Hz, H-5), 3.54 (~t, 1H, $J$ = 4.5 Hz, H-3), 3.26 (dd, 1H, $J$ = 14.1, 3.3 Hz, H-6'), 2.44 (m, 2H, H-7, H-7'), 1.43 ppm (s, 9H, $(C\underline{H}_3)_3$C-). $^{13}$C NMR (150 MHz, $CDCl_3$) δ: 155.3 ($\underline{C}$=O), 138.29, 138.27, 138.1 (3 × quat. benzyl), 134.8 (C-8), 128.4-127.4 (arom.), 117.5 (C-9), 80.8 (C-4), 79.7 ($(CH_3)_3\underline{C}$-), 76.7 (C-5), 75.9 (C-3), 72.6, 71.9, 70.6 (3 × O$\underline{C}H_2$Ph), 54.4 (C-2), 39.6 (C-6), 35.3 (C-7), 28.4 ppm ($(\underline{C}H_3)_3$C-).

**(1*R*,6*R*,7*S*,8*S*,8a*R*)-1-ethenyl-6,7,8-tribenzyloxyhexahydro[1,3]oxazolo[3,4-*a*]pyridin-3-one (4):**



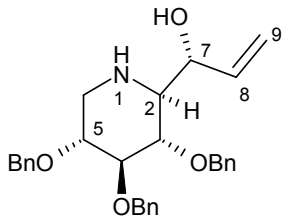

Important 1D-NOE interactions:
H-1 and H-8 (2.9%)
H-5' and H-8a (2.0%)

*Representative procedure:*

No precautions were taken to exclude moisture and air. To a solution of **3a** (494 mg, 0.86 mmol) in dioxane (4.3 mL), benzoquinone (185 mg, 2 equiv) was added, followed by $Yb(OTf)_3$ (53 mg, 0.1 equiv) and [1,2-bis(phenylsulfinyl) ethane] palladium acetate (White catalyst, 43 mg, 0.1 equiv). The flask was sealed with a rubber septum and the mixture was stirred at 75 °C for 4 h. Then, the mixture was cooled down and toluene (5 mL) was added, followed by silica gel (3 g, 230-400 mesh). The solvent was evaporated and the dry residue was loaded on a chromatography column. Flash chromatography (linear gradient, 100% hexanes to 100% ethyl acetate) yielded **4** (297 mg, 71%) as a pale orange oil that solidified upon standing.

HRMS: found: *m*/*z* = 486.2285; calcd. for $C_{30}H_{32}NO_5$ ($[M + H]^+$): 486.2280; elem. anal.: found: C – 74.21, H – 6.66, N – 2.67%; calcd. C – 74.21, H –6.43 , N – 2.88%; mp = 82 ÷ 84 °C; $[\alpha]_D^{23} = -21.9$; $R_f$ = 0.4 (hexanes: ethyl acetate 3:1). $^1$H NMR (600 MHz, $CDCl_3$) δ: 7.30 (m, arom.), 5.82 (ddd, 1H, *J* = 17.0, 10.6, 5.8 Hz, H-9), 5.33 (m, 1H, H-10), 5.25 (m, 1H, H-10'), 5.00 (d, 1H, *J* = 10.9 Hz, OC*H*$_2$Ph), 4.92 (d, 1H, *J* = 11.4 Hz, OC*H*$_2$Ph), 4.82 (d, 1H, *J* = 10.9 Hz, OC*H*$_2$Ph), 4.67 (m, 3H, OC*H*$_2$Ph), 4.37 (~ddt, 1H, *J* = 5.7, 4.4, 1.3 Hz, H-1), 4.13 (dd, 1H, *J* = 13.2, 5.4 Hz, H-5), 3.56 (m, 2H, H-6, H-7), 3.37 (m, 1H, H-8), 3.28 (dd, 1H, *J* = 9.5, 4.4 Hz, H-8a), 2.74 ppm (dd, 1H, *J* = 13.2, 10.0 Hz, H-5'). $^{13}$C NMR (150 MHz, $CDCl_3$) δ: 155.9 (C-3), 138.2, 137.57, 137.56 (3 × quat. benzyl), 134.1 (C-9), 128.5-127.8 (arom.), 118.1 (C-10), 85.7 (C-7), 79.8 (C-8), 77.7 (C-1), 77.4 (C-6), 75.9, 75.1, 73.2 (3 × O*C*H$_2$Ph), 61.8 (C-8a), 42.8 ppm (C-5).

**(2*S*,3*S*,4*S*,5*R*)-2-[(1*R*)-1-hydroxyprop-2-en-1-yl]-3,4,5-tribenzyloxypiperidine (5):**



To a stirred solution of **4** (503 mg, 1.04 mmol) in methanol (10 mL), KOH (1.1 g, 19 equiv) was added in few portions. The flask was sealed with a rubber septum and the mixture was stirred at 75 °C for 12 h. After cooling down to room temperature, water (20 mL) and ethyl acetate (100 mL) were added. Layers were separated and the aqueous one was washed with ethyl acetate (2 × 20 mL). The combined organic layers were washed with water (10 mL) and brine. Then, the mixture was dried and solvent was evaporated. The residue was chromatographed (flash chromatography, linear gradient: 100% hexanes to 100% ethyl acetate) to yield **5** (404 mg, 85%) as a colorless oil.

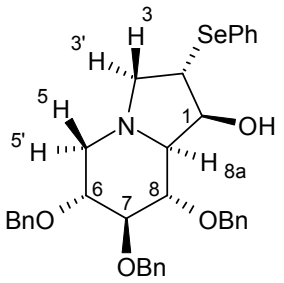
HRMS: found: *m*/*z* = 460.2488; calcd. for $C_{29}H_{34}NO_4$ ([M + H]$^+$): 460.2488; elem. anal.: found: C – 75.79, H – 7.16, N – 3.01%; calcd. C – 75.79, H – 7.24, N – 3.05%; $[\alpha]_D^{23} = 4.6$; $R_f$ = 0.3 (hexanes: ethyl acetate 2:3). $^1$H NMR (600 MHz, $CDCl_3$) δ: 7.30 (arom.), 5.87 (ddd, 1H, *J* = 17.2, 10.6, 3.9 Hz, H-8), 5.38 (m, 1H, H-9), 5.24 (m, 1H, H-9'), 4.99 (d, 1H, *J* = 11.0 Hz, OC$\underline{H_2}$Ph), 4.95 (d, 1H, *J* = 10.9 Hz, OC$\underline{H_2}$Ph), 4.86 (d, 1H, *J* = 11.0 Hz, OC$\underline{H_2}$Ph), 4.70 (m, 2H, OC$\underline{H_2}$Ph), 4.65 (d, 1H, *J* = 11.6 Hz, OC$\underline{H_2}$Ph), 4.47 (dd, 1H, *J* = 3.7, 1.8 Hz, H-7), 3.57 (m, 2H, H-3, H-4), 3.50 (m, 1H, H-5), 3.23 (dd, 1H, *J* = 11.6, 4.9 Hz, H-6), H- 2.57 (m, 1H, H-2), 2.50 ppm (dd, 1H, *J* = 11.3, 10.6 Hz, H-6'). $^{13}$C NMR (150 MHz, $CDCl_3$) δ: 139.0 (C-8), 138.8, 138.42, 138.37 (3 × quat. benzyl), 128.4-127.5 (arom.), 115.5 (C-9), 87.1 (C-4), 80.0 (C-5), 78.9 (C-3), 75.5, 75.3, 72.8 (3 × O$\underline{C}$H$_2$Ph), 69.4 (C-7), 62.5 (C-2), 47.9 ppm (C-6).

**Selenium mediated cyclization of 5**

*This reaction was performed under an argon atmosphere.*

To a stirred solution of **5** (287 mg, 0.63 mmol) in a mixture of dry DCM (5 mL) and dry pyridine (1 mL), at room temperature, phenylselenyl bromide (162 mg, 1.1 equiv) was added in one portion. After 10 min, triethylamine was added (1 mL). Then, solvents were evaporated. The residue was redissolved in hot toluene and concentrated again. The process was repeated 2 × times. Column chromatography (flash chromatography, linear gradient: 100% hexanes to 100% ethyl acetate) yielded **6b** as an off-white solid (38 mg, 10%) and **6a** as an off-white solid (272 mg, 71%).

**(1*S*,2*S*,6*R*,7*S*,8*S*,8a*R*)-2-(phenylselenyl)-6,7,8-tribenzyloxyoctahydroindolizine-1-ol (6a):**

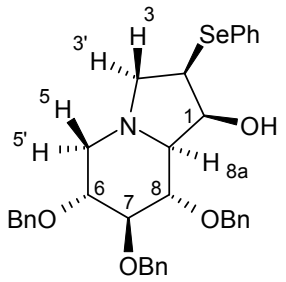



Important 1D-NOE interactions:
H-1 and H-8a (2.4%)
H-2 and H-3 (1.7%)
H-3 and H-5 (1.1%)
H-5' and H-8a (1.7%)
H-3' and H-8a (1.4%)
H-3' and H-5' (1.4%)

Important HMBC correlations:
C-3 and H-5; C-3 and H-5'; C-5 and H-3'

LRMS: *m*/*z*: 616.4 ([M + H]$^+$); elem. anal.: found: C – 68.33, H – 5.93, N – 2.17%; calcd. C – 68.40, H – 6.07, N – 2.28%; mp = 95 ÷ 97 °C; $[\alpha]_D^{23} = -81.1$; $R_f$ = 0.4 (hexanes:ethyl acetate 2:1). $^1$H NMR (600 MHz, $C_6D_6$) δ: 7.11 (m, arom.), 5.00 (d, 1H, *J* = 11.2 Hz, OC*H*$_2$Ph), 4.92 (m, 3H, OC*H*$_2$Ph), 4.56 (d, 1H, *J* = 12.0 Hz, OC*H*$_2$Ph), 4.50 (d, 1H, *J* = 12.0 Hz, OC*H*$_2$Ph), 4.42 (~d, 1H, *J* = 2.9 Hz, H-1), 3.84 (~t, 1H, *J* = 9.2 Hz, H-8), 3.68 (~td, 1H, *J* = 9.6, 5.0 Hz, H-6), 3.60 (~t, 1H, *J* = 8.9 Hz, H-7), 3.51 (~t, 1H, *J* = 7.9 Hz, H-2), 3.18 (dd, 1H, *J* = 9.7, 8.4 Hz, H-3), 2.93 (dd, 1H, *J* = 10.5, 5.0 Hz, H-5), 2.32 (dd, 1H, *J* = 9.5, 3.8 Hz, H-8a), 1.99 (dd, 1H, *J* = 9.8, 7.7 Hz, H-3'), 1.81 ppm (~t, 1H, *J* = 10.4 Hz, H-5'). $^{13}$C NMR (150 MHz, $C_6D_6$) δ: 139.82, 139.81, 139.4 (3 × quat. benzyl), 133.0-127.3 (arom.), 87.4 (C-7), 79.3 (C-6), 78.8 (C-1), 77.7 (C-8), 75.8, 74.6, 72.8 (3 × O*C*H$_2$Ph), 70.2 (C-8a), 59.1 (C-3), 54.3 (C-5), 45.6 ppm (C-2). $^{77}$Se NMR (114 MHz, $C_6D_6$) δ: 358.3 ppm (s, -*Se*Ph).

**(1*S*,2*R*,6*R*,7*S*,8*S*,8a*R*)-2-(phenylselenyl)-6,7,8-tribenzyloxyoctahydroindolizine-1-ol (6b):**

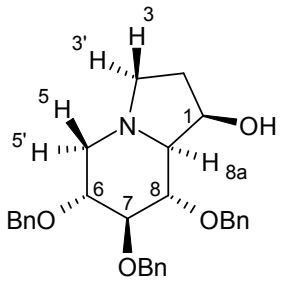



Important 1D-NOE interactions:
H-1 and H-8a (2.8%)
H-2 and H-8a (1.2%)
H-1 and H-2 (3.3%)
H-5 and H-3 (1.1%)
-O*H* and H-3 (0.4%)
-O*H* and H-8 (1.5%)

Important HMBC correlations:
C-5 and H-3'; C-3 and H-5; C-3 and H-5'

LRMS: *m*/*z*: 616.5 ([M + H]$^+$); elem. anal.: found: C – 68.16, H – 6.29, N – 2.13%; calcd. C – 68.40, H – 6.07, N – 2.28%; m.p. = decomp. (>50°C); $[\alpha]_D^{23} = -50.0$; $R_f$ = 0.7 (hexanes:ethyl acetate 2:1). $^1$H NMR (600 MHz, $C_6D_6$) δ: 7.21 (m, arom.), 5.05 (d, 1H, *J* = 11.3 Hz, OC*H*$_2$Ph), 4.96 (m, 3H, OC*H*$_2$Ph), 4.59 (d, 1H, *J* = 12.0 Hz, OC*H*$_2$Ph), 4.52 (d, 1H, *J* = 12.0 Hz, OC*H*$_2$Ph), 4.13 (m, 1H, H-1), 3.82 (~t, 1H, H-8), 3.62 (m, 1H, H-6), 3.57 (~t, 1H, H-7), 3.51 (ddd, 1H, *J* = 9.7, 5.5, 4.2 Hz, H-2), 2.99 (dd, 1H, *J* = 10.0, 4.1 Hz, H-3), 2.91 (dd, 1H, *J* = 10.4, 5.1 Hz, H-5), 2.44 (d, 1H, *J* = 9.8 Hz, -O*H*), 2.31 (~t, 1H, *J* = 9.8 Hz, H-3'), 1.91 (dd, 1H, *J* = 9.4, 3.1 Hz, H-8a), 1.82 ppm (~t, 1H, *J* = 10.3 Hz, H-5'). $^{13}$C NMR (150 MHz, $C_6D_6$) δ: 140.02, 140.00, 139.5 (3 × quat. benzyl), 133.6-127.4 (arom.), 87.4 (C-7), 79.2 (C-6), 78.4 (C-8), 75.8, 74.8, 72.9 (3 × O*C*H$_2$Ph), 71.9 (C-1), 71.7 (C-8a), 60.3 (C-3), 54.3 (C-5), 47.1 ppm (C-2). $^{77}$Se NMR (114 MHz, $C_6D_6$) δ: 323.8 ppm (s, -*Se*Ph).

**(1*R*,6*R*,7*S*,8*S*,8a*S*)-6,7,8-tribenzyloxyoctahydroindolizine-1-ol (7):**




Important 2D-NOESY interactions:
H-3' and H-5'; H-3 and H-5; H-3' and H-8a;
H-1 and H-8a

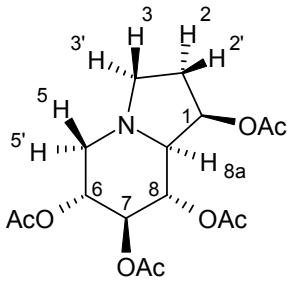
Important HMBC correlations:
C-5 and H-3'; C-3 and H-5; C-3 and H-5'

To a stirred solution of **6a** (108 mg, 0.18 mmol) in MeOH (1.0 mL) and THF (0.3 mL), a solution of $NiCl_2 \cdot 7H_2O$ (90 mg, 2 equiv) in MeOH (0.5 mL) was added. The resulting mixture was cooled to 0 °C and $NaBH_4$ (150 mg, 22 equiv) was added for 1 h in several portions. Then, the mixture was warmed to room temperature and stirred for another 1 h. After this time, the mixture was filtered through a pad of silica gel (3 g, 230-400 mesh), which was then thoroughly washed with ethyl acetate (100 mL). Solvent was evaporated and the residue was chromatographed (flash chromatography, 100% hexanes to 100% ethyl acetate) to yield **7** (48 mg, 60%) as a pale yellow oil.

HRMS: found: *m*/*z* = 460.2492; calcd. for $C_{29}H_{34}NO_4$ ($M + H^+$): 460.2488; elem. anal.: found: C – 75.66, H – 7.12, N – 2.89%; calcd. C – 75.79, H – 7.24, N – 3.05%; $[\alpha]_D^{23} = -38.5$ (*c* 1.0, DCM), lit.[1] $[\alpha]_D^{23} = +35.5$ (*c* 0.96, DCM); $R_f$ = 0.4 (DCM: methanol 20:1). $^1$H NMR (600 MHz, $CDCl_3$)[1] δ: 7.31 (arom.), 4.97 (d, 1H, *J* = 10.9 Hz, OC*H*$_2$Ph; lit. 4.99), 4.87 (m, 2H, OC*H*$_2$Ph; lit. 4.87), 4.80 (d, 1H, *J* = 11.3 Hz, OC*H*$_2$Ph; lit. 4.80), 4.70 (d, 1H, *J* = 11.6 Hz, OC*H*$_2$Ph; lit. 4.71), 4.65 (d, 1H, *J* = 11.6 Hz, OC*H*$_2$Ph; lit. 4.66), 4.23 (bs, 1H, H-1; lit. 4.23), 3.68 (m, 2H, H-8, H-6; lit. 3.68), 3.56 (~t, 1H, *J* = 9.0 Hz, H-7; lit. 3.56), 3.25 (dd, 1H, *J* = 10.6, 5.0 Hz, H-5; lit. 3.26), 3.09 (~td, 1H, *J* = 8.8, 2.5 Hz, H-3; lit. 3.08), 2.17 (m, 1H, H-2; lit. 2.06-2.26), 2.12 (m, 1H, H-3'; lit. 2.06-2.26), 2.00 (~t, 1H, *J* = 10.4 Hz, H-5'; lit. 2.00), 1.94 ppm (dd, 1H, *J* = 9.5, 3.6 Hz, H-8a; lit. 1.94), 1.74 (m, 1H, H-2'; lit. 1.75). $^{13}$C NMR (600 MHz, $CDCl_3$)[1] δ: 138.9, 138.8, 138.4 (3 × quat. benzyl), 128.5-127.5 (arom.), 87.3 (C-7; lit. 87.3), 79.2, 76.7 (C-6, C-8; lit. 79.2, 76.9), 75.6, 74.3, 72.9 (3 × O*C*H$_2$Ph; lit.75.6, 74.3, 72.9), 71.8 (C-8a; lit. 71.8), 70.8 (C-1; lit. 70.7), 54.4 (C-5; lit. 54.3), 51.6 (C-3; lit. 51.6), 33.6 ppm (C-2; lit. 33.6).

[1] For data of its enantiomer, see: Jensen, T.; Mikkelsen, M.; Lauritsen, A.; Andresen, T. L.; Gotfredsen, C. H.; Madsen, R. *J. Org. Chem.* **2009**, *74*, 8886.

**(1*R*,6*R*,7*S*,8*S*,8a*S*)-octahydroindolizine-1,6,7,8-tetrayl tetraacetate ((−)-castanospermine tetraacetate) (8):**




Important 2D-NOESY interactions:
H-1 and H-8a; H-1 and H-2; H-5 and H-3;
H-5' and H-3', H-3 and H-2'; H-3' and H-2

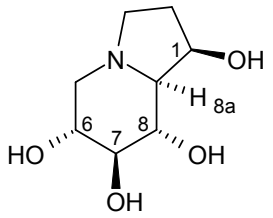
Important HMBC correlations:
C-5 and H-3'; C-3 and H-5; C-3 and H-5'

To a solution of **7** (50 mg, 0.11 mmol) in methanol (1.1 mL), palladium hydroxide on charcoal (20% (dry basis), <50% $H_2O$, 200 mg) was added under an argon atmosphere. Then, argon was replaced by hydrogen (from a balloon) and the reaction was carried out for 72 h. Then, the suspension was filtered through a pad of Celite and washed repeatedly with methanol. The solvent was evaporated and the residue was dissolved in pyridine (0.8 mL) and $Ac_2O$ (0.2 mL). DMAP was added (1 mg) and the mixture was stirred for 24 h. The solvent was evaporated and the residue was chromatographed (flash chromatography, linear gradient: 100% hexanes to 100% ethyl acetate in 30 min) to yield **8** as a white solid (31 mg, 79%).

HRMS: found: *m*/*z* = 358.1493; calcd. for $C_{16}H_{24}NO_8$ ($M + H^+$): 358.1502; elem. anal.: found: C – 53.88, H – 6.38, N – 3.75%; calcd. C – 53.78, H – 6.49, N – 3.92%; $[\alpha]_D^{23} = -44.9$ (*c* 1.0, DCM); lit.[2a] $[\alpha]_D^{25} = +42.7$, *c* 0.08, $CHCl_3$; m. p. = 105 ÷ 110 °C (decomp.); $R_f$ = 0.3 (hexanes: ethyl acetate 1:1; $KMnO_4$ stain). $^1$H NMR (600 MHz, $CDCl_3$)[2] δ: 5.36 (m, 1H, H-1; lit. 5.36), 5.21 (m, 1H, H-8; lit. 5.21), 5.08 (m, 2H, H-6, H-7; lit. 5.07), 3.40 (m, 1H, H-5; lit. 3.39), 3.22 (~td, 1H, *J* = 9.0, 2.2 Hz, H-3; lit. 3.20), 2.36 (m, 1H, H-2), 2.33 (dd, 1H, *J* = 9.8, 4.6 Hz, H-8a; lit. 2.32), 2.24 (m, 1H, H-3'; lit. 2.23), 2.08 (m, 1H, H-5'; lit. 2.10), 2.05, 2.03, 2.02, 1.97 (4 × s, 12H, 4 × C<u>*H*</u>$_3$C(O)O-), 1.86 ppm (~dtd, 1H, *J* = 14.4, 8.8, 1.9 Hz, H-2'). $^{13}$C NMR (150 MHz, $CDCl_3$)[2] δ: 170.5, 170.4, 169.9, 169.6 (4 × $CH_3$<u>*C*</u>(O)O-), 75.1 (C-7; lit. 75.2), 71.0 (C-1; lit. 71.1), 70.2 (C-6; lit. 70.2), 68.5 (C-8a; lit. 68.5), 68.2 (C-8; lit. 68.2), 52.9 (C-5; lit. 52.9), 51.9 (C-3; lit. 51.9), 31.6 (C-2; lit.31.6), 21.0, 20.8, 20.7, 20.6 ppm (4 × <u>*C*</u>H$_3$C(O)O-).

[2] In accordance with data for (+)-castanospermine tetraacetate: (a) Kim, N.-S.; Choi, J.-R.; Cha, J.-K. *J. Org. Chem.* **1993**, *58*, 7096. (b) Cronin, L.; Murphy, P. V. *Org. Lett.* **2005**, *7*, 2691.

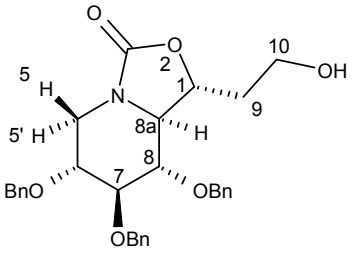
**(1*R*,6*R*,7*S*,8*S*,8a*S*)-octahydroindolizine-1,6,7,8-tetraol ((−)-castanospermine) (9):**




To a solution of **8** (20 mg, 0.06 mmol) in dry methanol (1 mL), MeONa (freshly prepared ~1M in MeOH, 50 μL) was added and the resulting mixture was stirred for 12 h at room temperature. Then, Amberlyst-15 (freshly activated with 5% aq. HCl, 0.5 g) was added. The resin was filtered off and washed thoroughly with 25% aq. $NH_3$. The solvent was evaporated to yield **9** ((−)-castanospermine) (10 mg, quant.). This product was characterized without further purification.

HRMS: found: *m*/*z* = 190.1077; calcd. for $C_8H_{16}NO_4$ ([M + $H^+$]): 190.1079; $[\alpha]_D^{23}$ = −73.7 (*c* 1, MeOH); lit.[3] $[\alpha]_D^{25}$ = −81.1, *c* 2.0, $H_2O$; lit.[2b] $[\alpha]_D^{25}$ = +78.6, *c* 0.25, $D_2O$; lit.[1] $[\alpha]_D^{21}$ = +72.4, *c* 0.22, $H_2O$; $^1$H NMR (600 MHz, $D_2O$, DSS[4] as standard)[1] δ: 4.40 (m, 1H, H-1; lit. 4.43-4.25), 3.60 (m, 2H, H-6, H-8; lit. 3.65-3.59), 3.31 (~t, 1H, *J* = 9.1 Hz, H-7; lit. 3.32), 3.16 (dd, 1H, *J* = 10.8, 5.0 Hz, H-5; lit. 3.17), 3.07 (~td, 1H, *J* = 9.0, 1.7 Hz, H-3; lit. 3.08), 2.32 (m, 1H, H-2; lit. 2.39-2.29), 2.20 (dd, 1H, *J* = 18.3, 9.2 Hz, H-3'; lit. 2.21), 2.04 (~t, 1H, *J* = 10.7 Hz, H-5'; lit. 2.04), 2.01 (dd, 1H, *J* = 9.9, 4.3 Hz, H-8a; lit. 2.02), 1.70 ppm (m, 1H, H-2'; lit. 1.71). $^{13}$C NMR (150 MHz, $D_2O$)[3] δ: 81.8 (C-7; lit. 81.8), 74.2 (C-8a; lit. 74.2), 72.9 (C-6; lit. 72.9), 72.4 (C-1; lit. 72.3), 71.7 (C-8; lit. 71.7), 58.2 (C-5; lit. 58.2), 54.3 (C-3; lit. 54.4), 35.5 ppm (C-2; lit. 35.5).

**(1*R*,6*R*,7*S*,8*S*,8a*R*)-6,7,8-tribenzyloxy-1-(2-hydroxyethyl)hexahydro[1,3]oxazolo[3,4-*a*]pyridin-3-one (10):**



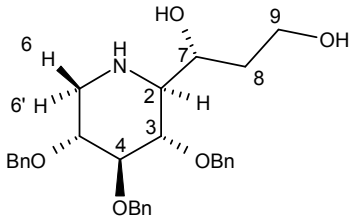

*This reaction was performed under an argon atmosphere.*

[3] Mulzer, J.; Dehmlow, H.; Buschmann, J.; Luger, P. *J. Org. Chem.* **1992**, *57*, 3194.
[4] 3-(Trimethylsilyl)-1-propanesulfonic acid sodium salt

To a stirred solution of **4** (420 mg, 0.87 mmol) in dry THF (5.7 mL), Wilkinson catalyst (40 mg, 5 mol%) was added in one portion. The resulting mixture was cooled to 0 °C and catecholborane (1M in THF, 3.0 mL, 3.4 equiv) was added with a syringe pump (15 min). The cooling bath was removed and the reaction was performed for 24 h at room temperature. Then, the mixture was cooled to 0 °C and NaOH (10% aq., 3 mL) was added dropwise (10 min), followed by $H_2O_2$ (30% aq., 3 mL). The cooling bath was removed and the mixture was stirred for another 24 h at room temperature. After this time, water (30 mL) was added and the mixture was washed with ethyl acetate (3 × 50 mL). The combined organic layers were washed with water (10 mL) and brine. Then, the mixture was dried and solvent was evaporated. The residue was chromatographed (flash chromatography, linear gradient: 100% hexanes to 100% ethyl acetate) to yield **10** (315 mg, 72%) as a white solid.

HRMS: found: *m*/*z* = 526.2211; calcd. for $C_{30}H_{33}NO_6$ ($[M + Na]^+$): 526.2206; elem. anal.: found: C – 71.58, H – 6.64, N – 2.68%; calcd. C – 71.55, H – 6.61, N – 2.78%; mp = 136 ÷ 138 °C; $[\alpha]_D^{23}$ = −32.9; $R_f$ = 0.3 (hexanes: ethyl acetate 1:1). $^1$H NMR (500 MHz, $CDCl_3$) δ: 7.32 (m, arom.), 5.01 (d, 1H, *J* = 10.9 Hz, OC*H*$_2$Ph), 4.92 (d, 1H, *J* = 11.3 Hz, OC*H*$_2$Ph), 4.82 (d, 1H, *J* = 10.9 Hz, OC*H*$_2$Ph), 4.68 (m, 3H), 4.13 (m, 2H, H-1, H-5), 3.66 (m, 2H, H-10,H-10'), 3.56 (m, 2H, H-7, H-8), 3.36 (m, 1H, H-8), 3.30 (dd, 1H, *J* = 9.5, 4.5 Hz, H-8a), 2.75 (dd, 1H, *J* = 13.1, 9.8 Hz, H-5'), 1.87 ppm (m, 2H, H-9, H-9'). $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 155.8 (C-3), 138.1, 137.6, 137.4 (3 × quat. benzyl), 128.7-127.8 (arom.), 85.7 (C-7), 80.2 (C-8), 77.5 (C-6), 76.3 (C-1), 75.9, 75.3, 73.2 (3 × O*C*H$_2$Ph), 61.4 (C-8a), 58.6 (C-10), 42.7 (C-5), 37.7 ppm (C-9).

**(2*S*,3*S*,4*S*,5*R*)-2-[(1*R*)-1,3-dihydroxypropyl]-3,4,5-tribenzyloxypiperidine (11):**




To a stirred solution of **10** (100 mg, 0.20 mmol) in methanol (2.0 mL), KOH (0.5 g, 45 equiv) was added in few portions. The flask was sealed with a rubber septum and the mixture was stirred at 75 °C for 12 h. After cooling down to room temperature, water (10 mL) and DCM (50 mL) were added. Layers were separated and the aqueous one was washed with DCM (2 × 20 mL). The combined organic layers were washed with water (10 mL) and brine. Then, the mixture was dried and solvent was evaporated. The residue was chromatographed (prep. TLC, 1 mm, DCM: MeOH 10:1) to yield **11** (65 mg, 68%) as a white solid.

HRMS: found: *m*/*z* = 478.2601; calcd. for $C_{29}H_{36}NO_5$ ($[M + H]^+$): 478.2593; elem. anal.: found: C – 72.83, H – 7.51, N – 3.02%; calcd. C – 72.93, H – 7.39, N – 2.93%; mp = 100 ÷ 102 °C; $[\alpha]_D^{23}$ = −28.8; $R_f$ = 0.4 (DCM: MeOH 10:1). $^1$H NMR (600 MHz, $CDCl_3$) δ: 7.30 (m., arom.), 4.99 (d, 1H, *J* = 10.9 Hz, OC*H*$_2$Ph), 4.94 (d, 1H, *J* = 11.2 Hz, OC*H*$_2$Ph), 4.85 (d, 1H, *J* = 10.9 Hz, OC*H*$_2$Ph), 4.68 (m, 3H, OC*H*$_2$Ph), 4.10 (m, 1H, H-7), 3.77 (m, 1H, H-9), 3.65 (ddd, 1H, *J* = 11.2, 5.2, 3.5 Hz, H-9'), 3.59 (~t, 1H, *J* = 9.0 Hz, H-4), 3.45 (m, 2H, H-3, H-5), 3.23 (dd, 1H, *J* = 13.1, 5.1 Hz, H-6), 2.47 (m, 2H, H-2, H-6'), 1.84 (m, 1H, H-8), 1.71 ppm (m, 1H, H-8'). $^{13}$C NMR (150 MHz, $CDCl_3$) δ: 138.7, 138.3, 138.2 (3 × quat. benzyl), 128.5-127.6 (arom.), 86.9 (C-4), 80.3 (C-5), 78.8 (C-3), 75.6, 75.1, 72.9 (3 × O*C*H$_2$Ph), 68.0 (C-7), 62.5 (C-2), 59.0 (C-9), 47.1 (C-6), 37.2 ppm (C-8).

**DPPA-mediated cyclization of 11 to 7**

*This reaction was performed under an argon atmosphere.*

To a stirred solution of **11** (42 mg, 0.09 mmol) in dry DCM (1 mL), at room temperature, dry $Et_3N$ (50 µL, 4 equiv) was added, followed by DPPA (diphenylphosphoryl azide, 50 µL, 2.6 equiv). The mixture was stirred for 12 h at room temperature. Then, water (10 mL) and DCM (50 mL) were added. Layers were separated, and the aqueous one was washed with DCM (2 × 20 mL). The combined organic layers were washed with brine. Then, the mixture was dried and solvent was evaporated. The residue was chromatographed (prep. TLC, 0.5 mm, DCM: MeOH 20:1) to yield **7** (32 mg, 80%) as a colorless oil. All spectral data matched those reported for compound **7**.