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Total Synthesis of Acanthacerebroside A and Astrocerebroside A via a Chiral Epoxide Intermediate Derived from L-Quebrachitol

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The chiral and stereoselective total synthesis of novel cerebrosides, acanthacerebroside A (**1**) and astrocerebroside A (**2**), isolated from starfish, is described. The phytosphingosine moieties in **1** and **2** were prepared by the coupling reaction of dialkylmagnesium reagents with the common epoxide intermediate, 2-(*t*-butoxycarbonyl)amino-1-*O*-(*t*-butyldiphenylsilyl)-2-deoxy-3-*O*-(4-methoxybenzyl)-D-4,5-anhydroribitol (**5**). The epoxide (**5**) was synthesized from naturally occurring cyclitol, L-quebrachitol via the conduramine derivative, which was prepared regio- and stereoselectively by the Pd-catalyzed azidation of the allyl carbonate derivative. Condensation of phytosphingosines with 2-acetoxy fatty acid residue, followed by glycosidation, furnished the total synthesis. This work established an effective synthetic pathway to a wide variety of cerebrosides containing various phytosphingosines and 2-hydroxy fatty acid residue; the first total synthesis of astrocerebroside A (**2**) fully confirmed the proposed structure.

Glycosphingolipids, ubiquitous components of eukaryotic cell surfaces, are known to play very important biological roles in cellular interactions and differentiation.[1)] Recently, many new glycosphingolipids containing a phytosphingosine (4-hydroxysphinganine) component, such as acanthacerebroside A (**1**) and astrocerebroside A (**2**), have been isolated from marine biological sources which exhibit significant antitumor, immunostimulatory, neuritogenic and growth-inhibitory activities.[2)] A structural study of these novel glycosphingolipids reveals that they usually have cerebroside (ceramide monohexoside) structures, and are composed of aldohexose residue, 2-hydroxy fatty acids, and long-chain bases (phytosphingosines) (Fig. 1).[3)] It is also shown that both the 2-hydroxy fatty acid moiety and phytosphingosine moiety have a wide variety of carbon chains.[2,3)] A pioneering study to elucidate the structures of cerebrosides isolated from marine sources by Komori and Higuchi revealed that the 2-hydroxy fatty acid moiety has a *R* configuration[3a,3b)] and that the phytosphingosine residue has a (2*S*,3*S*,4*R*) stereochemistry.[3c)] To clarify their biological activity, it is essential to isolate cerebrosides in pure form; however, these are usually isolated as a mixture (molecular species) of several cerebrosides containing a variety of phytosphingosine and 2-hydroxy fatty acid moeities, and their chromatographic separation is sometimes very difficult.[3a)] Due to their interesting and promising biological activity, it is highly desired to develop a synthetic method for the preparation of a wide variety of phytosphingosine-type cerebrosides. Although several total syntheses of ceramides and cerebrosides containing sphingosine component have been reported,[4)] synthetic studies on cerebrosides with phytosphingosine and 2-hydroxy fatty acid components have been limited.[5,6)] Recent reports on the successful total synthesis of cerebrosides of this family are: acanthacerebroside A (**1**)[5a)] and galactosyl ceramide by Komori,[5b)] and agelasphin by Akimoto.[5c)] In this paper we describe a novel methodology for the preparation of various phytosphingosines which utilizes chiral epoxide (**5**) as a common precursor, and the total synthesis of acanthacerebroside A (**1**)[2a)] and astrocerebroside A (**2**)[2b)] using the epoxide (**5**) as the key intermediate. A retrosynthetic analysis (Fig. 2) suggested that cerebrosides should be obtained by the glycosidation of ceramide (**ii**). The ceramide (**ii**) was envisioned to be prepared by the condensation of the 2-hydroxy fatty acid moiety (**iii**) and the phytosphingosine moiety (**iv**). The former was planned to be derived from D-mannitol, and the later to be prepared by the coupling reaction of chiral epoxide (**5**) with proper organometallic species. The key epoxide (**5**), in turn, was envisioned to be synthesized by a ring cleavage of conduramine (aminoconduritol) derivative (**4**), which was planned to be derived from L-quebrachitol (**3**), a naturally occurring optically active cyclitol, obtained in large quantities from the serum of the rubber tree.[7)]

Results and Discussion

Preparation of Conduramine Derivatives. To construct the phytosphingosine moiety starting from L-quebrachitol (**3**), a stereoselective introduction of the amino functionality into **3** was first explored (Scheme 1). 1L-*chiro*-Inositol (**6**) was prepared from **3** in 90% yield by a known procedure.[8)] The treatment of **6** with 2,2-dimethoxypropane afforded the tri-*O*-isopropylidene derivative (**7**), whose *trans*-*O*-isopropylidene group was selectively removed to give

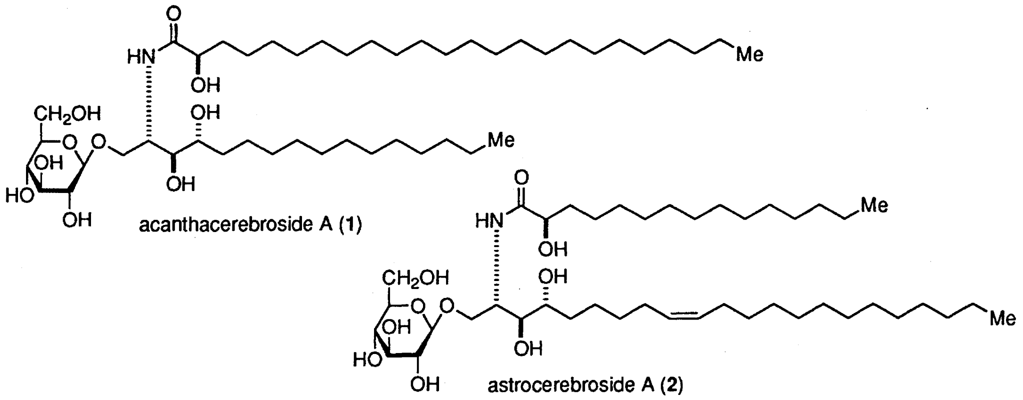


Fig. 1.

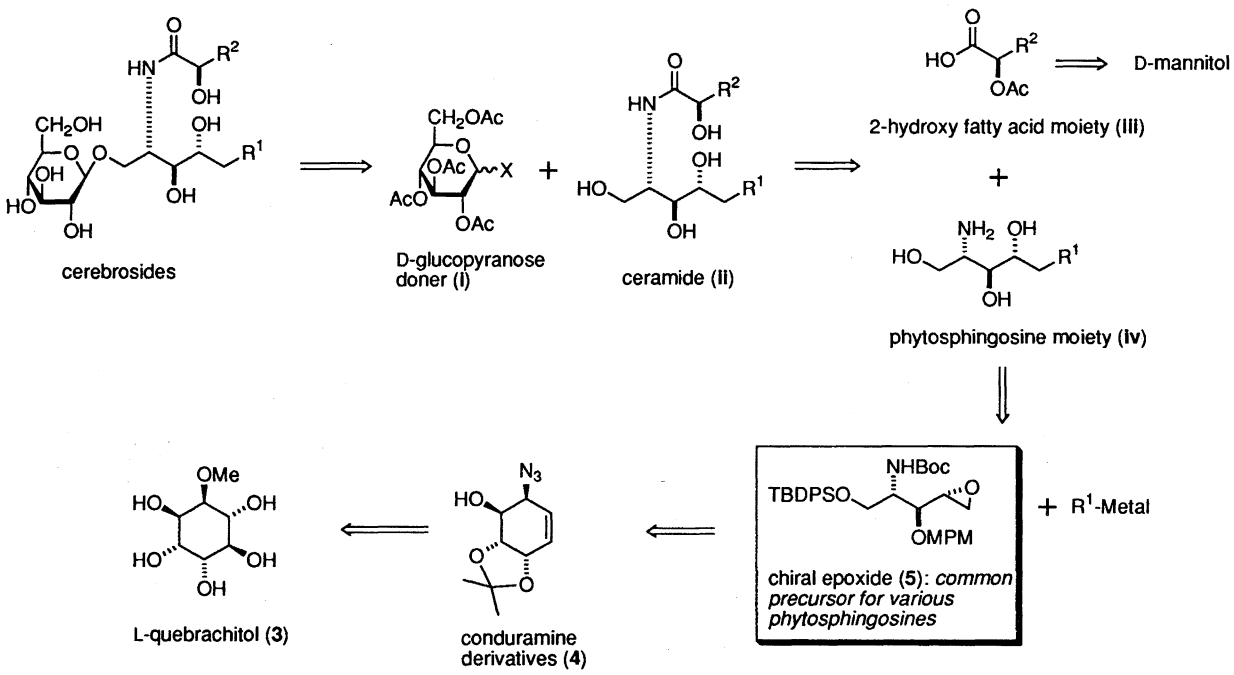
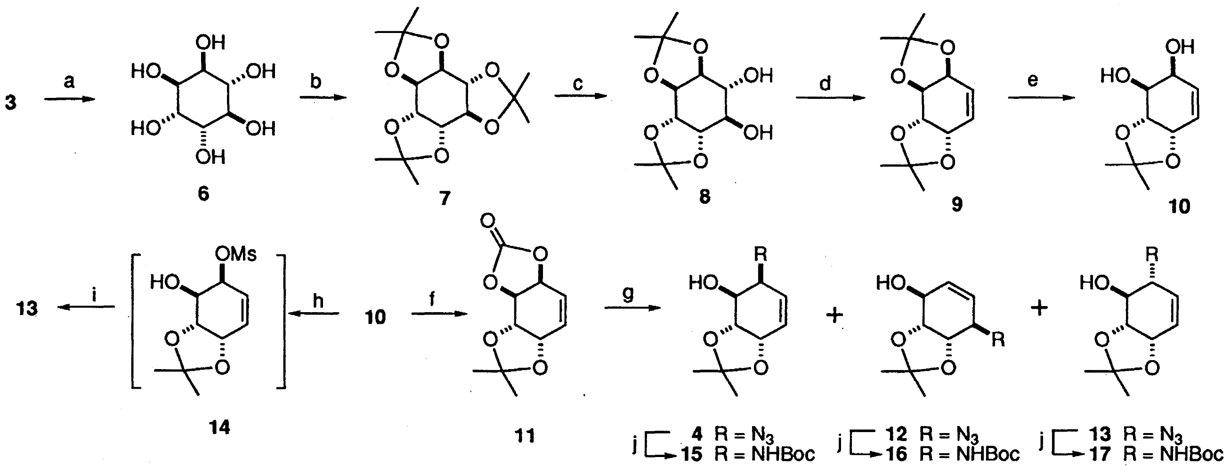


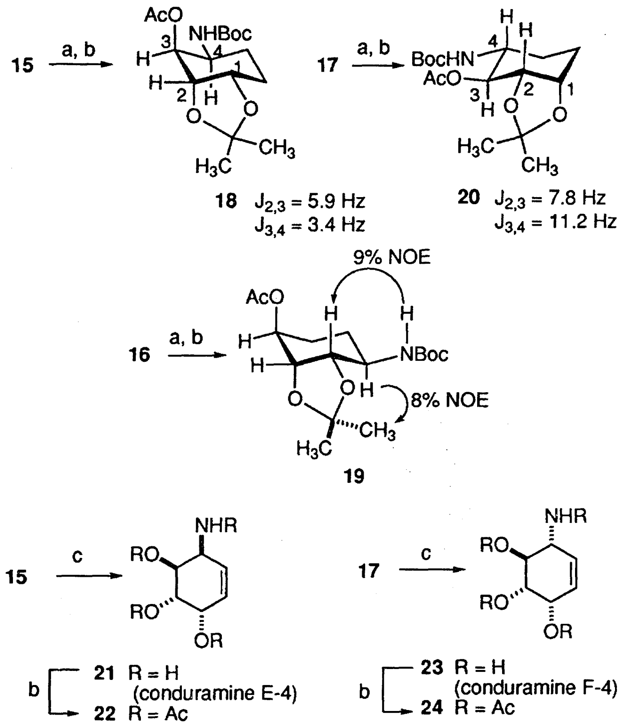
Fig. 2.



Scheme 1. Boc = $t\text{-}C_4H_9OC(O)$–. Reagents and conditions: a) see Ref. 8; b) 2,2-dimethoxypropane, DMF, p-TsOH, 70 °C; c) CSA, THF–MeOH, 0 °C; d) Ph_3P, I_2, imidazole, toluene, reflux; e) Amberlite IR-120B (H^+ form), THF–MeOH, r.t.; f) 1,1-carbonyldiimidazole, toluene, 50 °C; g) NaN_3, $(Ph_3P)_4Pd$, THF–H_2O, r.t.; h) MsCl, pyridine–CH_2Cl_2, −45 °C; i) NaN_3, DMF, r.t.; j) $LiAlH_4$, THF, 0 °C, then Boc_2O, r.t.

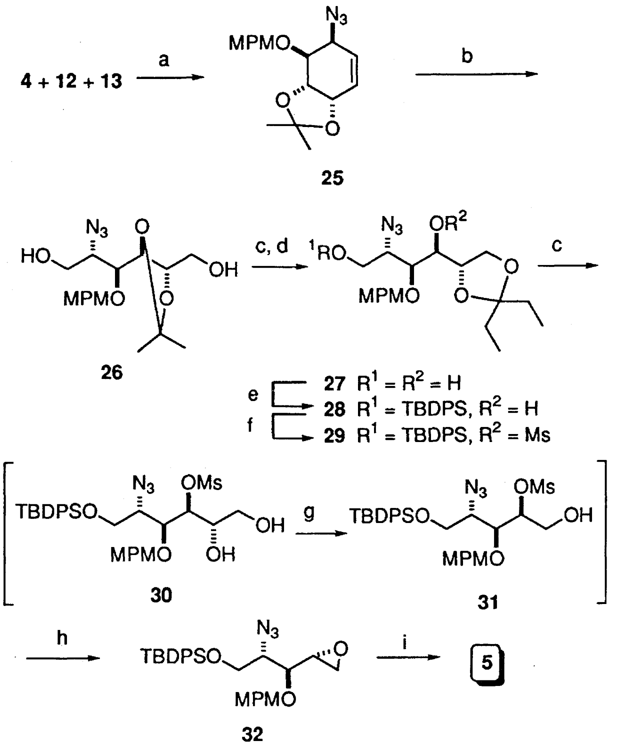
known **8**[8)] in 62% yield. The reaction of **8** with Ph_3P, imidazole and I_2 in toluene cleanly generated protected conduritol E (**9**) in 85% yield. The treatment of tetrahydrofuran (THF) solution of **9** with acidic resin afforded the mono-*O*-isopropylidene derivative (**10**) in 60% yield. The diol (**10**) was converted into cyclic carbonate (**11**) in 92% yield. The palladium-catalyzed azidation of **11** under the conditions developed by Murahashi[9)] [NaN_3, $Pd(PPh_3)_4$ (3 mol%) in aqueous THF] afforded an inseparable mixture of allylic azides (**4**, **12**, and **13**) in a ratio of 86 : 8 : 6 (determined with 270 MHz ^1H NMR) in 97% yield.[10)] Using over solvents (DMF, acetonitrile, or diethyl ether) or other catalysts {tris(dibenzylideneacetone)dipalladium(0)–$CHCl_3$ or $Pd(PPh_3)_4$-[1,4-bis(diphenylphosphino)butane]} reduced the yield of the products. It has been reported that the Pd-catalyzed azidation of allyl esters proceeded via inverted (π-allyl)palladium intermediates,[9a)] which underwent a nucleophilic attack of the azide ion along with an inversion of the configuration to afford allylic azides with a net retention of the stereochemistry. The formation of a small amount of inverted allylic azide (**13**) would be attributed to the palladium(0)-induced partial isomerization of the (π-allyl)palladium intermediate.[9a)] On the other hand, the reaction of **10** with methanesulfonyl chloride (MsCl) at −45 °C gave allylic mesylate (**14**), which was reacted with NaN_3 in *N*,*N*-dimethylformamide (DMF) to provide single allylic azide (**13**) in 56% yield from **10**. It is well known that allylic azides existed as an equilibrating mixture of two isomers.[9,11)] Indeed, rapid isomerization of **4** and **12** at room temperature, which resulted in the formation of an equilibrated mixture (**4** : **12** = ca. 10 : 1), was observed during an attempted separation by silica-gel chromatography. Interestingly, no isomerization was observed for another allylic azide (**13**). To confirm the structure of allylic azides, a mixture of **4**, **12**, and **13** was treated with $LiAlH_4$ to give the corresponding amines, which were converted into *t*-butyl carbamate derivatives. The products were cleanly separated by silica-gel chromatography to afford **15**, **16**, and **17** in 78, 7, and 5% isolated yields, respectively. The reduction of **13** (prepared from **14**), followed by carbamate formation, also gave **17** in 91% yield. The hydrogenation of these products followed by acetylation afforded **18**, **19**, and **20**. The ^1H NMR analyses of **18**, **19**, and **20** with spin–spin decoupling experiments and a NOE measurement clearly assigned their structures (Scheme 2). Removal of the protecting groups in **17** afforded **23**, which was identified as known conduramine F-4,[12a)] again confirming the assigned structure of **17**. A similar transformation of **15** provided (+)-conduramine E-4 (**21**). This is the first example of preparing conduramine E-4 and F-4 in an optically active form, which are expected to show inhibitory activity against some glycosidases.[12b,12c,12d)]

Preparation of Chiral Epoxide Intermediate. Having established the stereoselective preparation of conduramine derivatives, the transformation of **4** into the chiral epoxide (**5**) was then investigated (Scheme 3). 4-Methoxybenzyl ether formation of the mixture of allylic azides (**4**, **12**, and **13**), followed by chromatographic separation afforded **25** in 55% yield. Ozonolysis and a subsequent reductive workup of **25** generated acyclic diol **26** in 80% yield. After removing the *O*-isopropylidene group in **26**, the 1,2-diol moiety was protected as 1-ethylpropylidene acetal to give **27** (78%). The primary hydroxy group in **27** was protected as *t*-butyldiphenylsilyl ether to afford **28** (100% yield), whose secondary hydroxy function was converted into methanesulfonyl ester to give **29** quantitatively. The 1-ethylpropylidene acetal part in **29** was removed to give diol (**30**) in 75% yield, which was subjected to $Pb(OAc)_4$ oxidation, followed by reduction to give alcohol (**31**). Without isolation, **31** was treated with sodium methoxide to give an inverted epoxide (**32**) in 84% yield from **30**. Hydrogenation of **32** in the presence of di-*t*-butyl dicarbonate (Boc_2O) provided the the key intermediate, chiral epoxide (**5**) in 75% yield.



Scheme 2. Reagents and conditions: a) H_2, 10% Pd on carbon, EtOAc, r.t.; b) Ac_2O, pyridine, r.t.; c) TFA–CH_2Cl_2, then TFA–CH_2Cl_2–H_2O, r.t.

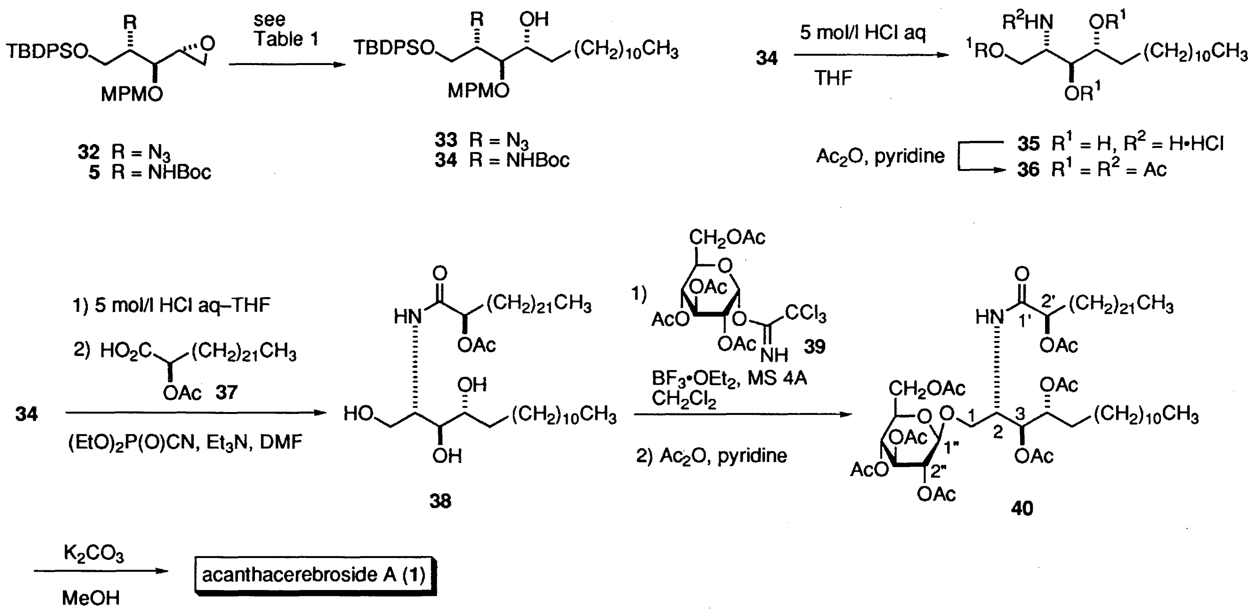
Synthesis of Phytosphingoshine. With the chiral epoxide (**5**), which contains the required functionalities with the correct stereochemistry in hand, the transformation of **5** into phytosphingosines was studied (Scheme 4). First, to synthesize phytosphingosine (**35**) found in acanthacerebroside A (**1**), coupling reactions of azido-epoxide (**32**) with undecylmagnesium bromide in the presence of various Cu(I) salts were examined.[13)] When **32** was reacted with excess undecylmagnesium bromide in the presence of CuCN (50 mol%) in Et_2O at 0 °C, the desired coupling product (**33**) was obtained, but only in 22% yield. The low yield of **33** was apparently due to the formation of unidentified more polar by-products. The IR spectra of the by-products showed no absorption of the azide function, implying that the Grignard reagent had reacted with the azide group. To overcome this problem, af-



Scheme 3. TBDPS = (t-C$_4$H$_9$)Ph$_2$Si–, Ms = CH$_3$SO$_2$–, MPM = 4-methoxybenzyl. Reagents and conditions: a) NaH, DMF, MPMCl, r.t., then separation; b) O$_3$, MeOH, −78 °C, then NaBH$_4$, MeOH, −78 °C—r.t.; c) AcOH–H$_2$O, 50 °C; d) 3-pentanone, p-TsOH, r.t.; e) TBDPS-Cl, imidazole, r.t.; f) MsCl, Et$_3$N, CH$_2$Cl$_2$, r.t.; g) Pb(OAc)$_4$, PhH, r.t., then NaBH$_4$, MeOH, r.t.; h) MeONa, MeOH, 0 °C; i) H$_2$, Pd–BaSO$_4$, Boc$_2$O, EtOAc–EtOH, r.t.

ter compound **32** was converted into **5**, the coupling reaction was again explored (Table 1). Although the reaction of **5** with undecylmagnesium bromide in the presence of CuCN (50 mol%) afforded the coupling product (**34**) in only 27% yield, better results were obtained when **5** was reacted with diundecylmagnesium,[14] prepared from an ethereal solution of undecylmagnesium bromide by adding 1,4-dioxane[14a,14b] followed by centrifuging; the desired product (**34**) was isolated in 62% yield. The presence of Cu salt was found to be essential for the coupling reaction. Interestingly, when azido-epoxide (**32**) was subjected to the same reaction condition (dialkylmagnesium+CuCN), the formation of compound **33** was not observed. The protecting group in **34** was removed by acid hydrolysis to give phytosphingosine (**35**), which, without isolation, was acetylated to provide **36** in 95% yield from **34**. The spectral (^{1}H and ^{13}C NMR) data as well as specific rotational value $\{[\alpha]_D^{19}+31$ (c 0.80, CHCl$_3$); lit,[3c] $[\alpha]_D^{25}+27.9$ (c 1.5, CHCl$_3$)] were in good agreement with those of the authentic compound reported by Komori,[3c,15] confirming that the **35** has the correct absolute structure.

Total Synthesis of Acanthacerebroside A. Having finished the synthesis of phytosphingosine (**35**), the total synthesis of acanthacerebroside A (**1**) was next examined. The condensation of **35** with (R)-2-acetoxytetracosanoic acid (**37**), prepared from D-mannitol by a procedure reported by Komori,[5a] under the conditions of Shioiri[16] [diethyl cyanophosphonate (DEPC), Et$_3$N] afforded the condensate **38** in 74% yield from **34**. β-Glycosidation of **38** was successfully achieved by Schmidt's protocol.[17] Thus, the treatment of **38** with glucopyranosyl trichloroacetimidate (**39**)[17] in the presence of BF$_3$·OEt$_2$ and molecular sieves 4A, followed by acetylation, afforded β-glucoside (**40**) in 52% yield. In the ^{1}H NMR spectrum of **40**, methylene protons at C-1 were observed at $\delta = 3.6$—3.9 and H-3 and H-4 were observed at $\delta = 5.1$ and 4.8, respectively, revealing that glycosidation had occurred at the C-1 position; also, the β-glucosidic linkage



Scheme 4.

Table 1. Reaction of Epoxides (**5** and **32**) with Undecylmagnesium Reagents

Run	Epoxide	Reagent	Solvent	Catalyst	Temperature	Product	Yield[a)]
				mol%	°C		%
1	**32**	n-$C_{11}H_{23}MgBr$	THF	CuCN (50)	−15	**33**	9
2	**32**	n-$C_{11}H_{23}MgBr$	Et_2O	CuI (50)	0	**33**	19
3	**32**	n-$C_{11}H_{23}MgBr$	Et_2O	CuBr–Me_2S (50)	0	**33**	22
4	**32**	n-$C_{11}H_{23}MgBr$	Et_2O	CuCN (50)	−15	**33**	25
5	**5**	n-$C_{11}H_{23}MgBr$	Et_2O	CuI (50)	0—r.t.	**34**	25
6	**5**	n-$C_{11}H_{23}MgBr$	Et_2O	CuCN (50)	0—r.t.	**34**	27
7	**5**	n-$C_{11}H_{23}MgBr$	Et_2O	CuCN (150), $BF_3 \cdot OEt_2$ (150)	0—r.t.	**34**	5
8	**5**	n-$C_{11}H_{23}MgBr$	Et_2O–THF–Me_2S	CuCN (50)	0—r.t.	**34**	19
9	**5**	$(n$-$C_{11}H_{23})_2Mg$	Et_2O	CuCN (50)	0—r.t.	**34**	62
10	**5**	$(n$-$C_{11}H_{23})_2Mg$	Et_2O	None	0—r.t.	—	0
11	**32**	$(n$-$C_{11}H_{23})_2Mg$	Et_2O	CuCN (50)	0—r.t.	—	0

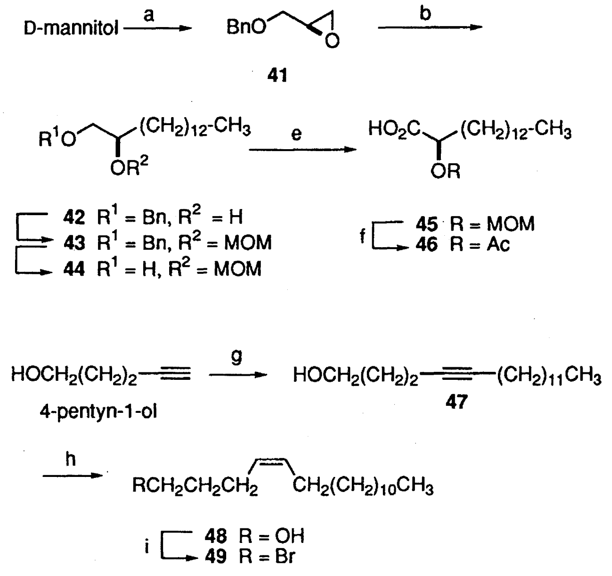
a) Isolated yield after purification by silica-gel chromatography.

was confirmed from the proton–proton spin coupling constant ($J_{1'',2''} = 8.1$ Hz). Finally, the *O*-acetyl groups in **40** were removed by basic methanolysis to furnish acanthacerebroside A (**1**) in 92% yield. The ^1H and ^{13}C NMR data were fully identical with those of the natural product, and the $[\alpha]_D$ value of synthetic **1** was in good accord with that reported for natural product by Higuchi and Komori.[2a)]

Total Synthesis of Astrocerebroside A. To demonstrate the usefulness of the epoxide (**5**) as the common precursor for the preparation of phytosphingsines with a variety of long-carbon chains, the total synthesis of astrocerebroside A (**2**), which was isolated from starfish,[2b)] *Astropecten latespinosus*, was then explored. The structure of **2** was elucidated by Higuchi and Komori by degradation and a mass spectral study, and was shown to possess the novel phytosphingosine moiety with a *Z*-olefinic bond.[2b)] The synthesis of the phytosphingosine (**51**) as well as the whole molecule has not been reported to data.

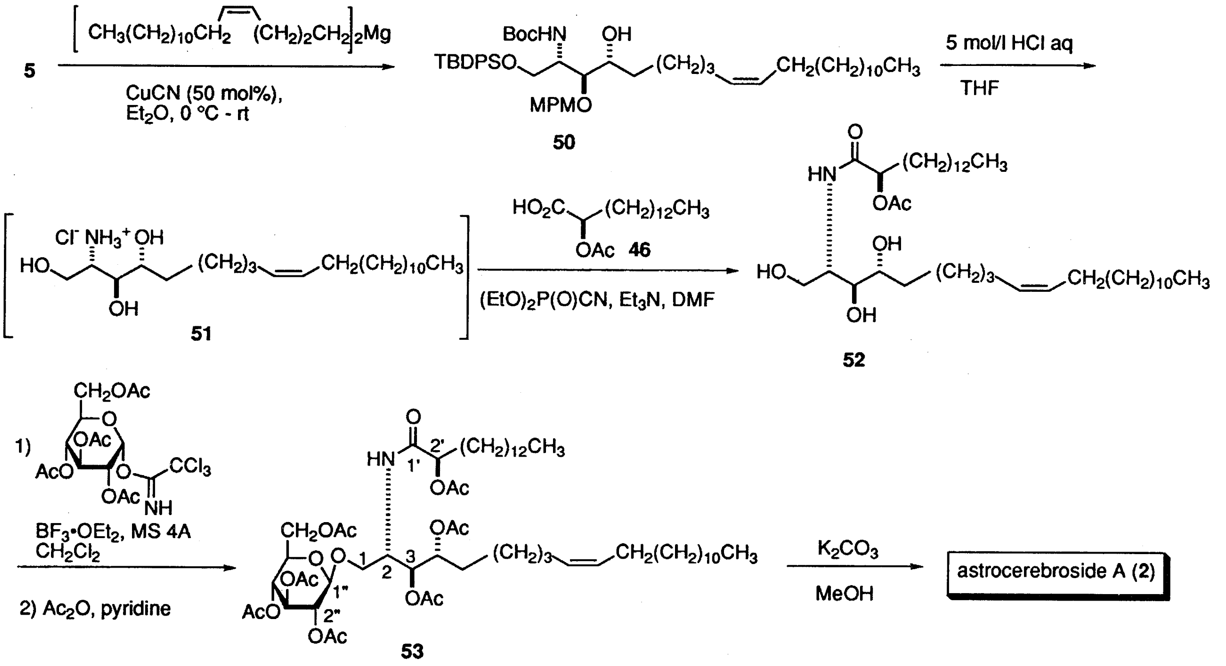
The synthesis of the requisite 2-hydroxy fatty acid portion (**46**) in **2** commenced with the known epoxide (**41**), prepared from D-mannitol.[19)] The reaction of **41** with didodecylmagnesium in the presence of CuCN afforded the coupling product (**42**) in 88% yield (Scheme 5). In this reaction, it was also found that dialkylmagnesium reagent gave better results, since the reaction of **41** with dodecylmagnesium bromide produced a significant amount of bromohydrine compound. After protection of the secondary hydroxy group in **42** as a methoxymethyl ether, the *O*-benzyl group in the resulting **43** was removed to give **44**. A Jones oxidation of **44**, followed by an exchange of the protecting group of secondary hydroxy function, furnished (*R*)-2-acetoxypentadecanoic acid (**46**).

For the preparation of phytoshingosine in astrocerebroside A, the precursor of organometallic compound, (4*Z*)-1-bromo-4-heptadecene (**49**), was synthesized from dodecyl bromide and 4-pentyn-1-ol. Thus, the reaction of dianion of 4-pentyn-1-ol with dodecyl bromide afforded **47** in 67% yield. Hydrogenation of **47** in the presence of the Lindlar catalyst provided *Z*-alkene (**48**) in 85% yield, whose primary hydroxy function was transformed into bromide to give **49**. The observed proton–proton spin coupling constant in **49** ($J_{4,5} = 11.0$ Hz) suggested that the geometry of the double bond in **49** should be *Z*.



Scheme 5. Bn=$C_6H_5CH_2$–, MOM=CH_3OCH_2–. Reagents and Conditions: a) see Ref. 19; b) $[CH_3(CH_2)_{10}CH_2]_2$-Mg, CuCN, Et_2O, r.t.; c) CH_3OCH_2Cl, $i$$Pr_2NEt$, CH_2Cl_2, r.t.; d) H_2, 10% Pd on carbon, EtOH, r.t.; e) Jones reagent, acetone, 0 °C; f) 2 mol dm^{-3} aqueous HCl-1,4-dioxane, 100 °C, then Ac_2O, pyridine, r.t.; g) n-BuLi (2.3 mol amt.), THF, −78—0 °C, then dodecyl bromide, HMPA, −40 °C—r.t.; h) H_2, Lindlar catalyst, EtOAc, r.t.; i) *N*-bromosuccinimide, Ph_3P, DMF, 0 °C.

Coupling of the epoxide (**5**) with **49**, and the total synthesis of astrocerebroside A were successfully achieved by the same procedure as that employed for the preparation of acanthacerebroside A (Scheme 6). The reaction of **5** with dialkylmagnesium reagent, generated from **49** by the action of magnesium followed by a treatment with 1,4-dioxane, in the presence of CuCN, cleanly provided **50** in 57% yield. Removal of all protecting groups in **50** with 5 mol dm^{-3} aqueous HCl afforded **51**, without isolation; **51** was treated with carboxylic acid (**46**) in the presence of DEPC and triethylamine to provide **52** in 60% yield from **50**. Glycosidation of **52** with glucopyranosyl trichloroacetimidate (**39**) in the presence of



Scheme 6.

BF$_3$·OEt$_2$ and molecular sieves 4A, followed by acetylation, afforded β-glucoside (**53**) in 46% yield. ^{1}H NMR spectrum of **53** showed the signals of H-1 at $\delta = 3.6$—3.9, and those of H-3 and H-4 at $\delta = 5.1$ and 4.9, respectively, revealing that glycosidation had occurred at the C-1 position; also, the observed proton–proton spin couping constant at $J_{1'',2''}$ (8.1 Hz) supported the β-glucosidic linkage. Finally, the *O*-acetyl groups in **53** were removed to furnish astrocerebroside A (**2**) in 93% yield. The ^{1}H and ^{13}C NMR data were fully identical with those of the natural product[2b] and the $[\alpha]_D$ value of synthetic **2** $\{[\alpha]_D^{21} +9$; lit,[2b] $[\alpha]_D^{21} +10.3]$ was in good accord with that reported for the natural product. This first total synthesis of **2** fully confirmed the proposed structure of the natural product assigned by Komori and Higuchi.[2b]

Conclusion

The development of a novel synthetic pathway to cerebrosides containing phytosphingosine moieties based on the utilization of the chiral epoxide (**5**) as the common intermediate has been described. L-Quebrachitol (**3**), an optically pure cyclitol obtained from the serum of the rubber tree, was effectively transformed into chiral epoxide (**5**), which contains the required functionalities with the correct stereochemistry for the preparation of phytosphingosines. The coupling reaction of **5** with dialkylmagnesium reagents could provide phytosphingosines with saturated and unsaturated carbon chains. The successful total synthesis of two cerebrosides, acanthacerebroside A (**1**) and astrocerebroside A (**2**), from the epoxide (**5**) in each 6-step reaction sequence revealed the effectiveness of this approach. Thus, it should now be possible to synthesize a wide variety of cerebrosides in this class using the methodology developed in this study. This work also showed the usefulness of L-quebrachitol (**3**) as a chiral building block for the preparation of natural products containing multiple stereocenters.

Experimental

Mps were determined on a Mitamura-riken micro hot stage and are uncorrected. ^{1}H NMR spectra were measured with JEOL JNM EX-90 (90 MHz) and JEOL JNM-GSX 270 (270 MHz) spectrometers, with tetramethylsilane used as the internal standard for solutions in deuteriochloroform, unless otherwise noted. ^{13}C NMR spectra were taken on a JEOL JNM-GSX 270 (67 MHz) spectrometer. Mass spectra were measured by JEOL JMS-DX 303 (EI, 70 eV) and JEOL GC Mate (FAB) spectrometers. Optical rotations were measured with a JASCO DIP-370 instrument, and values of $[\alpha]_D$ were recorded in units of 10^{-1} deg cm^2 g^{-1}. IR spectra were taken with JASCO IR-810 and JASCO FT/IR-200 spectrometers. Organic extracts were dried over anhydrous Na$_2$SO$_4$ and concentrated below 40 °C under reduced pressure.

1L-1,2 : 3,4 : 5,6-Tri-*O*-isopropylidene-*chiro*-inositol (7). To a solution of 1L-*chiro*-inositol[8] (**6**, 16.2 g, 90.1 mmol) in DMF (160 ml) and 2,2-dimethoxypropane (222 ml, 1.35 mol) was added *p*-toluenesulfonic acid hydrate (857 mg, 4.51 mmol). After being stirred at 70 °C for 42 h, the mixture was neutralized with triethylamine at 0 °C, and then concentrated. The resulting residue was dissolved in CH$_2$Cl$_2$, washed with water, and dried. Removal of the solvent left a syrup, which was chromatographed on a column of silica gel (210 g), with EtOAc–toluene (1 : 20) as an eluent, to afford compound **7** (22.5 g, 83%) as crystals: Mp 204—207 °C (from EtOAc); $[\alpha]_D^{27} +34$ (*c* 1.0, CHCl$_3$); IR (KBr) 2950, 2940, and 2900 cm^{-1}; ^{1}H NMR (270 MHz) $\delta = 1.35$, 1.45, and 1.52 (3s, each 6 H), 3.61—3.70 (m, 2 H), 4.32—4.45 (m, 4 H). Found: C, 59.65; H, 7.79%. Calcd for C$_{15}$H$_{24}$O$_6$: C, 59.98; H, 8.05%.

1L-1,2 : 5,6-Di-*O*-isopropylidene-*chiro*-inositol (8). To a solution of **7** (10.0 g, 33.4 mmol) in THF (100 ml) and MeOH (200 ml) at 0 °C was added camphorsulfonic acid (388 mg, 1.67 mmol); the mixture was stirred at 0 °C for 9 h. After the reaction mixture was neutralized at 0 °C by adding solid NaHCO$_3$, it was concentrated to give a residue, which was chromatographed on a column of silica gel (250 g), with EtOAc–toluene (1 : 1) as an eluent, to afford compound **8** (6.42 g, 74%) as crystals: Mp 145—146 °C (from EtOAc) (lit,[8] 153 °C); $[\alpha]_D^{27}-5$ (*c* 1.0, EtOH) {lit,[8] $[\alpha]_D^{27}-4.7$ (*c* 1.0, EtOH)}; IR (KBr) 3398 cm^{-1}; ^{1}H NMR (270 MHz) $\delta=1.36$ and 1.51 (2s, each 6 H), 3.1—3.3 (b, 2H), 3.51—3.60 (m, 2 H), 4.12—4.23 (m, 2 H), 4.33—4.38 (m, 2 H). Found: C, 55.26; H, 7.47%. Calcd for $C_{12}H_{20}O_6$: C, 55.37; H, 7.75%.

1D-(1,2/3,4)-1,2:3,4-Di-*O*-isopropylidene-5-cyclohexene-1,2,3,4-tetrol (9). To a solution of **8** (6.20 g, 23.8 mmol) in toluene (500 ml) were added triphenylphosphine (25.0 g, 95.3 mmol), imidazole (6.49 g, 95.3 mmol), and iodine (18.1 g, 71.5 mmol); the mixture was heated under reflux for 1 h. After cooling, the reaction mixture was diluted with EtOAc and washed successively with 10% aqueous sodium thiosulfate solution, saturated $NaHCO_3$ solution, and brine, and dried. Removal of the solvent left a syrup, which was chromatographed on a column of silica gel (300 g), with EtOAc–hexanes (1 : 25) as an eluent, to afford compound **9** (4.46 g, 83%) as crystals: Mp 51—54 °C (from EtOAc); $[\alpha]_D^{27}+35$ (*c* 1.0, $CHCl_3$); IR (KBr) 2950, 2940, and 2900 cm^{-1}; ^{1}H NMR (270 MHz) $\delta=1.37$ and 1.38 (2s, each 6 H), 4.52—4.57 (m, 4 H), 5.72 (m, 2 H). Found: C, 63.40; H, 8.10%. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02%.

1D-(1,2/3,4)-1,2-*O*-Isopropylidene-5-cyclohexene-1,2,3,4-tetrol (10). To a solution of **9** (2.23 g, 9.86 mmol) in THF (110 ml) and methanol (11 ml) was added Amberlite IR-120 resin (H$^+$ form, 2.23 g); the mixture was gently stirred at room temperature for 12 h. The insoluble material was removed by filtration and the filtrate was concentrated to give a residue, which was chromatographed on a column of silica gel (60 g) with EtOAc–toluene (1 : 40) as an eluent, to afford first, the starting material, compound **9** (0.71 g, 32%). Further elution with acetone–toluene (1 : 5) afforded compound **10** (1.08 g, 59%) as crystals: Mp 66—67 °C (from EtOAc); $[\alpha]_D^{26}-3$ (*c* 1.0, $CHCl_3$); IR (KBr) 3345 cm^{-1}; ^{1}H NMR (270 MHz) $\delta=1.39$ and 1.45 (2s, each 3 H), 1.89 (bs, 2 H), 3.99 (dd, 1 H, $J=3.4$, 6.8 Hz), 4.33 (dd, 1 H, $J=2.4$, 3.4 Hz), 4.38 (dd, 1 H, $J=6.4$, 6.8 Hz), 4.66 (dd, 1 H, $J=2.4$, 6.4 Hz), 5.94 (m, 2 H). Found: C, 57.78; H, 7.69%. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58%.

1D-(1,2/3,4)-1,2-*O*-Carbonyl-3,4-*O*-isopropylidene-5-cyclohexene-1,2,3,4-tetrol (11). A mixture of compound **10** (1.08 g, 5.80 mmol) and 1,1-carbonyldiimidazole (1.41 g, 8.70 mmol) in toluene (45 ml) was stirred at 50 °C for 40 min. The reaction mixture was concentrated to give a residue, which was chromatographed on a column of silica gel (18 g), with EtOAc–toluene (1 : 20) as an eluent, to afford compound **11** (840 mg, 92%) as crystals: Mp 113—115 °C (from EtOAc); $[\alpha]_D^{27}+74$ (*c* 1.0, $CHCl_3$); IR (KBr) 1820 cm^{-1}; ^{1}H NMR (270 MHz) $\delta=1.36$ and 1.39 (2s, each 3 H), 4.61—4.66 (m, 2 H), 5.07—5.13 (m, 2 H),5.78 (m, 1 H), 6.01—6.05 (m, 1 H). Found: C, 56.55; H, 5.59%. Calcd for $C_{10}H_{12}O_5$: C, 56.60; H, 5.70%.

An Inseparable Mixture of 1D-(1,2/3,4)-4-Azido-1,2-*O*-isopropylidene-5-cyclohexene-1,2,3-triol (4), 1D-(1,4/2,3)-4-Azido-2,3-*O*-isopropylidene-5-cyclohexene-1,2,3-triol (12), and 1D-(1,2,4/3)-4-Azido-1,2-*O*-isopropylidene-5-cyclohexene-1,2,3-triol (13). A mixture of compound **11** (2.32 g, 10.9 mmol), sodium azide (782 mg, 12.0 mmol), and tetrakis(triphenylphosphine)palladium(0) (379 mg, 0.328 mmol) in THF (100 ml) and water (20 ml) was stirred under Ar at room temperature for 1 h. The mixture was diluted with water and then extracted with EtOAc three times. The combined extracts was washed successively with 1 mol dm^{-3} aqueous HCl solution, saturated $NaHCO_3$ solution, and brine, and then dried. Removal of the solvent left a residue, which was chromatographed on a column of silica gel (80 g), with EtOAc–toluene (1 : 20) as an eluent, to afford a mixture of compounds **4**, **12**, and **13** (1.96 g, 85%) as a colorless syrup. ^{1}H NMR analysis showed that the ratio of **4**, **12**, and **13** was 86 : 8 : 6. IR (neat) 3450 and 2100 cm^{-1}; ^{1}H NMR (270 MHz, for the major isomer **4**) $\delta=1.39$ and 1.45 (2s, each 3 H), 2.36 (d, 1 H, $J=3.9$ Hz), 4.04 (ddd, 1 H, $J=3.4$, 3.9, 6.8 Hz), 4.16 (ddd, 1 H, $J=1.0$, 3.4, 4.4 Hz), 4.32 (dd, 1 H, $J=6.4$, 6.8 Hz), 4.67 (ddd, 1 H, $J=1.0$, 3.4, 6.4 Hz), 5.91 (ddd, 1 H, $J=1.0$, 4.4, 9.8 Hz), 6.05 (ddd, 1 H, $J=1.0$, 3.4, 9.8 Hz). Found: C, 50.94; H, 6.49; N, 19.58%. Calcd for $C_9H_{13}N_3O_3$: C, 51.18; H, 6.20; N, 19.89%.

Preparation of 13 from 10 by S_N2 Reaction. To a solution of compound **10** (948 mg, 5.09 mmol) in pyridine (18 ml) and CH_2Cl_2 (18 ml) at −45 °C was added methanesulfonyl chloride (0.512 ml, 6.62 mmol). After 1 h, additional methanesulfonyl chloride (0.512 ml, 6.62 mmol) was added at −45 °C; the resulting mixture was stirred at −45 °C for 1 h. To the reaction mixture were added methanol (1.2 ml) and water (6 ml); the whole mixture was stirred at −45 °C for 30 min. The mixture was concentrated to give a residue, which was dissolved in $CHCl_3$. The organic layer was washed with saturated $NaHCO_3$ solution and dried. Removal of the solvent left a syrup, which was chromatographed on a column of silica gel (4 g), with EtOAc–toluene (1 : 5) as an eluent, to afford compound **14** (927 mg, 69%) as a colorless syrup: ^{1}H NMR (270 MHz) $\delta=1.40$ and 1.46 (2s, each 3 H), 2.57 (d, 1 H, $J=3.9$ Hz), 3.13 (s, 3 H), 4.13 (ddd, 1 H, $J=3.9$, 3.9, 7.1 Hz), 4.35 (dd, 1 H, $J=6.1$, 7.1 Hz), 4.72 (dd, 1 H, $J=3.9$, 6.1 Hz), 5.20 (dd, 1 H, $J=3.9$, 4.4 Hz), 6.00 (dd, 1 H, $J=4.4$, 9.8 Hz), 6.10 (dd, 1 H, $J=3.9$, 9.8 Hz). This compound was used in the next reaction without further purification. To a solution of compound **14** (927 mg, 3.51 mmol) in DMF (36 ml) was added sodium azide (1.60 g, 24.5 mmol); the mixture was stirred at room temperature for 13 h. The mixture was diluted with $CHCl_3$ and washed with brine. The aqueous phase was extracted with $CHCl_3$ three times. The combined organic layer was dried and concentrated to give a residue, which was chromatographed on a column of silica gel (4 g), with EtOAc–toluene (1 : 10) as an eluent, to afford compound **13** (610 mg, 56% from **10**) as a colorless syrup: $[\alpha]_D^{26}+59$ (*c* 1.0, $CHCl_3$); IR (neat) 3450 and 2100 cm^{-1}; ^{1}H NMR (270 MHz) $\delta=1.40$ and 1.52 (2s, each 3 H), 3.66 (dd, 1 H, $J=8.8$, 8.8 Hz), 3.90 (ddd, 1 H, $J=1.5$, 2.4, 8.8 Hz), 4.10 (dd, 1 H, $J=6.4$, 8.8 Hz), 4.64 (ddd, 1 H, $J=1.0$, 3.4, 6.4 Hz), 5.76 (ddd, 1 H, $J=1.0$, 1.5, 9.8 Hz), 5.97 (ddd, 1 H, $J=2.4$, 3.4, 9.8 Hz). Found: C, 51.13; H, 6.48; N, 19.52%. Calcd for $C_9H_{13}N_3O_3$: C, 51.18; H, 6.20; N, 19.89%.

1D-(1,2/3,4)-4-(*t*-Butoxycarbonyl)amino-1,2-*O*-isopropylidene-5-cyclohexene-1,2,3-triol (15), 1D-(1,4/2,3)-4-(*t*-Butoxycarbonyl)amino-2,3-*O*-isopropylidene-5-cyclohexene-1,2,3-triol (16), and 1D-(1,2,4/3)-4-(*t*-Butoxycarbonyl)amino-1,2-*O*-isopropylidene-5-cyclohexene-1,2,3-triol (17). To a suspension of $LiAlH_4$ (75 mg, 1.98 mmol) in THF (3 ml) at 0 °C was added a solution of a mixture of compounds **4**, **12**, and **13** (140 mg) in THF (3 ml); the mixture was first stirred at 0 °C for 15 min, and then at room temperature for 3 h. The reaction mixture was quenched by adding water (4 ml) at 0 °C. To this mixture was added Boc_2O (256 mg, 1.42 mmol); the whole mixture was further stirred at room temperature for 4 h. The reaction mixture was diluted with EtOAc and washed successively with 1 mol dm^{-3} aqueous HCl solution, saturated $NaHCO_3$ solution, and brine, and dried. Removal of the solvent left a residue, which was chromatographed on a column of silica gel (12 g), with EtOAc–toluene (1 : 7) as an eluent, to afford first, compound **15** (148 mg, 78%) as a colorless syrup: $[\alpha]_D^{27}+105$ (*c* 1.0, $CHCl_3$); IR (neat) 3400 and 1680 cm^{-1}; ^{1}H NMR (270 MHz) $\delta=1.37$ and 1.41 (2s, each 3 H), 1.46 (s, 9 H), 2.35 (bs, 1 H), 4.15 (dd, 1 H, $J=4.6$, 4.6 Hz), 4.31 (dd, 1 H, $J=4.6$, 4.6 Hz), 4.34—

4.43 (m, 1 H), 4.61 (dd, 1 H, $J=3.9$, 4.6 Hz), 4.97 (d, 1 H, $J=7.3$ Hz), 5.71 (dd, 1 H, $J=2.2$, 10.3 Hz), 5.82—5.86 (m, 1 H). Found: C, 58.72; H, 8.45; N, 4.90%. Calcd for $C_{14}H_{23}NO_5$: C, 58.93; H, 8.13; N, 4.91%. Further elution gave compound **16** (13 mg, 7%) as a colorless syrup: $[\alpha]_D^{25}-41$ (c 1.0, $CHCl_3$); IR (neat) 3350 and 1680 cm^{-1}; ^{1}H NMR (270 MHz) $\delta=1.35$ (s, 3 H), 1.45 (s, 12 H), 2.63 (b, 1 H), 4.02 (m, 1 H), 4.16—4.27 (m, 3 H), 5.07 (b, 1 H), 5.80 (ddd, 1 H, $J=1.0$, 2.9, 9.8 Hz), 5.91 (ddd, 1 H, $J=2.2$, 2.2, 9.8 Hz). Further elution gave compound **17** (9 mg, 5%), whose physical and spectral data were identical with those of the sample prepared by S_N2 reaction (vide infra).

Preparation of 17 from 13. A similar treatment of compound **13** (13 mg, 0.063 mmol) to that described for the preparation of compounds **15**, **16**, and **17** afforded compound **17** (27 mg, 91%) as a colorless syrup: $[\alpha]_D^{27}-43$ (c 1.0, $CHCl_3$); IR (neat) 3400 and 1700 cm^{-1}; ^{1}H NMR (270 MHz) $\delta=1.39$ (s, 3 H), 1.46 (s, 9 H), 1.51 (s, 3 H), 2.1—2.2 (b, 1 H), 3.61 (dd, 1 H, $J=8.3$, 8.3 Hz), 4.08—4.22 (m, 2 H), 4.64 (m, 1 H), 4.77 (bd, 1 H, $J=6.1$ Hz), 5.76 (ddd, 1 H, $J=1.0$, 1.0, 11.0 Hz), 5.89 (ddd, 1 H, $J=1.2$, 3.4, 11.0 Hz). Found: C, 58.93; H, 8.36; N, 4.90%. Calcd for $C_{14}H_{23}NO_5$: C, 58.93; H, 8.13; N, 4.91%.

1D-(1,2/3,4)-3-*O*-Acetyl-4-(*t*-butoxycarbonyl)amino-1,2-*O*-isopropylidenecyclohexane-1,2,3-triol (18). A mixture of compound **15** (7.5 mg, 0.026 mmol) and 10% Pd on carbon (5 mg) in EtOAc (1 ml) was stirred under 1 atm of H_2 at room temperature for 18 h. The catalyst was removed by filtration, and the filtrate was concentrated to give a residue, which was treated with acetic anhydride (0.5 ml) and pyridine (0.5 ml) at room temperature for 8 h. Methanol was added to the reaction mixture at 0 °C. After being stirred at 0 °C for 15 min, the mixture was concentrated to give a residue, which was chromatographed on a column of silica gel (1 g), with EtOAc–toluene (1 : 5) as an eluent, to afford compounds **18** (8.2 mg, 96%) as a colorless syrup: ^{1}H NMR (270 MHz) $\delta=1.34$ and 1.51 (2s, each 3 H), 1.45 (s, 9 H), 1.65—1.76 (m, 1 H), 1.81—2.00 (m, 3 H), 2.10 (s, 3 H), 4.08 (dd, 1 H, $J=5.9$, 5.9 Hz), 4.06—4.14 (m, 1 H), 4.25—4.31 (m, 1 H), 4.49 (bd, 1 H, $J=6.4$ Hz), 5.01 (dd, 1 H, $J=3.4$, 5.9 Hz). HRMS (EI) Calcd for $C_{16}H_{28}NO_6$: ($M^+ + H$), 330.1917. Found: m/z 330.1913.

1D-(1,4/2,3)-1-*O*-Acetyl-4-(*t*-butoxycarbonyl)amino-2,3-*O*-isopropylidenecyclohexane-1,2,3-triol (19). A similar treatment of compound **16** (4.9 mg, 0.017 mmol) to that described for the preparation of compound **18** afforded **19** (4.6 mg, 82%) as a colorless syrup: ^{1}H NMR (270 MHz) $\delta=1.36$ and 1.53 (2s, each 3 H), 1.45 (s, 9 H), 1.58—1.68 (m, 2 H), 1.81—1.94 (m, 2 H), 2.07 (s, 3 H), 3.75—3.85 (m, 1 H), 4.00 (dd, 1 H, $J=5.1$, 6.4 Hz), 4.07 (dd, 1 H, $J=5.1$, 5.1 Hz), 4.54 (bd, 1 H, $J=6.4$ Hz), 5.08—5.13 (m, 1 H). HRMS (EI) Calcd for $C_{16}H_{27}NO_6$: (M^+), 329.1838. Found: m/z 329.1810.

1D-(1,2,4/3)-3-*O*-Acetyl-4-(*t*-butoxycarbonyl)amino-1,2-*O*-isopropylidenecyclohexane-1,2,3-triol (20). A similar treatment of compound **17** (5.2 mg, 0.018 mmol) to that described for the preparation of compound **18** afforded **20** (4.5 mg, 75%) as a colorless syrup: ^{1}H NMR (270 MHz) $\delta=1.36$ and 1.52 (2s, each 3 H), 1.42 (s, 9 H), 1.57—1.89 (m, 3 H), 2.10 (s, 3 H), 2.11—2.22 (m, 1 H), 3.47—3.58 (m, 1 H), 4.05 (dd, 1 H, $J=5.1$, 7.6 Hz), 4.31 (m, 1 H), 4.62 (bd, 1 H, $J=8.8$ Hz), 4.86 (dd, 1 H, $J=7.6$, 11.2 Hz). HRMS (EI) Calcd for $C_{16}H_{28}NO_6$: ($M^+ + H$), 330.1917. Found: m/z 330.1919.

1D-(1,2/3,4)-4-Amino-5-cyclohexene-1,2,3-triol [(+)-Conduramine E-1] (21). To a solution of compound **15** (196 mg, 0.687 mmol) in CH_2Cl_2 (2 ml) at 0 °C was added trifluoroacetic acid (2 ml); the mixture was first stirred at 0 °C for 10 min, and then at room temperature for 1 h. The reaction mixture was cooled to 0 °C, and water (1 ml) was added. The resulting mixture was stirred at 0 °C for 10 min, and then at room temperature for 3 h. The mixture was concentrated to give a residue, which was purified by a column of resin (Dowex 50W-X2, H$^+$ form, 15 ml) with water and 1 mol dm^{-3} aqueous NH_4OH to give compound **21** (64 mg, 64%) as crystals: Mp 159—162 °C (from water); $[\alpha]_D^{26}+344$ (c 0.9, H_2O); IR (KBr) 3344 cm^{-1}; ^{1}H NMR (270 MHz, D_2O) $\delta=3.37$—3.46 (m, 1 H), 3.80—3.86 (m, 2 H), 4.16—4.20 (m, 1 H), 5.58—5.67 (m, 2 H). Found: C, 48.65; H, 7.94; N, 9.19%. Calcd for $C_6H_{11}NO_3\cdot 1/5H_2O$: C, 48.44; H, 7.72; N, 9.41%.

1D-(1,2/3,4)-4-Acetamido-1,2,3-tri-*O*-acetyl-5-cyclohexene-1,2,3-triol (22). A solution of compound **21** (22 mg, 0.15 mmol) in acetic acid (0.5 ml) and pyridine (0.5 ml) was stirred at room temperature for 4 h. After the addition of methanol at 0 °C, the reaction mixture was concentrated to give a residue, which was chromatographed on a column of silica gel (1 g), with acetone–toluene (1 : 2) as an eluent, to afford compound **22** (44 mg, 94%) as crystals: Mp 176—180 °C (from EtOAc); $[\alpha]_D^{28}+203$ (c 0.3, $CHCl_3$); IR (KBr) 3250, 1750, 1640, and 1560 cm^{-1}; ^{1}H NMR (270 MHz) $\delta=2.01$ (s, 3 H), 2.07 (s, 9 H), 5.05—5.13 (m, 1 H), 5.32—5.39 (m, 2 H), 5.53—5.66 (m, 2 H), 5.80 (ddd, 1 H, $J=1.1$, 4.0, 10.3 Hz), 5.80 (dd, 1 H, $J=3.3$, 10.3 Hz). Found: C, 53.42; H, 6.48; N, 4.36%. Calcd for $C_{14}H_{19}NO_7$: C, 53.67; H, 6.11; N, 4.47%.

1D-(1,2,4/3)-4-Amino-5-cyclohexene-1,2,3-triol [(+)-Conduramine F-4] (23). A similar treatment of compound **17** (435 mg, 1.52 mmol) with CH_2Cl_2 (4.3 ml) and trifluoroacetic acid (4.3 ml) to that described for the preparation of compound **21** afforded **23** (203 mg, 92%) as crystals: Mp 184—186 °C (from water), [lit,[12a)] Mp 188—189 °C (for racemic compound)]; $[\alpha]_D^{26}+99$ (c 0.7, H_2O); IR (KBr) 3340 cm^{-1}; ^{1}H NMR (270 MHz, D_2O) $\delta=3.22$ (dd, 1 H, $J=2.7$, 8.1 Hz), 3.43 (dd, 1 H, $J=8.1$, 10.6 Hz), 3.48 (dd, 1 H, $J=4.4$, 10.6 Hz), 4.13 (dd, 1 H, $J=4.4$, 5.1 Hz), 5.58 (dd, 1 H, $J=1.8$, 9.9 Hz), 5.72 (ddd, 1 H, $J=2.7$, 5.1, 9.9 Hz). Found: C, 48.96; H, 7.99; N, 9.55%. Calcd for $C_6H_{11}NO_3\cdot 1/5H_2O$: C, 48.44; H, 7.72; N, 9.41%.

1D-(1,2,4/3)-4-Acetamido-1,2,3-tri-*O*-acetyl-5-cyclohexene-1,2,3-triol (24). A similar treatment of compound **23** (24 mg, 0.19 mmol) to that described for the preparation of compound **22** afforded **24** (52 mg, 90%) as a colorless syrup; $[\alpha]_D^{25}+81$ (c 1.0, $CHCl_3$); IR (neat) 3350, 3210, 1740, 1630, and 1570 cm^{-1}; ^{1}H NMR (270 MHz) $\delta=1.98$, 2.02, 2.08, 2.10 (4s, each 3 H), 4.78 (dd, 1 H, $J=8.4$, 8.4 Hz), 5.19 (dd, 1 H, $J=4.0$, 11.0 Hz), 5.30 (dd, 1 H, $J=8.4$, 11.0 Hz), 5.63 (ddd, 1 H, $J=1.5$, 2.9, 4.0 Hz), 5.72—5.77 (m, 1 H), 5.77—5.86 (m, 2 H). Found: C, 53.34; H, 6.40; N, 4.30%. Calcd for $C_{14}H_{19}NO_7$: C, 53.67; H, 6.11; N, 4.47%.

1D-(1,2/3,4)-4-Azido-1,2-*O*-isopropylidene-3-*O*-(4-methoxybenzyl)-5-cyclohexene-1,2,3-triol (25). To a solution of compound **4** (containing small amount of compounds **12** and **15**, 6.80 g, 32.0 mmol) in DMF (140 ml) was added NaH (30% in oil, 5.15 g, 129 mmol) at 0 °C; the resulting mixture was stirred at 0 °C for 30 min. To this suspension was added 4-methoxybenzyl chloride (5.24 ml, 39.0 mmol) at 0 °C; the mixture was stirred at room temperature for 2 h. Saturated $NaHCO_3$ solution (160 ml) was added at 0 °C. After stirring at 0 °C for 30 min, the mixture was diluted with water and the products were extracted with EtOAc. The organic layer was washed with brine, and then dried. Removal of the solvent left a residue, which was chromatographed on a column of silica gel (400 g), with EtOAc–toluene (1 : 50) as an eluent, to afford compound **25** (5.63 g, 56%) as a colorless syrup: $[\alpha]_D^{26}+21$ (c 0.9, $CHCl_3$); IR (neat) 2100 and 1515 cm^{-1}; ^{1}H NMR (270 MHz) $\delta=1.36$, 1.40, and 3.80 (3s, each 3 H), 3.81 (dd, 1 H, $J = 4.4$, 6.6 Hz), 3.97 (ddd, 1 H, $J = 1.1$, 4.0, 4.4 Hz), 4.38 (dd, 1 H, $J = 6.6$, 6.6 Hz), 4.65 (ddd, 1 H, $J = 0.7$, 3.3, 6.6 Hz), 4.70 (m, 2 H), 5.85 (ddd, 1 H, $J = 0.7$, 4.0, 9.9 Hz), 6.00 (ddd, 1 H, $J = 1.1$, 3.3, 9.9 Hz), 6.85—6.91 (m, 2 H), 7.28—7.33 (m, 2 H). Found: C, 61.32; H, 6.60; N, 12.63%. Calcd for $C_{14}H_{21}N_3O_4$: C, 61.62; H, 6.38; N, 12.68%.

2-Azido-2-deoxy-4,5-*O*-isopropylidene-3-*O*-(4-methoxybenzyl)-L-mannitol (26). Ozone was bubbled into a solution of compound **25** (2.47 g, 7.44 mmol) in methanol (50 ml) at −78 °C for 40 min. After confirming the disappearance of the starting material by TLC (EtOAc–hexanes, 1 : 2), excess ozone was removed by introducing a stream of Ar. To this solution at −78 °C was added $NaBH_4$ (704 mg, 18.6 mmol); the mixture was gradually warmed up to 0 °C over 2 h. The reaction mixture was neutralized with acetic acid at 0 °C, and then concentrated to give a residue, which was dissolved in EtOAc. The organic layer was washed with brine, and dried. Removal of the solvent left a residue, which was chromatographed on a column of silica gel (100 g), with EtOAc–toluene (1 : 2) as an eluent, to afford compound **26** (2.19 g, 80%) as a colorless syrup: $[\alpha]_D^{26} - 11$ (*c* 0.8, $CHCl_3$); IR (neat) 3450, 2100, and 1515 cm^{-1}; ^1H NMR (270 MHz) $\delta = 1.40$, and 1.51 (2s, each 3 H), 2.24 and 2.35 (2bs, each 1 H), 3.62 (dd, 1 H, $J = 5.1$, 9.5 Hz), 3.70 (d, 2 H, $J = 5.7$ Hz), 3.77—3.87 (m, 2 H), 3.80 (s, 3 H), 3.95 (dd, 1 H, $J = 5.1$, 10.6 Hz), 4.23 (dd, 1 H, $J = 5.7$, 6.2 Hz), 4.33 (dd, 1 H, $J = 6.2$, 6.2 Hz), 4.66 and 4.72 (2d, each 1 H, $J = 11.0$ Hz), 6.85—6.92 (m, 2 H), 7.26—7.33 (m, 2 H). Found: C, 55.20; H, 7.08; N, 11.22%. Calcd for $C_{17}H_{25}N_3O_6$: C, 55.58; H, 6.86; N, 11.44%.

5-Azido-5-deoxy-4-*O*-(4-methoxybenzyl)-1,2-*O*-(1-ethylpropylidene)-L-mannitol (27). A solution of compound **26** (4.14 g, 11.3 mmol) in acetic acid (85 ml) and water (15 ml) was stirred at 50 °C for 2 h. The reaction mixture was concentrated to give a residue, which was dissolved in 3-pentanone (85 ml). To this solution was added *p*-toluenesulfonic acid monohydrate (64 mg, 0.34 mmol); the mixture was stirred at room temperature for 5 h. The reaction mixture was first neutralized with triethylamine at 0 °C, and then concentrated to give a residue, which was chromatographed on a column of silica gel (120 g), with EtOAc–toluene (1 : 4) as an eluent, to afford compound **27** (3.48 g, 78%) as a colorless syrup: $[\alpha]_D^{26} + 18$ (*c* 0.8, $CHCl_3$); IR (neat) 3450, 2100, and 1515 cm^{-1}; ^1H NMR (270 MHz) $\delta = 0.90$ and 0.91 (2t, each 3 H, $J = 7.3$ Hz), 1.63 and 1.66 (2q, each 2 H, $J = 7.3$ Hz), 2.13 and 2.27 (2bs, each 1 H), 3.54—3.63 (m, 1 H), 3.67 (ddd, 1 H, $J = 4.7$, 4.8, 6.8 Hz), 3.72—3.81 (m, 1 H), 3.81 (s, 3 H), 3.88—4.03 (m, 4 H), 4.18 (ddd, 1 H, $J = 3.2$, 7.6, 8.8 Hz), 4.64 and 4.71 (2d, each 1 H, $J = 10.6$ Hz), 6.87—6.93 (m, 2 H), 7.26—7.33 (m, 2 H). Found: C, 57.41; H, 7.79; N, 10.60%. Calcd for $C_{19}H_{29}N_3O_6$: C, 57.71; H, 7.39; N, 10.63%.

2-Azido-1-*O*-(*t*-butyldiphenylsilyl)-2-deoxy-3-*O*-(4-methoxybenzyl)-5,6-*O*-(1-ethylpropylidene)-L-mannitol (28). To a solution of compound **27** (1.30 g, 3.28 mmol) in DMF (19 ml) at 0 °C were added imidazole (3.35 g, 49.2 mmol) and *t*-butylchlorodiphenylsilane (1.36 ml, 5.25 mmol). After first stirring at 0 °C for 10 min, and then at room temperature for 10 h, the reaction mixture was concentrated and diluted with EtOAc. The organic layer was washed with water and dried. Removal of the solvent left a syrup, which was chromatographed on a column of silica gel (100 g), with EtOAc–toluene (1 : 30) as an eluent, to afford compound **28** (2.12 g, 100%) as a colorless syrup: $[\alpha]_D^{15} + 23$ (*c* 1.1, $CHCl_3$); IR (neat) 3450, 2100, and 1515 cm^{-1}; ^1H NMR (270 MHz) $\delta = 0.90$ and 0.91 (2t, each 3 H, $J = 7.3$ Hz), 1.09 (s, 9 H), 1.63 (q, 4 H, $J = 7.3$ Hz), 2.13 (bd, 1 H, $J = 9.9$ Hz), 3.59—3.71 (m, 2 H), 3.75—3.81 (m, 2 H), 3.77 (s, 3 H), 3.91—4.02 (m, 3 H), 4.17 (ddd, 1 H, $J = 3.3$, 6.8, 8.6 Hz), 4.42 and 4.51 (2d, each 1 H, $J = 10.6$ Hz), 6.73—6.78 (m, 2 H), 6.96—7.02 (m, 2 H), 7.36—7.49 (m, 6 H), 7.66—7.70 (m, 4 H). Found: C, 66.04; H, 7.64; N, 6.45%. Calcd for $C_{35}H_{47}N_3O_6Si$: C, 66.32; H, 7.42; N, 6.63%.

2-Azido-1-*O*-(*t*-butyldiphenylsilyl)-2-deoxy-4-*O*-methanesulfonyl-3-*O*-(4-methoxybenzyl)-5,6-*O*-(1-ethylpropylidene)-L-mannitol (29). To a solution of compound **28** (618 mg, 0.975 mmol) in CH_2Cl_2 (12 ml) at 0 °C were added triethylamine (1.36 ml, 9.75 mmol) and methanesulfonyl chloride (0.14 ml, 1.81 mmol). The reaction mixture was first stirred at 0 °C for 10 min, and then at room temperature for 1 h. Water (1 ml) was added at 0 °C, and the resulting mixture was stirred at 0 °C for 10 min. The mixture was diluted with saturated $NaHCO_3$ solution, and extracted twice with $CHCl_3$. The combined organic layer was dried and concentrated to give a residue, which was chromatographed on a column of silica gel (20 g), with EtOAc–toluene (1 : 8) as an eluent, to afford compound **29** (693 mg, 100%) as a colorless syrup: $[\alpha]_D^{16} + 13$ (*c* 1.1, $CHCl_3$); IR (neat) 2100 and 1515 cm^{-1}; ^1H NMR (270 MHz) $\delta = 0.91$ and 0.94 (2t, each 3 H, $J = 7.7$ Hz), 1.09 (s, 9 H), 1.65 and 1.68 (2q, each 2 H, $J = 7.7$ Hz), 3.04 (s, 3 H), 3.64 (ddd, 1 H, $J = 2.9$, 6.2, 9.5 Hz), 3.76 (s, 3 H), 3.78 (dd, 1 H, $J = 6.2$, 10.6 Hz), 3.86 (dd, 1 H, $J = 1.5$, 9.5 Hz), 4.03 (dd, 1 H, $J = 2.9$, 10.6 Hz), 4.08 (dd, 1 H, $J = 6.6$, 8.6 Hz), 4.18 (dd, 1 H, $J = 5.9$, 8.8 Hz), 4.30 (ddd, 1 H, $J = 5.9$, 6.6, 8.1 Hz), 4.37 and 4.60 (2d, each 1 H, $J = 10.3$ Hz), 4.98 (dd, 1 H, $J = 1.5$, 8.1 Hz), 6.70—6.75 (m, 2 H), 6.93—6.98 (m, 2 H), 7.36—7.70 (m, 10 H). Found: C, 60.61; H, 7.23; N, 5.77%. Calcd for $C_{36}H_{49}N_3O_8SSi$: C, 60.73; H, 6.94; N, 5.90%.

2-Azido-1-*O*-(*t*-butyldiphenylsilyl)-2-deoxy-4-*O*-methanesulfonyl-3-*O*-(4-methoxybenzyl)-L-mannitol (30). A solution of compound **29** (1.687 g, 2.374 mmol) in acetic acid (51 ml) and water (9 ml) was stirred at 50 °C for 17 h. The reaction mixture was concentrated and co-distilled with toluene to afford a residue, which was chromatographed on a column of silica gel (120 g), with EtOAc–toluene (1 : 2) as an eluent, to afford compound **30** (1.138 g, 75%) as a colorless syrup: IR (neat) 3450, 2100, and 1515 cm^{-1}; ^1H NMR (270 MHz) $\delta = 1.10$ (s, 9 H), 2.20—2.60 (b, 2 H), 3.08 (s, 3 H), 3.69 (ddd, 1 H, $J = 2.7$, 2.7, 9.5 Hz), 3.76 (s, 3 H), 3.74—3.93 (m, 6 H), 3.96 (dd, 1 H, $J = 1.5$, 9.5 Hz), 4.05 (dd, 1 H, $J = 2.7$, 10.4 Hz), 4.38 and 4.56 (2d, each 1 H, $J = 10.4$ Hz), 4.93 (dd, 1 H, $J = 1.5$, 8.8 Hz), 6.70—6.75 (m, 2 H), 6.94—6.98 (m, 2 H), 7.35—7.72 (m, 10 H). This compound was used in the next reaction without further purification.

2-Azido-1-*O*-(*t*-butyldiphenylsilyl)-2-deoxy-3-*O*-(4-methoxybenzyl)-D-4,5-anhydroribitol (32). To a solution of compound **30** (1.138 g, 1.768 mmol) in benzene (20 ml) under dark at room temperature was added lead(IV) acetate (1.098 g, 2.476 mmol). After stirring at room temperature for 30 min, the insoluble material was removed by filtration through celite and washed with benzene. The filtrate and washings were first combined, and then concentrated, to give a residue, which was dissolved in methanol (20 ml). To this solution at 0 °C was added $NaBH_4$ (100 mg, 2.65 mmol); the mixture was stirred at room temperature for 1 h. The reaction mixture was neutralized with acidic resin (Amberlite IR 120B, H^+ form), and the insoluble material was removed by filtration. The filtrate was concentrated to give a residue, which was diluted with EtOAc, washed with brine, and then dried. Removal of the solvent afford crude primary alcohol derivative (**31**) as a colorless syrup. This was dissolved in methanol (20 ml) and treated with sodium methoxide (1 mol dm^{-3} solution, 2.1 ml, 2.1 mmol) at 0 °C. After stirring at room temperature for 4 h, the reaction mixture was neutralized with acetic acid at 0 °C and concentrated to afford a residue, which was dissolved in EtOAc and then washed with saturated $NaHCO_3$ solution and brine, and dried. Removal of the solvent left a residue, which was chromatographed on a column of silica gel (50 g), with EtOAc–toluene (1 : 10) as an eluent, to afford compound **32** (768 mg, 84%) as a colorless syrup: $[\alpha]_{\mathrm{D}}^{26}$ +29 (*c* 1.1, $CHCl_3$); IR (neat) 2100 and 1515 cm^{-1}; ^{1}H NMR (270 MHz) δ = 1.07 (s, 9 H), 2.66 (dd, 1 H, *J* = 2.6, 5.5 Hz), 2.71 (dd, 1 H, *J* = 3.7, 5.5 Hz), 3.06 (ddd, 1 H, *J* = 2.6, 3.7, 4.8 Hz), 3.45 (dd, 1 H, *J* = 4.8, 5.0 Hz), 3.62 (ddd, 1 H, *J* = 4.8, 5.0, 6.6 Hz), 3.79 (s, 3 H), 3.83 (dd, 1 H, *J* = 4.8, 10.6 Hz), 3.87 (dd, 1 H, *J* = 6.6, 10.6 Hz), 4.38 and 4.53 (2d, each 1 H, *J* = 11.0 Hz), 6.78—6.83 (m, 2 H), 7.09—7.14 (m, 2 H), 7.35—7.68 (m, 10 H). Found: C, 67.55; H, 7.01; N, 8.18%. Calcd for $C_{29}H_{35}N_3O_4Si$: C, 67.28; H, 6.81; N, 8.12%.

2-(*t*-Butoxycarbonyl)amino-1-*O*-(*t*-butyldiphenylsilyl)-2-deoxy-3-*O*-(4-methoxybenzyl)-D-4,5-anhydroribitol (5). A mixture of compound **32** (42 mg, 0.080 mmol), Boc_2O (88 mg, 0.40 mmol), and Pd–$BaSO_4$ (30 mg) in EtOAc (0.8 ml) and ethanol (0.2 ml) was stirred under 1 atm of H_2 at room temperature for 30 h. The catalyst was removed by filtration, and the filtrate was concentrated to give a residue, which was chromatographed on a column of silica gel (3.5 g), with EtOAc–hexanes (1 : 10) as an eluent, to afford compound **5** (36 mg, 75%) as a colorless syrup: $[\alpha]_{\mathrm{D}}^{26}$ +7 (*c* 1.2, $CHCl_3$); IR (neat) 1710 and 1515 cm^{-1}; ^{1}H NMR (270 MHz) δ = 1.07 and 1.43 (2s, each 9 H), 2.70 (dd, 1 H, *J* = 2.2, 5.5 Hz), 2.71 (dd, 1 H, *J* = 3.3, 5.5 Hz), 3.06 (m, 1 H), 3.57 (dd, 1 H, *J* = 4.4, 6.6 Hz), 3.75—3.93 (m, 3 H), 3.79 (s, 3 H), 4.34 and 4.58 (2d, each 1 H, *J* = 10.6 Hz), 4.86 (bd, 1 H, *J* = 8.5 Hz), 6.78—6.84 (m, 2 H), 7.08—7.15 (m, 2 H), 7.32—7.69 (m, 10 H); MS *m*/*z* (FAB, glycerol matrix) 592 (M^{+} + H; 33%), 553 (9), 536 (27). Found: C, 68.83; H, 7.87; N, 2.51%. Calcd for $C_{34}H_{45}NO_6Si$: C, 69.00; H, 7.66; N, 2.37%.

Preparation of Diundecylmagnesium Solution. An ethereal solution of undecylmagnesium bromide was prepared from Mg (165 mg, 6.79 mmol) and undecyl bromide (1.37 ml, 6.17 mmol) in diethyl ether (6.2 ml) under Ar. To this solution under Ar was added 1,4-dioxane (0.53 ml, 6.22 mmol) at room temperature; the mixture was vigorously stirred at room temperature for 2 h. The resulting suspension was centrifuged (2500 rpm, 10 min), and the supernatant layer was used as 1.0 mol dm^{-3} solution of diundecylmagnesium in diethyl ether.

(2*S*,3*S*,4*R*)-2-(*t*-Butoxycarbonyl)amino-1-(*t*-butyldiphenylsilyloxy)-3-(4-methoxybenzyloxy)-4-hexadecanol (34). To a stirred mixture of compound **5** (295 mg, 0.500 mmol) and CuCN (22 mg, 0.25 mmol) in diethyl ether (6 ml) at 0 °C was added diundecylmagnesium in diethyl ether (1.0 mmol solution, 2.0 ml, 2.0 mmol). After stirring at room temperature for 3 h, the reaction was quenched by the addition of a saturated aqueous NH_4Cl solution at 0 °C. The mixture was diluted with EtOAc and washed with saturated $NaHCO_3$ solution and brine, and then dried. Removal of the solvent left a residue, which was chromatographed on a column of silica gel (30 g), with EtOAc–toluene (1 : 50) as an eluent, to afford compound **34** (231 mg, 62%) as a colorless syrup: $[\alpha]_{\mathrm{D}}^{23}$ +6 (*c* 1.3, $CHCl_3$); IR (neat) 1710 and 1515 cm^{-1}; ^{1}H NMR (270 MHz) δ = 0.88 (t, 3 H, *J* = 7.1 Hz), 1.08 (s, 9 H), 1.26 (m, 20 H), 1.41 (s, 9 H), 1.47—1.55 (m, 2 H), 2.08 (bs, 1 H), 3.53 (dd, 1 H, *J* = 4.0, 5.9 Hz), 3.71—3.87 (m, 3 H), 3.79 (s, 3 H), 3.88—4.00 (m, 2 H), 4.45 and 4.58 (2d, each 1 H, *J* = 10.6 Hz), 4.81 (bd, 1 H, *J* = 8.5 Hz), 6.80—6.87 (m, 2 H), 7.12—7.19 (m, 2 H), 7.32—7.69 (m, 10 H). Found: C, 72.12; H, 9.57; N, 2.15%. Calcd for $C_{45}H_{69}NO_6Si$: C, 72.25; H, 9.30; N, 1.87%.

(2*S*,3*S*,4*R*)-2-Acetamido-tri-*O*-acetyl-1,3,4-hexadecanetriol (36). A solution of compound **34** (27 mg, 0.035 mmol) in THF (1 ml) and 5 mol dm^{-3} aqueous HCl solution (0.5 ml) was stirred at 60 °C for 12 h. The mixture was concentrated and co-distilled with ethanol and toluene to give crude (2*S*,3*S*,4*R*)-2-amino-1,3,4-hexadecanetriol hydrochloride (**35**). To a solution of crude **35** in methanol (1 ml) was added a 0.1 mol dm^{-3} solution of K_2CO_3 in methanol (0.5 mmol). After being stirred at room temperature for 30 min, the insoluble material was removed by filtration and the filtrate was concentrated to give a residue, which was dissolved in pyridine (0.5 ml) and acetic anhydride (0.4 ml). After being stirred at room temperature for 5 h, the reaction mixture was concentrated to give a residue, which was chromatographed on a column of silica gel (1 g), with EtOAc–toluene (1 : 1) as an eluent, to afford compound **36** (12 mg, 74%) as colorless syrup: $[\alpha]_{\mathrm{D}}^{19}$ +31 (*c* 0.8, $CHCl_3$) {lit,[3c] $[\alpha]_{\mathrm{D}}^{25}$ +27.9 (*c* 1.5, $CHCl_3$)}; IR (neat) 3300, 1750, 1650, and 1540 cm^{-1}; ^{1}H NMR (270 MHz) δ = 0.88 (t, 3 H, *J* = 6.6 Hz), 1.25 (m, 22 H), 2.03 (s, 3 H), 2.05 (s, 6 H), 2.08 (s, 3 H), 4.00 (dd, 1 H, *J* = 3.3, 11.7 Hz), 4.29 (dd, 1 H, *J* = 5.0, 11.7 Hz), 4.47 (m, 1 H), 4.94 (dt, 1 H, *J* = 3.5, 8.4 Hz), 5.10 (dd, 1 H, *J* = 3.1, 8.4 Hz), 5.93 (bd, 1 H, *J* = 9.2 Hz); ^{13}C NMR (67 MHz in $CDCl_3$) δ = 14.1, 20.8, 21.0, 22.7, 23.3, 25.5, 28.1, 29.3, 29.5, 29.5, 29.6, 31.9, 47.6, 62.8, 72.0, 72.9, 169.7, 170.1, 170.8, 171.1; MS *m*/*z* (FAB, glycerol matrix) 458 (M^{+} + H; 53%), 416 (22), 399 (11), 398 (50). The ^{1}H and ^{13}C NMR data were fully identical with those of the authentic compound reported by Komori.[3c]

(2*S*, 3*S*, 4*R*)- 2- [(*R*)- 2- Acetoxytetracosanoylamino]- 1, 3, 4-hexadecanetriol (38). A solution of compound **34** (18 mg, 0.024 mmol) in THF (1 ml) and 5 mol dm^{-3} aqueous HCl solution (0.5 ml) was stirred at 60 °C for 12 h. The reaction mixture was concentrated and co-distilled with ethanol and toluene to afford crude **35**, which was dissolved in DMF (1 ml). (*R*)-2-Acetoxytetracosanoic acid[5a] (**37**, 13 mg, 0.031 mmol) was added to this solution. To this mixture at 0 °C were added diethyl cyanophosphonate (7.5 µl, 0.048 mmol) and triethylamine (6.6 µl, 0.047 mmol). After being stirred at room temperature for 3 h, the reaction mixture was concentrated to give a residue, which was chromatographed on a column of silica gel (5 g), with methanol–$CHCl_3$ (1 : 30) as an eluent, to afford compound **38** (12 mg, 74%) as amorphous solid: $[\alpha]_{\mathrm{D}}^{22}$ +6 (*c* 0.8, $CHCl_3$); IR (neat) 3280, 1745, and 1660 cm^{-1}; ^{1}H NMR (270 MHz) δ = 0.88 (t, 6 H, *J* = 7.0 Hz), 1.17—1.58 (m, 62 H), 1.65—1.89 (m, 2 H), 2.16 (s, 3 H), 3.12 (b, 3 H), 3.58—3.68 (m, 2 H), 3.72 (dd, 1 H, *J* = 6.2, 11.0 Hz), 3.92 (dd, 1 H, *J* = 2.2, 11.0 Hz), 4.06—4.19 (m, 1 H), 5.07 (t, 1 H, *J* = 6.2 Hz), 6.90 (bd, 1 H, *J* = 7.3 Hz); ^{13}C NMR (67 MHz in $CDCl_3$) δ = 14.1, 20.1, 22.7, 24.9, 25.7, 29.3, 29.3, 29.4, 29.6, 29.7, 31.8, 31.9, 33.3, 53.0, 61.7, 72.6, 74.3, 76.3, 170.2, 171.1; MS *m*/*z* (FAB, glycerol matrix) 698 (M^{+} + H; 5%), 469 (2), 459 (35), 407 (100).

(2*S*,3*S*,4*R*)-2-[(*R*)-2-Acetoxytetracosanoylamino]-3,4-diacetoxy-1-*O*-(2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyl)-1-hexadecanol (40). To a stirred mixture of compound **38** (15.1 mg, 0.0216 mmol), 2,3,4,6-tetra-*O*-acetyl-*α*-D-glucopyranosyl trichloroacetimidate (**39**)[17] (21.3 mg, 0.0432 mmol), and molecular sieves 4A (10 mg) in dichloromethane (1 ml) at 0 °C under Ar was added $BF_3 \cdot OEt_2$ (13.5 µl, 0.108 mmol). After being stirred at 0 °C for 4 h, the reaction mixture was quenched by the addition of saturated aqueous sodium hydrogencarbonate solution. The product was extracted with EtOAc, washed with brine, and dried. Removal of the solvent afforded a residue, which was chromatographed on a column of silica gel (1 g), with acetone–toluene (1 : 10) as an eluent, to afford crude glucoside (15 mg). This was dissolved in pyridine (1 ml) and acetic anhydride (0.5 ml); the resulting solution was stirred at room temperature for 3 h. The mixture was concentrated to give a residue, which was chromatographed on a column of silica gel (1 g), with acetone–toluene (1 : 10) as an eluent, to afford compound

40 (4.8 mg, 48%) as amorphous solid: $[\alpha]_D^{22}+6$ (c 0.7, $CHCl_3$); IR (neat) 3350, 1745, and 1650 cm^{-1}; ^{1}H NMR (270 MHz) $\delta=0.88$ (t, 6 H, $J=7.0$ Hz), 1.15—1.89 (m, 64 H), 1.99 and 2.02 (2s, each 3 H), 2.05 (s, 6 H), 2.07, 2.09, and 2.24 (3s, each 3 H), 3.64—3.74 (m, 2 H), 3.86 (dd, 1 H, $J=3.2$, 11.0 Hz), 4.12 (dd, 1 H, $J=2.2$, 12.5 Hz), 4.21—4.32 (m, 2 H), 4.48 (d, 1 H, $J=8.1$ Hz), 4.82—4.89 (m, 1 H), 4.89 (dd, 1 H, $J=8.1$, 9.5 Hz), 5.06 (dd, 1 H, $J=9.5$, 9.5 Hz), 5.09—5.15 (m, 2 H), 5.19 (dd, 1 H, $J=9.5$, 9.5 Hz), 6.74 (bd, 1 H, $J=8.8$ Hz); ^{13}C NMR (67 MHz in $CDCl_3$) $\delta=14.1$, 20.5, 20.6, 20.7, 20.7, 20.9, 21.0, 22.7, 24.9, 25.6, 28.3, 29.3, 29.4, 29.5, 29.6, 29.6, 29.7, 29.7, 31.8, 31.9, 48.2, 61.8, 66.7, 68.1, 71.3, 71.7, 71.9, 72.7, 73.2, 74.0, 100.4, 169.3, 169.4, 169.8, 169.9, 170.2, 170.3, 170.6, 171.1; MS m/z (FAB, glycerol matrix) 1112 (M^++H; 100%), 1053 (86), 993 (25).

Acanthacerebroside A (1). To a stirred solution of compound **40** (8.5 mg, 7.6 μmol) in methanol (1 ml) at 0 °C was added a 0.05 mol dm^{-3} solution of K_2CO_3 in methanol (0.2 ml); the mixture was stirred at room temperature for 1 h. The reaction mixture was neutralized with acidic resin [Amberlite IR 120A (H^+ form)]. The insoluble material was removed by filtration and the filtrate was concentrated to give a residue, which was chromatographed on a column of silica gel (1 g), with MeOH–$CHCl_3$ (1 : 12) as an eluent, to afford **1** (5.8 mg, 92%) as amorphous solid: $[\alpha]_D^{22}+9$ (c 0.15, 1-propanol) {lit,[2a] +9.4 (c 0.6, 1-propanol)}; IR (neat) 3350 and 1650 cm^{-1}; ^{1}H NMR (270 MHz in pyridine-d_5) $\delta=0.875$ and 0.878 (2t, each 3 H, $J=7.0$ Hz), 1.15—2.25 (m, 64 H), 3.88 (m, 1 H), 4.03 (dd, 1 H, $J=7.8$, 8.0 Hz), 4.16—4.25 (m, 3 H), 4.26—4.40 (m, 2 H), 4.46—4.64 (m, 3 H), 4.74 (dd, 1 H, $J=6.6$, 10.7 Hz), 4.97 (d, 1 H, $J=7.8$ Hz), 5.29 (m, 1 H), 8.58 (d, 1 H, $J=9.2$ Hz); ^{13}C NMR (67 MHz in pyridine-d_5) $\delta=14.1$, 22.7, 25.7, 26.4, 29.4, 29.5, 29.8, 30.0, 30.2, 31.9, 34.0, 35.4, 51.5, 62.4, 70.4, 71.2, 72.2, 72.3, 75.0, 75.6, 78.3, 78.4, 105.4, 175.4; MS m/z (FAB, glycerol matrix) 818 (M^++H; 12%), 800 (2), 774 (4), 656 (9). The ^{1}H and ^{13}C NMR data were fully identical with those of the natural product reported by Higuchi and Komori.[2a]

***(R)*-1-(Benzyloxy)-2-pentadecanol (42).** To a mixture of compound **41**[19] (167 mg, 1.02 mmol) and CuCN (45 mg, 0.51 mmol) in diethyl ether (3.5 ml) under Ar at 0 °C was added an ethereal solution of didodecylmagnesium (1.0 mol dm^{-3}; 2.5 ml, 2.5 mmol), prepared from magnesium and dodecyl bromide by a similar procedure as that described for the preparation of a diundecylmagnesium solution (vide supra). After being stirred at room temperature for 2 h, the reaction mixture was quenched by the addition of saturated an aqueous NH_4Cl solution at 0 °C. The product was extracted with EtOAc, and the extract was washed with saturated $NaHCO_3$ solution and brine, and dried. Removal of the solvent left a residue, which was chromatographed on a column of silica gel (15 g), with EtOAc–toluene (1 : 50) as an eluent, to afford compound **42** (230 mg, 88%) as crystals: Mp 37.5—39 °C (from hexanes): $[\alpha]_D^{23}-3$ (c 1.3, $CHCl_3$); IR (neat) 3300, 1470, and 1455 cm^{-1}; ^{1}H NMR (270 MHz) $\delta=0.88$ (t, 3 H, $J=6.8$ Hz), 1.19—1.51 (m, 24 H), 2.18 (bs, 1 H), 3.32 (dd, 1 H, $J=8.1$, 9.5 Hz), 3.50 (dd, 1 H, $J=3.1$, 9.5 Hz), 3.76—3.86 (m, 1 H), 4.55 (s, 2 H), 7.26—7.39 (m, 5 H). Found: C, 78.59; H, 11.75%. Calcd for $C_{22}H_{38}O_2$: C, 78.99; H, 11.45%.

***(R)*-1-(Benzyloxy)-2-(methoxymethoxy)pentadecane (43).** To a solution of compound **42** (180 mg, 0.538 mmol) in CH_2Cl_2 (3.5 ml) at 0 °C were added *N*,*N*-diisopropylethylamine (0.466 ml, 2.68 mmol) and chloromethyl methyl ether (0.122 ml, 1.61 mmol). After being stirred at room temperature for 2 h, the reaction mixture was diluted with EtOAc and washed successively with a 1 mol dm^{-3} aqueous HCl solution, a saturated $NaHCO_3$ solution, and brine, and then dried. Removal of the solvent left a residue, which was chromatographed on a column of silica gel (10 g), with EtOAc–hexanes (1 : 15) as an eluent, to afford compound **43** (198 mg, 97%) as a colorless syrup: $[\alpha]_D^{23}+10$ (c 1.3, $CHCl_3$); IR (neat) 1470 and 1455 cm^{-1}; ^{1}H NMR (270 MHz) $\delta=0.88$ (t, 3 H, $J=7.0$ Hz), 1.21—1.35 (m, 22 H), 1.50—1.65 (m, 2 H), 3.38 (s, 3 H), 3.49 (d, 2 H, $J=5.4$ Hz), 3.73 (dt, 1 H, $J=5.1$, 10.3 Hz), 4.51 and 4.56 (2d, each 1 H, $J=10.3$ Hz), 4.67 and 4.77 (2d, each 1 H, $J=7.0$ Hz), 7.23—7.38 (m, 5 H). Found: C, 76.14; H, 11.26%. Calcd for $C_{24}H_{42}O_3$: C, 76.14; H, 11.18%.

***(R)*-2-(Methoxymethoxy)-1-pentadecanol (44).** A mixture of compound **43** (197 mg, 0.521 mmol) and 10% Pd on carbon (20 mg) in ethanol (4 ml) was stirred under 1 atm of H_2 at room temperature for 10 h. The catalyst was removed by filtration, and the filtrate was concentrated to give a residue, which was chromatographed on a column of silica gel (10 g), with EtOAc–hexanes (1 : 10) as an eluent, to afford compound **44** (147 mg, 98%) as a colorless syrup: $[\alpha]_D^{23}-30$ (c 1.0, $CHCl_3$); IR (neat) 3450 cm^{-1}; ^{1}H NMR (270 MHz) $\delta=0.88$ (t, 3 H, $J=7.0$ Hz), 1.24—1.55 (m, 24 H), 2.84 (bs, 1 H), 3.43 (s, 3 H), 3.47—3.63 (m, 3 H), 4.68 and 4.74 (2d, each 1 H, $J=7.0$ Hz). Found: C, 70.51; H, 12.87%. Calcd for $C_{17}H_{36}O_3$: C, 70.78; H, 12.58%.

***(R)*-2-(Methoxymethoxy)pentadecanoic Acid (45).** To a stirred solution of compound **44** (168 mg, 0.581 mmol) in acetone (3 ml) at 0 °C was added Jones reagent (2.67 mol dm^{-3} solution of CrO_3 in 4.1 mol dm^{-3} aqueous H_2SO_4; 1 ml, 2.67 mmol); the mixture was stirred at 0 °C for 5 h. After the addition of 2-propanol (1 ml) at 0 °C, the reaction mixture was first filtered through celite, and the filtrate was then neutralized with triethylamine, and concentrated to give a residue, which was chromatographed on a column of silica gel (10 g), with acetone–hexanes (1 : 12) as an eluent, to afford compound **45** (117 mg, 67%) as crystals: Mp 54.5—56 °C (from EtOH); $[\alpha]_D^{23}+26$ (c 0.9, $CHCl_3$); IR (KBr) 3000—3600 and 1730 cm^{-1}; ^{1}H NMR (270 MHz) $\delta=0.88$ (t, 3 H, $J=7.0$ Hz), 1.21—1.51 (m, 22 H), 1.76—1.86 (m, 2 H), 3.42 (s, 3 H), 4.17 (t, 1 H, $J=6.2$ Hz), 4.69 and 4.74 (2d, each 1 H, $J=6.6$ Hz); MS m/z (EI) 303 (M^++H; 1.3%), 302 (1.4), 285 (1.5), 270 (11), 257 (100).

***(R)*-2-Acetoxypentadecanoic Acid (46).** A solution of compound **45** (117 mg, 0.388 mmol) in 1,4-dioxane (5 ml) and 2 mol dm^{-3} aqueous HCl solution (0.5 ml) was stirred at 100 °C for 12 h. The mixture was concentrated and co-distilled with EtOH and toluene (each three times) to give an only residue, which was treated with pyridine (3 ml) and acetic anhydride (2 ml) at room temperature for 3 h. The reaction mixture was concentrated to give a residue, which was chromatographed on a column of silica gel (10 g), with acetone–hexanes (1 : 10) as an eluent, to afford compound **46** (91 mg, 78%) as crystals: Mp 43—44 °C (from EtOH); $[\alpha]_D^{23}+9$ (c 0.7, $CHCl_3$); IR (KBr) 3440—3560, 1730, and 1720 cm^{-1}; ^{1}H NMR (270 MHz) $\delta=0.88$ (t, 3 H, $J=7.0$ Hz), 1.19—1.49 (m, 22 H), 1.81—1.92 (m, 2 H), 2.14 (s, 3 H), 5.01 (t, 1 H, $J=5.9$ Hz); ^{13}C NMR (67 MHz in $CDCl_3$) $\delta=14.1$, 20.6, 22.7, 25.1, 29.1, 29.3, 29.5, 29.6, 30.9, 31.9, 71.9, 170.7, 176.1. Found: C, 67.79; H, 10.53%. Calcd for $C_{17}H_{32}O_4$: C, 67.96; H, 10.74%.

4-Heptadecyn-1-ol (47). To a solution of 4-pentyn-1-ol (3.0 ml, 32.2 mmol) in THF (100 ml) under Ar at −78 °C was added butyllithium (1.6 mol dm^{-3} solution in hexanes; 46.4 ml, 74.2 mmol) dropwise. The reaction mixture was gradually warmed up to 0 °C over a period of 3 h, and then cooled to −40 °C. To this solution were added HMPA (28.1 ml, 161 mmol) and dodecyl bromide (7.88 ml, 32.2 mmol); the whole mixture was first stirred at −40 °C for 30 min, and then at room temperature for 2 h. The mixture was diluted with saturated aqueous NH_4Cl solution and the product was extracted with EtOAc. The extract was washed with saturated aqueous $NaHCO_3$ solution and brine, and dried. Removal of the solvent left a residue, which was chromatographed on a column of silica gel (300 g), with EtOAc–toluene (1 : 20) as an eluent, to afford compound **47** (5.48 g, 67%) as a colorless syrup: IR (neat) 3340 cm^{-1}; ^1HNMR (270 MHz) $\delta=0.88$ (t, 3 H, $J=7.0$ Hz), 1.20—1.40 (m, 17 H), 1.41—1.51 (m, 2 H), 1.74 (tt, 1 H, $J=6.2$, 7.0 Hz), 2.13 and 2.28 (2ddt, each 1 H, $J=7.0$, 2.6, 2.2 Hz), 3.76 (t, 1 H, $J=6.2$ Hz); MS *m*/*z* (EI) 252 (M^+; 0.5%), 225 (0.1), 168 (8.4).

(4*Z*)-4-Heptadecen-1-ol (48). A mixture of compound **47** (930 mg, 3.66 mmol) and Lindlar catalyst (100 mg) in EtOAc (20 ml) was stirred under 1 atom of H_2 at room temperature for 72 h. The catalyst was removed by filtration, and the filtrate was concentrated to give a residue, which was chromatographed on a column of silica gel (10 g), with EtOAc–hexanes (1 : 40) as an eluent, to afford compound **48** (788 mg, 85%) as a colorless syrup: IR (neat) 3340 cm^{-1}; ^1HNMR (270 MHz) $\delta=0.88$ (t, 3 H, $J=7.0$ Hz), 1.23—1.38 (m, 18 H), 1.63 (tt, 2 H, $J=6.6$, 6.6 Hz), 1.68 (bs, 1 H), 2.00—2.15 (m, 4 H), 3.66 (t, 2 H, $J=6.6$ Hz), 5.35 and 5.42 (2ddt, each 1 H, $J=11.0$, 5.9, 1.1 Hz); MS *m*/*z* (EI) 255 (M^++H; 4.7%), 254 (7.9), 253 (17.1), 236 (13.7).

(4*Z*)-1-Bromo-4-heptadecene (49). To a solution of compound **48** (2.29 g, 9.00 mmol) in DMF (50 ml) at 0 °C were added triphenylphosphine (3.54 g, 13.5 mmol) and *N*-bromosuccinimide (1.92 g, 10.8 mmol). After being stirred at 0 °C for 2 h, the reaction mixture was diluted with hexanes, and successively washed with a 10% aqueous $Na_2S_2O_3$ solution, a saturated aqueous $NaHCO_3$ solution and brine, and then dried. Removal of the solvent left a residue, which was chromatographed on a column of silica gel (100 g), with hexanes as an eluent, to afford compound **49** (2.63 g, 92%) as a colorless liquid: IR (neat) 2920 cm^{-1}; ^1HNMR (270 MHz) $\delta=0.88$ (t, 3 H, $J=7.0$ Hz), 1.22—1.39 (m, 18 H), 1.90 (tt, 2 H, $J=6.6$, 6.6 Hz), 2.04 (m, 2 H), 2.18 (m, 2 H), 3.41 (t, 2 H, $J=6.6$ Hz), 5.29 (dtt, 1 H, $J=11.0$, 7.0, 1.5 Hz), 5.44 (dtt, 1 H, $J=11.0$, 7.3, 1.5 Hz); ^{13}CNMR (67 MHz in $CDCl_3$) $\delta=14.1$, 22.7, 25.6, 27.3, 29.3, 29.4, 29.5, 29.7, 31.9, 32.7, 33.3, 127.3, 131.8. Found: C, 64.05; H, 10.76%. Calcd for $C_{17}H_{33}Br$: C, 64.34; H, 10.48%.

(2*S*,3*S*,4*R*,9*Z*)-2-(*t*-Butoxycarbonyl)amino-1-(*t*-butyldiphenylsilyloxy)-3-(4-methoxybenzyloxy)-9-docosen-4-ol (50). To a stirred mixture of compound **5** (112 mg, 0.190 mmol) and CuCN (8.5 mg, 0.095 mmol) in diethyl ether (2 ml) at 0 °C was added bis[(4*Z*)-4-heptadecenyl)]magnesium in diethyl ether, prepared from magnesium and compound **49** by a similar procedure to that described for the preparation of a bis(undecyl)magnisium solution (vide supra) (1.0 mol dm^{-3} solution; 1.4 ml, 1.4 mmol). After stirring at room temperature for 3 h, the reaction was quenched by the addition of a saturated aqueous NH_4Cl solution at 0 °C. The mixture was diluted with EtOAc and washed with a saturated $NaHCO_3$ solution and brine, and then dried. Removal of the solvent left a residue, which was chromatographed on a column of silica gel (30 g), with EtOAc–toluene (1 : 50) as an eluent, to afford compound **50** (89 mg, 57%) as a colorless syrup: $[\alpha]_D^{23}+5$ (*c* 1.3, $CHCl_3$); IR (neat) 3440 and 1715 cm^{-1}; ^1HNMR (270 MHz) $\delta=0.88$ (t, 3 H, $J=7.0$ Hz), 1.08 (s, 9 H), 1.21—1.37 (m, 26 H), 1.41 (s, 9 H), 1.96—2.18 (m, 4 H), 2.49 (bs, 1 H), 3.52 (dd, 1 H, $J=4.4$, 6.2 Hz), 3.70—3.86 (m, 3 H), 3.79 (s, 3 H), 3.80—3.86 (m, 1 H), 4.45 and 4.57 (2d, each 1 H, $J=11.0$ Hz), 5.23 and 5.37 (2dtt, each 1 H, $J=11.1$, 3.7, 1.8 Hz), 6.79—6.82 (m, 2 H), 7.11—7.19 (m, 2 H), 7.32—7.48 (m, 6 H), 7.61—7.69 (m, 4 H). Found: C, 73.89; H, 9.93; N, 1.86%. Calcd for $C_{51}H_{79}NO_6Si$: C, 73.78; H, 9.59; N, 1.69%.

(2*S*,3*S*,4*R*,9*Z*)-2-[(*R*)-2-Acetoxypentadecanoylamino]-9-docosen-1,3,4-triol (52). A solution of compound **50** (57 mg, 0.068 mmol) in THF (1 ml) and 5 mol dm^{-3} aqueous HCl solution (0.8 ml) was stirred at 60 °C for 22 h. The reaction mixture was concentrated and co-distilled with ethanol and toluene (each three times) to afford crude **51** as a residue, which was dissolved in DMF (1 ml). Compound **46** (23 mg, 0.075 mmol) was added to this solution. To this mixture at 0 °C were added diethyl cyanophosphonate (22 µl, 0.136 mmol) and triethylamine (19 µl, 0.136 mmol). After being stirred at room temperature for 2 h, the reaction mixture was concentrated to give a residue, which was chromatographed on a column of silica gel (10 g), with methanol–$CHCl_3$ (1 : 30) as an eluent, to afford compound **52** (27 mg, 60%) as a colorless syrup: $[\alpha]_D^{19}+7$ (*c* 1.3, $CHCl_3$); IR (neat) 3300, 1745, and 1660 cm^{-1}; ^1HNMR (270 MHz) $\delta=0.88$ (t, 6 H, $J=7.0$ Hz), 1.16—1.59 (m, 50 H), 1.94—2.10 (m, 4 H), 2.16 (s, 3 H), 3.22 (bs, 3 H), 3.56—3.67 (m, 2 H), 3.72 (dd, 1 H, $J=5.1$, 11.4 Hz), 3.92 (dd, 1 H, $J=2.2$, 11.4 Hz), 4.07—4.18 (m, 1 H), 5.05 (dd, 1 H, $J=5.9$, 6.6 Hz), 5.32 (dtt, 1 H, $J=11.0$, 5.5, 1.8 Hz), 5.38 (dtt, 1 H, $J=11.0$, 5.9, 1.8 Hz), 6.91 (bd, 1 H, $J=7.7$ Hz); ^{13}CNMR (67 MHz in $CDCl_3$) $\delta=14.1$, 20.9, 22.7, 24.9, 25.3, 27.2, 27.3, 29.3, 29.3, 29.4, 29.7, 29.8, 31.8, 31.9, 33.1, 52.7, 61.5, 72.5, 74.4, 76.1, 129.4, 130.3, 170.4, 171.1; MS *m*/*z* (FAB, glycerol matrix) 654 (M^++H; 100%), 636 (53). Found: C, 71.85; H, 11.59; N, 2.09%. Calcd for $C_{39}H_{75}NO_6$: C, 71.62; H, 11.56; N, 2.14%.

(2*S*,3*S*,4*R*,9*Z*)-2-[(*R*)-2-Acetoxypentadecanoylamino]-3,4-diacetoxy-1-*O*-(2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyl)-9-docosen-1-ol (53). To a stirred mixture of compound **52** (9.6 mg, 0.015 mmol), 2,3,4,6-tetra-*O*-acetyl-*α*-D-glucopyranosyl trichloroacetimidate (14 mg, 0.029 mmol), and molecular sieves 4A (20 mg) in dichloromethane (1 ml) at 0 °C under Ar was added $BF_3 \cdot OEt_2$ (9.2 µl, 0.073 mmol). After being stirred at 0 °C for 4 h, the reaction mixture was quenched by the addition of a saturated aqueous sodium hydrogencarbonate solution. The product was extracted with EtOAc, washed with brine, and then dried. Removal of the solvent afforded a residue, which was chromatographed on a column of silica gel (1 g), with acetone–hexanes (1 : 5) as an eluent, to afford crude glucoside (7 mg). This was dissolved in pyridine (1 ml) and acetic anhydride (0.5 ml); the resulting solution was stirred at room temperature for 3 h. The mixture was concentrated to give a residue, which was chromatographed on a column of silica gel (1 g), with acetone–toluene (1 : 10) as an eluent, to afford compound **53** (6.4 mg, 40%) as amorphous solid: $[\alpha]_D^{18}+7$ (*c* 0.2, $CHCl_3$); IR (neat) 3350, 1750, and 1690 cm^{-1}; ^1HNMR (270 MHz) $\delta=0.88$ (t, 6 H, $J=7.0$ Hz), 1.18—1.91 (m, 54 H), 1.99 and 2.02 (2s, each 3 H), 2.04 (s, 6 H), 2.07, 2.09, and 2.23 (3s, each 3 H), 3.64—3.73 (m, 2 H), 3.86 (dd, 1 H, $J=2.9$, 10.6 Hz), 4.12 (dd, 1 H, $J=2.6$, 12.5 Hz), 4.20—4.33 (m, 2 H), 4.48 (d, 1 H, $J=8.1$ Hz), 4.83—4.89 (m, 1 H), 4.89 (dd, 1 H, $J=8.1$, 9.5 Hz), 5.03 (dd, 1 H, $J=9.5$, 9.5 Hz), 5.09—5.17 (m, 2 H), 5.18 (dd, 1 H, $J=9.5$, 9.5 Hz), 5.25—5.40 (m, 2 H), 6.70 (bd, 1 H, $J=8.8$ Hz); ^{13}CNMR (67 MHz in $CDCl_3$) $\delta=14.1$, 20.5, 20.6, 20.7, 20.7, 20.9, 21.0, 22.7, 24.9, 25.3, 27.1, 27.3, 28.2, 29.3, 29.4, 29.4, 29.5, 29.6, 29.7, 29.7, 29.8, 31.8, 31.9, 48.2, 61.7, 66.7, 68.1, 71.2, 71.7, 71.9, 72.7, 73.1, 74.0, 100.4, 129.2, 130.3, 169.2, 169.3, 169.8, 169.9, 170.2, 170.3, 170.6, 171.0; MS *m*/*z* (FAB, glycerol matrix) 1068 (M^++H; 74%), 1008 (17).

Astrocerebroside A (2). To a stirred solution of compound **53** (4.6 mg, 4.3 mmol) in methanol (1 ml) at 0 °C was added a 0.05 mol dm^{-3} solution of K_2CO_3 in methanol (0.3 ml); the mixture was stirred at room temperature for 1 h. The reaction mixture was neutralized with acidic resin [Amberlite IR 120A (H^+ form)]. The insoluble material was removed by filtration and the filtrate was concentrated to give a residue, which was chromatographed on a column of silica gel (1 g), with MeOH–$CHCl_3$ (1 : 12) as an eluent, to afford **2** (3.1 mg, 93%) as amorphous solid: $[\alpha]_D^{21} +9$ (c 0.2, 1-propanol) {lit,[2b)] $[\alpha]_D^{21} +10.3$ (c 1.0, 1-propanol)}; IR (neat) 3340 and 1630 cm^{-1}; ^1H NMR (270 MHz in pyridine-d_5) $\delta = 0.87$ (t, 6 H, $J = 7.0$ Hz), 1.18—2.35 (m, 54 H), 3.88 (m, 1 H), 4.02 (dd, 1 H, $J = 7.7$, 8.5 Hz), 4.16—4.24 (m, 3 H), 4.27—4.38 (m, 2 H), 4.46—4.62 (m, 3 H), 4.72 (dd, 1 H, $J = 6.8$, 10.0 Hz), 4.97 (d, 1 H, $J = 7.7$ Hz), 5.28 (m, 1 H), 5.47 (m, 2 H), 8.57 (bd, 1 H, $J = 8.8$ Hz); ^{13}C NMR (67 MHz in pyridine-d_5) $\delta = 14.1$, 22.7, 25.7, 26.1, 27.3, 27.6, 29.36, 29.42, 29.6, 29.8, 29.9, 30.3, 31.9, 33.9, 35.4, 51.5, 62.4, 70.3, 71.2, 72.2, 75.0, 75.6, 78.3, 78.4, 105.4, 129.9, 130.1, 175.4; MS m/z (FAB, glycerol matrix) 774 ($M^+ + H$; 20%), 756 (4). The ^1H and ^{13}C NMR data were fully identical to those of the natural product reported by Higuchi and Komori.[2b)]

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