spectrum of 1 in DMSO-d_6 and MeOH-d_4, table comparing antifungal activity of calophycin and amphotericin B, 300-MHz ^{1}H and 75-MHz ^{13}C NMR spectra of compounds 4, 6, 7, 9–12, 14, and 15 in $CDCl_3$, and 500-MHz ^{1}H NMR spectrum of synthetic 3 in $CDCl_3$ (22 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

A Route to Several Stereoisomers of Castanospermine

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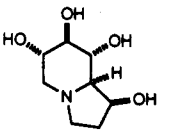
The following three stereoisomers of castanospermine have been prepared: (1*R*,6*R*,7*R*,8*S*,8a*R*)-1,6,7,8-tetrahydroxyindolizidine (1), (1*R*,6*S*,7*S*,8*S*,8a*R*)-1,6,7,8-tetrahydroxyindolizidine (2), and (1*R*,6*R*,7*S*,8*S*,8a*R*)-1,6,7,8-tetrahydroxyindolizidine (3). Each of these compounds was synthesized via asymmetric allylation of pentose derivatives with [(*Z*)-γ-(methoxymethoxy)allyl]diisopinocampheylborane, an approach which is, in principle, suitable for preparations of a total of eight stereoisomers of castanospermine. Compounds 1–3 were tested as possible inhibitors of various glycosidase enzymes and for anti-HIV-1 activity in cell cultures. They are very poor inhibitors of glycosidase enzymes; however, preliminary tests indicate indolizidines 1 and 3 have weak but significant anti-HIV activities.

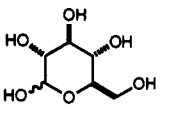
Introduction

Polyhydroxylated indolizidines show varied biological activities based on their ability to act as competitive inhibitors of glycosidase enzymes.[1-11] There is particular interest in inhibition of the glycoprotein-processing enzyme glucosidase I because this interferes with the processing of the surface glycoproteins of HIV-1, suppressing viral replication and virus-induced syncitia formation.[12]

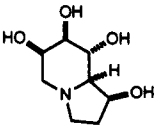
Castanospermine, isolated from *Castanospermum australe* and *Alexa leiopetala*,[13,14] is a potent glucosidase I inhibitor.[15] The stereochemistry of this molecule corresponds to the pyranose form of glucose; consequently, one might expect that, compared with its stereoisomers, castanospermine would be the most potent inhibitor of glucosidase enzymes. However, other observations imply this prediction is not necessarily correct. For instance, 6-epicastanospermine resembles mannose, but it is a poor inhibitor of several mannosidases and an effective inhibitor of amyloglucosidase.[16]



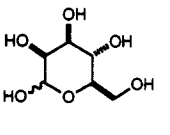
(+)-castanospermine



D-glucose



(+)-6-epicastanospermine



D-mannose

A theoretical study indicates topographic similarity with the mannopyranosyl cation, not with mannose itself, is the key to inhibition of mannosidase enzymes.[17] Calculations comparing castanospermine derivatives with the glucopyranosyl cation, however, have not been reported.[18] In any event their predictive value would be suspect since the mechanistic origins of the enzyme activity have not been elucidated and no structural information is available for the active sites of glucosidase I. At this time the *only* reliable way to formulate a structure/activity relationship for these compounds is to synthesize them and determine their biological activities.

Only eight of the 31 stereoisomers of castanospermine have been synthesized. Some of these were prepared by design[19-22] while others were obtained as byproducts en

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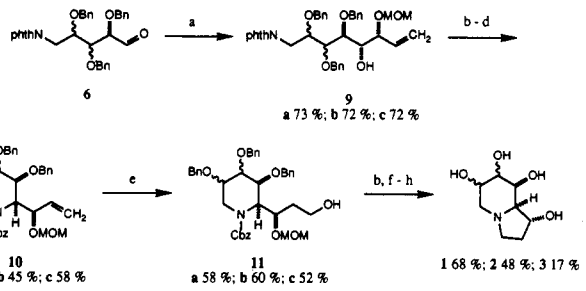
Scheme I. Syntheses of Stereoisomers 1–3[a]

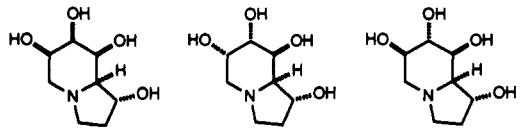


[a] Key: (a) (*Z*)-(MOMO)CHCHCH$_2$-^{d}BIpc$_2$, BF_3·OEt_2, then H_2O_2, $NaHCO_3$; (b) MsCl, NEt_3; (c) $MeNH_2$; (d) CbzCl, $NaHCO_3$; (e) BH_3·THF,then H_2O_2, $NaHCO_3$; (f) H_2, cat. Pd/C, MeOH; (g) $HCl_{(aq)}$; (h) ion exchange.

route to the parent compound.[23–27] Most routes utilize hexose derivatives with four of the five desired chiral centers already present; syntheses from smaller fragments tend to be relatively long in comparison. Few of these synthetic approaches are readily amenable to preparations of several stereoisomers in the series.

Recently, we began developing syntheses of castanospermine stereoisomers to provide an insight into the molecular basis of their biological activities. This project required selective routes suitable for the preparation of several stereoisomers. Ideally, the syntheses should be very similar so that once the practical problems associated with the very first preparation are overcome, access to other compounds in the series is relatively easy.

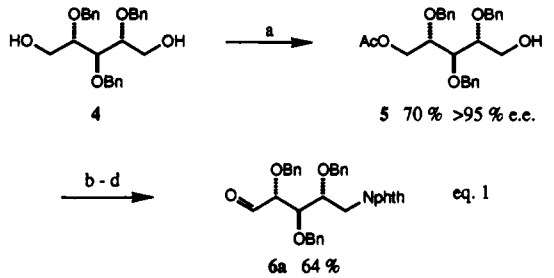
Methodology is presented here for highly selective preparations of (theoretically) eight castanospermine stereoisomers; three compounds in this series were actually prepared, i.e., the 1,6,7,8-tetrahydroxyindolizidines **1–3**.

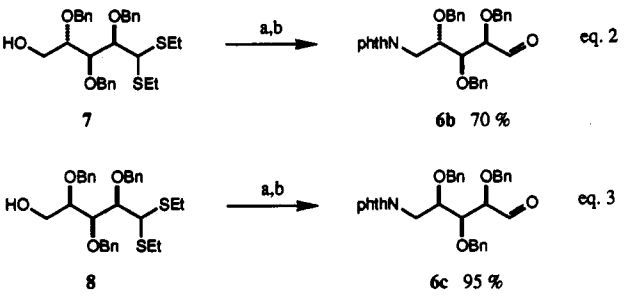


Results and Discussion

Our synthetic strategy[28] hinges upon formation of an acyclic precursor with all the desired chirality via asymmetric allylations of chiral aldehydes. One of the aldehydes (**6a**) was obtained via a biocatalytic, enantiogroup differentiation of the adonitol derivative **4**[29] to give monoacetate **5**; simple chemical manipulation of this ester gave the product (eq 1, where the conditions are (a) 4.0 mass equiv of *Candida cylindracea*, vinyl acetate, hexanes (0.005 M) (b) phthNH, DEAD, PPh_3, (c) TsOH, MeOH, and (d) $(COCl)_2$, DMSO, then NEt_3).

Aldehydes **6b** and **6c** were conveniently prepared (eqs 2 and 3, where the conditions are (a) phthNH, DEAD, PPh_3 and (b) $HgCl_2$, $CaCO_3$, $MeCN/H_2O$) from the corresponding thioacetals **7** and **8** derived from L-arabinose and D-xylose, respectively.[30]





Syntheses of compounds **1–3** from aldehydes **6a–c** are illustrated in Scheme I. Asymmetric allylations were effected using an optically active borane[31] chosen to pair in a constructive sense[32] with the Felkin–Anh bias[33–35] imposed by the α-chiral center of the substrate; this powerful transformation establishes a new C–C linkage and two chiral centers in a single step. Only one diastereomeric product was detected from each allylation reaction. Our previous studies had shown that acyclic systems similar to alkene **9** spontaneously close to give five-membered rings after mesylation of the alcohol and N-deprotection; however, it was not clear that the required nucleophilic displacement to form six-membered rings would be as facile. In the event, mesylation of the allylation products **9** and N-deprotection[36] gave derivatives which cyclized in refluxing ethanol. The cyclized products were isolated after N-protection, as the piperidines **10**. Hydroboration/oxidation of these alkenes to the alcohols **11** was difficult; BH_3·THF gave moderate yields whereas 9-BBN did not react in refluxing THF, and other hindered boranes were similarly unsuitable.

Ambient ^1H and ^{13}C NMR spectra of the piperidines **10** and **11** display "doubled" peaks which coalesce at elevated temperatures. This behavior is indicative of a relatively high activation energy for interconversions between two conformational isomers.

Mesylation and hydrogenolysis facilitated the second cyclization and almost complete deprotection; this is a slow reaction, requiring long reaction times and relatively large amounts of palladium on carbon. Acid-catalyzed hydrolysis of the intermediate MOM ether and ion-exchange chromatography gave the target compounds **1–3**. (Compound **2** was fully characterized as the tetraacetate due to difficulties associated with purification.)

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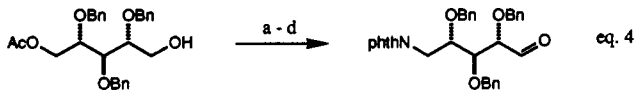
Monoacetate **6**, formed in the biocatalytic resolution described in eq 1, is optically active by virtue of its protecting functionality alone. Consequently, simple manipulation of protecting groups (eq 4, where the conditions are (a) $(COCl)_2$, DMSO, then NEt_3, (b) Ph_3PCH_2 then hydrolysis, (c) phthNH, DEAD, PPh_3, and (d) O_3, Me_2S) provided access to aldehyde **6d**, the enantiomer of **6a**.



5 **6d** 30 % eq. 4

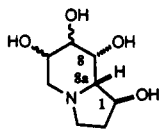
Theoretically, aldehyde **6d** could be carried through a sequence almost identical to that shown in Scheme I to give the enantiomer of target compound **1**.

Biological Activities

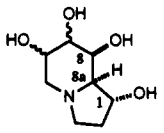
Indolizidines **1–3** showed no significant inhibitory activity against the following enzymes when tested at levels as high as 2×10^{-4} M: amyloglucosidase, yeast α-glucosidase, almond β-glucosidase, coffee bean α-galactosidase, calf liver β-galactosidase, jackbean α-mannosidase, or *Aspergillus fumagitis* β-mannosidase. Nevertheless, preliminary tests indicate compounds **1** and **3** have weak anti-HIV-1 activities in cells. Compound **2** is inactive against HIV-1 in the same assay.[37] Full details of these biological studies will be reported when more stereoisomers in the series have been prepared and tested.

Conclusions

Several steps in the strategy outlined above could be modified to obtain other stereoisomers of castanospermine. For instance, the enantiomers of **1–3** could be synthesized using this methodology since both optical isomers of the allylating reagent are readily available. Similar syntheses from other pentose derivatives (e.g., lyxose-derived aldehydes) should also be possible. Consequently, we are reasonably confident that the eight stereoisomers with 1*S*,8*R*,8a*S* or 1*R*,8*S*,8a*R* stereochemistries could be prepared using simple variants of the route described above.



1*S*,8*R*,8a*S*



1*R*,8*S*,8a*R*

Preparations of the other 23 stereoisomers require antiselective allylations and allylations which overcome the Felkin–Anh bias of the substrate. The current focus of our research is to develop the chemistry required for closely related synthetic sequences which could be applied to all the stereoisomers of castanospermine. Eventually, NMR data for the compounds will be used in conjunction with calculations to assess their solution conformations; this information then can be correlated with their biological activities to furnish meaningful structure/activity relationships. The fact that compounds **1** and **3** show some anti-HIV-1 activity adds further impetus to this research.

Experimental Section

General Procedures. Melting points are uncorrected. High-field NMR spectra were recorded on a 300- or 250-MHz instrument using $CDCl_3$ solvent unless otherwise stated. Chemical shifts are reported in δ ppm relative, in most cases, to $CHCl_3$ as an internal reference (7.25 ppm for ^1H and 77.1 ppm for ^{13}C). Occasionally, MeOH (3.31 ppm for ^1H and 49.6 ppm for ^{13}C) and dioxane (3.53 ppm for ^1H and 66.5 ppm for ^{13}C) were used as internal references. Where abbreviated DEPT sequence experiments were carried out during ^{13}C NMR experiments, the carbon multiplicities are listed as (C) quaternary, (CH_2) methylene, and (CH/CH_3) methine/methyl. The purity of all products was assessed as >95% via ^1H and ^{13}C NMR analyses. Thin-layer chromatography was performed on silica gel 60 F_{254} plates. Flash chromatography was performed on SP Silica Gel 60 (230–400 mesh ASTM). Tetrahydrofuran (THF) was distilled immediately before use from sodium benzophenone ketyl. Dichloromethane (CH_2Cl_2) was distilled immediately before use from CaH_2.

Methods used for measurements of inhibitory activities[3] and anti-HIV-1 properties have been described previously.[37]

2,3,4-Tri-*O*-benzyladonitol (4). Pyridine (36.0 mL, 444 mmol, 14.8 equiv) was added to 4.56 g (30.0 mmol, 1.00 equiv) of adonitol, 16.7 g (60.0 mmol, 2.00 equiv) of trityl chloride, and a catalytic amount of 4-(*N*,*N*'-dimethylamino)pyridine under N_2. The resulting green solution was stirred at 25 °C for 33 h. The reaction mixture was then poured into saturated NH_4Cl solution (150 mL) and extracted with CH_2Cl_2 (2 × 75 mL). The combined organic layers were washed with saturated NaCl solution (75 mL) and dried ($MgSO_4$). Removal of the volatiles in vacuo gave a yellow oil which was stirred under hexane for 8 h. The hexane was decanted off, and the crude 1,5-di-*O*-trityladonitol which remained was placed under high vacuum (1 mmHg) for 4 h. A viscous yellow oil formed which crystallized on standing: ^1H NMR δ 7.00–7.40 (m, 30 H), 3.60 (br s, 3 H), 3.25 (m, 4 H), 2.85 (br s, 2 H), 2.80 (br s, 1 H); ^{13}C NMR δ 128.6 (CH/CH_3), 128.0 (CH/CH_3), 127.2 (CH/CH_3), 87.2 (C), 73.3 (CH/CH_3), 71.9 (CH/CH_3), 65.0 (CH_2).

The crude 1,5-di-*O*-trityladonitol (~30.0 mmol, 1.00 equiv) and a catalytic amount of tetrabutylammonium iodide was added to a suspension of 14.1 g (300 mmol, 10.0 equiv) of 50% sodium hydride dispersion in oil in THF (250 mL) at 0 °C under N_2. After the mixture was stirred for 5 min at 0 °C followed by 30 min at 25 °C, 8.63 mL (72.6 mmol, 4.00 equiv) of benzyl bromide was added and the resulting gray suspension refluxed for 27 h. The reaction was then decanted (CAUTION!) into saturated NH_4Cl solution (400 mL), taking care to avoid as much as possible transferring the excess sodium hydride and solid residues. The aqueous layer was extracted with Et_2O (3 × 200 mL), and the combined organic fractions were dried ($MgSO_4$). Removal of volatiles in vacuo yielded the crude 1,5-di-*O*-trityl-2,3,4-tri-*O*-benzyladonitol as a red oil which was partially purified by passing through a short column of flash silica (50 % EtOAc in hexane): ^1H NMR δ 6.88–7.51 (m, 15 H), 4.66–4.70 (d, J = 9.5 Hz, 2 H), 4.42–4.54 (m, 4 H), 3.84–3.91 (m, 3 H), 3.27–3.41 (m, 4 H); ^{13}C NMR δ 128.9 (CH/CH_3), 128.5 (CH/CH_3), 128.3 (CH/CH_3), 128.1 (CH/CH_3), 127.8 (CH/CH_3), 127.3 (CH/CH_3), 127.1 (CH/CH_3), 86.7(C), 79.1 (CH/CH_3), 77.3 (CH/CH_3), 73.4 (CH_2), 72.7 (CH_2), 64.0 (CH_2).

p-Toluenesulfonic acid monohydrate (5.71 g, 30.0 mmol, 1.00 equiv) was added to the 1,5-di-*O*-trityl-2,3,4-tri-*O*-benzyladonitol (~30.0 mmol, 1.00 equiv) in 100 mL of MeOH and the resulting reaction mixture refluxed for 6 h. Volatiles were removed in vacuo yielding a brown oil. This was redissolved CH_2Cl_2 (250 mL), washed successively with 1 M NaOH (150 mL), saturated NH_4Cl solution (150 mL), and H_2O (150 mL), and then dried ($MgSO_4$). Removal of the volatiles in vacuo and purification by flash chromatography (30–40% EtOAc in hexane) gave the product **4** (5.3 g, 42%) as an oil: R_f 0.1 (20% EtOAc in hexane); ^1H NMR δ 7.27–7.38 (m, 15 H), 4.75 (s, 2 H), 4.63 (s, 4 H), 3.95 (t, J = 5.0 Hz, 1 H), 3.77 (m, 4 H), 3.73 (m, 2 H), 2.27 (br s, 2 H); ^{13}C NMR δ 137.8 (C), 128.5 (CH/CH_3), 128.1 (CH/CH_3), 127.9 (CH/CH_3), 78.8 (CH/CH_3), 78.7 (CH/CH_3), 74.2 (CH_2), 72.0 (CH_2), 61.1(CH_2); IR (neat) 3450 (br st), 1605 (md), 1585 (md) cm^{-1}; MS (EI, 70 eV) m/z (rel intensity) 423 [3, $(M+1)^+$], 422 (1, M^+); HRMS calcd for $C_{26}H_{30}O_5$ 422.20930, found 422.20914.

(2*S*,3*R*,4*R*)-1-*O*-Acetyl-2,3,4-tri-*O*-benzyladonitol (5). Hexane (232 mL) followed by 1.96 g (4 mass equiv) of the crude lipase obtained from *Candida cylindracea* (Sigma, EC 3.1.1.3) was added to a solution of 0.490 g (1.16 mmol, 1.00 equiv) of **4** in 2.14 mL (23.2 mmol, 20.0 equiv) of vinyl acetate. The resulting suspension was stirred at 25 °C for 30 h. The reaction was stopped by filtering through celite (washing with Et_2O). The volatiles were

(37) Montefiori, D. C.; Robinson, W. E.; Schuffman, S. S.; Mitchell, W. M. *J. Clin. Microbiol.* 1988, *26*, 231.

then removed in vacuo to give a yellow oil consisting of the monoacetate and diacetate formed in the reaction. Purification by flash chromatography (10–20% EtOAc in hexane) gave the product **5** (0.38 g, 70%) as a yellow oil: R_f 0.3 (20% EtOAc in hexane); $[\alpha]^{25}_D$ −9.0° (*c* 3.40, $CHCl_3$); >95% ee (from ^1H NMR using (+)-Eu(hfc)$_3$); ^1H NMR δ 7.26–7.41 (m, 15 H), 4.71 (s, 2 H), 4.62 (m, 4 H), 4.42 (dd, *J* = 2.8, 12.2 Hz, 1 H), 4.19 (dd, *J* = 5.7, 12.2 Hz, 1 H), 3.86 (m, 2 H), 3.74 (br s, 2 H), 3.70 (m, 1 H), 2.00 (s, 3 H); ^{13}C NMR δ 170.0 (C), 137.9 (C), 137.8 (C), 128.5 (CH/CH_3), 128.4 (CH/CH_3), 128.2 (CH/CH_3), 128.1 (CH/CH_3), 128.0 (CH/CH_3), 127.9 (CH/CH_3), 78.6 (CH/CH_3), 78.5 (CH/CH_3), 77.0 (CH/CH_3), 74.0 (CH_2), 72.2 (CH_2), 72.1 (CH_2), 63.6 (CH_2), 61.2 (CH_2), 21.0 (CH/CH_3); IR (neat) 3465 (br st), 1740 (st), 1605 (wk), 1585 (wk) cm^{-1}; MS (EI, 70 eV) *m*/*z* (rel intensity) 387 (1), 91 (100); HRMS calcd for $C_{28}H_{32}O_6$ 464.2199, found 464.2203. Anal. Calcd for $C_{28}H_{32}O_6$: C, 72.39; H, 6.94. Found: C, 72.20; H, 7.03.

1,5-Di-*O*-acetyl-2,3,4-tri-*O*-benzyladonitol (0.16 g, 28%) was also obtained as a yellow oil: ^1H NMR δ 7.32 (m, 15 H), 4.70 (s, 2 H), 4.67 (d, *J* = 11.6 Hz, 2 H), 4.61 (d, *J* = 11.6 Hz, 2 H), 4.45 (dd, *J* = 2.5, 11.9 Hz, 2 H), 4.21 (dd, *J* = 5.5, 11.9 Hz, 2 H), 3.87 (m, 3 H), 1.99 (s, 6 H); ^{13}C NMR δ 171.1 (C), 138.1 (C), 138.0 (C), 128.6 (CH/CH_3), 128.4 (CH/CH_3), 128.3 (CH/CH_3), 128.2 (CH/CH_3), 128.0 (CH/CH_3), 128.0 (CH/CH_3), 78.0 (CH/CH_3), 77.7 (CH/CH_3), 73.9 (CH_2), 72.5 (CH_2), 63.7 (CH_2), 21.2 (CH/CH_3); IR (neat) 1740 (st), 1605 (wk), 1495 (wk) cm^{-1}.

5-*N*-Phthalyl-2,3,4-tri-*O*-benzyl-D-ribose (6a). Diethyl azodicarboxylate (2.33 mL, 14.8 mmol, 2.00 equiv) was added to a suspension of 3.44 g (7.41 mmol, 1.00 equiv) of **5**, 3.88 g (14.8 mmol, 2.00 equiv) of triphenylphosphine, and 2.18 g (14.8 mmol, 2.00 equiv) of phthalimide in THF (24 mL) under N_2 at 0 °C. The resulting orange solution was stirred at 0 °C for 5 min and 25 °C for 12 h. Removal of the volatiles in vacuo gave an orange oil which was dissolved in Et_2O (18 mL) and left at −23 °C for 3 h. The solution containing crystals of the triphenylphosphine oxide byproduct was then filtered (washing with Et_2O), and the volatiles were removed in vacuo to give the crude (2*S*,3*R*,4*R*)-1-*O*-acetyl-5-*N*-phthalyl-2,3,4-tri-*O*-benzyladonitol as an orange oil: ^1H NMR δ 7.66–7.76 (m, 4 H), 7.25–7.41 (m, 10 H), 6.93–7.05 (m, 5 H), 4.88 (m, 1 H), 4.51–4.62 (m, 5 H), 4.37 (d, 10.0 Hz, 1 H), 4.20 (dd, 3.1, 9.6 Hz, 1 H), 4.10 (m, 2 H), 3.84 (m, 2 H), 3.69 (m, 1 H), 2.02 (s, 3 H); ^{13}C NMR δ 170.8 (C), 137.8 (C), 137.5 (C), 133.6 (CH/CH_3), 132.0 (CH/CH_3), 128.4 (CH/CH_3), 128.3 (CH/CH_3), 127.9 (CH/CH_3), 127.7 (CH/CH_3), 127.3 (CH/CH_3), 123.0 (CH/CH_3), 78.1 (CH/CH_3), 76.6 (CH/CH_3), 75.8 (CH/CH_3), 73.5 (CH_2), 72.7 (CH_2), 71.9 (CH_2), 63.0 (CH_2), 38.7 (CH_2), 20.9 (CH_2).

p-Toluenesulfonic acid monohydrate (4.21 g, 22.1 mmol, 3.00 equiv) was added to a solution of the crude (2*S*,3*R*,4*R*)-1-*O*-acetyl-5-*N*-phthalyl-2,3,4-tri-*O*-benzyladonitol in MeOH (35 mL) and stirred at 25 °C for 16 h. After this period, Et_2O (250 mL) and saturated $NaHCO_3$ (100 mL) were carefully added, the organic layer was collected, and the aqueous layer was extracted with Et_2O (100 mL). The combined organic fractions were dried ($MgSO_4$), and removal of the volatiles in vacuo followed by purification by flash chromatography (15–25% EtOAc in hexane) gave the (2*S*,3*R*,4*R*)-2,3,4-tri-*O*-benzyl-5-*N*-phthalyladonitol as an oil: ^1H NMR δ 7.60–7.75 (m, 4 H), 7.25–7.40 (m, 10 H), 6.90–7.10 (m, 5 H), 4.90 (d, 10 Hz, 1 H), 4.55–4.62 (m, 4 H), 4.05–4.40 (m, 4 H), 3.60–3.95 (m, 4 H); ^{13}C NMR δ 137.9 (C), 137.6 (C), 133.7 (CH/CH_3), 132.1 (CH/CH_3), 128.5 (CH/CH_3), 128.3 (CH/CH_3), 128.0 (CH/CH_3), 127.9 (CH/CH_3), 127.4 (CH/CH_3), 123.1 (CH/CH_3), 78.8 (CH/CH_3), 78.6 (CH/CH_3), 76.1 (CH/CH_3), 73.9 (CH_2), 72.6 (CH_2), 71.7 (CH_2), 60.4 (CH_2), 38.7 (CH_2); IR ($CHBr_3$) 3470 (br), 1770 (st), 1715 (st), 1495 (md) cm^{-1}; MS (EI, 70 eV) *m*/*z* (rel intensity) 552 [0.7, $(M+1)^+$], 551 (0.7, M^+), 91 (100); HRMS calcd for $C_{34}H_{33}NO_6$ 551.23076, found 551.22997.

Dimethyl sulfoxide (2.28 mL, 32.2 mmol, 4.00 equiv) was added to a solution of 1.41 mL (16.1 mmol, 2.00 equiv) of oxalyl chloride in CH_2Cl_2 (40 mL) under N_2 at −78 °C and the resulting colorless solution stirred at −78 °C for 20 min. A solution of (2*S*,3*R*,4*R*)-2,3,4-tri-*O*-benzyl-5-*N*-phthalyladonitol in CH_2Cl_2 (40 mL) was then added and the reaction allowed to warm to −35 °C over 75 min, after which 8.95 mL (64.4 mmol, 8.00 equiv) of Et_3N was added and the resulting precipitate allowed to warm to 25 °C and stirred for 8.5 h. After this period, CH_2Cl_2 (200 mL) and saturated NH_4Cl (75 mL) were added and the organic layer was collected, then washed with H_2O (75 mL) and dried ($MgSO_4$). Removal of the volatiles in vacuo and purification by flash chromatography (20–30% EtOAc in hexane) gave the product **6a** (2.62 g, 64%) as an oil: R_f 0.3 (25 % EtOAc in hexane); $[\alpha]^{27}_D$+27° (*c* 1.1, $CHCl_3$); ^1H NMR δ 9.42 (s, 1 H), 7.73 (m, 2 H), 7.66 (m, 2 H), 7.22–7.33 (m, 10 H), 7.12 (m, 5 H), 4.70 (m, 4 H), 4.58 (m, 2 H), 3.89–4.10 (m, 5 H); ^{13}C NMR δ 201.5 (CH/CH_3), 168.5 (C), 137.6 (C), 137.4 (C), 137.3 (C), 133.8 (CH/CH_3), 132.1 (C), 128.6 (CH/CH_3), 128.4 (CH/CH_3), 128.2 (CH/CH_3), 128.1 (CH/CH_3), 128.0 (CH/CH_3), 127.8 (CH/CH_3), 127.6 (CH/CH_3), 123.2 (CH/CH_3), 82.3 (CH/CH_3), 81.6 (CH/CH_3), 75.1 (CH/CH_3), 73.4 (CH_2), 73.0 (CH_2), 72.5 (CH_2), 38.0 (CH_2); IR ($CHBr_3$) 1770 (st), 1715 (st), 1615 (wk), 1495 (md) cm^{-1}; MS (EI, 70 eV) *m*/*z* (rel intensity) 519 (0.1), 91 (100).

5-*N*-Phthalyl-2,3,4-tri-*O*-benzyl-L-arabinose (6b). Diethyl azodicarboxylate (2.52 mL, 16.0 mmol, 2.00 equiv) was added to a solution of 4.21 g (8.00 mmol, 1.00 equiv) of **7**,[30] 4.19 g (16.0 mmol, 2.00 equiv) of triphenylphosphine, and 2.35 g (16.0 mmol, 2.00 equiv) of phthalimide in 25 mL of THF at 0 °C under N_2. The resulting orange solution was stirred at 0 °C for 5 min then 25 °C for 8.5 h. Removal of the volatiles in vacuo followed by purification by flash chromatography (10–20% EtOAc in hexane) gave 5-*N*-phthalyl-2,3,4-tri-*O*-benzyl-L-arabinose diethyl dithioacetal as an oil.

A portion of 3.20 g (32.0 mmol, 4.00 equiv) of calcium carbonate followed by 8.69 g (32.0 mmol, 4.00 equiv) of mercuric chloride was added to a solution of this dithioacetal in 121 mL of MeCN/H_2O (10:1). The resulting white precipitate was stirred at 25 °C for 30 min. The precipitate was then filtered (washing with MeCN) and removal of the volatiles in vacuo from the filtrate gave an orange oil. This oil was dissolved in CH_2Cl_2 (250 mL) and washed with 1 M KI solution (2 × 250 mL) and 30% $Na_2S_2O_3$ solution (250 mL) and then dried ($MgSO_4$). Removal of the volatiles in vacuo followed by purification by flash chromatography (10–20% EtOAc in hexane) gave the product **6b** (3.1 g, 70%) as colorless crystals (recrystallized from EtOAc/35–60 °C petroleum ether): mp 104–106 °C; R_f 0.3 (25% EtOAc in hexane); $[\alpha]^{24}_D$ −7.3° (*c* 1.1, $CHCl_3$); ^1H NMR δ 9.73 (s, 1 H), 7.75 (m, 2 H), 7.68 (m, 2 H), 7.26–7.38 (m, 10 H), 7.05 (m, 5 H), 4.72 (dd, *J* = 0.9, 11.2 Hz, 2 H), 4.60 (dd, *J* = 1.7, 11.2 Hz, 2 H), 4.45 (s, 2 H), 4.12 (dd, *J* = 6.6, 13.3 Hz, 1 H), 4.03 (s, 3 H), 3.92 (dd, *J* = 2.5, 13.9 Hz, 1 H); ^{13}C NMR δ 202.1 (CH/CH_3), 168.3 (C), 137.5 (C), 137.2 (C), 133.8 (CH/CH_3), 132.1 (C), 128.6 (CH/CH_3), 128.4 (CH/CH_3), 128.2 (CH/CH_3), 128.1 (CH/CH_3), 127.9 (CH/CH_3), 127.6 (CH/CH_3), 123.2 (CH/CH_3), 83.5 (CH/CH_3), 80.0 (CH/CH_3), 76.3 (CH/CH_3), 73.5 (CH_2), 72.6 (CH_2), 38.9 (CH_2); IR ($CHBr_3$) 1770 (md), 1710 (st), 1615 (wk), 1495 (md) cm^{-1}; MS (EI, 70 eV) *m*/*z* (rel intensity) 458 (1), 91 (100). Anal. Calcd for $C_{34}H_{31}NO_6$: C, 74.30; H, 5.69; N, 2.55. Found: C, 73.97; H, 5.76; N, 2.63.

5-*N*-Phthalyl-2,3,4-tri-*O*-benzyl-D-xylose (6c). The procedure used was analogous to the one described for **6b**; **8**[30] was converted to **6c** in 95% yield after flash chromatography (10–30% EtOAc in hexane); R_f 0.3 (25% EtOAc in hexane); ^1H NMR δ 9.70 (s, 1 H), 7.76 (m, 2 H), 7.69 (m, 2 H), 7.25–7.32 (m, 10 H), 7.08 (m, 5 H), 4.80 (d, *J* = 11.8 Hz, 1 H), 4.74 (d, *J* = 11.4 Hz, 1 H), 4.61 (d, *J* = 11.5 Hz, 1 H), 4.58 (d, *J* = 11.8 Hz, 1 H), 4.50 (d, *J* = 11.7 Hz, 1 H), 4.37 (d, *J* = 11.7 Hz, 1 H), 4.06 (m, 2 H), 3.87 (m, 3 H); ^{13}C NMR δ 201.4 (CH/CH_3), 168.2 (C), 137.5 (C), 137.1 (C), 133.9 (CH/CH_3), 132.1 (C), 128.5 (CH/CH_3), 128.2 (CH/CH_3), 128.1 (CH/CH_3), 127.6 (CH/CH_3), 123.2 (CH/CH_3), 81.4 (CH/CH_3), 79.2 (CH/CH_3), 75.1 (CH/CH_3), 73.9 (CH_2), 73.5 (CH_2), 73.1 (CH_2), 38.3 (CH_2); IR ($CHBr_3$) 1770 (st), 1715 (st), 1605 (wk), 1495 (wk) cm^{-1}; MS (EI, 70 eV) *m*/*z* (rel intensity) 474 (1), 92 (100).

5-*N*-Phthalyl-2,3,4-tri-*O*-benzyl-L-ribose (6d). Dimethyl sulfoxide (4.00 mL, 56.4 mmol, 4.00 equiv) was added to a solution of 2.46 mL (28.2 mmol, 2.00 equiv) of oxalyl chloride in CH_2Cl_2 (40 mL) under N_2 at −78 °C and the resulting colorless solution stirred at −78 °C for 20 min. A solution of 6.57 g (14.1 mmol, 1.00 equiv) of **5** in CH_2Cl_2 (40 mL) was added, and the reaction was allowed to warm to −35 °C over 60 min. After this period, 16.3 mL (112.8 mmol, 8.00 equiv) of Et_3N was added, and the resulting precipitate allowed to warm to 25 °C and stirred for 6 h. Addition of 200 mL of CH_2Cl_2 and 100 mL of saturated NH_4Cl and separation of the organic layer gave a solution which was washed with H_2O and dried ($MgSO_4$). Removal of the volatiles in vacuo and purification by flash chromatography (15–30% EtOAc in hexane)

gave 2,3,4-tri-*O*-benzyl-5-*O*-acetyl-L-ribose which was used without further purification: R_f 0.66 (25% EtOAc in hexane); $[\alpha]^{25}_D$ −33° (*c* = 1.0, $CHCl_3$); ^1H NMR δ 9.46 (s, 1 H), 7.25–7.36 (m, 15 H), 4.49–4.74 (m, 7 H), 4.10 (s, 2 H), 3.92 (s, 2 H), 1.97 (s, 3 H); ^{13}C NMR δ 201.3 (C), 171.0 (C), 137.2 (C), 128.5 (CH/CH_3), 128.4 (CH/CH_3), 128.2 (CH/CH_3), 128.1 (CH/CH_3), 128.0 (CH/CH_3), 127.8 (CH/CH_3), 81.9 (CH/CH_3), 80.0 (CH/CH_3), 75.2 (CH/CH_3), 73.3 (CH_2), 72.6 (CH_2), 72.5 (CH_2), 62.2 (CH_2), 20.9 (CH/CH_3); IR (neat) 1730 cm^{-1}.

n-Butyllithium (11.1 mL, 23.5 mmol, 2.50 equiv) was added dropwise to a solution of methyltriphenylphosphonium bromide in THF (50 mL) at −35 °C and the solution stirred for 30 min. A solution of 4.34 g (9.40 mmol, 1.00 equiv) of 2,3,4-tri-*O*-benzyl-5-*O*-acetyl-L-ribose was added and the solution stirred at −35 °C for 30 min, allowed to warm to 25 °C, and stirred for 4 h and then refluxed for 12 h. Removal of the volatiles in vacuo gave a brown oil which was dissolved in Et_2O (200 mL) and filtered through Celite, and the volatiles evaporated. The oil was purified by flash chromatography (10–20% EtOAc in hexane) giving (2*S*,3*R*,4*R*)-2,3,4-tris(benzyloxy)-hex-5-en-1-ol which was used without further purification: R_f 0.85 (25% EtOAc in hexane); $[\alpha]^{25}_D$ −30° (*c* = 1.0, $CHCl_3$); ^1H NMR δ 7.25–7.38 (m, 15 H), 5.92 (m, 1 H), 5.22 (dd, *J* = 1.7, 10.4 Hz, 1 H), 5.15 (dd, *J* = 0.6, 17 Hz, 1 H), 4.38–4.87 (m, 6 H), 4.08 (dd, *J* = 3.8, 6.4 Hz, 1 H), 3.89 (dd, *J* = 3.8, 8.0 Hz, 1 H), 3.80 (m, 2 H), 3.58 (m, 1 H); ^{13}C NMR δ 138.0 (C), 135.0 (CH/CH_3), 128.4 (CH/CH_3), 128.2 (CH/CH_3), 127.9 (CH/CH_3), 127.7 (CH/CH_3), 119.8 (CH_2), 81.2 (CH/CH_3), 81.1 (CH/CH_3), 78.5 (CH/CH_3), 74.2 (CH_2), 71.7 (CH_2), 70.4 (CH_2), 61.0 (CH_2); IR (neat) 3425, 1500, 1470 cm^{-1}.

Diethyl azodicarboxylate (2.4 mL, 15.2 mmol, 2.00 equiv) was added to a suspension of 3.17 g (7.6 mmol, 1.00 equiv) of (2*S*,3*R*,4*R*)-2,3,4-tris(benzyloxy)hex-5-en-1-ol, 3.97 g (15.2 mmol, 2.00 equiv) of triphenylphosphine, and 2.23 g (15.2 mmol, 2.00 equiv) of phthalimide in THF (25 mL) under N_2 at 0 °C. The resulting orange solution was stirred at 0 °C for 5 min and at 25 °C for 12 h. Removal of the volatiles in vacuo gave an orange oil which was dissolved in Et_2O (25 mL) and left at −23 °C for 3 h. The resulting solution containing crystals of the triphenylphosphine oxide byproduct was then filtered (washing with Et_2O) and the volatiles were removed in vacuo to give the crude (2*S*,3*R*,4*R*)-1-phthalimido-2,3,4-tris(benzyloxy)hex-5-ene as a yellow oil. This was purified by flash chromatography (10–20% EtOAc in hexane) and recrystallized from EtOH: R_f 0.72 (25% EtOAc in hexane); $[\alpha]^{20}_D$ −7° (*c* = 1.0, $CHCl_3$); ^1H NMR δ 7.65–7.83 (m, 5 H), 7.25–7.42 (m, 9 H), 6.98–7.04 (m, 5 H), 5.95 (m, 1 H), 5.38 (m, 2 H), 4.84 (m, 2 H), 4.36–4.66 (m, 4 H), 4.06–4.11 (m, 2 H), 3.80 (m, 1 H); ^{13}C NMR δ 168.5 (C), 138.0 (C), 137.5 (C), 133.6 (CH/CH_3), 132.0 (CH/CH_3), 128.2 (CH/CH_3), 128.0 (CH/CH_3), 127.5 (CH/CH_3), 123.0 (CH/CH_3), 119.5 (CH_2), 82.0 (CH/CH_3), 81.0 (CH/CH_3), 76.0 (CH/CH_3), 73.5 (CH_2), 51.5 (CH_2), 70.5 (CH_2), 41.0 (CH_2), 38.5 (CH_2); IR 1775, 1700 cm^{-1}.

Ozone was bubbled through a solution of 2.04 g (3.63 mmol, 1.00 equiv) of (2*S*,3*R*,4*R*)-1-phthalimido-2,3,4-tris(benzyloxy)-hex-5-ene in CH_2Cl_2 (12 mL) and MeOH (4 mL) at −78 °C until the solution turned a pale blue. Dimethyl sulfide (1.1 mL, 14.5 mmol, 4.00 equiv) was then added and the solution stirred at −78 °C for 5 min and then allowed to warm to 25 °C. Removal of the volatiles in vacuo gave a clear oil which was purified by flash chromatography (10–20% EtOAc in hexane) to give the product **6d** (1.48 g, 30%) as an oil: R_f 0.6 (25% EtOAc in hexane); $[\alpha]^{25}_D$ −29° (*c* = 1.0, $CHCl_3$); ^1H NMR δ 9.45 (s, 1 H), 6.8–7.8 (m, 19 H), 4.3–4.9 (m, 6 H), 3.7–4.2 (m, 5 H), 3.45 (s, 3 H), 3.43 (s, 3 H); ^{13}C NMR δ 168.5 (C), 137.0 (C), 133.5 (CH/CH_3), 132.0 (CH/CH_3), 128.3 (CH/CH_3), 128.1 (CH/CH_3), 127.9 (CH/CH_3), 127.8 (CH/CH_3), 127.7 (CH/CH_3), 127.5 (CH/CH_3), 127.3 (CH/CH_3), 122.0 (CH_2), 82.0 (CH/CH_3), 81.4 (CH/CH_3), 74.8 (CH/CH_3), 73.2 (CH/CH_3), 72.7 (CH_2), 72.2 (CH_2), 37.8 (CH_2); IR (neat) 1780, 1720, 1610 cm^{-1}.

(2*R*,3*R*,4*S*,5*R*,6*R*)-5-Hydroxy-6-[(methoxymethyl)oxy]-1-*N*-phthalyl-2,3,4-tris(benzyloxy)oct-7-enamine (9a). A 1.5 M solution of *sec*-butyllithium in cyclohexane (2.49 mL, 3.74 mmol, 1.20 equiv) was added to a solution of 0.457 g (4.49 mmol, 1.44 equiv) of (methoxymethyl)allyl ether in THF (7.5 mL) under N_2 at −78 °C. The resulting dark yellow solution was stirred at −78 °C for 20 min. A solution of 3.74 mmol (1.20 equiv) of *B*-methoxydiisopinocampheylborane (derived from (+)-α-pinene via diisopinocampheylborane) in THF (8.5 mL) was then added and the resulting yellow solution stirred at −78 °C for 1 h. A portion of 0.609 mL (4.95 mmol, 1.59 equiv) of boron trifluoride etherate followed immediately by a precooled solution (−78 °C) of 1.71 g (3.11 mmol, 1.00 equiv) of **6a** in THF (11 mL) was then added to this solution. The resulting yellow solution was stirred at −78 °C for 30 min and then left at −23 °C for 12 h. Saturated $NaHCO_3$ (7.5 mL) followed by H_2O_2 (7.5 mL of a 30% by weight solution in water) was then added and the reaction heated to 40 °C for 2 h. Et_2O (100 mL) was added and the organic layer collected after shaking. The aqueous layer was extracted with Et_2O (50 mL), and the combined organic layers were then dried ($MgSO_4$). Removal of the volatiles in vacuo and purification by flash chromatography (20–30% EtOAc in hexane) gave the product **9a** (1.5 g, 73%) as an oil: R_f 0.2 (25% EtOAc in hexane); $[\alpha]^{25}_D$ +20° (*c* 3.6, $CHCl_3$); ^1H NMR δ 7.72 (m, 2 H), 7.66 (m, 2 H), 7.29–7.42 (m, 10 H), 6.92–7.05 (m, 5 H), 5.75 (m, 1 H), 5.27 (s, 1 H), 5.22 (d, *J* = 3.2 Hz, 1 H), 4.93 (d, *J* = 11.3 Hz, 1 H), 4.86 (d, *J* = 10.9 Hz, 1 H), 4.75 (d, *J* = 11.3 Hz, 1 H), 4.53–4.68 (m, 4 H), 4.38 (d, *J* = 12.0 Hz, 1 H), 4.35 (m, 1 H), 4.14 (m, 3 H), 3.86 (m, 3 H), 3.34 (s, 3 H); ^{13}C NMR δ 168.2 (C), 138.1 (C), 137.5 (C), 135.1 (CH/CH_3), 133.5 (CH/CH_3), 131.9 (C), 128.2 (CH/CH_3), 128.0 (CH/CH_3), 127.8 (CH/CH_3), 127.6 (CH/CH_3), 127.5 (CH/CH_3), 127.2 (CH/CH_3), 122.8 (CH/CH_3), 119.1 (CH_2), 94.3 (CH_2), 79.1 (CH/CH_3), 78.0 (CH/CH_3), 77.8 (CH/CH_3), 76.0 (CH/CH_3), 74.1 (CH/CH_3), 73.3 (CH_2), 73.2 (CH_2), 71.7 (CH_2), 55.7 (CH/CH_3), 38.9 (CH_2); IR ($CHBr_3$) 3470 (br md), 1775 (md), 1710 (st), 1615 (wk), 1495 (md) cm^{-1}; MS (EI, 70 eV) *m/z* (rel intensity) 528 (1), 91 (100).

(2*S*,3*S*,4*S*,5*R*,6*R*)-5-Hydroxy-6-[(methoxymethyl)oxy]-1-*N*-phthalyl-2,3,4-tris(benzyloxy)oct-7-enamine (9b). The procedure used was analogous to the one described for **9a**; **6b** was converted to **9b** in 72% yield after flash chromatography (20–30% EtOAc in hexane): R_f 0.2 (25% EtOAc in hexane); $[\alpha]^{25}_D$ −53° (*c* 1.3, $CHCl_3$); ^1H NMR δ 7.73 (m, 2 H), 7.68 (m, 2 H), 7.23–7.43 (m, 10 H), 6.93–7.02 (m, 5 H), 5.88 (m, 1 H), 5.28–5.33 (m, 2 H), 4.94 (d, *J* = 11.4 Hz, 1 H), 4.52–4.83 (m, 6 H), 4.13–4.36 (m, 5 H), 3.89 (m, 2 H), 3.77 (dd, *J* = 3.7, 8.2 Hz, 1 H), 3.39 (s, 3 H), 3.36 (d, *J* = 8.4 Hz, 1 H); ^{13}C NMR δ 168.2 (C), 138.0 (C), 137.5 (C), 135.3 (CH/CH_3), 133.6 (CH/CH_3), 132.0 (C), 128.3 (CH/CH_3), 128.0 (CH/CH_3), 127.7 (CH/CH_3), 127.6 (CH/CH_3), 127.3 (CH/CH_3), 122.9 (CH/CH_3), 119.0 (CH_2), 94.2 (CH_2), 79.0 (CH/CH_3), 77.8 (CH/CH_3), 77.0 (CH/CH_3), 74.1 (CH_2), 73.9 (CH/CH_3), 73.0 (CH_2), 71.7 (CH_2), 56.0 (CH/CH_3), 38.9 (CH_2); IR ($CHBr_3$) 3470 (br md), 1770 (st), 1710 (st), 1615 (wk), 1495 (md) cm^{-1}; MS (EI, 70 eV) *m/z* (rel intensity) 528 (1), 91 (100).

(2*R*,3*S*,4*S*,5*R*,6*R*)-5-Hydroxy-6-[(methoxymethyl)oxy]-1-*N*-phthalyl-2,3,4-tris(benzyloxy)oct-7-enamine (9c). The procedure used was analogous to the one described for **9a**; **6c** was converted to **9c** in 72% yield after flash chromatography (20–30% EtOAc in hexane): R_f 0.2 (25% EtOAc in hexane); $[\alpha]^{25}_D$ +18° (*c* 0.82, $CHCl_3$); ^1H NMR δ 7.74 (m, 2 H), 7.68 (m, 2 H), 7.22–7.44 (m, 10 H), 6.98–7.12 (m, 5 H), 5.91 (m, 1 H), 5.24–5.30 (m, 2 H), 4.59–4.85 (m, 7 H), 4.45 (d, *J* = 11.9 Hz, 1 H), 4.29 (d, *J* = 7.6 Hz, 1 H), 4.14 (m, 1 H), 3.92 (m, 5 H), 3.38 (s, 3 H), 2.97 (br s, 1 H); ^{13}C NMR δ 168.3 (C), 137.9 (C), 137.8 (C), 137.5 (C), 135.4 (CH/CH_3), 133.7 (CH/CH_3), 132.0 (C), 128.7 (CH/CH_3), 128.5 (CH/CH_3), 128.4 (CH/CH_3), 128.3 (CH/CH_3), 128.1 (CH/CH_3), 127.9 (CH/CH_3), 127.8 (CH/CH_3), 127.7 (CH/CH_3), 127.5 (CH/CH_3), 123.1 (CH/CH_3), 119.0 (CH_2), 94.2 (CH_2), 78.3 (CH/CH_3), 77.2 (CH/CH_3), 76.4 (CH/CH_3), 75.5 (CH/CH_3), 73.9 (CH_2), 73.7 (CH/CH_3), 73.2 (CH_2), 72.8 (CH_2), 56.0 (CH/CH_3), 38.8 (CH_2); IR ($CHBr_3$) 3465 (br st), 1775 (st), 1715 (st), 1615 (wk), 1495 (md) cm^{-1}; MS (EI, 70 eV) *m/z* (rel intensity) 529 (1), 528 (1), 91 (100).

(2*S*,3*S*,4*R*,5*R*)-1-Carbobenzoxy-3,4,5-tris(benzyloxy)-2-[(1*R*)-1-[(methoxymethyl)oxy]prop-2-enyl]piperidine (10a). Methanesulfonyl chloride (0.891 mL, 11.5 mmol, 7.00 equiv) was added to a solution of 1.07 g (1.64 mmol, 1.00 equiv) of **9a** and 1.83 mL (13.1 mmol, 8.00 equiv) of Et_3N in CH_2Cl_2 (8.5 mL) under N_2 at −78 °C. The resulting yellow precipitate was stirred at −78 °C for 30 min and then allowed to warm to 25 °C over 30 min. A 100-mL portion of CH_2Cl_2 was added and the resulting organic layer washed with 1 M NaOH (25 mL), saturated NH_4Cl solution (25 mL), and H_2O (25 mL). Removal of the volatiles in vacuo gave the crude mesylate of **9a** as an oil: ^1H NMR δ 7.68–7.77 (m,

4 H), 7.25–7.47 (m, 10 H), 6.87–6.99 (m, 5 H), 5.56 (m, 1 H), 5.27 (m, 1 H), 5.02 (d, J = 7.5 Hz, 1 H), 4.91 (d, J = 9.1 Hz, 1 H), 4.53–4.72 (m, 5 H), 4.30 (m, 1 H), 4.09–4.15 (m, 3 H), 3.88 (s, 2 H), 3.51 (m, 1 H), 3.38 (s, 3 H), 2.89 (s, 3 H); ^{13}C NMR δ 138.3 (C), 137.9 (C), 137.7 (C), 134.6 (CH/CH$_3$), 134.4 (CH/CH$_3$), 132.9 (C), 130.2 (CH/CH$_3$), 129.9 (CH/CH$_3$), 129.2 (CH/CH$_3$), 129.0 (CH/CH$_3$), 128.9 (CH/CH$_3$), 128.3 (CH/CH$_3$), 123.9 (CH/CH$_3$), 122.5 (CH$_2$), 96.7 (CH$_2$), 85.7 (CH/CH$_3$), 78.3 (CH/CH$_3$), 77.7 (CH/CH$_3$), 77.1 (CH/CH$_3$), 76.5 (CH/CH$_3$), 74.4 (CH$_2$), 73.5 (CH/CH$_3$), 72.7 (CH$_2$), 56.6 (CH/CH$_3$).

A 40% by weight solution of methylamine in H_2O (4.24 mL, 49.2 mmol, 30.0 equiv) was added to a suspension of the mesylate in EtOH (20 mL). The resulting solution was stirred at 25 °C for 9 h then refluxed for 48 h. Removal of the volatiles in vacuo gave an oil which was dissolved in CH_2Cl_2 (150 mL) and washed with 1 M NaOH (20 mL). Removal of the volatiles in vacuo gave the crude N-unprotected piperidine as an oil: ^{1}H NMR δ 7.20–7.67 (m, 15 H), 5.75 (m, 1 H), 5.21–5.33 (m, 3 H), 4.51–4.74 (m, 8 H), 4.20 (m, 1 H), 4.13 (t, 8.6 Hz, 1 H), 3.78 (m, 1 H), 3.47 (m, 1 H), 3.32 (s, 3 H), 3.29–3.40 (m, 2 H).

Saturated $NaHCO_3$ solution (12 mL) was added to a solution of the piperidine in THF (10 mL). The resulting emulsion was cooled to 0 °C and stirred vigorously while 0.375 mL (2.62 mmol, 1.60 equiv) of benzyl chloroformate was added. The reaction was stirred at 25 °C for 48 h. EtOAc (75 mL) was added and collected after shaking. The remaining aqueous layer was extracted with EtOAc (2 × 75 mL), and the combined organic fractions were dried ($MgSO_4$). Removal of the volatiles in vacuo and purification by flash chromatography (5–10% EtOAc in hexane) gave the product **10a** (0.66 g, 63%) as an oil: R_f 0.2 (10% EtOAc in hexane); $[\alpha]^{25}_D$ +19° (c 1.2, $CHCl_3$); ^{1}H NMR (2 conformations) δ 7.27–7.40 (m, 20 H), 5.59 (m, 1 H), 5.03–5.21 (m, 4 H), 4.91 (m, 2 H), 4.46–4.81 (m, 8 H), 4.18 (m, 1 H), 4.14 (m, 1 H, 1st conformation), 3.94 (m, 1 H, second conformation), 3.46 (m, 1 H), 3.31 (m, 1 H), 3.20 (s, 3 H, first conformation), 3.19 (s, 3 H, second conformation), 3.00 (m, 1 H); ^{13}C NMR (two conformations) δ 155.5 (C), 155.4 (C), 141.0 (C), 138.9 (C), 138.1 (C), 137.9 (C), 135.6 (CH/CH$_3$), 135.1 (CH/CH$_3$), 128.6 (CH/CH$_3$), 128.5 (CH/CH$_3$), 128.2 (CH/CH$_3$), 128.1 (CH/CH$_3$), 127.8 (CH/CH$_3$), 127.6 (CH/CH$_3$), 127.5 (CH/CH$_3$), 127.0 (CH/CH$_3$), 123.2 (CH/CH$_3$), 119.3 (CH$_2$), 119.1 (CH$_2$), 95.1 (CH$_2$), 94.9 (CH$_2$), 78.2 (CH/CH$_3$), 78.1 (CH/CH$_3$), 76.7 (CH/CH$_3$), 76.5 (CH/CH$_3$), 75.6 (CH/CH$_3$), 75.1 (CH/CH$_3$), 74.9 (CH/CH$_3$), 74.5 (CH$_2$), 71.3 (CH$_2$), 71.1 (CH$_2$), 71.0 (CH$_2$), 70.7 (CH$_2$), 67.6 (CH$_2$), 67.5 (CH$_2$), 65.3 (CH$_2$), 55.8 (CH/CH$_3$), 55.7 (CH/CH$_3$), 54.4 (CH/CH$_3$), 53.9 (CH/CH$_3$), 39.3 (CH$_2$), 38.9 (CH$_2$); IR (neat) 1705 (st), 1605 (wk) 1585 (wk) cm^{-1}; MS (EI, 70 eV) m/z (rel intensity) 628 (0.1), 627 (0.1), 91 (100). Anal. Calcd for $C_{39}H_{43}NO_7$: C, 73.45; H, 6.80; N, 2.20. Found: C, 73.54; H, 6.77; N, 2.57.

(2*S*,3*S*,4*S*,5*S*)-1-Carbobenzoxy-3,4,5-tris(benzyloxy)-2-[(1*R*)-1-[(methoxymethyl)oxy]prop-2-enyl]piperidine (10b). The procedure used was analogous to the one described for **10a**; **9b** was converted to **10b** in 45% yield after flash chromatography (0–20% EtOAc in hexane): R_f 0.6 (25 % EtOAc in hexane); $[\alpha]^{27}_D$ +22° (c 0.97, $CHCl_3$); ^{1}H NMR (two conformations) δ 7.27–7.36 (m, 20 H), 5.82 (m, 1 H), 5.12–5.29 (m, 4 H), 4.36–4.92 (m, 10 H), 4.21 (m, 2 H), 3.88 (br s, 1 H, first conformation), 3.85 (br s, 1 H, second conformation), 3.74 (br s, 1 H, first conformation), 3.66 (br s, 1 H, second conformation), 3.21 (s, 3 H, first conformation), 3.17 (s, 3 H, second conformation), 2.95 (d, J = 14.5 Hz, 1 H, first conformation), 2.85 (d, J = 17.5 Hz, 1 H, second conformation); ^{13}C NMR (two conformations) δ 156.3 (C), 156.1 (C), 138.8 (C), 138.2 (C), 136.4 (CH/CH$_3$), 136.3 (CH/CH$_3$), 128.4 (CH/CH$_3$), 128.2 (CH/CH$_3$), 128.1 (CH/CH$_3$), 128.0 (CH/CH$_3$), 127.8 (CH/CH$_3$), 127.7 (CH/CH$_3$), 127.6 (CH/CH$_3$), 127.5 (CH/CH$_3$), 127.4 (CH/CH$_3$), 118.5 (CH$_2$), 118.4 (CH$_2$), 94.0 (CH$_2$), 78.2 (CH/CH$_3$), 77.9 (CH/CH$_3$), 76.6 (CH/CH$_3$), 76.4 (CH/CH$_3$), 73.2 (CH$_2$), 73.1 (CH$_2$), 72.7 (CH$_2$), 72.3 (CH$_2$), 72.0 (CH/CH$_3$), 70.8 (CH$_2$), 70.5 (CH$_2$), 67.5 (CH$_2$), 67.4 (CH$_2$), 56.5 (CH/CH$_3$), 56.0 (CH/CH$_3$), 55.8 (CH/CH$_3$), 42.7 (CH$_2$), 42.1 (CH$_2$); IR (CHBr$_3$) 1685 (st), 1605 (wk), 1585 (wk) cm^{-1}; MS (EI, 70 eV) m/z (rel intensity) 576 (1), 91 (100). Anal. Calcd for $C_{39}H_{43}NO_7$: C, 73.45; H, 6.80; N, 2.20. Found: C, 72.90; H, 6.94; N, 2.64.

(2*S*,3*S*,4*S*,5*R*)-1-Carbobenzoxy-3,4,5-tris(benzyloxy)-2-[(1*R*)-1-[(methoxymethyl)oxy]prop-2-enyl]piperidine (10c). The procedure used was analogous to the one described for **10a**; **9c** was converted to **10c** in 58% yield after flash chromatography (0–10% EtOAc in hexane): R_f 0.2 (10 % EtOAc in hexane); $[\alpha]^{25}_D$ −5.2° (c 1.1, $CHCl_3$); ^{1}H NMR (two conformations) δ 7.27–7.37 (m, 20 H), 5.74 (m, 1 H), 5.09–5.31 (m, 4 H), 4.33–4.93 (m, 10 H), 4.32 (m, 1 H, first conformation), 4.11 (m, 1 H, second conformation), 3.91 (m, 1 H), 3.66 (m, 1 H), 3.43 (m, 1 H), 3.26 (s, 3 H, first conformation), 3.24 (s, 3 H, second conformation), 2.81 (m, 1 H); ^{13}C NMR (two conformations) δ 155.5 (C), 155.4 (C), 141.0 (C), 138.8 (C), 138.0 (C), 135.3 (CH/CH$_3$), 135.0 (CH/CH$_3$), 133.8 (CH/CH$_3$), 128.4 (CH/CH$_3$), 128.3 (CH/CH$_3$), 128.2 (CH/CH$_3$), 127.9 (CH/CH$_3$), 127.7 (CH/CH$_3$), 127.6 (CH/CH$_3$), 127.5 (CH/CH$_3$), 127.3 (CH/CH$_3$), 126.8 (CH/CH$_3$), 123.0 (CH/CH$_3$), 119.4 (CH$_2$), 119.2 (CH$_2$), 93.9 (CH$_2$), 81.8 (CH/CH$_3$), 81.5 (CH/CH$_3$), 79.6 (CH/CH$_3$), 79.4 (CH/CH$_3$), 77.6 (CH/CH$_3$), 77.4 (CH/CH$_3$), 77.2 (CH/CH$_3$), 75.4 (CH$_2$), 75.3 (CH$_2$), 73.0 (CH$_2$), 72.8 (CH$_2$), 72.6 (CH$_2$), 72.5 (CH$_2$), 67.6 (CH$_2$), 67.5 (CH$_2$), 64.8 (CH$_2$), 55.8 (CH/CH$_3$), 55.0 (CH/CH$_3$), 54.5 (CH/CH$_3$), 43.0 (CH$_2$), 42.7 (CH$_2$); IR (CHBr$_3$) 1700 (st), 1605 (wk) cm^{-1}; MS (EI, 70 eV) m/z (rel intensity) 576 (1), 91 (100). Anal. Calcd for $C_{39}H_{43}NO_7$: C, 73.45; H, 6.80; N, 2.20. Found: C, 73.87; H, 7.14; N, 2.72.

(2*S*,3*S*,4*R*,5*R*)-1-Carbobenzoxy-3,4,5-tris(benzyloxy)-2-[(1*R*)-3-hydroxy-1-[(methoxymethyl)oxy]propyl]piperidine (11a). A 1.0 M solution of borane–tetrahydrofuran complex in THF (1.65 mL, 1.65 mmol, 2.50 equiv) was added to a solution of 0.420 g (0.659 mmol, 1.00 equiv) of **10a** in THF (6.6 mL) under N_2 at 0 °C. The resulting solution was stirred at 25 °C for 3.75 h. After the solution was cooled to 0 °C, EtOH (6.5 mL) was carefully added followed by saturated $NaHCO_3$ solution (6.5 mL) and H_2O_2 (6.5 mL of a 30% by weight solution in H_2O). The reaction was stirred at 25 °C for 17 h and then heated to 50 °C for 2 h. The solution was diluted with 100 mL of Et_2O and washed with 1 M NaOH (25 mL), saturated NH_4Cl solution (25 mL), and H_2O (25 mL) then dried ($MgSO_4$). Removal of the volatiles in vacuo and purification by flash chromatography (20–30% EtOAc in hexane) gave the product **11a** (0.25 g, 58%) as a colorless oil: R_f 0.2 (40% EtOAc in hexane); ^{1}H NMR (two conformations) δ 7.22–7.36 (m, 20 H), 5.10 (m, 2 H), 4.90 (m, 2 H), 4.78 (m, 3 H), 4.63 (m, 1 H), 4.49 (m, 3 H), 4.27 (m, 1 H), 4.18 (s, 1 H), 4.05 (m, 1 H), 3.74 (m, 2 H), 3.57 (m, 2 H), 3.15 (s, 3 H, first conformation), 3.13 (s, 3 H, second conformation), 2.98 (m, 1 H), 1.79 (m, 1 H), 1.42 (m, 1 H); ^{13}C NMR (two conformations) δ 155.7 (C), 138.6 (C), 138.0 (C), 137.9 (C), 136.1 (C), 128.6 (CH/CH$_3$), 128.4 (CH/CH$_3$), 128.2 (CH/CH$_3$), 128.1 (CH/CH$_3$), 127.8 (CH/CH$_3$), 127.5 (CH/CH$_3$), 127.4 (CH/CH$_3$), 127.3 (CH/CH$_3$), 98.8 (CH$_2$), 77.1 (CH/CH$_3$), 76.8 (CH/CH$_3$), 76.6 (CH/CH$_3$), 75.7 (CH/CH$_3$), 75.6 (CH/CH$_3$), 74.8 (CH$_2$), 74.7 (CH$_2$), 71.2 (CH$_2$), 70.9 (CH$_2$), 67.8 (CH$_2$), 67.7 (CH$_2$), 58.4 (CH$_2$), 58.2 (CH$_2$), 55.6 (CH/CH$_3$), 54.9 (CH/CH$_3$), 54.4 (CH/CH$_3$), 39.2 (CH$_2$), 38.8 (CH$_2$), 34.9 (CH$_2$), 34.8 (CH$_2$); IR (neat) 3490 (br st), 1700 (st), 1605 (wk), 1585 (wk) cm^{-1}; MS (EI, 70 eV) m/z (rel intensity) 624 (0.3), 91 (100).

(2*S*,3*S*,4*S*,5*S*)-1-Carbobenzoxy-3,4,5-tris(benzyloxy)-2-[(1*R*)-3-hydroxy-1-[(methoxymethyl)oxy]propyl]piperidine (11b). The procedure used was analogous to the one described for **11a**; **10b** was converted **11b** in 60% yield after flash chromatography (20–30% EtOAc in hexane): R_f 0.2 (40% EtOAc in hexane); $[\alpha]^{25}_D$ +72° (c 3.5, $CHCl_3$); ^{1}H NMR (at 327 K) δ 7.26–7.36 (m, 20 H), 5.16 (d, J = 12.4 Hz, 1 H), 5.09 (d, J = 12.4 Hz, 1 H), 4.43–4.75 (m, 9 H), 4.19 (m, 3 H), 3.87 (dd, J = 2.9, 8.9 Hz, 1 H), 3.77 (m, 2 H), 3.69 (m, 1 H), 3.32 (s, 3 H), 3.06 (m, 1 H), 1.94 (m, 1 H), 1.74 (m, 1 H); ^{13}C NMR δ 156.2 (C), 138.5 (C), 138.1 (C), 136.4 (C), 128.5 (CH/CH$_3$), 128.3 (CH/CH$_3$), 128.1 (CH/CH$_3$), 128.0 (CH/CH$_3$), 127.7 (CH/CH$_3$), 127.6 (CH/CH$_3$), 127.5 (CH/CH$_3$), 98.4 (CH$_2$), 77.5 (CH/CH$_3$), 77.4 (CH/CH$_3$), 77.3 (CH/CH$_3$), 76.7 (CH/CH$_3$), 76.4 (CH/CH$_3$), 73.1 (CH$_2$), 72.7 (CH$_2$), 72.4 (CH$_2$), 72.3 (CH$_2$), 70.9 (CH$_2$), 67.7 (CH$_2$), 58.7 (CH$_2$), 56.2 (CH/CH$_3$), 55.8 (CH/CH$_3$), 43.0 (CH$_2$), 35.2 (CH$_2$); IR (neat) 3490 (br st), 1700 (st), 1605 (wk), 1585 (wk) cm^{-1}; MS (EI, 70 eV) m/z (rel intensity) 656 [0.2, (M+1)$^+$], 91 (100).

(2*S*,3*S*,4*S*,5*R*)-1-Carbobenzoxy-3,4,5-tris(benzyloxy)-2-[(1*R*)-3-hydroxy-1-[(methoxymethyl)oxy]propyl]piperidine (11c). The procedure used was analogous to the one described for **11a**; **10c** was converted to **11c** in 52% yield after flash chromatography (20–30% EtOAc in hexane): R_f 0.2 (40% EtOAc in hexane); $[\alpha]^{23}_D$ +46° (c 5.9, $CHCl_3$); ^{1}H NMR (two confor-

mations) δ 7.26–7.36 (m, 20 H), 5.09 (m, 2 H), 4.56–4.87 (m, 8 H), 4.39 (m, 1 H), 4.10 (m, 1 H), 3.37–3.86 (m, 6 H), 3.35 (s, 3 H, first conformation), 3.36 (s, 3 H, second conformation), 2.69 (m, 1 H), 1.83 (m, 1 H), 1.64 (m, 1 H); ^{13}C NMR (two conformations) δ 155.5 (C), 155.3 (C), 138.5 (C), 138.0 (C), 137.8 (C), 136.1 (C), 128.5 (CH/CH_3), 128.3 (CH/CH_3), 128.2 (CH/CH_3), 128.1 (CH/CH_3), 128.0 (CH/CH_3), 127.9 (CH/CH_3), 127.7 (CH/CH_3), 127.6 (CH/CH_3), 98.7 (CH_2), 98.5 (CH_2), 81.3 (CH/CH_3), 81.2 (CH/CH_3), 79.7 (CH/CH_3), 79.6 (CH/CH_3), 77.5 (CH/CH_3), 76.2 (CH/CH_3), 75.9 (CH/CH_3), 75.2 (CH_2), 72.8 (CH_2), 72.6 (CH_2), 72.5 (CH_2), 67.7 (CH_2), 67.6 (CH_2), 58.3 (CH_2), 58.1 (CH_2), 56.2 (CH/CH_3), 54.8 (CH/CH_3), 54.2 (CH/CH_3), 42.8 (CH_2), 42.5 (CH_2), 34.5 (CH_2); IR (neat) 3490 (br st), 1700 (st), 1605 (wk), 1585 (wk) cm^{-1}; MS (EI, 70 eV) *m/z* (rel intensity) 638 (0.3), 637 (0.3), 536 (16), 91 (100).

(1*R*,6*R*,7*R*,8*S*,8a*R*)-1,6,7,8-Tetrahydroxyindolizidine [(−)-1,6,8-triepicastanospermine] (1). Methanesulfonyl chloride (0.172 mL, 2.23 mmol, 7.00 equiv) was added to a solution of 0.208 g (0.318 mmol, 1.00 equiv) of **11a** and 0.355 mL (2.54 mmol, 8.00 equiv) of Et_3N in CH_2Cl_2 (8.0 mL) under N_2 at −78 °C. The resulting yellow precipitate was stirred at −78 °C for 30 min and then allowed to warm to 25 °C over 1 h. The solution was diluted with CH_2Cl_2 (100 mL) and washed with 1 M NaOH (25 mL), saturated NH_4Cl (25 mL), H_2O (25 mL), then dried ($MgSO_4$). Removal of the volatiles in vacuo and purification by flash chromatography (20–30% EtOAc in hexane) gave the mesylate of **11a** as an oil: ^{1}H NMR (two conformations) δ 7.25–7.37 (m, 20 H), 5.12 (m, 2 H), 4.70–4.90 (m, 4 H), 4.40–4.70 (m, 6 H), 4.15–4.70 (m, 4 H), 3.20–3.40 (m, 3 H), 3.41 (s, 3 H), 3.06 (s, 3 H), 2.70–2.75 (m, 2 H); ^{13}C NMR (two conformations) δ 155.5 (C), 155.3 (C), 138.0 (C), 137.5 (C), 137.0 (C), 136.0 (C), 128.3 (CH/CH_3), 128.2 (CH/CH_3), 128.0 (CH/CH_3), 127.6 (CH/CH_3), 127.4 (CH/CH_3), 127.1 (CH/CH_3), 127.0 (CH/CH_3), 98.2 (CH_2), 77.1 (CH/CH_3), 76.6 (CH/CH_3), 76.5 (CH/CH_3), 75.6 (CH/CH_3), 75.0 (CH/CH_3), 74.8 (CH_2), 71.0 (CH_2), 70.7 (CH_2), 67.6 (CH_2), 67.5 (CH_2), 67.3 (CH_2), 66.9 (CH_2), 60.1 (CH_2), 55.4 (CH/CH_3), 54.0 (CH/CH_3), 53.0 (CH/CH_3), 38.5 (CH_2), 38.0 (CH_2), 36.8 (CH/CH_3), 36.4 (CH/CH_3), 32.1 (CH_2).

Palladium on activated carbon (10%, 0.130 g, 0.122 mmol, 0.384 equiv) was added to a solution of the mesylate in EtOH (10 mL) and the resulting suspension stirred under 1250 psi of H_2 at 25 °C for 4 d. The suspension was then filtered through Celite (washing thoroughly with EtOH). Removal of the volatiles in vacuo gave the mesylate salt of (1*R*,6*R*,7*R*,8*S*,8a*R*)-1-*O*-(methoxymethyl)-6,7,8-trihydroxyindolizidine as a colorless semicrystalline oil.

A solution of this mesylate salt in THF (6.0 mL) was acidified with 4 M HCl (20 mL) and heated to 65 °C for 9 h. Removal of the volatiles in vacuo and purification by ion-exchange chromatography (using Amberlite IRA-400 (OH) followed by Dowex 50X8-100 ion-exchange resins) gave the product **1** (0.041 g, 68%) as an oil. The stereochemistry was confirmed via COSY, HETCOR, and NOE NMR experiments: $[\alpha]^{27}_D$ −28° (*c* 0.95, MeOH); ^{1}H NMR (D_2O, ref MeOH) δ 4.30 (dd, *J* = 8.5, 11.7 Hz, 1 H, H-1), 4.05 (s, 1 H, H-8), 3.95 (s, 1 H, H-6), 3.63 (s, 1 H, H-7), 3.10 (d, *J* = 12.2 Hz, 1 H, H-5′), 2.94 (t, *J* = 8.7 Hz, 1 H, H-3′), 2.46 (q, *J* = 9.1 Hz, 1 H, H-3), 2.35 (d, *J* = 12.3 Hz, 1 H, H-5), 2.23 (m, 1 H, H-2′), 2.08 (d, *J* = 7.4 Hz, 1 H, H-8a), 1.63 (m, 1 H, H-2); ^{13}C NMR (D_2O, ref MeOH) δ 73.2 (CH/CH_3), 70.5 (CH/CH_3), 70.1 (CH/CH_3), 70.0 (CH/CH_3), 69.3 (CH/CH_3), 56.6 (CH_2), 52.2 (CH_2), 31.8 (CH_2); IR (neat) 3385 (br st), 2930 (md), 1105 (md) cm^{-1}; MS (EI, 70 eV) *m/z* (rel intensity) 189 (25, M^+), 145 (100); HRMS calcd for $C_8H_{15}NO_4$ 189.100 09, found 189.100 16.

(1*R*,6*S*,7*S*,8*S*,8a*R*)-1,6,7,8-Tetrahydroxyindolizidine [1,7,8-triepicastanospermine] (2). The procedure used was analogous to the one described for **1**: **11b** was converted to **2** in 48% yield after ion-exchange chromatography: ^{13}C NMR (D_2O, ref MeOH) δ 70.8 (CH/CH_3), 69.1 (CH/CH_3), 68.5 (CH/CH_3), 67.4 (CH/CH_3), 65.8 (CH/CH_3), 52.5 (CH_2), 52.4 (CH_2), 31.8 (CH_2); MS (EI, 70 eV) *m/z* (rel intensity) 203 (6), 189 (8, M^+), 93 (100); HRMS calcd for $C_8H_{15}NO_4$ 189.100 09, found 189.100 16.

An impurity was present that could not be removed by ion exchange chromatography, so the tetraacetate was formed and purified by flash chromatography (0–5% MeOH in $CHCl_3$). The stereochemistry was confirmed via COSY and NOESY NMR experiments: ^{1}H NMR ($CDCl_3$) δ 5.31 (t, *J* = 3.2 Hz, 1 H), 5.16 (m, 1 H), 5.07 (t, *J* = 2.7 Hz, 1 H), 4.88 (m, 1 H), 3.05 (m, 2 H), 2.62 (dd, *J* = 2.0, 7.4 Hz, 1 H), 2.49 (m, 2 H), 2.37 (m, 1 H), 2.15 (s, 3 H), 2.13 (s, 3 H), 2.04 (s, 3 H), 1.98 (s, 3 H), 1.65 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 170.0 (C), 169.9 (C), 71.8 (CH/CH_3), 67.1 (CH/CH_3), 67.0 (CH/CH_3), 66.8 (CH/CH_3), 64.7 (CH/CH_3), 51.9 (CH_2), 50.1 (CH_2), 30.0 (CH_2), 21.1 (CH/CH_3), 21.0, (CH/CH_3), 20.9 (CH/CH_3); MS (EI, 70 eV) *m/z* (rel intensity) 358 [0.4, $(M+1)^+$], 43 (100); HRMS calcd for $C_{16}H_{23}NO_8$ 357.142 33, found 357.141 56.

(1*R*,6*R*,7*S*,8*S*,8a*R*)-1,6,7,8-Tetrahydroxyindolizidine [(−)-1,6,7,8-tetraepicastanospermine] (3). The procedure used was analogous to the one described for **1**: **11c** was converted to **3** in 17% yield after ion-exchange chromatography. The stereochemistry was confirmed via COSY and NOESY NMR experiments: $[\alpha]^{25}_D$ −33° (*c* 0.31, MeOH); ^{1}H NMR (D_2O, ref MeOH) δ 4.40 (dt, 1 H, H-1), 4.01 (m, 1 H, H-8), 3.94 (t, *J* = 3.4 Hz, 1 H, H-7), 3.87 (m, 1 H, H-6), 3.12 (m, 2 H, H-3′ and H-5′), 2.88 (m, 1 H, H-5), 2.83 (m, 1 H, H-3), 2.74 (m, 1 H, H-8a), 2.29 (m, 1 H, H-2′), 1.72 (m, 1 H, H-2); ^{13}C NMR (D_2O, ref. dioxane) δ 68.9 (CH/CH_3), 68.8 (CH/CH_3), 68.6 (CH/CH_3), 68.2 (CH/CH_3), 67.8 (CH/CH_3), 53.4 (CH_2), 51.9 (CH_2), 29.9 (CH_2); MS (EI, 70 eV) *m/z* (rel intensity) 189 (24, M^+), 91 (100); HRMS calcd for $C_8H_{15}NO_4$ 189.100 09, found 189.100 16.

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Supplementary Material Available: Spectra for the key compounds prepared (35 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.