Facile Asymmetric Syntheses of 1-Deoxycastanospermine and 1-Deoxy-8a-*epi*-castanospermine

Stephen F. Martin,* Hui-Ju Chen, and Chih-Ping Yang

Department of Chemistry and Biochemistry, The University of Texas, Austin, Texas 78712

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The asymmetric syntheses of 1-deoxycastanospermine (6) and 1-deoxy-8a-*epi*-castanospermine (7) have been completed. A key step in these syntheses was the stereoselective addition of 2-furyllithium to the 4-*O*-*tert*-butyldiphenylsilyl-protected threose derivative 13 to give the C(7)–C(8) syn-adduct 14 as the major product. The diastereoselectivity of this reaction is particularly noteworthy since the related addition of 2-furyllithium to the corresponding 4-*O*-benzyl-protected aldehyde 8 proceeded in the *opposite* stereochemical sense to give primarily the C(7)–C(8) anti-adduct 10. Oxidation of the furan ring in 14 followed by refunctionalization led to the azido ketone 20, which was then converted into the imine 22 by several procedures. Depending upon the reaction conditions, stereoselective reduction of 22 furnished primarily either 23 or 24. Hydrolysis of the pyranoid acetal moiety in 23 and 24 followed by reductive amination gave 6 or 7, respectively.

Introduction

We have been interested in exploiting hydropyranones 2 that are produced by oxidative processing of furyl carbinols 1 as key intermediates in the asymmetric synthese of a variety of oxygenated natural products (Scheme I). Recent applications of this strategy from our laboratories have resulted in concise syntheses of Prelog-Djerassi lactone, tirandamycin, the seco acids of erythronolides A and B, and KDO.[1] As an extension of this work, we were intrigued by the possibility of using this transformation in the formulation of a novel entry to the highly hydroxylated alkaloids of the indolizidine family.[2] This class of alkaloids has attracted considerable attention because a number of members act as competitive inhibitors of glucosidases. Of the polyhydroxylated indolizidine alkaloids, castanospermine (3)[2c,3] and its derivatives have been the most frequent targets for synthetic investigations[4,5] owing to the documented potential of these substances as drug candidates for treating a variety of disease states including cancer and viral infections.[6] Application of the general strategy outlined in Scheme I to the problem of the synthesis of 3 is depicted in retrosynthetic format in Scheme II. One of the attractive features of this approach lay in its inherent flexibility since a variety of non-natural analogues could be available for biological testing by simply altering the stereochemistry at C(6)–C(8) in the starting carbinol 5. We wish to report the successful implementation of the basic elements of this strategy for the asymmetric synthesis of polyhydroxylated indolizidine alkaloids by its application to the preparation of 1-deoxycastanospermine (6) and 1-deoxy-8a-*epi*-castanospermine (7), a heretofore unknown compound.

Results and Discussion

Execution of the first phase of the synthetic plan required the preparation of a suitable protected derivative of the furyl carbinol 5, which we envisioned would be accessible via the stereoselective addition of 2-furyllithium to a protected derivative of threose. In this context, it is noteworthy that Mukaiyama had previously observed that the addition of 2-furyllithium to 8 gave mixtures of 9 and 10 in virtually equal amounts.[7] However, when the reaction was conducted in the presence of zinc bromide,

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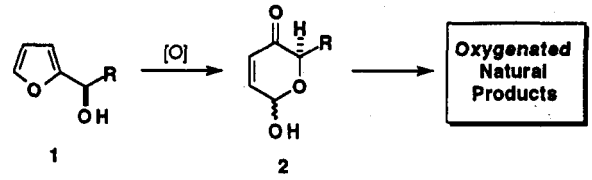
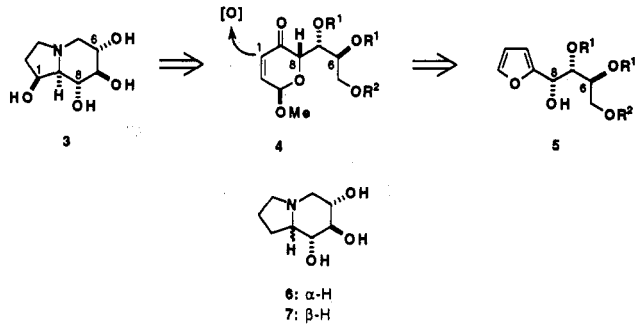
Scheme I



1 2

Scheme II



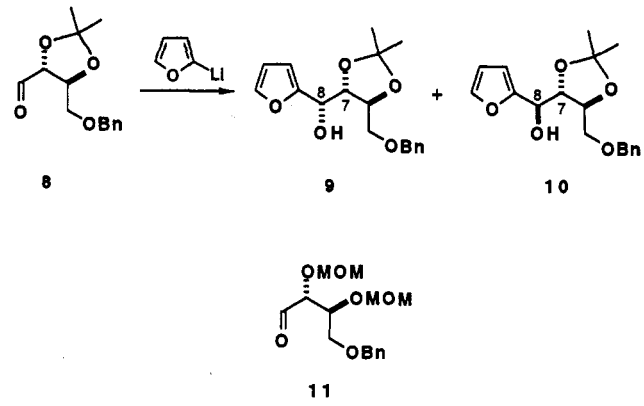
3 4 5

10 was obtained with >98% diastereoselectivity. The stereochemical outcome of this addition is consistent with either the β-chelate model or the Felkin–Anh model, but inasmuch as a coordinating metal ion was required for good selectivity, the former seems more likely. Since 10 has the undesired C(7)–C(8) anti-stereochemistry, we queried whether addition of 2-furyllithium to a threose derivative might be induced via an α-chelated transition state so that an adduct having the requisite C(7)–C(8) syn-relationship could be prepared.

To address this question, we first examined the stereoselectivity of the reaction of 2-furyllithium with the known aldehyde 11[8] in the presence of Lewis acids such as magnesium bromide and zinc bromide, conditions that were designed to promote nucleophilic addition via an α-chelated transition state. Even though the desired C(7)–C(8) syn-isomer was the major product under these conditions, the diastereoselectivity of this reaction never exceeded 2:1, and a more stereoselective process was clearly indicated.

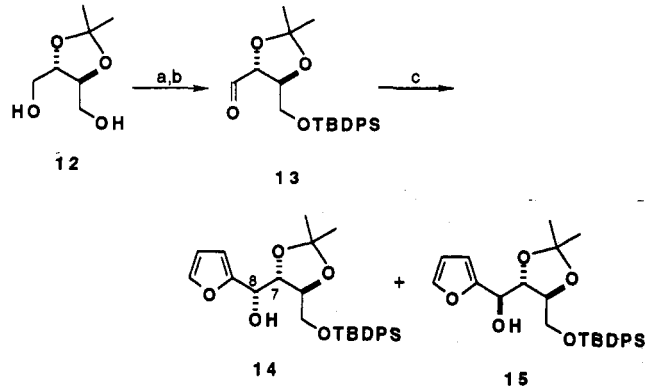
The reactions of 8 and 11 with different nucleophiles suggested that the diastereoselectivity of such additions depends upon the presence of Lewis acids and the specific nature of the hydroxyl protecting groups. Consequently, it seemed possible that using some combination of Lewis acid and hydroxyl protecting groups could lead to the enhanced formation of the desired C(7)–C(8) syn-adduct. We reasoned that if the transition state for the addition of 2-furyllithium to 8 to furnish 10 was organized by a β-chelate involving zinc, then replacement of the benzyl group on the γ-hydroxyl function with a bulkier protecting group might favor addition via an α-chelate to provide the C(7)–C(8) syn-adduct. In the event, the aldehyde 13 was prepared by selective protection and oxidation of the known diol 12[9] (Scheme IV).[10] The addition of 2-furyllithium to 13 in the absence of Lewis acids not surprisingly gave a mixture (1–2:1) of 14 and 15. However, when the

Scheme III



8 9 10 11

Scheme IV[a]



12 13 14 15

[a] (a) *n*-BuLi (1 equiv), TBDPS-Cl, rt; (b) $(COCl)_2$, DMSO, Et_3N, −78 °C; (c) 2-furyllithium, $ZnBr_2$ (excess), THF, −20 °C.

reaction was conducted in the presence of an excess of zinc bromide, a mixture (12:1) of 14 and 15 was obtained from which 14 was isolated in 90% yield after chromatographic separation. This complete reversal of stereochemistry in the addition of nucleophiles to 8 and 13 is remarkable, but the true origin of the effect remains obscure. We executed several preliminary ^1H NMR experiments in an attempt to gain insights regarding the precise nature of any chelated derivatives of 8 and 13 that might be present in solution, but these studies were inconclusive. Further investigations will be required to understand the fundamental basis for this phenomenon, but the ability to alter the diastereoselectivity in the additions of organometallic reagents to aldehydes derived from tartaric acid by simply changing the *distal* hydroxyl protecting group of threose derivatives is significant.

The furyl carbinol 14 was then transformed into the mixture (2:1) of protected hydropyranones 16 and 17 by oxidation[11] and methylation of the anomeric hydroxyl group (Scheme V). Since the stereochemistry at the anomeric center of 16 and 17 will eventually be lost, both could be converted into 1-deoxycastanospermine (6); however, in order to simplify characterization of the intermediates, only the major isomer 16 was carried forward. Reduction of 16 into the alcohol 18 was most effectively accomplished using K-Selectride in the presence

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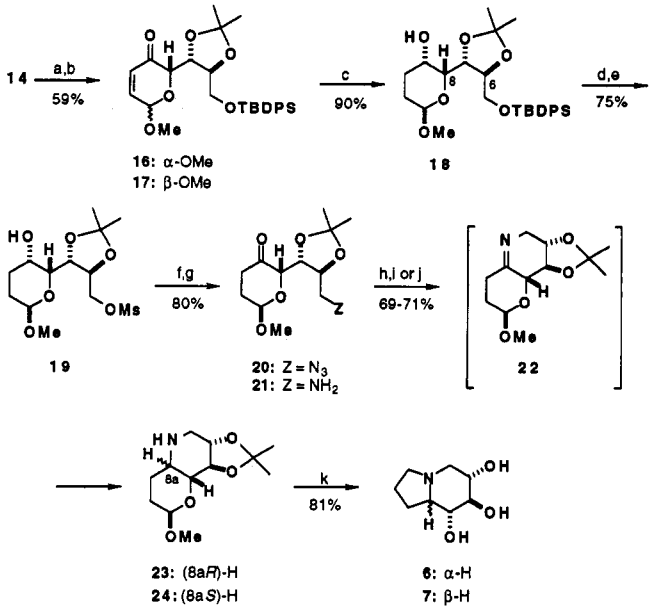
(10) The structure assigned to each compound was in accord with its spectral (^1H and ^{13}C NMR, IR, and mass) characteristics. Yields cited are for compounds judged to be >95% pure by ^1H NMR.

(11) Ho, T.-L.; Sapp, S. G. *Synth. Commun.* **1983**, *13*, 207.

Scheme V[a]

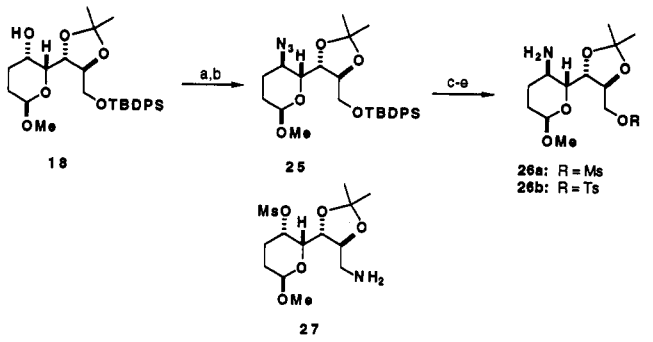


[a] (a) *tert*-BuOOH/VO(acac)$_2$, CH_2Cl_2, rt; (b) MeI/Ag_2O, rt; (c) K-Selectride, EtOH (2 equiv)/THF, −100 °C; (d) Bu_4NF, THF, 0 °C; (e) MsCl, Et_3N, DMAP, CH_2Cl_2, −40 °C; (f) NaN_3, DMF, 100 °C; (g) $(COCl)_2$, DMSO, NMM, −78 °C; (h) PPh_3, PhH, 70 °C; (i) $TiCl_4$; LAH/THF, Et_3N, CH_2Cl_2, −100 °C; (j) H_2 (70 psi), 10% Pd–C, MeOH; (k) H_3O^+; H_2 (70 psi), 10% Pd–C, MeOH.

of 2 equiv of ethanol,[12] but catalytic hydrogenation could also be employed. The C(5) hydroxyl group was then deprotected, and the intermediate diol was selectively converted into the mesylate **19**; small quantities (ca. 10%) of the dimesylate were typically obtained as a byproduct. Nucleophilic displacement of the mesylation with azide followed by oxidation of the alcohol by a Swern oxidation gave the key intermediate ketone **20**.

In the next phase of the synthesis, it was necessary to examine various tactics for transforming **20** into the desired target **6** or its epimer **7**. The key issue that needed to be resolved was the stereochemical course of the reduction of the cyclic imine **22**, which could be produced in situ by the cyclization of the amino ketone **21**. In one series of experiments, the azido ketone array in **20** was converted into the intermediate imine **22** by treatment of **20** with triphenylphosphine.[13] After exploring a number of hydride reductants, we discovered that the reduction of **22** proceeded with an acceptable level of stereoselectivity using lithium aluminum hydride in the presence of a Lewis acid such as titanium tetrachloride giving a mixture (4.4:1) of **23** and **24**. Sequential hydrolysis of the two cyclic acetal protecting groups followed by a second intramolecular reductive amination delivered 1-deoxycastanospermine (**6**). The **6** thus prepared was identical with an authentic sample.[14] Alternatively, reduction of the azido ketone **20** by catalytic hydrogen furnished exclusively **24**, which was readily converted into 1-deoxy-8a-*epi*-castanospermine (**7**) by hydrolysis of the hydropyranoid acetal and reductive amination. The biological activity of **7** was

Scheme VI[a]



[a] (a) MsCl, Et_3N, DMAP, CH_2Cl_2, rt; (b) NaN_3, DMF, 120 °C; (c) Bu_4NF, THF, 0 → 25 °C; (d) MsCl (or TsCl), Et_3N, DMAP, CH_2Cl_2, 0 → 25 °C; (e) H_2, 10% Pd–C, MeOH, rt.

evaluated in an α-glucosidase I enzyme assay, but it was not a good inhibitor, exhibiting an $IC_{50} > 200$ μg/mL.[15]

Since the reductive amination sequence leading from **20** to **23** was not highly stereoselective, we explored several other tactics for effecting the conversion of the intermediate alcohol **18** into **23** (Scheme VI). In particular, **18** was converted into the amino mesylate or tosylate **26a** or **26b**, respectively, by a straightforward sequence of reactions. Unfortunately all attempts to induce the efficient cyclization of either **26a** or **26b** by an intramolecular N-alkylation were unavailing; either starting material or unidentifiable polymeric substances were obtained. Thinking that the acetonide array might impose strain upon the transition state for cyclization, we also briefly examined the cyclization of the corresponding diol; however, none of the desired bicyclic amine was isolated. In a related series of experiments, we also prepared **27** as a potential precursor of **23** but were unable to induce its cyclization.

The successful synthesis of 1-deoxycastanospermine (**6**) and 1-deoxy-8a-*epi*-castanospermine (**7**) demonstrates for the first time the efficacy of the general plan outlined in Scheme I for the asymmetric synthesis of polyhydroxylated alkaloids. Further applications of this strategy to the synthesis of highly oxygenated natural products are in progress and will be reported in due course.

Experimental Section

General Procedures. Unless noted otherwise, all starting materials were obtained from commercial suppliers and were used without further purification. THF was distilled from potassium/benzophenone ketyl under nitrogen prior to use. DMF and DMSO were distilled under reduced pressure from calcium hydride and stored over 4-Å molecular sieves under argon. CH_2Cl_2, triethylamine, diisopropylethylamine, and *N*-methylmorpholine were distilled from calcium hydride and stored under argon. All reactions involving organometallic reagents or other moisture sensitive reactants were executed under an atmosphere of dry nitrogen or argon using oven-dried and/or flame-dried glassware. Flash chromatography was performed using silica gel 60 (230–400 mesh ASTM) with the indicated solvent. Melting points are uncorrected. ^1H NMR spectra were recorded at the indicated field strength as solutions in deuteriochloroform ($CDCl_3$), unless otherwise indicated. Chemical shifts are expressed in parts per million (ppm, δ) downfield from TMS and are referenced to $CDCl_3$ (7.24 ppm) as internal standard. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; comp, complex multiplet; br, broad. Coupling constants are given in hertz (Hz). ^{13}C NMR spectra were recorded at the indicated field strength as solutions in $CDCl_3$

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(13) Pearson, W. H.; Szura, D. P.; Postich, M. J. *J. Am. Chem. Soc.* **1992**, *114*, 1329.

(14) We thank Professor A. C. Richardson (Kings College, London) for copies of the ^1H NMR spectra of 1-deoxycastanospermine and Dr. Norton Peet (Marion Merrell Dow) for an authentic sample of 1-deoxycastanospermine for comparison.

(15) We thank Dr. Mohinder Kang (Marion Merrell Dow, Inc.) for conducting this assay.

unless otherwise indicated. Chemical shifts are reported in parts per million (ppm, δ) downfield from TMS and are referenced to the center line of $CDCl_3$ (77.0 ppm) as internal standard. IR spectra were recorded either neat on sodium chloride plates or as solutions as indicated and reported in wavenumbers (cm^{-1}).

4-*O*-(*tert*-Butyldiphenylsilyl)-2,3-*O*-isopropylidene-L-threitol. To a solution of 2,3-*O*-isopropylidene-L-threitol (**12**) (3.5 g, 21.8 mmol) in THF (109 mL) was added *n*-BuLi (3.7 N, 6.1 mL, 22.6 mmol) dropwise at 0 °C. The resulting solution was stirred at 0 °C for 40 min, whereupon *tert*-butylchlorodiphenylsilane (6.6 g, 24.2 mmol) was added. After stirring at 0 °C for 1 h and then at room temperature for 4 h, the reaction was quenched by adding saturated aqueous $NaHCO_3$ (30 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The crude material was purified by flash chromatography (hexane/EtOAc = 3:1) to give the product as a colorless oil (7.7 g, 88%): ^1H NMR (500 MHz) δ 7.68–7.37 (comp, 10 H), 4.07 (ddd, *J* = 8.1, 4.5, 4.2 Hz, 1 H), 3.97 (ddd, *J* = 8.1, 6.2, 4.0 Hz, 1 H), 3.82 (dd, *J* = 10.7, 4.0 Hz, 1 H), 3.81 (m, 1 H), 3.74 (dd, *J* = 10.7, 6.2 Hz, 1 H), 3.66 (ddd, *J* = 11.9, 7.9, 4.5 Hz, 1 H), 2.11 (dd, *J* = 7.9, 4.8 Hz, 1 H), 1.41 (s, 3 H), 1.39 (s, 3 H), 1.06 (s, 9 H); ^{13}C NMR (125 MHz) δ 135.6, 132.9, 132.8, 129.9 (2 C's), 127.8, 109.2, 79.5, 77.5, 64.2, 62.6, 27.1, 27.0, 26.8, 19.2; IR ($CHCl_3$) ν 3580, 3476, 1006 cm^{-1}; mass spectrum (CI) *m/z* 401.2155 [$C_{23}H_{33}O_4Si$ (M + H) requires 401.2148], 343, 265 (base), 187.

4-*O*-(*tert*-Butyldiphenylsilyl)-2,3-*O*-isopropylidene-L-threose (13). A solution of DMSO (12.1 g, 155 mmol) in anhydrous CH_2Cl_2 (35 mL) was added dropwise to a solution of oxalyl chloride (9.7 g, 77.4 mmol) in CH_2Cl_2 (190 mL) at −78 °C. After stirring for 5 min, a solution of 4-*O*-(*tert*-butyldiphenylsilyl)-2,3-*O*-isopropylidene-L-threitol (23.6 g, 58.9 mmol) in CH_2Cl_2 (75 mL) was added. The cloudy mixture was stirred at −78 °C for 15 min, and Et_3N (29.8 g, 294 mmol) was added dropwise. The resulting solution was warmed to room temperature and stirred for 1 h. Water (100 mL) was added, and the layers were separated. The organic layer was concentrated, and the residue was diluted with hexane/Et_2O (1:1) (200 mL) and washed with H_2O (3 × 100 mL) and saturated brine (50 mL). The aqueous layers were combined and extracted with Et_2O (2 × 100 mL). The combined organic fractions were dried (Na_2SO_4) and concentrated under reduced pressure to afford **13** as a yellow oil, which was used in the next step without further purification.

[*R*-(*R,*R**)]-1-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-3,3-dimethyl-α-(2-furanyl)-2,4-dioxolane-5-methanol (14) and [*S*-(*R**,*R**)]-1-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-3,3-dimethyl-α-(2-furanyl)-2,4-dioxolane-5-methanol (15).** To a solution of furan (24.1 g, 350 mmol) in anhydrous THF (350 mL) at −60 °C was added *n*-BuLi (2.87 N, 82 mL, 235 mmol), and the resulting solution was stirred at −10 °C for 2 h. After cooling to −20 °C, a solution of $ZnBr_2$ (35.0 g, 155 mmol) in THF (100 mL) was added dropwise while maintaining the temperature below −10 °C. A solution of **13** (23.5 g, 58.8 mmol) and $ZnBr_2$ (30.0 g, 133 mmol) in THF (200 mL) was added dropwise to the reddish solution and the stirring continued at −20 to −25 °C for 4 h. The reaction was quenched by adding saturated aqueous $NaHCO_3$ (600 mL) at 0 °C, and the mixture was filtered through a pad of Celite. The filter cake was washed with CH_2Cl_2 (200 mL), and the layers of the filtrate were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 200 mL). The combined organic fractions were washed with saturated $NaHCO_3$ (3 × 200 mL), dried (Na_2SO_4), and concentrated under reduced pressure. Flash chromatography (hexane/EtOAc = 3:1) of the residue provided **14** (24.7 g, 90%) and **15** (2.0 g, 7%) as colorless oils.

For **14**: ^1H NMR (300 MHz) δ 7.70–7.37 (comp, 10 H), 7.33 (br s, 1 H), 6.34–6.31 (comp, 2 H), 4.89 (dd, *J* = 5.6, 3.7 Hz, 1 H), 4.40 (dd, *J* = 7.8, 5.6 Hz, 1 H), 4.15 (m, 1 H), 3.70 (dd, *J* = 11.0, 4.5 Hz, 1 H), 3.51 (dd, *J* = 11.0, 3.8 Hz, 1 H), 2.94 (d, *J* = 3.7 Hz, 1 H), 1.42 (s, 3 H), 1.40 (s, 3 H), 1.05 (s, 9 H); ^{13}C NMR (75 MHz) δ 152.9, 142.1, 135.6, 132.9, 129.7, 127.7, 110.3, 109.5, 107.5, 79.2, 78.3, 68.2, 63.9, 27.1, 27.0, 26.8, 19.2; IR ν ($CHCl_3$) 3580, 3394 cm^{-1}; mass spectrum (CI) *m/z* 467.2265 [$C_{27}H_{35}O_5Si$ (M + H) requires 467.2254], 449, 391, 313, 154 (base).

For **15**: ^1H NMR (300 MHz) δ 7.68–7.35 (comp, 10 H), 7.33 (br s, 1 H), 6.33–6.30 (comp, 2 H), 4.73 (dd, *J* = 7.0, 5.0 Hz, 1 H), 4.43 (dd, *J* = 7.8, 5.0 Hz, 1 H), 4.07 (m, 1 H), 3.65 (dd, *J* = 11.0, 4.8 Hz, 1 H), 3.47 (dd, *J* = 11.0, 4.1 Hz, 1 H), 2.68 (d, *J* = 7.0 Hz, 1 H), 1.44 (s, 6 H), 1.05 (s, 9 H); ^{13}C NMR (75 MHz) δ 153.4, 142.3, 135.6, 133.0, 129.7, 127.7, 110.3, 109.9, 107.7, 79.5, 77.9, 68.1, 63.5, 27.3, 27.2, 26.8, 19.2; IR ($CHCl_3$) ν 3440 cm^{-1}; mass spectrum (CI) *m/z* 467.2263 [$C_{27}H_{35}O_5Si$ (M + H) requires 467.2254], 450, 391, 331, 221 (base).

[2*S*-[2α(2*R,4*R**),6α]]-2-[1-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-3,3-dimethyl-2,4-dioxolan-5-yl]-6-methoxy-2*H*-pyran-3(6*H*)-one (16) and [2*S*-[2α(2*R**,4*R**),6β]]-2-[1-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-3,3-dimethyl-2,4-dioxolan-5-yl]-6-methoxy-2*H*-pyran-3(6*H*)-one (17).** A solution of anhydrous *t*-BuOOH (3.0 M, 14.1 mL, 42.3 mmol) in 2,2,4-trimethylpentane was added dropwise at 0 °C to a solution of **14** (18.0 g, 38.6 mmol) and $VO(acac)_2$ (66.6 mg, 0.3 mmol) in CH_2Cl_2 (80 mL). The resulting reddish solution was stirred at 0 °C for 1 h and then at room temperature for 3.5 h. The pale yellow solution was filtered through a short column of silica gel and eluted with EtOAc. Removal of the volatiles under reduced pressure, followed by flash chromatography (hexane/EtOAc = 1:1) provided the intermediate hydropyranone as a pale yellow solid (15.1 g, 81%), which was immediately dissolved in MeI (60 mL) containing Ag_2O (14.5 g, 62.6 mmol). The suspension was stirred at room temperature for 58 h and then filtered through a short column of silica gel. The filtrate was concentrated under reduced pressure, and the residue was diluted with CH_2Cl_2 (50 mL) and washed with 20% aqueous $NaHCO_3$ (20 mL) and H_2O (20 mL). The organic layer was dried (Na_2SO_4), concentrated under reduced pressure, and the crude material was purified by flash chromatography (hexane/EtOAc = 3:1) to give **16** (7.5 g, 39% overall) and **17** (3.8 g, 20% overall) as colorless oils.

For **16**: ^1H NMR (300 MHz) δ 7.71–7.35 (comp, 10 H), 6.85 (dd, *J* = 10.1, 3.5 Hz, 1 H), 6.08 (d, *J* = 10.1 Hz, 1 H), 5.19 (d, *J* = 3.5 Hz, 1 H), 4.71 (br s, 1 H), 4.56–4.54 (comp, 2 H), 3.77–3.76 (comp, 2 H), 3.50 (s, 3 H), 1.42 (s, 3 H), 1.41 (s, 3 H), 1.05 (s, 9 H); ^{13}C NMR (75 MHz) δ 193.7, 143.2, 135.7, 135.6, 133.3, 133.1, 129.7, 129.6, 128.5, 127.7, 127.6, 109.9, 94.3, 78.3, 76.8, 73.7, 64.4, 56.6, 27.4, 26.8, 26.7, 19.2; IR ($CHCl_3$) ν 1698, 1642 cm^{-1}; mass spectrum (CI) *m/z* 497.2379 [$C_{28}H_{37}O_6Si$ (M + H) requires 497.2359], 465, 439, 200, 172 (base).

For **17**: ^1H NMR (300 MHz) δ 7.73–7.25 (comp, 10 H), 6.87 (dd, *J* = 10.5, 1.5 Hz, 1 H), 6.12 (dd, *J* = 10.5, 1.6 Hz, 1 H), 5.26 (br s, 1 H), 4.63 (dd, *J* = 8.0, 2.8 Hz, 1 H), 4.43 (m, 1 H), 4.37 (dd, *J* = 2.8, 1.0 Hz, 1 H), 3.80 (dd, *J* = 11.0, 4.1 Hz, 1 H), 3.72 (dd, *J* = 11.0, 3.8 Hz, 1 H), 3.54 (s, 3 H), 1.44 (s, 3 H), 1.43 (s, 3 H), 1.06 (s, 9 H); ^{13}C NMR (75 MHz) δ 193.3, 146.7, 135.7, 133.3, 133.2, 129.6, 129.5, 127.7, 109.8, 97.1, 77.8, 77.5, 77.3, 64.1, 56.4, 27.3, 26.8, 19.3; IR ($CHCl_3$) ν 1698 1641 cm^{-1}; mass spectrum (CI) *m/z* 496.2275 ($C_{28}H_{36}O_6Si$ requires 496.2281), 465, 439 (base), 311, 154.

[2*S*-[2α(2*R,4*R**),3β,6α]]-2-[1-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-3,3-dimethyl-2,4-dioxolan-5-yl]-6-methoxy-3,4,5,6-tetrahydro-2*H*-pyran-3-ol (18).** A solution of **16** (435 mg, 0.88 mmol) and anhydrous EtOH (81 mg, 1.76 mmol) in anhydrous THF (2.5 mL) was cooled to −100 °C, and K-Selectride (0.5 M in THF, 3.5 mL, 1.75 mmol) was added dropwise with stirring. After 2 h at −100 °C, the cooling bath was removed, and the reaction was quenched at 0 °C by adding 10% aqueous Na_2HPO_4 (7 mL) and 30% H_2O_2 (3.5 mL). The resulting mixture was stirred at room temperature for 30 min, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL), and the organic layers were combined, dried (Na_2SO_4), and concentrated under reduced pressure. The crude material was purified by flash chromatography (CH_2Cl_2/EtOAc = 10:1) to afford **18** (404 mg, 92%) as a colorless oil: ^1H NMR (500 MHz) δ 7.70–7.36 (comp, 10 H), 4.71 (d, *J* = 3.3 Hz, 1 H), 4.20 (dd, *J* = 8.0, 5.6 Hz, 1 H), 4.07 (dt, *J* = 8.0, 4.5 Hz, 1 H), 4.00 (br d, *J* = 3.8 Hz, 1 H), 3.86 (dd, *J* = 10.9, 4.5 Hz, 1 H), 3.82 (br d, *J* = 5.6 Hz, 1 H), 3.81 (dd, *J* = 10.9, 4.5 Hz, 1 H), 3.28 (s, 3 H), 2.90 (d, *J* = 3.8 Hz, 1 H), 2.11 (m, 1 H), 1.92 (m, 1 H), 1.75 (m, 1 H), 1.53 (m, 1 H), 1.44 (s, 3 H), 1.42 (s, 3 H), 1.06 (s, 9 H); ^{13}C NMR (125 MHz) δ 135.7, 135.6, 133.2, 133.1, 129.7 (2 C's), 127.7, 109.6, 98.6, 79.4, 78.2, 70.2, 64.4, 64.3, 54.8, 72.2, 26.9, 26.8, 25.0, 23.6, 19.2; IR ($CHCl_3$) ν 3500 cm^{-1}; mass spectrum (CI) *m/z* 500.2579 ($C_{28}H_{40}O_6Si$ requires 500.2594), 469, 391 (base), 255, 154.

[2*S*-[2α(2*R,4*R**),3β,6α]]-2-[1-(Hydroxymethyl)-3,3-dimethyl-2,4-dioxolan-5-yl]-6-methoxy-3,4,5,6-tetrahydro-2*H*-pyran-3-ol.** To a solution of **18** (390 mg, 0.8 mmol) in THF (10 mL) at 0 °C was added dropwise *n*-Bu_4NF (1.0 M in THF, 0.8 mL, 0.8 mmol) at 0 °C, and the solution was stirred for 15 min. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography (EtOAc/CH_2Cl_2 = 6:1) to provide the diol as a colorless oil (190 mg, 91%): ^1H NMR (500 MHz) δ 4.74 (d, *J* = 2.6 Hz, 1 H), 4.05–4.00 (comp, 3 H), 3.81–3.77 (comp, 2 H), 3.74 (dd, *J* = 7.8, 1.2 Hz, 1 H), 3.37 (s, 3 H), 2.49 (br s, 1 H), 2.23 (br s, 1 H), 2.10–1.98 (comp, 2 H), 1.76 (m, 1 H), 1.58 (m, 1 H), 1.43 (s, 3 H), 1.41 (s, 3 H); ^{13}C NMR (125 MHz) δ 109.4, 98.5, 80.8, 76.6, 71.7, 63.9, 63.4, 55.1, 27.0, 26.9, 24.7, 23.6; IR ($CHCl_3$) ν 3597, 3472 cm^{-1}; mass spectrum (CI) *m*/*z* 263.1496 [$C_{12}H_{23}O_6$ (M + H) requires 263.1495], 247, 231 (base), 173.

[2*S*-[2α(2*R,4*R**),3β,6α]]-2-[1-[[(Methylsulfonyl)oxy]methyl]-3,3-dimethyl-2,4-dioxolan-5-yl]-6-methoxy-3,4,5,6-tetrahydro-2*H*-pyran-3-ol (19).** Crushed, activated 4-Å molecular sieves (ca. 250 mg) were added to a solution of the above diol (200 mg, 0.76 mmol), Et_3N (86 mg, 0.85 mmol) and 4-(dimethylamino)pyridine (10 mg, 0.08 mmol) in CH_2Cl_2 (10 mL). The resulting mixture was cooled to −40 °C, MsCl (89 mg, 0.78 mmol) was added dropwise, and stirring was continued at −40 °C for 1 h. After warming to room temperature, the molecular sieves were removed by filtration, and the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography (EtOAc/CH_2Cl_2 = 5:1) to give **19** (213 mg, 82%) and the di-O-mesylated derivative (48 mg, 15%) as colorless oils. For **19**: ^1H NMR (500 MHz) δ 4.72 (d, *J* = 2.5 Hz, 1 H), 4.58 (dd, *J* = 11.1, 2.1 Hz, 1 H), 4.28 (dd, *J* = 11.1, 6.7 Hz, 1 H), 4.21 (m, 1 H), 3.99 (t, *J* = 8.0 Hz, 1 H), 3.95 (br s, 1 H), 3.74 (dd, *J* = 8.0, 1.2 Hz, 1 H), 3.37 (s, 3 H), 3.07 (s, 3 H), 2.04 (s, 1 H), 2.03 (br s, 1 H), 2.01 (br s, 1 H), 1.75 (m, 1 H), 1.58 (m, 1 H), 1.45 (s, 3 H), 1.42 (s, 3 H); ^{13}C NMR (125 MHz) δ 110.4, 98.3, 78.5, 74.8, 71.9, 70.1, 63.8, 55.1, 37.7, 27.0, 26.96, 24.8; IR ($CHCl_3$) ν 3590, 1360, 1176 cm^{-1}; mass spectrum (CI) *m*/*z* 340.1150 ($C_{13}H_{24}O_8S$ requires 340.1192), 309 (base), 213.

[2*S*-[2α(2*R,4*R**),3β,6α]]-2-[1-(Azidomethyl)-3,3-dimethyl-2,4-dioxolan-5-yl]-6-methoxy-3,4,5,6-tetrahydro-2*H*-pyran-3-ol.** A mixture of **19** (271 mg, 0.8 mmol) and NaN_3 (517 mg) in anhydrous DMF (10 mL) was stirred at 100 °C for 3 h. The mixture was cooled to room temperature and partitioned between Et_2O (50 mL) and H_2O (25 mL). The aqueous layer was extracted with Et_2O (50 mL), and the organic layers were combined and washed with H_2O (3 × 20 mL). The aqueous layers were collected and extracted with Et_2O/hexane (1:1) (3 × 20 mL). The organic fractions were combined, dried ($MgSO_4$), and concentrated under reduced pressure. The crude material was purified by flash chromatography (CH_2Cl_2/EtOAc = 4:1) to yield a colorless oil (197 mg, 86%): ^1H NMR (500 MHz) δ 4.70 (br d, *J* = 2.0 Hz, 1 H), 4.10 (ddd, *J* = 8.0, 6.0, 2.8 Hz, 1 H), 4.01 (t, *J* = 8.0 Hz, 1 H), 3.96 (m, 1 H), 3.71 (dd, *J* = 8.0, 1.1 Hz, 1 H), 3.62 (dd, *J* = 13.0, 2.8 Hz, 1 H), 3.36 (dd, *J* = 13.0, 6.0 Hz, 1 H), 2.08 (d, *J* = 6.2 Hz, 1 H), 2.05–1.97 (comp, 2 H), 1.75 (m, 1 H), 1.57 (m, 1 H), 1.47 (s, 3 H), 1.42 (s, 3 H); ^{13}C NMR (125 MHz) δ 110.2, 98.4, 79.7, 75.7, 71.9, 63.8, 54.9, 53.0, 27.1, 27.0, 24.8, 23.6; IR (neat) ν 3420, 2120 cm^{-1}; mass spectrum (CI) *m*/*z* 288.1547 [$C_{12}H_{22}N_3O_5$ (M + H) requires 288.1559], 272, 256, 228 (base).

[2*S*-[2α(2*R,4*R**),6α]]-2-[1-(Azidomethyl)-3,3-dimethyl-2,4-dioxolan-5-yl]-6-methoxy-4,5-dihydro-2*H*-pyran-3(6*H*)-one (20).** Oxalyl chloride (63 mg, 0.50 mmol) was added with stirring to a solution of DMSO (77 mg, 1.00 mmol) in CH_2Cl_2 (0.5 mL) at −78 °C. After stirring for 15 min, a solution of a portion of the above material (47 mg, 0.16 mmol) in CH_2Cl_2 (1.5 mL) was added. The resulting solution was stirred for 30 min, and then 4-methylmorpholine (117 mg, 1.16 mmol) was added at −78 °C. The reaction was allowed to warm up to room temperature and stirred for 1 h. After removal of the volatiles under reduced pressure, the residue was purified by flash chromatography (hexane/EtOAc = 3:1) to give **20** (43 mg, 92%) as a colorless oil: ^1H NMR (500 MHz) δ 4.92 (t, *J* = 4.5 Hz, 1 H), 4.33 (ddd, *J* = 7.6, 5.3, 3.2 Hz, 1 H), 4.29 (dd, *J* = 7.6, 3.7 Hz, 1 H), 4.27 (d, *J* = 3.7, 1 H), 3.50 (dd, *J* = 13.1, 3.2 Hz, 1 H), 3.42 (s, 3 H), 3.29 (dd, *J* = 13.1, 5.3 Hz, 1 H), 2.53 (m, 1 H), 2.43 (m, 1 H), 2.28 (m, 1 H), 1.98 (m, 1 H), 1.45 (s, 3 H), 1.39 (s, 3 H); ^{13}C NMR (125 MHz) δ 207.8, 110.3, 97.8, 76.5, 75.9, 73.8, 55.4, 52.3, 34.5, 28.9, 27.2, 26.6; IR (neat) ν 2130, 1740 cm^{-1}; mass spectrum (CI) *m*/*z* 286.1392 [$C_{12}H_{20}N_3O_5$ (M + H) requires 286.1403] 258, 228 (base), 200.

[3*S*-(4*R,4a*R**,6*R**,8a*R**)]-6-Methoxy-3,4-(isopropylidenedioxy)-5-oxadecahydroquinoline (23).** A solution containing PPh_3 (10.2 mg) and **20** (10.3 mg, 0.04 mmol) in benzene (0.5 mL) was stirred at 72 °C for 3 h. After being cooled to room temperature, the benzene was removed to give a yellow oil, which was dissolved in CH_2Cl_2 (1 mL) containing Et_3N (2.2 mg, 0.02 mmol) under argon. The solution was cooled to −100 °C, whereupon $TiCl_4$ (8.7 mg, 0.05 mmol) was added dropwise with stirring. After 10 min, $LiAlH_4$ (1.0 M in THF, 144 μL, 0.14 mmol) was added dropwise, and the resulting mixture was stirred at −100 °C for 1 h. The reaction was quenched by adding Et_3N (100 μL) and saturated aqueous $NaHCO_3$ (0.2 mL). The mixture was allowed to warm to room temperature with stirring over a period of 30 min, whereupon anhydrous K_2CO_3 and $MgSO_4$ were added to remove excess water. The solids were removed by filtration, and the organic filtrate was concentrated under reduced pressure to give a colorless oil that was a mixture of **23** and **24** (4.4:1 by ^1H NMR). This mixture was separated by flash chromatography (CH_2Cl_2/MeOH = 15:1) to yield **23** (4.5 mg, 56%) as a white solid and **24** as a colorless oil (1.0 mg, 13%). For **23**: mp 119.5–120.5 °C; ^1H NMR (500 MHz) δ 4.45 (dd, *J* = 9.6, 2.3 Hz, 1 H), 3.54 (s, 3 H), 3.53 (t, *J* = 9.1 Hz, 1 H), 3.41 (ddd, *J* = 11.0, 9.1, 4.3 Hz, 1 H), 3.31 (dd, *J* = 11.0, 4.3 Hz, 1 H), 3.26 (dd, *J* = 9.1, 8.7 Hz, 1 H), 2.75 (t, *J* = 11.0 Hz, 1 H), 2.36 (m, 1 H), 1.98 (m, 1 H), 1.92 (m, 1 H), 1.62 (m, 1 H), 1.52–1.43 (comp, 1 H), 1.47 (s, 3 H), 1.45 (s, 3 H); ^{13}C NMR (125 MHz) δ 110.5, 102.6, 81.0, 79.2, 76.7, 56.8, 56.7, 47.3, 30.7, 28.2, 26.9, 26.6; IR ($CHCl_3$) ν 3342, 1720, 1680 cm^{-1}; mass spectrum (CI) *m*/*z* 244.1563 [$C_{12}H_{22}NO_4$ (M + H) requires 244.1549], 212, 186 (base), 154.

[3*S*-(4*R,4a*R**,6*R**,8a*S**)]-6-Methoxy-3,4-(isopropylidenedioxy)-5-oxadecahydroquinoline (24).** A solution of **20** (10.2 mg, 0.04 mmol) in absolute methanol (1 mL) containing Pd/C (10%) (5.5 mg) was shaken under an atmosphere of H_2 (70 psi) at room temperature for 19 h. The mixture was then filtered, and the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography (CH_2Cl_2/MeOH = 10:1) to provide **24** (6.2 mg, 71%) as a colorless oil: ^1H NMR (500 MHz) δ 4.76 (d, *J* = 3.3 Hz, 1 H), 4.30 (d, *J* = 1.6 Hz, 1 H), 3.84 (ddd, *J* = 10.8, 9.5, 4.4 Hz, 1 H), 3.42–3.38 (comp, 2 H), 3.40 (s, 3 H), 2.70 (dd, *J* = 11.8, 10.8 Hz, 1 H), 2.66 (t, *J* = 2.1 Hz, 1 H), 2.15 (m, 1 H), 1.82 (m, 1 H), 1.67 (m, 1 H), 1.57 (m, 1 H), 1.47 (s, 3 H), 1.44 (s, 3 H); ^{13}C NMR (125 MHz) δ 109.2, 97.7, 81.3, 71.2, 66.1, 54.8, 51.2, 48.1, 26.8, 24.2, 23.1; IR ($CHCl_3$) ν 3338, 1668 cm^{-1}; mass spectrum (CI) *m*/*z* 244.1559 [$C_{12}H_{22}NO_4$ (M + H) requires 244.1549], 212, 186, 149 (base).

1-Deoxycastanospermine (6). A solution of **23** (10.8 mg, 0.04 mmol) in THF (ca. 0.1 mL) and aqueous HCl (4 N, 0.5 mL) was stirred at room temperature for 20 h. The volatiles were removed under reduced pressure, and the residue was diluted with MeOH (5 mL) and neutralized with K_2CO_3(s). The mixture was filtered to remove excess K_2CO_3(s), and the filtrate was concentrated under reduced pressure. The residue was diluted with CH_2Cl_2/MeOH (3:1) (10 mL), the mixture was filtered to remove any solids, and the filtrate was concentrated under reduced pressure. The resulting yellow oil (50.1 mg) was dissolved in absolute MeOH (0.6 mL) containing Pd/C (10%) (5.0 mg), and the mixture was shaken under an atmosphere of H_2 (75 psi) at room temperature for 23 h. The catalyst was removed by filtration, and the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography (CH_2Cl_2/MeOH = 3:2) to give **6** (6.2 mg, 81%) as a white solid: mp 177–179.5 °C (lit.[5a] 178–181 °C); $[\alpha]^{22}_D$ = +47.8° (*c* = 0.006, MeOH); lit.[5a] $[\alpha]_D$ = +50.6° (*c* = 0.2, MeOH); the spectral data were identical with that of an authentic sample.[14]

1-Deoxy-8a-*epi*-castanospermine (7). A solution of **24** (20.2 mg, 0.08 mmol) in THF (ca. 0.1 mL) and aqueous HCl (4 N, 0.5 mL) was stirred at room temperature for 16 h. After removal of the volatiles under reduced pressure, the residue was diluted with MeOH (5 mL) and neutralized with K_2CO_3(s). The mixture was filtered to remove excess K_2CO_3, and the filtrate was concentrated under reduced pressure. The residue was diluted with CH_2Cl_2/MeOH (3:1) (10 mL), and the mixture was filtered to remove any solids. After concentration of the filtrate, the

resulting yellow oil (35.2 mg) was dissolved in absolute MeOH (1 mL) containing Pd/C (10%) (9.0 mg), and the mixture was shaken under an atmosphere of H_2 (70 psi) at room temperature for 23 h. The catalyst was removed by filtration, and the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography (CH_2Cl_2/MeOH = 3:2) to yield 7 (10.8 mg, 75%) as a white solid: mp 149–150 °C; $[\alpha]^{22}_D$ = +41.8° (c = 0.0057, MeOH); ^{1}H NMR (d_5-pyridine) (500 MHz) δ 4.48 (m, 1 H), 4.18 (dd, J = 3.3, 0.7 Hz, 1 H), 3.80 (dd, J = 9.2, 3.3 Hz, 1 H), 3.47 (dd, J = 10.2, 5.2 Hz, 1 H), 2.96 (m, 1 H), 2.24 (t, J = 10.2 Hz, 1 H), 2.20–2.13 (comp, 2 H), 2.06 (dd, J = 17.3, 8.5 Hz, 1 H), 1.70 (m, 1 H), 1.65–1.56 (comp, 2 H); ^{13}C NMR (125 MHz) δ 78.6, 70.2, 69.4, 67.1, 58.1, 54.0, 25.1, 22.9; mass spectrum (CI) m/z 174.1135 [$C_8H_{16}NO_3$ (M + H) requires 174.1130] (base), 156, 154, 123.

[2*S*-[2α(2*R,4*R**),3β,6α]]-2-[1-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-3,3-dimethyl-2,4-dioxolan-5-yl]-3-[(methylsulfonyl)oxy]-6-methoxy-3,4,5,6-tetrahydro-2*H*-pyran.** To a solution of 18 (296 mg, 0.59 mmol) in CH_2Cl_2 (1.5 mL) containing Et_3N (120 mg, 1.18 mmol) and 4-(dimethylamino)pyridine (8.4 mg, 0.07 mmol) at 0 °C was added MsCl (102 mg, 0.89 mmol). The resulting solution was stirred at 0 °C for 10 min and then at room temperature for 3.5 h. The solvent was evaporated under reduced pressure, and the residue was purified by flash chromatography (CH_2Cl_2) to afford a colorless oil (288 mg, 84%): ^{1}H NMR (500 MHz) δ 7.73–7.36 (comp, 10 H), 4.83 (br s, 1 H), 4.59 (br s, 1 H), 4.16 (dd, J = 9.2, 7.2 Hz, 1 H), 4.03 (ddd, J = 7.2, 4.1, 2.4 Hz, 1 H), 3.97 (dd, J = 11.2, 2.4 Hz, 1 H), 3.77 (dd, J = 11.2, 4.1 Hz, 1 H), 3.74 (dd, J = 9.2, 1.1 Hz, 1 H), 3.23 (s, 3 H), 3.03 (s, 3 H), 2.15–2.09 (comp, 3 H), 1.61 (m, 1 H), 1.43 (s, 3 H), 1.41 (s, 3 H), 1.06 (s, 9 H); ^{13}C NMR (125 MHz) δ 135.8, 135.7, 129.6, 127.6 (2 C's), 109.8, 97.8, 82.3, 75.8, 72.8, 71.4, 63.9, 54.9, 38.0, 27.3, 27.1, 26.8, 23.8, 23.6, 19.3; IR ($CHCl_3$) ν 2859, 1428, 1356, 1172 cm^{-1}; mass spectrum (CI) m/z 579.2436 [$C_{29}H_{43}O_8SSi$ (M + H) requires 579.2448], 547, 489, 425, 347, 227 (base).

[2*S*-[2α(2*R,4*R**),3α,6α]]-2-[1-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-3,3-dimethyl-2,4-dioxolan-5-yl]-3-azido-6-methoxy-3,4,5,6-tetrahydro-2*H*-pyran (25).** A solution of a portion of the above material (31 mg, 0.05 mmol) and NaN_3 (36 mg, 0.55 mmol) in DMF (2 mL) was stirred at 105 °C for 15 h. The mixture was cooled to room temperature, diluted with pentane (5 mL), and filtered. The filtrate was concentrated, and the residue was purified by flash chromatography (hexane/EtOAc = 10:1) to yield **25** (25 mg, 87%) as a colorless oil: ^{1}H NMR (500 MHz) δ 7.72–7.26 (comp, 10 H), 4.66 (dd, J = 3.3, 0.9 Hz, 1 H), 4.33 (dt, J = 7.8, 4.4 Hz, 1 H), 4.22 (dd, J = 7.8, 3.2 Hz, 1 H), 3.81 (dd, J = 11.0, 4.4 Hz, 1 H), 3.78 (dd, J = 11.0, 4.4 Hz, 1 H), 3.73 (dd, J = 10.0, 3.2 Hz, 1 H), 3.28 (s, 3 H), 3.27 (m, 1 H), 1.95–1.90 (comp, 2 H), 1.83 (m, 1 H), 1.73 (m, 1 H), 1.45 (s, 3 H), 1.43 (s, 3 H), 1.07 (s, 9 H); ^{13}C NMR (125 MHz) δ 135.7, 135.6, 133.3, 133.2, 129.7, 129.6, 127.7, 109.5, 97.3, 78.8, 77.8, 70.3, 64.9, 56.8, 54.7, 28.6, 27.3, 26.9, 26.8, 23.9, 19.3; IR (neat) ν 2100 cm^{-1}; mass spectrum (CI) m/z 525.2642 ($C_{28}H_{39}N_3O_5Si$ requires 525.2659), 440, 388, 179, 154 (base).

[2*S*-[2α(2*R,4*R**),3α,6α]]-2-[1-(Hydroxymethyl)-3,3-dimethyl-2,4-dioxolan-5-yl]-3-azido-6-methoxy-3,4,5,6-tetrahydro-2*H*-pyran.** To a solution of **25** (89 mg, 0.17 mmol) in THF (2 mL) was added *n*-Bu_4NF (1.0 M in THF, 0.5 mL, 0.5 mmol) dropwise at 0 °C. The resulting solution was stirred at 0 °C for 30 min and then at room temperature for 1 h. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography (CH_2Cl_2/EtOAc = 8:1) to give a colorless oil (45 mg, 92%): ^{1}H NMR (300 MHz) δ 4.70 (d, J = 2.5 Hz, 1 H), 4.25 (dt, J = 7.9, 5.0 Hz, 1 H), 4.04 (dd, J = 7.9, 5.0 Hz, 1 H), 3.82 (dt, J = 11.6, 5.0 Hz, 1 H), 3.71 (m, 1 H), 3.69 (dd, J = 9.9, 5.0 Hz, 1 H), 3.35 (s, 3 H), 3.28 (td, J = 9.9, 5.7 Hz, 1 H), 2.37 (dd, J = 6.8, 5.0 Hz, 1 H), 1.99–1.91 (comp, 2 H), 1.86 (m, 1 H), 1.77 (m, 1 H), 1.46 (s, 3 H), 1.45 (s, 3 H); ^{13}C NMR (75 MHz) δ 109.6, 97.2, 78.6, 78.3, 70.7, 63.1, 58.1, 54.7, 28.5, 27.1, 26.6, 24.0; IR ($CHCl_3$) ν 3440, 2125 cm^{-1}; mass spectrum (CI) m/z 288.1555 [$C_{12}H_{22}N_3O_5$ (M + H) requires 288.1559], 272, 260, 256, 202, 198 (base).

[2*S*-[2α(2*R,4*R**),3α,6α]]-2-[1-[[(Methylsulfonyl)oxy]methyl]-3,3-dimethyl-2,4-dioxolan-5-yl]-3-azido-6-methoxy-3,4,5,6-tetrahydro-2*H*-pyran.** To a solution of the hydroxy azide prepared as above (231 mg, 0.80 mmol) in CH_2Cl_2 (2 mL) containing 4-(dimethylamino)pyridine (12 mg, 0.09 mmol) and Et_3N (167 mg, 1.65 mmol) at 0 °C was added MsCl (138 mg, 1.20 mmol), and the resulting solution was stirred at 0 °C for 1 h. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography (CH_2Cl_2/EtOAc = 30:1) to give a colorless oil (280 mg, 95%): ^{1}H NMR (300 MHz) δ 4.68 (d, J = 2.6 Hz, 1 H), 4.46 (dd, J = 10.7, 2.8 Hz, 1 H), 4.38 (ddd, J = 7.6, 5.6, 2.8 Hz, 1 H), 4.28 (dd, J = 10.7, 5.6 Hz, 1 H), 3.99 (dd, J = 7.6, 5.1 Hz, 1 H), 3.68 (dd, J = 9.8, 5.1 Hz, 1 H), 3.34 (s, 3 H), 3.25 (td, J = 9.8, 5.5 Hz, 1 H), 3.08 (s, 3 H), 1.98–1.82 (comp, 3 H), 1.76 (m, 1 H), 1.46 (s, 3 H), 1.45 (s, 3 H); ^{13}C NMR (75 MHz) δ 110.7, 97.3, 78.1, 76.3, 70.8, 69.7, 58.3, 54.9, 37.7, 28.6, 27.0, 26.7, 23.9; IR ($CHCl_3$) ν 2105, 1361, 1177 cm^{-1}; mass spectrum (CI) m/z 365.1273 [$C_{13}H_{23}N_3O_7S$ (M) requires 365.1257], 338, 334, 306 (base), 239.

[2*S*-[2α(2*R,4*R**),3α,6α]]-2-[1-[[(Tolylsulfonyl)oxy]methyl]-3,3-dimethyl-2,4-dioxolan-5-yl]-3-azido-6-methoxy-3,4,5,6-tetrahydro-2*H*-pyran.** To a solution of [2*S*-[2α-(2*R**,4*R**),3α,6α]]2-[1-(hydroxymethyl)-3,3-dimethyl-2,4-dioxolan-5-yl]-3-azido-6-methoxy-3,4,5,6-tetrahydro-2*H*-pyran (20 mg, 0.07 mmol) in CH_2Cl_2 (1 mL) containing 4-(dimethylamino)-pyridine (8.6 mg, 0.07 mmol) was added TsCl (17 mg, 0.09 mmol), and the resulting solution was stirred at room temperature for 1 h. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography (CH_2Cl_2/EtOAc = 50:1) to give a colorless oil (29 mg, 94%): ^{1}H NMR (300 MHz) δ 7.82 (d, J = 8.2 Hz, 2 H), 7.35 (d, J = 8.1 Hz, 2 H), 4.64 (d, J = 2.9 Hz, 1 H), 4.32 (ddd, J = 7.6, 5.4, 3.7 Hz, 1 H), 4.23 (dd, J = 10.5, 3.7 Hz, 1 H), 4.10 (dd, J = 10.5, 5.4 Hz, 1 H), 3.96 (dd, J = 7.6, 4.7 Hz, 1 H), 3.64 (dd, J = 10.0, 4.7 Hz, 1 H), 3.31 (s, 3 H), 3.21 (td, J = 10.0, 5.6 Hz, 1 H), 2.45 (s, 3 H), 1.95–1.82 (comp, 3 H), 1.73 (m, 1 H), 1.41 (s, 3 H), 1.35 (s, 3 H); ^{13}C NMR (75 MHz) δ 144.9, 132.8, 129.8, 128.0, 110.6, 97.3, 78.4, 75.8, 70.6, 70.0, 57.9, 54.8, 28.6, 26.9, 26.7, 23.9, 21.6; IR ($CHCl_3$) ν 2105 cm^{-1}; mass spectrum (CI) m/z 441.1554 ($C_{19}H_{27}N_3O_7S$ requires 441.1570), 414, 410, 382 (base).

[2*S*-[2α(2*R,4*R**),3α,6α]]-2-[1-[[(Methylsulfonyl)oxy]methyl]-3,3-dimethyl-2,4-dioxolan-5-yl]-3-amino-6-methoxy-3,4,5,6-tetrahydro-2*H*-pyran (26a).** A solution of [2*S*-[2α-(2*R**,4*R**),3α,6α]]-2-[1-[[(methylsulfonyl)oxy]methyl]-3,3-dimethyl-2,4-dioxolan-5-yl]-3-azido-6-methoxy-3,4,5,6-tetrahydro-2*H*-pyran (15 mg, 0.04 mmol) in absolute MeOH (0.5 mL) containing Pd/C (10%) (4 mg) was shaken under an atmosphere of H_2 (70 psi) at room temperature for 2.5 h. The catalyst was removed by filtration, and the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography (CH_2Cl_2/MeOH = 10:1) to give **26a** as colorless oil (12 mg, 90%): ^{1}H NMR (500 MHz) δ 4.65 (d, J = 2.7 Hz, 1 H), 4.61 (dd, J = 14.4, 6.0 Hz, 1 H), 4.27 (dd, J = 14.4, 6.2 Hz, 1 H), 4.25 (m, 1 H), 3.85 (t, J = 8.0 Hz, 1 H), 3.41 (t, J = 8.0 Hz, 1 H), 3.34 (s, 3 H), 3.07 (s, 3 H), 2.74 (td, J = 10.0, 4.1 Hz, 1 H), 1.80–1.72 (comp, 2 H), 1.69 (m, 1 H), 1.61 (m, 1 H), 1.44 (s, 6 H); ^{13}C NMR (125 MHz) δ 110.6, 97.4, 79.1, 78.8, 75.2, 70.3, 54.8, 51.7, 37.7, 29.0, 26.9; IR ($CHCl_3$) ν 3382, 3313 cm^{-1}; mass spectrum (CI) m/z 340.1413 [$C_{13}H_{26}NO_7S$ (M + H) requires 340.1430], 308 (base), 244, 212.

[2*S*-[2α(2*R,4*R**),3α,6α]]-2-[1-[[(Tolylsulfonyl)oxy]methyl]-3,3-dimethyl-2,4-dioxolan-5-yl]-3-amino-6-methoxy-3,4,5,6-tetrahydro-2*H*-pyran (26b).** A solution of [2*S*-[2α-(2*R**,4*R**),3α,6α]]-2-[1-[[(tolylsulfonyl)oxy]methyl]-3,3-dimethyl-2,4-dioxolan-5-yl]-3-azido-6-methoxy-3,4,5,6-tetrahydro-2*H*-pyran (19 mg, 0.04 mmol) in absolute MeOH (0.5 mL) containing Pd/C (10%) (5 mg) was shaken under an atmosphere of H_2 (70 psi) at room temperature for 2 h. The catalyst was removed by filtration, and the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography (CH_2Cl_2/MeOH = 10:1) to give **26b** as colorless oil (17 mg, 93%): ^{1}H NMR (300 MHz) δ 7.81 (d, J = 8.4 Hz, 2 H), 7.34 (d, J = 8.1 Hz, 2 H), 4.53 (d, J = 1.6 Hz, 1 H), 4.40 (dd, J = 10.3, 2.2 Hz, 1 H), 4.17 (ddd, J = 8.0, 6.1, 2.2 Hz, 1 H), 4.06 (dd, J = 10.3, 6.1 Hz, 1 H), 3.78 (t, J = 8.0 Hz, 1 H), 3.33 (t, J = 8.0 Hz, 1 H), 3.25 (s, 3 H), 2.68 (td, J = 8.0, 4.0 Hz, 1 H), 2.45 (s, 3 H), 1.77–1.52 (comp, 4 H), 1.56 (br s, 2 H), 1.38 (s, 3 H), 1.34 (s, 3 H); ^{13}C NMR (75 MHz) δ 144.7, 133.0, 129.7, 128.1, 110.5, 97.2, 79.1, 78.5, 75.2, 70.5, 54.7, 51.6, 29.0, 27.0, 26.9, 26.8, 21.6; IR ($CHCl_3$) ν 3382,

3313 cm^{-1}; mass spectrum (CI) m/z 416.1745 [$C_{19}H_{30}NO_7S$ (M + H) requires 416.1743], 384 (base), 244, 230.

[2*S*-[2α(2*R,4*R**),3β,6α]]-2-[1-(Azidomethyl)-3,3-dimethyl-2,4-dioxolan-5-yl]-3-[(methylsulfonyl)oxy]-6-methoxy-3,4,5,6-tetrahydro-2*H*-pyran.** To a solution of [2*S*-[2α-(2*R**,4*R**),3β,6α]]-2-[1-(azidomethyl)-3,3-dimethyl-2,4-dioxolan-5-yl]-6-methoxy-3,4,5,6-tetrahydro-2*H*-pyran-3-ol (22 mg, 0.08 mmol) in CH_2Cl_2 (1 mL) containing 4-(dimethylamino)pyridine (1.5 mg, 0.01 mmol) and Et_3N (15 mg, 0.15 mmol) at 0 °C was added MsCl (13 mg, 0.11 mmol), and the resulting solution was stirred at room temperature for 30 min. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography (CH_2Cl_2/EtOAc = 30:1) to give a colorless oil (26 mg, 93%): ^1H NMR (500 MHz) δ 4.81 (m, 1 H), 4.71 (d, J = 2.3 Hz, 1 H), 4.07 (ddd, J = 7.6, 5.8, 2.6 Hz, 1 H), 3.83 (dd, J = 9.1, 7.6 Hz, 1 H), 3.76 (dd, J = 9.1, 1.3 Hz, 1 H), 3.64 (dd, J = 13.1, 2.6 Hz, 1 H), 3.35 (dd, J = 13.1, 5.8 Hz, 1 H), 3.34 (s, 3 H), 3.09 (s, 3 H), 2.16–2.08 (comp, 3 H), 1.63 (m, 1 H), 1.44 (s, 3 H), 1.41 (s, 3 H); ^{13}C NMR (125 MHz) δ 110.5, 98.0, 80.5, 75.4, 74.1, 71.3, 55.1, 52.7, 38.1, 27.1, 26.9, 23.6, 23.5; IR ($CHCl_3$) ν 2106 cm^{-1}; mass spectrum (CI) m/z 366.1331 [$C_{13}H_{24}N_3O_7S$ (M + H) requires 366.1335], 338 (base), 323, 306.

[2*S*-[2α(2*R,4*R**),3β,6α]]-2-[1-(Aminomethyl)-3,3-dimethyl-2,4-dioxolan-5-yl]-3-[(methylsulfonyl)oxy]-6-methoxy-3,4,5,6-tetrahydro-2*H*-pyran (27).** A solution of the above material (19 mg, 0.05 mmol) in absolute MeOH (1 mL) containing Pd/C (10%) (6 mg) was shaken under an atmosphere of H_2 (70 psi) at room temperature for 17 h. The catalyst was removed by filtration, and the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography (CH_2Cl_2/MeOH = 10:1) to give **27** as colorless oil (16 mg, 89%): ^1H NMR (500 MHz) δ 4.81 (br s, 1 H), 4.72 (d, J = 2.2 Hz, 1 H), 3.94 (ddd, J = 6.9, 6.4, 3.5 Hz, 1 H), 3.80 (d, J = 9.1, 6.9 Hz, 1 H), 3.77 (dd, J = 9.1, 1.0 Hz, 1 H), 3.36 (s, 3 H), 3.09 (s, 3 H), 3.06 (m, 1 H), 2.89 (dd, J = 13.1, 6.4 Hz, 1 H), 2.18–2.07 (comp, 3 H), 1.64–1.61 (comp, 3 H), 1.39 (s, 6 H); ^{13}C NMR (125 MHz) δ 109.4, 98.0, 83.1, 75.8, 74.8, 71.2, 55.1, 44.6, 38.1, 27.3, 27.1, 23.7, 23.6; IR ($CHCl_3$) ν 3387, 3320 cm^{-1}; mass spectrum (CI) m/z 340.1424 [$C_{13}H_{26}NO_7S$ (M + H) requires 340.1430] (base), 308, 244.

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