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Total Synthesis and Biological Activities of (+)-Sulfamisterin (AB5366) and its Analogues

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Abstract The first total synthesis of (+)-sulfamisterin (AB5366), a naturally occurring α-substituted α-amino acid derivative possessing a sulfonated hydroxy function, is described. Overman rearrangement of an allylic trichloroacetimidate derived from D-tartrate effectively generated the tetrasubstituted carbon containing a nitrogen substituent. Construction of the amino acid moiety and sulfonation of the hydroxy group, followed by deprotection completed the total synthesis, which fully confirmed the proposed absolute structure of the natural product. The possible stereoisomers of (+)-sulfamisterin and their desulfonated derivatives were also synthesized. Biological assessment of all synthetic compounds revealed that natural (+)-sulfamisterin and its 3-epimer as well as their desulfonated derivatives possessing 2*S*-configuration strongly inhibit the serine palmitoyl transferase both *in vitro* and *in vivo*, whereas compounds with 2*R*-configuration were found to show much weaker inhibitory activity.

Keywords sulfamisterin, AB5366, total synthesis, sulfamisterin analogues, SPT inhibitory activity

Introduction

(+)-Sulfamisterin (AB5366 **1**) is an antifungal agent isolated from the culture broths of *Pycnidiella* sp. AB5366 in 1996 [1,2] and reported to be an inhibitor of serine palmitoyl transferase (SPT) [3]. The structural study by spectral and X-ray crystallographic analysis showed that **1** has an α-substituted α-amino acid structure with a sulfonated hydroxy function [2] (Fig. 1). Compound **1** has a structure that resembles myriocin [4,5], a well-known SPT inhibitor as well as strong immunosuppressant. Recently, detailed SPT inhibitory activities of sulfamisterin and its simple analogues obtained by chemical transformation of the natural product have been reported [3]. With interest in the structure-activity relationship of sulfamisterin, we embarked on the synthesis of **1** and its possible stereoisomers (**2**~**4**). In this paper, we report the first total synthesis of **1** and its stereoisomers (**2**~**4**) as well as their desulfonated analogues (**5**~**8**) starting from tartrates using Overman rearrangement [6,7] as the key transformation. SPT inhibitory activities both *in vitro* and *in vivo* of these compounds (**1**~**8**) are also reported.

Results and Discussion

Total Synthesis of (+)-Sulfamisterin and its C-3 Epimer

The known (2*S*,3*S*)-3-benzyloxybutane-1,2,4-triol [8] (**9a**) derived from diisopropyl D-tartrate in 2 step reaction, was treated with 2-methoxypropene in the presence of pyridinium *p*-toluenesulfonate (PPTS) to afford a mixture

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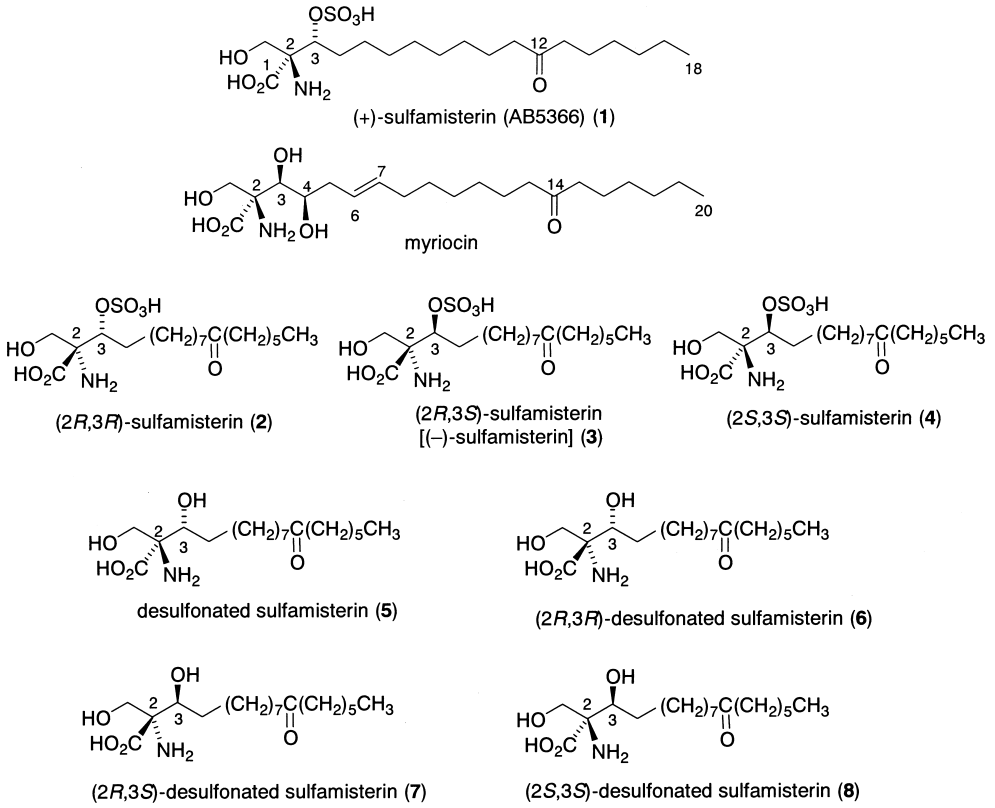
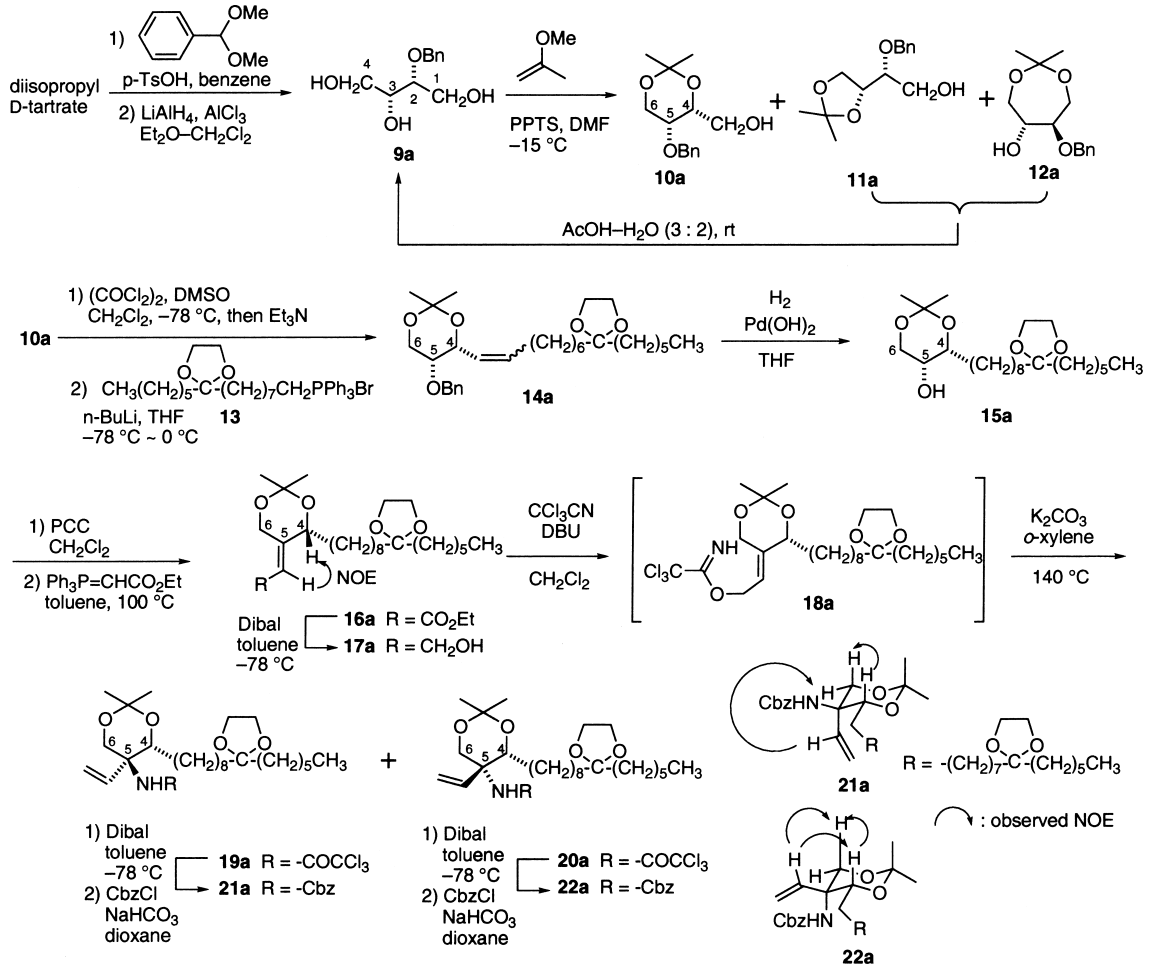


Fig. 1 Structures of (+)-sulfamisterin, myriocin and sulfamisterin analogues.

of the known acetonides [9] **10a**, **11a** and **12a** (Scheme 1). Separation of the mixture by a silica gel chromatography afforded **10a** in 27% isolated yield along with a mixture of **11a** and **12a** (68% yield). Acid hydrolysis of a mixture of **11a** and **12a** gave the starting triol **9a** in 87% yield, which could be reused to provide additional amount of **10a**. Swern oxidation of **10a** gave an aldehyde, which without purification, was reacted with Wittig reagent generated from phosphonium salt [10] **13** and *n*-BuLi to give **14a** in 45% yield from **10a** as a mixture of geometrical isomers (*E* : *Z*=*ca.* 1 : 4). Catalytic hydrogenation of **14a** afforded saturated alcohol **15a** in 88% yield. The observed coupling constants in **15a** ($J_{4,5}$ and $J_{5,6}$<3.5 Hz) revealed the *cis* relationship of C-4 and C-5 substituents, supporting the assigned structure. PCC oxidation of **15a** followed by reaction with $Ph_3P{=}CHCO_2Et$ gave **16a** as a single isomer in 97% yield. The observed NOE between a vinyl proton and H-4 clearly suggested the *E*-geometry of the double bond. Diisobutylaluminum hydride (Dibal) reduction of **16a** afforded allyl alcohol **17a** in 95% yield.

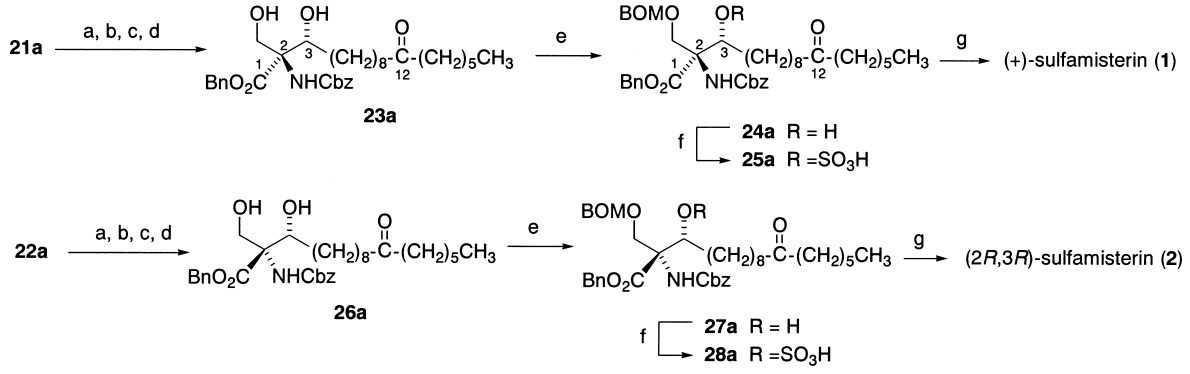
With the allylic alcohol **17a** in hand, we then examined the Overman rearrangement. Thus, an *o*-xylene solution of allylic trichloroacetimidate **18a** prepared from **17a** by the action of CCl_3CN and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) was heated at 140°C in a sealed tube under argon in the presence of solid potassium carbonate [11] to afford the diastereomeric rearranged products, which were easily and cleanly separated by silica gel chromatography to provide **19a** and **20a** in 50 and 45% isolated yields, respectively. HPLC analysis of **20a** and **20b** (prepared from dimethyl L-tartrate, *vide infra*) with chiral column (chiralcel OD) showed that the optical purities of **20a** and **20b** are both >99% ee, respectively, indicating no racemization had occurred during the transformation of **15a** to **19a** and **20a**. The protecting group of nitrogen (*N*-trichloroacetyl group) in **19a** was converted into *N*-benzyloxycarbonyl (Cbz) group by two step reactions to give **21a**, quantitatively. Similar treatment of **20a** afforded **22a** (97% yield). NOE experiments of **21a** and **22a** clearly showed that the tetrasubstituted carbon in **21a** possessed *S* configuration whereas that in **22a** is *R* configuration, respectively.

Ozonolysis of **21a**, followed by further oxidation and esterification, and subsequent acid hydrolysis afforded diol **23a** in 50% yield (Scheme 2). The primary hydroxy group in **23a** was selectively protected as a benzyloxymethyl ether to give **24a** (64% yield), whose remaining hydroxy group was sulfonated by the action of SO_3-pyridine [12] to afford **25a**, quantitatively. Hydrogenolysis of **25a** in the presence



Scheme 1

Bn=–CH_2Ph, Cbz=–C(O)OCH_2Ph.



Scheme 2

BOM=–CH_2OCH_2Ph. Reagents and conditions: (a) O_3, EtOH, −78°C then Me_2S; (b) $NaClO_2$, NaH_2PO_4, $HOSO_2NH_2$, *t*-BuOH–H_2O; (c) BnOH, *N*-ethyl-*N'*-(3-dimethylaminopropyl)carbodiimide (WSCD), DMAP, CH_2Cl_2; (d) AcOH - H_2O (3 : 2); (e) BOMCl, *i*-Pr_2NEt, CH_2Cl_2, 40°C; (f) SO_3-pyridine complex, pyridine, 80°C; (g) H_2, $Pd(OH)_2$, MeOH.

of $Pd(OH)_2$, followed by treatment with weak acidic resin (IRC-76, H^+ form) and purification with LH-20 provided (+)-sulfamisterin (**1**) in 57% yield. The spectral (^1H and ^{13}C NMR) data for synthetic **1** were fully identical with those of natural (+)-sulfamisterin, and the $[\alpha]_D$ value of synthetic **1** showed good agreement {$[\alpha]_D^{25}$ +3.6° (*c* 0.62, MeOH)} with that of natural product {$[\alpha]_D^{23}$ +2.0° (*c* 1.0, MeOH) [1]; $[\alpha]_D^{23}$ +3.1° (*c* 0.50, MeOH), measured in our laboratory}. Therefore, total synthesis of (+)-sulfamisterin has been accomplished, confirming the proposed absolute structure of the natural product.

Similar treatment of **22a** as described for the preparation of **1** from **21a** afforded (2*R*,3*R*)-sulfamisterin (**2**), a C-3 epimer of natural sulfamisterin, in 7 step reactions and in 58% overall yield from **22a**.

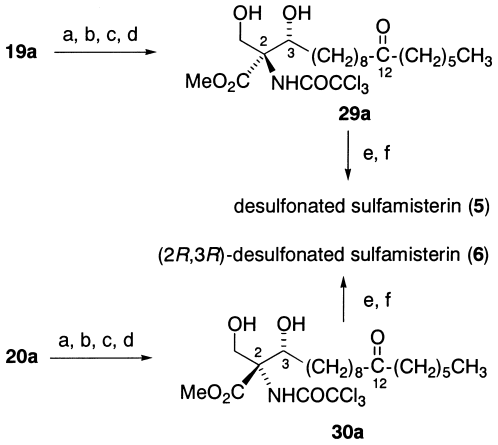
Preparation of Sulfamisterin Analogues

To obtain information of the biological role of the sulfate function, synthesis of desulfonated analogues of sulfamisterin was carried out (Scheme 3). Thus, ozonolysis of **19a**, followed by oxidation and esterification, and subsequent deprotection of an acetonide and a ketal groups by acid hydrolysis afforded **29a** in 57% yield. Saponification of **29a** with 12% aqueous NaOH - MeOH followed by neutralization with acidic resin (IRC-76) furnished desulfonated sulfamisterin (**5**) in 53% yield. Similar treatment of **20a** afforded (2*R*,3*R*)-desulfonated sulfamisterin (**6**).

The enantiomers of **1**, **2**, **5** and **6** were synthesized starting from dimethyl L-tartrate (Scheme 4). Thus, the same reaction sequences as used for preparation of **19a** and **20a** from diisopropyl D-tartrate were applied to dimethyl L-tartrate to give a diastereomeric pair of **19b** (enantiomer of **19a**) and **20b** (enantiomer of **20a**). By the same reactions as employed for preparation of **1** and **5** from **19a**, one of rearranged product **19b** was successfully transformed into (−)-sulfamisterin (**3**) and (2*R*,3*S*)-desulfonated sulfamisterin (**7**). Similar transformation of another rearranged product **20b** provided (2*S*,3*S*)-sulfamisterin (**4**) and (2*S*,3*S*)-desulfonated sulfamisterin (**8**).

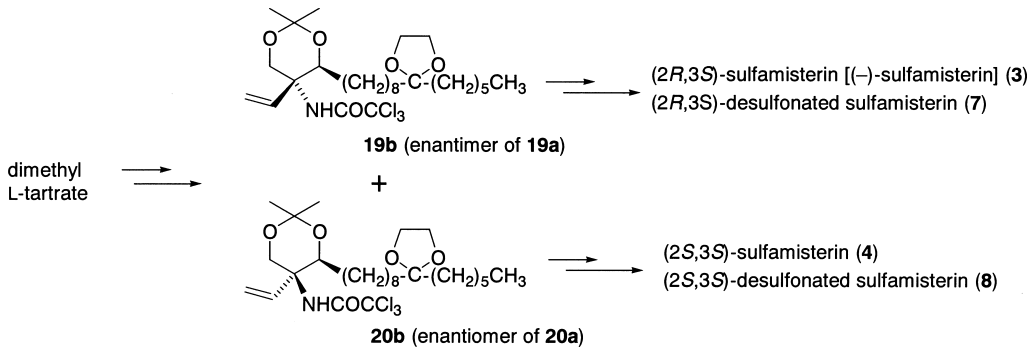
Biological Activities

The inhibitory activities of synthetic compounds against SPT were measured according to a method described previously [3]. The results were shown in Table 1 and 2. The *in vitro* assay with the Chinese hamster ovary (CHO) cell homogenates by measuring the radioactivity of incorporated [^3H]-serine revealed that (+)-sulfamisterin (**1**) (possessing 2*S*,3*R* absolute configuration) strongly inhibit the SPT activity. Interestingly, 3-epi-(+)-sulfamisterin (**4**) as well as derivatives without a sulfate function, desulfonated sufamisterin (**5**) and (2*S*,3*S*)-desulfonated sufamisterin (**8**) were found to be also strong inhibitors. However, compounds with 2*R* configuration (**2**, **3**, **6** and **7**) showed much weaker inhibitory activity. This tendency was



Scheme 3

Reagents and conditions: (a) O_3, EtOH, −78°C then Me_2S; (b) $NaClO_2$, NaH_2PO_4, $HOSO_2NH_2$, *t*-BuOH - H_2O; (c) Me_3SiCHN_2, MeOH - benzene; (d) 6 M HCl aq - THF (1 : 2), rt; (e) 12% NaOH aq - MeOH (1 : 2); (f) IRC-76 resin (H^+ form).



Scheme 4

also observed in *in vivo* assay in which the amount of several sphingolipids synthesized by CHO cells were measured. Whereas compounds possessing 2*S* configuration (**1**, **4**, **5** and **8**) inhibited the biosynthesis of sphingomyelin, glucosylceramide and ceramide with a concentration as low as 11.25 μM, compounds with 2*R* configuration (**2**, **3**, **6** and **7**) were found to be weaker than those with 2*S* configuration. The fact that all compounds did not inhibit the synthesis of phosphatidylethanolamine and phosphatidylserine as well as previous results [3] suggested that sulfamistein and its analogues suppress sphingolipid biosynthesis through the inhibition of SPT. These results revealed that in sulfamisterin-type compounds, 1) the 2*S* configuration is essential for the high SPT inhibitory activity; 2) the configuration at C-3 is not an important factor; and 3) sulfonation of a hydroxy function at C-3 does not significantly affect the activity. These findings should be important and useful for the design of new SPT inhibitors.

Table 1 The activity of SPT (%) measured in the presence of compounds **1**~**8** *in vitro* at various concentrations.[a]

Compound	Concentration			
	100 μM	10 μM	1 μM	0.01 μM
1	3.7	3.0	4.0	18.1
2	3.5	9.0	35.6	98.3
3	3.8	7.2	30.0	99.9
4	2.8	3.0	3.5	18.4
5	3.3	6.5	5.4	27.5
6	4.0	7.0	30.5	98.1
7	4.8	12.5	39.1	98.8
8	2.5	4.2	3.7	11.3

[a] CHO cell homogenates were treated with compounds at the concentration indicated in the reaction buffer containing palymitoyl CoA and [^{3}H]-serine at 37°C for 20 minutes. The observed relative radioactivities, measured with a liquid scintillation counter (%, the amount when the assay was carried out without compounds corresponds to 100% SPT activity) of the lipid products extracted from the reaction mixture, are shown. The activity without palmitoyl CoA was considered as 0%. For detailed experimental procedures, see ref. 3.

Table 2 Inhibition of sphingolipid synthesis *in vivo* by compounds **1**~**8**.[a]

Compound	SM[b]	GlcCer[c]	Cer[d]	PS[e]	PE[f]
1	13.5 (23.7)	6.2 (3.4)	3.0 (3.2)	88.2 (104.0)	95.9 (91.4)
2	96.5 (95.5)	103.3 (74.1)	94.6 (79.2)	101.1 (116.2)	107.0 (107.7)
3	90.8 (36.8)	101.9 (11.5)	100.2 (2.3)	97.5 (105.9)	101.5 (99.0)
4	19.3 (25.4)	5.6 (5.5)	6.9 (2.3)	92.5 (105.9)	92.0 (99.0)
5	12.4 (23.4)	0.6 (1.9)	2.8 (1.8)	89.5 (98.8)	86.9 (92.1)
6	104.1 (126.0)	111.2 (89.4)	113.0 (88.7)	98.2 (108.8)	109.6 (125.9)
7	89.9 (138.6)	88.1 (139.2)	100.1 (154.7)	89.1 (114.0)	94.4 (129.9)
8	12.9 (28.4)	2.4 (3.9)	3.2 (2.5)	94.2 (106.7)	90.5 (102.2)

[a] CHO cells were treated with compounds overnight at the concentration of 11.25 μM and then cells were labeled with [^{14}C]-serine for 2 hours. Newly synthesized lipids were analyzed and their observed relative radioactivities (%, the amount when cells were cultured without compounds corresponds to 100%) are shown (numbers in parentheses denote the activities measured at the concentration of 45 μM). For detailed experimental procedures, see ref. 3. [b] sphingomyerin. [c] glucosylceramide. [d] ceramide. [e] phosphatidylserine. [f] phosphatidylethanolamine.

Experimental

General

IR spectra were taken with a JASCO FT/IR-200 spectra. Mass spectra are recorded on a JEOL GC Mate spectrometer with EI (70 eV) or FAB mode. Melting points were determined on a Mitamura-Riken micro hot stage. Optical rotations were recorded using a sodium lamp with a JASCO DIP-370 instrument with 1 dm tube. ^{1}H (at 300 MHz) and ^{13}C NMR (at 75 MHz) spectra were measured with JEOL JNM Lambda 300 (300 MHz) or Varian MVX-300 (300 MHz) spectrometers. Chemical shifts are reported as δ values in ppm relative to tetramethylsilane or chloroform as internal references. Organic extracts were dried over Na_2SO_4 and concentrated below 40°C under reduced pressure. For column chromatography, Merck silicagel 60 (230~400 or 75~230 mesh) was used, unless otherwise noted. Preparative TLC was performed on precoated Merck PLC plate (silicagel 60 F254 on glass plates, 0.25 mm).

2-*O*-Benzyl-D-threitol (9a)

To a solution of diisopropyl D-tartrate (9.0 g, 38.4 mmol) in 90 ml of benzene at room temperature were added benzaldehyde dimethyl acetal (6.35 ml, 42.3 mmol) and 10-camphorsulfonic acid (CSA, 446 mg, 1.92 mmol), and the mixture was heated at reflux for 2 days. After cooling, the reaction mixture was neutralized with Et_3N (0.3 ml) and diluted with EtOAc. The resulting mixture was washed with water and dried. Removal of the solvent gave a residue, which was purified by column chromatography (200 g silica gel, 1/1 EtOAc/hexane as an eluent) to afford a benzylidene derivative (13.5 g, quant.) as a pale yellow syrup. To a suspension of $LiAlH_4$ (5.55 g, 146 mmol) in diethyl ether (80 ml) and CH_2Cl_2 (75 ml) was added the benzylidene derivative (13.5 g, 38.4 mmol) at 0°C. After stirring at 0°C for 40 minutes, to the reaction mixture was added $AlCl_3$ (16.7 g, 125 mmol) in diethyl ether (80 ml) dropwise at 0°C, and the mixture was heated at reflux for 2.5 hour. After cooling to 0°C, to the mixture were added with water (20 ml), 15 wt% NaOH aq (100 ml) and water (25 ml). The insoluble material was removed by filtration through celite (THF as an eluent), and the filtrate was dried. Removal of the solvent afforded crystalline residue, which was recrystallized from benzene to give **9a** (5.6 g, 63%) as white crystals; m.p. 74~75°C; $[\alpha]_D^{23}$ −15° (*c* 0.92, MeOH) {lit. [8] m.p. 75~76°C; $[\alpha]_D^{23}$ −15° (*c* 0.96, MeOH)}; IR ν_{max} (KBr disc) 3200~3400, 2940, 2900, 1450, 1330, 1200, 1125, 1090, 1050, 1035, 990 cm^{-1}; HR FAB-MS *m/z* for $C_{11}H_{17}O_4$ $(M+H)^+$, Calcd: 213.1127, Found: 213.1126; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.40 (1H, bt, *J*=5.4 Hz, primary OH), 2.59 (1H, bt, *J*=6.6 Hz, primary OH), 2.86 (1H, d, *J*=5.7 Hz, secondary OH), 3.55~3.59 (1H, m, H-3), 3.64~3.92 (5H, m, H-1, H-2, H-4), 4.59 (1H, d, *J*=11.4 Hz, benzyl), 4.72 (1H, d, *J*=11.4 Hz, benzyl), 7.30~7.42 (5H, m, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 61.0, 63.2, 71.9, 72.6, 79.4, 128.2, 128.4, 128.9, 137.8.

3-*O*-Benzyl-2,4-*O*-isopropylidene-D-threitol (10a)

To a solution of triol **9a** (2.17 g, 10.2 mmol) and pyridinium *p*-toluenesulfonate (PPTS, 251 mg, 1.0 mmol) in DMF (25 ml) was added dropwise 2-methoxypropene (1.6 ml, 15.3 mmol) in DMF (5 ml) at −15°C. After being stirred at −15°C for 7 hour, the resulting mixture was neutralized with Et_3N. The reaction mixture was diluted with EtOAc and washed with brine. The organic layer was dried and concentrated to afford the residue, which was purified by flash chromatography (100 g silica gel, 1 : 3 to 2 : 1 EtOAc/hexane as an eluent) to give **10a** (700 mg, 27%) as white crystals and a mixture of **11a** and **12a** (1.77 g, 68%) as a colorless syrup; **10a**: m.p. 61~62°C; $[\alpha]_D^{24}$ −65° (*c* 1.55, $CHCl_3$) {lit. [8] for **10b** (enantiomer of **10a**): m.p. 60~61°C; $[\alpha]_D$ +64° (*c* 0.3, $CHCl_3$)}; IR ν_{max} (neat) 3450, 2990, 2940, 2875, 1455, 1385, 1200, 1120, 1080, 1055, 1025 cm^{-1}; HR FAB-MS *m/z* for $C_{14}H_{21}O_4$ $(M+H)^+$, Calcd: 253.1440, Found: 253.1453; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.46, 1.47 (3H×2, 2s, $Me_2C<$), 1.94~2.10 (1H, m, OH), 3.25~3.35 (1H, m, H-5), 3.62 (1H, ddd, *J*=4.5, *J*=8.7, *J*=11.4 Hz, H-4), 3.80~3.88 (1H, m, H-1a), 3.91 (1H, dd, *J*=2.4, *J*=12.9 Hz, H-6a), 3.95~4.03 (1H, m, H-1b), 4.04 (1H, dd, *J*=2.1, *J*=12.9 Hz, H-6b), 4.44 (1H, d, *J*=12.3 Hz, benzyl), 4.76 (1H, d, *J*=12.3 Hz, benzyl), 7.24~7.44 (5H, m, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 19.1, 28.9, 61.1, 62.9, 69.9, 70.7, 71.6, 98.8, 127.9, 128.0, 128.5, 137.8. The isomeric compounds **11a** and **12a** could be converted into **9a** by the following procedure and reused: The mixture of **11a** and **12a** (1.77 g, 7.02 mmol) was dissolved in 60% aq AcOH (13 ml) at room temperature. After stirring for 32 hour, the reaction mixture was concentrated to give a residue, which was recrystallized from benzene to afford triol **9a** (1.30 g, 87%) as white crystals.

(4*R*,5*R*)-5-Benzyloxy-4-[8-(2-hexyl-[1,3]dioxolan-2-yl)-oct-1-enyl]-2,2-dimethyl-[1,3]dioxane (14a)

To a solution of $(COCl)_2$ (2.0 mol/liter in CH_2Cl_2, 3.9 ml, 7.8 mmol) was added dropwise DMSO (1.11 ml, 15.6 mmol) at −78°C for 40 minutes under argon. To this

mixture was added a solution of alcohol **10a** (657 mg, 2.60 mmol) in CH_2Cl_2 (16 ml) at −78°C. The reaction mixture was stirred at −78°C for 40 minutes and then treated with Et_3N (3.26 ml, 23.4 mmol). The resulting suspension was further stirred at 0°C for 30 minutes, and then diluted with Et_2O. The organic layer was washed with saturated NH_4Cl aq solution and dried. Evaporation of the solvents gave crude aldehyde (720.0 mg). To a solution of phosphonium salt **13** [10] (6.22 g, 10.4 mmol) in dry THF (19 ml) was added dropwise *n*-butyl lithium (1.59 mol/liter in hexane, 8.50 ml, 13.5 mmol) at −78°C and the mixture was stirred for 15 minutes at room temperature. After cooling at −78°C, to the mixture was added a solution of the crude aldehyde (720 mg) in THF (9 ml) dropwise *via* a cannula. After stirring for 15 minutes, to the mixture was added *t*-BuOH (1.2 ml) and then the dark red solution was warmed to room temperature. The resulting mixture was diluted with EtOAc, and washed with saturated NH_4Cl aq and brine, and then dried. Removal of the solvent gave a residue, which was purified by flash chromatography (70 g silica gel, EtOAc/toluene=1/40 to 1/15 as an eluent) to give coupling product **14a** (574 mg, 45%) as a mixtures of geometrical isomers (*E* : *Z*=*ca.* 1 : 4); IR ν_{max} (neat) 2930, 2840, 1455, 1380, 1370, 1200, 1130, 1090, 1070 cm^{-1}; *Anal* Found: C, 73.75; H, 9.87%. Calcd for $C_{30}H_{48}O_5$: C, 73.73; H, 9.90%; ^1H NMR (300 MHz, $CDCl_3$) δ: 0.88 (3H, t, *J*=6.8 Hz, $CH_2C\underline{H}_3$), 1.47, 1.49 (3H×2, 2s, $Me_2C<$), 1.22～1.64 (20H, m, 10×–CH_2–), 1.88～2.16 (2H, m, C=CHC$\underline{H}_2$–), 3.17 (1H, m, H-5), 3.92 (4H, s, –$O(CH_2)_2O$–), 3.94～4.01 (2H, m, H-4, H-6a), 4.57 (1H, d *J*=12.5 Hz, benzyl), 4.71 (1H, d, *J*=12.5 Hz, benzyl), 4.68～4.78 (1H, m, H-6b), 5.54～5.82 (2H, m, –CH=CH–), 7.24～7.44 (5H, m, Ph).

(4*R*,5*R*)-4-[8-(2-Hexyl-[1,3]dioxolan-2-yl)-octyl]-2,2-dimethyl-[1,3]dioxan-5-ol (15a)

A mixture of **14a** (402 mg, 0.82 mmol) and 20% $Pd(OH)_2$ on activated carbon (107 mg) in THF (1.5 ml) was hydrogenated at room temperature under atmospheric pressure of H_2 for 2 hour. After addition of K_2CO_3 (50 mg) to the mixture, the insoluble material was removed by filtration through celite (EtOAc as an eluent). The filtrate was concentrated to give a residue, which was purified by column chromatography (10 g silica gel, 1/8 to 1/4 EtOAc/hexane as an eluent) to afford alcohol **15a** (289 mg, 88%) as a colorless syrup; $[\alpha]_D^{22}$ −3.9° (*c* 0.93, $CHCl_3$); IR ν_{max} (neat) 3460, 2930, 2855, 1460, 1380, 1200, 1080 cm^{-1}; HR FAB-MS *m*/*z* for $C_{23}H_{45}O_5$ $(M+H)^+$, Calcd: 401.3267, Found: 401.3266; *Anal* Found: C, 68.84; H, 10.92%. Calcd for $C_{23}H_{44}O_5$: C, 68,96; H, 11.07%; ^1H NMR (300 MHz, $CDCl_3$) δ: 0.88 (3H, t, *J*=6.6 Hz, $CH_2C\underline{H}_3$), 1.20～1.63 (26H, m, 13×–CH_2–), 1.42, 1.46 (3H×2, 2s, $Me_2C<$), 2.53 (1H, d, =11.7 Hz, OH), 3.31 (1H, m, H-5), 3.76～3.88 (2H, m, H-6a, H-4), 3.92 (4H, s, –$O(CH_2)_2O$–), 4.04 (1H, dd, *J*=1.2, *J*=12.3 Hz, H-6b); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.1, 18.4, 22.6, 23.8, 24.8, 29.4, 29.5, 29.6, 29.7, 29.9, 31.3, 31.8, 37.1, 64.8, 65.1, 66.2, 72.1, 98.8, 111.9.

(4*R*)-{4-[8-(2-Hexyl-[1,3]dioxolan-2-yl)-octyl]-2,2-dimethyl-[1,3]dioxan-5-ylidene}-acetic Acid Ethyl Ester (16a)

To the mixture of alcohol **15a** (413 mg, 1.03 mmol) and 4A molecular sieves (330 mg) in dry CH_2Cl_2 (17 ml) was added a slurry of NaOAc (592 mg, 7.21 mmol), PCC (778 mg, 3.61 mmol) and 4A molecular sieves (330 mg) in CH_2Cl_2 (17 ml) at room temperature and the mixture was stirred at room temperature for 2 hour. The resulting precipitate was filtered off over celite and thoroughly washed with diethyl ether. The filtrate was concentrated to give a crude ketone (470 mg), which was used in the next reaction without further purification. To a solution of the ketone (470 mg) in toluene (14.1 ml) was added $Ph_3P=CHCO_2Et$ (1.26 g, 3.61 mmol) and the mixture was heated at 100°C for 14 hour. The resulting mixture was cooled and concentrated to give a residue, which was purified by flash chromatography (35 g silica gel, 1/25 to 1/15 EtOAc/hexane as an eluent) to afford unsaturated ester **16a** (469 mg, 97% for 2 steps) as a colorless syrup; $[\alpha]_D^{18}$ +78° (*c* 0.83, $CHCl_3$); IR ν_{max} (neat) 2980, 2930, 2855, 1715, 1650, 1460, 1380, 1370, 1210, 1150, 1040 cm^{-1}; EI-MS *m*/*z* 453 (M^+−Me, 11%), 410 (16), 383 (79), 325 (16) and 157 (100); HR EI-MS *m*/*z* for $C_{26}H_{45}O_6$ (M^+−Me), Calcd: 453.3216, Found: 453.3218; *Anal* Found: C, 69.05; H, 10.24%. Calcd for $C_{27}H_{48}O_6$: C, 69.19; H, 10.32%; ^1H NMR (300 MHz, $CDCl_3$) δ: 0.88 (3H, t, *J*=6.6 Hz, $CH_2C\underline{H}_3$), 1.22～1.82 (29H, m, 13×–CH_2–, $OCH_2C\underline{H}_3$), 1.38, 1.39 (3H×2, 2s, $Me_2C<$), 3.93 (4H, s, –$O(CH_2)_2O$–), 4.16 (2H, q, *J*=7.1 Hz, $OC\underline{H}_2CH_3$), 4.32 (1H, m, H-4), 4.64 (1H, ddd, *J*=2.0, *J*=2.0, *J*=17.8 Hz, H-6a), 5.02 (1H, dd, *J*=2.0, *J*=17.8 Hz, H-6b), 5.61 (1H, dd, *J*=2.0, *J*=2.0 Hz, –C=C$\underline{H}$–); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.1, 14.2, 22.6, 23.8, 24.3, 25.1, 29.4, 29.4, 29.5, 29.6, 29.9, 31.4, 31.8, 37.1, 60.1, 61.9, 64.9, 69.6, 100.4, 110.8, 111.9, 162.6, 166.0.

(4*R*)-2-{4-[8-(2-Hexyl-[1,3]dioxolan-2-yl)-octyl]-2,2-dimethyl-[1,3]dioxan-5-ylidene}-ethanol (17a)

To a solution of ester **16a** (374 mg, 0.80 mmol) in toluene (9.0 ml) was added dropwise DIBAL-H (1.01 mol/liter in

toluene, 2.76 ml, 2.79 mmol) at −78°C under argon. After being stirred at −78°C for 30 minutes, to the solution was added acetone (2.5 ml) and stirring was further continued for 10 minutes at 0°C. To the resulting mixture was added excess $Na_2SO_4 \cdot 10H_2O$ and the mixture was stirred for 1 hour. The insoluble material was removed by filtration through celite, and the filtrate was concentrated to give a residue, which was purified by column chromatography (20 g silica gel, 1/7 to 1/3 EtOAc/hexane as an eluent) to afford allylic alcohol **17a** (322 mg, 95%) as a colorless syrup; $[\alpha]_D^{21}$ +68° (*c* 1.10, $CHCl_3$); IR ν_{max} (neat) 3380～3500, 2985, 2930, 2850, 1455, 1380, 1370, 1225, 1160, 1080 cm^{-1}; EI-MS *m/z* 425 (M^+−H, 1.1%), 411 (M^+−Me, 16), 355 (13), 341 (34), 281 (30) and 157 (100); HR EI-MS *m/z* for $C_{25}H_{45}O_5$ (M^+−H), Calcd: 425.3267, Found: 425.3264; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.88 (3H, t, *J*=6.6 Hz, $CH_2C\underline{H}_3$), 1.22～1.82 (27H, m, 13×–CH_2–, OH), 1.37, 1.41 (3H×2, 2s, Me_2C<), 3.92 (4H, s, –$O(CH_2)_2O$–), 4.12 (2H, m, H-4, H-6a), 4.22～4.42 (3H, m, H-6b, –$C\underline{H}_2OH$), 5.42 (1H, dt, *J*=1.7, *J*=6.6 Hz, –C=C$\underline{H}$–); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.1, 22.6, 23.1, 23.8, 23.8, 25.2, 25.8, 25.9, 29.4, 29.5, 29.5, 29.6, 29.9, 31.8, 32.0, 37.1, 58.1, 59.4, 64.8, 70.1, 99.8, 111.9, 119.6, 141.2.

(4*R*,5*S*)-2,2,2-Trichloro-*N*-{4-[8-(2-hexyl-[1,3]dioxolan-2-yl)-octyl]-2,2-dimethyl-5-vinyl-[1,3]dioxan-5-yl}-acetamide 19a and Its (4*R*,5*R*) Isomer 20a

To a solution of allylic alcohol **17a** (508 mg, 1.19 mmol) in CH_2Cl_2 (15 ml) were added trichloroacetonitrile (0.30 ml, 2.98 mmol) and DBU (34.8 μl, 0.233 mmol) at 0°C, and the mixture was stirred at 0°C for 2 hour. The resulting mixture was concentrated to give a residue, which was passed through a short column of silica gel (6 g, 1/10 EtOAc/hexane containing 1% Et_3N as an eluent) to afford roughly purified imidate **18a** (651 mg) as a yellow syrup. To a solution of crude **18a** (651 mg) in *o*-xylene (65 ml) was added K_2CO_3 (130 mg), and the mixture was heated at 140°C in a sealed tube for 89 hour under argon. The resulting mixture was concentrated to give a residue, which was purified by column chromatography (57 g silica gel, 1/150 EtOAc/toluene as an eluent) to afford first, rearranged products **19a** (336 mg, 49%) as a colorless syrup; $[\alpha]_D^{20}$ +21° (*c* 0.22, $CHCl_3$); IR ν_{max} (neat) 3430, 2930, 2860, 1725, 1505, 1460, 1380, 1200, 1100 cm^{-1}; HR FAB-MS *m/z* for $C_{27}H_{47}C_{l3}NO_5$ $(M+H)^+$, Calcd: 570.2520, Found: 570.2534; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.87 (3H, t, *J*=6.6 Hz, $CH_2C\underline{H}_3$), 1.20～1.62 (26H, m, 13×–CH_2–), 1.43, 1.58 (3H×2, 2s, Me_2C<), 3.76 (1H, d, *J*=11.1 Hz, H-6a), 3.91 (4H, s, –$O(CH_2)_2O$–), 4.57 (1H, dd, *J*=6.3, *J*=8.7 Hz, H-4), 4.61 (1H, d, *J*=11.1 Hz, H-6b), 5.23 (1H, d, *J*=17.7 Hz, –CH=C$\underline{H}$H), 5.40 (1H, d, *J*=11.1 Hz, –CH=CH$\underline{H}$), 6.44 (1H, dd, *J*=11.1, *J*=17.7 Hz, –C$\underline{H}$=CH_2,), 6.46 (1H, s, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.1, 19.4, 22.6, 23.8, 25.5, 28.7, 29.4, 29.4, 29.5, 29.6, 29.9, 31.8, 37.1, 57.9, 64.9, 65.3, 70.7, 92.8, 99.5, 111.9, 114.5, 135.8, 160.8.

Further elution (1/50 EtOAc/toluene as an eluent) gave isomeric product **20a** (306 mg, 45%) as a colorless syrup; $[\alpha]_D^{21}$ −19° (*c* 1.09, $CHCl_3$); IR ν_{max} (neat) 3405, 2930, 2850, 1730, 1505, 1385, 1370, 1200, 1110, 1080, 1055 cm^{-1}; HR FAB-MS *m/z* for $C_{27}H_{47}Cl_3NO_5$ $(M+H)^+$, Calcd: 570.2520, Found: 570.2531; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.88 (3H, t, *J*=6.6 Hz, $CH_2C\underline{H}_3$), 1.15～1.65 (26H, m, 13×–CH_2–), 1.42, 1.48 (3H×2, 2s, Me_2C<), 3.78 (1H, dd, *J*=1.5, *J*=9.3 Hz, H-4), 3.86 (1H, d, *J*=12.0 Hz, H-6a), 3.92 (4H, s, –$O(CH_2)_2O$–), 4.20 (1H, d, *J*=12.0 Hz, H-6b), 5.15 (1H, d, *J*=18.0 Hz, –CH=C$\underline{H}$H), 5.32 (1H, d, *J*=11.4 Hz, –CH=CH$\underline{H}$), 5.89 (1H, dd, *J*=11.4, *J*=18.0 Hz, –C$\underline{H}$=CH_2), 7.15 (1H, s, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.1, 18.4, 22.6, 23.8, 25.8, 28.6, 29.2, 29.4, 29.4, 29.5, 29.6, 29.9, 31.8, 37.1, 58.3, 64.3, 64.9, 76.0, 93.2, 99.3, 111.9, 116.6, 134.0, 161.2. Optical purities of **20a** was confirmed to be >99% ee (determined by HPLC [DAICEL CHIRALCEL OD, 4.6 mm ID, 250 mml, *i*-PrOH/hexane=1/50, flow rate=1.5 ml/minute, retention volume for **20a**: 7.3 ml, **20b**: 6.1 ml]).

(4*R*,5*S*)-{4-[8-(2-Hexyl-[1,3]dioxolan-2-yl)-octyl]-2,2-dimethyl-5-vinyl-[1,3]dioxan-5-yl}-carbamic Acid Benzyl Ester (21a)

To a solution of **19a** (67 mg, 0.117 mmol) in toluene (2.0 ml) was added dropwise DIBAL-H (1.01 mol/liter in toluene, 0.23 ml, 0.23 mmol) at −78°C under argon. After being stirred at −78°C for 10 minutes, to the solution was added acetone (0.5 ml) and the mixture was stirred for 10 minutes at 0°C. To the resulting mixture was added excess $Na_2SO_4 \cdot 10H_2O$ and the mixture was further stirred at 0°C for 1.5 hour. The insoluble material was removed by filtration through celite (EtOAc as an eluent) and the filtrate was concentrated to afford crude amine (62.3 mg). To a solution of the crude amine (62.3 mg) in 1,4-dioxane (2 ml) were added $NaHCO_3$ (79 mg, 0.94 mmol) and carbobenzoxy chloride (CbzCl, 0.13 ml, 0.94 mmol) at room temperature and the mixture was stirred for 8 hour. The resulting mixture was diluted with EtOAc and washed with brine, and dried. Removal of the solvent gave a residue, which was purified by chromatography (5 g silica gel, 1/20 to 1/10, EtOAc/hexane as an eluent) to give carbamate **21a** (66 mg, quant.) as a colorless syrup; $[\alpha]_D^{22}$ +16° (*c* 1.12, $CHCl_3$); IR ν_{max} (neat) 3350, 2930, 2855,

1725, 1505, 1455, 1380, 1260, 1235, 1200, 1080, 1060 cm^{-1}; HR FAB-MS *m/z* for $C_{33}H_{54}NO_6$ $(M+H)^+$, Calcd: 560.3951, Found: 560.3961; *Anal* Found: C, 70.80; H, 9.50; N, 2.46%. Calcd for $C_{33}H_{53}NO_6$: C, 70.81; H, 9.54; N, 2.50%; ^1H NMR (300 MHz, $CDCl_3$) δ: 0.88 (3H, t, J=6.6 Hz, $CH_2C\underline{H}_3$), 1.18～1.62 (26H, m, 13×–CH_2–), 1.42, 1.56 (3H×2, 2s, Me_2C<), 3.80 (1H, d, J=11.4 Hz, H-6a), 3.92 (4H, s, –$O(CH_2)_2O$–), 4.38 (1H, bs, H-4), 4.49 (1H, d, J=11.4 Hz, H-6b), 4.74 (1H, s, NH), 5.07 (2H, s, –$NHCO_2C\underline{H}_2Ph$), 5.18 (1H, d, J=18.0 Hz, –CH=C$\underline{H}$H), 5.30 (1H, d, J=11.1 Hz, –CH=CH$\underline{H}$), 6.33 (1H, dd, J=11.1, J=18.0 Hz, –C$\underline{H}$=CH_2), 7.32～7.38 (5H, m, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.1, 19.4, 22.6, 23.8, 23.8, 25.8, 28.9, 29.3, 29.4, 29.5, 29.5, 29.6, 29.9, 31.8, 37.1, 55.9, 64.8, 66.5, 66.7, 72.0, 99.1, 111.9, 114.1, 128.2, 128.3, 128.6, 136.1, 136.6, 154.6.

(4*R*,5*R*)-{4-[8-(2-Hexyl-[1,3]dioxolan-2-yl)-octyl]-2,2-dimethyl-5-vinyl-[1,3]dioxan-5-yl}-carbamic Acid Benzyl Ester (22a)

By the same reaction conditions as described for the preparation of **21a** from **19a**, compound **20a** (60 mg, 0.10 mmol) was converted to carbamate **22a** (57 mg, 97% for 2 steps); colorless syrup; $[\alpha]_D^{24}$ −25° (*c* 0.94, $CHCl_3$); IR ν_{max} (neat) 3430, 2930, 2855, 1730, 1505, 1495, 1455, 1380, 1260, 1235, 1200, 1100, 1070 cm^{-1}; HR FAB-MS *m/z* for $C_{33}H_{54}NO_6$ $(M+H)^+$, Calcd: 560.3951, Found: 560.3939; *Anal* Found: C, 70.85; H, 9.50; N, 2.47%. Calcd for $C_{33}H_{53}NO_6$: C, 70.81; H, 9.54; N, 2.50%; ^1H NMR (300 MHz, $CDCl_3$) δ: 0.88 (3H, t, J=6.6 Hz, $CH_2C\underline{H}_3$), 1.15～1.64 (26H, m, 13×–CH_2–), 1.41, 1.46 (3H×2, 2s, Me_2C<), 3.69 (1H, dd, J=1.8, J=9.6 Hz, H-4), 3.84 (1H, d, J=11.7 Hz, H-6a), 3.92 (4H, s, –$O(CH_2)_2O$–), 4.17 (1H, d, J=11.7 Hz, H-6b), 5.04 (1H, d, J=12.3 Hz, –$NHCO_2C\underline{H}HPh$), 5.12 (1H, d, J=12.3 Hz, –$NHCO_2CH\underline{H}Ph$), 5.11 (1H, d, J=18.0 Hz, –CH=C$\underline{H}$H), 5.25 (1H, d, J=11.4 Hz, –CH=CH$\underline{H}$), 5.35 (1H, s, NH), 5.92 (1H, dd, J=11.4, J=18.0 Hz, –C$\underline{H}$=CH_2), 7.30～7.40 (5H, m, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.1, 18.6, 22.6, 23.8, 25.9, 28.4, 29.2, 29.4, 29.5, 29.6, 29.9, 31.8, 37.1, 56.5, 64.8, 65.1, 66.5, 76.3, 99.0, 111.9, 115.5, 128.0, 128.1, 128.5, 136.5, 136.9, 155.6.

(2*S*,3*R*)-2-Benzyloxycarbonylamino-3-hydroxy-2-hydroxymethyl-12-oxo-octadecanoic Acid Benzyl Ester (23a)

Ozone was introduced into a solution of carbamate **21a** (19 mg, 0.034 mmol) in EtOH (2 ml) at −78°C for 10 minutes. After purging of excess ozone with a stream of Ar gas, to the solution was added Me_2S (25 μl, 0.34 mmol) and the mixture was stirred at −78°C for 1 hour. The resulting mixture was diluted with EtOAc and washed with brine, and dried. Removal of the solvent gave crude aldehyde (20 mg) as a pale yellow syrup. To a solution of the crude aldehyde in *t*-BuOH (0.7 ml) and water (0.7 ml) were added $NaH_2PO_4 \cdot 2H_2O$ (10.6 mg, 0.068 mmol), $HOSO_2NH_2$ (9.7 mg, 0.1 mmol) and $NaClO_2$ (9.0 mg, 0.1 mmol) at room temperature. After stirring for 16 hour at room temperature, the reaction mixture was quenched with 20 wt% aq solution of $Na_2S_2O_3$. The aq phase was extracted with $CHCl_3$ (×6). The combined organic layer was washed with 20% aq solution of $Na_2S_2O_3$, and dried. Evaporation of the solvent afforded crude carboxylic acid (22 mg) as a white solid. To a solution of the crude carboxylic acid (22 mg) in CH_2Cl_2 (1 ml) were added WSCD (13 mg, 0.068 mmol), DMAP (2 mg, 0.017 mmol) and benzyl alcohol (7.0 μl, 0.068 mmol) at 0°C. After being stirred at room temperature for 60 hour, the mixture was diluted with EtOAc and washed with brine and dried. Removal of the solvent gave a residue, which was purified by chromatography (1.2 g silica gel, 1/30 EtOAc/toluene as an eluent) to afford a benzyl ester (15 mg) as a colorless syrup; IR ν_{max} (neat) 3340, 2920, 2855, 1730, 1715, 1500, 1455, 1255, 1225, 1080, 1050, 1030 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 0.88 (3H, t, J=6.6 Hz, CH_2CH_3), 1.10～1.68 (26H, m, 13×–CH_2–), 1.41, 1.59 (3H×2, 2s, Me_2C<), 3.92 (4H, s, –$O(CH_2)_2O$–), 4.12 (1H, bs, H-4), 4.21 (1H, d, J=15.0 Hz, H-6a), 4.40 (1H, d, J=15.0 Hz, H-6b), 5.07 (2H, s, –$NHCO_2C\underline{H}_2Ph$), 5.24 (2H, s, –$CCO_2C\underline{H}_2Ph$), 5.47 (1H, s, NH), 7.28～7.44 (10H, m, Ph). To the benzyl ester (15 mg, 0.034 mmol) was added 60% aq AcOH solution, and the mixture was heated at 50°C for 19 hour. The mixture was concentrated and residual acetic acid was azeotropically removed with EtOH to afford a yellow syrup, which was purified by column chromatography (0.7 g silica gel, 1/5 to 1/2 EtOAc/hexane as an eluent) to give diol **23a** (10 mg, 50% for 4 steps) as colorless syrup; $[\alpha]_D^{23}$ +4.9° (*c* 1.41, $CHCl_3$); IR ν_{max} (neat) 3400, 2930, 2855, 1740, 1710, 1510, 1500, 1455, 1260, 1215, 1060, 1030 cm^{-1}; HR FAB-MS *m/z* for $C_{34}H_{50}NO_7$ $(M+H)^+$, Calcd: 584.3587, Found: 584.3581; *Anal.* Found: C, 69.96; H, 8.46; N, 2.32%. Calcd for $C_{34}H_{49}NO_7$: C, 69.95; H, 8.46; N, 2.40%; ^1H NMR (300 MHz, $CDCl_3$) δ: 0.88 (3H, t, J=6.6 Hz, CH_2CH_3), 1.14～1.64 (22H, m, 11×–CH_2–), 2.37 (2H×2, 2t, J=6.9 Hz, H-11, H-13), 3.00 (1H, bs, OH), 3.63 (1H, bs, OH), 3.92～4.10 (3H, m, –CH_2OH, H-3), 5.10 (2H, s, –$NHCO_2CH_2Ph$), 5.22 (2H, bs, –CCO_2CH_2Ph), 5.88 (1H, s, NH), 7.34 (10H, bs, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.0, 22.5, 23.8, 23.8, 25.9, 28.9, 29.1, 29.2, 31.5, 31.6, 42.7, 42.8, 64.2, 67.3, 67.6, 69.0, 74.0, 128.1,

128.2, 128.3, 128.4, 128.6, 135.4, 135.9, 157.1, 170.9, 211.9.

(2*S*,3*R*)-2-Benzyloxycarbonylamino-2-benzyloxymethoxymethyl-3-hydroxy-12-oxo-octadecanoic Acid Benzyl Ester (24a)

To a solution of **23a** (50 mg, 0.086 mmol) in CH_2Cl_2 were added *i*-Pr_2NEt (37.2 μl, 0.214 mmol) and BOM-Cl (59.2 μl, 0.427 mmol) at 0°C. After stirring at 35°C for 23 hour, the resulting mixture was diluted with $CHCl_3$ and washed with brine, and the organic layer was dried. Removal of the solvent gave a residue, which was purified by flash chromatography (8 g silica gel, 1/10 to 1/6 EtOAc/hexane as an eluent) to afford BOM ether **24a** (39 mg, 64%) as a colorless syrup; $[\alpha]_D^{24}$ +35° (*c* 0.90, $CHCl_3$); IR ν_{max} (neat) 3400, 2930, 2855, 1740, 1710, 1500, 1455, 1250, 1220, 1040, 1030 cm^{-1}; HR FAB-MS *m*/*z* for $C_{42}H_{58}NO_8$ $(M+H)^+$, Calcd: 704.4162, Found: 704.4182; ^1H NMR (300 MHz, $CDCl_3$) δ: 0.88 (3H, t, *J*=6.3 Hz, $CH_2C\underline{H}_3$), 1.10～1.65 (22H, m, 11×–CH_2–), 2.38 (4H, t, *J*=7.1 Hz, H-11, H-13), 3.72～3.80 (2H, m, –C<u>H</u>HOBOM, H-3), 4.17 (1H, d, *J*=9.8 Hz, –CH<u>H</u>OBOM), 4.28 (1H, d, *J*=12.4 Hz, OH), 4.41 (1H, d, *J*=11.7 Hz, –C<u>H</u>HOCH_2Ph), 4.47 (1H, d, *J*=11.7 Hz, –CH<u>H</u>OCH_2Ph), 4.63 (1H, d, *J*=6.8 Hz, –CH_2OC<u>H</u>HPh), 4.67 (1H, d, *J*=6.8 Hz, –CH_2OCH<u>H</u>Ph), 5.08 (1H, d, *J*=11.9 Hz, –NHCO$_2$C<u>H</u>HPh), 5.13 (1H, d, *J*=11.9 Hz, –NHCO$_2$CH<u>H</u>Ph), 5.16 (1H, d, *J*=12.4 Hz, –CCO$_2$C<u>H</u>HPh), 5.29 (1H, d, *J*=12.4 Hz, –CCO$_2$CH<u>H</u>Ph), 5.85 (1H, s, NH), 7.22～7.38 (15H, m, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.2, 22.7, 24.0, 26.3, 29.1, 29.4, 29.5, 29.6, 31.8, 33.1, 43.0, 43.0, 67.5, 67.8, 68.2, 69.7, 70.1, 74.1, 95.1, 128.1, 128.3, 128.4, 128.6, 128.7, 128.7, 135.6, 136.2, 137.3, 157.0, 170.5, 211.9.

(2*S*,3*R*)-2-Benzyloxycarbonylamino-2-benzyloxymethoxymethyl-12-oxo-3-sulfooxy-octadecanoic Acid Benzyl Ester (25a)

To a solution of alcohol **24a** (11 mg, 0.016 mmol) in pyridine (1 ml) was added SO_3-pyridine complex (25 mg, 0.16 mmol) at room temperature. After stirring at 80°C for 2 hour, the reaction mixture was diluted with MeOH at room temperature. Removal of the solvent gave a residue, which was purified by flash chromatography (1 g silica gel, 1/10 MeOH/$CHCl_3$ as an eluent) afforded **25a** (12 mg, quant.) as a colorless syrup; $[\alpha]_D^{23}$ +12° (*c* 0.80, MeOH); IR ν_{max} (neat) 3420, 2930, 2855, 1735, 1720, 1710, 1505, 1455, 1260, 1230, 1050, 1030, 960 cm^{-1}; HR FAB-MS *m*/*z* for $C_{42}H_{58}NO_{11}S$ $(M-H)^-$, Calcd: 782.3574, Found: 782.3578; ^1H NMR (300 MHz, CD_3OD) δ: 0.89 (3H, t, *J*=6.3 Hz, $CH_2C\underline{H}_3$), 1.02～1.62 (22H, m, 11×–CH_2–), 2.42 (2H, t, *J*=7.3 Hz, H-11), 2.43 (2H, t, *J*=7.3 Hz, H-13), 4.20 (2H, s, –C$\underline{H}_2$OBOM), 4.48 (1H, d, *J*=11.7 Hz, –C<u>H</u>HOCH_2Ph), 4.52 (1H, d, *J*=11.7 Hz, –CH<u>H</u>OCH_2Ph), 4.66 (2H, s, –CH_2OC$\underline{H}_2$Ph), 4.76 (1H, d, *J*=8.7 Hz, H-3), 5.02 (2H, s,–NHCO$_2$C$\underline{H}_2$Ph), 5.10 (1H, d, *J*=12.3 Hz, –CCO$_2$C<u>H</u>HPh), 5.24 (1H, d, *J*=12.3 Hz, –CCO$_2$CH<u>H</u>Ph), 7.18～7.42 (15H, m, Ph); ^{13}C NMR (75 MHz, CD_3OD) δ: 14.4, 23.6, 24.9, 24.9, 26.9, 30.0, 30.3, 30.3, 30.4, 30.4, 32.5, 32.8, 43.5, 67.0, 67.4, 68.5, 70.2, 81.4, 95.7, 128.6, 128.8, 129.0, 129.2, 129.3, 129.4, 129.4, 129.6, 129.7, 136.9, 138.2, 139.3, 157.0, 171.4, 214.4.

(+)-Sulfamisterin (1)

To a solution of **25a** (12 mg, 0.016 mmol) in MeOH (1 ml) was added 20% $Pd(OH)_2$ on activated carbon (10 mg) at room temperature and the mixture was hydrogenated under atmospheric pressure of H_2 for 15 hour. The insoluble material was removed by filtration through celite and the filtrate was concentrated to give a residue, which was purified by a column of Sephadex LH-20 (95 ml, MeOH as an eluent). The fractions containing **1** were collected and concentrated to give a residue, which was treated with IRC-76 resin (H^+ form). The resin was removed by filtration and the filtrate was concentrated to afford (+)-sulfamisterin (**1**) (3.0 mg, 57%) as white solids; $[\alpha]_D^{21}$ +3.6° (*c* 0.62, MeOH) {natural sulfamisterin: lit. [1] $[\alpha]_D^{23}$ +2.0° (*c* 1.0, MeOH); $[\alpha]_D^{28}$ +3.1° (*c* 0.50, MeOH), measured in our laboratory}; IR ν_{max} (neat) 3435, 2930, 2855, 1710, 1660, 1645, 1520, 1405, 1385, 1290, 1230, 1060 cm^{-1}; HR FAB-MS *m*/*z* for $C_{19}H_{36}NO_8S$ $(M-H)^-$, Calcd: 438.2161, Found: 438.2171; ^1H NMR (300 MHz, CD_3OD) δ: 0.90 (3H, t, *J*=6.6 Hz, $CH_2C\underline{H}_3$), 1.28～1.90 (22H, m, 11×–CH_2–), 2.43 (2H, t, *J*=7.2 Hz, H-11), 2.44 (2H, t, *J*=7.2 Hz, H-13), 3.84 (1H, d, *J*=11.7 Hz, –C<u>H</u>HOH), 4.12 (1H, d, *J*=11.7 Hz, –CH<u>H</u>OH), 4.60 (1H, dd, *J*=9.8, *J*=2.7 Hz, H-3); ^{13}C NMR (75 MHz, CD_3OD) δ: 14.4, 23.6, 24.9, 24.9, 26.9, 30.0, 30.3, 30.4, 30.4, 30.5, 32.0, 32.8, 43.5, 43.5, 61.2, 69.6, 79.6, 171.2, 214.4. The ^1H and ^{13}C NMR data were fully identical with those of natural sulfamisterin.

(2*R*,3*R*)-2-Benzyloxycarbonylamino-3-hydroxy-2-hydroxymethyl-12-oxo-octadecanoic Acid Benzyl Ester (26a)

By the same reaction conditions as described for the preparation of **23a** from **21a**, compound **22a** (47 mg, 0.07 mmol) was converted to diol **26a** (33 mg, 56% for 4 steps); a colorless syrup; $[\alpha]_D^{21}$ +18° (*c* 1.01, $CHCl_3$); IR

ν_{max} (neat) 3405, 2930, 2850, 1730, 1705, 1510, 1455, 1275, 1220, 1060, 1030 cm^{-1}; HR FAB-MS *m/z* for $C_{34}H_{50}NO_7$ $(M+H)^+$, Calcd: 584.3587, Found: 584.3589; *Anal* Found: C, 69.66; H, 8.39; N, 2.37%. Calcd for $C_{34}H_{49}NO_7$: C, 69.95; H, 8.46; N, 2.40%; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.88 (3H, t, J=6.6 Hz, $CH_2C\underline{H}_3$), 1.04～1.62 (22H, m, 11×–CH_2–), 2.29 (1H, bs, OH), 2.37 (2H, t, J=7.2 Hz, H-11), 2.38 (2H, t, J=7.2 Hz, H-13), 4.00～4.32 (4H, m, –C$\underline{H}_2$OH, H-3, OH), 5.07 (1H, d, J=12.3 Hz, –NHCO$_2$C$\underline{H}$HPh), 5.12 (1H, d, J=12.3 Hz, –NHCO$_2$CH$\underline{H}$Ph), 5.18 (1H, d, J=12.0 Hz, –CCO$_2$C$\underline{H}$HPh), 5.28 (1H, d, J=12.0 Hz, –CCO$_2$CH$\underline{H}$Ph), 6.10 (1H, s, NH), 7.32～7.38 (10H, m, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.2, 22.7, 24.0, 26.0, 29.1, 29.4, 29.5, 29.5, 31.8, 33.0, 43.0, 43.0, 64.3, 67.6, 68.3, 69.3, 74.4, 128.3, 128.6, 128.8, 128.8, 135.0, 135.9, 156.8, 171.2, 212.0.

(2*R*,3*R*)-2-Benzyloxycarbonylamino-2-benzyloxymethoxymethyl-3-hydroxy-12-oxo-octadecanoic Acid Benzyl Ester (27a)

By the same reaction conditions as described for the preparation of **24a** from **23a**, compound **26a** (80 mg, 0.138 mmol) was converted to BOM ether **27a** (81 mg, 83%); colorless syrup; $[\alpha]_D^{22}$ +8.9° (*c* 1.35, $CHCl_3$); IR ν_{max} (neat) 3410, 2930, 2855, 1740, 1705, 1505, 1455, 1280, 1250, 1220, 1050, 1030 cm^{-1}; HR FAB-MS *m/z* for $C_{42}H_{58}NO_8$ $(M+H)^+$, Calcd: 704.4162, Found: 704.4175; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.88 (3H, t, J=6.6 Hz, $CH_2C\underline{H}_3$), 1.00～1.62 (22H, m, 11×–CH_2–), 2.37 (2H, t, J=7.2 Hz, H-11), 2.38 (2H, t, J=7.2 Hz, H-13), 4.04 (1H, dt, J=2.4, J=10.5 Hz, H-3), 4.10 (1H, d, J=10.2 Hz, –C$\underline{H}$HOBOM), 4.33 (1H, d, J=10.2 Hz, –CH$\underline{H}$OBOM), 4.42 (2H, s, –C$\underline{H}_2$OCH$_2$Ph), 4.61 (1H, d, J=6.6 Hz, –CH$_2$OC$\underline{H}$HPh), 4.64 (1H, d, J=6.6 Hz, –CH$_2$OCH$\underline{H}$Ph), 4.67 (1H, d, J=10.5 Hz, OH), 5.02 (1H, d, J=12.3 Hz, –NHCO$_2$C$\underline{H}$HPh), 5.10 (1H, d, J=12.3 Hz, –NHCO$_2$CH$\underline{H}$Ph), 5.15 (1H, d, J=12.0 Hz, –CCO$_2$C$\underline{H}$HPh), 5.27 (1H, d, J=12.0 Hz, –CCO$_2$CH$\underline{H}$Ph), 6.28 (1H, s, NH), 7.23～7.36 (15H, m, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.0, 22.5, 23.9, 25.8, 29.0, 29.3, 29.4, 31.6, 33.1, 42.8, 42.8, 67.3, 68.1, 68.7, 68.9, 69.3, 74.6, 94.6, 127.7, 127.8, 128.0, 128.3, 128.4, 128.5, 128.5, 128.6, 128.7, 134.8, 135.9, 137.5, 156.7, 170.7, 211.7.

(2*R*,3*R*)-2-Benzyloxycarbonylamino-2-benzyloxymethoxymethyl-12-oxo-3-sulfooxy-octadecanoic Acid Benzyl Ester (28a)

By the same reaction conditions as described for the preparation of **25a** from **24a**, compound **27a** (20 mg, 0.028 mmol) was converted to sulfate **28a** (23 mg, quant.); colorless syrup; $[\alpha]_D^{23}$ +14° (*c* 1.08, MeOH); IR ν_{max} (neat) 3400, 2930, 2855, 1730, 1715, 1700, 1520, 1505, 1455, 1290, 1220, 1050 cm^{-1}; HR FAB-MS *m/z* for $C_{42}H_{56}NO_{11}S$ $(M-H)^-$, Calcd: 782.3574, Found: 782.3573; ^{1}H NMR (300 MHz, CD_3OD) δ: 0.89 (3H, t, J=6.6 Hz, $CH_2C\underline{H}_3$), 1.08～1.74 (22H, m, 11×–CH_2–), 2.41 (2H, t, J=7.5 Hz, H-11), 2.42 (2H, t, J=7.5 Hz, H-13), 4.01 (1H, d, J=10.2 Hz, –C$\underline{H}$HOBOM), 4.38 (1H, d, J=10.2 Hz, –CH$\underline{H}$OBOM), 4.52 (2H, s, –C$\underline{H}_2$OCH$_2$Ph), 4.67 (1H, d, J=6.9 Hz, –CH$_2$OC$\underline{H}$HPh), 4.73 (1H, d, J=6.9 Hz, –CH$_2$OCH$\underline{H}$Ph), 4.81 (1H, dd, J=1.8, 8.7 Hz, H-3), 4.91 (1H, d, J=12.3 Hz, –NHCO$_2$C$\underline{H}$HPh), 4.99 (1H, d, J=12.3 Hz, –NHCO$_2$CH$\underline{H}$Ph), 5.15 (2H, s, –CCO$_2$C$\underline{H}_2$Ph), 7.18～7.42 (15H, m, Ph); ^{13}C NMR (75 MHz, CD_3OD) δ: 14.4, 23.6, 24.9, 24.9, 26.9, 30.0, 30.3, 30.4, 30.5, 30.5, 31.8, 32.8, 43.5, 67.3, 67.4, 68.2, 70.4, 79.2, 79.3, 95.8, 128.7, 128.8, 128.9, 129.1, 129.2, 129.4, 129.4, 129.5, 137.1, 138.1, 139.2, 157.4, 171.0, 214.4.

(2*R*,3*R*)-Sulfamisterin (3-epi-sulfamisterin) (2)

By the same reaction conditions as described for the preparation of sulfamisterin (**1**) from **25a**, compound **28a** (23 mg, 0.028 mmol) was converted to (2*R*,3*R*)-sufamisterin (**2**) (7.4 mg, 58%); white solid; $[\alpha]_D^{23}$ +5.6° (*c* 0.70, $CHCl_3$); IR ν_{max} (neat) 3420, 2930, 2860, 1710, 1650, 1635, 1510, 1470, 1410, 1260, 1220, 1060 cm^{-1}; HR FAB-MS *m/z* for $C_{19}H_{36}NO_8S$ $(M-H)^-$, Calcd: 438.2152, Found: 438.2152; ^{1}H NMR (300 MHz, CD_3OD) δ: 0.90 (3H, t, J=6.6 Hz, $CH_2C\underline{H}_3$), 1.28～1.80 (22H, m, 11×–CH_2–), 2.44 (4H, t, J=7.2 Hz, H-11, H-13), 3.98 (1H, d, J=11.7 Hz, –C$\underline{H}$HOH), 4.04 (1H, d, J=11.7 Hz, –CH$\underline{H}$OH), 4.68 (1H, dd, J=9.8, J=2.5 Hz, H-3); ^{13}C NMR (75 MHz, CD_3OD) δ: 14.4, 23.6, 24.9, 24.9, 26.7, 30.0, 30.3, 30.4, 30.4, 30.5, 32.0, 32.8, 43.5, 43.5, 64.3, 70.3, 79.0, 170.7, 214.4.

(2*S*,3*R*)-3-Hydroxy-2-hydroxymethyl-12-oxo-2-(2,2,2-trichloro-acetylamino)-octadecanoic Acid Methyl Ester (29a)

Ozone was introduced into a solution of carbamate **19a** (114 mg, 0.199 mmol) in MeOH (3.4 ml) at −78°C for 15 minutes. After purging of excess ozone with a stream of Ar gas, to the solution was added Me_2S (0.15 ml, 1.99 mmol) and the mixture was stirred at −78°C for 1 hour. The resulting mixture was diluted with EtOAc and washed with brine, and dried. Removal of the solvent gave crude aldehyde (114 mg) as a yellow syrup. To a solution of the

crude aldehyde in *t*-BuOH (1.7 ml) and water (1.7 ml) were added $NaH_2PO_4 \cdot 2H_2O$ (62.1 mg, 0.398 mmol), $HOSO_2NH_2$ (58.0 mg, 0.597 mmol) and $NaClO_2$ (54.0 mg, 0.597 mmol) at room temperature. After stirring for 24 hour at room temperature the reaction mixture was quenched with 20 wt% aq solution of $Na_2S_2O_3$. The aq phase was extracted with $CHCl_3$ (×5). The combined organic layer was washed with 20 wt% aq solution of $Na_2S_2O_3$, and dried. Removal of the solvent afforded crude carboxylic acid (125 mg) as white solids. To a solution of the crude carboxylic acid (125 mg) in MeOH/benzene (3.8 ml, 1/4) was added Me_3SiCHN_2 (2.0 mol/liter in hexane, 0.13 ml, 0.259 mmol) at room temperature. The mixture was stirred for 13 hour at room temperature and concentrated to give a residue, which was purified by chromatography (6 g silica gel, 1/10 to 1/5 EtOAc/hexane as an eluent) to afford methyl ester (87.4 mg) as a colorless syrup. To a solution of the methyl ester (87.4 mg) in THF (2.2 ml) was added 6 N HCl aq (1.1 ml) at 0°C, and the mixture was stirred at room temperature for 5 hour. The reaction mixture was diluted with $CHCl_3$ and washed with brine, and dried. Removal of the solvent gave a residue, which was purified by column chromatography (6 g silila gel, 1/6 EtOAc/toluene as an eluent) to afford diol **29a** (59 mg, 57% for 4 steps) as a syrup; $[\alpha]_D^{24}$ +14° (*c* 1.09, $CHCl_3$); IR ν_{max} (neat) 3370, 2930, 2855, 1750, 1715, 1515, 1460, 1375, 1230, 1035 cm^{-1}; HR FAB-MS *m/z* for $C_{22}H_{39}Cl_3NO_6$ $(M+H)^+$, Calcd: 518.1843, Found: 518.1833; ^1H NMR (300 MHz, $CDCl_3$) δ: 0.86 (3H, t, *J*=6.5 Hz, $CH_2C\underline{H}_3$), 1.36～1.53 (22H, m, 11×–CH_2–), 2.37 (4H, t, *J*=7.4 Hz, H-11, H-13), 3.81 (3H, s, $CO_2C\underline{H}_3$), 4.03 (1H, bt, *J*=6.1 Hz, H-3), 4.08 (1H, d, *J*=11.9 Hz, –C<u>H</u>HOH), 4.18 (1H, d, *J*=11.9 Hz, –CH<u>H</u>OH), 7.91 (1H, s, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.3, 22.8, 24.1, 24.1, 26.1, 29.2, 29.4, 29.5, 30.3, 31.9, 32.0, 43.0, 43.2, 53.5, 63.1, 69.8, 73.9, 92.7, 162.7, 170.4, 212.5.

Desulfonated Sulfamisterin (5)

To a solution of **29a** (41 mg, 0.079 mmol) in MeOH (1.3 ml) was added 12 wt% aq NaOH solution (0.6 ml) at room temperature. The mixture was stirred at 50°C for 18 hour, and then neutralized with IRC-76 resin (H^+ form). The resin was removed by filtration through a glass filter, and the filtrate was concentrated to give a residue, which was purified by column chromatography (3.5 g silica gel, MeOH/$CHCl_3$=1/5 as an eluent) to give roughly purified **5**. This was further purified by gel filtration (Sephadex LH-20, 95 ml, MeOH as an eluent) to afford desulfonated sufamisterin (**5**) (15 mg, 53%) as an amorphous solid; $[\alpha]_D^{19}$ +11° (*c* 0.49, pyridine); IR ν_{max} (KBr disc) 3400, 2930, 2850, 1710, 1640, 1540, 1510, 1470, 1400, 1385, 1285, 1130, 1050 cm^{-1}; HR FAB-MS *m/z* for $C_{19}H_{38}NO_5$ $(M+H)^+$, Calcd: 360.2750, Found: 360.2764; ^1H NMR (300 MHz, CD_3OD) δ: 0.90 (3H, t, *J*=6.7 Hz, $CH_2C\underline{H}_3$), 1.30～1.54 (22H, m, 11×–CH_2–), 2.43 (4H, t, *J*=7.3 Hz, H-11, H-13), 3.80～3.86 (1H, m, H-3), 3.80 (1H, d, *J*=11.7 Hz, –C<u>H</u>HOH), 3.93 (1H, d, *J*=11.7 Hz, –CH<u>H</u>OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.4, 23.6, 24.9, 27.3, 30.0, 30.3, 30.5, 30.5, 32.7, 32.8, 43.5, 43.5, 62.5, 69.8, 72.3, 174.0, 214.4.

(2*R*,3*R*)-3-Hydroxy-2-hydroxymethyl-12-oxo-2-(2,2,2-trichloro-acetylamino)-octadecanoic Acid Methyl Ester (30a)

By the same reaction conditions as described for the preparation of **29a** from **19a**, compound **20a** (142 mg, 0.249 mmol) was converted to diol **30a** (90 mg, 70% for 4 steps); colorless syrup; $[\alpha]_D^{22}$ +3.1° (*c* 0.47, $CHCl_3$); IR ν_{max} (neat) 3360, 2930, 2855, 1715, 1505, 1455, 1370, 1290, 1230, 1160, 1125, 1075, 1040 cm^{-1}; HR FAB-MS *m/z* for $C_{22}H_{39}Cl_3NO_6$ $(M+H)^+$, Calcd: 518.1843, Found: 518.1859; ^1H NMR (300 MHz, $CDCl_3$) δ: 0.86 (3H, t, *J*=6.7 Hz, $CH_2C\underline{H}_3$), 1.25～1.53 (22H, m, 11×–CH_2–), 2.36 (4H, t, *J*=7.4 Hz, H-11, H-13), 3.86 (3H, s, $CO_2C\underline{H}_3$), 4.14～4.19 (1H, m, H-3), 4.14 (1H, d, *J*=11.8 Hz, –C<u>H</u>HOH), 4.28 (1H, d, *J*=11.8 Hz, –CH<u>H</u>OH), 8.11 (1H, s, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.0, 22.5, 23.8, 23.8, 23.8, 25.6, 28.9, 29.1, 29.2, 29.2, 31.6, 32.6, 42.7, 42.8, 53.7, 63.0, 70.7, 73.5, 92.3, 162.6, 170.9, 211.9.

(2*R*,3*R*)-Desulfonated Sulfamisterin (6)

By the same reaction conditions as described for the preparation of **5** from **29a**, compound **30a** (90 mg, 0.174 mmol) was converted to (2*R*,3*R*)-desulfonated sulfamisterin (**6**) (18 mg, 29%); amorphous solid; $[\alpha]_D^{20}$ +8.2° (*c* 0.49, pyridine); IR ν_{max} (KBr disc) 3400, 2930, 2850, 1710, 1630, 1510, 1470, 1415, 1380, 1320, 1285, 1130, 1115, 1090, 1050 cm^{-1}; HR FAB-MS *m/z* for $C_{19}H_{38}NO_5$ $(M+H)^+$, Calcd: 360.2750, Found: 360.2751; ^1H NMR (300 MHz, CD_3OD) δ: 0.90 (3H, t, *J*=5.8 Hz, $CH_2C\underline{H}_3$), 1.28～1.53 (22H, m, 11×–CH_2–), 2.43 (4H, t, *J*=7.3 Hz, H-11, H-13), 3.81 (1H, t, *J*=6.3 Hz, H-3), 3.83 (1H, d, *J*=11.1 Hz, –C<u>H</u>HOH), 3.98 (1H, d, *J*=11.1 Hz, –CH<u>H</u>OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.4, 23.6, 24.9, 27.4, 30.3, 30.3, 30.5, 30.5, 32.6, 32.8, 43.5, 64.8, 71.1, 71.5, 173.5, 214.4.

2-*O*-Benzyl-L-threitol (9b) (Enantiomer of 9a)

To a solution of dimethyl L-tartrate (30.0 g, 168 mmol) in

300 ml of benzene at room temperature were added benzaldehyde dimethyl acetal (27.8 ml, 185 mmol) and $TsOH \cdot H_2O$ (320 mg, 1.68 mmol), and the mixture was heated at reflux for 2 days. After cooling to room temperature, the reaction mixture was neutralized with 0.3 ml of Et_3N and diluted with EtOAc. The resulting mixture was washed with water and dried. Removal of the solvent afforded yellow crystal. Recrystallization from hexane gave pure benzylidene derivative (42.3 g, 94%) as white crystals; m.p. 74~75°C; $[\alpha]_D^{19}$ −45° (*c* 2.19, MeOH) {lit. [8] m.p. 70°C; $[\alpha]_D$ −42° (*c* 0.50, $CHCl_3$)} To a suspension of $LiAlH_4$ (8.3 g, 218 mmol) in diethyl ether (100 ml) and CH_2Cl_2 (95 ml) was added the benzylidene derivative (16.6 g, 62.3 mmol) at 0°C. After stirring for 40 minutes, to the reaction mixture was added $AlCl_3$ (25.0 g, 187 mmol) in diethyl ether (100 ml) dropwise at 0°C, and the mixture was heated at reflux for 2.5 hour. After cooling to 0°C, to the mixture were added with water (20 ml), 15 wt% NaOH aq (100 ml) and water (25 ml). The insoluble material was removed by filtration through celite (THF as an eluent), and the filtrate was dried. Removal of the solvent afforded crystalline residue, which was recrystallized from benzene to give **9b** (11.3 g, 86%) as white crystals; m.p. 75.5~76°C;$[\alpha]_D^{24}$ +16° (*c* 1.60, MeOH). Spectral data were fully identical with those of **9a**.

Starting from **9b**, compounds **3**, **4**, **7**, and **8** were synthesized by the same procedure as described for the preparation **1**, **2**, **5**, and **6**, respectively.

10b; m.p. 60~62°C; $[\alpha]_D^{25}$ +59° (*c* 0.40, $CHCl_3$). **15b**; $[\alpha]_D^{21}$ +3.4° (*c* 1.52, $CHCl_3$). **16b**; $[\alpha]_D^{22}$ −78° (*c* 1.38, $CHCl_3$). **17b**; $[\alpha]_D^{23}$ −64° (*c* 0.80, $CHCl_3$). **19b**; $[\alpha]_D^{22}$ −22° (*c* 0.55, $CHCl_3$). **20b**; $[\alpha]_D^{23}$ +20° (*c* 0.69, $CHCl_3$). **21b**; $[\alpha]_D^{24}$ −14° (*c* 1.09, $CHCl_3$). **22b**; $[\alpha]_D^{23}$ +25° (*c* 1.06, $CHCl_3$). **23b**; $[\alpha]_D^{23}$ −5.1° (*c* 0.97, $CHCl_3$). 24b; $[\alpha]_D^{20}$ −37° (*c* 0.75, $CHCl_3$). **25b**; $[\alpha]_D^{23}$ −11° (*c* 0.94, MeOH). **3**; $[\alpha]_D^{27}$ −4.5° (*c* 0.55, MeOH). **26b**; $[\alpha]_D^{23}$ −16° (*c* 0.55, $CHCl_3$). **27b**; $[\alpha]_D^{22}$ −7.9° (*c* 0.44, $CHCl_3$). **28b**; $[\alpha]_D^{25}$ −12° (*c* 0.38, MeOH). **4**; $[\alpha]_D^{20}$ −5.3° (*c* 0.41, MeOH). **29b**; $[\alpha]_D^{22}$ −14° (*c* 1.11, $CHCl_3$). **7**; $[\alpha]_D^{23}$ −9.3° (*c* 0.36, pyridine). **30b**; $[\alpha]_D^{22}$ −5.1° (*c* 1.18, $CHCl_3$). **8**; $[\alpha]_D^{19}$ −6.0° (*c* 0.43, pyridine).

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